SPRINGER HANDBOOK OF AUDITORY RESEARCH
Series Editors: Richard R. Fay and Arthur N. Popper

Sheryl Coombs
Horst Bleckmann
Richard R. Fay
Arthur N. Popper
Editors

The Lateral Line System

Springer

Springer Handbook of Auditory Research

For further volumes:
http://www.springer.com/series/2506

Sheryl Coombs • Horst Bleckmann
Richard R. Fay • Arthur N. Popper
Editors

The Lateral Line System

Springer

Editors
Sheryl Coombs
Department of Biological Sciences
and JP Scott Center for Neuroscience
Mind and Behavior
Bowling Green State University
Bowling Green, OH, USA

Richard R. Fay
Marine Biological Laboratory
Woods Hole, MA, USA

Horst Bleckmann
Institute of Zoology
University of Bonn
Bonn, Germany

Arthur N. Popper
Department of Biology
University of Maryland
College Park, MD, USA

ISSN 0947-2657 ISSN 2197-1897 (electronic)
ISBN 978-1-4614-8850-7 ISBN 978-1-4614-8851-4 (eBook)
DOI 10.1007/978-1-4614-8851-4
Springer New York Heidelberg Dordrecht London

Library of Congress Control Number: 2013951428

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

This volume is dedicated to Phyllis Cahn, Sven Dijkgaaf, and Peter Görner, three early pioneers in the study of the mechanosensory lateral line. Phyllis organized and edited the proceedings of the very first international conference on the lateral line and provided some of the first experimental evidence for a precise role of the lateral line in the schooling behavior of fish. Sven conducted countless behavioral experiments on the function of the lateral line in the context of natural behaviors, leading him to champion the view that this system functioned as a system of "touch-at-a distance" rather than an accessory organ of hearing. Peter, together with his co-workers Barbara Claas and Heinrich Münz, studied the role of the lateral line system in surface feeding and prey localization by Xenopus. *The breadth and depth of their combined neurophysiological and behavioral (neuroethological) studies are still unmatched.*

Series Preface

The following preface is the one that we published in Volume 1 of the Springer Handbook of Auditory Research back in 1992. As anyone reading the original preface or the many users of the series will note, we have far exceeded our original expectation of eight volumes. Indeed, with books published to date and those in the pipeline, we are now set for more than 50 volumes in SHAR, and we are still open to new and exciting ideas for additional books.

We are very proud that there seems to be consensus, at least among our friends and colleagues, that SHAR has become an important and influential part of the auditory literature. While we have worked hard to develop and maintain the quality and value of SHAR, the real value of the books is very much because of the numerous authors who have given their time to write outstanding chapters and to our many coeditors who have provided the intellectual leadership to the individual volumes. We have worked with a remarkable and wonderful group of people, many of whom have become great personal friends of both of us. We also continue to work with a spectacular group of editors at Springer, currently Ann Avouris. Indeed, several of our past editors have moved on in the publishing world to become senior executives. To our delight, this includes the current president of Springer US, Dr. William Curtis.

But the truth is that the series would and could not be possible without the support of our families, and we want to take this opportunity to dedicate all of the SHAR books, past and future, to them. Our wives, Catherine Fay and Helen Popper, and our children, Michelle Popper Levit, Melissa Popper Levinsohn, Christian Fay, and Amanda Fay, have been immensely patient as we developed and worked on this series. We thank them and state, without doubt, that this series could not have happened without them. We also dedicate the future of SHAR to our next generation of (potential) auditory researchers—our grandchildren—Ethan and Sophie Levinsohn; Emma Levit; and Nathaniel, Evan, and Stella Fay.

Preface 1992

The Springer Handbook of Auditory Research presents a series of comprehensive and synthetic reviews of the fundamental topics in modern auditory research. The volumes are aimed at all individuals with interests in hearing research including advanced graduate students, postdoctoral researchers, and clinical investigators. The volumes are intended to introduce new investigators to important aspects of hearing science and to help established investigators to better understand the fundamental theories and data in fields of hearing that they may not normally follow closely.

Each volume presents a particular topic comprehensively, and each serves as a synthetic overview and guide to the literature. As such, the chapters present neither exhaustive data reviews nor original research that has not yet appeared in peer-reviewed journals. The volumes focus on topics that have developed a solid data and conceptual foundation rather than on those for which a literature is only beginning to develop. New research areas will be covered on a timely basis in the series as they begin to mature.

Each volume in the series consists of a few substantial chapters on a particular topic. In some cases, the topics will be ones of traditional interest for which there is a substantial body of data and theory, such as auditory neuroanatomy (Vol. 1) and neurophysiology (Vol. 2). Other volumes in the series deal with topics that have begun to mature more recently, such as development, plasticity, and computational models of neural processing. In many cases, the series editors are joined by a coeditor having special expertise in the topic of the volume.

Richard R. Fay, Falmouth, MA
Arthur N. Popper, College Park, MD

SHAR logo by Mark B. Weinberg, Bethesda, Maryland, used with permission.

Volume Preface

Approximately every 20 years, lateral line researchers feel the urge to publish a book on this fascinating yet somewhat enigmatic flow-sensing system. This book is the latest of three volumes dedicated solely to the lateral line system, with the first two being published as conference proceedings (Cahn, P. H., 1967, *Lateral Line Detectors*. Bloomington: Indiana University Press; Coombs, S., Görner, P., & Münz, H., 1989, *The Mechanosensory Lateral Line: Neurobiology and Evolution*. New York: Springer). In keeping with the spirit of SHAR, this new book differs from earlier conference proceedings in that it is not a collection of research papers presented at a conference but rather a set of invited chapters from leading experts in the field. Each chapter serves as a guide to the relevant literature (especially from the last 20 years) and to the key concepts and issues surrounding the development, evolution, neurobiology, and function of the lateral line.

Readers might ask why the lateral line system, possessed by only fish and aquatic amphibians, is included in a series of books on the auditory sciences. There are several good reasons for including it, not the least of which is historical precedence for linking the two systems together into a single "acousticolateralis" system. Coombs and Bleckmann provide a brief historical account of this long-term association and how it has influenced the evolution of our thinking on the lateral line system. In addition, their chapter highlights some of the key discoveries in the field up until the time of the second lateral line volume in 1989. Braun and Sand continue the acousticolateralis theme by discussing areas of functional overlap and nonoverlap between the two systems.

A primary reason for the historical linking of lateral line and auditory systems together is the obvious fact that sense organs in both systems use mechanosensory hair cells. Indeed, the ease of access to the superficially located hair cells of the lateral line system make this sense a powerful model system for addressing basic questions on hair cell biology. This is seen in the chapter by Coffin, Brignuli, Raible, and Rubel, which discusses how the lateral line system of zebrafish is currently being used as a powerful model system for molecular and genetic studies of hair cell loss and regeneration as well as a tool (bioassay) for screening ototoxic agents.

More basic information about the structure and development of the lateral line system in zebrafish as well as in a wide variety of other species can be found in the chapter by Webb. This chapter serves as a source of inspiration and information on other species that could be used as new model systems for addressing other interesting questions, such as the relationship between structure and function or the developmental mechanisms that underlie the evolution of anatomical diversity.

For readers seeking a primer on the physical principles governing the response properties of the lateral line, the chapters by McHenry and Liao and by van Netten and McHenry explain the basic hydrodynamic and biomechanical features of the flow-sensing lateral line while summarizing the key research in each area. They additionally demonstrate how important it will be for future researchers to integrate computational modelling and flow-visualization techniques with more traditional neurophysiological and behavioral techniques for a much better understanding of the lateral line system.

No book on the lateral line would be complete without a chapter on the behavioral relevance of this sensory system to the lives of fish. Indeed, great strides in our understanding of this system have come from a deeper appreciation of how flow impacts the daily lives of fish, a common thread throughout many chapters. Accordingly, the chapter by Montgomery, Bleckmann, and Coombs focuses on the role of the lateral line in natural fish behaviors in the rich tradition of sensory ecology and neuroethology. The overall goal of this chapter is to provide a better understanding of the neurobiological basis of behavior by considering how fish use their lateral line system to meet life's basic necessities, such as finding food or avoiding predators, and how both behavior and the environment shape the information that is available to the lateral line.

Following through on that same theme, the chapters by Chagnaud and Coombs and by Bleckmann and Mogdans examine how behaviorally relevant information is shaped and encoded by the peripheral and central nervous systems. In their chapter, Wullimann and Grothe provide background information on the organization and evolution of the central nervous system, taking into account the relationship between the lateral line and the closely related auditory and electrosensory systems.

As always with SHAR volumes, this volume builds on past contributions in the series. Although we have not yet had a book on the lateral line, there are related chapters in a number of volumes. These include *Comparative Hearing: Fish and Amphibians* (Vol. 11, edited by Fay and Popper); *Electroreception* (Vol. 21, edited by Bullock, Hopkins, Popper, and Fay); and *Fish Bioacoustics* (Vol. 32, edited by Webb, Fay, and Popper).

Sheryl Coombs, Bowling Green, OH
Horst Bleckmann, Bonn, Germany
Richard R. Fay, Falmouth, MA
Arthur N. Popper, College Park, MD

Contents

Contributors

Horst Bleckmann Institute of Zoology, University of Bonn, Bonn, Germany

Christopher B. Braun Department of Psychology, Hunter College (CUNY), New York, NY, USA

Heather Brignull Department of Biological Structure, University of Washington, Seattle, WA, USA

Boris Philippe Chagnaud Department of Biology II, Ludwig-Maximilians-University Munich, Munich, Germany

Allison B. Coffin Neuroscience Program, Washington State University, Vancouver, WA, USA

Sheryl Coombs Department of Biological Sciences and JP Scott Center for Neuroscience, Mind and Behavior, Bowling Green State University, Bowling Green, OH, USA

Benedikt Grothe Graduate School of Systemic Neurosciences & Department Biology II, Ludwig-Maximilians-Universität Munich, Munich, Germany

James C. Liao Whitney Laboratory for Marine Bioscience, Department of Biology, University of Florida, St. Augustine, FL, USA

Matthew J. McHenry Department of Ecology and Evolutionary Biology, 321 Steinhaus Hall, University of California, Irvine, Irvine, CA, USA

Joachim Mogdans Institute of Zoology, University of Bonn, Bonn, Germany

John Montgomery School of Biological Sciences and Department of Marine Science, University of Auckland, Auckland, New Zealand

David W. Raible Department of Biological Structure, University of Washington, Seattle, WA, USA

Edwin W. Rubel Virginia Merrill Bloedel Hearing Research Center, University of Washington, Seattle, WA, USA

Olav Sand Department of Molecular Biosciences, Physiology Program, University of Oslo, 1041, Blindern, Oslo, Norway

Sietse M. van Netten Department of Artificial Intelligence and Cognitive Engineering, University of Groningen, Nijenborgh, The Netherlands

Jacqueline F. Webb Center for Biotechnology and Life Sciences, Department of Biological Sciences, University of Rhode Island, Kingston, RI, USA

Mario F. Wullimann Graduate School of Systemic Neurosciences and Department Biology II, Ludwig-Maximilians-Universität Munich, Munich, Germany

The Gems of the Past: A Brief History of Lateral Line Research in the Context of the Hearing Sciences

Sheryl Coombs and Horst Bleckmann

Keywords Acousticolateralis • Adaptive filter • Auditory • Efferent system • Electrosensory • Hair cell • Historical review • Inner ear • Lateral line • Modifiable efference copy • Octavolateralis

1 Introduction

In this day and age of Internet search engines, information overload, online journals, and pressures to publish at record-breaking paces, it is somewhat dismaying, but perhaps understandable, that the contributions of our academic forefathers are too often lost and forgotten. Yet, as any true scholar knows, the older literature contains many "gems" that young investigators coming into their fields would do well to read and understand. In reading some of these classics, they will be surprised as well as inspired by the many insights and research ideas that the older literature contains and that are ripe for the plucking. One such example in lateral line research is the classic 50-page review paper by Dijkgraaf (1962), a veritable gold mine of information for anyone interested in the lateral line. The goal of this chapter is to inspire an interest in the classics by identifying and highlighting some of the key players, discoveries, and debates that have shaped our understanding of lateral line function, especially in the context of the hearing sciences. More details on the

S. Coombs (✉)
Department of Biological Sciences and J. P. Scott Center for Neuroscience, Mind and Behavior, Bowling Green State University, Bowling Green, OH 43403, USA
e-mail: scoombs@bgsu.edu

H. Bleckmann
Institute of Zoology, University of Bonn, 53115 Bonn, Germany

S. Coombs et al. (eds.), *The Lateral Line*, Springer Handbook of Auditory Research 48,
DOI 10.1007/2506_2013_11, © Springer Science+Business Media New York 2013,
Published online: 29 June 2013

history of the field can be found in several early reviews (Parker, 1904; Johnson, 1917; Wright, 1951; Dijkgraaf, 1962) and two lateral line conference proceedings (Cahn, 1967; Coombs et al., 1989).

2 Early Notions on the Sensory Nature and Function of the Lateral Line

The earliest description of the lateral line was published in the 17th century by Stenonis (aka Stensen, Steno; 1664), who, according to Leydig (1868), described lateral line structures (canal pores) in elasmobranchs (sharks, skates, and rays). A few years later, Lorenzini (1678) reported additional pored structures that would later be called the ampullae of Lorenzini. The notion that these and other superficially located ampullary and tuberous organs on freshwater bony fishes might have an entirely different function from that of the "ordinary" lateral line did not become clearly evident until the discovery of electroreceptors nearly three centuries later (Lissmann & Machin, 1958; Murray, 1960; Bullock et al., 1961). Thus, throughout most of scientific history, mechanosensory and electrosensory organs have been lumped together under the lateral line umbrella as if they were one and the same system. Even though there is now ample evidence that each system is unique in its own right, responding to fundamentally different types of stimuli and with separate pathways and processing regions in the brain (McCormick, 1982), the term "lateral line" is still used in connection with both systems (e.g., lateral line nerves that innervate electroreceptors). This is, in no small part, due to the close developmental and evolutionary ties between the two systems (see the chapter by Wullimann & Grothe). Nevertheless, the term lateral line is becoming increasingly reserved for the mechanosensory component alone, and this is the convention adopted here and in most of the other chapters in this volume.

Likely biased by his own research interests in glands and lymph nodes, Stenonis (1664) proposed slime (mucus) production as the main function of the lateral line. This view of lateral line function remained essentially unchanged for the next 200 years until the German anatomist Franz Leydig published his influential paper on the "sixth sense" (Leydig, 1868) (Fig. 1). Leydig's paper reviewed the anatomical evidence for the sensory nature of the lateral line, beginning with his discovery of large, easily identified sense organs in the wide head canals of the ruffe (*Gymnocephalus cernua*), which Leydig called "Nervenknöpfe" (nerve buttons; Fig. 2) (Leydig, 1850, 1851), and culminating with the discovery by Schulze (1861) (Fig. 1) of a second type of sense organ ("Seitenorgane") on the skin surface of fish and aquatic amphibians (Fig. 3). These two types of sense organs are now recognized as belonging to two distinct submodalities of the lateral line: canal (CN) and superficial (SN) neuromasts. Each submodality can be distinguished in terms of not only developmental and morphological characteristics (chapter by

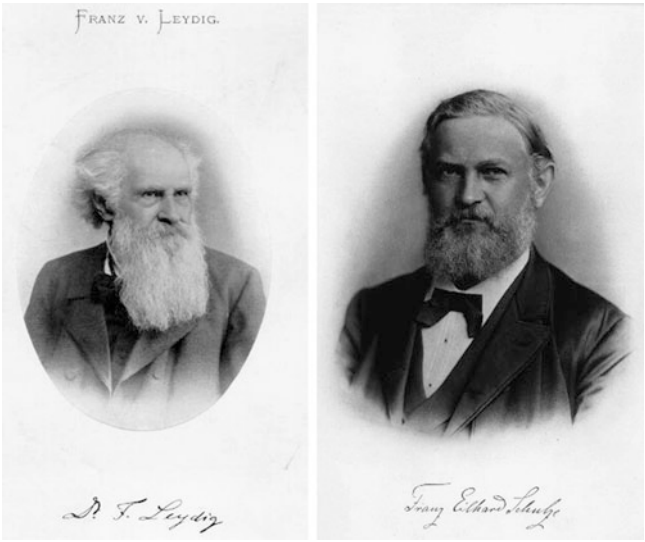

Fig. 1 Two 19th-century pioneers—Franz Leydig and Franz Schulze—who provided some of the first anatomical evidence for the sensory nature of lateral line sense organs, as illustrated in Figs. 2 and 3

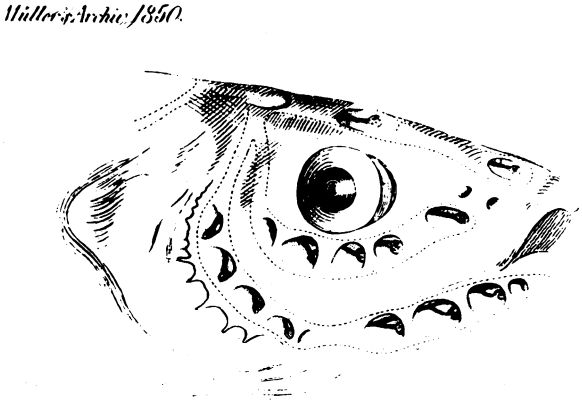

Fig. 2 Large canal neuromasts (Nervenknöpfe) on the head of the ruffe (*Gymnocephalus cernua*). The canal roof has been removed to reveal the underlying neuromasts in the supraorbital, infraorbital, and preopercular-mandibular canals. [From Leydig (1850) as reprinted in Dijkgraaf (1989)]

Webb), but also function, as evidenced from hydrodynamic (chapter by McHenry & Liao), biomechanical (chapter by van Netten & McHenry), physiological (chapter by Chagnaud & Coombs), and behavioral (chapter by Montgomery, Bleckmann, & Coombs) studies.

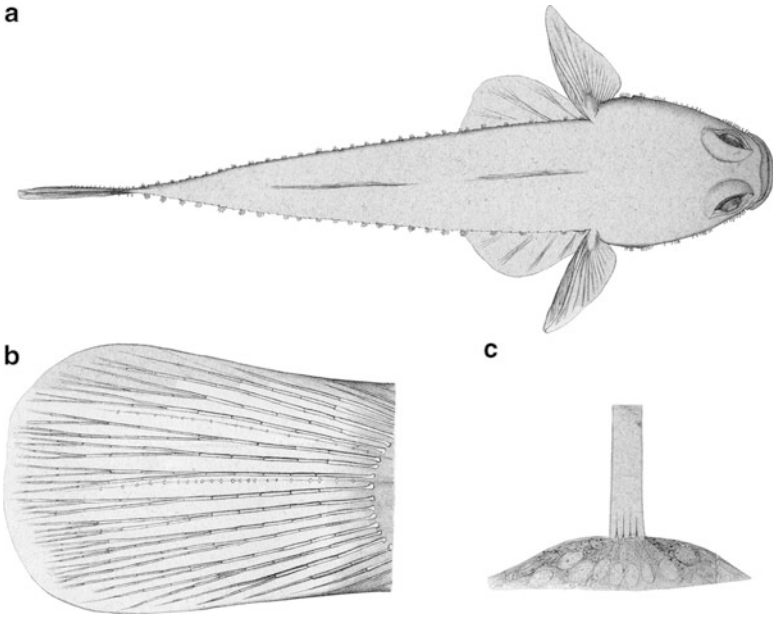

Fig. 3 Superficial neuromasts (Seitenorganröhren) along the lateral surface of the trunk (as seen from a dorsal view, **a**) and along the caudal fin rays (**b**) of the sand goby (*Pomatoschistus minutus*). In (**c**), a cephalic neuromast from a 16-mm larval *Triton taeniatus* (current genus species unknown) illustrating the pear-shaped sensory cells (hair cells) with their apical hairs projecting into an overlying cupula. [From Schulze (1850)]

3 The Big Debate: Is the Lateral Line a Sense of Hearing, Touch, or Something in Between?

When Schulze (1861) identified the features (pear-shaped sensory cells innervated by nerve fibers) that revealed the sensory nature of his Seitenorgane (Fig. 3b), he also described for the first time the fragile and nearly translucent structure (cupula) that covered them (Fig. 3b). Many years later, Schulze made the important discovery that the cupulae of these SNs could be displaced by weak water currents, leading him to suggest that water motions, but perhaps also low-frequency sound waves, were the relevant stimuli (Schulze, 1870). Following up on this idea, Dercum (1879) proposed that even CNs could be stimulated by water motions over the skin surface (and canal pores) by virtue of induced fluid motions inside the canals. It is now known from the classic work of Sir Eric Denton and Sir John Gray (reviewed in Denton and Gray, 1988, 1989) that accelerating flows (or, in other words, pressure differences) along canal pores cause fluid movements inside the canal (see also the chapters by McHenry & Liao and Chagnaud & Coombs).

The first experimental evidence that the lateral line responds to flowing water, what Sven Dijkgraaf (1989) would later call the "true" function of the lateral line,

was provided by the German ichthyologist Bruno Hofer (1908). Hofer observed the ability of blinded northern pike (*Esox lucius*) to orient to water currents and to avoid collisions with the walls of the aquarium. Both of these behaviors were abolished when the lateral line nerves were cut. From these experiments, Hofer concluded that fish use their lateral line to "feel at a distance," and further that rheotaxis (orientation to water currents) must be the principal behavioral function of the lateral line. Dijkgraaf (1934) challenged the rheotaxis idea after repeating the experiments of Lyon (1904) to confirm that rheotaxis relied mainly on visual and, to a lesser extent, tactile senses, but not the lateral line. Ironically, some 60 years later, Montgomery et al. (1997) discovered a subtle role for lateral line SNs, but not CNs, in the ability of fish to orient to slow but not fast currents.

Unfortunately, Hofer's little-known finding (having been published in an obscure fisheries journal) was overlooked (Dijkgraaf, 1989), and the prevailing view during most of the 19th and well into the 20th century was that the lateral line was an accessory organ of hearing specialized for the detection of low-frequency sound. Lowenstein (1967) credits the pivotal review paper of Mayser (1882) for the popularity of this view, which persisted for many decades, despite evidence that the inner ear and not the lateral line mediated behavioral responses of fish to low-frequency sound (von Frisch, 1923; von Frisch & Stetter, 1932). According to Lowenstein (1967), Mayser was a physician at the County Psychiatric Hospital in Munich, who, after an extensive review of the literature, proclaimed that "the mucous canals of fishes are nothing else than an accessory hearing organ spread over the whole body surface" (p. 5).

It is worth noting that the primary support for a hearing function of the lateral line was the shared anatomical characteristics of the two systems, including receptor cell structure (e.g., Schulze, 1861), close proximity during development (Wilson & Mattocks, 1897), and nerve fibers that appeared to originate from the same area of the hindbrain, the so-called acoustic tubercle (Mayser, 1882; see also the chapter by Braun & Sand). The evidence for a common termination site for both lateral line (including electrosensory component) and auditory nerve fibers was later augmented by the classic neuroanatomical studies of Pearson (1936a, b), Larsell (1967), and others on the "acousticolateralis area" of the hindbrain (reviewed in the chapter by Wullimann & Grothe).

Direct physiological evidence for lateral line responses to "sound" was not provided until the classic study of Harris and van Bergeijk (1962) on the responses of lateral line nerve fibers to the low-frequency vibrations of a nearby sound source. Their paper was very instructive, not only because it provided direct physiological evidence of responsiveness, but also because it provided additional insight as to the physical nature of the stimulus likely to excite the lateral line. Harris and van Bergeijk (1962) emphasized for biologists what was already known by physicists: that in the near field of a sound source, water behaves as if it is both compressible and incompressible, and thus both water motions (bulk flow) and propagated sound pressure waves are generated. Given that the near-field duality extends over distances significantly greater than a typical fish body length, especially at low frequencies (e.g., ~2 m at 100 Hz and 20 m at 10 Hz), the near field takes on

additional biological significance for fish. Knowing that the lateral line is actually responding to the local incompressible flow rather than the pressure wave, as Dijkgraaf (1934) and also Harris and van Berjeijk (1962) correctly assumed, the argument about the function of the lateral line and what fish "perceive" through the lateral line now becomes one of semantics and how sound and hearing are defined. If sound is defined strictly as propagated pressure waves, then it would be difficult to conclude that the "typical"[1] lateral line is an accessory organ of hearing. If, however, sound close to the source is defined as a combination of both flow and propagated pressure waves, then the idea of the lateral line as an accessory organ of hearing is quite plausible.[1]

van Bergeijk (1967) was careful to point out that although he and Harris could not "say very much about *what* the fish perceives" (p. 73) from their physiological studies, they could at the very least, say something about "the class of stimuli that fish *could* perceive" (p. 73). Although it is nearly impossible to know *what* fish actually perceive through their lateral line, the seminal studies of Catherine McCormick tell us that information from the lateral line in most fishes is processed by areas and pathways in the brain that are separate from those that process either auditory or electrosensory information (McCormick, 1982, 1989; reviewed in the chapter by Wullimann & Grothe). Thus, if the concept of labeled lines (separate pathways for different sensory modalities) applies to sensory perceptions, it follows that lateral line perceptions, called "svenning" by Platt et al. (1989) in honor of Sven Dijkgraaf, are distinct from the auditory perceptions of hearing.

In the foreword to Phyllis Cahn's 1967 book *Lateral Line Detectors*, George von Békésy (who won the Nobel Prize in Medicine or Physiology for his research on the function of the mammalian cochlea) wrote "When thinking about the lateral line system in fish, I always found myself starting with the physical stimulus, then going over to physiology, from there to gross anatomy and histology, and then back to physics again, and finally trying to make both ends of this ring fit"(p. ix). This fundamental approach to understanding sensory function was typical of many sensory psychologists and physiologists at the time (especially in America) and was certainly consistent with the approach that Harris and van Bergeijk (1962) took to understand sensory function at the level of isolated lateral line sense organs. In contrast, Dijkgraaf's seminal behavioral work in the Netherlands, likely inspired by the European ethologists Konrad Lorenz and Niko Tinbergen, paved the way for a fuller appreciation for the behavioral relevance of the lateral line at the level of the whole animal (as reviewed in the chapter by Montgomery, Bleckmann, & Coombs). Among other things, Dijkgraaf (1934, 1947) was instrumental in following up on Hofer's (1908) original studies to

[1] There are rare cases in which parts of the lateral line system may be adapted for pressure detection via a close association with compressible gas cavities, e.g., clupeids (Denton & Blaxter, 1976; Gray, 1984), chaetodontids (Webb & Blum, 1990), and some silurids (Bleckmann et al., 1991). There is also evidence that the lateral line/gas cavity association may be involved in ultrasound detection in some clupeids (Wilson et al., 2009).

show that blinded fish could detect nearby stationary obstacles by virtue of the distortions they created in the fish's self-generated flow field. Dijkgraaf called this ability *Ferntastsinn* or "touch-at-a-distance." Remarkably, Knox (1825) had similar ideas a century earlier when he proposed that this was a system of "touch, so modified, however, as to hold an intermediate place between the sensations of touch and hearing" (as quoted by Parker, 1904, p.186). In any event, touch-at-a-distance is now generally accepted as a more apt description of lateral line function than hearing, and there is now considerable hydrodynamic and behavioral evidence for this ability in blind cavefish (*Astyanax mexicanus*; reviewed in Windsor et al., 2008, 2010).

Semantics aside, it is becoming abundantly clear that low-frequency vibrations of a nearby body are capable of evoking neural responses from both lateral line and auditory nerve fibers, as well as both conditioned and unconditioned behaviors (reviewed in the chapter by Braun & Sand). This should be of particular interest to researchers interested in fish bioacoustics because many, if not all, biologically relevant sound sources produce complex hydroacoustic near fields that are capable of stimulating both the ear and lateral line of fish. Although in most fishes the ability of the lateral line to respond to the hydrodynamic (incompressible flow) component of a sound source is limited to the near field, many fish behaviors are as well. Thus, the different bits and pieces of information that each sense encodes are likely to be combined in the nervous system in as yet unknown ways to affect behavior. As Braun and Sand suggest in their chapter, many questions remain about the functional overlap between the two mechanosensory modalities—perhaps most importantly, how and where in the brain is information from the two senses integrated and to what behavioral effect?

4 Historical Contributions of Lateral Line Research to the Hearing Sciences

Although the auditory and lateral line systems of fish and amphibians are now regarded as separate sensory systems, the striking similarities and functional overlap between them continue to inform us about shared principles of operation. The sections that follow provide examples of how lateral line research has contributed to the hearing sciences in particular, but also to a broader understanding of hair cell systems in general.

4.1 A Unifying Concept of Hair Cell Function

Åke Flock's anatomical and physiological studies on the lateral line canal system of the freshwater burbot (*Lota lota*) in the 1960s and early 1970s (Flock & Wersäll,

1962; Flock, 1965a, b; Harris et al., 1970) were instrumental in providing a conceptual framework of hair cell function that could explain the variability of observed physiological responses in different systems, including those in the cochlea, semicircular canals, and otolithic end organs of vertebrates. As was well known at the time, hair cells in all of these end organs share basic features, including most especially the anatomical asymmetry of the hair bundle, which gives rise to the directional sensitivity of the hair cell (reviewed in the chapter by Chagnaud & Coombs). Flock's hypothesis of how hair cells respond to opposite directions of displacement (now known to be correct) helped to resolve the apparent discrepancies between extracellular responses recorded from different hair cell end organs. That is, the summed extracellular responses from cochlear and semicircular canal hair cells faithfully followed the frequency of the stimulus, whereas those in the lateral line exhibited a doubling of the frequency – the so-called *double microphonic* response (Jielof et al., 1952) (Fig. 4).

Flock was astute enough to realize that the differences were based on the grouping of hair cells into two, oppositely oriented, populations in the lateral line, but into a single population of similar orientations in the cochlea and crista ampullaris of the semicircular canals. He reasoned that it would be impossible to get any microphonic responses at all from the lateral line if the receptor potentials of oppositely oriented hair cells were equal in amplitude because they would effectively cancel each other out. Based on this reasoning, he and his colleague Jan Wersäll proposed a theory of hair cell function that included a nonlinear component; that is, that displacement of the stereovilli in the best excitatory direction causes a depolarizing response, whereas an equal displacement in the opposite direction causes a hyperpolarizing response of much smaller magnitude (Flock & Wersäll, 1962) (Fig. 4). Flock then went on to demonstrate via several clever experiments that he could turn a double microphonic response into a single microphonic response by simultaneously biasing the responses of opposing populations of hair cells with a static displacement of the cupula, effectively eliminating the contribution of one population (Flock 1965b). It goes without saying that Flock's contributions to hair cell function scarcely ended there; his initial work on the lateral line launched a long and distinguished career in the hearing sciences.

4.2 The Octavolateralis Efferent System

There is no question that both the lateral line and the auditory system of fish share a common efferent supply from the octavolateralis efferent nucleus in the hindbrain and that with rare exceptions, efferent innervation is a fundamental feature of all vertebrate hair cell systems (Roberts & Meredith, 1989). For reasons still not well understood, efferent innervation does not extend to the closely allied electrosensory system (Bodznick, 1989). Early lateral line studies played a substantial role in determining the pharmacology of the efferent synapse (Russell, 1971b; Flock & Russell, 1973; Flock & Lam, 1974), as well as the inhibitory

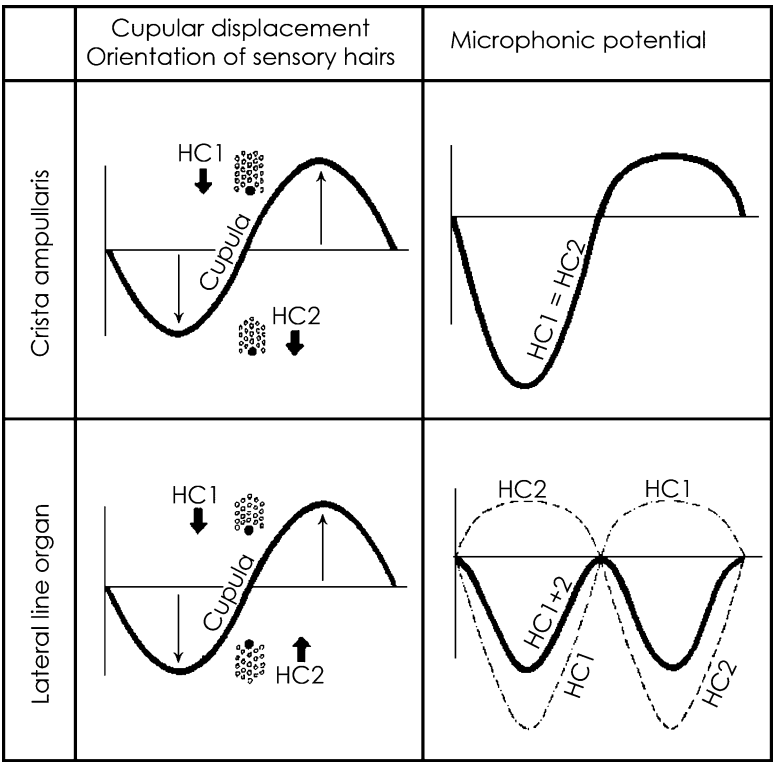

Fig. 4 Illustration from Flock and Wersäll (1962) to explain how the summed extracellular (microphonic) potentials of two hair cell organs can differ when their overlying cupula is sinusoidally displaced in two opposing directions (thin arrows). The microphonic potential of lateral line neuromasts (bottom panel) is twice the frequency of the sinusoidal stimulus, whereas that of the crista ampullaris (vestibular sense organ in the semicircular canals, top panel) is the same. The difference arises because all hair cells (HCs) in the crista ampullaris have the same orientation, whereas those in the lateral line are divided into two, oppositely oriented populations. HC orientation is determined by the arrangement of stereovilli (open circles) relative to a single, eccentrically placed kinocilium (filled circle). Because depolarizing responses of individual HCs to stimulus directions in the best excitatory direction (in the direction of the kinocilium, as indicated by the thick arrows) are larger in magnitude than hyperpolarizing responses to the opposite direction, oppositely oriented populations of hair cells in the lateral line system give rise to a summed potential that is double the frequency of the applied stimulus

effects of the efferent system on spontaneous and evoked activity (Russell, 1971a; Flock & Russell, 1973). It is now known that the efferent system has both excitatory and inhibitory effects that mediate complex, context-dependent modulation of hair cell gain through both feed-forward and feedback loops (reviewed by Köppl, 2011 and in the chapter by Chagnaud & Coombs). Toward that end, lateral line studies have contributed to our understanding of how the efferent system operates in animal behavior (Roberts, 1972; Roberts & Russell, 1972; Tricas & Highstein, 1990, 1991). From these studies, it has been shown that the

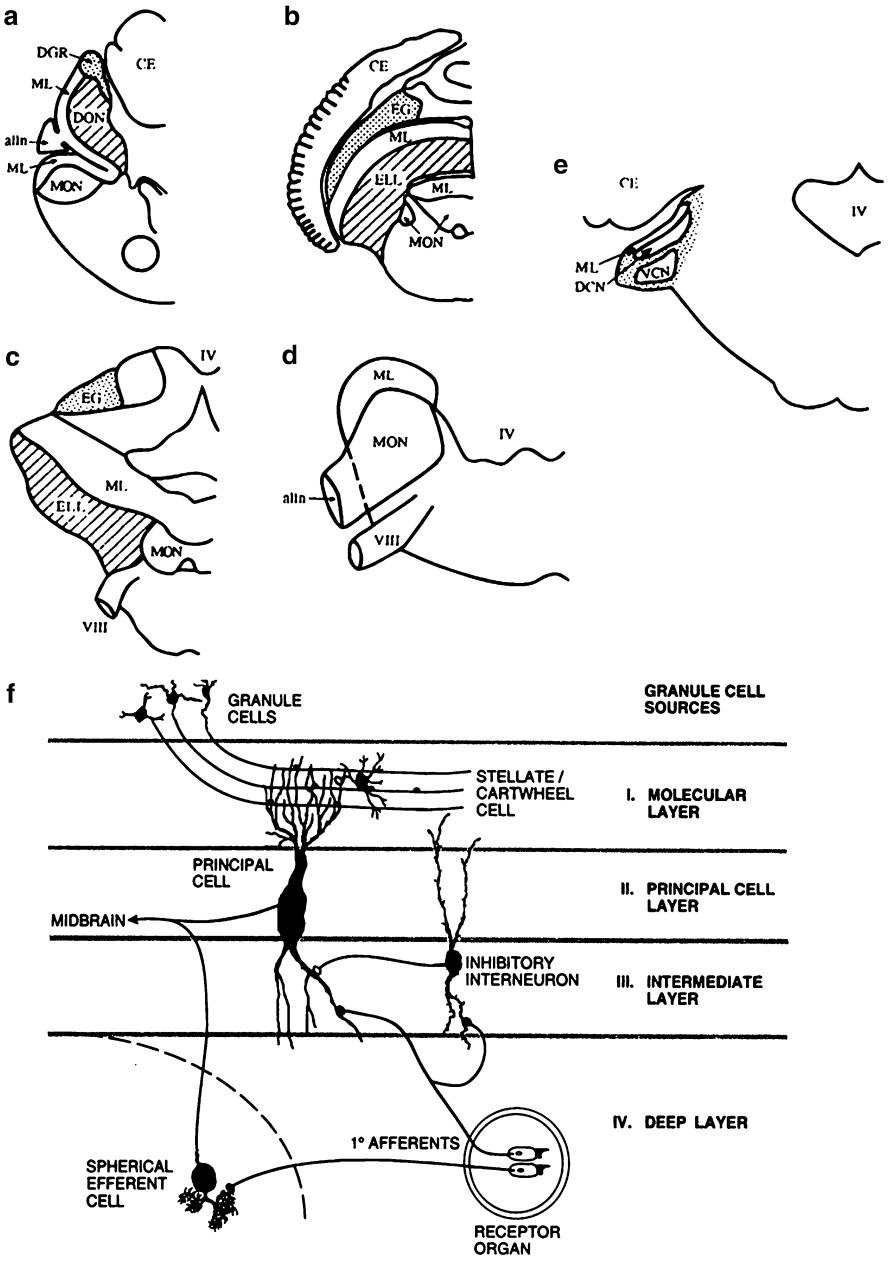

Fig. 5 Example of how comparisons across different octavolateralis systems can reveal basic principles of organization and operation. First-order, brain stem nuclei (hatched areas in **a**–**e**) all share common associations with an overlying molecular layer (ML) of parallel fibers from granule cell masses (stippled regions), which provide descending inputs to the principal (output) cells in the nucleus (**f**). Different octavolateralis nuclei include (1) the mechanosensory lateral line

efferent system can be activated by stimulation of different sensory modalities, such as touch and vision (Roberts & Russell, 1972; Tricas & Highstein, 1990), but also by motor acts (e.g., vocalization, swimming motions) that cause self-stimulation of octavolateralis sense organs (sensory reafference) (Tricas & Highstein, 1991; Weeg et al., 2005).

4.3 Adaptive Filters in First-Order Octavolateralis Brain Stem Nuclei

The octavolateralis efferent system is but one strategy that animals can employ for improving signal-to-noise ratios—especially in the presence of self-generated noise. Mechanisms such as this are extremely important, because the exquisite mechanical sensitivity of hair cells to displacements in the nanometer range render them useless in noisy environments capable of interfering with the detection of biologically relevant signals. Although biomechanical and neural filters for separating signals and noise along different stimulus dimensions (e.g., frequency, intensity, location, or time) are powerful strategies for dealing with this problem, there is yet another strategy that animals use. This strategy relies on prior knowledge of often-repeated and thus "expected" noises that can be adaptively filtered out to improve signal-to-noise ratios. As first discovered by Bell (1981, 1982), the electrosensory lateral line lobe in the medulla of weakly electric mormyrid fish contains an adaptive filter or modifiable efference copy mechanism that constructs a negative image of the expected temporal pattern of reafferent input. Evidence for similar adaptive filter mechanisms in the brain stem regions of other groups of other electric fish, as well as in lateral line (mechanosensory) brain stem regions of both electroreceptive and nonelectroreceptive species, suggests that common features (i.e., cerebellar-like circuitries) are responsible (Fig. 5) (reviewed in Montgomery et al., 1995, Bell et al., 1997, 2008). Interestingly, the shared features extend to the dorsal cochlear nucleus of mammals (reviewed in Montgomery et al., 1995; Bell et al., 1997), and comparisons among different

Fig. 5 (continued) nucleus, the medial octavolateralis nucleus (MON), of all fishes (**a**–**d**), (2) electrosensory nuclei, the dorsal octavolateralis nucleus (DON) in cartilaginous fishes (**a**) and the electrosensory lateral line lobe (ELL) in bony fishes (**b** and **c**), and (3) the dorsal cochlear nucleus (DCN) of the mammalian auditory system (E). Granule cell masses in cartilaginous and bony fishes are called the dorsal granular ridge (DGR, **a**) and the eminentia granularis (EG, **b**,**c**), respectively. In addition, octavolateralis nuclei have similar cell types and circuitries (**f**), including cerebellar-like Purkinje cells, which function as the principal (output) cells of the nuclei and receive primary afferent input from sense organs on their ventral dendrites, but parallel fiber input from granule cells on their apical dendrites. Parallel fibers in the molecular layer convey information from granule cells, which receive multiple inputs, including motor corollary discharge to inform animals about self-generated noises. [Adapted from Montgomery et al. (1995)]

octavolateralis systems have fueled recent advances in our understanding of the underlying circuits and adaptive filter mechanisms in these brain stem structures (reviewed in Requarth & Sawtell, 2011).

5 Gems of the Future

There is no doubt that lateral line research will continue to be an integral part of the hearing sciences. Current research on the lateral line system of the zebrafish (*Danio rerio*) is a stellar example. The zebrafish lateral line serves not only as a useful bioassay for screening ototoxic agents (Ou et al., 2010), but also as a powerful model system for molecular, cellular, and genetic studies of hair cell loss and regeneration (reviewed in the chapter by Coffin, Brignull, Raible, & Rubel), as well as pattern formation, development, and morphogenesis (e.g., Dambly-Chaudiére et al., 2003; Nagiel et al., 2008; Ma and Raible, 2009).

Research on the lateral line has clearly made (and will continue to make) significant contributions to the hearing sciences. However, it is well worth remembering that lateral line research makes equally important contributions to our understanding of how flow information is utilized by fish and aquatic amphibians in a wide range of amazing behaviors, from simple (e.g., orientation to currents) to more complex (e.g., synchronized schooling maneuvers (reviewed in the chapter by Montgomery, Bleckmann, & Coombs). Given that there are more than 30,000 species of fish, the structural variations in the lateral line across species is a veritable gold mine of structure–function relationships to explore (see the chapter by Webb). Moreover, there is the growing promise that future research on structure–function relationships, as well as on the processing of flow information by the central nervous system (see the chapter by Bleckmann & Mogdans), will inspire novel flow-sensing technologies (e.g., Yang et al., 2006, 2010) and engineering applications, such as the sensory guidance of autonomous underwater vehicles to explore foreign and hostile environments. Thus, this fascinating system will continue to inspire classic research for years to come and in ways not yet imagined.

References

Bell, C. B. (1981). An efference copy modified by reafferent input. *Science*, 214, 450–453.

Bell, C. B. (1982). Properties of a modifiable efference copy in electric fish. *Journal of Neurophysiology* 47, 1043–1056

Bell, C., Bodznick, D., Montgomery, J., & Bastian, J. (1997). The generation and subtraction of sensory expectations within cerebellum-like structures. *Brain, Behavior and Evolution*, 50(1), 17–31.

Bell, C. B., Han, V., & Sawtell, N. B. (2008). Cerebellum-like structures and their implications for cerebellar function. *Annual Review of Neuroscience,* 31, 1–24.

Bleckmann, H., Niemann, U., & Fritzsch, B. (1991). Peripheral and central aspects of the acoustic and lateral line system of a bottom dwelling catfish, *Ancistrus* sp. *Journal of Comparative Neurology,* 314, 452–466.

Bodznick, D. A. (1989). Comparisons between electrosensory and mechanosensory lateral line systems. In S. Coombs, P. Görner & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 653–678). New York: Springer-Verlag.

Bullock, T. H., Hagiwara, S., Kusano, K., & Negishi, K. (1961). Evidence for a category of electroreceptors in the lateral line of gymnotid fishes. *Science*, 134, 1426–1427.

Cahn, P. H., Ed. (1967). *Lateral line detectors*. Bloomington: Indiana University Press.

Coombs, S., Görner, P., & Münz, H. (1989). *The mechanosensory lateral line—neurobiology and evolution* (1st ed.). New York: Springer.

Dambly-Chaudiére, C., Sapede, D., Soubiran, F., Decorde, K., Gompel, N., & Ghysen, A. (2003). The lateral line of zebrafish: A model system for the analysis of morphogenesis and neural development in vertebrates. *Biology of the Cell (Paris)*, 95(9), 579–587.

Denton, E. J., & Blaxter, J. H. (1976). The mechanical relationships between the clupeid swimbladder, inner ear and lateral line. *Journal of Marine Biological Association*, 56, 787–807.

Denton, E. J., & Gray, J. A. B. (1988). Mechanical factors in the excitation of the lateral lines of fishes. In J. Atema, R. R. Fay, A. N. Popper, & W. N. Tavolga (Eds.), *Sensory biology of aquatic animals* (pp. 595–617). New York: Springer.

Denton, E. J., & Gray, J. A. B. (1989). Some observations on the forces acting on neuromasts in fish lateral line canals. In S. Coombs, P. Görner & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 229–246). New York: Springer-Verlag.

Dercum, F. (1879). The lateral sensory apparatus of fishes. *Proceedings of the Academy of Natural Sciences of Philadelphia*, 152–154.

Dijkgraaf, S. (1934). Untersuchungen über die Funktion der Seitenorgane an Fischen. *Zeitschrift für vergleichende Physiologie*, 20, 162–214.

Dijkgraaf, S. (1947). Über die Reizung des Ferntastsinnes bei Fischen und Amphibien. *Experientia*, 3, 206–208.

Dijkgraaf, S. (1962). The functioning and significance of the lateral-line organs. *Biological Review*, 38, 51–105.

Dijkgraaf, S. (1989). A short personal review of the history of lateral line research. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 7–14). New York: Springer-Verlag.

Flock, Å. (1965a). Electron microscopic and electrophysiological studies on the lateral line canal organ. *Acta Oto-Laryngologica*, 199, 1–90.

Flock, Å. (1965b). Transducing mechanisms in the lateral line canal organ receptors. *Cold Spring Harbor Symposia on Quantitative Biology*, 30, 133–145.

Flock, Å., & Wersäll, J. (1962). A study of the orientation of the sensory hairs of the receptor cells in the lateral line organ of fish, with special reference to the function of the receptors. *Journal of Cell Biology*, 15, 19–27.

Flock, Å., & Russell, I. J. (1973). Efferent nerve fibres: Postsynaptic action on hair cells. *Nature New Biology*, 243, 89–91.

Flock, Å., & Lam, D. M. K. (1974). Neurotransmitter synthesis in inner ear and lateral line sense organs. *Nature*, 249, 142–144.

Gray, J. (1984). Interaction of sound pressure and particle acceleration in the excitation of the lateral-line neuromasts of sprats. *Proceedings of the Royal Society of London B: Biological Sciences*, 220, 299–325.

Harris, G. G., & van Bergeijk, W. A. (1962). Evidence that the lateral-line organ responds to near-field displacements of sound sources in water. *Journal of the Acoustical Society of America*, 34, 1831–1841.

Harris, G. G., Frishkopf, L. S., & Flock, Å. (1970). Receptor potentials from hair cells of the lateral line. *Science*, 167, 76–79.

Hofer, B. (1908). Studien über die Hautsinnesorgane der Fische. I. Die Funktion der Seitenorgane bei den Fischen. *Berichte der königlichen Bayerischen Biologischen Versuchsstation München*, 1, 115–164.

Jielof, R., Spoor, A., & deVries, H. (1952). The microphonic activity of the lateral line. *Journal of Physiology*, 116, 137–157.

Johnson, S. E. (1917). Structure and development of the sense organs of the lateral canal system of selachians (*Mustelus canis and Squalus acanthias*). *Journal of Comparative Neurology*, 28, 1–74.

Knox, R. (1825). On the theory of the existence of a sixth sense in fishes; supposed to reside in certain peculiar tubular organs, found immediately under the integuments of the head in sharks and rays. *Journal of Science*, 2, 12–16.

Köppl, C. (2011). Evolution of the octavolateral efferent system. In D. K. Ryugo, R. R. Fay, & A. N. Popper (Eds.), *Auditory and vestibular efferents* (pp. 217–259). New York: Springer.

Larsell, O. (1967). *The comparative anatomy and histology of the cerebellum from myxinoids through birds.* Minneapolis: The University of Minnesota Press.

Leydig, F. (1850). Über die Schleimkanäle der Knochenfische. *Müllers Archiv für Anatomie und Physiologie*, 170–181.

Leydig, F. (1851). Über die Nervenköpfe in den Schleimkanälen von *Lepidoleprus umbrina* und *corvina*. *Müllers Archiv für Anatomie und Physiologie*, 235–240.

Leydig, F. (1868). Über Organe eines sechsten Sinnes. *Nova Acta Academia Curios*, 34(5).

Lissmann, H. W., & Machin, K. E. (1958). The mechanism of object location in *Gymnarchus niloticus.* Cuv. *Journal of Experimental Biology,* 35, 451–486.

Lorenzini, S. (1678). Observazioni inforno alle Torpedini. Firenze, 1678, London, 1705, Angl.

Lowenstein, O. (1967). The concept of the acousticolateral system. In P. H. Cahn (Ed.), *Lateral line detectors* (pp. 3–11). Bloomington: Indiana University Press.

Lyon, E. P. (1904). On rheotropism. I. Rheotropism in fishes. *American Journal of Physiology*, 12, 149–161.

Ma, E. Y., & Raible, D. W. (2009). Signaling pathways regulating zebrafish lateral line development. *Current Biology*, 19(9), R381–R386.

Mayser, P. (1882). Vergleichend anatomische Studien über das Gehirn der Knochenfische mit besonderer Berücksichtigung der Cyprinoiden. *Zeitschrift für wissenschaftliche Zoologie*, 36, 259–364.

McCormick, C. A. (1982). The organization of the octavolateralis area in actinopterygian fishes: A new interpretation. *Journal of Morphology*, 171, 159–181.

McCormick, C. A. (1989). Central lateral line mechanosensory pathways in bony fish. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 341–364). New York: Springer-Verlag.

Montgomery, J. C., Coombs, S., Conley, R. A., & Bodznick, D. A. (1995). Hindbrain sensory processing in lateral line, electrosensory and auditory systems: A comparative overview of anatomical and functional similarities. *Auditory Neuroscience*, 1, 207–231.

Montgomery, J. C., Baker, C. F., & Carton, A. G. (1997). The lateral line can mediate rheotaxis in fish. *Nature*, 389, 960–963.

Murray, R. W. (1960). Electrical sensitivity of the ampullae of lorenzini. *Nature*, 187, 957.

Nagiel, A., Andor-Ardó, D., & Hudspeth, A. (2008). Specificity of afferent synapses onto plane-polarized hair cells in the posterior lateral line of the zebrafish. *The Journal of Neuroscience*, 28(34), 8442.

Ou, H. C., Santos, F., Raible, D. W., Simon, J. A., & Rubel, E. W. (2010). Drug screening for hearing loss: Using the zebrafish lateral line to screen for drugs that prevent and cause hearing loss. *Drug Discovery Today*, 15(7–8), 265–271.

Parker, G. H. (1904). The function of the lateral line organs in fishes. *Bulletin of the US Bureau of Fisheries*, 24, 185–207.

Pearson, A. A. (1936a). The acoustico-lateral centers and cerebellum, with fiber connections, of fishes. *Journal of Comparative Neurology*, 65, 201–294.

Pearson, A. A. (1936b). The acustico-lateral nervous system in fishes. *Journal of Comparative Neurology*, 64, 235–273.

Platt, C., Popper, A. N., & Fay, R. R. (1989). The ear as part of the octavolateralis system. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 633–651). New York: Springer-Verlag.

Requarth, T., & Sawtell, N. B. (2011). Neural mechanisms for filtering self-generated sensory signals in cerebellum-like circuits. *Current Opinion in Neurobiology*, 21(4), 602–608.

Roberts, B. L. (1972). Activity of lateral-line organs in swimming dogfish. *Journal of Experimental Biology*, 56, 105–118.

Roberts, B. L., & Russell, I. J. (1972). The activity of lateral-line efferent neurones in stationary and swimming dogfish. *Journal of Experimental Biology*, 57, 435–448.

Roberts, B. L., & Meredith, G. E. (1989). The efferent system. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 445–459). New York: Springer-Verlag.

Russell, I. J. (1971a). The pharmacology of efferent synapses in the lateral-line system of *Xenopus laevis*. *Journal of Experimental Biology*, 54, 643–658.

Russell, I. J. (1971b). The role of the lateral-line efferent system in *Xenopus laevis*. *Journal of Experimental Biology*, 54, 517–522.Schulze, F. E. (1861). Über die Nervenendigung in den sogenannten Schleimkanälen der Fische und über entsprechende Organe der durch Kiemen atmenden Amphibien. *Archiv für Anatomie*, *Physiologie und wissenschaftliche Medizin*, 28, 759–769.

Schulze, F. E. (1870). Über die Sinnesorgane der Seitenlinie bei Fischen und Amphibien. *Archiv für Mikroskopie und Anatomie*, 6, 62–88.

Stenonis (alias Steno or Stensen), N. (1664). *De muscalis et glandulis observationum specimen cum epistolisduabus anatomicis; de anatome rajae*. [*from Leydig*, 1868 *and Johnson*, 1917]. Amsterdam: Hafniae: Literis Matthiae Godicchenii.

Tricas, T. C., & Highstein, S. M. (1990). Visually mediated inhibition of lateral line primary afferent activity by the octavolateralis efferent system during predation in the free-swimming toadfish, *OPSANUS tau*. *Experimental Brain Research*, 83, 233–236.

Tricas, T. C., & Highstein, S. M. (1991). Action of the octavolateralis efferent system upon the lateral line of free-swimming toadfish, (*Opsanus tau*). *Journal of Comparative Physiology A*, 169, 25–37.

van Bergeijk, W. A. (1967). Introductory comments on lateral line function In P. H. Cahn (Ed.), *Lateral line detectors* (pp. 73–79). Bloomington: Indiana University Press.

von Frisch, K. (1923). Ein Zwergwels der kommt wenn man ihm pfeift. *Biologisches Zentralblatt*, 43, 439–446.

von Frisch, K., & Stetter, H. (1932). Untersuchungen über den Sitz des Gehörsinns bei der Elrize. *Zeitschrift für vergleichende Physiologie*, 17, 686–801.

Webb, J. F., & Blum, S. D. (1990) A swimbladder-lateral line connection in the butterflyfish genus *Chaetodon* (Perciformes: Chaetodontidae). *American Zoologist*, 30, 98.

Weeg, M. S., Land, B. R., & Bass, A. H. (2005). Vocal pathways modulate efferent neurons to the inner ear and lateral line. *Journal of Neuroscience*, 25(25), 5967–5974.

Wilson, H. V., & Mattocks, J. E. (1897). The lateral sensory anlage in the salmon. *Anatomischer Anzeiger*, 13, 658–660.

Wilson, M., Montie, E. W., Mann, K. A., & Mann, D. A. (2009). Ultrasound detection in the gulf menhaden requires gas-filled bullae and an intact lateral line. *Journal of Experimental Biology*, 212(21), 3422.

Windsor, S. P., Tan, D., & Montgomery, J. C. (2008). Swimming kinematics and hydrodynamic imaging in the blind mexican cavefish (*Astyanax fasciatus*). *The Journal of Experimental Biology*, 211, 2950–2959.

Windsor, S. P., Norris, S. E., Cameron, S. M., Mallinson, G. D., & Montgomery, J. C. (2010). The flow fields involved in hydrodynamic imaging by blind mexican cave fish (*Astyanax fasciatus*).

part I: Open water and heading towards a wall. *Journal of Experimental Biology*, 213(22), 3819–3831.

Wright, M. R. (1951). The lateral line system of sense organs. *Quarterly Review of Biology*, 26, 264–280.

Yang, Y., Chen, J., Engel, J., Pandya, S., Chen, N., Tucker, C., Coombs, S., Jones, D. L., & Liu, C. (2006). Distant touch hydrodynamic imaging with an artificial lateral line. *Proceedings of the National Academy of Sciences of the USA*, 103(50), 18891–18895.

Yang, Y., Nguyen, N., Chen, N., Lockwood, M., Tucker, C., Hu, H., Bleckmann, H., Liu, C., & Jones, D.L. (2010). Artificial lateral line with biomimetic neuromasts to emulate fish sensing. *Bioinspiration & Biomimetics*, 5(1), 016001.

Morphological Diversity, Development, and Evolution of the Mechanosensory Lateral Line System

Jacqueline F. Webb

Keywords Agnatha • Amphibia • Cupula • Dermatocranium • Elasmobranch • Hair cell • Mantle cell • Neuromast • Placode • Sensory • Support cell • Teleost

1 Introduction

The mechanosensory lateral line system is a primitive feature of vertebrates that is found in all fishes and in larval and adult aquatic amphibians (Coombs et al., 1988; Northcutt, 1989; Webb, 1989b). It has critical roles in feeding, swimming, navigation, and communication behaviors (see the chapters by Montgomery, Coombs, & Bleckmann; Chagnaud & Coombs; Bleckmann & Mogdans; and Braun & Sand). It has also been the subject of anatomical studies for over a century. Late 19th- and 20th-century monographs have detailed both the structure and development of the neuromasts and lateral line canals in marine and freshwater fishes (e.g., Allis, 1889; Pehrson, 1944a; Lekander, 1949), and expeditionary reports have described neuromasts, and in some cases their innervation, in open ocean and deep-sea species (e.g., Garman, 1899). The fact that the lateral line canals, especially those on the head, are integrated within a conserved subset of bones of bony fishes has ensured that the lateral line system has figured prominently in studies of the evolution of the fish skull (e.g., Parker, 1904; Hensel, 1976). Their preservation in the fossil record has allowed important comparisons of lateral line morphology in extinct and extant taxa (e.g., Grande and Bemis, 1991, 1998; Ahlberg & Clack, 1998; Grande, 2010). The lateral line system continues to be important in the fields of taxonomy and systematics, where the lateral line canals are a source of

J.F. Webb (✉)
Department of Biological Sciences, Center for Biotechnology and Life Sciences, University of Rhode Island, Kingston, RI 02881, USA
e-mail: Jacqueline_webb@mail.uri.edu

S. Coombs et al. (eds.), *The Lateral Line*, Springer Handbook of Auditory Research 48,
DOI 10.1007/2506_2013_12, © Springer Science+Business Media New York 2013,
Published online: 29 June 2013

morphological characters used in species descriptions and phylogenetic analyses (e.g., Di Dario & de Pinna, 2006; Parenti, 2008; Stephens, 2010).

The lateral line system has also played important roles in the fields of comparative neuroanatomy and developmental biology. Patterns of neuromast innervation have been used in the analysis of the evolution of the nervous system in vertebrates (Northcutt, 1989 and Section 2.2). The lateral line system has attracted attention in the reinvigorated field of evolutionary developmental biology (Webb, 1989a; Northcutt, 1997; Jeffery, 2001), which exploits new tools for the study of the developmental genetics of the lateral line system in model species such as zebrafish (*Danio rerio*; Sections 3.1 and 5.2.1) and medaka (*Oryzias latipes*; Wittbrodt et al., 2002; Yasuoka et al., 2004).

From the perspectives of both evolutionary developmental biology and neuroethology, the structural organization, evolution, and behavioral roles of the lateral line system are particularly interesting, especially when compared to other vertebrate sensory systems. First, the neuromast receptor organs that compose the system are not located in a pair of complex organs on the head, but are distributed over the head and body in stereotyped patterns established during embryogenesis (see Section 3.1). Second, the neuromasts demonstrate a great deal of morphological diversity with respect to both size and shape, which suggests variation in function at the level of individual receptor organs (Section 3.2). Third, the location of neuromasts either on the skin or in canals (Section 2.1.1) determines their functional attributes and provides complementary roles in lateral line–mediated behaviors (see the chapters by van Netten & McHenry and Chagnaud & Coombs). Lastly, the dual identity of the lateral line system as both a structural component of the skull of bony fishes and a sensory system critical for various aspects of behavior provides a rich context in which to analyze its adaptive evolution in response to different structural (constructional) and functional constraints and adaptive opportunities.

This chapter draws upon insights from morphological, physiological, behavioral, and developmental studies of the lateral line system, especially those carried out over the past two decades. It (1) reviews principles of lateral line structural organization and defines sources of morphological (and potential functional) variation among fishes; (2) describes the embryonic and postembryonic development of the lateral line system; (3) examines how variation in adult lateral line morphology among species can be explained by examining developmental patterns; and (4) describes the lateral line system in key species used in biomechanical, neurophysiological, and neuroethological studies.

2 Structural Organization of the Lateral Line System

The neuromast receptor organs, the functional units of the lateral line system, are composed of directionally sensitive sensory hair cells (Fig. 1a). Two types of neuromasts, canal neuromasts (CNs) and superficial neuromasts (SNs), constitute two sensory submodalities in jawed fishes (see the chapters by van Netten &

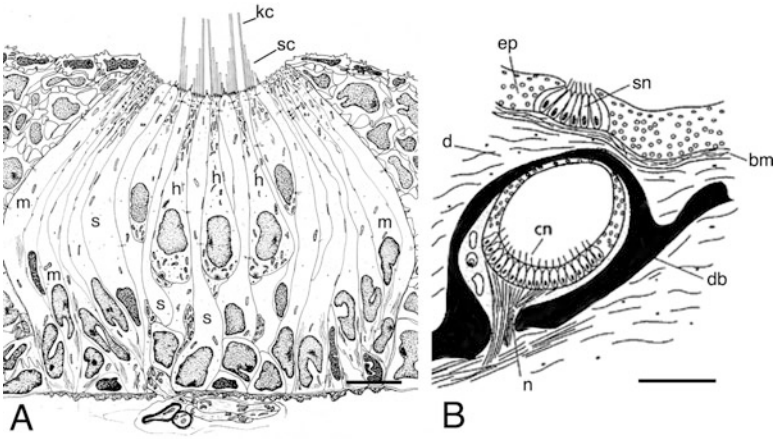

Fig. 1 Structure of neuromasts in teleost fishes. (**a**) Superficial neuromast in Nile tilapia (*Oreochromis niloticus*) indicating the apical kinocilium (kc) and stereocilia (sc) of each hair cell (h), nonsensory mantle cells (m), and support cells (s). Scale bar = 10 μm. (From Münz, 1979.) (**b**) Schematic representation of neuromasts in the cyprinid *Hybopsis aestivalis* showing a superficial neuromast with ciliated hair cells (sn) in the epidermis (ep) and much larger canal neuromast with ciliated hair cells (cn; support cells and mantle cells not illustrated). The lateral line nerve (n) moves through a nerve foramen in a cranial canal (dermal bone, db) within the dermis d, (below basement membrane, bm) to innervate the hair cells in the canal neuromast. Scale bar = 50μm. (From Webb, 2011)

McHenry and Chagnaud & Coombs and Fig. 1b); only SNs are found in the extant jawless fishes (Section 6.3) and in larval and aquatic adult amphibians (Section 7). The sensory neurons that innervate the neuromasts on the head and trunk comprise several lateral line nerves (Puzdrowski, 1989; Northcutt & Bemis, 1993; Piotrowski & Northcutt, 1996; Northcutt et al., 2000). These are no longer considered to be branches of the other vertebrate cranial nerves (e.g., V, VII, IX, X; discussed by Northcutt, 1989). The cell bodies of the bipolar sensory neurons that compose the lateral line nerves compose distinct sensory ganglia and have discrete central projections to the medulla oblongata (hindbrain) that are distinct from those that receive input from the auditory and electrosensory systems (see chapters by Wullimann & Grothe and Bleckmann & Mogdans).

2.1 Structure of Neuromasts

Neuromasts are small epithelial organs (typically 10–500 μm diameter) composed of mechanosensory hair cells (not unlike those of the vertebrate inner ear) and nonsensory cells (Fig. 1a). Each hair cell has a ciliary bundle extending from its apical surface that is composed of a single kinocilium (a true cilium), which may be

quite long, and several shorter stereovilli (microvilli) located to one side of it, which are graded in length (Flock, 1965a, b). The placement of the kinocilium relative to the stereocilia defines a hair cell's structural and functional polarity, and the direction of a water flow relative to the orientation of the ciliary bundle determines how a hair cell will respond to it. Deflections of the kinocilium away from the stereocilia will cause an excitatory response, whereas deflections of the kinocilium toward the stereocilia will cause an inhibitory response (see the chapter by Chagnaud & Coombs). Hair cells with opposing orientations (180° to each other) are spatially intermingled within a neuromast, thus defining its axis of best physiological sensitivity (Fig. 2). In the small neuromasts of fish embryos and larvae, hair cells cover the neuromast's entire surface (Raible & Kruse, 2000; Webb & Shirey, 2003), but in the larger neuromasts of juvenile and adult fishes, hair cells are generally restricted to a smaller, round or oval region of the neuromast (the "sensory zone," Jakubowski, 1967b, or "sensory strip," Coombs et al., 1988; Fig. 2) that is surrounded by nonsensory cells. The morphology of the ciliary bundles (e.g., relative length of the kinocilium, number and length of stereocilia) may vary among hair cells within a neuromast (e.g., Song and Northcutt, 1991; Marshall, 1996; Faucher et al., 2003) and between CNs and SNs in the same individual, which should have interesting functional consequences.

Two types of nonsensory cells, the support ("supporting") cells and mantle cells, are generally recognized based on their location within the neuromast (Blaxter, 1987; Münz, 1979) and on differential gene expression (reviewed in Chitnis et al., 2011). Support cells are scattered among the hair cells and extend from the apical surface of the neuromast to below the hair cells (Fig. 1a). It has been shown that support cells differentiate into hair cells, thus accounting for the processes of hair cell turnover (Williams & Holder, 2000) and regeneration (Hernández et al., 2007; Behra et al., 2009; Namdaran et al., 2012; reviewed by Chitnis et al., 2011; also see the chapter by Coffin, Brignull, Raible, and Rubel). In contrast, the mantle cells, which surround the population of hair cells, define the neuromast's shape (Rouse & Pickles, 1991b; Williams & Holder, 2000; Ghysen & Dambly-Chaudière, 2007; Fig. 2) and are thought to secrete the cupula. Neuromasts are surrounded by the large squamous (flat) epithelial cells that compose the general surface epithelium and the lining of the lateral line canals (Figs. 1a and 2).

The ciliary bundles of all of the hair cells in a neuromast extend into a single, elongate cupula, which serves as the biomechanical interface between the neuromast and the surrounding environment, and is thus critical for neuromast function (Windsor & McHenry, 2009; see the chapters by van Netten & McHenry and Chagnaud & Coombs). The base of the cupula covers the entire neuromast; thus neuromast size and shape determines the shape of the base of the cupula, which is of functional significance (see the chapter by van Netten & McHenry). For instance, in zebrafish larvae, the height of the cupula in SNs is, on average, twice that of its kinocilia and four times that of the diameter of the cupular base (Van Trump & McHenry, 2008), but cupular length varies considerably among SNs within an individual defining variation in their frequency response (Van Trump & McHenry,

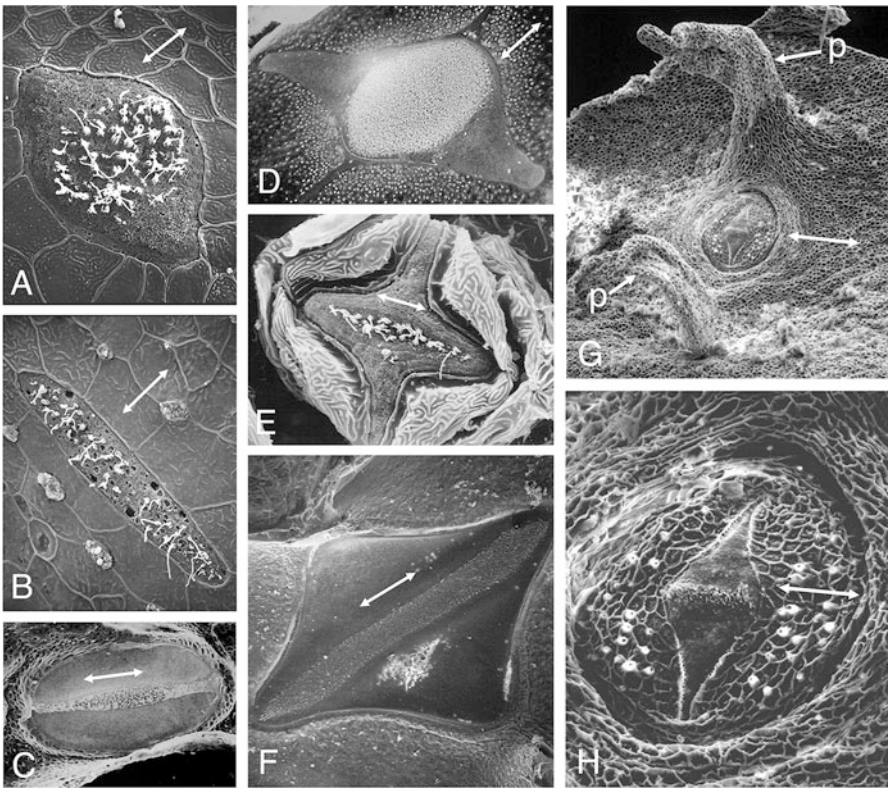

Fig. 2 Morphological variation in CNs (canal neuromasts) and SNs (superficial neuromasts) in teleost fishes. (**a**) SN on trunk of windowpane flounder (*Scophthalmus aquosus*). (**b**) CN in narrow canal of zebrafish (*Danio rerio*). (**c**) CN in narrow canal of mottled sculpin (*Cottus bairdi*). (**d**) CN in widened canal in clown knifefish (*Notopterus chitala*). (**e**) SN from the blind side of the head of California tongue sole (*Symphurus atricauda*). (**f**) CN in widened canal in rex sole (*Glyptocephalus* sp.). (**a–f** from Webb, 2011. Reprinted with permission of Elsevier, Inc.). (**g**) SN from the dorsal most of five horizontal lines of neuromasts on the trunk of an adult plainfin midshipman (*Porichthys notatus*), showing the pair of papillae (p) that accompany each of the trunk neuromasts. (**h**) Close-up of the SN in G, showing the elongate sensory zone containing the hair cells in the center of the neuromast. Arrows indicate hair cell orientation, which is parallel to the long axis of the canal in all canal neuromasts

2008). Cupulae may be damaged at hatch, but are repaired (Van Trump & McHenry, 2008) and grow continuously (Vischer, 1989; Mukai & Kobayashi, 1992). Münz (1979) noted that the cupula is composed of two distinct layers: a central layer that overlies the sensory strip and supporting cells and an outer layer that overlies the surrounding mantle cells. Kelly and van Netten (1991) described a fibrillar core to the cupula. Münz (1979) suggested that the central layer of the cupula is secreted by the support cells, so the outer layer is likely secreted by the mantle cells (as suggested by Blaxter, 1987). However, it has also been suggested

that only the mantle cells secrete the cupula (Rouse & Pickles, 1991b; Ghysen & Dambly-Chaudière, 2007).

2.1.1 Canal versus Superficial Neuromasts

CNs and SNs define two sensory submodalities in bony fishes that are characterized by different morphological and functional attributes (see the chapters by McHenry & Liao and van Netten & McHenry). Their overall distribution is also distinct; the location of CNs is limited by their association with the lateral line canals on the head and trunk, but the number and spatial distribution of SNs on the head, trunk, and tail tend to demonstrate a great deal of variation among species.

CNs are found in the epithelium lining the bottom of the lateral line canals, and one neuromast is found between two adjacent canal pores. This pattern is the result of the process of canal morphogenesis (Section 3.3). The placement of CNs between pores allows them to be deflected by water flows generated by pressure differences at adjacent canal pore positions. Although fewer in number, CNs are typically larger than SNs in juvenile (Blaxter, 1987; Tarby & Webb, 2003) and adult fishes (Münz, 1989; Webb, 1989c; Song & Northcutt, 1991; Fig. 1b). On the head, CN size and shape appear to be correlated with the type of canal in which they are found (Section 4.1.1). For instance, neuromasts in narrow cranial canals tend to be round or oval with their major axis parallel to canal axis (Fig. 2c), whereas neuromasts in widened cranial canals tend to be much larger, with a secondary morphological axis perpendicular to the canal axis resulting in a diamond shape (e.g., Garman, 1899; Jakubowski, 1963, 1967b, 1974; Figs. 2 and 3). However, in some species with narrow canals, the CNs are elongated perpendicular to the canal axis (e.g., zebrafish, Webb & Shirey, 2003; Fig. 2b; goldfish [*Carassius auratus*], Schmitz et al., 2008; seabass [*Dicentrarchus labrax*], Faucher et al., 2003). These neuromasts likely respond differently than those arranged parallel to the length of the canal owing to the difference in the shape of the cupula. But, regardless of neuromast shape, the axis of best physiological sensitivity (directional orientation) of the hair cells in a canal neuromast is always parallel to the length of the canal (Fig. 2), thus ensuring the ability of a neuromast to respond to water movements along the length of the canal (Fig. 2).

SNs are diverse with respect to their morphology, developmental origin, and evolutionary history. Their morphology and distribution have been described in detail in only a small number of species (e.g., Puzdrowski, 1989; Song & Northcutt, 1991; Schmitz et al., 2008; Asaoka et al., 2011, 2012 , but nevertheless, some generalizations can be made. SNs tend to be round or diamond-shaped (Fig. 2a; Münz, 1979; Webb, 1989c; Song et al., 1995) and occur singly, in lines, or in clusters (Fig. 3c–e). Some SNs that sit in pits or grooves on the skin (especially in non-teleost fishes and amphibians) have been historically referred to as “pit organs,” and linear series of such neuromasts have been referred to as “pit lines” (Lekander, 1949; Nelson, 1972; Song & Northcutt, 1991). Northcutt and Bleckmann (1993) determined that the “pit organs” in the axolotl (*Ambystoma*

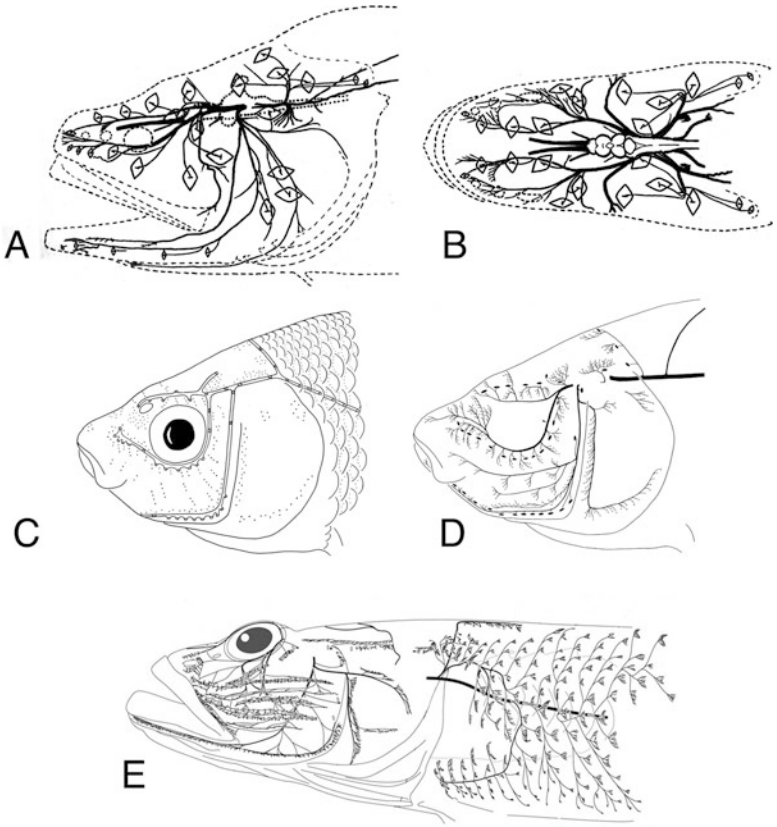

Fig. 3 Innervation of the lateral line system. (**a**, **b**) Lateral and dorsal view of the head of *Bassozetus nasus* (family Ophidiidae), a deep-sea species with widened canals. Large diamond-shaped neuromasts are innervated by branches of the lateral line nerves. Canals are not illustrated. The line at the end of each nerve branch indicates the shape of the "sensory strip" within the neuromast (Garman, 1899). (**c**, **d**) CNs (in narrow canals) and SNs and their innervation in goldfish (*Carrasius auratus*). (From Puzdrowski, 1989. Reprinted with permission of S. Karger AG, Basel). (**e**) Innervation of CNs and the highly proliferated SNs on the head and trunk of the goby (*Glossogobius olivaceus*) (Asaoka et al., 2012)

mexicanum) are similar to other neuromasts both morphologically and physiologically, and thus they need not be considered a special class of sensory organs. Other SNs may sit flush with the skin surface (Webb, 1989c) or on top of stalks, filaments, or papillae, which is particularly common among deep-sea (Marshall, 1996; Gibbs, 1999; Pietsch, 2009) and cave-dwelling fishes (e.g., Moore & Burris, 1956). In some bottom-associated fishes, SNs may be proliferated (e.g., Figs. 2 and 3) and/or are found between non-sensory accessory structures that appear to protect the neuromast and/or alter the hydrodynamic environment of the neuromast (Appelbaum & Schemmel, 1983; Nakae & Sasaki, 2010; Section 5.4; Fig. 2g, h).

SNs may be homologues of CNs that present in canals of ancestral or sister species ("replacement neuromasts," Coombs et al., 1988), or SNs may accompany CNs that are contained within existing canals ("accessory neuromasts," sensu Lekander, 1949; Coombs et al., 1988) in teleost fishes. "Replacement neuromasts" sit flush on the skin, or in some cases in incompletely formed canals (grooves), which are interpreted to be the result of a paedomorphic reduction (incomplete development) of the canals (Webb, 1989a; Section 4.1.1). From a functional standpoint, the evolutionary reduction of lateral line canals represents a transition from CNs to SNs, which represents a change in function (from accelerometer to velocimeter). In contrast, "accessory neuromasts" are found in the epithelium adjacent to or overlying canals (Fig. 3d) have hair cell orientations that tend to be either parallel to and/or perpendicular to the axis of the canal (Marshall, 1986; Webb, 1989c; Schmitz et al., 2008). On the trunk, accessory neuromasts are often located on each lateral line scale. Their hair cell orientation is generally parallel or perpendicular to the length of the trunk canal, and thus to the body axis (Webb, 1989c). Accessory SNs may occur in lines or stitches with similar orientations, or in pairs with perpendicular (orthogonal) orientations (Coombs et al., 1988; Webb, 1989c) and provide complementary responses to that of the CNs (see the chapter by van Netten and McHenry). SNs with perpendicular orientations in close proximity to one another can respond to stimuli from a variety of directions. Hair cell orientation among SNs on the head tends to be more variable with reference to the body axis, given the three-dimensional nature of the head and the curvature of the canals that they accompany, such as the infraorbital, which follows the circumference of the orbit (Webb, 1989c; Schmitz et al., 2008).

2.2 *Innervation of the Lateral Line System*

The pattern of neuromast innervation and the organization of central projections in the hindbrain are conserved among bony fishes (see the chapter by Wullimann & Grothe and Fig. 3). Peripherally, dorsal and ventral branches of the anterior lateral line nerve (ALLN) innervate CNs and SNs around the orbit and on the mandible. A middle lateral line nerve (MLLN) innervates a small number of CNs and SNs at the posterior margin of the head in many (but not all) teleosts (Puzdrowski, 1989; Gibbs, 1999). The posterior lateral line nerve (PLLN) is typically divided into two branches that innervate the dorsal and main neuromast lines on the trunk, respectively, and a third branch that, interestingly, innervates the supratemporal line (or the CNs of the supratemporal commissure) on the head (Fig. 3d; Puzdrowski, 1989; Song & Northcutt, 1991; Raible & Kruse, 2000).

A recent series of remarkably detailed papers by Sasaki and colleagues has described the pattern of innervation of the lateral line system in several species of the family Tetraodontidae (triggerfishes, pufferfishes, ocean sunfishes), all of which have only SNs (Nakae & Sasaki, 2005, 2006), and pattern of innervation in other taxa that have only CNs (Nakae & Sasaki, 2010). Related studies

described the distribution and innervation of the highly proliferated SNs in several gobies [Gobioidei] (Asaoka et al., 2011a,b; Fig. 3e) and in a deep-sea perciform (Nakae et al., 2006). The pattern of neuromast innervation on the trunk has been used as a source of characters for an exploration of phylogenetic relationships among taxa (Fukuda et al., 2010; Tamanaka et al., 2010). Collectively, these studies have demonstrated that the concept of "replacement neuromasts" (Coombs et al., 1988) is supported by the similarity of the innervation of CNs and SNs found in the same locations in related taxa. Further, the pattern of innervation of proliferated SNs on the head and trunk appears to be the result of the simple addition of nerve branches of the major lateral line nerves. These papers demonstrate that comparisons of innervation patterns among related taxa can shed light on the nature of the homology of neuromast lines located in similar positions on the head and trunk in different species.

3 Development of the Lateral Line System

A functional lateral line system composed of small SNs is present in newly hatched larvae of bony fishes. Dramatic changes that occur in body size, swimming capabilities, and the morphology of the system in larvae and juveniles with the growth of neuromasts and formation of the lateral line canals, change the hydrodynamic context in which neuromasts function. Thus, an understanding of the pattern of lateral line development is essential for an appreciation of changes in lateral line function and thus its behavioral roles through a fish's life history. Further, the morphological evolution of the lateral line system as well as the nature of structure–function relationships are best appreciated when patterns (and underlying mechanisms) of development are considered. Conversely, an appreciation for morphological diversity among species is likely to assist in the interpretation of developmental patterns.

The analysis of early lateral line development started more than a century ago with the pioneering work of Harrison, Stone, and Landacre (reviewed by Northcutt, 1989, 1994, 2003). Over the past two decades, an extensive body of work has explored the genetic mechanisms underlying early lateral line development primarily in two model fish species, zebrafish (*Danio rerio*) and medaka (*Oryzias latipes*). An in-depth treatment of the early development of the lateral line system on the trunk of zebrafish is provided in recent reviews (Aman & Piotrowski, 2009, 2011; Ma & Raible, 2009; Gallardo et al., 2010; Chitnis et al., 2012; see also the chapter by Coffin, Brignull, Raible, & Rubel). Here an overview of patterns of lateral line development is provided, with insights from recent studies that show how an understanding of developmental mechanisms may shed light on the generation of evolutionary diversity.

The development of the lateral line system starts in the embryo. Both the neuromasts and the sensory neurons that innervate them arise from cranial ectodermal lateral line placodes located rostral and caudal to the otic (ear) placode (Baker &

Bronner-Fraser, 2001; Schlosser, 2010; Modrell et al., 2011a, b). Interestingly, the electrosensory organs also arise from the lateral line placodes in the non-teleost bony fishes, chondrichthyans, and amphibians in which they are found (Northcutt et al., 1994, 1995; Northcutt, 2003; Modrell et al., 2011a,b; Gillis et al., 2012). After the appearance of the lateral line placodes, development of the lateral line system in bony fishes occurs as a series of three phases (Webb, 1989a). First, the migration of placode-derived lateral line primordia (on the trunk) or elongation of primordia in sensory ridges (on the head) establishes the spatial distribution of neuromasts (Section 3.1). Neuromast maturation, growth, and proliferation and then morphogenesis of the lateral line canals commence in late-stage larvae and continue through metamorphosis (transformation to the juvenile stage; see Sections 3.2 and 3.3). Canal morphogenesis does not occur in jawless fishes and amphibians (Sections 6.3 and 7)—they have exclusively SNs. The pattern and process of canal morphogenesis are not well known in the cartilaginous fishes (sharks, skates, rays, chimeras; Section 6.2).

3.1 Migration of Neuromast Primordia and Sensory Neurons and Spatial Patterning of Neuromasts

On the trunk of zebrafish, placode-derived lateral line primordia migrate along defined paths, from the head to the caudal peduncle and onto the caudal fin (Fig. 4). As a primordium migrates, "rosettes" of cells (protoneuromasts) form within it and are deposited as clusters of cells from which hair cells then differentiate, forming a neuromast (Lopez-Shier et al., 2004; Yasuoka et al., 2004; Fig. 4b). Three migrating primordia contribute to the development of the trunk neuromasts, and hair cell orientation in a given neuromast correlates with its origin in a particular primordium (Nuñez et al., 2009; Ghysen et al., 2012; Fig. 4c–f). Each primordium leaves a trail of cells, the "interneuromast" cells, that differentiate into additional neuromasts (Grant et al., 2005; Lopez-Schier & Hudspeth, 2005). Interestingly, these cells may be those that comprise the "connecting strand" described in several species of bony fishes (Allis, 1889; Clapp, 1889; Peters, 1973; Fig. 4). When the primordia start migrating, some placode-derived cells stay behind and differentiate into the bipolar sensory neurons whose cell bodies will form the lateral line ganglia. One neurite of each sensory neuron will project to the hindbrain centrally and the other comigrates with the neuromast primordium to innervate a neuromast peripherally (Gilmour et al., 2004; Schuster et al., 2010; reviewed in Chitnis et al., 2012).

The genetic control of the spatial patterning and innervation of the trunk neuromasts has been explored through detailed experimental studies in zebrafish (e.g., Sapède et al., 2002; Lopez-Schier et al., 2004; reviewed in Chitnis et al., 2012). Comparisons of the migration paths and resultant patterning of the neuromasts on the trunk in wild-type and mutant zebrafish

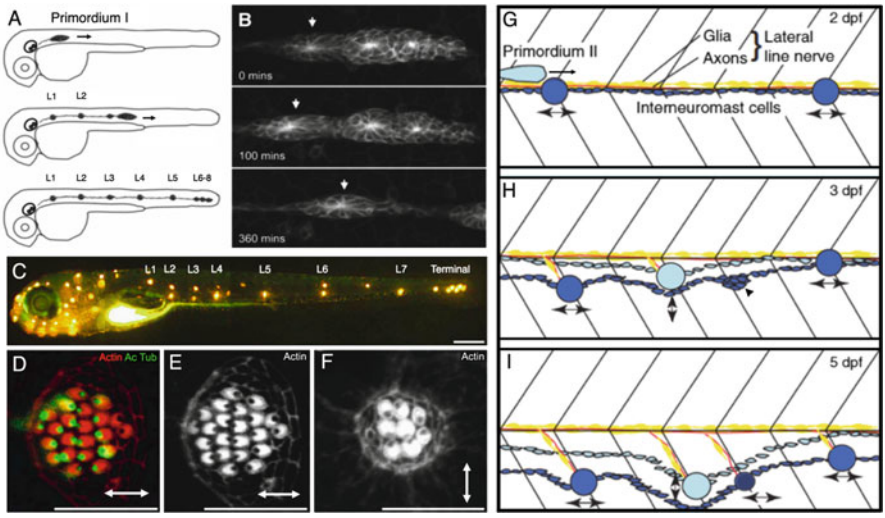

Fig. 4 Migration of lateral line primordia and differentiation of neuromasts on the trunk of zebrafish (*Danio rerio*). (**a**) Migration of Primordium I (arrow indicates direction of migration) in a zebrafish yolk-sac embryo, showing the deposition of neuromasts (L1–L5, L6–8 = terminal neuromasts), the trail of interneuromast cells between them, and the lateral line nerve (axons, red; glia, yellow). (**b**) Images of the migrating Primordium I from a time-lapse movie (0–360 minutes, confocal microscopy) of a transgenic larva with primordium labeled with green fluorescent protein (GFP). Arrows indicate the proto-neuromasts in the form of a rosette. (**a**, **b** from Chitnis et al., 2011. Reproduced with permission of John Wiley & Sons, Inc.) (**c**) Zebrafish larva (6 dpf) fluorescently stained with 4-Di-2-ASP showing head neuromasts and trunk neuromasts (L1–L7, terminal; neuromasts of both sides of fish are visible). (**d**) Neuromast L1 with double labeling for actin in stereocilia and anti-acetylated tubulin in kinocilia of hair cells revealing rostrocaudal orientation (double-headed arrow). (**e**) Same type of neuromast stained just for actin in stereocilia; dark spots are positions of kinocilia. (**f**) Similar labeling of a dorsoventrally oriented neuromast (double-headed arrow). (**c–f** from Lopez-Shier et al., 2004. Reprinted with permission of Elsevier, Inc.) (**g**) Diagrammatic representation of the trunk of a zebrafish embryo (2 dpf), indicating myosepta and horizontal septum (zigzag and horizontal black lines, respectively), after migration of Primordium I along the horizontal septum, which has laid down two neuromasts (medium blue) at myosepta, leaving interneuromast cells between them. Primordium II (light blue) is shown starting to migrate along the same path (arrow). Double-headed arrows indicate hair cell orientation of the two neuromasts (rostrocaudal, as in **d**, **e**). (**h**) One day later (3 dpf), Primordium II has migrated along the same path as Primordium I and has deposited a neuromast (light blue, with dorsoventral hair cell orientation, as in (**f**) at a myoseptum, between the two neuromasts previously deposited by Primordium I. Interneuromast cells (dark blue, arrowhead) have begun to aggregate. (**i**) At 5 dpf, the neuromasts derived from Primordium I (medium blue) and Primordium II (light blue) have migrated ventrally, and branches of the myelinated lateral line nerve (red, yellow) have comigrated with the neuromasts. Interneuromast cells of Primordium I (dark blue) have differentiated into an intercalary neuromast with rostrocaudal hair cell orientation. (**g–i** modified from Whitfield, 2004. Reprinted with permission of Elsevier, Inc.) Scale bars: **C** =100 μm, **d–f** = 10 μm

(Sapède et al., 2002; Lopez-Schier & Hudspeth, 2005), medaka (Yasuoka et al., 2004), and in a small number of other teleosts (Pichon & Ghysen, 2004; Wada et al., 2008; Ghysen et al., 2012), are beginning to reveal how variation in spatial patterning of trunk neuromasts can generate the interspecific variation found among adult fishes.

On the head, placode-derived primordia extend within the ectoderm and may appear as elongate ridges in which neuromasts differentiate in elasmobranchs (O'Neill et al., 2007; Gillis et al., 2012), bony fishes (Northcutt, 2003; Gibbs & Northcutt, 2004), and amphibians (Northcutt et al., 1994, 1995). This process establishes the general distribution of canal neuromasts, which are in lines dorsal to the orbit (supraorbital line), ventral to the orbit (infraorbital line), and on the cheek and lower jaw (preopercular and mandibular lines, respectively). The differentiation of additional superficial neuromasts on the head (e.g., "pit lines" and accessory neuromasts) is not well studied.

3.2 *Neuromast Maturation, Growth, and Proliferation*

Neuromasts first appear in embryos and larvae as small, round organs (<10 μm in diameter; Fig. 5) on the head and trunk (Raible & Kruse, 2000; Wada et al., 2010;

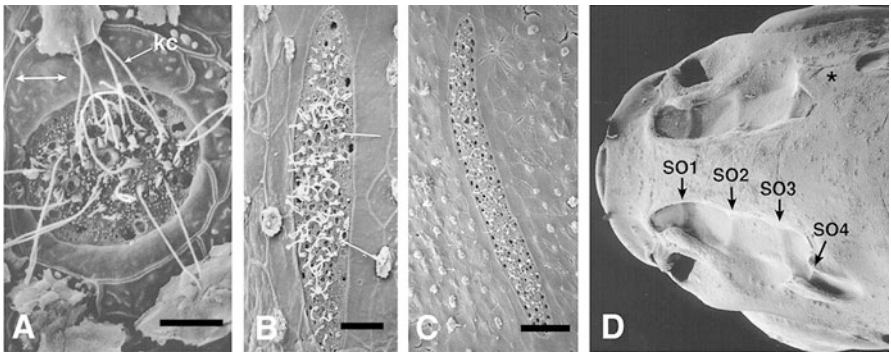

Fig. 5 Ontogeny of CNs in the supraorbital (SO) canal of the zebrafish (*Danio rerio*). Rostral is to left in all images. (**a**) Presumptive SO canal neuromast (SO3, see **d**) in a 9-mm larva, with round shape and very long kinocilia (kc). Double-headed arrow indicates the axis of hair cell polarization and the long axis of the canal into which this neuromast will become incorporated. (**b**) SO3 continues to elongate perpendicular to the canal axis (15 mm juvenile), and (**c**) SO3 has become extremely elongate (23 mm juvenile). Note that the hair cells extend to the edges of the neuromast, and the clearly defined outer perimeter of the neuromast is surrounded by squamous epithelial cells. (**d**) Bilateral SO canal grooves on the dorsal surface of the head (23 mm SL juvenile) indicating its location medial to the naris and the location of the four CNs (SO1–4) in the left groove. Asterisk indicates where the canal segment over neuromast SO4 has already enclosed in the right SO canal. Scale bars: **a–c** = 25 μm. (From Webb & Shirey, 2003. Reprinted with permission of John Wiley & Sons, Inc)

Ghysen et al., 2012) and are important for behavior at hatch (reviewed in Blaxter & Fuiman, 1989). They contain just a few hair cells with ciliary bundles (Lopez-Shier et al., 2004) that are embedded in an elongate cupula (e.g., Iwai, 1964; Mukai et al., 1994; Mukai & Kobayashi, 1995). The axis of best physiological sensitivity defined by hair cell orientation is apparent in these neuromasts and appears to be maintained throughout a neuromast's lifespan (Münz, 1989; Webb, 1989c; Vischer, 1989).

"Primary" (1^o) and "secondary" (2^o) neuromasts have been defined in young fishes (e.g., Blaxter, 1987; Coombs et al., 1988, 1992) based on relative timing of differentiation (1^o neuromasts differentiate earlier than 2^o neuromasts, e.g., before hatch vs. after hatch) or whether a neuromast is a presumptive canal neuromast that will become enclosed in a lateral line canal, or if it will remain superficial. Those described as 1^o tend to be the presumptive CNs, and those described as 2^o tend to remain superficial. In young larvae, all SNs tend to be similar in size and shape, whether they are presumptive CNs (destined to become CNs), replacement neuromasts (SNs that are homologues of CNs), or SNs that will remain on the skin (Webb & Shirey, 2003). Interestingly, recent studies of neuromast patterning on the trunk of zebrafish have revealed that the timing and location of a neuromast's differentiation, its hair cell orientation (polarity), and its fate (e.g., CNs, SNs that are replacement neuromasts, or other SNs) correlate with its origin in a particular migrating primordium (Lopez-Shier et al., 2004; Ghysen et al., 2012).

Presumptive CNs experience an increase in size and change in shape with an increase in hair cell number concurrent with the start of canal morphogenesis (Fig. 5; Webb, 1999; Fuiman et al., 2004). Once the full complement of presumptive CNs is established, their number appears to stabilize as canal morphogenesis proceeds. An understanding of the relationship between the dynamics of hair cell population (e.g., hair cell differentiation and turnover; Rouse & Pickles, 1991a; Williams & Holder, 2000; Ma et al., 2008) and the ontogeny of neuromast size and shape (which deserve more study) is likely to provide a robust explanation for the unappreciated diversity of neuromast morphologies found among adult fishes.

In contrast to CNs, SNs remain small (Janssen et al., 1987; Diaz et al., 2003; Webb & Shirey, 2003; Section 5.2.1), but their number tends to increase relative to the number of presumptive CNs (Fuiman et al., 2004; Faucher et al., 2005). SN proliferation has reached an extreme in several well-known taxa, including goldfish (Fig. 3c, d; Section 5.2.2) and Mexican blind cavefish (*Astyanax mexicanus*; Section 5.2.3). Among the gobies, known for their reduced cranial canals and abundant SNs, *Glossogobius olivaceus* is particularly notable, with more than 4800 SNs on the head, trunk, and tail (Asaoka et al., 2012; Nakae et al., 2012a; Fig. 3e).

The developmental origins of the neuromasts that arise as a result of proliferation are diverse: They may differentiate directly from placode-derived primordia, from interneuromast cells (see Section 3.1), or via budding where a "founder" neuromast may give rise to additional ("accessory") neuromasts. Such neuromasts may form linear series (stitches) on the opercular bone (Wada et al., 2010), on the scales of the trunk (Ghysen & Dambly-Chaudière, 2007; Beckmann et al., 2010), or on the membranes between fin rays on the caudal fin (Wada et al., 2008). Integrated

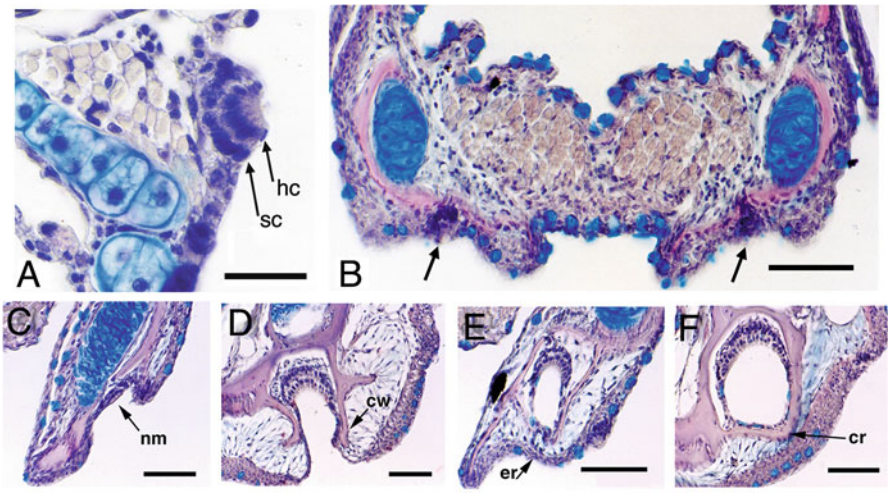

Fig. 6 Morphogenesis of lateral line canals (stages II–V, see Webb & Shirey, 2003) on the head of zebrafish (*Danio rerio*). (**a**) SN (in SO series; see Fig. 5) on day of hatch, showing hair cells (hc) and support cells (sc). (**b**) Mandible showing Meckel's cartilage (blue) and presumptive CNs (arrows, stage I). (**a**, **b** from Webb, 2011. Reprinted with permission of Elsevier, Inc.) (**c**) Presumptive CN (nm) at bottom of epithelial depression (stage IIa, 11 mm SL). (**d**) Presumptive CN in canal groove (stage IIb, 20 mm SL) with ossified canal walls (pink, cw). (**e**) CN in canal enclosed by ossified canal walls (pink) and epithelial roof (er, stage III, 12 mm SL). (**f**) CN enclosed in canal with ossified canal roof (pink, cr, 22 mm SL). (**c–f** from Webb & Shirey, 2003. Reprinted with permission of John Wiley & Sons Inc.). Scale bars: **a** = 10 μm, **b–f** = 50 μm

comparative studies of development and innervation will be necessary to distinguish presumptive CNs from "replacement neuromasts" and other SNs in larvae and to determine the developmental relationship (if any) between canal neuromasts and the accessory SNs that accompany them.

3.3 Morphogenesis of the Lateral Line Canals in Bony Fishes

The cranial lateral line canals generally begin to form near the end of the larval period (Fuiman et al., 2004), and thus days or even weeks after fertilization (e.g., ~4 weeks post-fertilization in zebrafish; Webb & Shirey, 2003; Fig. 5). The morphogenesis of canal segments around individual neuromasts (Jollie, 1984a,c) can be described as occurring in four sequential stages, starting with the location of a neuromast on the epithelium, followed by formation of a depression/groove in which the neuromast sits and ossification of canal walls on either side of the neuromast, enclosure of the neuromast in a soft tissue canal segment , and finally the ossification of the roof of the canal segment (Tarby & Webb, 2003; Fig. 6). As they form, adjacent canal

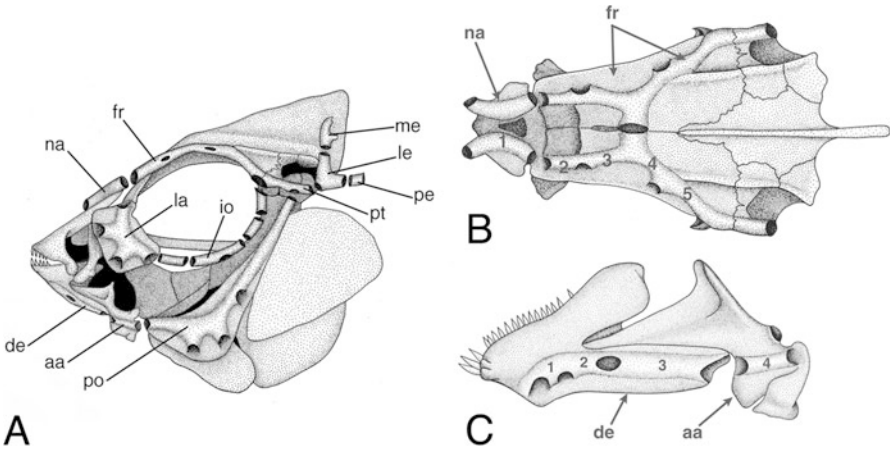

Fig. 7 Skull of the convict cichlid (*Amatitlania nigrofasciata* = *Archocentrus nigrofasciatus*), illustrating the pored lateral line canals contained in the dermatocranial bones. (**a**) Lateral view showing the supraorbital canal in the nasal (na) and frontal (fr) bones, infraorbital canals in the lacrimal (la) and infraorbital series (e.g., io), preopercular canal in the preoperculum (po), mandibular canal in the dentary (de) and angulo-articular (aa), otic canal in the pterotic (pt), supratemporal commissure in the lateral and medial extrascapular bones (le, me), and post-otic canal in the posttemporal bone (pe). (**a** from Webb, 2000. Reprinted with permission of Academic Press/Elsevier, Inc.). (**b**) Dorsal view showing the supraorbital canal in the nasal and frontal bones. (**c**) Ventrolateral view showing the mandibular canal in the dentary and angulo-articular bones. Numbers in **b** and **c** indicate the location of neuromasts within the supraorbital and mandibular canals. (**b**, **c** from Tarby & Webb, 2003. Reprinted with permission of Wiley & Sons, Inc)

segments then grow toward one another and fuse, leaving a common pore between them. This explains the alternating positions of CNs and canal pores in the lateral line canals of bony fishes (Webb & Northcutt, 1997; Figs. 5 and 7). Interestingly, canal segments in adjacent bones do not fuse, preserving the mobility of joints and the integrity of other articulations and bone sutures. Instead, the soft tissue lining the canals forms tubular extensions at the junction between adjacent bones, preserving the continuity of the canal lumen. The process of canal morphogenesis is coincident with the integration of the canals into a conserved subset of dermatocranial bones (Fig. 6; Webb & Shirey, 2003). Canal diameter starts to increase even before initial canal ossification of canal segments is completed and continues to increase as a fish grows (Tarby & Webb, 2003; Moore & Webb, 2008). This process is the result of bone remodeling, as indicated by the activity of osteoclasts on the inner wall of the canals (Moore & Webb, 2008). Increases in neuromast size and canal diameter, improvement of swimming capabilities (including increases in swimming velocity) and associated increases in Reynolds number, all result in changes in lateral line function through the life history of a fish.

Formation of the trunk canals occurs in concert with the development of the scales, subsequent to the migration of the posterior lateral line primordia. When presumptive CNs are initially patterned on the trunk, one neuromast is typically

positioned in the epithelium over each myomere (trunk muscle segment; Fig. 4). Then toward the end of the larval stage, scales begin to develop at the caudal peduncle, their development continues in a caudal to rostral wave (reviewed in Sire & Akimenko, 2004), and one lateral line scale forms under each presumptive CN. A tubular lateral line canal segment then forms in that scale and encloses the presumptive CN in a process resembling cranial canal morphogenesis (Wonsettler & Webb, 1997). Additional neuromasts (accessory SNs as well as SNs that will remain on the skin overlying the scales) generally appear after the presumptive CNs appear or as canal formation starts.

4 Diversity of the Lateral Line System in Bony Fishes

The morphological diversity of the lateral line system in bony fishes is defined by variation in the morphology and extent of development of the cranial lateral line canals; the number, placement, and extent of development of the trunk canals; and the distribution of superficial neuromasts on the skin of the head, trunk, and tail. Coombs et al. (1988) and Webb (1989a) presented comprehensive reviews of the structural diversity of the lateral line system, and Kasumyan (2003) contributed a valuable review that includes the Russian literature, which is often overlooked. Table 1 provides key references that describe lateral line morphology and development for each of the orders or suborders of actinopterygian (ray-finned) fishes; comparable resources for sarcopterygians fishes are found in Section 6.1. Sections 4.1 and 4.2 integrate more recent literature and reveal how an understanding of patterns of lateral line development can shed light on evolutionary diversification of the lateral line system.

4.1 Cranial Lateral Line Canals

The morphology of the cranial lateral line canals in bony fishes is characterized by both conserved patterns and a limited number of variations (Webb, 1989b). Canals are typically found over the eye (supraorbital canal), under the eye (infraorbital canal), and on the cheek and continuing onto the lower jaw (preopercular and mandibular). These canals come together just caudal to the eye as the otic canal, and then the post-otic canal, which continues onto the trunk as the trunk canal contained in the lateral line scales. The right and left cranial canals may come together as a common pore of the paired supraorbital canals on the top of the head (e.g., Fig. 7b), or more caudally as a supratemporal commissure. This configuration is conserved among bony fishes, and the canals are found in a conserved subset of dermatocranial bones (Fig. 7).

Among the non-teleost actinopterygian (ray-finned) fishes, the bichirs (e.g., *Polypterus* spp.), gars (e.g., *Lepisosteus* spp.), and bowfin (*Amia calva*) have a

Table 1 Key sources on the morphology and development of the lateral line system in ray-fin fishes

Taxon	References
Actinopterygii	
Polypteriformes	Jollie, 1984b; Piotrowski & Northcutt, 1996
Acipenseriformes	Pehrson, 1944b; Disler, 1971; Grande & Bemis, 1991; Gibbs & Northcutt, 2004; Hilton et al., 2011; Modrell et al., 2011b; Song & Song, 2012
Lepisosteiformes	Jollie, 1984a; Song & Northcutt, 1991; Grande, 2010
Amiiformes	Allis, 1899; Beckwith, 1907; Grande & Bemis, 1998
Teleostei	
Osteoglossomorpha	Omarkhan, 1948; Nelson, 1969; Kershaw, 1970
Elopomorpha	Allis, 1903; Asano, 1962; Hama, 1978; Nielsen & Bertelsen, 1985; Zacchei & Tavolaro, 1988; Okamura et al., 2002
Clupeomorpha	Nelson, 1983, 1984; Stephens, 1985, 2010; Di Dario, 2004; Di Dario & de Pinna, 2006
Ostariophysi	Lekander, 1949
Gonorynchiformes	—
Cypriniformes[a]	Reno, 1966, 1969, 1971; Kapoor, 1970; Disler, 1971; Hoyt, 1972; Hensel, 1976; Metcalfe, 1989; Puzdrowski, 1989; Webb & Shirey, 2003; Fujita & Hosoya, 2005; Schmitz et al., 2008; Dezfuli et al., 2009; Takeuchi et al., 2011
Characiformes	Schemmel, 1973; Tekye, 1990; Jeffery 2001, 2008; Montgomery et al., 2001; Franz-Odendaal & Hall, 2006; Yoshizawa et al., 2010
Siluriformes	Arratia & Huaquin, 1995; Adriaens et al., 1997; Northcutt et al., 2000; Aquino & Schaefer, 2002; Schafer & Aquino, 2002; Northcutt, 2003; Roth, 2010
Gymnotiformes	Lundberg & Mago-Leccia, 1986; Vischer, 1989
Protacanthopterygii[b]	
Salmoniformes	Moy-Thomas, 1941; Disler, 1971; Jollie, 1984c
Esociformes	Pehrson, 1944a; Nelson, 1972; Jollie, 1975
Myctophiformes	Lawry, 1972a,b
Paracanthopterygii	
Percopsiformes	Moore & Burris, 1956
Gadiformes	Garman, 1899; Marshall, 1965; Jakubowski, 1967a; Bialowiec & Jakubowski, 1971; Fange et al., 1972; Halama, 1977; Otsuka & Nagai, 1997
Amblyopsiformes	Poulson, 1963
Ophidiiformes	Garman, 1899; Gibbs, 1999
Batrachoidiformes	Clapp, 1889; Greene, 1899
Lophiiformes	Garman, 1899; Caruso, 1989; Marshall, 1996; Pietsch, 2009; Nakae & Sasaki, 2010
Acanthopterygii[c]	
Atherinomorpha	
Atheriniformes	Cahn et al., 1968
Beloniformes	Parin & Astakhov, 1982; Yabumoto & Uyeno, 1984; Montgomery & Saunders, 1985; Ishikawa, 1994; Yasuoka et al., 2004; Parenti, 2008; Wada et al., 2010

(continued)

Table 1 (continued)

Taxon	References
Cyprinodontiformes	Rosen & Mendelson, 1960; van Bergeijk & Alexander, 1962; Cernuda-Dernuda & Garcia-Fernandez, 1992; Guarnieri et al., 1993
Percomorpha[d]	
Stephanoberyciformes and Beryciformes	Garman, 1899; Jakubowski, 1974; De Sylva & Eschmeyer, 1977; Paxton, 1989; Moore, 1993; Marshall, 1996
Zeiformes	Nakae & Sasaki, 2010
Gasterosteiformes	Honkanen, 1993; Wark & Peichel, 2010
Synbranchiformes	Britz & Kottelat, 2003
"Scorpaeniformes"	McAllister, 1968; Rass, 1970; Sideleva, 1981; Yabe, 1985; Janssen et al., 1987; Jones & Janssen, 1992; Lannoo, 2009
Perciformes	
Percoidei	Disler, 1950, 1971; Branson & Moore, 1962; Jakubowski, 1963, 1966, 1967b; Disler & Smirnov, 1977; Siming & Hongxi, 1986; Rouse & Pickles, 1991b; Janssen, 1997; Poling & Fuiman, 1997; Diaz et al., 2003; Faucher et al., 2003, 2005; Nakae and Sasaki, 2005
Elassomatoidei	Branson & Moore, 1962
"Labroidei"	Branson, 1961; Peters, 1973; Munz, 1979, 1989; Webb, 1988, 1989c, 1990a,b; Tarby & Webb, 2003
Zoarcoidei	Laverack & Bevan, 1991; Nazarkin, 2011
Notothenoidei	Coombs & Montgomery, 1994; Montgomery et al., 1994; Balushkin, 1996; Prokofiev & Kukuev, 2009
Trachinoidei	Carton & Montgomery, 2004; Nakae et al., 2006
Blennioidei	Makushok, 1961; Yatsu, 1986; Wellenreuther et al., 2010; Nakae et al., 2012
Gobioidei	Miller & Wongrat, 1979, 1991; Marshall, 1986; Rouse & Pickles, 1991b; Gill et al., 1992; Ahnelt & Scattolin, 2003; Bassett et al., 2006; Asaoka et al., 2011, 2012.
Scombroidei	Kawamura et al., 2003; Ghysen et al., 2010, 2012
Pleuronectiformes	Sakamoto, 1984; Fukuda et al., 2009; Voronina, 2009; Applebaum & Schemmel, 1983
Tetraodontiformes	Nakae & Sasaki, 2005, 2006, 2010

Taxonomy follows Nelson (2006). For additional older references see Coombs et al. (1988) and Webb (1989b).
[a]See Section 3.1 for a brief review of early development of the lateral line system in zebrafish.
[b]Protacanthopterygian orders for which data are not available: Argentiniformes, Osmeriformes, Stomiiformes, Ateleopodiformes, Lampriformes, Polymixiiformes.
[c]Data not available for Mugiliformes.
[d]Percomorph suborders for which limited or no data are available: Pholidichthyoidei, Icosteoidei, Kurtoidei, Scombrolabracoidei, Channoidei, Caproidei, Gobiesocoidei, Callionymoidei, Acanthuroidei, Stromateoidei, Anabantoidei (but see Gosline, 1970; Nakae and Sasaki, 2010).

full complement of ossified head and trunk canals (Allis, 1889; Song & Northcutt, 1991; Jollie, 1984b). The sturgeons (e.g., *Acipenser* spp.) and paddlefishes (e.g., Mississippi paddlefish [*Polyodon spathula*]), have somewhat reduced dermatocranial bones and tubular canal ossicles travel through soft tissues of the

head and extend onto the rostrum (Grande & Bemis, 1991; Gibbs & Northcutt, 2004; Hilton et al., 2011). A trunk canal is absent in the paddlefishes, but a canal travels within the lateral series of bony scutes on the trunk of sturgeons (Hilton et al., 2011). Among the sarcopterygian (lobe-finned) fishes, some have well-developed dermatocranial bones and lateral line canals and others others demonstrate a reduction in both the dermatocranial bones and cranial lateral line canals (see Section 6.1).

Among teleost fishes, the cranial lateral line canals are found in the same dermal bones regardless of variation in the shape of the head, or size and shape of those bones (see Gregory, 1933; Fig. 8). One canal neuromast is found between adjacent canal pores (Figs. 3 and 7), a pattern that is the result of the process of canal morphogenesis (Section 3.3). It also allows a pressure differential at adjacent pores (caused by an external water flow) to cause the deflection of the cupula of the canal neuromast positioned between pores. These conserved morphological patterns suggest that there is a basic developmental relationship among neuromasts, canals, and dermatocranial bones with which they are associated (Jollie, 1984c; De Beer 1985; Adriaens et al., 1997). In addition, the diversity of canal morphologies found among taxa can illustrate how variation in canal morphology among species may arise as the result of heterochrony (changes in developmental timing; Webb, 1989a).

4.1.1 Diversity of Cranial Lateral Line Canals

Five types of cranial lateral line canals are found among bony fishes: three variations on narrow canals (narrow-simple, narrow-branched, narrow with widened tubules), reduced canals, and widened canals (categorization modified from Coombs et al., 1988; Webb, 1989b; Fig. 9).

A simple narrow canal pattern is the most common pattern found among bony fishes. Narrow canals tend to be well ossified, uniform in diameter, and they are pierced by small bony pores (between neuromast positions) from which a soft tissue tubule extends through the skin to end in a terminal pore open to the environment (Figs. 8d and 9a). Narrow-branched canals are similar to simple narrow canals, but each bony canal pore is extended into a highly branched tubule located in the soft tissues overlying the bones that ends in a large number of terminal pores (e.g., herrings and relatives; Webb, 1989b; Florida gar [*Lepisosteus platyrhincus*], Song & Northcutt, 1991; blue cod [*Parapercis colias*], Carton & Montgomery, 2004; Fig. 9d). The occurrence of this pattern is likely underestimated because the soft tissue overlying the bones into which the branched tubules extend is not present in dry skeletons or is rendered transparent in the cleared and stained skeletal preparations that are so often used to describe skull bone morphology (Potthoff, 1984). Another variation on narrow canals, narrow with widened tubules, is defined by narrow and well-ossified canals with canal pores that extend into pouch-like tubules ("sinuses," Nelson, 1969) in the epithelium overlying the canals, and

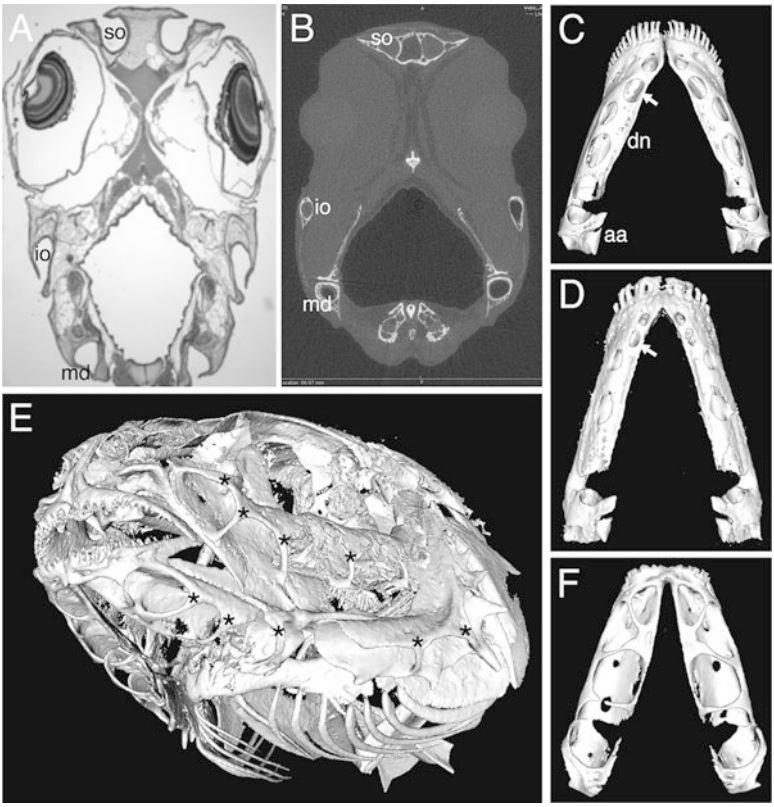

Fig. 8 Visualization of the lateral line canals in two African cichlids (*Aulonocara baenschi*, widened lateral line canals, and *Tramitichromis* sp., narrow canals) and in the Eurasian ruffe (*Gymnocephalus cernuus*, widened canals) using histology and 2-D and 3-D microCT (μCT) imaging. (**a**) Transverse histological section (8 μm thickness) from a juvenile *Aulonocara baenschi* showing widened supraorbital (so), infraorbital (io), and mandibular (md) canals, demonstrating pores to outside, at the level of the eyes (e). (**b**) μCT slice (16 μm thickness) of an adult *A. baenschi* showing the ossification (white) of the supraorbital, infraorbital, and mandibular canals (as in **a**). (**c**) Ventral view of the mandible (dentary [dn] and angulo-articular [aa] bones), containing the mandibular canal in *A. baenschi* (same individual as in **b**), showing the large canal pores (arrows) characteristic of widened canals. (**d**) Mandible of *Tramitichromis* sp., with narrow canals, demonstrating smaller pores (arrows). (**e**) Skull of *G. cernuus* (lateroventral view) with very large pores bounded by thin bony bridges (*) that characterize the widened infraorbital, mandibular, and preopercular canals. (**f**) Mandible of *G. cernuus* with very large pores defined by the thin bony bridges that compose the canal roof under which the CNs sit. The large nerve foramina, through which the lateral line nerves pass to innervate the neuromasts, are clearly visible in the floor of the canal. Images generated using OsiriX (v.3.6.1, 64-bit, http://www.osirix-viewer.com/)

terminate in one or more pores in the skin. This pattern appears to be quite limited in its distribution and is found in some osteoglossomorphs (e.g., African arowana [*Heterotis niloticus*] and arapaima, [*Arapaima gigas*]; Nelson, 1969) and elopomorphs (e.g., Conger eel [*Conger* sp.]; Allis, 1903) and some notothenioids Montgomery, et al., 1994).

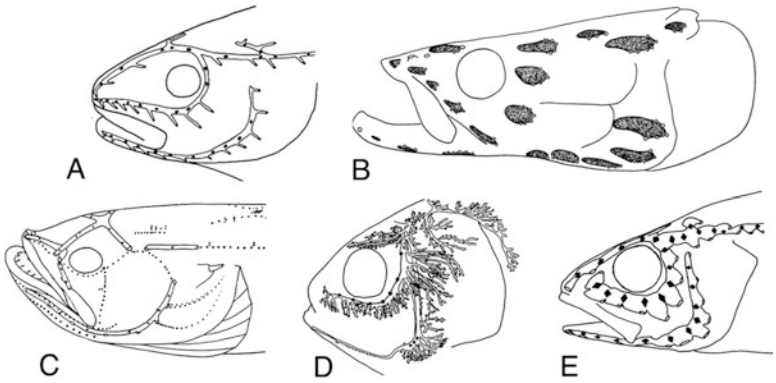

Fig. 9 Five patterns of cranial canal systems found among teleost fishes. (**a**) Narrow-simple canal system (saithe, *Pollachius virens*). (Modified from Marshall, 1965, with permission from Elsevier, Inc.). (**b**) Narrow canals with widened tubules (*Arapaima*) (From Nelson, 1969. Courtesy of The American Museum of Natural History.) (**c**) Reduced canal system with lines of superficial neuromasts (dots) in the plainfin midshipman (*Porichthys notatus*). (From Greene, 1899.) (**d**) Narrow with branched canal system (Atlantic menhaden, *Brevoortia tyrannus*). (Redrawn from Hoss & Blaxter, 1982. Reprinted with permission by Wiley & Sons, Inc.). (**e**) Widened canal system in common pecarina (*Percarina demidoffi*). (From Jakubowski, 1967, reprinted with permission of the author)

Reduced canals are defined by the loss of a portion of one or more (typically narrow) canals, as the result of the truncation or slowing of canal development leaving SNs ("replacement neuromasts," canal neuromast homologues) on the skin (Webb, 1989a,b; Fig. 9c). The degree of canal reduction is variable among taxa and represents a shift from a predominance of CNs to a greater number of SNs (and is often accompanied by SN proliferation; Section 2.1.1). Although many fishes have lost small portions of individual canals (often the ends of canals; Section 5.4), a more extensive loss of canals is seen in, for instance, pigmy sunfishes (*Elassoma*; Branson & Moore, 1962), killifishes (e.g., *Fundulus* spp.), medaka (*Oryzias latipes*; Parenti, 2008), and gobies (suborder Gobioidei, e.g., Asaoka et al., 2011a,b). Head canals are completely absent in, for instance, three-spine stickleback (*Gasterosteus aculeatus*, in contrast to other stickleback species; Honkanen, 1993; Wark & Peichel, 2010), and in all tetraodontiforms (e.g., pufferfishes, triggerfishes, sunfishes; Nakae & Sasaki, 2005, 2006, 2010).

Widened lateral line canals are defined by large bony pores and canal diameters that are much larger than those of narrow canals. They may cover much of the head and are quite noticeable in live and preserved specimens (Garman, 1899; Jakubowski, 1963; Marshall, 1996; Figs. 8 and 9). They may be weakly ossified with only thin bony bridges (the canal roof) sitting over each of the CNs, making the bones appear quite delicate (Fig. 8e, f; Kershaw, 1970). The large pores bounded by the bony bridges are covered by a tympanum-like epithelium (van Netten & van Maarseveen, 1994; explaining the source of the term "membranous canals" used by some authors, e.g., Janssen, 2004). The epithelium is typically

pierced by one small pore between adjacent bony bridges. The CNs in widened canals are quite large, especially when compared to those in comparably sized fishes with narrow canals. In these CNs, hair cell orientation is parallel to the canal, but these neuromasts also have a prominent morphological axis perpendicular to the length of the canal, resulting in a square or diamond shape that is reflected in the shape of the base of the cupula.

Among the four cranial canal patterns, widened lateral line canals are the most limited in distribution, having evolved convergently in only about 15 families of teleost fishes (reviewed in Coombs et al., 1988; Webb, 1989b; Figs. 8 and 9). Notably, widened canals are found in some coastal marine drums (Chao, 1978), fishes in several deepwater marine families (Garman, 1899; Paxton, 1989; Marshall, 1996; Sasaki et al., 2006), and on the blind side of the head of some flounders (McDonnell, 1871; Sakamoto, 1984). Widened canals are also found convergently in freshwater taxa, for instance, in African butterflyfish (*Pantodon buchholzi*; Kershaw, 1970), a cave catfish (*Rhamdia guasarensis*; DoNascimiento et al., 2004), pirate perch (*Aphredoderus sayanus*, accompanied by an unusual proliferation of SNs; Moore & Burris, 1956), a sunfish (*Lepomis humilis*; Branson & Moore, 1962), Eurasian ruffe (*Gymnocephalus cernuus*, Section 5.6.1), and some cichlids (Section 5.6.2). Widened canals may characterize only the dorsal-most or ventral-most canals in an individual (Reno, 1971; Sakamoto, 1984), which is likely the result of adaptations for lateral line–mediated feeding on prey at the surface or in the benthos, respectively.

The convergent evolution of widened canals in such a wide range of taxa from a spectrum of habitat types (including the deep sea), the higher sensitivity of widened canals (especially to lower frequencies), and the demonstrated ability of fishes with widened canals to feed in lowlight environments all suggest that widened canals are an adaptation for prey detection, especially in environments with low light or low hydrodynamic noise and/or in behavioral contexts where fishes can afford to be more sensitive to biologically relevant hydrodynamic stimuli (discussed in Webb et al., 2008; Schwalbe et al., 2012).

4.2 Diversity of the Lateral Line System on the Trunk

Unlike the canals on the head, whose number and placement are conserved, the number andplacement, as well as the degree of development of the trunk canals, define variation in the trunk canals among bony fishes. The presence of three lines of trunk neuromasts (the dorsal, main and ventral lines) is considered to be a primitive characteristic of gnathostomes (jawed fishes), but only the dorsal and main lines are found in living jawed fishes (the cartilaginous and bony fishes; Northcutt, 1989). In bony fishes, the main line of neuromasts is the series generally enclosed in a trunk canal, and the other lines of neuromasts (if present) remain superficial.

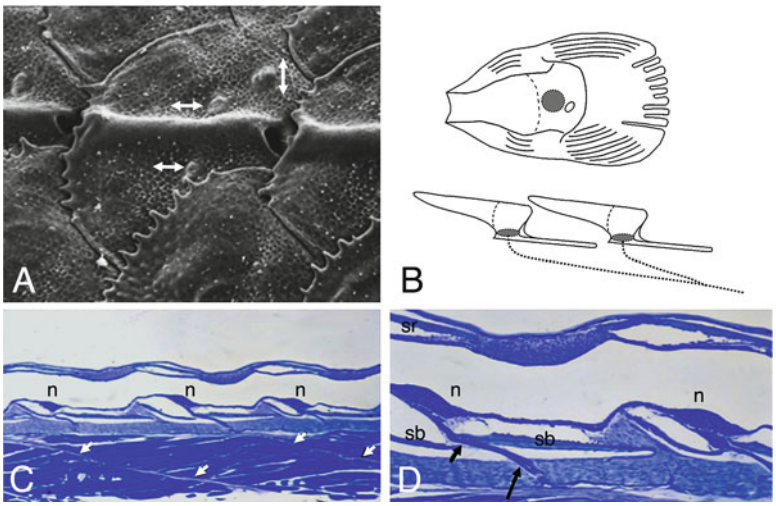

Fig. 10 Lateral line scales and trunk canal (rostral to right). (**a**) Lateral line scales in the convict cichlid (*Amatitlania nigrofasciata* = *Archocentrus nigrofasciatus*), illustrating the tubular canal segments in overlapping scales and the pores between them. Double-headed arrows indicate hair cell orientation of SNs that accompany the lateral line canal segment in each scale. The canal neuromast within the canal segment has a rostrocaudal orientation, parallel to the SNs just dorsal and ventral to the canal. (**b**) Lateral line scales in the greenling (*Hexagrammos decagrammos*) derived from cleared and stained material. A single scale in dorsal view (top) indicates the position of the canal neuromast within it (gray circle), the nerve foramen through which the branch of the lateral line nerve passes (open circle), and the configuration of two adjacent scales (bottom), each composed of a short tubular section containing a neuromast innervated by a branch of the posterior lateral line nerve, and cantilevered canal roof and scale base. (Modified from Wonsettler & Webb, 1997. Reprinted with permission of John Wiley & Sons, Inc.) (**c**) Horizontal section through the length of the tubular trunk canal in a flatfish (*Hippoglossoides* sp., out of the plane of the pores to the outside). Three neuromasts (n) are positioned in register with the trunk canal segments separated by myosepta (arrows). (**d**) Close-up of C showing the neuromast sitting over the scale base (sb) and under the canal roof (scale roof, sr). The nerve branch innervating the neuromast is seen traversing the foramen in the scale base (sb) and then the dense connective tissue beneath the scales (arrows)

4.2.1 Lateral Line Scales

The single trunk canal typical of most bony fishes is contained within a horizontal (rostrocaudal) series of overlapping lateral line scales (Fig. 10). Each lateral line scale typically incorporates a cylindrical, ossified, canal segment (Webb, 1989b,c; Wonsettler & Webb, 1997) that terminates in anterior and posterior pores (suprascalar and infrascalar pores, respectively; Coombs et al., 1988), and one CN is generally found in the canal segment of each lateral line scale (Webb, 1989c; Song & Northcutt 1991; Faucher et al., 2003). In addition to the anterior and posterior pores of the canal segment, one or more canal tubules may extend from the middle of the canal segment, increasing the number of pores that

provide access to the external environment (e.g., Webb, 1990a). At a gross level, the lateral line scales and the lateral line canal contained within them appear to be two-dimensional in nature, but the overlapping lateral line scales, hollow lateral line canals, and the innervation of the CNs have a complex geometry that is revealed only at a microscopic level (Fig. 10).

In fully scaled species, the trunk canal may be partially or completely lost, but canal neuromast homologues are retained as replacement SNs in the epithelium overlying the lateral line scales ("pitted lateral line scales," Webb, 1988, 1990b). In other species, all scales may be lost with the exception of the lateral line scales. In some taxa that otherwise lack scales, the lateral line scales are reduced to only ossified plates with soft tissue canal segments (Asano, 1962; Paxton, 1989). These variations suggest selection for the presence of either SNs or CNs, but behavioral and/or ecological explanations are elusive. Lateral line scale number varies among taxa, so that this metric is often used by taxonomists to distinguish among closely related species. Descriptions of the morphology of lateral line scales are scattered throughout the ichthyology literature, but only a few attempts have been made to understand patterns of lateral line scale evolution (Webb, 1990a; Voronina, 2009; Voronina & Hughes, 2011).

Functionally, the size of the lateral line scales, most often inversely correlated with scale number, determines the spacing of the anterior and posterior pores of each canal segment along the canal and this has important implications for trunk canal function (discussed in Coombs & van Netten, 2006). Further, the presence of one neuromast within each canal segment of the trunk canal indicates that the spatial patterning of the lateral line scales must somehow be related to the earlier spatial patterning of the presumptive CNs (see Section 3.1), but the relationship between these two developmental processes has not been explored. Mutations that cause changes in patterning of trunk neuromasts in zebrafish (Section 3.1) and medaka (Yasuoka et al., 2004) can provide a novel context for understanding the genetic basis for differences in neuromast number, and thus by extension, variation in lateral line scale number and its functional implications.

4.2.2 Diversity of Trunk Canal Patterns

Eight trunk canal patterns are found among teleost fishes and are defined by the placement and extent of a single canal, or by the presence of multiple canals (Webb, 1989b, 1990a,b; Fig. 11).

One trunk canal typically extends down the length of the body to the caudal peduncle. In more basal teleost groups (e.g., Osteoglossomorpha, Elopomorpha, Salmoniformes) the canal follows a straight course, extending along the horizontal septum (Fig. 11a). In many members of the Cypriniformes, the canal tends to dip downward, especially in deeper bodied species, and then returns to the level of the horizontal septum as it approaches the caudal peduncle (Coombs et al., 1988). In more advanced teleosts (e.g., Acanthopterygii), the trunk canal arches above the pectoral fin (which is located higher on the flank than in basal teleosts) before

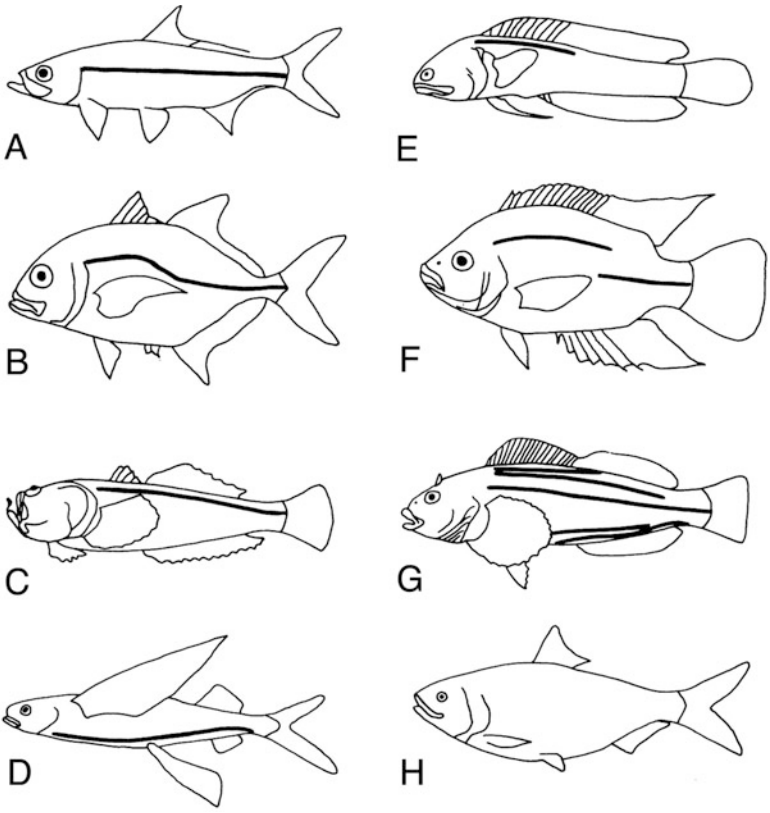

Fig. 11 Eight trunk canal patterns found among teleost fishes. (**a**) Complete—straight. (**b**) Complete—arched. (**c**) Dorsally placed. (**d**) Ventrally placed. (**e**) Incomplete. (**f**) Disjunct. (**g**) Multiple, (**h**) Absent. (Modified from Webb, 1989b. Reprinted with permission of S. Karger AG, Basel)

returning to the horizontal septum and continuing onto the caudal peduncle (Fig. 11b). The placement of the base of the pectoral fin higher on the trunk may restrict the placement of the canal to a position above the fin base. Alternatively, the placement of the canal may be adaptive, facilitating the detection of water flows that are diverted over the pectoral fins during swimming (discussed in Webb, 1989b), but these hypotheses have not been tested.

In a small number of benthic fishes, one trunk canal is placed high on the body (e.g., stargazers, family Uranoscopidae; Fig. 11c), and in some fishes that live just under the water surface, one canal is located low on the body (e.g., African butterflyfish, *Pantodon buchholzi*; flying fishes, family Exocoetidae; Webb, 1989b; Fig. 11d). Interestingly, the single canal found in such taxonomically diverse species may not be homologous, but homologies could be established based on innervation patterns (see Nakae & Sasaki, 2010), or on the identification of the migrating primordia from which the neuromasts originate (Section 3.1) and

subsequent patterns of canal morphogenesis (Section 3.3). In other words, the formation of canals around different lines of SNs (e.g., those of the dorsal vs. main neuromast lines; Northcutt, 1989) may explain differences in the vertical position of a single canal among species (see Balushkin, 1996).

In some teleost families, a single trunk canal may be incomplete, extending from the first lateral line scale to a point partially down the trunk (Fig. 11e). This morphology can be explained as the result of the truncation of canal development as it proceeds rostro-caudally (Webb, 1989a,c, 1990b). An incomplete trunk canal is typically followed by replacement neuromasts (SNs) that sit on the lateral line scales and continue down the trunk to the caudal peduncle; these SNs retain the rostrocaudal orientation found in the CNs of ancestral species with complete trunk canals (Webb, 1988, 1989a).

In a small number of percomorph fishes, most notably the cichlids, a single trunk canal is typically divided into an arched anterior portion and a straight posterior portion, defining a disjunct trunk canal (Webb, 1989b; Fig. 11f; Section 5.6.2). The development of the disjunct trunk canal is quite unusual: The trunk neuromasts presumably differentiate in a series extending from the head to the caudal peduncle and scales form beneath them (as in other teleosts). However, the anterior portion of the trunk canal then develops in a rostrocaudal direction (as a complete trunk canal does in other fishes), whereas the posterior portion of the canal then develops in a caudorostral direction (Webb, 1989a,c). The variations on a disjunct canal found among species of cichlids are likely explained as the result of heterochrony (variation in the timing of canal development; Webb, 1990b).

Multiple trunk canals are also found in a small number of teleost families (reviewed in Webb, 1989b; Fig. 11g). The number of canals appears to vary from two to five, and complex interconnections between adjacent canals may be present (Stichaeidae, Makushok, 1961). In greenlings (*Hexagrammos* spp.), which lack such interconnections, neuromasts are found in only one of the five trunk canals (Wonsettler & Webb, 1997). So, although it may be tempting to suggest that multiple canals provide enhanced sensitivity to water flows, the absence of neuromasts within most of the canals counters this functional argument. Further, the mechanism that could explain how canals develop in the absence of neuromasts remains a subject of speculation (discussed in Wonsettler & Webb, 1997). However, the recent discovery that several migrating primordia give rise to the neuromasts in zebrafish (Section 3.1) provides a context for examining the development and evolution of such complex trunk canal patterns in adult fishes (Section 4.2.2).

The absence of a trunk canal (e.g., expressed as “no lateral line” in identification keys and textbooks) represents an extreme in trunk canal reduction (Fig. 11h). For example, a trunk canal is absent in herrings, anchovies, and their relatives (Clupeiformes, Section 5.1) and in mullets (Mugiliformes). Small cichlids in the genus *Biotoecus* have a line of SNs with rostrocaudal orientation (interpreted as homologues of trunk CNs), which is accompanied by pairs of SNs with dorsoventral hair cell orientation (Webb, 1988, 1989c, 1990b). Although the absence of a trunk canal often correlates with the proliferation of SNs, the tetraodontiforms

(which completely lack CNs) have a relatively small number of SNs in a single trunk line (e.g., Nakae & Sasaki, 2010).

Finally, many teleosts have one or more canals or, more typically, one or more lines of SNs that extend along the membranes between the fin rays of the caudal fin (Asaoka et al., 2011, 2012), and their development has been investigated in some detail in zebrafish (Wada et al., 2008).

5 The Lateral Line System of Model Species Used in Experimental Studies

The range of species used in experimental studies of lateral line function is still limited to small, hardy, coastal, or freshwater teleosts. They were chosen because they are particularly suitable for laboratory studies, have either unremarkable or particularly interesting lateral line morphologies, and/or demonstrate what appeared to be lateral line–mediated behaviors that warranted investigation. In this section, the major features of the lateral line system of species used in studies of lateral line (and auditory) function and/or behavior are described and placed into a broader taxonomic and comparative anatomical context.

5.1 Clupeomorpha: Herrings, Alewives, Sardines, and Anchovies

Clupeomorph fishes have served as important models for the study of the role of the lateral line system in both prey detection and schooling (Denton & Gray, 1983, 1993; Blaxter, 1987; Blaxter & Fuiman, 1989). Most members of this group are coastal, planktivorous, schooling fishes that have narrow-branched cranial lateral line canals, but lack a trunk canal (Nelson, 1983; Blaxter, 1987; Stephens, 2010; Fig. 9d). The clupeomorph fishes are of particular interest because they all have a recessus lateralis complex, a unique three-way connection between anterior bullae (air-filled extensions of the swim bladder), the fluid-filled cranial lateral line canals, and the inner ears. This three-way connection enhances sound pressure reception (reviewed in Braun & Grande, 2008) and may be involved in communication during rapid schooling maneuvers of herring that produce transient pressure pulses (Gray and Denton, 1991), and in the ability of some members of the subfamily Alosinae to hear in the ultrasonic range (Wilson, et al., 2009). In addition, detailed descriptions of interspecific variation in the morphology of the recessus lateralis and associated lateral line canals have been used for a reassessment of phylogenetic relationships within the Clupeomorpha (Di Dario, 2004; Di Dario & de Pinna, 2006). The anchovies (family Engraulidae) have a rostral organ that is formed by portions of the supraorbital and ethmoidal canals that are connected by a

commissural canal across the snout. A membrane separates the lumen of the rostral organ from that of the supraorbital and infraorbital canals; the rostral organ contains neuromasts that are larger than those in the rest of the cranial canals, suggesting a distinct but yet unknown function (Nelson, 1984).

5.2 *Otophysi: Zebrafish, Goldfish, and Mexican Blind Cavefish*

The otophysan fishes, which comprise three quarters of the world's freshwater fishes, have a Weberian apparatus (Weber, 1820), a morphological specialization of the anterior vertebrate that forms a unique mechanical linkage between the swim bladder and the inner ear, which enhances auditory capabilities (reviewed in Braun & Grande, 2008). The morphology of the Weberian apparatus varies considerably among species (Bird & Hernandez, 2007). Otophysan fishes generally have narrow cranial lateral line canals and a single trunk canal (if present). The lateral line system has been described in detail in only a small number of Cypriniformes (minnows, e.g., goldfish, zebrafish), Characiformes (e.g., blind cavefish), and Siluriformes (catfishes, see Table 1).

5.2.1 Zebrafish

The zebrafish (zebra danio, *Danio rerio*) has become the preeminent model for the experimental analysis of vertebrate development (Haffter et al., 1996; Dambly-Chaudière et al., 2003; Detrich et al., 2010). The early development of its lateral line system (to 5 days post-fertilization) has been studied intensively as a model for cell migration and spatial patterning (Section 3.1) and for mechanisms of hair cell differentiation and regeneration (see the chapter by Coffin, Brignull, Raible & Rubel). The zebrafish has also become a model for the analysis of neuromast biomechanics (see the chapter by van Netten & McHenry) and hydrodynamics (Van Trump & McHenry, 2008; Suli et al., 2012; see the chapter by McHenry & Liao) in larval fishes as well as for the developmental (see the chapter by Coffin, Brignull, Raible & Rubel) and physiological analysis (Higgs et al., 2003; Zeddies & Fay, 2005) of hearing.

Adult zebrafish have a full complement of narrow lateral line canals on the head and a small number of SNs. The cranial canals are well ossified, with the exception of the supraorbital canal, which has an unossified canal roof, a morphology that may facilitate feeding on prey at the water's surface (Fang, 2003; Webb & Shirey, 2003). The CNs are quite unusual in that instead of having a major morphological axis parallel to the axis of the canal (typical of species with narrow canals), these neuromasts have a major axis perpendicular to the axis of the canal. In addition, the population of hair cells extends to the perimeter of these long, narrow neuromasts

(Fig. 5), a feature that becomes apparent as the cranial canals start forming (several weeks after fertilization; Webb & Shirey, 2003). This unusual CN morphology is also found in the silverjaw minnow (*Notropis buccatus* = *Ericymba buccata*, Webb, unpubl. observ.) and in some European freshwater percids (Jakubowski, 1967b; discussed in Coombs et al., 1992), suggesting an interesting and yet unexplored case of convergent evolution, presumably in response to common behavioral and/or ecological demands among representatives of these important groups of freshwater fishes. The trunk of zebrafish is characterized by a proliferation of SNs in several lines. A very short incomplete canal is found in just the first two or three lateral line scales behind the operculum, which contains neuromasts like those in the cranial canals (Webb & Shirey, 2003; Fig. 5). Several other lines of SNs are positioned along the length of the trunk and their SNs are proliferated as small vertical stitches (Nuñez, et al., 2009). Each of the stitches arises from a single founder neuromast via budding (Metcalfe et al., 1985) and the neuromasts in a stitch all share the same hair cell orientation and innervation (Ghysen et al., 2012). In addition, several lines of SNs sit on the membranes between the fin rays of the caudal fin ("caudal lateral line neuromasts"; Wada et al., 2008).

5.2.2 Goldfish

The goldfish (*Carrasius auratus*) has been used in the study of lateral line physiology (Coombs et al., 1996; Chagnaud et al., 2007, 2008) and the role of the lateral line system in prey detection and swimming behavior (see the chapter by McHenry & Liao). It has also been a key species in fundamental studies of fish hearing (Fay & Edds-Walton, 2008; Coombs et al., 2010; Popper & Fay, 2011). Goldfish have well-developed, narrow cranial lateral line canals and a single trunk canal, as well as proliferated SNs on both the head (in linear series) and trunk. In addition, between three and nine neuromasts are found in a linear series on each scale of the body (Puzdrowski, 1989; Schmitz et al., 2008; Fig. 3c, d), which is similar to the SN distribution in some other cypriniform fishes (Beckmann et al., 2010). Despite being located in narrow canals, the CNs have a diamond shape with a secondary axis perpendicular to the length of the canal (Schmitz et al., 2008), while the orientation of the hair cells remains parallel with the length of the canal. The goldfish is one of the few species for which the hair cell orientation in thousands of CNs and SNs have been mapped and described in detail (Puzdrowski, 1989; Schmitz et al., 2008).

5.2.3 Mexican Blind Cavefish

The Mexican tetra (*Astyanax mexicanus*, family Characidae) includes two morphs, a sighted (surface) form and a blind (cave) form. The blind form ("Mexican blind cavefish") demonstrates modifications in the morphology of all major sensory systems and in associated behaviors, pigmentation, skeleton, and body shape

(Jeffery, 2008). It has been used to examine the role of the lateral line in rheotactic behavior (Baker & Montgomery, 1999), "hydrodynamic imaging" of the environment (Windsor et al., 2008; see also the chapters by McHenry & Liao and Montgomery, Coombs, & Bleckmann), and feeding behavior (Yoshizawa et al., 2010). It has also become an important model for evolutionary developmental biology (Franz-Odendaal & Hall, 2006; Jeffery, 2008), the analysis of the genetic basis for adaptive changes in sensory morphology and associated behaviors (Jeffery, 2005; Yoshizawa et al., 2010), and the role of nonvisual senses in spatial navigation and cognition (e.g., Tekye 1989; Burt de Perera & Braithwaite, 2005).

Both surface and cave morphs are characterized by well-ossified narrow cranial canals containing neuromasts that are larger than their SNs (Schemmel, 1973; Van Trump et al., 2010) and a trunk canal (which dips slightly below the horizontal septum, as in many cyprinids). The cave morph is well known for the proliferation of SNs on the head, which is often attributed to the need to enhance nonvisual sensory systems to facilitate prey detection and other behaviors. The surface form also has proliferated SNs, but to a lesser degree (Schemmel, 1973 Yoshizawa et al., 2010). Like goldfish, both forms also have a short line of SNs on each scale of the body (Tekye, 1990; Yoshizawa et al., 2010; Van Trump et al., 2010). Thus, it appears that the moderate proliferation of SNs in the surface morph likely served as a preadaptation for the evolution of a cave-dwelling habit.

5.3 *Salmoniformes: Trouts, Charrs and Salmon*

The family Salmonidae (trouts, charrs, salmons) is a commercially important group known for its extensive migrations and complex life histories. Rainbow trout (*Oncorhynchus mykiss*) has been used for the analysis of lateral line function in prey detection, swimming, and schooling (reviewed in Webb et al., 2008; see also McHenry & Liao), and for their rheotactic and station-holding abilities in turbulent flow (reviewed in Bleckmann et al., 2012). Rainbow trout and other salmonids typically have a full set of well-ossified narrow canals (Collinge, 1895; Jollie, 1984c), which contain a relatively large number of elongate CNs (parallel with the canal axis; Schmitz et al., 2008), and have a correspondingly large number of rather closely positioned canal pores, when compared to other teleosts. Many of the lines of SNs found on the head of other taxa are apparently absent in salmonids (Jollie, 1984c). The complete trunk canal is contained in numerous small lateral line scales that follow a straight course to the caudal peduncle.

5.4 *Batrachidiformes: Toadfishes and Plainfin Midshipman*

The oyster toadfish (*Opsanus tau*) and Lusitanian toadfish (*Halobatrachus didactylus*) are cryptic, benthic ambush predators that communicate acoustically

and have been used in key studies of lateral line and auditory anatomy and physiology, and vocal behavior (e.g., Vasconcelos & Ladich, 2008; Edds-Walton & Fay, 2009; Vasconcelos et al., 2011). The morphology and development of the lateral line system of *Opsanus tau* (=*Batrachus tau*) was described in detail by Clapp (1889). *Opsanus tau* has somewhat reduced narrow canals in which some canals are only partially formed, and the infraorbital canal has been completely lost; these canals appear to have been replaced by SNs (Fig. 9c). In addition to the cranial CNs, more than 200 SNs occur in simple lines on the head and trunk. A trunk canal is absent. Paired "flaps" (Clapp, 1889) are found on either side of each of the SNs on the head and trunk, which likely affect neuromast function by filtering water flows that can intercept a neuromast.

The plainfin midshipman (*Porichthys notatus*) is an important model for the study of the physiological interaction of the auditory and lateral line systems (Weeg & Bass, 2000, 2002) and the analysis of the physiological and hormonal control of the auditory and vocal motor systems (Bass, 2008; Sisneros, 2009; Zeddies et al., 2010). Its lateral line system was described in conjunction with that of its bioluminescent organs (Greene, 1899). The cranial canals are somewhat reduced, as in the toadfishes, with lines of SNs in the place of the infraorbital canal and the dorsal-most portion of the preopercular canal. In contrast to toadfishes, a mandibular line of SNs is present in addition to a mandibular canal, and other lines of SNs are present on the head. As in the toadfishes, a trunk canal is absent, but this species has five longitudinal lines of slender-diamond shaped neuromasts distributed in register with the five longitudinal lines of serial photophores (Greene, 1899). Each neuromast is flanked by a pair of "dermal papillae" (Greene 1899; a more slender version of the fleshy "flaps" in oyster toadfish; Fig. 2g) with an elongate sensory strip at the center of these neuromasts that is composed of a dense hair cell population (Fig. 2h). Each neuromast is elongated, with papillae at its tips, and hair cell orientation perpendicular to the long axis of the neuromast. Thus, the flow of water over a neuromast is restricted to a path that is parallel to the axis of best physiological sensitivity defined by hair cell orientation (Fig. 2g) and can thus provide an effective stimulus. However, among the five lines, the orientation of the long axis of the neuromasts, and thus their hair cell orientation varies so that each line is composed of series of neuromasts with either dorsoventral, rostrocaudal, or oblique hair cell orientation. This variation in neuromast orientation among the five trunk lines may explain the physiological heterogeneity reported for SNs by Weeg and Bass (2002).

5.5 *"Scorpaeniformes": Mottled Sculpin*

The mottled sculpin (*Cottus bairdi*), a freshwater member of the family Cottidae, has been used for key studies in the analysis of lateral line function, particularly in the context of prey detection (Hoekstra & Janssen, 1985; Coombs & Conley,

1997; Coombs et al., 2001; Kanter & Coombs, 2003). Like many cottids, the mottled sculpin has well-ossified narrow cranial lateral line canals, but the ends of several of the canals appear to be reduced, and SNs (replacement neuromasts) are present instead. A mandibular accessory line is composed of SNs with hair cells oriented perpendicular to the axis of the mandibular canal. Scales are absent, but a trunk canal composed of soft tissue canal segments is present.

5.6 *Percomorpha: Eurasian Ruffe, Cichlids, Butterflyfishes*

The percomorphs, the most speciose and morphologically diverse group of teleost fishes, includes several model species used for functional studies of the lateral line system.

5.6.1 The Eurasian Ruffe

The Eurasian ruffe (*Gymnocephalus cernua* [= *Acerina cernua*]; family Percidae) was the species in which the lateral line system was first identified as a sensory system (Leydig, 1850). More than a century later, the Eurasian ruffe was used in novel studies of the biomechanics and physiology of CNs and their cupulae (Gray & Best, 1989; reviewed in Coombs & van Netten, 2006; see also the chapter by van Netten & McHenry). It has quite prominent widened cranial lateral line canals with large bony pores (Jakubowski, 1963), which are covered by skin (van Netten & van Maarseveen, 1994) that is pierced by very small pores. Each of the very large diamond-shaped CNs (Jakubowski, 1963) sits under a slender bony bridge (Fig. 8e), which represents the remnant of the canal roof. This morphology has facilitated access to the neuromasts and their cupulae in physiological studies that have provided key insights into neuromast and cupular biomechanics (reviewed in Coombs & van Netten, 2006). In addition, Eurasian ruffe is an invasive species in the North American Great Lakes and is thus of great ecological importance because of its impacts on native fishes. The possession of more sensitive widened lateral line canals, which can likely account for its ability to feed successfully under low light conditions, may account for the success of this species in both native and nonnative habitats (discussed in Schwalbe et al., 2012).

5.6.2 Cichlids

The Cichlidae, the most speciose non-otophysan family of freshwater fishes (several thousand species in >200 genera), is distributed in lakes and rivers of South and Central America, Africa, and Madagascar. The lateral line system is typically composed of narrow cranial canals and a disjunct trunk canal (e.g., Webb, 1989c; Tarby & Webb, 2003). Accessory SNs form simple lines in the vicinity of the

cranial canals and dorsal and ventral to each segment of the trunk canal. SNs are also found around the naris, on the dorsal surface of the head, on the cheek, and on the operculum (Peters, 1973; Webb, 1989c; Song et al., 1995).

The oscar (*Astronotus ocellatus*), which has a lateral line system typical of most cichlids (narrow cranial canals, disjunct trunk canal), has been used for studies of the development, innervation, and physiology of the auditory system (e.g., Chang et al., 1992; Yan & Popper, 1993; Lu et al., 1996). More recently, this species has been used to study the detection and discrimination by the lateral line system of low-frequency dipole stimuli in still and flowing waters (Mogdans and Nauroth, 2011). In contrast to the oscar (and most cichlids), a few African genera from Lake Tanganyika and Lake Malawi have widened cranial canals. The peacock cichlids of Lake Malawi (*Aulonocara* spp., Meyer et al. 1987), for instance, have widened canals that have been described (somewhat inaccurately) as having "deep pits" (Fryer, 1959), "enlarged cephalic pores" (Konings, 1990), or an "enlarged lateral line system" (Konings, 2007; Fig. 8a, b, c). These fish are also reported to employ an unusual feeding strategy in which they repeatedly swim in short bursts and glide just a few millimeters above the sandy sediments and strike at invertebrate prey in the substrate (Konings, 2007). The correlation between a widened cranial lateral line canal morphology and their particular feeding behavior has been the basis for the assertion that the widened lateral line canals mediate prey detection (Fryer, 1959). Recent experimental work has shown that, in the laboratory, *Aulonocara stuartgranti* uses the same feeding strategy as it does in the field, and detects invertebrate prey using its lateral line system, especially in the dark (Schwalbe et al., 2012).

5.6.3 Butterflyfishes

Butterflyfishes (family Chaetodontidae) are important members of coral reef communities worldwide and have narrow, well-ossified cranial canals and a single trunk canal. In addition, the genus *Chaetodon* is defined by the presence of a "laterophysic connection" (Webb, 1998), a unique relationship between anterior cylindrical horns of the swim bladder and a medial opening in the wall of the lateral line canal in the supracleithral bone (Smith et al., 2003). Like the recessus lateralis of clupeomorph fishes (Section 5.1), the laterophysic connection is thought to impart sound pressure sensitivity to the lateral line system, and the swim bladder horns likely enhance pressure sensitivity of the ear in adult *Chaetodon* (Webb et al., 2010), although a direct test of this hypothesis is still lacking.

The morphology of the laterophysic connection varies among *Chaetodon* subfamilies (Smith et al., 2003) and correlates with the morphology of the swim bladder (Webb et al., 2006), suggesting that the swim bladder contributes to the acoustic function of the laterophysic connection. This is particularly interesting because it is now known that sound production is important in the social behavior of butterflyfishes (Tricas et al., 2006; Boyle & Tricas, 2010, 2011). The ears in

Chaetodon lack those features found in fishes with otophysic connections (discussed in Webb et al., 2010), but nevertheless, late larvae and juveniles of spotfin butterflyfish (*Chaetodon ocellatus*) were found to be more sensitive to sound pressure than damselfishes of the same size, which lack swim bladder horns (Webb et al., 2012). The timing of the development of the swim bladder horns, and thus the presence of a laterophysic connection only in individuals larger than those typically seeking out coral reef habitats, suggests that the behavioral role of the laterophysic connection is limited to post-settlement, reef-based behaviors (Webb et al., 2012).

6 The Lateral Line System of Other Fishes

The lateral line system of the Sarcopterygii (lobe-finned bony fishes), Chondrichthyes (cartilaginous fishes), and "Agnatha" (jawless fishes) is of great evolutionary interest, but has not received the same attention that the lateral line system of bony fishes has received.

6.1 Sarcopterygians: Coelocanths and Lungfishes

The living coelocanth (*Latimeria chalumnae*) and the Australian lungfish (*Neoceratodus forsteri*) have cranial lateral line canals embedded within well-ossified dermatocranial bones (Hensel, 1986; Kemp, 1999; Hensel & Balon, 2001), as do many fossil sarcopterygians and closely related early tetrapods (primitive amphibians; Graham-Smith, 1978; Ahlberg & Clack, 1998). One neuromast is found between adjacent canal pores in their cranial canals, as in actinopterygian fishes (Webb & Northcutt, 1997), and a lateral line canal is present on the trunk. In contrast, the African lungfishes (*Protopterus* spp.) and the South American lungfish (*Lepidosiren paradoxa*) have partially or completely lost their cranial lateral line canals, respectively (Webb & Northcutt, 1997; Jørgensen, 2010). When present, these canals are located in soft tissue within the dermis, and are not associated with any of the dermatocranial bones. Multiple CNs are found between canal pore positions in these soft tissue canals, which is interpreted as being convergent with the condition in elasmobranchs (Webb & Northcutt, 1997). Where a canal is lacking, a dense line of SNs (presumably replacement neuromasts) is present in addition to short lines of other SNs, which have described as "pit lines" (Webb & Northcutt, 1997). These lungfishes lack scales and a trunk canal; the South American lungfish has three lines of small SNs that extend down the trunk (Webb & Northcutt, 1997; Jørgensen, 2010).

6.2 *Chondrichthyans: Sharks, Skates, Rays, Chimaeras*

The lateral line system of chondrichthyan fishes differs fundamentally from that of bony fishes with respect to the distribution, morphology, and development of the lateral line canals and morphology of the CNs.

The lateral line system of elasmobranchs (sharks, skates, rays) is composed of CNs as well as SNs ("pit organs"; Peach & Rouse, 2000; Peach & Marshall 2009). The cranial lateral line canals sit in the dermis, are cylindrical, small in diameter, and are composed of soft tissue. Periodic tubules emerge from the canals and extend to the skin's surface as pores. The canals are not associated with the cranial cartilages that compose the skull, in contrast to the canals of bony fishes that are associated with certain dermal bones of the skull (Section 4.1). The course of the canals varies among species, may be somewhat circuitous, and correlates with head shape and body form (e.g., Chu & Wen, 1979; Jordan et al., 2009). In hammerhead sharks (*Sphryna* spp.), for instance, some canals extend onto the cephalofoil, the large lateral extensions of the head that characterize these fishes (Chu & Wen, 1979). In the dorsoventrally flattened skates and rays, well-developed canals are found on both the dorsal and ventral surfaces of the head, some of which have spread onto the greatly expanded pectoral fins, which are fused to the head (Chu & Wen, 1979; Jordan et al., 2009). The homology of some of these canals is uncertain (Disler, 1961), but can likely be revealed by examining their innervation (Abe et al., 2012) and development. A trunk canal is typically found between modified placoid scales and extends down the mid-flank and onto the upper lobe of the heterocercal caudal fin in sharks. The ecological and behavioral significance of canal distributions (Maruska, 2001; Jordan et al., 2009; Shibuya et al., 2010), and the contribution of the lateral line system to multimodal sensory integration among species with different morphologies (Gardiner et al., 2012), are important areas of inquiry.

The neuromasts of elasmobranchs have been described as being composed of a "continuous" or "nearly continuous" sensory epithelium (Johnson, 1917), which is in distinct contrast to the neuromasts of bony fishes, which are well-defined, focal populations of hair cells separated by epithelial cells that compose the lining of the lateral line canals. A length of sensory epithelium, or what has also been described as "several [densely placed] neuromasts" (Webb & Northcutt, 1997), sits between adjacent canal pores. The hair cells have well-defined ciliary bundles that are oriented 180° to one another, parallel with the canal axis. This raises questions about the shape and extent of the cupulae and how water flows might stimulate and evoke a response from such a continuous population of hair cells.

Some species of rays (e.g., Atlantic stingray [*Dasyatis sabina*]) and sawfishes (family Pristidae, Wueringer et al., 2011) also have nonpored canals, which likely have a function distinct from that of pored canals on their ventral surface (Maruska & Tricas, 2004; Shibuya et al., 2010). It is thought that deformation of the skin overlying these canals in Atlantic stingray stimulates the CNs ("mechanotactile

hypothesis"; Maruska & Tricas, 1998, 2004). Torpedo rays, electric rays, and stingrays also have vesicles of Savi (Chu & Wen, 1979), pouches on the ventral side of the snout, which contain either one discrete neuromast (in stingrays, *Dasyatis spp*.), or one large and two smaller discrete neuromasts (in torpedo rays [*Torpedo* spp.], Maruska, 2001). Like the nonpored canals in the Atlantic stingray, the vesicles of Savi are not open to the external environment and are thought to provide a tactile sense (Maruska, 2001). In addition, SNs occur singly or in clusters and sit between modified placoid scales generally dorsal to the trunk canal in sharks (Peach & Rouse, 2000; Maruska, 2001; Peach & Marshall, 2009).

As in bony fishes, the lateral line system of elasmobranchs is derived from cranial placodes (Section 3), but the pattern of lateral line canal morphogenesis appears to differ quite substantially from that in bony fishes (Johnson, 1917; Holmgren, 1940; Disler, 1961). Further, in bony fishes, differentiation of the presumptive CNs occurs well before the start of canal morphogenesis, but in elasmobranchs, the relative timing of these two processes, and the temporal–spatial pattern of canal morphogenesis (e.g., the direction of the progression of morphogenesis along a canal's length), remain unclear.

In the chimaeras (Holocephali), the other major group of Chondrichthyes, the distribution of lateral line canals is similar to that found in elasmobranchs (Lisney, 2010), but the cranial canals may either be narrow and tubular (family Callorhynchidae) or in the form of open grooves (families Rhinochimaeridae, Chimaeridae). Members of the Rhinochimeridae have long snouts onto which lateral line canals extend, suggesting that they use their lateral line system (probably in addition to the electroreceptors) to detect benthic prey within sediments (Lisney, 2010). As in elasmobranchs, the CNs of chimaeras are elongate and almost continuous along the length of a canal (Ekström von Lubitz, 1981). However, in some members of the family Chimaeridae (e.g., spotted ratfish [*Hydrolagus collei*]) open canal grooves on the lateral and ventral surfaces of the snout contain discrete neuromasts that are located between periodic canal dilations (Fields et al., 1993), which appear to be unique among fishes. As expected, hair cell orientation in CNs is generally parallel with the canal axis, but hair cells with orientations perpendicular to the canal axis have been documented in *Chimaera monstrosa* (Ekström von Lubitz, 1981).

6.3 "Agnathans": Hagfishes and Lampreys

The lateral line system of the living lampreys (order Petromyzontiformes) is composed entirely of SNs (Northcutt, 1989), which are reported to sit in pits flanked by pairs of "hillocks" and are arranged in rows on the head and body (Lane & Whitear, 1982). The hair cells have a kinocilium longer than the stereocilia, providing directional polarity as in jawed fishes (Lane & Whitear, 1982), but the neuromasts are reported to lack cupulae (Braun, 1996; Gelman et al., 2006).

The filter feeding ammocoetes larvae of lampreys already have a functional lateral line system with neuromasts that are structurally similar to those of adults and respond to a vibrating sphere (Gelman et al., 2006).

Among hagfishes (order Myxiniformes), only members of the family Eptatretidae are known to have a lateral line system; it is apparently absent in the family Myxinidae (Braun, 1996). In the Pacific hagfish (*Eptatretus stoutii*) the system consists of a series of short, unpigmented depressions or grooves rostral and caudal to the eye spot (Northcutt, 1989) that vary in number and position among individuals (Fernholm, 1985) and increase in size through life (Braun & Northcutt, 1997). The depressions contain flask-shaped sensory receptor cells that have a single cilium and a corolla of shorter stereovilli (microvilli), and a cupula is not present; they are thus unlike the directionally polarized hair cell bundles in the well-developed neuromasts of jawed fishes. Sensory cells in the grooves are innervated by bundles of cranial nerve fibers that form two nerves that project to the hindbrain. The nature of sensory cell function in these animals is not clear, but they are thought to transduce hydrodynamic disturbances. Little is known about hagfish embryology (Ota et al., 2007), but one study provides evidence that the lateral line system of "agnathans" develops from a cranial placodes (Wicht & Northcutt, 1995).

7 The Lateral Line System of Amphibians

Like the South American lungfish, larval and adult aquatic amphibians have a lateral line system composed exclusively of SNs. These neuromasts are generally proliferated into stitches (lines of similarly oriented neuromasts) on the head and trunk, which demonstrate a considerable degree of interspecific variation (Lannoo, 1985, 1987a,b, 1988; Smith et al., 1988). Experimental work on the aquatic African clawed toad (*Xenopus laevis*) has contributed to our fundamental understanding of the physiology and behavioral role of the lateral line system in amphibians (reviewed in Fritzsch & Neary, 1998; Simmons et al., 2004). The neuromasts and sensory neurons that innervate them are known to develop from lateral line placodes as in fishes (see Section 3.1). Early studies of neuromast regeneration in frogs and salamanders (reviewed in Wright, 1951), and more recent experimental work on axolotl (*Ambystoma mexicanum*; Corwin et al., 1989) provided the first evidence for hair cell regeneration in vertebrates. Those amphibians with direct development (e.g., lack a larval stage; some salamanders, caecilians, and anurans) have suppressed formation of the neuromasts (Schlosser, 1999). The regression of both the neuromasts and their innervation at metamorphosis (Wahnschaffe et al., 1987; Fritzsch, 1989) can shed light on how the system was lost with the evolutionary origin of terrestrial amniotes.

8 Summary

The mechanosensory lateral line system is composed of neuromast receptor organs on the skin or in canals that occur in stereotyped patterns determined by developmental processes that take place in embryos and larvae. Structural diversity in the lateral line system occurs at several levels of organization, including variation in hair cell bundle morphology among hair cells within a neuromast, size and shape of CNs and SNs within and among species, morphology and extent of development of lateral line canals on the head and trunk, and the number and distribution of SNs among species. The lateral line canals create a different hydrodynamic environment for the CNs in contrast to that experienced by SNs, thus defining two sensory submodalities with complementary functional attributes for flow detection. These are now reasonably well understood as the result of elegant experimental work in a small number of species of bony fishes, and of a much smaller number of studies in elasmobranch fishes and in amphibians. Even though the system has been studied at different anatomical, temporal (developmental, ontogenetic), and comparative scales, a robust understanding of the functional implications of different aspects of morphological diversity in the lateral line system has not yet been revealed.

9 Suggestions for Future Research

Several approaches that use the tools of comparative biology are likely to yield significant insights for our understanding of the structural and functional evolution of the lateral line system.

1. The mapping of features of lateral morphology on independently derived cladograms ("character mapping") will reveal evolutionary trends in morphology (e.g., Webb, 1989b; Coombs et al., 1992), which when coupled with data on physiology, behavior, and ecology, should reveal interesting patterns of functional and adaptive evolution.
2. The study of the development of the lateral line system in closely related species with divergent adult morphologies will shed light on the developmental basis for the structural and functional evolution of the system. In addition, the integration of what is known about the development of the lateral line system in model species (e.g., zebrafish) with studies of lateral line development in other taxa will enhance this effort.
3. The morphology of the lateral line system should be studied among ecologically diverse species found within well-defined taxa to seek putative adaptive trends. For instance, variation in lateral line morphology described among related species within families of freshwater fishes (e.g., Centrarchidae, Branson & Moore, 1962; Percidae, Jakubowski, 1967b; Cottidae, McAllister, 1968) and

marine fishes (stichaeids, Makushok, 1961; Gadidae, Halama, 1977; triplefins, Wellenreuther et al., 2010; Nakae et al., 2012b) can provide a valuable context for comparative functional studies. This is especially true for those groups that include well-studied model species (e.g., the Cyprinidae, including zebrafish and goldfish; the Cottidae, including mottled sculpin, and the Percidae, including Eurasian ruffe).

4. Families in which ecological correlates of lateral line morphology are already evident deserve study. For instance, large canal pores (which characterize widened canal systems) occur in those species in a family that tend to occupy greater depths (Garman, 1899; McAllister, 1968) or lower visibility habitats (Branson & Moore, 1962) when compared to other members of the family. This suggests that they live in environments where vision may be limited and where lower levels of hydrodynamic noise might enhance the utility of the lateral line system.

The ability to carry out such comparative studies depends on the identification of related species for which there is both a demonstrable variation in lateral line morphology *and* a robust hypothesis of phylogenetic relationships. Such studies may also be complicated by the inevitability that one or more species of interest may be too large (or small) to work with, inaccessible or unavailable for study (e.g., deep sea species), and/or not hardy enough for experimental work. Thus, the taxa in which comparative functional studies can be done are relatively limited. However, only continuing investigations of variation in lateral line morphology among species will reveal those taxa in which instructive studies may be carried out.

Finally, several investigative and methodological approaches also need to be more fully exploited.

1. Early taxonomic and descriptive morphological work, dating to the 19th century, provides a great deal of anatomical detail, which tends to be overlooked, but this work has predicted the outcomes of work done more recently using more sophisticated methods. Access to this older literature is no longer limited as the result of the development of remarkable electronic resources that are continuously expanding (e.g., Biodiversity Heritage Library, http://www.biodiversitylibrary.org/).
2. The terminology used to describe features of the lateral line system (lateral line canals, neuromasts, innervation) differs among research communities (systematic ichthyology, evolutionary morphology, physiology, developmental biology) and needs to be unified. Structural and developmental homologies should drive the unification of terminology, and precedence in the literature from all fields must be documented and acknowledged. Collaborative efforts will certainly facilitate this.
3. The discovery and analysis of lateral line morphology, and especially complex connections between the lateral line and ear and/or swim bladder (such as the *recessus lateralis*, Section 5.1, and laterophysic connection, Section 5.6.3) that broaden the function roles of the lateral line system, would benefit from

analyses of hard and soft tissues using histology in conjunction with micro-computed tomographic (μCT) imaging (Fig. 8; Webb et al., 2006, 2012; Wilson et al., 2009).

4. Finally, at a practical level, an understanding of the structure and function of the lateral line system in economically important species will inform fisheries and aquaculture practices as they relate to the biology of predator avoidance, prey detection, and the ability of fishes to navigate around man-made obstacles. It will also reveal more about the role that sensory systems play as human activities continue to impinge on natural habitats by altering sensory environments (e.g., increased turbidity, and alteration of hydrodynamic regimes), thus altering the relative importance of different sensory modalities, including mechanoreception by the lateral line system.

Acknowledgments This chapter is dedicated to the memory of Dr. Karel F. Liem (Harvard University) who, through his instruction, mentorship, and enthusiasm, instilled in me a career-long interest in comparative and developmental morphology. Several colleagues provided valuable insights about the identity of the cells composing neuromasts via a lively e-mail interchange and members of the Webb Lab provided valuable comments that improved the manuscript. This work was supported by NSF grant IOS-0843307 and the College of the Environment and Life Sciences, University of Rhode Island.

References

Abe, Y., Asaoka, R., Nakae, M., & Sasaki, K. (2012). Ambiguities in the identification of batoid lateral line systems clarified by innervation. *Ichthyological Research*, 59, 189–192.

Adriaens, D., Verraes, W., & Taverne, L. (1997). The cranial lateral-line system in *Clarias gariepinus* (Burchell, 1822) (Siluroidei: Clariidae): Morphology and development of canal related bones. *European Journal of Morphology*, 35, 181–208.

Ahlberg, P. E., & Clack, J. A. (1998). Lower jaws, lower tetrapods—a review based on the Devonian genus *Acanthostega*. *Transactions of the Royal Society of Edinburgh: Earth Sciences*, 89, 11–46.

Allis, E. P. (1889). The anatomy and development of the lateral line system in *Amia calva*. *Journal of Morphology*, 2, 463–542+ plates.

Allis, E. P. (1903). The laterosensory system in the Muraenidae. *Int. Mschr. Anat. Physiol.* 20, 125–170 + plates.

Aman, A., & Piotrowski, T. (2009). Multiple signaling interactions coordinate collective cell migration of the posterior lateral line primordium. *Cell Adhesion and Migration*, 3, 365–368.

Aman, A., Nguyen, M., & Piotrowski, T. (2011). Wnt/beta-catenin dependent cell proliferation underlies segmented lateral line morphogenesis. *Developmental Biology*, 349, 470–482.

Appelbaum, S., & Schemmel, C. (1983). Dermal sense organs and their significance in the feeding behaviour of the common sole *Solea vulgaris*. *Marine Ecology Progress Series*, 13, 29–36.

Aquino, A. E., & Schaefer, S.A. (2002). Structural diversity of the temporal region of catfishes: Convergence in functional integration of sensory systems. *Zoologischer Anzeiger*, 241, 223–244.

Arratia, G., & Huaquin, L. (1995). Morphology of the lateral line system and of the skin of diplomystid and certain primitive loricarioid catfishes and systematic and ecological considerations. *Bonner Zoologische Monographien*, 36, 1–110.

Asano, H. (1962). Studies on the congrid eels of Japan. *Bulletin of the Misaki Marine Biological Institute*, *Kyoto University*, 1, 1–143.

Asaoka, R., Nakae, M., & Sasaki, K. (2011). Description and innervation of the lateral line system in two gobioids, *Odontobutis obscura* and *Pterobobius elapoides* (Teleostei: Perciformes). *Ichthyological Research*, 58, 51–61.

Asaoka, R., Nakae, M., & Sasaki, K. (2012). The innervation and adaptive significance of extensively distributed neuromasts in *Glossogobius olivaceus* (Perciformes: Gobiidae). *Ichthyological Research*, 59, 143–150.

Baker, C. F., & Montgomery, J. C. (1999). The sensory basis of rheotaxis in the blind Mexican cave fish, *Astyanax fasciatus*. *Journal of Comparative Physiology Z: Neuroethology, Sensory, Neural, and Behavioral Physiology*, 184, 519–527.

Baker, C. V. H., & Bronner-Fraser, M. (2001). Vertebrate cranial placodes I. Embryonic induction. *Developmental Biology*, 232, 1–61.

Balushkin, A. V. (1996). Structure and evolution of the trunk lateral lines of the Notothenoidei (Perciformes). *Journal of Ichthyology*, 36, 419–429.

Bass, A. H. (2008). Steroid-dependent plasticity of vocal motor systems: Novel insights from teleost fish. *Brain Research Reviews*, 57, 299–308.

Bassett, D. K., Carton A. G., & Montogmery J. C. (2006). Flowing water decreases hydrodynamic signal detection in a fish with an epidermal lateral-line system. *Marine and Freshwater Research*, 57, 611–617.

Beckmann, M., Eros, T., Schmitz, A., & Bleckmann, H. (2010). Number and distribution of superficial neuromasts in twelve common European cypriniform fishes and their relationship to habitat occurrence. *International Review of Hydrobiology*, 95, 273–284.

Beckwith, C. J. (1907). The early development of the lateral line system of *Amia calva*. *Biological Bulletin*, 14, 23–34.

Behra, M., Bradsher, J., Sougrat, R., Gallardo, V., Allende, M. L., & Burgess, S. M. (2009). Phoenix is required for mechanosensory hair cell regeneration in the zebrafish lateral line. PLoS Genetics. 5: e1000455.

Bialowiec, L., & Jakubowski, M. (1971). The anatomical structure, topography, and innervation of lateral-line organs in *Gaidropsarus mediterraneus* L. (Gadidae, Pisces). *Acta Biologica Cracoviensia*, *Series Zoologica*, 14, 257–265.

Bird, N. C., & Hernandez, L. P. (2007). Morphological variation in the Weberian apparatus of Cypriniformes. *Journal of Morphology*, 268, 739–757.

Blaxter, J. H. S. (1987). Structure and development of the lateral line. *Biological Reviews*, 62, 471–514.

Blaxter, J. H. S., & Fuiman, L. A. (1989). Function of the free neuromasts of marine teleost larvae. In S. Coombs, P. Görner, & H. Münz, H. (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 481–499). New York: Springer-Verlag.

Bleckmann, H., Pryzbilla, A., Klein, A., Schmitz, A., Kunze, S., & Brucker, C. (2012). Station holding of trout: Behavior, physiology and hydrodynamics. *Notes on Numerical Fluid Mechanics and Multidisciplinary Design*, 119, 161–177.

Boyle, K. S., & Tricas, T. C. (2010). Pulse sound generation, anterior swim bladder buckling, and associated muscle activity in the pyramid butterflyfish, *Hemitaurichthys polylepis*. *Journal of Experimental Biology*, 213, 3881–3893.

Boyle, K. S., & Tricas, T. C. (2011). Sound production in the longnose butterflyfishes (genus *Forcipiger*): Cranial kinematics, muscle activity and honest signals. *Journal of Experimental Biology*, 214, 3829–3842.

Branson, B. A. (1961). The lateral-line system in the Rio Grande perch *Cichlasoma cyanoguttatum* (Baird and Girard). *American Midland Naturalist*, 65, 446–458.

Branson, B. A., & Moore, G. A. (1962). The lateralis components of the acoustico-lateralis system in the sunfish family Centrarchidae. *Copeia*, 1962, 1–108.

Braun, C. B. (1996). The sensory biology of the living jawless fishes: A phylogenetic assessment. *Brain, Behavior, and Evolution*, 48, 262–276.

Braun, C. B., & Northcutt, R. G. (1997). The lateral line system of hagfishes (Craniata: Myxinoidea). *Acta Zoologica (Stockholm)*, 78, 247–268.

Braun, C. B., & Grande, T. (2008). Evolution of peripheral mechanisms for the enhancement of sound reception. In J. F. Webb, R. R. Fay, & A. N. Popper (Eds.), *Fish bioacoustics* (pp. 99–144). New York: Springer-Verlag.

Britz, R., & Kottelat, M. (2003). Descriptive osteology of the family Chaeudhuriidae (Teleosteii, Synbranchiformes, Mastacembeloidei), with a discussion of its relationships. *American Museum Novitates*, 3418, 1–62.

Burt de Perera, T., & Braithwaite, V. A. (2005). Laterality in a non-visual sensory modality—the lateral line of fish. *Current Biology*, 15, R241–R24.

Cahn, P. H., Shaw, E., & Atz, E. H. (1968). Lateral-line histology as related to the development of schooling in the atherinid fish, *Menidia*. *Bulletin of Marine Science*, 18, 660–670.

Carton, A. G., & Montgomery, J. C. (2004). A comparison of lateral line morphology of blue cod and torrentfish: Two sandperches of the family Pinguipedidae. *Environmental Biology of Fishes*, 70, 123–131.

Caruso, J. H. (1989). Systematics and distribution of chaunacid anglerfishes (Pisces: Lophiiformes). *Copeia*, 1989, 153–165.

Chagnaud, B. H., Bleckmann, H., & Hofmann, M. H. (2007). Karman vortex street detection by the lateral line. *Journal of Comparative Physiology, A*, 193, 753–763.

Chagnaud, B. P., Bleckmann, H., & Hofmann, M. H. (2008). Detecting flow velocity and flow direction by spatial and temporal analysis of flow fluctuations. *Journal of Neuroscience*, 28, 4479–4487.

Chang, J. S. Y., Popper, A. N., & Saidel, W. M. (1992). Heterogeneity of sensory hair cells in a fish ear. *Journal of Comparative Neurology*, 324, 621–640.

Chao, L. N. (1978). A basis for classifying Western Atlantic Sciaenidae (Teleostei: Perciformes). National Oceanic and Atmospheric Administration Technical Report. National Marine Fisheries Service, Rockville, MD. Circular 415, 1–64.

Chitnis, A. J., Nogare, D. D., & Matsuda, M. (2011). Building the posterior lateral line system in zebrafish. *Developmental Neurobiology*, 72, 234–255.

Chu, Y. T., & Wen, M. C. (1979). *Monograph of fishes of China (No. 2): A study of the lateral-line canals system and that of lorenzini ampulla and tubules of elasmobranchiate fishes of China*. Shanghai: Science and Technology Press.

Clapp, C. M. (1889). The lateral line system of *Batrachus tau*. *Journal of Morphology*, 15, 223–264.

Collinge, W. E. (1895). On the sensory canal system of fishes. Teleostei—Suborder A. *Physostom*i. *Proceedings of the Zoological Society of London*, 63, 274–299.

Coombs, S., & Montgomery, J. (1994). Function and evolution of superficial neuromasts in an Antarctic nototheniod fish. Brain, Behavior and Evolution, 44, 287–298

Coombs, S., & Conley, R. A. (1997). Dipole source localization by mottled sculpin. I. Approach strategies. *Journal of Comparative Physiology A*, 180, 387–399.

Coombs, S., & van Netten, S. (2006). The hydrodynamics and structural mechanics of the lateral line system. In R. E. Shadwick & G. V. Lauder (Eds.), *Fish biomechanics* (pp. 103–139). San Diego: Elsevier.

Coombs, S., Janssen, J., & Webb, J. F. (1988). Diversity of lateral line systems: Phylogenetic and functional considerations. In J. Atema, R. R. Fay, A. N. Popper, & W. N. Tavolga (Eds.), *Sensory biology of aquatic animals* (pp. 553–593). New York: Springer-Verlag.

Coombs, S., Janssen, J., & Montgomery, J. (1992). Functional and evolutionary implications of peripheral diversity in lateral line systems. In D. B. Webster, A. N. Popper, & R. R. Fay (Eds.). *Evolutionary biology of hearing* (pp. 267–294). New York: Springer-Verlag.

Coombs, S., Braun, C., & Donovan, B. (2001). The orienting response of Lake Michigan mottled sculpin is mediated by canal neuromasts. *Journal of Experimental Biology*, 204, 337–348.

Coombs, S., Fay, R. R., & Elepfandt, A. (2010). Dipole source encoding and tracking by the goldfish auditory system. *Journal of Experimental Biology*, 213, 3536–3547.

Corwin, J. T., Balak, K. J., & Borden, P. C. (1989). Cellular events underlying the regenerative replacement of lateral line sensory epithelia in amphibians. In S. Coombs, P. Görner, & H. Münz, H. (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 161–183). New York: Springer-Verlag.

Dambly-Chaudière, C., Sapede, D., Soubiran, F., Decorde, K., Gompel, N., & Ghysen, A. (2003). The lateral line of zebrafish: A model system for the analysis of morphogenesis and neural development in vertebrates. *Biology of the Cell*, 95, 579–587.

De Beer, G. R. (1985). *The development of the vertebrate skull*. Chicago: University of Chicago Press.

Denton, E. J., & Gray, J. A. B. (1983). Mechanical factors in the excitation of clupeid lateral lines. *Proceedings of the Royal Society of London B*, 218, 1–26.

Denton, E. J., & Gray, J. A. B. (1993). Stimulation of the acoustico-lateralis system of clupeid fish by external sources and their own movements. *Philosophical Transactions of the Royal Society of London Biological Sciences*, 341, 113–127.

Dezfuli, B. S., Capuano, S., Magosso, S., Giari, L., & Berti, R. (2009). The lateral line system in larvae of the blind cyprinid cavefish, *Phreatichthys andruzzii*. *The Anatomical Record*, 292, 423–430.

Diaz, J. P., Prié-Granié, M., Kentouri, M., Varsamos, S., & Connes, R. (2003). Development of the lateral line system in the sea bass. *Journal of Fish Biology*, 62, 24–40.

Di Dario, F. (2004). Homology between the recessus lateralis and cephalic sensory canals, with the proposition of additional synapomorphies for the Clupeiformes and the Clupeoidei. *Zoological Journal of the Linnaean Society*, 141, 257–270.

Di Dario, F., & de Pinna, M. C. C. (2006). The supratemporal system and the pattern of ramification of cephalic sensory canals in *Denticeps clupeoides* (Denticipitoidei, Teleostei): Additional evidence for monophyly of Clupeiformes and Clupeoidei. *Papéis Avulsos de Zoologia (São Paulo)*, 46, 107–123.

Disler, N. N. (1950). Development of the sense organs of the lateral line system of the perch and ruffe. *Trudy Instituta Morfologii Zhivotnykh Imeni A. H. Severtsova*, 2, 85–139 (translated from Russian by A. R. Gosline & W. A. Gosline).

Disler, N. N. (1961). On the structure of the laterosensory system in sharks and rays. *Acta Zoologica*, 42, 163–175.

Disler, N. N. (1971). *Lateral line sense organs and their importance in fish behavior*. Jerusalem: Israel Program for Scientific Translations.

Disler, N. N., & Smirnov, S. A. (1977). Sensory organs of the lateral-line canal system in two percids and their importance in behavior. *Journal of the Fisheries Research Board of Canada*, 34, 1492–1503.

DoNascimiento, C., Provenzano, F., & Lundberg, J. G. (2004). *Rhamdia guasarensis* (Siluriformes: Heptapteridae), a new species of cave catfish from the Sierra de Perijá, northwestern Venezuela. *Proceedings of the Biological Society of Washington*, 117, 564–574.

Edds-Walton, P. L., & Fay, R. R. (2009). Physiological evidence for binaural directional computations in the brainstem of the oyster toadfish, *Opsanus tau* (L.). *Journal of Experimental Biology*, 212, 1483–1493.

Ekström von Lubitz, D. K. (1981). Ultrastructure of the lateral-line sense organs of the ratfish, *Chimaera monstrosa*. *Cell and Tissue Research*, 215, 651–665.

Fang, F. (2003). Phylogenetic analysis of the Asian cyprinid genus *Danio* (Teleostei, Cyprinidae). *Copeia*, 2003, 714–728.

Fange, R., Larsson, A., & Lidman, U. (1972). Fluids and jellies of the acusticolateralis system in relation to body fluids in *Coryphaenoides rupestris* and other fishes. *Marine Biology*, 17, 180–185.

Faucher, K., Aubert, A., & Lagardére, J-P. (2003). Spatial distribution and morphological characteristics of the trunk lateral line neuromasts of the sea bass (*Dicentrarchus labrax*, L.; Teleostei, Serranidae). *Brain, Behavior, and Evolution*, 62, 223–232.

Faucher, K., Lagardére, J-P., & Aubert, A. (2005). Quantitative aspects of the spatial distribution and morphological characteristics of the sea bass (*Dicentrarchus labrax* L.; Teleostei, Serranidae) trunk lateral line neuromasts. *Brain, Behavior and Evolution*, 65, 231–243.

Fay, R. R., & Edds-Walton, P. L. (2008). Structures and functions of the auditory nervous system of fishes. In J. F. Webb, R. R. Fay, & A. N. Popper (Eds.). *Fish bioacoustics* (pp. 49–98). New York: Springer-Verlag.

Fernholm, B. (1985). The lateral line system of cyclostomes. In R. E. Foreman, A. Gorbman, J. M. Dodd, & R. Olsson, R. (Eds.), *Evolution and biology of primitive fishes* (pp. 113–122). New York: Plenum Press.

Fields, R. D., Bullock, T. H., & Lange, G. D. (1993). Ampullary sense organs, peripheral, central and behavioral electroreception in chimeras (*Hydrolagus*, Holocephali, Chondrichthyes). *Brain, Behavior and Evolution*, 41, 269–289.

Flock, A. (1965a). Electron microscopic an delectrophysiological studies on the lateral line canal organ. *Acta Otolaryngologica Supplementum*. S199, 7–90.

Flock, A. (1965b). Transducing mechanisms in the lateral line canal organ receptors. *Cold Spring Harbor Symposia on Quantitative Biology*, 30, 133–145.

Franz-Odendaal, T. A., & Hall, B. K. (2006). Modularity and sense organs in the blind cavefish, *Astyanax mexicanus*. *Evolution and Development*, 8, 94–100.

Fritzsch, B. (1989). Diversity and regression in the amphibian lateral line and electrosensory system. In S. Coombs, P. Görner, & H. Münz, H. (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 99–114). New York: Springer-Verlag.

Fritzsch, B., & Neary, T. J. (1998). The octavolateralis system of mechanosensory and electrosensory organs. In H. Heatwole, & E. M. Dawley (Eds.), *Amphibian biology*, Vol. 3 (pp. 878–922). Australia: Surrey Beattey & Sons.

Fryer, G. (1959). The trophic interrelationships and ecology of some littoral communities of Lake Nyasa with especial reference to the fishes, and a discussion of the evolution of a group of rock-frequenting Cichlidae. *Proceedings of the Zoological Society of London*, 132,153–281.

Fuiman, L. A., Higgs, D. M., & Poling, K. R. (2004). Changing structure and function of the ear and lateral line system of fishes during development. *American Fisheries Society Symposium*, 40, 117–144.

Fujita, T., & Hosoya, K. (2005). Cephalic lateral line systems in the Far Eastern species of the genus *Phoxinus* (Cyprinidae). *Ichthyological Research*, 52, 336–342.

Fukuda, E., Nakae, M., Asaoka, R., & Sasaki, K. (2010). Branching patterns of trunk lateral line nerves in Pleuronectiformes: Uniformity and diversity. *Ichthyological Research*, 57, 148–160.

Gallardo, V. E., Liang, J., Behra, M., Elkahloun, A., Villablanca, E. J., Russo, V., Allende, M. L., & Burgess, S. M. (2010). Molecular dissection of the migrating posterior lateral line primordium during early development in zebrafish. *BMC Developmental Biology*, 10, 120.

Gardiner, J. M., Hueter, R. E., Maruska, K. P., Sisneros, J. A., Casper, B. M., Mann, D. A., & Demski, L. S. (2012). Sensory physiology and behavior of elasmobranchs. In J. C. Carrier, J. A. Musick, & M. R. Heithaus (Eds.), *Biology of sharks and their relatives*, Vol. I. Boca Raton, FL: CRC Press.

Garman, S. (1899). Reports on an exploration off the west coasts of Mexico, Central and South America, and off the Galapogos Islands, in charge of Alexander Agassiz, by the United States Fish Commission Steamer "Albatross" during 1891, Lieut. Commander Z.L. Tanner, USN, Commanding. XXVI—The Fishes. *Memoirs of the Museum of Comparative Zoology*, 24, 1–431 + 97 plates.

Gelman, S., Ayali, A., Tytell, E. D., & Cohen, A. H. (2006). Larval lampreys possess a functional lateral line system. *Journal of Comparative Physiology A*, 193, 271–277.

Ghysen, A., & Dambly-Chaudière, C. (2007). The lateral line microcosmos. *Genes & Development*, 21, 2118–2130.

Ghysen, A., Schuster, K., Coves, D., De La Gandara, F., Papandroulakis, N., & Ortega, A. (2010). Development of the posterior lateral line system in *Thunnus thynnus*, the Atlantic blue-fin tuna,

and in its close relative *Sarda sarda*. *International Journal of Developmental Biology*, 54, 1317–1322.

Ghysen, A., Dambly-Chaudière, C., Coves, D., de la Gandara, F., & Ortega, A. (2012). Developmental origin of a major difference in sensory patterning between zebrafish and Bluefin tuna. *Evolution and Development*, 14, 204–211.

Gibbs, M. A. (1999). Lateral line morphology and cranial osteology of the rubynose brotula, *Cataetyx rubrirostris*. *Journal of Morphology*, 241, 265–274.

Gibbs, M. A., & Northcutt, R. G. (2004). Development of the lateral line system in the shovelnose sturgeon. *Brain, Behavior and Evolution*, 64, 70–84.

Gillis, J. A., Modrell, M. S., Northcutt, R. G., Catania, K. C., Luer, C. A., & Baker, C. V. H. (2012). Electrosensory ampullary organs are derived from lateral line placodes in cartilaginous fishes. *Development*, 139, 3142–3146.

Gilmour, D., Knaut, H., Maischein, H. M., & Nüsslein-Volhard, C. (2004). Towing of sensory axons by their migrating target cells in vivo. *Nature Neuroscience*, 7, 491–492.

Gosline, W. A. (1970). A reinterpretation of the teleostean fish order Gobiesosiformes. *Proceedings of the California Academy of Sciences*, 38, 363–382.

Graham-Smith, W. (1978). On the lateral lines and dermal bones in the parietal region of some crossopterygian and dipnoan fishes. *Philosophical Transactions of the Royal Society of London*, 282, 41–105.

Grande, L. (2010). *An empirical synthetic pattern study of gars (Lepisosteiformes) and closely related species, based mostly on skeletal anatomy—the resurrection of Holostei*. American Society of Ichthyologists and Herpetologists, Lawrence, KS. Special Publication no. 6.

Grande, L., & Bemis, W. E. (1991). Osteology and phylogenetic relationships of fossil and recent paddlefishes (Polyodontidae) with comment on the interrelationships of Acipenseriformes. *Journal of Vertebrate Paleontology*, *Special Memoir no. 1*, 11 (Supplement), 1–121.

Grande, L., & Bemis, W. E. (1998). A comprehensive phylogenetic study of amiid fishes (Amiidae) based on comparative skeletal anatomy. An empirical search for interconnected patterns of natural history. *Journal of Vertebrate Paleontology*, *Special Memoir* no. 4, 18 (Supplement), 1–690 + ix.

Grant, K. A., Raible, D. W., & Piotrowski, T. (2005). Regulation of latent sensory hair cell precursors by glia in the zebrafish lateral line. *Neuron*, 45, 69–80.

Gray, J. A. B., & Best, A. C. G. (1989). Patterns of excitation of the lateral line of the ruffe. *Journal of the Marine Biological Association of the United Kingdom*, 69, 289–306.

Gray, J. A. B., & Denton, E. J. (1991). Fast pressure pulses and communication between fish. *Journal of the Marine Biological Association of the United Kingdom*, 71, 83–106.

Greene, C. W. (1899). The phosphorescent organs in the toadfish, *Porichthys notatus* Girard. *Journal of Morphology*, 15, 667–696.

Gregory, W. K. (1933). Fish skulls: A study of the evolution of natural mechanisms. *Transactions of the American Philosophical Society*, 23, 75–481.

Haffter, P., Granato, M., Brand, M., Mullins, M. C., Hammerschmidt, M., Kane, D. A., Odenthal, J., van Eeden, F. J., Jiang, Y. J., Heisenberg, C. P., Kelsh, R. N., Furutani-Seiki, M., Vogelsang, E., Beuchle, D., Schach, U., Fabian, C., & Nüsslein-Volhard, C. (1996). The identification of genes with unique and essential functions in the development of the zebrafish. *Development*, 123, 1–36.

Halama, L. (1977). Anatomical structure of the lateral-line organs and related bones in the Gadidae (Pisces). *Acta Biologica Cracoviensia Series Zoologia*, 20, 41–63.

Hama, K. (1978). A study of the fine structure of the pit organ of the common Japanese sea eel *Conger myriaster*. *Cell and Tissue Research*, 189, 375–388.

Hensel, K. (1976). Morphology of lateral line canal system of the genera *Abramis*, *Blicca* and *Vimba* with regard to their ecology and systematic position. *Acta Universitatis Carolinae Biologica*, 1975–1976, 105–149.

Hensel, K. (1986). Morphologie et interprétation des canaux et canalicules sensoriels céphaliques de *Latimeria chalumnae* Smith, 1939 (Osteichthyes, Crossopterygii, Coelacathiformes).

Bulletin du Museum National d'Histoire Naturelle. 4e Serie. Section A. Zoologie, Biologie et Ecologie Animales, 2, 379–407.

Hensel, K., & Balon, E. K. (2001). The sensory canal systems of the living coelocanth, *Latimeria chalumnae*: A new installment. *Environmental Biology of Fishes*, 61, 117–124.

Hernández, P. P., Olivar, F. A., Sarrazn, A. F., Sandoval, P. C., & Allende, M. L. (2007). Regeneration in zebrafish lateral line neuromasts: Expression of the neural progenitor cell marker Sox2 and proliferation-dependent and -independent mechanisms of hair cell renewal. *Developmental Neurobiology*, 67, 637–654.

Higgs, D. M., Rollo, A. K., Souza, M. J., & Popper, A. N. (2003). Development of form and function in peripheral auditory structures of the zebrafish (*Danio rerio*). *Journal of the Acoustical Society of America*, 113, 1145–1154.

Hilton, E. J., Grande, L., & Bemis, W. E. (2011). Skeletal anatomy of the shortnose sturgeon, *Acipenser brevirostrum* Lesueur 1818, and the systematics of sturgeons (Acipenseriformes, Acipenseridae). *Fieldiana, Life and Earth Sciences*, 3, 1–168.

Hoekstra, D., & Janssen, J. (1985). Non-visual feeding behavior of the mottled sculpin, *Cottus bairdi*, in Lake Michigan. *Environmental Biology of Fishes*, 12, 111–117.

Holmgren, N. (1940). Studies on the head in fishes: Embryological, morphological and phylogenetical researches (Part I). *Acta Zoologica*, 21, 51–267.

Honkanen, T. (1993). Comparative study of the lateral-line system of the three-spined stickleback (*Gasterosteus aculeatus*) and the nine-spined stickleback (*Pungitius pungitius*). *Acta Zoologica (Stockholm)*, 74, 331–336.

Hoss, D. E. & Blaxter, J. H. S. (1982). Development and function of the swimbladder-inner ear system in the Atlantic menhaden, *Brevoortia tyrannus* (Latrobe). *Journal of Fish Biology*, 21, 131–142.

Hoyt, R. D. (1972). Anatomy and osteology of the cephalic lateral-line system of the silverjaw minnow, *Ericymba buccata* (Pisces: Cyprinidae). *Copeia*, 1972, 812–816.

Ishikawa, Y. (1994). Innervation of lateral line system in the medaka, Oryzias latipes. *The Fish Biology Journal Medaka*, 6, 17–24.

Iwai, T. (1964). Development of cupulae in free neuromasts of the Japanese medaka, *Oryzias latipes* (Temminck et Schlegel). *Bulletin of the Misaki Marine Biological Institute, Kyoto University*, 5, 31–37.

Jakubowski, M. (1963). Cutaneous sense organs of fishes. I. The lateral-line organs in the stone-perch (*Acerina cernua* L.). *Acta Biologica Cracoviensia*, *Series Zoologia*, 6, 59–78.

Jakubowski, M. (1966). Cutaneous sense organs of fishes. V. Canal system of lateral-line organs in *Mullus barbatus ponticus* Essipov and *Spicara smaris* L. (topography, innervation, structure). *Acta Biologica Cracoviensia*, *Series Zoologia*, 9, 225–237.

Jakubowski, M. (1967a). Cutaneous sense organs of fishes. Part VI. The structure, topography and innervation of lateral line organs in the burbot, *Lota lota*. *Acta Biologica Cracoviensia*, *Series Zoologia*, 10, 39–47.

Jakubowski, M. (1967b). Cutaneous sense organs of fishes. Part VII. The structure of the system of lateral-line canal organs in the Percidae. *Acta Biologica Cracoviensia*, *Series Zoologia*, 10, 69–81.

Jakubowski, M. (1974). Structure of the lateral-line canal system and related bones in the berycoid fish *Hoplostethus mediteranneus* Cuv. et Val. (Trachichthyidae, Pisces). *Acta Anatomica*, 87, 261–274.

Janssen, J. (2004). Lateral line sensory ecology. In G. von der Emde, G., J. Mogdans, & B. G. Kapoor (Eds.), *The senses of fish—Adaptations for the reception of natural stimuli* (pp. 231–264). Boston: Kluwer Academic.

Janssen, J., Coombs, S., Hoekstra, D., & Platt, C. (1987). Anatomy and differential growth of the lateral line system of the mottled sculpin, *Cottus bairdi* (Scorpaeniformes: Cottidae). *Brain, Behavior and Evolution*, 30, 210–229.

Jeffery, W. R. (2001). Cavefish as a model system in evolutionary developmental biology. *Developmental Biology*, 231, 1–12.

Jeffery, W. R. (2005). Adaptive evolution of eye degeneration in the Mexican blind cavefish. *Journal of Heredity*, 96, 1–12.
Jeffery, W. R. (2008). Emerging model systems in evo-devo: Cavefish and microevolution of development. *Evolution and Development*, 10, 265–272.
Johnson, S. E. (1917). Structure and development of the sense organs of the lateral canal system of selachians (*Mustelus canis* and *Squalus acanthias*). *Journal of Comparative Neurology*, 28, 1–74.
Jollie, M. (1975). Development of the head skeleton and pectoral girdle in *Esox*. *Journal of Morphology*, 147, 61–88.
Jollie, M. (1984a). Development of cranial and pectoral girdle bones of *Lepisosteus* with a note on scales. *Copeia*, 1984, 476–502.
Jollie, M. (1984b). Development of the head and pectoral skeleton of *Polypterus* with a note on scales (Pisces: Actinopterygii). *Journal of Zoology, London*, 204, 469–507.
Jollie, M. (1984c). Development of the head skeleton and pectoral girdle of salmons, with a note on the scales. *Canadian Journal of Zoology*, 62, 1757–1778.
Jones, W. R., & Janssen, J. (1992). Lateral line development and feeding behavior in the mottled sculpin, *Cottus bairdi* (Scorpaeniformes: Cottidae). *Copeia*, 1992, 485–492.
Jordan, L. K., Kajiura, S. M., & Gordon, M. S. (2009). Functional consequences of structural differences in stingray sensory systems. Part I: Mechanosensory lateral line canals. *Journal of Experimental Biology*, 212, 3037–3043.
Jørgensen, J. M. (2010). Mechanoreceptive neuromasts and electroreceptive ampullary organs, In J. M. Jørgensen, & J. Joss (Eds.), *The biology of lungfishes* (pp. 477–492). Boca Raton, FL: CRC Press.
Kanter, M., & Coombs, S. (2003). Rheotaxis and prey detection in uniform currents by Lake Michigan mottled sculpin (*Cottus bairdi*). *Journal of Experimental Biology*, 206, 59–70.
Kapoor, A. S. (1970). Development of dermal bones related to sensory canals of the head in the fishes *Ophicephalus punctatus* Bloch (Ophicephalidae) and *Wallago attu* B., & Schn. (Siluridae). *Zoological Journal of the Linnean Society*, 49, 69–97.
Kasumyan, A. O. (2003). The lateral line in fish: Structure, function and role in behavior. *Journal of Ichthyology*, 43 (Supplement 2), S175–S213.
Kawamura, G., Masuma S., Tezuka, N., Koiso, M., Jinbo, T., & Namba, K. (2003). Morphogenesis of sense organs in the bluefin tuna *Thunnus orientalis*. In H. I. Browman & A. B. Skiftesvik (Eds.), *The fish big bang*: *Proceedings of the 26th annual larval fish conference* (pp. 123–135). Bergen, Norway: Institute of Marine Research.
Kelly, J. P., & van Netten, S. M. (1991). Topography and mechanics of the cupula in the fish lateral line. I. Variation of cupular structure and composition in three dimensions. *Journal of Morphology*, 207, 23–36.
Kemp, A. (1999). Sensory lines and rostral skull bones in lungfish of the family Neoceratodontidae (Osteichthyes: Dipnoi). *Alcheringa*, 23, 289–307.
Kershaw, D. R. (1970). The cranial osteology of the 'butterfly fish', *Pantodon buchholzi* Peters. *Zoological Journal of the Linnean Society*, 49, 5–19.
Konings, A. (1990). *Koning's book of cichlids and other Fishes of Lake Malawi*. Neptune City, NJ: TFH Publications.
Konings, A. (2007). *Malawi cichlids in their natural habitat*, 4th ed. El Paso, TX:: Cichlid Press.
Lane, E. B., & Whitear, M. (1982). Sensory structures at the surface of fish skin. II. Lateralis system. *Zoological Journal of the Linnean Society*, 76, 19–28.
Lannoo, M. J. (1985). Neuromast topography in *Ambystoma* larvae. *Copeia*, 1985, 535–539.
Lannoo, M. J. (1987a). Neuromast topography in anuran amphibians. *Journal of Morphology*, 191, 115–129.
Lannoo, M. J. (1987b). Neuromast topography in urodele amphibians. *Journal of Morphology*, 191, 247–263.

Lannoo, M. J. (1988). The evolution of the amphibian lateral line system and its bearing on amphibian phylogeny. *Zeitschrift fur Zoologische Systematik und Evolutionforschung*, 26, 128–134.

Lannoo, M. J. (2009). Nervous and sensory systems in sub-Arctic and Antarctic snailfishes of the genus *Paraliparis* (Teleostei: Scorpaeniformes: Liparidae). *Copeia*, 2009, 732–739.

Laverack, M. S., & Bevan, M. D. (1991). The lateral line of the butterfish, *Pholis gunnellus* L. *Marine Behavior and Physiology*, 19, 15–26.

Lawry, J. V., Jr. (1972a). A presumed near field pressure receptor in the snout of the lantern fish, *Tarletonbeania crenularis* (Myctophidae). *Marine Behaviour and Physiology*, 1, 295–303.

Lawry, J. V., Jr. (1972b). The trigeminofacial innervation of the cephalic lateral line organs and photophores of the lantern fish *Tarletonbeania crenularis* (Myctophidae). *Marine Behaviour and Physiology*, 1, 285–293.

Lekander, B. (1949). The sensory line system and the canal bones in the head of some Ostariophysi. *Acta Zoologica (Stockholm)*, 30, 1–131.

Leydig, F. (1850). Ueber die Schleimkanale der Knochenfische. *Müller's Archiv fur Anatomie, Physiologie und Wissenschaftliche Medicin, Jahrgang 1850*, 170–181.

Lisney, T. J. (2010). A review of the sensory biology of chimaeroid fishes (Chondrichthyes; Holocephali). *Reviews in Fish Biology and Fisheries*, 20, 571–590.

Lopez-Schier, H., & Hudspeth, A. J. (2005). Supernumerary neuromasts in the posterior lateral line of zebrafish lacking peripheral glia. *Proceedings of the National Academy of Sciences of the USA*, 102, 1496–1501.

Lopez-Shier, H., Starr, C. J., Kappler, F. A., Kollmar, R., & Hudspeth, A. J. (2004). Directional cell migration establishes the axes of planar polarity in the posterior lateral-line organ of the zebrafish. *Developmental Cell*, 7, 401–412.

Lu, Z., Popper, A. N., & Fay, R. R. (1996). Behavioral detection of acoustic particle motion by a teleost fish, *Astronotus ocellatus*: Sensitivity and directionality. *Journal of Comparative Physiology A*, 179, 227–233.

Lundberg, J. G., & Mago-Leccia, F. (1986). A review of *Rhabdolichops* (Gymnotiformes, Sternopygidae), a genus of South American freshwater fishes, with decriptions of four new species. *Proceedings of the Academy of Natural Sciences of Philadelphia*, 138, 53–85.

Ma, E. Y., & Raible, D. W. (2009). Signaling pathways regulating zebrafish lateral line development. *Current Biology*, 19, R381–R386.

Ma, E. Y., Rubel, E. W., & Raible, D. W. (2008). Notch signaling regulates the extent of hair cell regeneration in the zebrafish lateral line. *Journal of Neuroscience*, 28, 2261–2273.

Makushok, V. M. (1961). [Some peculiarities in the structure of the seismosensory system of the northern blenniids (Stichaeoidae, Blennioidei, Pisces).]. *Trudy Instituta Okeanologii*, 43, 225–269. [English translation by A. R. Gosline, published by United States National Museum].

Marshall, N. J. (1965). Systematic and biological studies of the Macrourid fishes (Anacanthini-Teleostii). *Deep Sea Research*, 12, 299–322.

Marshall, N. J. (1986). Structure and general distribution of free neuromasts in the black goby, *Gobius niger*. *Journal of the Marine Biological Association of the United Kingdom*, 66, 323–333.

Marshall, N. J. (1996). The lateral line systems of three deep-sea fish. *Journal of Fish Biology*, 49 (Supplement), 239–258.

Maruska, D. P. (2001). Morphology of the mechanosensory lateral line system in elasmobranch fishes: Ecological and behavioral considerations. *Environmental Biology of Fishes*, 60, 47–75.

Maruska, K. P., & Tricas, T. C. (1998). Morphology of the mechanosensory lateral line system in the Atlantic stingray, *Dasyatis sabina*: The mechanotactile hypothesis. *Journal of Morphology*, 238, 1–22.

Maruska, K. P., & Tricas, T. C. (2004). Test of the mechanotactile hypothesis: Neuromast morphology and response dynamics of mechanosensory lateral line primary afferents in the stingray. *Journal of Experimental Biology*, 207, 3463–3476.

McAllister, D. E. (1968). Mandibular pore pattern in the sculpin family Cottidae. *Bulletin of the National Museum of Canada*, 223, 58–69.
McDonnell, R. (1871). On the system of the "lateral line" in fishes. *Transactions of the Royal Irish Academy, Science*, 24, 161–188.
Metcalfe, W. K. (1989). Organization and development of the zebrafish posterior lateral line. In S. Coombs, P. Görner, & H. Münz, H. (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 147–159). New York: Springer-Verlag.
Metcalfe, W. K., Kimmel, C. B., & Schabtach, E. (1985). Anatomy of the posterior lateral line system in young larvae of the zebrafish. *Journal of Comparative Neurology*, 233, 377–389.
Meyer, M. K., Riehl, R., & Zetzsche, H. (1987). A revision of the cichlid fishes of the genus *Aulonocara* Regan, 1922 from Lake Malawi, with descriptions of six new species (Pisces, Perciformes, Cichlidae). *Courier Forschungsinstitut Senckenberg*, 94, 7–53.
Modrell, M. S., Bemis, W. E., Northcutt, R. G., Davis, M. C., & Baker, C. V. H. (2011a). Electrosensory ampullary organs are derived from lateral line placodes in bony fishes. *Nature Communications*, 2, 496.
Modrell, M. S., Buckley, D., & Baker, C. V. (2011b). Molecular analysis of neurogenic placode development in a basal ray-finned fish. *Genesis*, 49, 278–294.
Mogdans J., & Nauroth I. E. (2011). The oscar, *Astronotus ocellatus*, detects and discriminates dipole stimuli with the lateral line system. *Journal of Comparative Physiology A*, 197, 959–968.
Montgomery, J., & Saunders, A. J. (1985). Functional morphology of the piper *Hyporhamphus ihi* with reference to the role of the lateral line in feeding. *Proceedings of the Royal Society of London B: Biological Sciences*, 224, 197–208.
Montgomery, J., Coombs, S., & Janssen, J. (1994). Form and function relationships in lateral line systems: Comparative data from six species of Antarctic notothenioid fish. *Brain, Behavior and Evolution*, 44, 299–306.
Montgomery, J., Coombs, S., & Baker, C. F. (2001). The mechanosensory lateral line system of the hypogean form of *Astyanax fasciatus*. *Environmental Biology of Fishes*, 62, 87–96.
Moore, G. A., & Burris, W. E. (1956). Description of the lateral-line system of the pirate perch, *Aphredoderus sayanus*. *Copeia*, 1956, 18–20.
Moore, J. A. (1993). Phylogeny of the Trachichthyiformes (Teleostei: Percomorpha). *Bulletin of Marine Sciences*, 52, 114–136.
Moore, M. E., & Webb, J. F. (2008). Dermal bone remodeling in the cranial lateral line canals of zebrafish: The role of osteoclasts. *Integrative and Comparative Biology*, 47, e142.
Moy-Thomas, J. A. (1941). Development of the frontal bones of the rainbow trout. *Nature*, 147, 681–682.
Mukai, Y., & Kobayashki, H. (1992). Cupular growth rate of free neuromasts in three species of cyprinid fish. *Nippon Suisan Gakkaishi*, 58, 1849–1853.
Mukai, Y., & Kobayashki, H. (1995). Development of free neuromasts with special reference to sensory polarity in larvae of the willow shiner, *Gnathopogon elongates caerulescens* (Teleostei, Cyprinidae). *Zoological Science*, 12, 125–131.
Mukai, Y., Yoshikawa, H., & Kobayashi, H. (1994). The relationship between the length of the cupulae of free neuromasts and feeding ability in larvae of the willow shiner *Gnathopogon elongates caerulescens* (Teleostei, Cyprinidae). *Journal of Experimental Biology*, 197, 399–403.
Münz, H. (1979). Morphology and innervation of the lateral line system in *Sarotherodon niloticus* (L.) (Cichlidae, Teleostei). *Zoomorphologie*, 93, 73–86.
Münz, H. (1989). Functional organization of the lateral line periphery. In S. Coombs, P. Görner, & H. Münz, H. (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 285–298). New York: Springer-Verlag.
Nakae, M., & Sasaki, K. (2005). The lateral line system and its innervation in the boxfish *Ostracion immaculatus* (Tetraodontiformes: Ostraciidae): Description and comparisons with other tetraodontiform and perciform conditions. *Ichthyological Research*, 52, 343–353.

Nakae, M., & Sasaki, K. (2006). Peripheral nervous system of the ocean sunfish, *Mola mola* (Tetraodontiformes: Molidae). *Ichthyological Research*, 53, 233–246.

Nakae, M., & Sasaki, K. (2010). Lateral line system and its innervation in Tetraodontiformes with outgroup comparisons: Descriptions and phylogenetic implications. *Journal of Morphology*, 271, 559–579.

Nakae, M., Asai, S., & Sasaki, K. (2006). The lateral line system and its innervation in *Champsodon snyderi* (Champsodontidae): Distribution of approximately 1000 neuromasts. *Ichthyological Research*, 53, 209–215.

Nakae, M., Asaoka, R., Wada, H., & Sasaki, K. (2012a). Fluorescent dye staining of neuromasts in live fishes: An aid to systematic studies. *Ichthyological Research*, 59, 286–290.

Nakae, M., Katayama, E., Asaoka, R., Hirota, M., & Sasaki, K. (2012b). Lateral line system in the triplefin *Enneapterygius etheostomus* (Perciformes: Tripterygiidae): New implications for taxonomic studies. *Ichthyological Research*, 59, 268–271.

Namdaran, P, Reinhart, K. E., Owens, K. N., Raibel, D. W., & Rubel, E. W. (2012). Identification of modulators of hair cell regeneration in the zebrafish lateral line. *The Journal of Neuroscience*, 32, 3516–3528.

Nazarkin, M. V. (2011). Morphology of two eastern Pacific eelpouts (Pisces, Zoarcidae, Lycodes) in connection with features of distribution of species with a double lateral line. *Journal of Ichthyology*, 51, 209–216.

Nelson, G. J. (1969). Infraorbital bones and their bearing on the phylogeny and geography of osteoglossomorphs fishes. *American Museum Novitates*, 2394, 1–37.

Nelson, G. J. (1972). Cephalic sensory canals, pitlines, and the classification of esocoid fishes, with notes on galaxiids and other teleosts. *American Museum Novitates*, 2492, 1–49.

Nelson, G. J. (1983). *Anchoa argentivittata*, with notes on other eastern Pacific anchovies and the Indo-Pacific genus *Encrasicholina*. *Copeia*, 1983, 48–54.

Nelson, G. J. (1984). Notes on the rostral organ of anchovies (Family Engraulidae). *Japanese Journal of Ichthyology*, 31, 86–87.

Nelson, J. S. (2006). *Fishes of the world*, 4th ed., Hoboken, NJ: John Wiley & Sons.

Nielsen, J. G., & Bertelsen, E. (1985). The gulper-eel family Saccopharyngidae (Pisces, Anguilliformes). *Steenstrupia*, 11, 157–206.

Northcutt, R. G. (1989). The phylogenetic distribution and innervation of craniate mechanoreceptive lateral lines. In S. Coombs, P. Görner, & H. Münz, H. (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 17–78). New York: Springer-Verlag.

Northcutt, R. G. (1997). Evolution of gnathostome lateral line ontogenies. *Brain, Behavior and Evolution*, 50, 25–37.

Northcutt, R. G. (2003). Development of the lateral line system in the channel catfish. In H. I. Browman, & A. B. Skiftesvik (Eds)., *The big fish bang: Proceedings of the 26th annual larval fish conference* (pp. 137–159). Bergen, Norway: Institute of Marine Research.

Northcutt, R. G., & Bemis, W. E. (1993). Cranial nerves of the coelocanth, *Latimeria chalumnae* [Osteichthyes: Sarcopterygii: Actinistia] and comparisons with other craniata. *Brain, Behavior and Evolution*, *42* (Supplement 1), 1–77.

Northcutt, R. G., & Bleckmann, H. (1993). Pit organs in axolotls: A second class of lateral line neuromasts. *Journal of Comparative Physiology A*, 172, 439–446.

Northcutt, R. G., Catania, K. C., & Riley, B. B. (1994). Development of lateral line organs in the axolotl. *Journal of Comparative Neurology*, 340, 480–514.

Northcutt, R. G., Brändle, K., & Fritzsch, B. (1995). Electroreceptors and mechanosensory lateral line organs arise from single placodes in axolotls. *Developmental Biology*, 168, 358–373.

Northcutt, R. G., Holmes, P. H., & Albert, J. S. (2000). Distribution and innervation of lateral line organs in the channel catfish. *Journal of Comparative Neurology*, 421, 570–592.

Nuñez, V. A., Sarrazin, A. F., Cubedo, N., Allende, M. L., Dambly-Chaudière, C., & Ghysen, A. (2009). Postembryonic development of the posterior lateral line in the zebrafish. *Evolution and Development*, 11, 391–404.

Okamura, A., Oka, H. P., Yamada, Y., Utoh, T., Mikawa, N., Horie, N., & Tanaka, S. (2002). Development of lateral line organs in leptocephali of the freshwater eel *Anguilla japonica* (Teleostei, Anguilliformes). *Journal of Morphology*, 254, 81–91.

Omarkhan, M. (1948). The lateral sensory canals of larval *Notopterus*. *Proceedings of the Zoological Society of London*, 118, 938–972.

O'Neill, P., McLole, R. G., & Baker, C. V. H. (2007). A molecular analysis of neurogenic placode and cranial sensory ganglion development in the shark, *Scyliorhinus canicula*. *Developmental Biology* 304, 156–181.

Ota, K. G., Kuraku, S., & Kuratani, S. (2007). Hagfish embryology with reference to the evolution of neural crest. *Nature*, 446, 672–675.

Otsuka, M., & Nagai, S. (1997). Neuromast formation in the prehatching embryos of the cod-fish, *Gadus macrocephalus Tilesius*. *Zoological Science*. 14, 475–481.

Parenti, L. R. (2008). A phylogenetic analysis and taxonomic revision of ricefishes, *Oryzias* and relatives (Beloniformes, Adrianichthyidae). *Zoological Journal of the Linnean Society*, 154, 494–610.

Parin, N. V., & Astakhov, D. A. (1982). Studies on the acoustico-lateralis system of beloniform fishes in connection with their systematics. *Copiea*, 1982, 276–291.

Parker, G. J. (1904). The function of the lateral-line organs in fishes. In *Contributions from the Biological Laboratory of the Bureau of Fisheries at Woods Hole*, *Massachusetts* (pp. 183–207).

Paxton, J. R. (1989). Synopsis of the whalefishes (family Cetomimidae) with descriptions of four new genera. *Records of the Australian Museum*, 41, 135–206.

Peach, M. B., & Rouse, G. W. (2000). The morphology of the pit organs and lateral line canal neuromasts of *Mustelus antarcticus* (Chondrichthyes: Triakidae). *Journal of the Marine Biological Association of the United Kingdom*, 80, 155–162.

Peach, M. B., & Marshall, N. J. (2009). The comparative morphology of pit organs in elasmobranchs. *Journal of Morphology*, 270, 688–701.

Pehrson, T. (1944a). The development of latero-sensory canal bones in the skull of *Esox lucius*. *Acta Zoologica (Stockholm)*, 25, 135–157.

Pehrson, T. (1944b). Some observations on the development and morphology of the dermal bones in the skull of *Acipenser* and *Polyodon*. *Acta Zoologica (Stockholm)*, 25, 27–48.

Peters, H. M. (1973). Anatomie und Entwicklungsgeschichte des Lateralissystems von *Tilapia* (Pisces, Cichlidae). *Zeitschrift fur Morphologie der Tiere*, 74, 89–161.

Pichon, R., & Ghysen, A. (2004). Evolution of posterior lateral line development in fish and amphibians. *Evolution & Development*, 6, 187–193.

Pietsch, T. W. (2009). *Oceanic anglerfishes*: *Extraordinary diversity in the deep sea*. Berkeley: University of California Press.

Piotrowski, T., & Northcutt, R. G. (1996). The cranial nerves of the Senegal bichir, *Polypterus senegalus* (Osteichthyes: Actinopterygii: Cladistia). *Brain, Behavior and Evolution*, 47, 55–102.

Poling, K. R., & Fuiman, L. A. (1997). Sensory development and concurrent behavioural changes in Atlantic croaker larvae. *Journal of Fish Biology*, 51, 402–421.

Popper, A. N., & Fay, R. R. (2011). Rethinking sound detection by fishes. *Hearing Research*, 273, 25–36.

Potthoff, T. (1984). Clearing and staining techniques. In H. G. Moser (Ed.), *Ontogeny and systematics of fishes* (pp. 35–37). Lawrence, KS: Allen Press.

Poulson, T. L. (1963). Cave adaptations in amblyopsid fishes. *American Midland Naturalist*. 70, 257–290.

Prokofiev, A. M., & Kukuev, E. I. (2009). Systematics and distribution of black swallowers of the genus *Chiasmodon* (Perciformes: Chiasmodontidae). *Journal of Ichthyology*, 49, 899–939.

Puzdrowski, R. L. (1989). Peripheral distribution and central projections of the lateral-line nerves in goldfish, *Carassius auratus*. *Brain, Behavior and Evolution*, 34, 110–131.

Raible, D. W., & Kruse, G. J. (2000). Organization of the lateral line system in embryonic zebrafish. *Journal of Comparative Neurology*, 421, 189–198.

Rass, T. S. (1970). *Greenlings: Taxonomy, biology, interoceanic transplantation*. Transactions of the Institute of Oceanology, Vol. 59. Jerusalem: Israel Program for Scientific Translations. (Translated from Russian.)

Reno, H. W. (1966). The infraorbital canal, its lateral-line ossicles and neuromasts, in the minnows *Notropis volucellus* and *N. buchanani*. *Copeia*, 1966, 403–413.

Reno, H. W. (1969). Cephalic lateral-line systems of the cyprinid genus *Hybopsis*. *Copiea*, 1969, 736–773.

Reno, H. W. (1971). The lateral-line system of the silverjaw minnow, *Ericymba buccata* Cope. *Southwestern Naturalist*, 15, 347–358.

Rosen, D. E., & Mendelson, J. R. (1960). The sensory canals of the head in poeciliid fishes (Cyprinodontiformes), with reference to dentitional types. *Copeia*, 1960, 203–210.

Roth, A. (2010). Development of the lateral line mechanoreceptors in the catfish *Silurus glanis*. *Naturwissenschaften*, 97, 645–653.

Rouse, G. W., & Pickles, J. O. (1991a). Paired development of hair cells in neuromasts of the teleost lateral line. *Proceedings of the Royal Society of London*, 246, 123–128.

Rouse, G. W., & Pickles, J. O. (1991b). Ultrastructure of free neuromasts of *Bathygobius fuscus* (Gobiidae) and canal neuromasts of *Apogon cyanosoma* (Apogonidae). *Journal of Morphology*, 209, 111–120.

Sakamoto, K. (1984). Interrelationships of the family Pleuronectidae (Pisces: Pleuronectiformes). *Memoirs of the Faculty of Fisheries: Hokkaido University (Japan)*, 31(1–2), 95–215.

Sapède, D., Gompel, N., Dambly-Chaudière, C., & Ghysen, A. (2002). Cell migration in the postembryonic development of the fish lateral line. *Development*, 129, 605–615.

Sasaki, K., Tanaka, T., & Takata, Y. (2006). Cranial morphology of *Ateleopus japonicus* (Ateleopodidae: Ateleopodiformes), with a discussion on metamorphic mouth migration and lampridiform affinities. *Ichthyological Research*, 53, 254–263.

Schaefer, S. A., & Aquino, A. E. (2000). The postotic laterosensory canal pterotic branch homology in catfishes. *Journal of Morphology*, 246, 213–227.

Schemmel, C. (1973). Les organs sensoriels cutanes du genre *Astyanax* (Pisces, Characidae) ches les formes occupant des biotopes souterrains. *Annales de Spéléologie*, 28, 209–219.

Schlosser, G. (1999). Loss of ectodermal competence for lateral line placode formation in the direct developing frog, *Eleutherodactylus coqui*. *Developmental Biology*, 213, 354–369.

Schlosser, G. (2010). Making senses: Development of vertebrate cranial placodes. *Internatiional Review of Cell and Molecular Biology*, 283, 129–234.

Schmitz, A., Bleckmann, H., & Mogdans, J. (2008). Organization of the superficial neuromast system in goldfish, *Carrasius auratus*. *Journal of Morphology*, 269, 751–761.

Schuster, K., Dambly-Chaudière, C., & Ghysen, A. (2010). Glial cell line-derived neurotrophic factor defines the path of developing and regenerating axons in the lateral line system of zebrafish. *Proceedings of the National Academy of Sciences of the USA*, 107, 19531–19536.

Schwalbe, M. A. B., Bassett, D. K., & Webb, J. F. (2012). Feeding in the dark: Lateral line mediated feeding behavior in the peacock cichlid, *Aulonocara stuartgranti*. *Journal of Experimental Biology*, 215, 2060–2071.

Shibuya, A., Zuanon, J., De Araújo, M. L. G., & Tanaka, S. (2010). Morphology of lateral line canals in Neotropical freshwater stingrays (Chondrichthyes: Potamotraygonidae) from Negro River, Brazilian Amazon. *Neotropical Ichthyology*, 8, 867–876.

Sideleva, V. G. (1981). Structural features of the seismosensory system of freshwater sculpins and Baikal oil-fishes (Cottidae and Comephoridae) in connection with a pelagic mode of life. *Journal of Ichthyology*, 20, 119–124.

Siming, D., & Hongxi, Z. (1986). Comparative studies of the lateral line canal system of families to be related with the Carangidae. In T. Uyeno, R. Arai, T. Taniuchi, & K. Matsuura (Eds.), *Indo-Pacific fish biology: Proceedings of the second international conference on Indo-Pacific fishes* (pp. 561–569). Tokyo: Ichthyological Society of Japan.

Simmons, A. M., Costa, L. M., & Gerstein, H. B. (2004). Lateral line-mediated rheotactic behavior in tadpoles of the African clawed frog (*Xenopus laevis*). *Journal of Comparative Physiology A*, 190, 747–758.

Sire, J. Y., & Akimenko, M. A. (2004). Scale development in fish: a review, with description of *sonic hedgehog (shh)* expression in the zebrafish (*Danio rerio*). *International Journal of Developmental Biology*, 48, 233–247.

Sisneros, J. A. (2009). Adaptive hearing in the vocal plainfin midshipman fish: Getting in tune for the breeding season and its implications for acoustic communication. *Integrative Zoology*, 4, 33–42.

Smith, S. C., Lannoo, M. J., & Armstrong, J. B. (1988). Lateral-line neuromast development in *Ambystoma mexicanum* and a comparison with *Rana pipiens*. *Journal of Morphology*, 198, 367–379.

Smith, W. L., Webb, J. F., & Blum, S. D. (2003). The evolution of the laterophysic connection with a revised phylogeny and taxonomy of butterflyfishes (Teleost: Chaetodontidae). *Cladistics*, 19, 287–306.

Song, J., & Northcutt, R. G. (1991). Morphology, distribution and innervation of the lateral-line receptors of the Florida gar, *Lepisosteus platyrhincus*. *Brain, Behavior and Evolution*, 37, 10–37.

Song, W., & Song, J. (2012). Morphological structure and peripheral innervation of the lateral line system in the Siberian sturgeon (*Acipenser baerii*). *Integrative Zoology*, 7, 83–93.

Song, J., Yan, H. Y., & Popper, A. N. (1995). Damage and recovery of hair cells in fish canal (but not superficial) neuromasts after gentamicin exposure. *Hearing Research*, 91, 63–71.

Stephens, R. R. (1985). The lateral line system of the gizzard shad, *Dorosoma cepedianum* Lesueur (Pisces: Clupeidae). *Copeia*, 1985, 540–556.

Stephens, R. R. (2010). A description of the cephalic lateralis system of *Anchoa mitchilli* (Valenciennes) (Clupeomorpha: Engraulidae) with identification of synapomorphies for the Engraulidae. *Proceedings of the Biological Society of Washington*, 123, 8–16.

Suli, A., Watson, G. M., Rubel, E. W., & Raible, D. W. (2012). Rheotaxis in larval zebrafish is mediated by lateral line mechanosensory hair cells. *PLoS One*, 7, 1–6.

Takeuchi, H., Tokuda, K., Kanagawa, N., & Hosoya, K. (2011). Cephalic lateral line canal system of the golden venus chub, *Hemigrammocypris rasborella* (Teleostei: Cypriniformes) *Ichthyological Research*, 58, 175–179.

Tamanaka, Y., Nakae, M., Fukuda, E., & Sasaki, K. (2010). Monophyletic origin of the dorsally arched lateral line in Teleostei: Evidence from nerve innervation patterns. *Ichthyological Research*, 57, 49–61.

Tarby, M. L., & Webb, J. F. (2003). Development of the supraorbital and mandibular lateral line canals in the cichlid, *Archocentrus nigrofasciatus*. *Journal of Morphology*, 254, 44–57.

Tekye, T. (1989). Learning and remembering the environment in the blind cave fish, *Anoptichthys jordani*. *Journal of Comparative Physiology A*, 164, 655–662.

Tekye, T. (1990). Morphological differences in neuromasts of the blind cave fish *Astyanax hubbsi* and the sighted river fish *Astyanax mexicanus*. *Brain, Behavior and Evolution*, 35, 23–30.

Tricas, T. C., Kajiura, S. M., & Kosaki, R. K. (2006). Acoustic communication in territorial butterflyfish: Test of the sound production hypothesis. *Journal of Experimental Biology*, 209, 4994–5004.

van Bergeijk, W. A., & Alexander, S. (1962). Lateral line canal organs on the head of *Fundulus heteroclitus*. *Journal of Morphology*, 110, 333–346.

Van Netten, S. M., & van Maarseveen, F. T. P. W. (1994). Mechanophysiological properties of the supraorbital lateral line canal in ruffe (*Acerina cernua* L.). *Proceedings of the Royal Society of London B: Biological Sciences*, 256, 239–246.

Van Trump, W. J., & McHenry, M. J. (2008). The morphology and mechanical sensitivity of lateral line receptors in zebrafish larvae (*Danio rerio*). *Journal of Experimental Biology*, 211, 2105–2115.

Van Trump, W. J., Coombs, S., Duncan, K., & McHenry, M. J. (2010). Gentamicin is ototoxic to all hair cells in the fish lateral line system. *Hearing Research*, 261, 42–50.
Vasconcelos, R., & Ladich, F. (2008). Development of vocalization, auditory sensitivity and acoustic communication in the Lusitanian toadfish *Halobatrachus didactylus*. *Journal of Experimental Biology*, 211, 502–509.
Vasconcelos, R. O., Fonseca, P. J., Amorim, M. C. P., & Ladich, F. (2011). Representation of complex vocalizations in the Lusitanian toadfish auditory system: Evidence of fine temporal frequency and amplitude discrimination. *Proceedings of the Royal Society of London B: Biological Sciences*, 278, 826–834.
Vischer, H. A. (1989). The development of lateral-line receptors in *Eigenmannia* (Teleostei, Gymnotiformes). I. The mechanoreceptive lateral-line system. *Brain, Behavior, and Evolution*, 33, 205–222.
Voronina, E. P. (2009). Structure of lateral-line scales in representatives of families of the order Pleuronectiformes. *Journal of Ichthyology*, 49, 940–961.
Voronina, E. P., & Hughes, D. R. (2011). Types and developmental pathways of lateral line scales in some teleost species. *Acta Zoologica (Stockholm)*, DOI: 10.1111/j.1463–6395.2011.00534.x
Wada, H., Hamaguchi, S., & Sakaizumi, M. (2008). Development of diverse lateral line patterns on the teleost caudal fin. *Developmental Dynamics*, 237, 2889–2902.
Wada, H., Ghysen, A., Satou, C., Higashijima, S., Kawakami, K., Hamaguchi, S., & Sakaizumi, M. (2010). Dermal morphogenesis controls lateral line patterning during postembryonic development of teleost fish. *Developmental Biology*, 340, 583–594.
Wahnschaffe, U., Bartsch, U., & Fritzsch, B. (1987). Metamorphic changes in the lateral-line system of Anura. *Anatomy and Embryology*, 175, 431–442.
Wark, A. R., & Peichel, C. L. (2010). Lateral line diversity among ecologically divergent threespine stickleback populations. *Journal of Experimental Biology*, 213, 108–117.
Webb, J. F. (1988). *Comparative morphology and evolution of the lateral line system in the labroid fishes (Pisces: Perciformes)*. Ph.D. dissertation, Boston University.
Webb, J. F. (1989a). Developmental constraints and evolution of the lateral line system in teleost fishes. In S. Coombs, P. Görner, & H. Münz, H. (Eds.), *The mechanosensory lateral line: neurobiology and evolution* (pp. 79–98). New York: Springer-Verlag.
Webb, J. F. (1989b). Gross morphology and evolution of the mechanosensory lateral line system in teleost fishes. *Brain, Behavior and Evolution*, 33, 34–53.
Webb, J. F. (1989c). Neuromast morphology and lateral line trunk ontogeny in two species of cichlids: An SEM study. *Journal of Morphology*, 202, 53–68.
Webb, J. F. (1990a). Comparative morphology and evolution of the lateral line system in the Labridae (Perciformes: Labroidei). *Copeia*, 1990, 137–146.
Webb, J. F. (1990b). Ontogeny and phylogeny of the trunk lateral line system in cichlid fishes. *Journal of Zoology (London)*, 221, 405–418.
Webb, J. F. (1998). Laterophysic connection: A unique link between the swim bladder and the lateral-line system in *Chaetodon* (Perciformes: Chaetodontidae). *Copeia*, 1998, 1032–1036.
Webb, J. F. (1999). Diversity of fish larvae in development and evolution. In B. K. Hall & M. H. Wake (Eds.), *Origin and evolution of larval forms* (pp. 109–158). San Diego: Academic Press.
Webb, J. F. (2000). Mechanosensory lateral line: Functional morphology and neuroanatomy. In G. Ostrander (Ed.), *Handbook of experimental animals: - The laboratory fish* (pp. 236–244). London: Academic Press.
Webb, J. F. (2011). Lateral line structure. In A. P. Farrell (Ed.), *Encyclopedia of fish physiology: From genome to environment*, Vol. 1 (pp. 336–346). San Diego: Academic Press.
Webb, J. F., & Northcutt, R. G. (1997). Morphology and distribution of pit organs and canal neuromasts in non-teleost bony fishes. *Brain, Behavior and Evolution*, 50, 139–151.
Webb, J. F., & Shirey, J. E. (2003). Post-embryonic development of the lateral line canals and neuromasts in the zebrafish. *Developmental Dynamics*, 228, 370–385.

Webb, J. F., Smith, W. L., & Ketten, D. R. (2006). The laterophysic connection and swim bladder in butterflyfishes in the genus *Chaetodon* (Perciformes: Chaetodontidae). *Journal of Morphology*, 267, 1338–1355.

Webb, J. F., Montgomery, J., & Mogdans, J. (2008). Mechanosensory lateral line and fish bioacoustics. In J. F. Webb, R. R. Fay, & A. N. Popper (Eds.), *Fish bioacoustics* (pp. 145–182). New York: Springer-Verlag.

Webb, J. F., Herman, J. L., Woods, C. F., & Ketten, D. R. (2010). The ears of butterflyfishes: Hearing generalists on noisy coral reefs? *Journal of Fish Biology*, 77, 1434–1451.

Webb, J. F., Walsh, R. M., Casper, B., Mann, D. A., Kelly, N., & Cicchino, N. (2012). Ontogeny of the ear, hearing capabilities, and laterophysic connection in the spotfin butterflyfish (*Chaetodon ocellatus*). *Environmental Biology of Fishes*, DOI 10.1007/s10641–012–9991–7.

Weber, E. H. (1820). *De aure et auditu hominis et animalium: Pars I—De aure animalium aquatilium*. Leipzig: Gehard Fleischer.

Weeg, M. S., & Bass, A. H. (2000). Central lateral line pathways in a vocalizing fish. *Journal of Comparative Neurology*, 418, 41–64.

Weeg, M. S., & Bass, A. H. (2002). Frequency response properties of lateral line SNs in a vocal fish, with evidence for acoustic sensitivity. *Journal of Neurophysiology*, 88, 1252–1262.

Wellenreuther, M., Brock, M., Montgomery, J., & Clements, K.D. (2010). Comparative morphology of the mechanosensory lateral line system in a clade New Zealand triplefin fishes. *Brain, Behavior and Evolution*, 75, 292–308.

Whitfield, T. T. (2005). Lateral line: precocious phenotypes and planar polarity. *Current Biology*, 15, R67–70.

Wicht, H., & Northcutt, R. G. (1995). Ontogeny of the head of the Pacific hagfish (*Eptatretus stouti* Myxinoidea): Development of the lateral line system. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 349, 119–134.

Williams, J. A., & Holder, N. (2000). Cell turnover in neuromasts of zebrafish larvae. *Hearing Research*, 143, 171–181.

Wilson, M., Montie, E. W., Mann, K. A., & Mann, D. A. (2009). Ultrasound detection in the Gulf menhaden requires gas-filled bullae and an intact lateral line. *Journal of Experimental Biology*, 212, 3422–3427.

Windsor, S. P., & McHenry, M. J. (2009). The influence of viscous hydrodynamics on the fish lateral-line system. *Comparative and Integrative Biology*, 49, 691–701.

Windsor, S. P., Tan, D., & Montgomery, J. C. (2008). Swimming kinematics and hydrodynamic imaging in the blind Mexican cave fish (*Astyanax fasciatus*). *Journal of Experimental Biology*, 211, 2950–2959.

Wittbrodt, J, Shima, A., & Schartl, M. (2002). Medaka—A model organism from the Far East. *Nature Reviews Genetics*, 3, 53–64.

Wonsettler, A. L., & Webb, J. F. (1997). Morphology and development of the multiple lateral line canals on the trunk in two species of *Hexagrammos* (Scorpaeniformes: Hexagrammidae). *Journal of Morphology*, 233, 195–214.

Wright, M. R. (1951). The lateral line system of sense organs. *Quarterly Review of Biology*, 26, 264–280.

Wueringer, B. E., Peverell, S. C., Seymour, J., Squire, L., & Collin, S. P. (2011). Sensory systems in sawfishes. 2. The lateral line. *Brain, Behavior and Evolution*, 78, 150–161.

Yabe, M. (1985). Comparative osteology and myology of the superfamily Cottoidea (Pisces: Scorpaeniformes) and its phylogenetic classification. *Memoirs of the Faculty of Fisheries Hokkaido University*, 32, 1–130.

Yabumoto, Y., & Uyeno, T. (1984). Osteology of the rice fish, *Oryzias latipes*. *Bulletin of the Kitakyushu Museum of Natural History*, 5, 143–161.

Yan, H. Y., & Popper, A. N. (1993). Acoustic intensity discrimination by the cichlid fish *Astronotus ocellatus*. *Journal of Comparative Physiology*, 173, 347–351.

Yasuoka, A., Hirose, Y., Yoda, H., Aihara, Y., Suwa, H., Niwa, K., Sasado, T., Morinaga, C., Deguchi, T., Henrich, T., Iwanami, N., Kunimatsu, S., Abe, K., Kondoh, H., & Furutani-Seiki, M. (2004).

Mutations affecting the formation of posterior lateral line system in Medaka, *Oryzias latipes*. *Mechanisms of Development*, 121, 729–738.

Yatsu, A. (1986). Phylogeny and zoogeography of the subfamilies Xiphisterinae and Cebidichthyinae (Blennioidei, Stichaeidae). In T. Uyeno, R. Arai, T. Taniuchi, & K. Matsuura, K. (Eds.), *Indo-Pacific fish biology: Proceedings of the second international conference on Indo-Pacific fishes* (pp. 663–678). Tokyo: Ichthyological Society of Japan.

Yoshizawa, M., Goricki, S., Soares, D., & Jeffery, W. R. (2010). Evolution of a behavioral shift mediated by SNs helps cavefish find food in darkness. *Current Biology*, 20, 1631–1636.

Zacchei, A. M., & Tavolaro, P. (1988). Lateral line system during the life cycle of *Anguilla anguilla* (L.). *Bollettino di Zoologia*, 3, 145–153.

Zeddies, D. G. & Fay, R. R. (2005). Development of the acoustically evoked behavioral response in zebrafish to pure tones. *Journal of Experimental Biology*, 208, 1363–1372.

Zeddies, D. G., Fay, R. R., Alderks, P. W., Shaub, K. S., & Sisneros, J. A. (2010). Sound source localization by the plainfin midshipman fish, *Porichthys notatus*. *Journal of the Acoustical Society of America*, 127, 3104–3113.

The Hydrodynamics of Flow Stimuli

Matthew J. McHenry and James C. Liao

Keywords Boundary layer • Hair cell • Kármán gait • Lateral line • Localization • Neuromast • Predation • Reynolds number • Rheotaxis • Swimming • Turbulence • Vortex street • Unsteady flow

1 Introduction

The lateral line system allows a fish to respond to changes in its surroundings by detecting flow stimuli. The velocity, acceleration, pressure gradient, and shear stress of water at the surface of a fish may all serve as stimuli that yield cues about environmental change. All of these stimuli are governed by hydrodynamics. Therefore, an application of hydrodynamic principles offers insight into the information provided by the lateral line system. The present chapter aims to explain these principles and to illustrate how they may be applied to understand the role of the lateral line system in fish behavior.

M.J. McHenry (✉)
Department of Ecology & Evolutionary Biology, University of California, 321 Steinhaus Hall, Irvine, CA 92697, USA
e-mail: mmchenry@uci.edu

J.C. Liao
The Whitney Laboratory for Marine Bioscience, Department of Biology, University of Florida, 9505 Ocean Shore Blvd., St., Augustine, FL 32080, USA

S. Coombs et al. (eds.), *The Lateral Line*, Springer Handbook of Auditory Research 48,
DOI 10.1007/2506_2013_13, © Springer Science+Business Media New York 2013,
Published online: 29 June 2013

2 Hydrodynamic Principles

Hydrodynamic theory is concerned with the forces generated by water motion. Although this motion can be highly complex, it emerges from just two fundamental fluid forces. Inertial force is generated by the acceleration of water. Viscous force is created by a fluid's ability to adhere to itself and to surfaces. The relative magnitude of these forces, as estimated by the Reynolds number, indicates where a flow resides in a continuum between perfectly smooth (i.e., viscous-dominated) and completely turbulent (i.e., inertia-dominated). For the present discussion, the Reynolds number provides a major indicator of the nature of flow at the surface of the body, where flow stimuli are detected by mechanosensory neuromasts.

2.1 Dynamic Properties of a Fluid

Any flow field may be thought of as a tremendous number of infinitesimal volumes, each of which approximates a cube. These fluid cubes exert forces on one another and the obstacles that they encounter. Imagine extracting one of these cubes and suspending it in space under zero gravity. If you were to push the cube with your finger, it would accelerate at a rate determined by the force that you exert upon it, as predicted by Newton's Second Law:

$$\text{Force} = \text{mass} \times \text{acceleration}. \tag{1}$$

This equation can be reformulated to apply more broadly to fluid flows. The mass of the cube is equal to the product of its density (ρ) and infinitesimal volume (dV) (Fig. 1a). This volume is equal to the product of the area upon which the force acts (dS) and the linear dimension (dx) in the direction of the force (i.e., along the x- axis, Fig. 1a). When surrounded by water in a flow field, the cube's acceleration (du/dt) is created by a difference in the pressures acting to propel and resist the cube's motion (dp). Therefore, Eq. (1) for a volume of fluid may be rewritten as follows (Batchelor, 1967):

$$dp/dx = -\rho du/dt. \tag{2}$$

This relationship, one form of the Euler equations, has implications for flow sensing. For example, it indicates that fluid acceleration varies with the pressure gradient. This explains why canal neuromasts, which are sensitive to pressure gradients, are often described as acceleration detectors (see Section 3 and the chapter by van Netten & McHenry). However, a major assumption of this flow model is that the viscosity of the water may be neglected. Inviscid models are

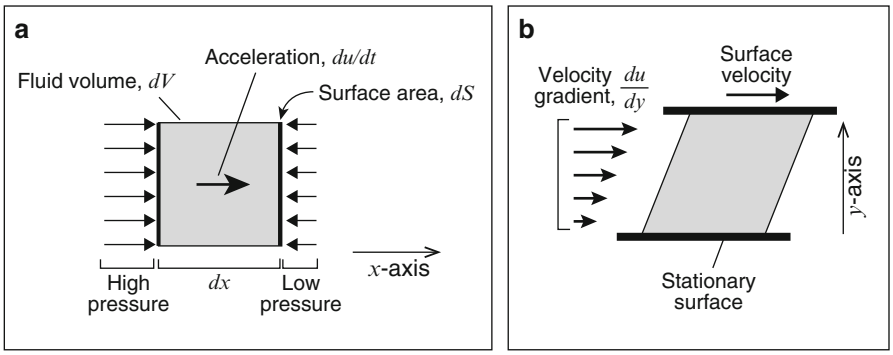

Fig. 1 The dynamic properties of a fluid. (**a**) A volume of fluid (gray box) accelerates in a pressure gradient (dp/dx, Eq. 2), which here decreases along the x-axis. (**b**) Shearing is generated in the fluid between two parallel surfaces (Eq. 3). In the case pictured, the top surface moves at a velocity parallel to a stationary surface. Fluid adhering to both surfaces creates a velocity gradient (du/dy)

reasonable under some conditions that are relevant to the lateral line system (see Section 4.1), but viscosity plays a key role in many aspects of flow sensing (see Sections 4.2 and 4.3).

Viscosity causes a fluid to resist shearing, which can be understood by returning to our virtual experiment. Imagine sliding a small volume of water between your forefinger and thumb. This motion causes the surface of your fingers to shear the fluid as they apply force directed parallel to the direction of motion (Fig. 1b). This force is proportional to both the rate of sliding between your fingers and water's viscosity. It is therefore not surprising that honey, with a relatively high viscosity, would be easier to feel between your fingers than water. Viscosity causes a fluid to adhere to a surface and thereby causes your forefinger to carry a layer of fluid as it slides in one direction and another layer to adhere to your thumb, moving in the opposite direction. This generates a gradient in flow velocity (du/dy), where y is perpendicular to the surfaces) in the space between your fingers (Fig. 1b). The force that creates this gradient per unit area of fluid is known as the shear stress (τ, with units of Pa) and it is proportional to the dynamic viscosity of the fluid (μ):

$$\tau = \mu \, du/dy. \tag{3}$$

This relationship, known as Newton's law of friction (Schlichting, 1979), demonstrates how shear stress relates to a spatial gradient in velocity. It follows that a steep gradient in flow velocity makes a relatively large contribution to the viscous force that may act on a submerged body.

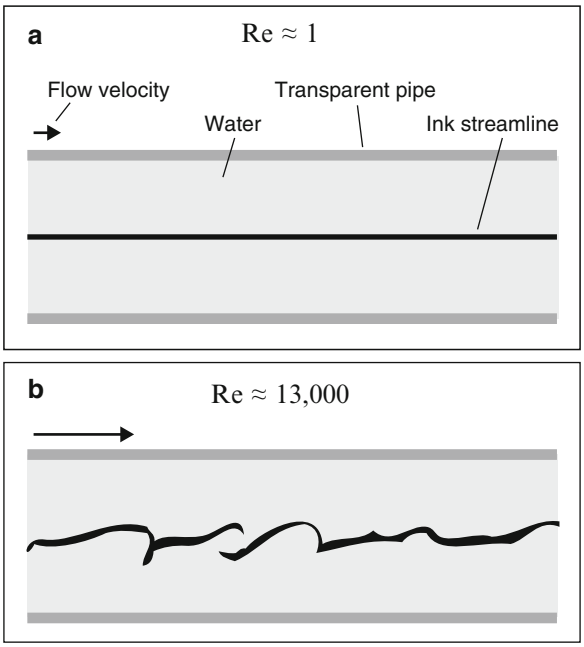

Fig. 2 Flow patterns vary with Reynolds number (Re). This principle was illustrated by the experiments of Osborne Reynolds, who examined flow through the center of a glass cylinder by means of an ink streamline, which is shown schematically here. (**a**) At relatively low Re values, the ink passes through the pipe as a straight line due to the laminar flow throughout its cross-section. (**b**) If flow speed is increased, higher Reynolds numbers are attained (Eq. 4) and the flow becomes turbulent at Re > 13,000 but may occur lower values due the geometry and texture of the surface over which the water flows (Reynolds, 1883; Van Dyke, 1982)

2.2 Reynolds Number

Flow patterns vary with the relative magnitude of viscous and inertial forces. As demonstrated by Osborne Reynolds, turbulence occurs when inertial forces are substantially greater than viscous forces (Reynolds, 1883). Reynolds found that flow is distinctly non-turbulent at low speeds or in liquids with a high viscosity (Fig. 2a) (Van Dyke, 1982). In this condition, known as laminar flow, the water throughout a pipe's cross section is directed downstream without lateral motion. Reynolds found that laminar flow could become turbulent by increasing flow speed, pipe diameter, or the density of water (Fig. 2b). He deduced that turbulence consistently appeared at a particular value of the following ratio of these parameters:

$$\mathrm{Re} = \rho u l / \mu, \tag{4}$$

where l is a characteristic length (e.g., the diameter of a pipe). This ratio, now known as the Reynolds number, may be mathematically derived (from Eqs. 2 and 3) as the ratio of inertial to viscous force (Schlichting, 1979). Therefore, Re indicates the hydrodynamic regime of a flow field by approximating the relative magnitude of these forces.

The Reynolds number serves as a key hydrodynamic index that may be easily calculated from measurements of length and speed. For example, the Reynolds number for a gliding fish (e.g., *Astyanax fasciatus;* Windsor et al., 2008) can be computed using the body length, gliding speed ($l = 5$ cm, $u = 12$ cm s^{-1}), and known physical properties of water ($\rho \approx 1000$ kg m^{-3}, $\mu \approx 0.001$ Pa s). The resulting value (Re ≈ 6000) suggests that the inertial force is dominant in determining the flow around the body. In this regime, models that neglect viscosity may predict large-scale flow patterns with reasonable accuracy.

Reynolds number calculations demonstrate how flow sensing is affected by hydrodynamics at multiple levels of organization. In the example of the gliding fish considered above, the Re value for a superficial neuromast on the rostrum uses the diameter of the neuromast as the characteristic length ($l \approx 10$ μm). Using the same speed of gliding and physical constants as above yields a low Reynolds number value (Re ≈ 1.2), which indicates that viscous forces are of a significant magnitude to flow at the receptor level.

2.3 Viscous Boundary Layers

Flow is sensed at the surface of a fish's body and viscosity plays a key role at this interface. By adhering to the surface, a spatial gradient in velocity is created between the surface and freestream flow. This gradient, known as the boundary layer, varies with the nature of freestream flow and the shape of the body. For a flat surface, boundary layers created by unidirectional or oscillating flows are well characterized by classical mathematical models (Prandtl, 1904; Schlichting, 1979). These models offer a first-order approximation of water motion over a fish's body that may be detected by the lateral line system.

The creation of a boundary layer is most easily understood for unidirectional flow, as seen in gliding fish (Daniel, 1981; Anderson et al., 2001). As a fish glides forward, water moves over the body in the opposite direction, like stacked layers running parallel to the surface. Before encountering the fish, these layers travel together with equal velocity and consequently displace over an equivalent distance for an interval of time (Fig. 3a*i*). As this fluid encounters the body, viscous adhesion slows the layer closest to the surface and thereby reduces its displacement (Fig. 3a*ii*). As the fluid continues to move along, layers further away are eventually slowed by the fluid closest to the surface (Fig. 3a*iii*–*iv*). This process establishes a spatial gradient of monotonically increasing velocity with distance from the surface (Fig. 3b). The distance from the surface where velocity is nearly equal to the freestream (u_∞) is called the boundary layer thickness (δ_{DC}). This is commonly

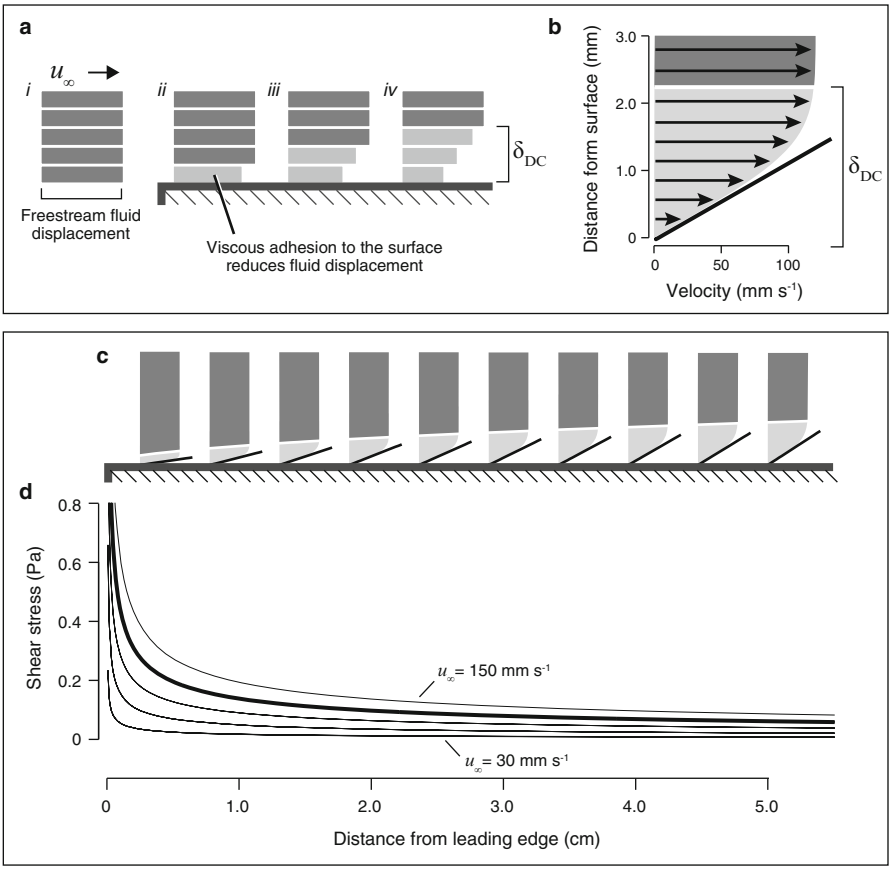

Fig. 3 The viscous boundary layer over a flat plate in unidirectional flow. (**a**) A schematic illustration of the displacement of layers of fluid as they move right-ward, over a flat surface. (*i*) Before encountering the surface, all layers of fluid displace by an equal amount for some interval of time (denoted by the horizontal length of each dark gray bar), determined by the freestream velocity, u_∞. (*ii*) As this fluid moves over the surface, the layer closest to the surface adheres to it and displaces less (light gray bar) than layers further away. (*iii*) Viscous adhesion between layers reduces the displacement of the layers further from the surface. (*iv*) This process proceeds to create the boundary layer, which is reflected in a gradient of displacement that increases with distance from the surface. (**b**) A boundary layer consequently exhibits a monotonic increase in velocity with distance. The boundary layer thickness (δ_{DC}) occurs at a distance at which the velocity is close to the freestream value. The shear stress at the surface is inversely proportional to the slope of the tangent line drawn for the velocity gradient. (**c**) A series of these tangent lines illustrates how the shear stress reduces as water moves further along a surface. This occurs while the boundary layer thickness (light gray region) increases. (**d**) The change in shear stress is shown as a function of position along the plate for variable freestream velocity (in increments of 30 mm s^{-1}) for the surface in (**c**)

defined as either $\delta_{DC} = 0.99u_\infty$ (used presently) or $\delta_{DC} = 0.90u_\infty$ (Batchelor, 1967). The boundary layer thickness increases with position along the surface (Fig. 3a, c), as indicated by the following relationship, derived from a consideration of viscous forces (Schlichting, 1979):

$$\delta_{DC} = 5\sqrt{\frac{\mu x}{\rho u_\infty}}, \tag{5}$$

where x is the distance along the surface from the leading edge.

Superficial neuromasts protruding from the surface of the body generally must detect a stimulus from within the boundary layer, where they are deflected by viscous drag (McHenry et al., 2008). This force varies with the velocity of flow, which depends on the height from the surface due to the boundary layer (see the chapter by van Netten & McHenry). The shear stress at the surface also varies with viscosity and the velocity gradient at the surface (Eq. 3) and thereby approximates the stimulus detected by a superficial neuromast (Rapo et al., 2009; Windsor & McHenry, 2009). For unidirectional flow over a flat plate (Fig. 3d), the shear stress is given by the following equation (Schlichting, 1979):

$$\tau_{surf} = 0.332\sqrt{\frac{\mu\rho u_\infty}{x}}. \tag{6}$$

Assuming the body's surface is nearly flat, this relationship indicates how the shear stress decreases with the velocity gradient along the body (Fig. 3c).

The boundary layer generated by oscillatory flow has a displacement amplitude that decreases at close proximity to the surface (Fig. 4a, b). The viscous interaction with the surface also creates a phase shift in the timing of velocity of up to 45° with respect to freestream flow (Fig. 4c). As a consequence, there are moments in an oscillation when the fluid close to the surface flows in the opposite direction from the freestream (e.g., at 1.7 ms and 6.7 ms in Fig. 4a). This variation in amplitude and phase emerges from the following model of the boundary layer profile for a pressure field over a flat plate (Batchelor, 1967; van Netten, 2006):

$$u(y, \omega, t) = u_\infty \cos(\omega t) - u_\infty \exp\left(-\frac{y}{\delta_{AC}}\right)\cos\left(\omega t - \frac{y}{\delta_{AC}}\right), \tag{7}$$

where δ_{AC} is the boundary layer thickness for oscillatory flow. This boundary layer thickness is defined as follows:

$$\delta_{AC} = \sqrt{\frac{2\mu}{\rho\omega}}. \tag{8}$$

The amplitude and phase of velocity within the boundary layer varies with the frequency of oscillation (Fig. 4a–c). At relatively high frequencies, inertial forces

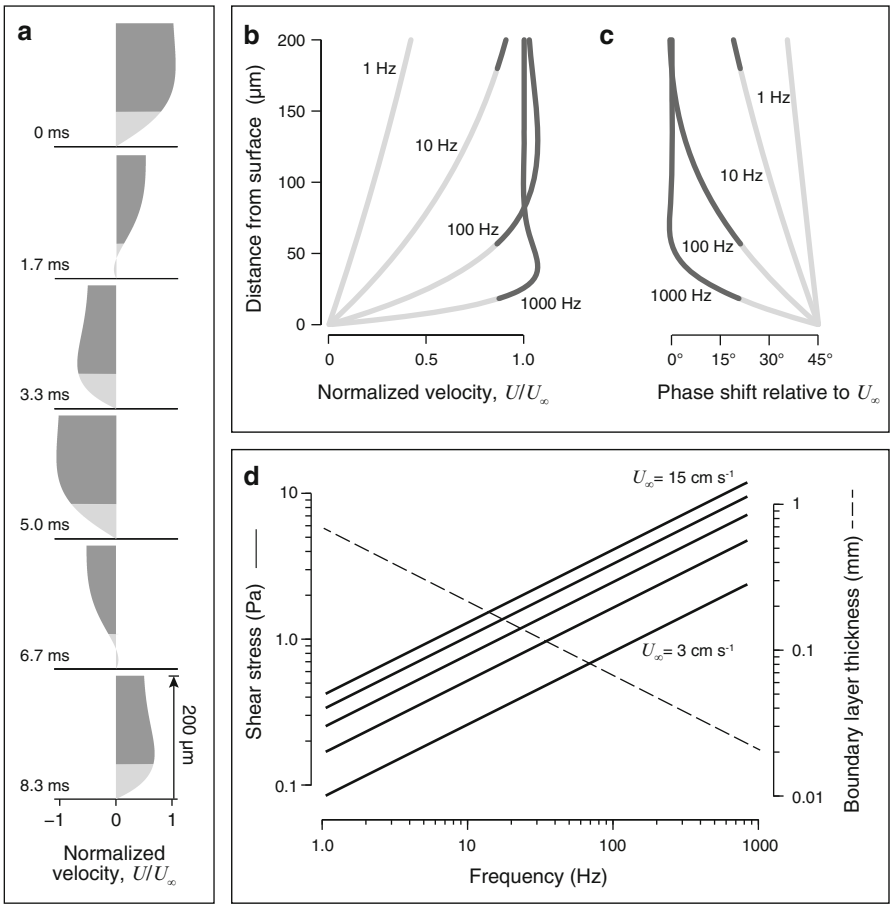

Fig. 4 The boundary layer over a flat plate in oscillating flow. (**a**) The boundary layer creates variation in the amplitude and timing of flow velocity as a function for distance from the surface. (**a–c**) The boundary layer thickness (δ_{AC}, Eq. 8) is denoted in light gray. Variation in (**b**) amplitude and (**c**) phase are shown as a function of distance from the surface for a variety of stimulus frequencies. (**d**) The surface shear stress (solid lines) and boundary layer thickness (dashed line) vary with stimulus frequency. The shear stress also varies with the amplitude of freestream velocity, as illustrated by the curves generated by stimuli ranging between 3 cm s $^{-1}$ and 15 cm s^{-1} in 3 cm s $^{-1}$ intervals

become more important and thereby reduce the boundary layer thickness (Eq. 8). As a consequence, the shear stress at the surface increases 10-fold over an increase in stimulus frequency from 1 Hz to 100 Hz (Fig. 4d), which is a range that encompasses the sensitivity of superficial neuromasts (McHenry et al., 2008). Therefore, the boundary layer serves as a mechanical filter that attenuates flow velocity for superficial neuromasts to an increasing degree at lower frequencies (see the chapter by van Netten & McHenry for details).

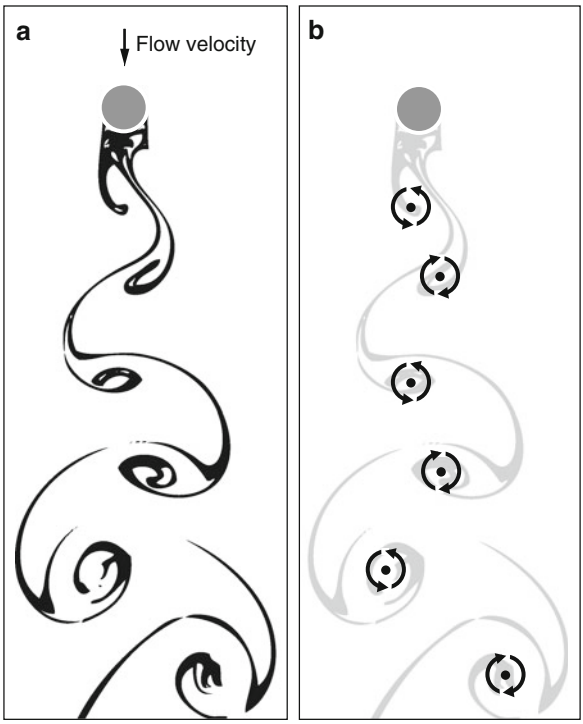

Fig. 5 The Kármán vortex street in the wake of a cylinder. (**a**) The wake behind a cylinder (gray circle) was visualized with smoke (in black) that was illuminated with a light sheet at Re = 140 (Van Dyke, 1982). (**b**) The vortex street is redrawn (in light gray) to illustrate the centers of vorticity within the drag wake (filled circles). The handedness of this vorticity (denoted by black arrows) alternates as vortices are shed on the left and right sides of the cylinder. Once shed, vortices are transported downstream with regular spacing in the direction of flow velocity

2.4 Vortices and Turbulence

Flow in a fish's environment is generally not unidirectional, nor does it oscillate at a single frequency, but is rather a heterogeneous combination of stimuli. This turbulence may provide a fish with information about environmental conditions or may hinder flow sensing by providing a source of noise. The chaos inherent to turbulence makes it a challenging frontier of fluid dynamics research (Muddada & Patnaik, 2011) and becomes an even more complicated subject when the flow field interacts with an animal's body. However, it is possible to create coherent vortices that provide a tractable means to study their influence on flow sensing and behavior (Sutterlin & Waddy, 1975; Webb, 1998; Liao et al., 2003a; Montgomery et al., 2003).

A stationary bluff body (e.g., a cylinder) in rapid flow creates a turbulent wake with a periodic shedding of vortices (Fig. 5). This trail of vorticity, called a Kármán vortex street (Kármán, 1954), occurs over a range of Reynolds numbers ($100 < Re < 150{,}000$) wherein inertial forces are strong enough to drive the creation of

vortices, but viscous forces maintain coherence in the wake. The frequency and spacing of vortices shed by a cylinder may be controlled for experimentation by altering the flow velocity and cylinder diameter. The relationship between these parameters is articulated by the Strouhal number (St):

$$\mathrm{St} = \frac{fd}{u}. \tag{9}$$

where f is the expected vortex shedding frequency and d is the cylinder diameter. A rigid geometry in flow is characterized by a fixed Strouhal number for flows in the inertial regime. For instance, measurements of the shedding frequency at a controlled flow speed have $\mathrm{St} \approx 0.2$ (Schewe, 1983; Blevins, 1990). It follows that an increase in cylinder diameter or a decrease in speed creates a proportionate decrease in shedding frequency. Once shed, a vortex is carried downstream by the prevailing current. Studies that manipulate the Kármán street behind a bluff body have been used to investigate the effect of turbulence on flow sensing in swimming fish (see Section 4.5).

3 Stimulus Detection by Neuromasts

It is necessary to define what neuromasts are capable of sensing to differentiate the flow stimuli that matter to a fish. This is a subject that is explored extensively in subsequent chapters (van Netten & McHenry; Chagnaud & Coombs) and is therefore only summarized for the purposes of the present discussion. The superficial and canal neuromasts of the fish lateral line system operate in a similar manner (Fig. 6). For both, water motion generates drag on a microscopic gelatinous structure, called a cupula, that extends from the skin of a fish into the water. Embedded within the extracellular matrix of the cupula are the hair bundles, each of which originates from a single hair cell and includes microvilli (commonly called stereocilia) and a nonmotile kinocilium (see chapter by Webb). The hair bundles contain the molecular machinery for mechanotransduction (Hudspeth, 1982). Therefore, a change in the membrane potential of the hair cells is generated as the hair bundles bend in response to fluid forces on the cupula (Fig. 7). Depolarization in the membrane results in the release of neurotransmitter glutamate to increase the firing rate of action potentials in the afferent neurons that innervate the hair cells (Flock, 1965; Liao, 2010).

The cupula of a superficial neuromast projects from the surface of the body, where it is directly exposed to flow (Figs. 6b and 7). With rare exceptions (e.g., *Astyanax fasciatus*, Teyke, 1990), the cupula of a superficial neuromast is around 50 μm tall (Mönz, 1989; Van Trump & McHenry, 2008), which generally resides within the boundary layer. For example, the boundary layer is 94 μm thick for a 36-Hz stimulus (Eq. 8), which is a frequency of maximal sensitivity in some species (Kroese & Schellart, 1992). This thickness increases to 1.4 mm at a position of 1 cm along the surface of the body (Eq. 5) for a gliding fish (see Section 2.2). This indicates that the boundary layer reduces the speed of flow that excites a superficial neuromast.

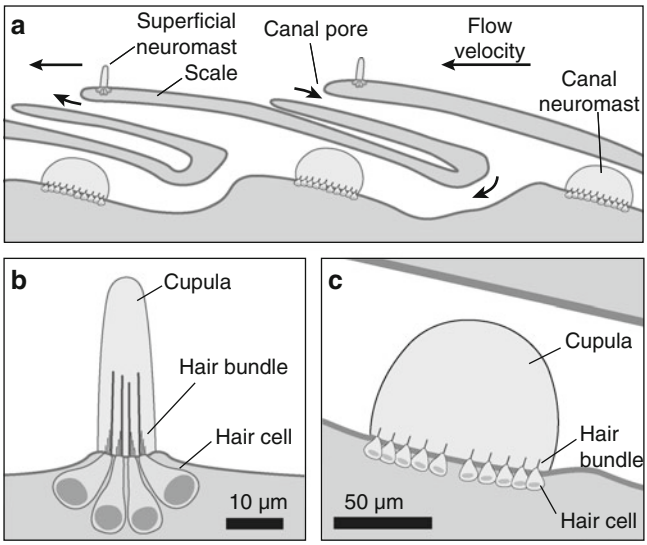

Fig. 6 The superficial and canal neuromasts of the lateral line system of fish. Schematic illustrations show (**a**) the relative position and major anatomical features of (**b**) superficial and (**c**) canal neuromasts. (**a**) The superficial neuromasts extend into the water surrounding the body, where they are directly exposed to water flow. Canal neuromasts are recessed in a channel beneath the scales, where they encounter flow when a pressure difference exists between the pores that open the channel to the surface (Weber & Schiewe, 1976; Kroese & Schellart, 1992). (**b**, **c**) Neuromasts consist of mechanosensory hair cells, a gelatinous cupula, and support cells (not shown). The hair bundle of each hair cell extends into the cupula and thereby detects deflections of the cupula created by fluid forces

The stimuli to which superficial neuromasts are sensitive may be considered in a variety of ways. Neurophysiological recordings of these receptors generally favor the notion that they are velocity sensitive (e.g., Görner, 1963), at least for frequencies below 50 Hz (Kroese & Schellart, 1992). As detailed in the chapter by van Netten and McHenry, this conclusion is consistent with our understanding for the biophysics of these receptors for frequencies above a few Hertz (see also Section 2.2). Viscous drag deflects the elastic hair cells within the cupula to generate its velocity sensitivity (McHenry et al., 2008). However, given the spatial variation in velocity that is created by the boundary layer and ambient flow conditions, it is not always apparent which velocity to consider as the stimulus for a superficial neuromast. For this reason, the shear stress at the surface (Eq. 3) can offer a more direct indication of the stimulus for these receptors (Rapo et al., 2009; Windsor & McHenry, 2009). The shear stress is proportional to viscosity and explicitly considers the velocity gradient (Eq. 3).

The position of a canal neuromast beneath the scales (Fig. 6c) enables these receptors to detect stimuli differently from superficial neuromasts. Although the cupula of a canal neuromast should also deflect in proportion to velocity due to viscous drag (Fig. 6a), this flow may be generated only when there is a pressure

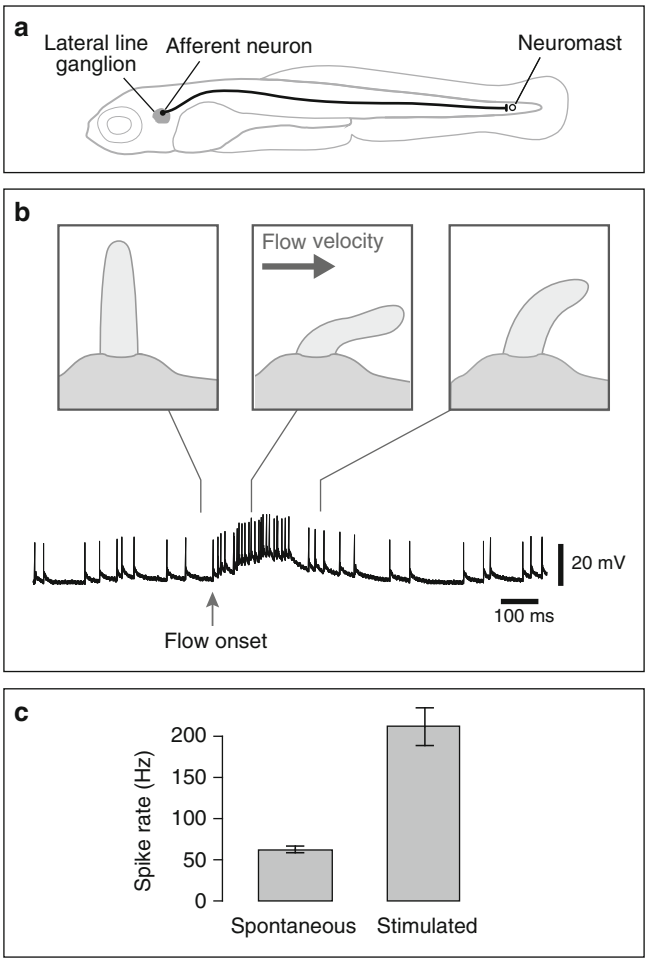

Fig. 7 Flow stimulus encoding by a lateral line afferent neuron (Liao, 2010). (**a**) Schematic illustration of the body of a 5-day old post-fertilization zebrafish larva with the location of an individual superficial neuromast and its innervation from a single afferent neuron highlighted. The cell body to this neuron resides within the lateral line ganglion. (**b**) A whole-cell patch recording from this cell body demonstrates the changes in the frequency of action potentials (i.e., spike rate) that are elicited by a microjet flow stimulus directed toward the P6 neuromast. Schematic drawings of the deflections of the cupula were traced from video-recordings of this experiment. (**c**) The mean values (± 1 SE) of spike rate demonstrate a more than threefold increase above the spontaneous rate that was generated by the stimulus

difference at the pores that open the canal to the surface (Denton & Gray, 1989). In accordance with Euler's equation (Eq. 2), a pressure difference in a flow field may be generated by the acceleration of flow over the surface of the body. It is for this reason that a number of neurophysiological measurements have concluded that canal neuromasts function as acceleration detectors (Coombs & Montgomery, 1992;

Kroese & Schellart, 1992). However, pressure differences along the body may also be generated by spatial differences in velocity. This effect is apparent in the following expanded form of the Euler equation, which allows for spatial variation in velocity (Batchelor, 1967):

$$\frac{dp}{dx} = -\rho\left(\frac{du}{dt} + u\frac{du}{dx}\right). \tag{10}$$

This relationship demonstrates how the pressure gradient may vary with either flow acceleration (du/dt) or a spatial gradient in velocity ($u\ du/dx$). Therefore, it is more precise to define the stimulus for a canal neuromast as the pressure gradient over the body's surface or the pressure difference at the canal pores (Denton & Gray, 1988, 1989).

4 Case Studies

A deep understanding for flow sensing requires an explicit consideration of the stimuli to which the lateral line system is exposed. This notion is perhaps best illustrated by the prey localization behavior of predators. Investigators of this system have been able to interpret behavior in terms of the nervous stimuli generated by canal neuromasts, which may be predicted from a consideration of inviscid hydrodynamics. In contrast, obstacle detection by blind cavefish requires a consideration of viscous forces. The viscous boundary layer is also an essential component of flow sensing by larval prey fish when detecting a predator's strike. Despite these advances, it remains unresolved how flow stimuli are used by a fish to modulate swimming in still water and the Kármán gaiting adopted by fish in a turbulent flow field.

4.1 Prey Localization

Research on prey localization in fish offers the most comprehensive understanding of flow sensing in any animal. The mottled sculpin (*Cottus bairdi*) is a nocturnal predator that preys on swimming *Daphnia* in complete darkness. This is achieved by directing its approach toward the prey in the dark (Hoekstra & Janssen, 1985) and then capturing it with a suction feeding strike (Hoekstra & Janssen, 1986). Prey localization and capture require a functioning lateral line system (Hoekstra & Janssen, 1985), and this behavior can be elicited by a vibrating sphere stimulus in place of the prey (Coombs & Conley, 1997b). Therefore, the lateral line is both a necessary and sufficient sensory system for nocturnal predation in the mottled sculpin.

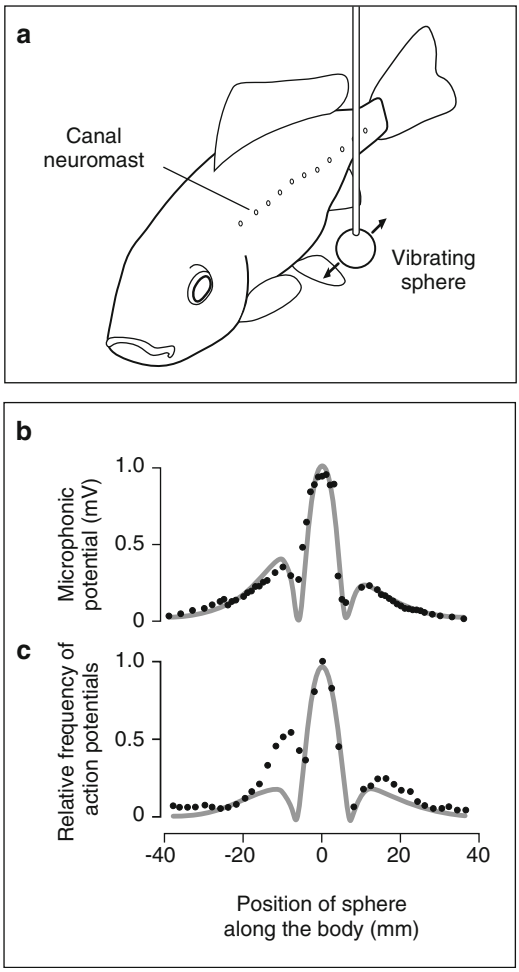

Fig. 8 Neurophysiology of prey localization. Recordings of the responses of neuromasts and lateral line afferent nerves to a vibrating sphere show a "Mexican hat" spatial pattern that may be predicted from hydrodynamic models. (**a**) These recordings were performed on anesthetized fish that were exposed to a vibrating sphere at a precisely controlled position with respect to the body. Plots show the amplitude of (**b**) microphonic potentials for individual neuromasts and (**c**) extracellular recordings of afferent fibers, which were recorded (circles) as a function of the position of the sphere along the length of the body. These patterns were predicted by the pressure gradient (gray line) generated by a dipole sphere. (**b**) The microphonic recordings were reported by Ćurčić-Blake and van Netten (2006) for a sphere positioned 1 cm away from the body of ruffe (body length: 10–13 cm). (**c**) Under similar experimental conditions, the relative afferent stimulus (which varies with the frequency of action potentials) was recorded in the goldfish (*Carassius auratus,* 9–12 cm) by Coombs et al. (1996)

The ability to stimulate the unconditioned predation behavior from a vibrating sphere has provided experimentalists with a critical tool for investigating the role of the lateral line system (Fig. 8a). The sphere offers a stimulus that is well controlled,

which has allowed for repeatable behavioral experiments and a neurophysiological preparation. These approaches have led to the finding that the variation in behavioral sensitivity with stimulus frequency follows the same trend as measured in the acceleration-sensitive fibers, but not velocity-sensitive fibers, in mottled sculpin (Coombs & Janssen, 1990). This suggests a dominant role for the canal neuromasts in mediating prey localization.

The stimuli detected by the canal neuromasts offer insight into an interesting feature of the prey localization behavior. Mottled sculpin exhibit the lowest accuracy at striking a vibrating sphere in the dark when they approach their target head-on. Strikes are significantly more accurate when approaching with an oblique body orientation that exposes the trunk lateral line to the source (Coombs & Conley, 1997b). This suggests that the trunk canal neuromasts offer enhanced spatial cues for localizing prey.

Major insight into these cues has emerged from mathematical models of the flow stimulus. The dipole pressure field generated by a vibrating sphere can be predicted from classic fluid dynamic theory that neglects the viscosity of the fluid (Kalmijn, 1988; Kalmijn 1989). Because of this inviscid assumption, the dipole model cannot predict boundary layer flows and hence the shear stress that stimulates the superficial neuromasts. However, this limitation does not matter to a consideration of the pressure gradients created by a vibrating sphere that stimulate the canal neuromasts (Fig. 8b, c). The extracellular potentials created by lateral line afferent neurons were recorded in the mottled sculpin for a range of positions of a vibrating sphere with respect to the body of an anesthetized fish. The frequency of action potentials that encode the intensity of flow was found to vary with a "Mexican hat" pattern as a function of the position of the sphere (Fig. 8c). A very similar spatial distribution is predicted for the amplitude of the pressure gradient in the mottled scuplin (Coombs & Conley, 1997a). This match between the flow model and neural response has been replicated in goldfish (*Carassius auratus*) (Coombs, 1994; Coombs et al., 1996; Goulet et al., 2008) and therefore appears in more than just nocturnal species. When this experiment was conducted in the ruffe (*Gymnocephalus cernuus* L.), the potentials generated by the hair cells of individual canal neuromasts were found to reflect closely the "Mexican hat" pattern (Fig. 8b, Ćurčić-Blake & van Netten, 2006). Further, computational fluid dynamics modeling (CFD) supported the assumption that viscosity may be neglected in models of dipole detection by the canal neuromasts (Rapo et al., 2009).

It remains unclear what cues are extracted from the array of neuromasts that determine the distance and orientation of a prey from a dipole field. The position of a vibrating sphere theoretically may be resolved through the use of a wavelet transformation (Ćurčić-Blake & van Netten, 2006) or from the zero-crossings and peaks in values of pressure gradient (Goulet et al., 2008) detected by the superficial neuromast stimuli. However, the spatial activation pattern varies in a complex way—not only with source position, but also source distance and orientation. Behavioral experiments to manipulate these factors revealed that the ability of mottled sculpin to determine source position is not guided by amplitude peaks (Coombs and Patton, 2009). Moreover, investigations into the central processing of

the lateral line system have yet to distinguish what cues are derived from this spatial pattern of stimuli (Bleckmann, 2008; see also the chapter by Bleckmann & Mogdans).

4.2 Obstacle Detection

The success of inviscid flow theory in modeling prey localization (Fig. 8b, c) appears to suggest that canal neuromasts are uninfluenced by the viscosity of water. This idea was put to the test with mathematical models of obstacle detection in the Mexican blind cavefish (*Astyanax mexicanus*). These animals use their lateral line system to sense changes in self-generated flow to avoid colliding with obstacles (Windsor et al., 2008). The hydrodynamic disturbances generated by these obstacles have been modeled with both an inviscid potential flow model (Hassan, 1985; 1992a,b) and a CFD model that included viscosity (Windsor et al., 2010a,b) (Fig. 9).

Both models considered the flow generated on the surface of the body as it glides toward and along a flat wall. A comparison of their results shows that the magnitude and pattern of the predicted pressure gradient differ substantially when viscosity is included. For example, when gliding along a wall, the CFD model predicts a change in pressure on the surface of the body that is more than 50 times greater than what is predicted by the potential flow model (Windsor et al., 2010a). Furthermore, the CFD model exhibits a substantially greater elevation in the pressure gradient as the distance decreases between the fish and the wall. Unlike the potential flow model, the CFD model can predict how the boundary layer around the body of a gliding fish is altered by its interaction with the wall. This demonstrates that the viscous interaction between the wall and the fish can substantially affect the pressure gradient on the surface of the fish's body. This finding holds even at high Reynolds numbers (Re = 6000), where one might predict a negligible contribution from viscosity. Therefore, the viscosity of water can influence flow sensing, even in flow that is governed largely by inertial hydrodynamics.

4.3 Predator Evasion

Although viscosity may be entirely neglected (e.g., prey localization) or have an indirect effect (e.g., obstacle detection) on the stimuli detected by canal neuromasts, viscous fluid dynamics are fundamental to sensing by superficial neuromasts. Creating a stimulus that may be detected by these receptors requires water motion relative to the body of a fish. Relative flow velocity is created in larval fish when attacked by a suction-feeding predator, which triggers a fast-start escape response in the larva to evade capture (McHenry et al., 2009).

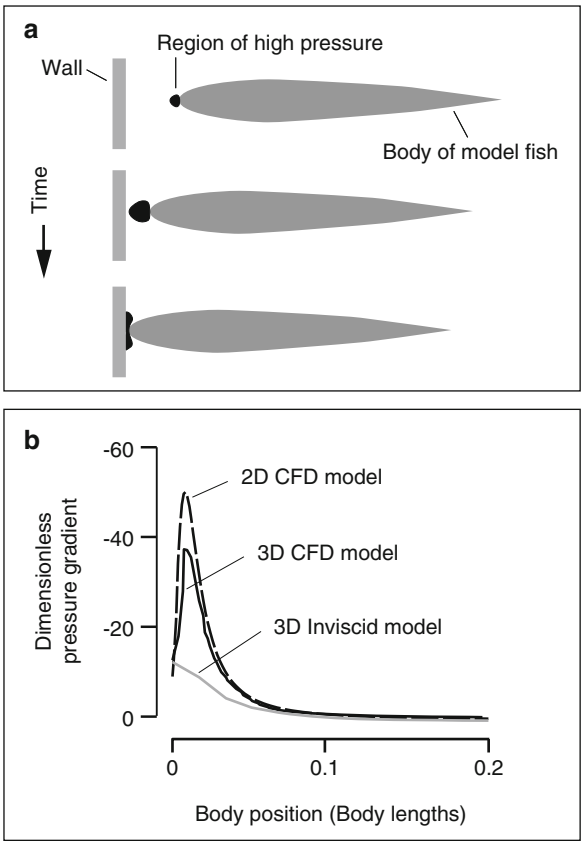

Fig. 9 Mathematical models of the flow around a Mexican blind cavefish as it glides toward a wall. This event has been modeled with potential flow theory (3D Inviscid model: Hassan, 1992) that neglects viscosity and computational fluid dynamics (CFD) models in 2D and 3D that include viscosity (Windsor et al., 2010). (**a**) Simulations of the approach (Re = 6000) reveal a region of high pressure (black shape) at the anterior-most point on the body that spreads laterally as the body approaches the wall. (**b**) The pressure gradient, the stimulus detected by canal neuromasts, predicted by this event differs between mathematical models. The 3D CFD model (black line) predicts a smaller maximum value than the 2D CFD model (dashed line), but a much greater value than the inviscid model (gray line). This demonstrates a case in which viscosity influences the flow stimulus for the canal neuromasts

Suction feeding is achieved by the rapid expansion of a predator's buccal cavity. This motion creates low pressure that accelerates water into the mouth with the funnel-shaped streamlines (Fig. 10a). Despite this complexity to the flow field, velocities directly in front of the mouth are nearly laminar and therefore relatively simple (Ferry-Graham et al., 2003; Higham et al., 2005). Because prey are generally targeted at this location, it is appropriate to apply the Euler equation (Eq. 10) to calculate changes in flow for a prey (Wainwright & Day, 2007). This flow may

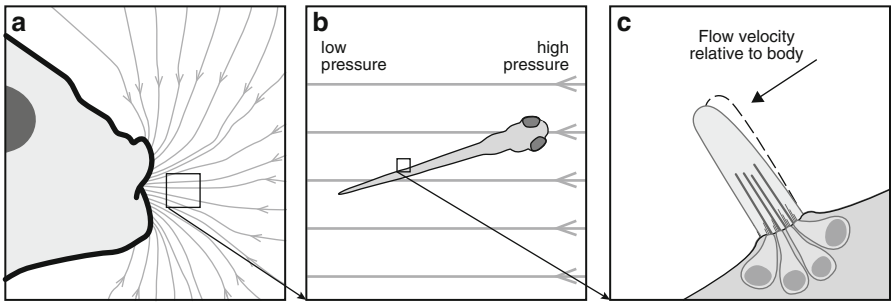

Fig. 10 Predator detection by a prey fish. (**a**) The flow field generated by a suction feeding sunfish (*Lepomis macrochirus,* shown from a lateral view) is illustrated with streamlines measured with particle tracking velocimetry (Higham et al., 2005). (**b**) Like the surrounding water, a fish prey (drawn as a larva from a dorsal view) is drawn toward the predator due to the low pressure generated by suction. (**c**) The flow velocity relative to the body is sensed by the deflection of the superficial neuromasts (Stewart & McHenry, 2010)

be approximated under experimental conditions that expose larval prey to a pressure gradient at a controlled rate to stimulate the escape response (McHenry et al., 2009).

For a larval fish exposed to this stimulus, flow acceleration is inversely proportional to density for both the body of a prey fish and the water. Therefore, the flow velocity relative to the prey depends on the density of the prey (ρ_{body}) relative to the water (ρ_{water}), as indicated by the specific gravity ($SG = \rho_{body}/\rho_{water}$). By modeling the relative flow predicted from measurements of specific gravity, the flow velocity of a predator's strike is substantially attenuated by the larva's body being carried along with the water. This is indicated by the maximum flow velocity from the larva's frame of reference during a strike, which is a small fraction (<6%) of the value from the earth-bound frame of reference. Further, subtle variation in the specific gravity can have a large influence on relative flow. For example, the specific gravity decreases by about 5% when the gas bladder inflates in zebrafish larvae (*Danio rerio*), at 4–5 days after fertilization, which causes the maximum relative velocity to decrease by 80% (Stewart & McHenry, 2010). Therefore, the ability of a larval fish to sense a predator is governed by a fluid–structure interaction between the body and flow field.

4.4 Propulsion

It is an old speculation that the lateral line system influences how a fish coordinates the kinematics of freestream swimming (Schulze, 1870). If such a mechanism exists, then it is not qualitatively apparent from watching the swimming of a fish that has had its lateral line system ablated (Dijkgraaf, 1963). Instead, the lateral line could provide stimuli that allow a fish to subtly tune its swimming to reduce the drag on the body. One version of this idea was formulated as the active drag reduction hypothesis (Lighthill, 1995).

The active drag reduction hypothesis is supported by research on clupeoid fishes. These animals possess a modified canal system that is considered to be highly sensitive to differences in pressure across the cranium (Denton & Gray, 1983, 1993). For this reason, a potential flow model of these pressure differences was devised to determine how this stimulus could influence swimming kinematics to minimize drag (Lighthill, 1993). This model predicts that drag should be minimized when the yaw angle of the head oscillates in phase with its lateral velocity. In addition, the optimal amplitude of changes in yaw and lateral velocity may be predicted from the shape of the fish's head. Measurements of the kinematics of swimming in Atlantic herring, a clupeoid species (*Clupea harengus* L.), supported these predictions (Rowe et al., 1993). However, these predictions were not supported by the kinematics of the golden shiner (*Notemigonus crysoleucas*), which does not school as strongly as clupeoid species. The golden shiner swims with head kinematics that do not minimize drag, and ablating the lateral line system does not elevate drag (McHenry et al., 2010). Although these results suggest that fish do not generally use the lateral line system to minimize pressure differences on the head, it remains possible that flow stimuli can be used to tune swimming kinematics in other ways. For example, lateral line inputs may assist in stabilizing swimming under turbulent conditions (Liao, 2006), or separation in the boundary layer may be avoided by sensory feedback (Anderson et al., 2001).

One of the challenges to understanding the role of the lateral line system in swimming is determining the stimuli detected by the neuromasts during locomotion. Measurements of the boundary layer over the surface of a swimming fish (Fig. 11) offer a glimpse into the stimuli detected by the superficial neuromasts (Fig. 3) (Anderson et al., 2001). Like the flow over a plate (Fig. 3d), the shear stress over the body is greatest near its leading edge, followed by a monotonic decline. This indicates that viscous drag and the stimulus detected by the superficial neuromasts is greatest in the anterior region of the body. However, the thickness of a fish's body and the flow created for propulsion influence the boundary layer, such that it deviates from flow over a plate. For example, skin friction remains elevated in the cranial region, anterior to the widest region of the body (Fig. 10b), rather than the precipitous drop-off seen in a flat plate (Fig. 3c). Therefore, an examination of the flow stimuli during locomotion requires experimental or theoretical approaches that extend beyond the simple cases considered by classical theory.

4.5 Kármán Gaiting

A broad diversity of fishes inhabit turbulent environments, and this variation in flow can have a strong influence on swimming behavior (Webb, 1998). Perhaps the most dramatic example is offered by the Kármán gait (Liao et al., 2003a), which is the synchronization of swimming kinematics to vortices in a Kármán vortex street (Fig. 12a).

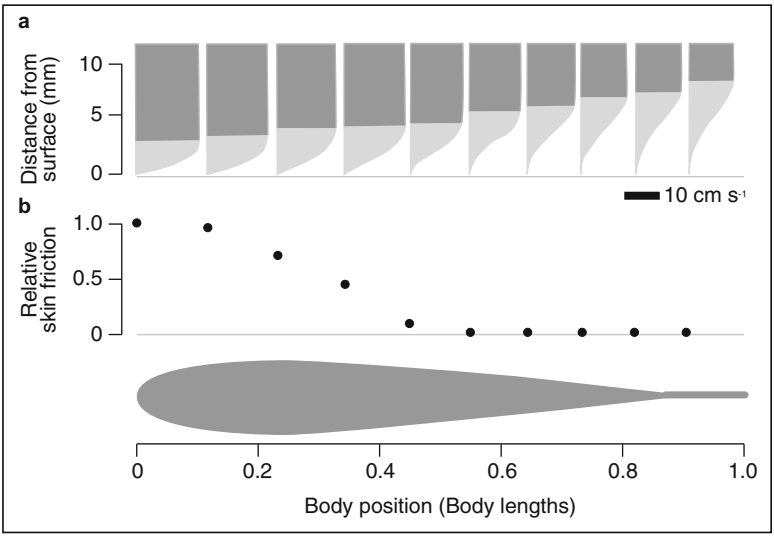

Fig. 11 Boundary layers over the surface of the body (length = 9 cm) of a swimming scup, *Stenotomus chrysops* (Anderson et al., 2001). (**a**) Flow velocities were measured by particle tracking velocimetry from a series of recordings. These profiles allow for the calculation of (**b**) skin friction (Eq. 3) on the surface of the body, which is normalized by the maximum value. These measurements demonstrate how the anterior half of the body is the major site of viscous drag production and offers a substantially stronger stimulus for the superficial neuromasts. The silhouette of the body of the fish from a dorsal view (in gray) illustrates the approximate shape of the body

When Kármán gaiting behind a cylinder, rainbow trout (*Oncorhynchus mykiss*) exhibit a lower tailbeat frequency and larger lateral body amplitude and curvature than seen during swimming in uniform flow of comparable velocity (Liao et al., 2003b). Simultaneous visualization of the flow and fish motions show that the body slaloms between oncoming vortices, moving with the lateral component of the sinusoidal flow rather than actively swimming through each vortex center (Fig. 12a). This motion is the result of a shift in the timing of lateral body motion relative to the vortices that pass along the body. For example, the center of mass oscillates antiphase (i.e., 180° phase shift) to move to its farthest lateral distance from a vortex core as it passes that body position (Fig. 12b). This slaloming is further facilitated by the head's motion away from a vortex (100° phase shift) and the tail moving toward the vortex as it approaches (230° phase shift).

Kármán gaiting emerges from a fluid–structure interaction between the body of the fish and the forces generated by the wake. Muscle recordings in trout revealed that only the anterior red muscles in the trunk are reliably activated during this behavior. This low level of muscle activity suggests that muscles primarily play a role in controlling body posture and stiffness (Liao, 2004). In contrast, trout swimming in freestream flow exhibit propagating waves of muscle activity along the whole body that serve to power body undulation. In addition, trout in a Kármán

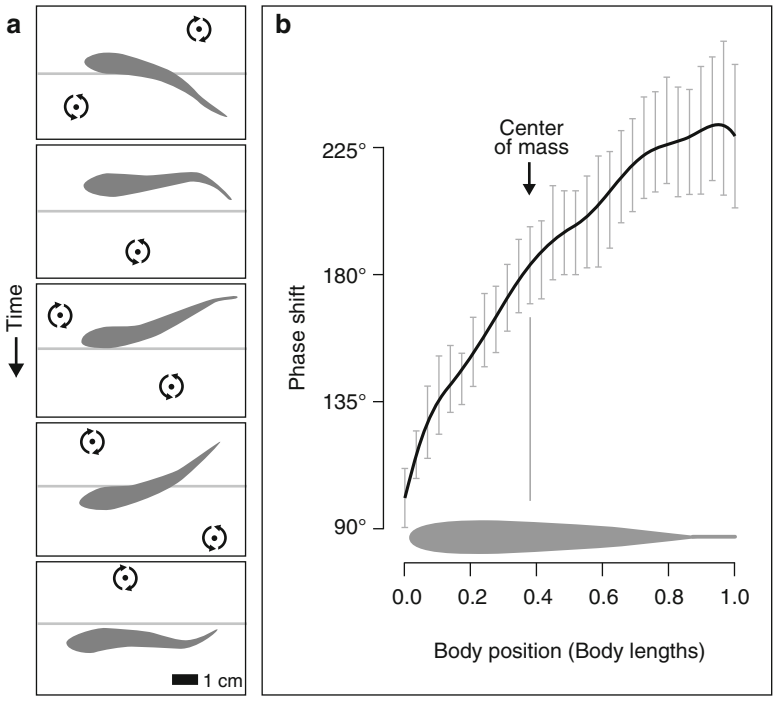

Fig. 12 Trout (*Oncorhynchus mykiss*) adopt a Kármán gait when holding station in a vortex street in the wake of an obstacle in flow. (**a**) A dorsal view of the body of the trout (in gray) illustrates the slaloming around vortices (centered at the rotating arrows) that is characteristic of this gait, measured in the wake of a semicylinder (Liao et al., 2003b). The centers of vortices (see Fig. 5) were measured with particle tracking velocimetry and the kinematics of swimming were recorded simultaneously. (**b**) These measurements revealed that the phase shift of lateral undulations is coordinated with respect to vortex shedding. Mean values (± 1 SE) for the phase shift demonstrate that the center of mass oscillates in antiphase (i.e., 180°) with the vortices and that the anterior and posterior regions are respectively directed away and toward the passing vortex

street at times actively move their pectoral fins to enable them to hold station without any muscle activity in the trunk. This demonstrates that Kármán gaiting can balance thrust and drag solely through fin action and the intrinsic compliance of the musculoskeletal system (Liao et al., 2003a,b).

Respirometry measurements demonstrated that Kármán gaiting allows a fish to use less oxygen when swimming. This indicates that fish can use some of the energy of environmental vortices to passively generate thrust (Taguchi & Liao, 2011). It has been proposed that the lateral translation of the body and its angular changes due to the vortex street may allow the body to act as a sail and thereby tack upstream passively (Liao et al., 2003a). This idea is supported by experimental and theoretical research on the hydrodynamics of fish-like foils, which can generate thrust when placed in oscillating flow (Wu & Chwang, 1975; Beal, 2003). Consequently, a dead trout towed behind a cylinder can passively generate thrust and move upstream on a slack line when they happen to synchronize with vortices

(Liao, 2004; Beal et al., 2006). Therefore, no muscle activity is required to maintain station, or even move upstream, in a vortex street if a body has the appropriate compliance.

The lateral line system plays a role in coordinating the Kármán gait. This was indicated by experiments that blocked the lateral line system by treating trout with a solution of cobalt chloride (Karlsen & Sand, 1987). This treatment altered the kinematics of Kármán gaiting (Liao, 2006), relative to control animals. Trout with a blocked lateral line exhibited faster body wave speed, lower maximum body curvature, lower tail-beat amplitude, and a longer and more variable body wavelength. It is unclear whether this effect may be attributed to stimuli detected by canal or superficial neuromasts. Similar experiments demonstrated that the lateral line is necessary to entrain in the relatively stable, low-pressure suction region directly behind a cylinder (Sutterlin & Waddy, 1975; Montgomery et al., 2003). Trout swimming under illuminated conditions choose to spend most of their time swimming in a turbulent vortex street, even with a blocked lateral line. In contrast, this behavior is rarely exhibited in the same species when swimming in the dark (Liao, 2006). Therefore, the lateral line system plays a role in the *ability* to Kármán gait and the visual system appears to be important in the *preference* of fish to exhibit this behavior.

5 Summary

Hydrodynamics provides a basis for understanding the stimuli detected by the lateral line system. Models of these stimuli have employed inviscid hydrodynamic theory (Kalmijn, 1988), which can accurately predict some stimuli detected by canal neuromasts (e.g., Coombs et al., 1996). However, there are circumstances where viscosity influences the flow detected by canal neuromasts (e.g., Fig. 11b) and viscous boundary layers are essential to the functioning of superficial neuromasts (McHenry et al., 2008). It is therefore fortuitous that computational modeling (e.g., Rapo et al., 2009) and flow visualization techniques (e.g., Anderson et al., 2001) are increasingly practical approaches for biological investigation. Studies adopting these techniques would do well to involve more natural levels of noise and turbulence in the environment. The integration of biomechanics with neurophysiological and behavioral approaches offers great promise for a deeper understanding of the lateral line system.

References

Anderson, E. J., McGillis, W. R., & Grosenbaugh, M. A. (2001). The boundary layer of swimming fish. *Journal of Experimental Biology*, 204, 81–102.

Anderson, J. M. (1996). Vorticity control for efficient propulsion. In *Applied ocean science engineering, MIT* (pp. 1–193). Cambridge: MIT/Woods Hole Oceanographic Institution.

Batchelor, G. (1967). *An introduction to fluid dynamics*. New York: Cambridge University Press.
Beal, D. N. (2003). *Propulsion through wake synchronization using a flapping foil*. Doctoral Dissertation, Massachusetts Institute of Technology.
Beal, D. N., Hover, F. S., Triantafyllou, M. S., Liao, J. C., & Lauder, G. V. (2006). Passive propulsion in vortex wakes. *Journal of Fluid Mechanics,* 549, 385–402.
Bleckmann, H. (2008). Peripheral and central processing of lateral line information. *Journal of Comparative Physiology A*, 194, 145–158.
Blevins, R. D. (1990). *Flow induced vibration,* 2nd ed. Malabar, FL: Krieger..
Coombs, S. (1994). Nearfield detection of dipole sources by the goldfish (*Carassius auratus*) and the mottled sculpin (*Cottus bairdi*). *Journal of Experimental Biology*, 190, 109–129.
Coombs, S., & Janssen, J. (1990). Behavioral and neurophysiological assessment of lateral line sensitivity in the mottled sculpin, *Cottus-bairdi*. *Journal of Comparative Physiology A*, 167, 557–567.
Coombs, S., & Montgomery, J. C. (1992). Fibers innervating different parts of the lateral line system of an antarctic notothenioid, *Trematomus-Bernacchii*, have similar frequency responses, despite large variation in the peripheral morphology. *Brain Behavior and Evolution*, 40, 217–233.
Coombs, S., & Conley, R. A. (1997a). Dipole source localization by the mottled sculpin. 2. The role of lateral line excitation patterns. *Journal of Comparative Physiology A*, 180, 401–415.
Coombs, S., & Conley, R. A. (1997b). Dipole source localization by mottled sculpin. 1. Approach strategies. *Journal of Comparative Physiology A,* 180, 387–399
Coombs, S., & Patton, P. (2009). Lateral line stimulation patterns and prey orienting behavior in the Lake Michigan mottled sculpin (*Cottus bairdi*). *Journal of Comparative Physiology A*, 195, 279–297.
Coombs, S., Hasting, M., & Finneran, J. (1996). Modeling and measuring lateral line excitation patterns to changing dipole source locations. *Journal of Comparative Physiology A*, 178, 359–371.
Ćurčić-Blake, B., & van Netten, S. M. (2006). Source location encoding in the fish lateral line canal. *Journal of Experimental Biology*, 209, 1548–1559.
Daniel, T. (1981). Fish mucus: *In situ* measurements of polymer drag reduction. *Biological Bulletin,* 160, 376–382.
Denton, E. J., & Gray, J. A. B. (1983). Mechanical factors in the excitation of clupeid lateral lines. *Proceedings of the Royal Society B: Biological Sciences,* 218, 1–26.
Denton, E. J., & Gray, J. A. B. (1988). Mechanical factors in the excitation of the lateral lines of fishes. In J. Atema, R. R. Fay, A. N. Popper, & W. N. Tavolga (Eds.), *Sensory biology of aquatic animals*(pp. 595–618). New York: Springer.
Denton, E. J., & Gray, J. A. B. (1989). Some observations on the forces acting on neuromasts in fish lateral line canals. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 79–97). New York: Springer-Verlag.
Denton, E. J., & Gray, J. A. B. (1993). Stimulation of the acoustico-lateralis system of clupeid fish by external sources and their own movements. *Philosophical Transactions: Biological Sciences,* 341, 113–127.
Dijkgraaf, S. (1963). The functioning and significance of lateral-line organs. *Biological Reviews of the Cambridge Philosophical Society*, 38, 51–105.
Dinklo, T. (2005). *Mechano- and electrophysiological studies on cochlear hair cells and superficial lateral line cupulae*. Doctoral dissertation, University of Groningen.
Ferry-Graham, L. A., Wainwright, P. C., & Lauder, G. V. (2003). Quantification of flow during suction feeding in bluegill sunfish. *Zoology*, 106, 159–168.
Flock, Å. (1965). Transducing mechanisms in lateral line canal organ receptors. *Cold Spring Harbor Symposia on Quantitative Biology*, 30, 133–145.
Görner, P. (1963). Untersuchungen zur Morphologie und Elektrophysiologie des Seitenlinienorgans vom Krallenfrosch (*Xenopus laevis* Daudin). *Journal of Comparative Physiology A*, 47, 316–338.

Goulet, J., Engelmann, J., Chagnaud, B. P., Franosch, J.-M. P., Suttner, M. D., & Hemmen, J. L. (2008). Object localization through the lateral line system of fish: Theory and experiment. *Journal of Comparative Physiology A*, 194, 1–17.

Hassan, E. S. (1985). Mathematical analysis of the stimulus of the lateral line organ. *Biological Cybernetics*, 52, 23–36.

Hassan, E. S. (1992a). Mathematical description of the stimuli to the lateral line system of fish derived from a three-dimensional flow field analysis. II. The case of gliding alongside or above a plane surface. *Biological Cybernetics*, 66, 453–461.

Hassan, E. S. (1992b). Mathematical description of the stimuli to the lateral line system of fish derived from a three-dimensional flow field analysis. I. The cases of moving in open water and of gliding towards a plane surface, *Biological Cybernetics,* 66, 443–452.

Higham, T. E., Day, S. W., & Wainwright, P. C. (2005). Sucking while swimming: Evaluating the effects of ram speed on suction generation in bluegill sunfish *Lepomis macrochirus* using digital particle image velocimetry. *Journal of Experimental Biology,* 208, 2653–2660.

Hoekstra, D., & Janssen, J. (1985). Non-visual feeding behavior of the mottled sculpin, *Cottus bairdi,* in Lake Michigan. *Environmental Biology of Fishes,* 12, 111–117.

Hoekstra, D., & Janssen, J. (1986). Lateral line receptivity in the mottled sculpin. *Copeia*, 1986, 91–96.

Hudspeth, A. J. (1982). Extracellular current flow and the site of transduction by vertebrate hair cells. *Journal of Neuroscience*, 2, 1–10.

Kalmijn, A. J. (1988). Hydrodynamic and acoustic field detection. In J. Atema, R. R. Fay, A. N. Popper, & W. N. Tavolga (Eds.), *Sensory biology of aquatic animals*. (pp. 83–130). New York: Springer-Verlag.

Kalmijn, A. J. (1989). Functional evolution of lateral line and inner ear sensory systems. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 187–215). New York: Springer-Verlag.

Karlsen, H. E., & Sand, O. (1987). Selective and reversible blocking of the lateral line in freshwater fish. *Journal of Experimental Biology*, 133, 249–262.

Kármán, von, T. (1954). *Aerodynamics: Selected topics in the light of their historical development*. Ithaca, NY: Cornell University Press.

Kroese, A. B. A., & Schellart, N. A. M. (1992). Velocity-sensitive and acceleration-sensitive units in the trunk lateral line of the trout. *Journal of Neurophysiology*, 68, 2212–2221.

Liao, J. C. (2004). Neuromuscular control of trout swimming in a vortex street: Implications for energy economy during the Kármán gait. *Journal of Experimental Biology*, 207, 3495–3506.

Liao, J. C. (2006). The role of the lateral line and vision on body kinematics and hydrodynamic preference of rainbow trout in turbulent flow. *Journal of Experimental Biology,* 209, 4077–4090.

Liao, J. C. (2010). Organization and physiology of posterior lateral line afferent neurons in larval zebrafish. *Biology Letters, 6,* 402–405.

Liao, J. C., Beal, D. N., Lauder, G. V., & Triantafyllou, M. S. (2003a). The Kármán gait: Novel body kinematics of rainbow trout swimming in a vortex street. *Journal of Experimental Biology,* 206, 1059–1073.

Liao, J. C., Beal, D. N., Lauder, G. V., & Triantafyllou, M. S. (2003b). Fish exploiting vortices decrease muscle activity. *Science*, 302, 1566–1569.

Lighthill, J. (1993). Estimates of pressure differences across the head of a swimming clupeid fish. *Philosophical Transactions: Biological Sci*ences, 341, 129–140.

Lighthill, J. (1995). The role of the lateral line in active drag reduction by clupeoid fishes. *Animal Locomotion Symposium by the Society for Experimental Biology,* 49, 35–48.

McHenry, M. J., Strother, J. A., & van Netten, S. M. (2008). Mechanical filtering by the boundary layer and fluid-structure interaction in the superficial neuromast of the fish lateral line system. *Journal of Comparative Physiology A*, 194, 795–810.

McHenry, M. J., Feitl, K. E., Strother, J. S., & Van Trump, W. J. (2009). Larval zebrafish rapidly sense the water flow of a predator's strike. *Biology Letters,* 5, 477–497.

McHenry, M. J., Michel, K. B., & Stewart, W. J. (2010). Hydrodynamic sensing does not facilitate active drag reduction in the golden shiner (*Notemigonus crysoleucas*). *Journal of Experimental Biology,* 213, 1309–1319.

Montgomery, J. C., McDonald, F., Baker, C. F., Carton, A. G., & Ling, N. (2003). Sensory integration in the hydrodynamic world of rainbow trout. *Proceedings of the Royal Society B: Biological Sciences,* 270, S195–S197.

Muddada, S., & Patnaik, B. S. V. (2011). Understanding complex systems. In S. Banerjee, M. Mitra, & L. Rondoni (Eds.), *Understanding complex systems* (pp. 87–136). Berlin: Springer.

Mönz, H. (1989). Functional organization of the lateral line periphery. In S. Coombs, P. Görner, & H. Mönz (Eds.). *The mechanosensory lateral line: Neurobiology and Evolution* (pp. 285–297). New York: Springer-Verlag.

Prandtl, L. (1904). Über Flüssigkeitsbewegung bei sehr kleiner Reibung. *Proceedings Third International Kongreß Heidelberg*, S, 484–491.

Rapo, M. A., Jiang, H., & Grosenbaugh, M. A. (2009). Using computational fluid dynamics to calculate the stimulus to the lateral line of a fish in still water. *Journal of Experimental Biology,* 212*,* 1494–1505.

Reynolds, O. (1883). An experimental investigation of the circumstances which determine whether the motion of water shall be direct or sinuous, and the law of resistance in parallel channels. *Philosophical Transactions of the Royal Society*, 174, 935–982.

Rowe, D. M., Denton, E. J., & Batty, R. S. (1993). Head turning in herring and some other fish. *Proceedings of the Royal Society B: Biological Sciences*, 341, 141–148.

Schewe, G. (1983). On the force fluctuations acting on a circular cylinder in crossflow from subcritical up to transcritical Reynolds numbers. *Journal of Fluid Mechanics,* 133, 265–285.

Schlichting, H. (1979). *Boundary-layer theory*. New York: Springer-Verlag.

Schulze, F. E. (1870). Über die Nervenendigung in den sogenannten Schleimkanälen der Fische und über entsprechende Organe der durch Kiemen athmenden Amphibien. *Archive für Anatomische Physiologie Leipzig*, 759–769.

Stewart, W. J., & McHenry, M. J. (2010). Sensing the strike of a predator fish depends on the specific gravity of a prey fish. *Journal of Experimental Biology*, 213, 3769–3777.

Sutterlin, A., & Waddy, S. (1975). Possible role of posterior lateral line in obstacle entrainment by brook trout (*Salvelinus-Fontinalis*). *Journal of Fisheries Research Board of Canada*, 32, 2441–2446.

Taguchi, M., & Liao, J. C. (2011). Rainbow trout consume less oxygen in turbulence: The energetics of swimming behaviors at different speeds. *Journal of Experimental Biology,* 214, 1428–1436.

Teyke, T. (1990).Morphological differences in neuromasts of the blind cave fish *Astyanax hubbsi* and the sighted river fish *Astyanax mexicanus*. *Brain Behavior and Evolution*, 35, 23–30.

Van Dyke, M. (1982). *An album of fluid motion*. Palo Alto, CA: Parabolic Press.

van Netten, S. M. (2006). Hydrodynamic detection by cupulae in a lateral line canal: Functional relations between physics and physiology. *Biological Cybernetics*, 94, 67–85.

Van Trump, W. J., & McHenry, M. J. (2008). The morphology and mechanical sensitivity of lateral line receptors in zebrafish larvae (*Danio rerio*). *Journal of Experimental Biology,* 211, 2105–2115.

Wainwright, P. C., & Day, S. W. (2007). The forces exerted by aquatic suction feeders on their prey. *Journal of the Royal Society Interface*, 4, 553–560.

Webb, P. W. (1998). Entrainment by river chub *Nocomis micropogon* and smallmouth bass *Micropterus dolomieu* on cylinders. *Journal of Experimental Biology*, 201, 2403–2412.

Weber, D. D., & Schiewe, M. H. (1976). Morphology and function of the lateral line of juvenile steelhead trout in relation to gas-bubble disease. *Journal of Fish Biology,* 9, 217–233.

Windsor, S. P., & McHenry, M. J. (2009). The influence of viscous hydrod3842ynamics on the fish lateral-line system. *Integrative and Comparative Biology*, 49, 691–701.

Windsor, S. P., Tan, D., & Montgomery, J. C. (2008). Swimming kinematics and hydrodynamic imaging in the blind Mexican cave fish (*Astyanax fasciatus*). *Journal of Experimental Biology,* 211, 2950–2959.

Windsor, S., Norris, S., & Cameron, S. (2010a). The flow fields involved in hydrodynamic imaging by blind Mexican cave fish (*Astyanax fasciatus*). Part I: Open water and heading towards a wall. *Journal of Experimental Biology,* 213, 3819–3831.

Windsor, S., Norris, S. E., Cameron, S. M., Mallinson, G. D., & Montgomery, J. C. (2010b). The flow fields involved in hydrodynamic imaging by blind Mexican cave fish (*Astyanax fasciatus*). Part II: Gliding parallel to a wall. *Journal of Experimental Biology,* 213, 3832–3842.

Wu, T. Y., & Chwang, A. T. (1975). *Extraction of flow energy by fish and birds in a wavy stream*. New York: Plenum Press.

The Biophysics of the Fish Lateral Line

Sietse M. van Netten and Matthew J. McHenry

Keywords Cupula • Flow sensing • Hair cells • Kinocilia • Micromechanics • Microphonic • Nanometer • Neurobiology • Neuromast • Stereocilia • Swimming

1 Introduction

A distinctive feature of fishes is their ability to sense water flow with two types of receptors, called neuromasts, which are the functional units of the peripheral lateral line system. The superficial neuromasts (SNs) possess mechanosensory hair cells and project from the skin into the water at the body's surface. This is similar to the flow-sensitive organs of amphibians (Kramer, 1933), cephalopods (Budelmann & Bleckmann, 1988), coelenterates (Watson & Hessinger, 1989), and other invertebrates (Budelmann, 1989). However, fish also possess canal neuromasts (CNs), which are recessed below the body's surface, within cranial bones and scales on the trunk (Fig. 1a; see also the chapter by Webb). This second type of receptor provides a fish with an additional stream of information and thereby contributes a second submodality to the lateral line system. This chapter describes how the two submodalities are sensitive to distinct features of a flow stimulus because of biophysical differences between SNs and CNs.

S.M. van Netten (✉)
Department of Artificial Intelligence and Cognitive Engineering, University of Groningen, Nijenborgh 9, 9747 Groningen, The Netherlands
e-mail: s.m.van.netten@rug.nl

M.J. McHenry
Department of Ecology and Evolutionary Biology, University of California, 321 Steinhaus Hall, Irvine, CA 92617, USA
e-mail: mmchenry@uci.edu

S. Coombs et al. (eds.), *The Lateral Line*, Springer Handbook of Auditory Research 48,
DOI 10.1007/2506_2013_14, © Springer Science+Business Media New York 2013,
Published online: 29 June 2013

1.1 The Morphology of Neuromasts

Much of the biophysical difference between SNs and CNs stems from their distinct morphology. Both types include hair cells in a cluster within a sensory epithelium, or macula, but a SN typically contains about 10 of these cells (Fig. 1b), which is many fewer than the hundreds, or sometimes thousands, of hair cells within a CN (Fig. 1c; Dijkgraaf, 1963). A hair cell transduces small deflections into changes in membrane potential with mechanically gated ion channels that are located within the hair bundle of the cell (Hudspeth, 1989). The hair bundle consists of a kinocilium and microvilli (often referred to as stereocilia) on the apical surface of the cell that extend into a gelatinous structure called the cupula. Although there are noteworthy exceptions (Coombs et al., 1988), the CN cupula is generally hemispherical with a diameter in the hundreds of microns (Fig. 1c). The much smaller SN cupula is bullet shaped and is around 10 μm in width and 50–100 μm in height (Fig. 1b). In either neuromast, the cupula serves to transmit hydrodynamic forces from the flow of water near the surface of the body to deflect the hair bundles and thereby generates a nervous response. In this respect, CNs and SNs are governed by similar biophysics.

1.2 The Sensitivity of Neuromasts

Differences between SNs and CNs are reflected in a variety of physiological measurements. The hair cells within a neuromast change their membrane potential as the cupula is deflected. These deflections can be measured with optical techniques (van Netten & Kroese, 1987) and the resulting changes in voltage can be monitored by extracellular microphonic recordings (Kuiper, 1956). Changes in the membrane potential are encoded as a train of action potentials transmitted along afferent neurons toward the central nervous system. The frequency of these action potentials may also be recorded to measure the physiological response to a flow stimulus (Görner, 1963; Kroese et al. 1978; Coombs & Janssen, 1989; Kroese & Schellart, 1992; see also the chapter by Chagnaud & Coombs). Therefore, cupular deflection, microphonic potentials, and afferent action potentials are responses that vary with the magnitude of a stimulus and the sensitivity of the neuromast.

The sensitivity of a receptor, such as a neuromast, may be defined as the ratio of response output to stimulus input. The stimulus for a neuromast is conventionally provided by an oscillating sphere placed at sufficient distance to be unaltered by the presence of the body. The stimulus at this proximity is consequently defined as the freestream flow (Fig. 1a). With this arrangement, the sensitivity of a neuromast may be defined as the ratio of the amplitude of a response variable to the amplitude of a stimulus variable. For example, the sensitivity of the hair cells to stimulus velocity may be calculated by dividing the amplitude of microphonic potentials by the

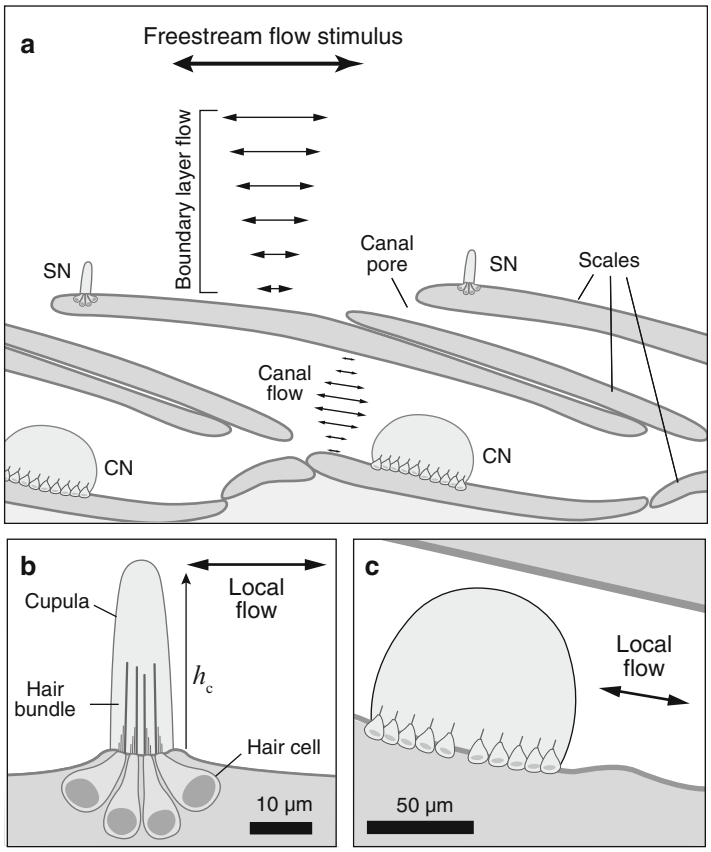

Fig. 1 The anatomy of lateral line neuromasts. Schematic illustrations show (**a**) the relative position and major anatomical features of (**b**) superficial and (**c**) canal neuromasts (Weber & Schiewe, 1976; Kroese & Schellart, 1992). (**a**) The superficial neuromasts extend into the water surrounding the body, where they are directly exposed to a flow stimulus. Canal neuromasts are enclosed in a channel that is formed of bone (on the head) or scales (on the trunk), where they encounter flow when a pressure difference exists between the pores that open the channel to the surface. Viscous hydrodynamics create a boundary layer at the surface and attenuate flow velocity within the canal and thereby filter a flow stimulus. (**b, c**) Neuromasts consist of mechanosensory hair cells, a gelatinous cupula, and support cells (not shown). The hair bundle of each hair cell extends into the cupula and thereby detects deflections of the cupular structure created by fluid forces. (**b**) The flow near the level of a cupula, local flow, may be defined at the height of the cupula for an SN (**b**) or the center of the canal for a CN (**c**)

amplitude of freestream velocity. The phase relationship between stimulus and response may also be encapsulated in this measure of sensitivity, as discussed in Sections 3.1 and 3.2.

The threshold sensitivity indicates the smallest stimulus that is required to create a response by a receptor. This limit of a receptor's performance depends on the strength of the response compared to the noise that is inherent to the receptor.

As discussed in Section 2.3, the transducer noise and Brownian motion are sources of noise in hair cells and have to be exceeded by a stimulus to produce a change in the firing rate of afferent neurons.

Sensitivity and threshold sensitivity have the potential to vary with the frequency of a stimulus. The frequency response indicates how sensitivity varies over a series of measurements over a range of stimulus frequency. The frequency response can be used to test whether a neuromast is sensitive to the velocity or acceleration of a flow stimulus. For example, sensitivity defined as the ratio of microphonic amplitude to velocity amplitude is predicted to remain constant across frequencies for a velocity-sensitive neuromast. In such a neuromast, microphonic potentials are in addition predicted to oscillate in phase with the freestream velocity. In contrast, the acceleration of freestream flow is phase-shifted by 90° and exhibits an amplitude that is proportional to frequency. Therefore, an acceleration-sensitive neuromast generates microphonic potentials that are phase-shifted by 90° with respect to freestream velocity. Such a neuromast would exhibit a sensitivity that is proportional to stimulus frequency, which is equivalent to a 20-dB increase per decade of frequency. As detailed in Section 2, such interpretations of frequency response measurements have supported the characterization of neuromasts as velocity (SN) and acceleration (CN) sensitive for a particular range of frequencies (Coombs & Janssen, 1989; Kroese & Schellart, 1992; see also the chapter by Chagnaud & Coombs).

2 Transfer Functions and the Frequency Response

The frequency response of a neuromast depends on how its hydrodynamics, structural dynamics, and neurophysiology vary with stimulus frequency. Each of these components may be modeled to examine their contribution to neuromast sensitivity. A model of a frequency response may be formulated as a transfer function [$H(f)$]. A transfer function is defined as the ratio of a response variable to a stimulus variable and therefore serves as a mathematical expression of sensitivity, as defined in Section 1.2. The transfer function generally uses complex notation that may be evaluated to yield the frequency response. In particular, the magnitude (i.e., absolute value) and argument of the transfer function respectively provide the amplitude and phase of the frequency response. For example, the hair bundle deflection generated by a velocity signal may be predicted (see Section 3.1) from a transfer function that is based on a biophysical model of cupular dynamics. Evaluating the magnitude and argument over a range of frequency values yields a prediction of the frequency response that may be compared with measurements from a physiological experiment. In the present context, a transfer function reveals how neuromasts filter different frequency components of a stimulus and offers a basis for understanding the salient differences between SNs and CNs.

2.1 Canal Neuromasts

Denton and Gray (1983, 1988, 1989) used a combination of physiological measurements with physical and mathematical modeling to study the biophysics of flow sensing in CNs. Their research on sprat examined the relationship between cupular deflection and the flow within the canal and how that flow varies in relation to freestream flow. These authors proposed that acceleration sensing emerges in the CN system due to dynamics at two levels. First, the velocity of flow within a canal is induced by pressure differences between its pores. Because a pressure gradient is proportional to the acceleration of freestream flow, the velocity within the canal is thus proportional to the temporal derivative of freestream velocity (Denton & Gray, 1983). Second, they proposed that a CN deflects with a displacement in proportion to the flow velocity within the canal owing to the viscous drag that acts upon the cupula. Therefore, the combined properties of the canal and CN cupula serve to encode the freestream acceleration of a flow stimulus.

Submicrometer measurements of cupular motion support this acceleration-sensing model for a restricted frequency range (van Netten, 2006). By measuring deflection in the CN at multiple positions within the cupula, it was revealed that the cupula slides as a rigid body along the surface of the sensory epithelium (van Netten & Kroese, 1987). These deflections are resisted by the spring-like hair bundles that anchor the cupula to the epithelium. A biophysical model of these dynamics predicts a constant cupular deflection per canal flow velocity across increases in frequency, up to about tens of Hertz in ruffe (*Gymnocephalus cernua*; Fig. 2d, green curve).

The hydrodynamics of the canal are also consistent with CN acceleration-sensing, as modeled with the hydrodynamics of a cylindrical channel (cf. van Netten, 2006). At low frequencies, the flow induced by a pressure gradient is governed by viscous interaction, known as Hagen–Poiseuille flow. The velocity of this flow adopts a parabolic profile with its most rapid flow in the center due to the viscous adhesion of water close to the channel wall (cf. van Netten, 2006). This condition has been modeled in general for channels (Sexl, 1930) and specifically for the lateral line (using a lumped parameter description; Denton & Gray, 1988). The model predicts that velocity within the canal is proportional to the acceleration of a freestream stimulus, which has been experimentally validated (Denton & Gray, 1983, 1988; Tsang, 1997). In accordance with this model, a transfer function of channel flow velocity per freestream acceleration is constant up to frequencies of tens of Hertz (Fig. 2c, green curve).

Mechanical filtering by the CN cupula and canal becomes more complicated at frequencies above tens of Hertz. The elasticity of the hair bundles causes the cupula to resonate, which creates an elevated ratio of cupular deflection to the canal flow velocity within the canal, known as the local velocity (Fig. 2d). The peak amplitude arises at a resonant frequency (~100 Hz), which depends on the stiffness provided by the hair cells and mass of the cupula and entrained water (van Netten, 1991). This is apparent in the almost hemispherically shaped cupulae of ruffe (van Netten

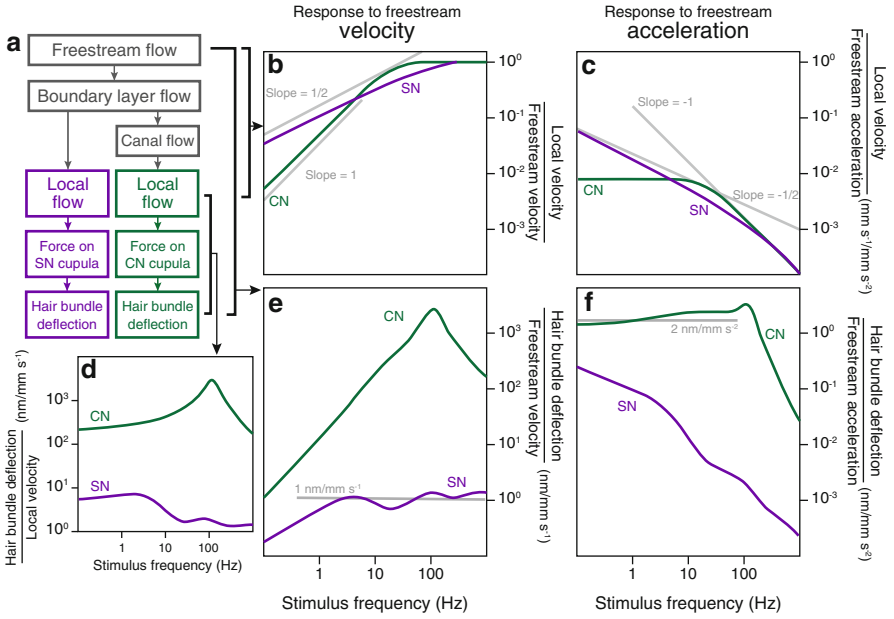

Fig. 2 The frequency responses of neuromasts. Transfer functions were used to model each component of the frequency response for the CNs (in green) and SNs (in purple) illustrated in Fig. 1. (**a**) A flow chart illustrates how these components alter a stimulus before it is encoded by the deflection of the hair bundles within a neuromast. This includes the boundary layer and canal flows (in gray) that alter the local flow that creates fluid forces that act on the cupula. (**b – f**) Each transfer function represents variation in a measure of sensitivity with the stimulus frequency. In this context, sensitivity is defined as a ratio of a response amplitude to a stimulus amplitude. In all plots, parameters for canal and CN transfer functions are taken from fits to measured cupular dynamics of ruffe (*Gymnocephalus cerua*) supraorbital canal neuromasts (van Netten, 2006). Parameters of SNs resulted from model-fits to measured cupular dynamics (Sendin et al., unpublished data.) for zebrafish (*Danio rerio*; McHenry et al., 2008). Lines of constant slope (in gray) are plotted for comparison. (**b, c**) The sensitivity of local velocity with respect to the velocity (**b**) and acceleration (**c**) of freestream flow. Local flow is defined at the location of the tip of the cupula for SNs and the center of the canal for CNs. These frequency responses are created for SNs by the boundary layer and for CNs by canal flows (Fig. 1). (**d**) The sensitivity of hair bundle deflection to local flow velocity depends on a fluid–structure interaction between the cupula, hair bundles and local flow. (**e**, **f**) These dynamics and the hydrodynamics of the boundary layer and canal combine to influence the sensitivity of the hair bundles to freestream flow. This overall sensitivity of the hair cells to a stimulus may be defined with respect to the velocity of freestream (**e**) or acceleration (**f**) of freestream flow. Constant overall sensitivity is indicated for SN of freestream (**e**) and CN (**f**) with a numerical value and a flat line (in gray) stretching across the appropriate frequency range

& Kroese, 1987) and the more elliptically shaped cupulae in the clown knife fish (Wiersinga-Post & van Netten, 2000). In the high-frequency range, the inertia of water causes flow in the canal to move in proportion to, and in phase with, the freestream stimulus. As a consequence, the amplitude of local canal velocity declines as stimulus frequency increases (Fig. 2c). The cutoff frequency that

marks this transition of canal filtering is inversely proportional to the square of the canal radius and therefore has the potential to vary with the body of a fish or between species (van Netten, 2006). This amounts to a cutoff frequency of approximately 20 Hz in ruffe, which have relatively large canals (Fig. 2c, green curve). This cutoff frequency is consequently predicted to be lower in the many species with smaller canals (see the chapter by Webb).

The flow signals detected by a CN depend on the combined filtering characteristics of both the cupula and canal. These composite properties may be examined by calculating the product of transfer functions, for the cupula and canal (i.e., Fig. 2c × Fig. 2d = Fig. 2f, green curves). In ruffe, the resonance peak created by the mass and stiffness of the cupula is somewhat higher than the cutoff frequency of the canal (~20 Hz). As a result, the attenuation in velocity created by canal hydrodynamics (Fig. 2c, green curve) at high frequency effectively removes the raise in sensitivity that is created by cupular resonance (Fig. 2d, green curve). This is also reflected in the frequency response of the discharge rate of afferent neurons (Wubbels, 1992), which can thus be mostly accounted for by the mechanical filtering of the canal and cupula. Additional electrical filtering by the hair cells exhibits a high-frequency cutoff that is close to the mechanical cutoff frequencies (Wiersinga-Post & van Netten, 2000). This may also explain the additional phase delay usually found in afferent responses (cf. Wubbels, 1992), as compared to accompanying phase delays (~ −180°) of the combined mechanical filtering at high frequencies.

2.2 *Superficial Neuromasts*

Deflection measurements of the cupulae in zebrafish (*Danio rerio*) suggest that SNs operate in a fundamentally different manner from CNs. The elongated cupula of a SN bends in flow (Dinklo, 2005), which is unlike the rigid-body motion of the CN (van Netten, 1988). The forces transmitted to the hair bundles in the SN thus also depend on the beam dynamics of the cupula, which vary with its material properties and dimensions (McHenry et al., 2008). This material is a compliant mucopolysaccaride gel (Young's modulus <100 Pa), which allows the cupula to bend with high flexibility (McHenry & van Netten, 2007). Although located at the surface of the body, a SN is exposed to hydrodynamic filtering that is similar to the filtering provided by the CN canal. As in the canal, water adheres to the surface of the skin and thereby creates a spatial velocity gradient, here called the boundary layer (Schlichting, 1979). The boundary layer and the fluid–structure interaction with the cupula provide two layers of mechanical filtering in the SN frequency response.

The role of the boundary layer in SN sensitivity may be modeled with hydrodynamic theory (Schlichting, 1979). This model is formulated as a transfer function that describes sensitivity of local velocity (at the height of the cupula, $h_c = 45$ μm; cf. Van Trump & McHenry, 2008) relative to the stimulus velocity in the freestream (Fig. 2b, purple curve). As detailed in the chapter by McHenry and Liao, the boundary layer may be characterized by the thickness from the body's surface at

which the flow velocity approximates freestream flow. In oscillatory flow, the boundary layer thickness decreases with frequency as inertial forces increasingly overcome viscosity and the flow velocity decreases near the surface. For low frequencies (<100 Hz), the velocity at the cupular height varies as a fractional (power of 0.5) time derivative of the freestream velocity (cf. Kalmijn, 1988), which is apparent from the 0.5 slope of the transfer function (i.e., 10 dB/decade, Fig. 2b, purple curve). This contrasts canal filtering (20 dB/decade, Fig. 2b, green curve), which provides a "full" derivative with respect to the freestream at low frequencies. At higher frequencies, the boundary layer thickness reduces to below the cupula height and, as a consequence, the SN cupula is acted upon by the full freestream stimulus. In this manner, the boundary layer functions as a high-pass filter with a cutoff frequency determined by the cupula height.

The mechanical filtering generated by the SN cupula has been considered by a mathematical model. By treating the cupula as a flexible beam in flow and modeling the forces generated by fluid motion, this model predicts the deflection of hair bundles for an oscillatory stimulus (McHenry et al., 2008). This model has been applied to the SN cupulae of zebrafish (*Danio rerio*) (Dinklo, 2005), which possess a morphology that is representative of SNs in many species of fish (Münz, 1989). A modified version of this model is presented here that incorporates new observations from experimental measures of cupula response using a micro fluid-jet stimulus (Sendin et al., unpublished data). This modified model predicts a nearly constant level of sensitivity to local flow (defined at $h_c = 45$ μm) for frequencies up to a few Hertz (Fig. 2d, purple curve). The exact cutoff frequency is determined by cupular dimensions (here both diameter and height), its material stiffness, as well as hair bundle stiffness. Beyond this cutoff, a slow decline in sensitivity is exhibited with increasing frequency.

The combined filtering provided by the cupula and boundary layer may be determined by the product of their transfer functions, which represents the sensitivity of hair bundle deflection to freestream stimulus velocity (Fig. 2b × Fig. 2d = Fig. 2e, purple curves). This result demonstrates that the SN hair bundles deflect in proportion to flow velocity, with high-pass filtering. However, it appears likely that the neurophysiology of the hair cells may attenuate signals at frequencies beyond tens of Hertz, as observed in several studies of afferent responses and extracellular receptor potentials (Kroese, 1978; Kroese & Schellart, 1992; Sendin et al., unpublished data).

2.3 Threshold Sensitivity

The frequency response can also provide a basis for estimating the threshold sensitivity of a neuromast, which is the minimum stimulus that may be detected. In the CN of ruffe, the constant acceleration-sensitivity below the cutoff frequency (~100 Hz) has an approximate value of 2 nm of hair bundle displacement

per mm s^{-2} of flow acceleration (Fig. 2f, green curve). The threshold sensitivity may be calculated as the acceleration necessary to deflect the hair cells to a degree equal to the noise that is inherent to mechanotransduction. In particular, the transducer noise and Brownian motion for the 1000 hair cells of ruffe are estimated to be 0.20 nm (root mean square). (cf. van Netten, 2006). For low frequencies, a comparable signal would be generated by a stimulus with an acceleration amplitude of about 0.10 mm s^{-2}. This estimate of threshold sensitivity for supraorbital canal neuromasts is on the same order of magnitude as reports of behavioral measurements for sensitivity. For example, the mottled sculpin (*Cottus bairdi*) responds to flow near the cranium with an acceleration of about 0.18 mm s^{-2} (−75 dB re 1 m s^{-2} ; Coombs & Janssen, 1990).

The different morphology of SNs creates a lower threshold sensitivity than CNs. Zebrafish SNs possess approximately 20 hair cells (Van Trump & McHenry, 2008), which suggests a noise level of 1.45 nm r.m.s. For frequencies greater than a few Hertz, the SN sensitivity to velocity is 1 nm hair bundle displacement per mm s^{-1} of stimulus velocity (Fig. 2e). This suggests that a velocity amplitude of 1.45 mm s^{-1} is sufficient to produce a threshold response. This value is less than, but not inconsistent with, measurements of the threshold from recordings of afferent neurons from the same species (7 mm s^{-1}; Liao, 2010).

The superior response of CNs over SNs is maintained over a broad spectrum of frequencies for the same freestream stimulus. For example, a 20-Hz oscillation with an acceleration amplitude of 100 mm s^{-2} creates an amplitude of velocity equal to 0.79 mm s^{-1}. This stimulus would create hair bundle deflections of 200 nm in the CN and 0.79 nm in SN. Therefore, the CN response is 1000 times greater than threshold, whereas the SN response is about half of its threshold. Such disparities in sensitivity are evident for both velocity (Fig. 2e) and acceleration stimuli (Fig. 2f). This result is mostly due to the much larger cupula and greater numbers of hair cells in CNs, as indicated by the responses to flow at the level of the cupula (Fig. 2d). For example, CNs are 50 times more sensitive than SNs in the frequency range up to a few Hertz for a velocity stimulus at the SN cupular tip (h_c = 45 μm). An even greater disparity is generated at higher frequencies (>10 Hz), where CN cupulae resonate and SN cupular responses decline. However, the boundary layer within the canal impedes local flow more than the boundary layer at the surface at low frequencies (<4 Hz), which causes the overall sensitivity values of CNs to approach that of SNs. Nevertheless, this phenomenon does not alter the general conclusion that CNs have a much higher response than SNs in the bandwidth considered (Figs. 2e, f).

3 Responses in the Time Domain

A transfer function gives a complete representation of a linear filter and may therefore be used to calculate how a neuromast responds to a flow stimulus in the time domain. This calculation follows a procedure that is commonly described in

textbooks on linear signal processing (e.g., Lathi, 1998). However, this approach is rarely employed to understand animal sensory systems, despite the insight that it offers by articulating the signals that are encoded by the peripheral nervous system.

Here a brief practical introduction on time-domain filtering is presented with an illustration of its applications to the lateral line system. These calculations require signal processing software (e.g., Matlab, Matcad, Igor, Origin, Octave, Labview) to determine the complex fast-Fourier transform (FFT) and an inverse fast-Fourier transform (IFFT). The FFT converts a signal that varies with time (i.e., defined in the time domain) into a series of complex numbers that vary with frequency (i.e., defined in the frequency domain). The absolute value and phase of these complex values constitute the spectrum of the signal in the frequency domain. It is in the frequency domain that the response of a sensor (e.g., an SN or CN) to a stimulus may be calculated. The result, a response signal, may then be determined for the time domain with IFFT. IFFT does the reverse of FFT by converting complex frequency-domain signals into time-domain signals, which are real numbers.

3.1 Calculating a Filtered Signal in the Time Domain

Determining the response of a sensor to a stimulus requires first converting a signal, y, from the time domain into the frequency domain. This signal must be recorded at a sufficiently high sample rate that the period between samples, ΔT, is much shorter than the duration of the most rapid events in the signal. The first step toward filtering y is to add a series of zeros at the beginning and end that are both equal in duration to the (finite) impulse response of the filter to be used, a procedure known as zero-padding. The zero-padded signal is then converted into the frequency domain ($y \rightarrow \text{FFT} \rightarrow Y$) to produce a spectrum, Y, that possesses the same number of samples, N, as in the time domain. The increment between frequency values for this spectrum, Δf, is determined by the sample period and total number of samples [$\Delta f = (N\Delta T)^{-1}$].

As explained in Section 2, the frequency response of a sensor indicates how it filters a stimulus, as dictated by its transfer function, H. Calculating the response of the sensor requires evaluating the transfer function for the same frequencies as those contained in the signal spectrum. This evaluation produces values, H_{eval}, that are calculated as follows:

$$\begin{aligned} H_{\text{eval}} &= H(n\,\Delta f), \text{ for } n \in (0,\ 1\ .\ .\ .N/2-1), \\ &= H^{*}((N-n)\,\Delta f), \text{ for } n \in (N/2\ .\ .\ .N-1), \end{aligned} \tag{1}$$

where n is a series of N integers. The first part of the this definition evaluates H_{eval} up to half the number of frequency values [$n \in (0, 1\ .\ .\ .N/2-1)$], so that the highest frequency represented is a single sample less than half of the sample rate

[i.e., $(N/2)\Delta f = (2\Delta T)^{-1}$]. The second part of the definition of H_{eval} is related to the negative frequencies, which are also required in complex notation. The values at these negative frequencies are equal to the complex conjugate of the transfer function at the corresponding positive frequencies [i.e., $H(-f) = H^*(f)$] and are a translated copy of the discrete values of H defined for $n \in (N/2 \ldots N-1)$. As a consequence, a plot of values at negative frequencies is a mirror image of the values at these positive frequencies.

Using the frequency-domain representations of both the stimulus and sensor allows for the final calculation to determine the response in the time domain. Within the frequency domain, the response, S, is calculated as the pairwise product of elements in Y and H_{eval}. This response spectrum is then converted back to the time domain ($S \rightarrow$IFFT$\rightarrow s$) to reveal the sensor's responses, s. These responses are equivalent to the discretized version of the stimulus signal, y, convolved with the impulse response h, as indicated by the following equation:

$$s = \int_{-\infty}^{t} y(t')h(t-t')dt' \tag{2}$$

3.2 The Response to a Simple Stimulus

Time-domain filtering may be demonstrated by its application in a simple example. Consider a dimensionless stimulus composed of two frequency components, defined by the following equation:

$$y = a_{\text{low}} \sin(2\pi f_{\text{low}} t) + a_{\text{high}} \sin(2\pi f_{\text{high}} t), \tag{3}$$

where f_{low} and f_{high} respectively define low (1 Hz) and high (100 Hz) frequency components with amplitude values of a_{low} (1.25) and a_{high} (0.75) for the signal y. A series of values such as a stimulus measurement may be determined by sampling this function during a time interval ($0\text{ s} < t < 2\text{ s}$, $N = 1024$; Fig. 3a). The spectrum of this stimulus (Y, found via FFT) reflects its major frequency components with peaks in amplitude at 1 Hz and 100 Hz (Fig. 3b).

To illustrate how two sensors may differ in their response to this stimulus, the responses to both a low-pass and high-pass first-order filter are now considered. Such sensors are described by the following transfer functions (Lathi, 1998):

$$H_{\text{low}} = 1/(1 + (f/f_c)i), \tag{4}$$

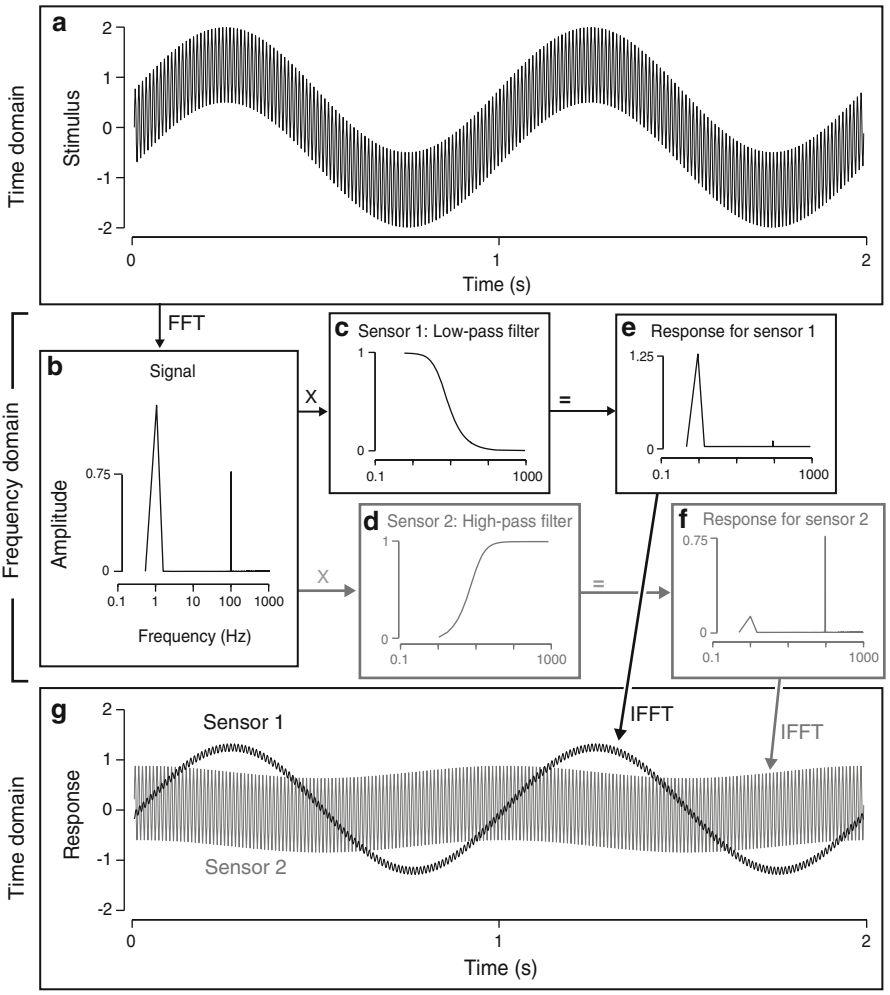

Fig. 3 Time-domain filtering employed to calculate the response of two sensors with distinct filtering characteristics. (**a**) For the purposes of illustration, the stimulus is modeled as a time-varying signal created by the sum of two sine functions (Eq. 1; see text for parameter values). This signal is converted from the time domain into (**b**) the frequency domain using a fast-Fourier transform (FFT). The resulting spectrum consists of a series of complex numbers for each frequency, the amplitude of which is shown. (**c**, **d**) In this example, the stimulus is detected by two sensors that possess distinct frequency response characteristics. (**c**) Sensor 1 is most sensitive to low frequencies and therefore functions as a low-pass filter. (**d**) In contrast, sensor 2 operates as a high-pass filter. (**e**, **f**) The response of both sensor 1 (**e**) and sensor 2 (**f**) is calculated in the frequency domain as the product of the signal spectrum (**b**) and the sensor spectra (**c, d**). These signals are then transformed into the time domain with IFFT. (**g**) The responses of sensor 1 (black) and sensor 2 (gray) demonstrate how the sensors respond differently to the same stimulus

$$H_{\text{high}} = 1 - (1/(1 + (f/f_c)i)), \tag{5}$$

where f_c is the cutoff frequency for each sensor ($f_c = 10$ Hz, in this example) and i denotes the (positive complex) root of -1 (Fig. 3c, d). These equations are evaluated to find their frequency responses. For example, the low-pass sensor maintains a relatively high-amplitude response to frequencies below the cutoff (Fig. 3c). Therefore, its response spectrum (Fig. 3e) maintains a high amplitude at 1 Hz, which is reflected in its response in the time domain (Fig. 3g). Conversely, the high-pass sensor attenuates the low-frequency components in favor of high frequencies that pass through to the response (Fig. d, f, g). These same steps may be employed to examine the differences between how SNs and CNs respond to a flow stimulus, based on their specific transfer functions.

3.3 The Responses to a Swimming Fish

The differences in frequency response between CNs and SNs are also reflected in their time-domain responses. An example is provided by a swimming goldfish (*Carassius auratus*; after Kalmijn, 1989). The displacement of the fluid increases on the approach of a neuromast (positive displacement in Fig. 4a) and subsequently passes zero (~0.25 s) before moving beyond the neuromast to produce a negative displacement. Most of the spectral power for this relatively slow stimulus signal is below 10 Hz, which is at the low end of the frequency range of the lateral line system (Fig. 2e, f).

The response of a SN to this stimulus (Fig. 4b, solid) was calculated with time-domain filtering (Section 3.1; cf. Fig. 3). This calculation used the transfer function to yield a displacement response for SN hair bundles (Fig. 2e, purple curve). This response appears to be almost identical in shape to the velocity of the stimulus (Fig. 4b, dashed line). This result illustrates how a SN can be considered a high-fidelity velocity detector for a low-frequency stimulus, even while the properties of a fractional time derivative of the boundary layer have been fully accounted for (cf. Goulet et al., 2012).

The CN response contrasts that of the SN for the same stimulus. The CN response (Fig. 4c, solid line) was calculated using time-domain filtering with the transfer function for the CN (Fig. 2f, green curve), applied to the stimulus acceleration (Fig. 4c, dashed line). The CN hair cell bundles sense a time waveform that closely follows the acceleration of the fluid flow. In addition, the CN hair bundles respond with a deflection that is about 50 times greater than in the SN (CN maximum ~1 μm vs. SN maximum ~20 nm; Fig. 4b, c), which is consistent with the differences in sensitivity interpreted from the frequency response (Section 2.3; Fig. 2d).

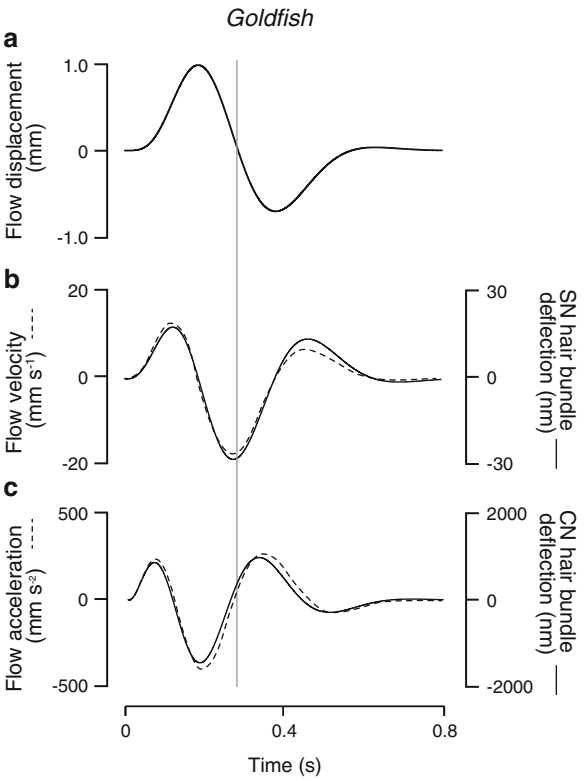

Fig. 4 Responses of SN and CN to a swimming goldfish calculated with time-domain filtering (Section 3.1; Fig. 3). (**a**) Freestream water displacement produced by a quietly approaching (positive going phase) and passing (negative going phase) goldfish (after Kalmijn, 1989; p. 204). (**b**) Hair cell displacement response of a SN (solid line) compared to the water velocity (dashed line) derived from the displacement shown in (**a**). (**c**) Hair cell displacement response of a CN (solid line) compared to the water acceleration (dashed line) derived from the displacement shown in (**a**). Parameters used for the transfer functions of SN and CN to calculate the filtered time responses were the same as used for Fig. 2. The vertical line indicates the time of passing by the neuromast ($t = 0.25$ s)

3.4 The Responses to Swimming Zooplankton

Biological flow stimuli can offer a broad range of frequency components, as illustrated by zooplankton that are detected by fish predators (Montgomery, 1989). For example, the crustaceans *Daphnia* and *Diaptomus* swim with appendages that create contrasting flow signals. *Daphnia* swimming is powered by a pair of antennae that propel the body in discrete pulses. *Diaptomus* use a series of swimmerets along the abdomen that operate with high frequency and low amplitude to move the body forward at a relatively steady rate. To examine how

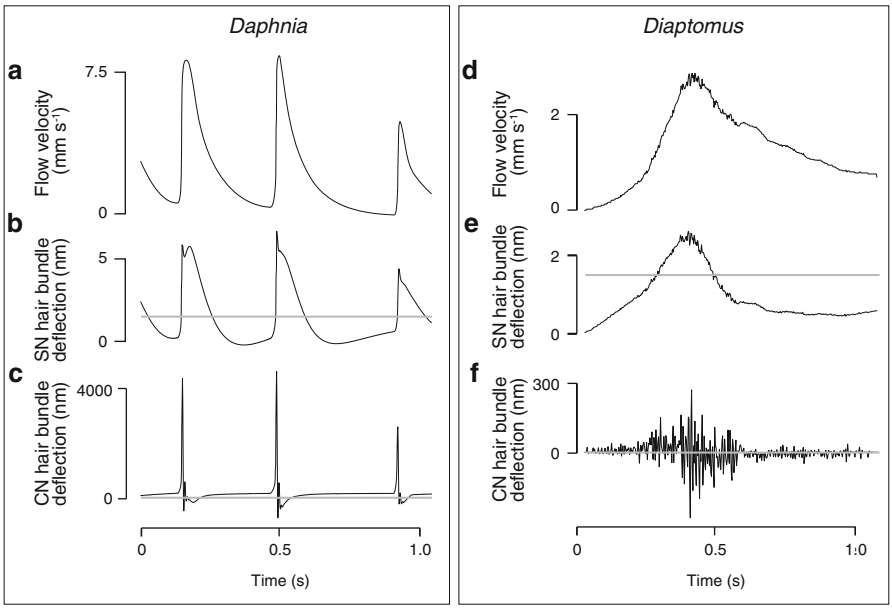

Fig. 5 Detecting the flow created by zooplankton. The flow velocity generated by two species of crustacean was measured by hot-wire anemometry (Montgomery, 1989). For each, we calculated the response of hair bundle deflection to the flow stimulus for both CN and SN biophysical models (Fig. 2) using time-domain filtering (Section 3.1; Fig. 3). The horizontal gray lines illustrate the threshold deflection (Section 2.3) for the SN (**b, e**) and CN (**c**, **f**). According to this calculation, (**a**) the velocity stimulus created by *Daphnia* was detected with high fidelity by (**b**) the SN neuromast. (**c**) In contrast, the CN neuromast responded with a high-intensity deflection to only the most rapid events in the stimulus. (**d–f**) Similar results were predicted for the stimulus generated by *Diaptomus*. (**d**) The flow velocity created by this animal is well reflected by (**e**) the small deflections of the SN, but (**f**) the rapid events are reflected in the large-amplitude response of the CN

CNs and SNs filter these different signals, the responses of both types may be calculated by time-domain filtering (Section 3.1).

Daphnia (Fig. 5a–c) swim with an oscillatory motion at a relatively low frequency and these pulses are interrupted by recovery strokes (Fig. 5). When exposed to this stimulus, the SN hair bundle deflections largely mirror the velocity of this flow pattern (Fig. 5b) with a relatively low amplitude. Therefore, SNs offer good fidelity to the velocity profile of this stimulus. In contrast, CNs accentuate the rapid events in a velocity signal and attenuate relatively slow flows. As a consequence, a CN responds with a high-amplitude deflection to the onset of the power stroke, but shows little response to the recovery stroke of *Daphnia*. The CN response thereby serves as an event marker for the initiation of propulsive cycles, but not a comprehensive reflection of changes in velocity.

The contrast in filtering between a SN and CN is even more dramatic for the stimulus produced by *Diaptomus* (Fig. 5d). The modeled SN response reflects

nearly all features of the velocity of the stimulus (Fig. 5e). However, much of this response is below transducer noise levels and therefore unlikely to be detected by SNs (van Netten et al., 2003; see also Section 2). SNs therefore encode the slow changes in flow as the zooplankton achieves high speeds. In contrast, the CN response filters out this slow change and emphasizes the high-frequency (~50 Hz) oscillations produced by the swimmerets with a far superior signal-to-noise ratio than the SN signal (Fig. 5f). Therefore, the SN and CN responses reflect complementary components of the stimulus produced by *Diaptomus*.

4 Unresolved Questions

Fundamental questions remain about the biophysics of lateral line neuromasts. Although a comprehensive picture is emerging for how CNs filter and encode stimuli, there remains less certainty about SNs. For example, it is not clear whether the hair cells within SNs possess the same filtering properties as in CNs. This uncertainty complicates our understanding for the role of each submodality in behavior (see also the chapter by Chagnaud & Coombs), and behavioral studies largely have yet to determine how SNs and CNs individually influence the behavior of fishes.

4.1 Are the Hair Cells within SNs and CNs Different?

It is increasingly clear how canal neuromasts detect flow stimuli. Biophysical models of the canal and CN cupula can successfully predict the extracellular potentials of the hair cells (Ćurčić-Blake & van Netten, 2006) and the afferent action potentials (Coombs & Janssen, 1990; Kroese & Schellart, 1992; Goulet et al., 2008) for an oscillatory flow stimulus. The dominance of mechanical properties in the CN frequency response is facilitated by the relative broad tuning of its hair cells (Kroese & van Netten, 1989), and there is evidence that in ruffe (*Gymnocephalus cernua*) the low-pass filtering of a CN hair cell exhibits a temperature-dependent cutoff frequency that under normal habitat conditions is tuned to mechanical properties (Wiersinga-Post & van Netten, 2000).

Mechanics may not similarly dictate the frequency response of superficial neuromasts. Studies on SN afferent activity indicate cutoff frequencies for a velocity stimulus on the order of tens of Hertz (Kroese & Schellart, 1992), which is not predicted by biophysical models so far (Fig. 2d). Therefore, the neurophysiology of SN hair cells may attenuate high frequencies in a manner that is not similarly found in CN hair cells. However, this issue remains unresolved because of possible differences between the flow stimulus used in neurophysiological measurements (e.g., Kalmijn, 1988) and that considered by biophysical models (e.g., McHenry et al., 2008).

A difference in the physiological or mechanical properties of hair cells has the potential to affect the limits of sensitivity in SNs and CNs. By neglecting such a difference, the present modeling results suggest that SNs generate relatively small hair bundle displacements as compared to CNs when exposed to the same oscillatory stimulus (e.g., Fig. 4, 5). This result emerges predominantly from the larger dimensions of CNs. In addition, the expected equivalent noise levels of SNs are higher mainly because of the fewer hair cells of SNs (see Münz, 1989, for data; van Netten et al., 2003). Together this results in an overall superior signal-to-noise ratio of hair bundle responses of a single CN as compared to those of a SN (see Section 2.3). This view is supported by threshold measurements of afferent neurons of both SNs and CNs in the mottled sculpin (Coombs & Janssen, 1989). However, it remains possible that SNs could compensate for their fewer numbers of hair cells with higher sensitivity in each hair cell. Also, afferent fibers may enhance the signal component over the noise by contacting many SNs (Münz, 1989) and thereby integrate the responses of hair cells of several cupulae. On the other hand, a less sensitive SN should detect high intensities, where CNs would be saturated. This means that a lower SN sensitivity could provide information about high-amplitude events, assuming a fixed and similar operational displacement range of the hair cells in both types of neuromasts.

The comparison we made is based on results from SNs in zebrafish and the rather large CNs in the ruffe. In other fish species the ratio of absolute hair bundle responses to the same stimulus may differ. Nevertheless, it is to be expected that because of the general morphological differences that govern their biophysical detection properties, SNs respond with smaller hair bundle deflection than those of CNs at higher frequencies, up to hundreds of Hertz (Fig. 2e, f).

4.2 Do CNs and SNs Play Different Roles in Behavior?

Experiments on predatory behavior offer compelling evidence for an integral role of CNs. The ability to detect and localize prey in mottled sculpin is likely limited by the sensitivity and threshold of the lateral line (Coombs & Janssen, 1990). CNs are better suited to this task over the less sensitive SNs (Fig. 2), particularly for the relatively high frequencies generated by the swimming motions of zooplankton (Fig. 5; Section 3). Indeed, this behavior was unaltered by ablating the SNs, but was extinguished by a chemical ablation of the entire system, including CN neuromasts (Coombs et al., 2001). In contrast, SNs appear to play an important role in prey fish. Zebrafish larvae, which lack CNs, require SNs to evade a predator (Stewart et al., 2013). This ability depends on the motion of the body relative to the surrounding water (Stewart et al., 2010) and becomes less sensitive during swimming (Feitl et al., 2010).

The canal lateral line system may offer advantages in detecting stimuli in environments with high currents. When exposed to a constant unidirectional flow, an oscillatory stimulus remains detectable to fibers innervating CNs, but not SNs in

trout (*Oncorhynchus mykiss*) and goldfish (Engelmann et al., 2000, 2002). This result is consistent with the frequency response of CNs, which filters out direct currents more strongly due to the hydrodynamics of the canal (Fig. 2b). Although exhibiting lower sensitivity for a wide range of frequencies (Fig. 2e, f), SNs are apparently saturated by rapid unidirectional flow and consequently become insensitive to an additional oscillatory flow stimulus, such as what might be generated by a prey (Fig. 5).

If not saturated, SNs may enable a fish to detect turbulent flows. In light of recent findings (Van Trump et al., 2010), the results of experiments on trout that combined an aminoglycoside treatment with mechanical ablation may be interpreted as demonstrating that SNs affect the duration of entrained swimming behind obstacles in flow (Montgomery et al., 2003). Consistent with this finding, experiments on goldfish suggest that posterior lateral line afferents shown to respond to vortex rings most likely innervate SNs (Chagnaud et al., 2006). Such flows, and those generated by self-motion and other animals, are characterized by high spectral power for frequencies around 10 Hz (Bleckmann et al., 1991), where SNs exhibit relatively high sensitivity (Fig. 2f; Coombs and Janssen, 1990). Therefore, SNs appear to play a role in behaviors that depend on relatively high-intensity turbulent flows.

Given the sensitivity of SNs to unidirectional flow, one might expect this submodality to play a role in the rheotactic (orienting) behaviors of fish to environmental currents. However, current evidence on this matter is inconclusive. Support has been provided by behavioral experiments that used aminoglycoside antibiotics to differentially ablate neuromasts. These antibiotics create a chemical disturbance of hair cell response by blocking hair cell transduction channels (Kroese et al., 1989; Marcotti et al., 2005; see also the chapter by Coffin et al.). Streptomycin is equally effective in creating this effect in the hair cells of both SNs and CN. However, gentamicin reportedly affected only the hair cells of canal neuromasts (Song et al., 1995). Taking advantage of this effect, behavioral experiments on rheotaxis attempted to differentially ablate SNs and CNs in combination with a mechanical ablation to eliminate only SNs (Montgomery et al., 1997). However, recent studies suggest that gentamicin actually blocks a large percentage of both SNs and CNs (Van Trump et al., 2010). Thus, it is difficult to explain why rheotaxis was affected by streptomycin (intended to block both CNs and SNs) but not gentamicin (intended to selectively block CNs). In support of a role of SNs in rheotaxis, mechanical ablation of SNs on the skin surface significantly reduced the rheotactic response in much the same manner as streptomycin, which blocks both CNs and SNs. Thus, there is some evidence that SNs, but not CNs, are important to rheotaxis, but only at relatively slow flows.

5 Summary

The two submodalities of the fish lateral line system are sensitive to different aspects of a flow stimulus owing to the biophysics of the neuromasts. In SNs, boundary layer hydrodynamics and fluid–structure interaction mechanics combine

to create a sensor that is velocity sensitive with high-pass filtering. The cutoff frequency for this filter is on the order of a few Hertz and varies with the dimensions of the cupula and number of hair cells. CNs are generally at least more than an order of magnitude more sensitive than SNs and respond in proportion to flow acceleration over a wide range of frequencies. They exhibit low-pass filtering with a cutoff frequency in the hundreds of Hertz, which is determined by the size of the cupula and the canal. Therefore, the sensitivity of the two submodalities encompasses distinct regimes of stimulus intensity and frequency.

These differences between the types of neuromast are reflected in their filtered responses in the time domain. SNs are predicted to generate responses with high fidelity to the velocity of many biological stimuli (Fig. 5a, e). CNs exhibit a stronger response (Fig. 5c, f), but preferentially sense high-frequency components. Consistent with this result, CNs appear to be employed in behaviors that are limited by neuromast sensitivity or benefit from their ability to filter out direct currents. In contrast, SNs may aid behaviors that depend on information gleaned from high-intensity flows. Despite these advances, a comprehensive understanding of the respective roles of the two submodalities remains elusive. Investigations that integrate behavioral experiments with neurophysiology and biophysics offer great potential for understanding this distinctive sensory system of fish.

References

Bleckmann, H., Breithaupt, T., Blickhan, R., & Tautz, J. (1991). The time course and frequency content of hydrodynamic events caused by moving fish, frogs, and crustaceans. *Journal of Comparative Physiology A*, 168, 749–757.

Budelmann, B. (1989). Hydrodynamic receptor systems in invertebrates. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line* (pp. 607–631). New York: Springer.

Budelmann, B., & Bleckmann, H. (1988). A lateral line analogue in cephalopods: Water waves generate microphonic potentials in the epidermal head lines of *Sepia* and *Lolliguncula*. *Journal of Comparative Physiology A*, 164, 1–5.

Chagnaud, B. P., Bleckmann, H., & Engelmann, J. (2006). Neural responses of goldfish lateral line afferents to vortex motions. *The Journal of Experimental Biology*, 209, 327–342.

Coombs, S., & Janssen, J. (1989). Peripheral processing by the lateral line of the mottled sculpin (*Cottus bairdi*). In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line* (pp. 299–319). New York: Springer.

Coombs, S., & Janssen, J. (1990). Behavioral and neurophysiological assessment of lateral line sensitivity in the mottled sculpin, *Cottus-bairdi*. *Journal of Comparative Physiology A*, 167, 557–567.

Coombs, S., Janssen, J., & Webb, J. F. (1988). Diversity of lateral line systems: Evolutionary and functional considerations. In J. Atema, R. R. Fay, A. N. Popper, & W. N. Tavolga (Eds.), *Sensory biology of aquatic animals* (pp. 553–593). New York: Springer.

Coombs, S., Braun, C. B., & Donovan, B. (2001). The orienting response of Lake Michigan mottled sculpin is mediated by canal neuromasts. *Journal of Experimental Biology*, *204*, 337–348.

Ćurčić-Blake, B., & van Netten, S. (2006). Source location encoding in the fish lateral line canal. *Journal of Experimental Biology*, 209, 1548–1559.

Denton, E. J., & Gray, J. (1983). Mechanical factors in the excitation of clupeid lateral lines. *Proceedings of the Royal Society B: Biological Sciences*, 218, 1–26.

Denton, E. J., & Gray, J. A. B. (1988). Mechanical factors in the excitation of the lateral lines of fishes. In J. Atema, R. R. Fay, A. N. Popper, & W. N. Tavolga (Eds.), *Sensory biology of aquatic animals* (pp. 595–618). New York: Springer.

Denton, E., & Gray, J. (1989). Some observations on the forces acting on neuromasts in fish lateral line canals. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line* (pp. 229–246). New York: Springer.

Dijkgraaf, S. (1963). The functioning and significance of the lateral-line organs. *Biological Reviews*, 38, 51–105.

Dinklo, T. (2005). *Mechano- and electrophysiological studies on cochlear hair cells and superficial lateral line cupulae*. Doctoral dissertation, University of Groningen.

Engelmann, J., Hanke, W., Mogdans, J., & Bleckmann, H. (2000). Neurobiology: Hydrodynamic stimuli and the fish lateral line. *Nature*, 408, 51–52.

Engelmann, J., Hanke, W., & Bleckmann, H. (2002). Lateral line reception in still- and running water. *Journal of Comparative Physiology A,* 188, 513–526.

Feitl, K. E., Ngo, V., & McHenry, M. J. (2010). Are fish less responsive to a flow stimulus when swimming? *The Journal of Experimental Biology*, 213, 3131–3137.

Görner, P. (1963). Untersuchungen zur Morphologie und Elektrophysiologie des Seitenlinienorgans vom Krallenfrosch (*Xenopus laevis* Daudin). *Zeitschrift für vergleichende Physiologie*, 47, 316–338.

Goulet, J., Engelmann, J., Chagnaud, B. P., Franosch, J.-M. P., Suttner, M. D., & Hemmen, J. L. (2008). Object localization through the lateral line system of fish: Theory and experiment. *Journal of Comparative Physiology A*, 194, 1–17.

Goulet, J., van Hemmen, J. L., Jung, S. N., Chagnaud, B. P., Scholze, B., & Engelman, J. (2012). Temporal precision and reliability in the velocity regime of a hair-cell sensory system: The mechanosensory lateral line of goldfish, *Carassius auratus*. *Journal of Neurophysiology*, 107, 2581–2593.

Hudspeth, A. J. (1989). How the ear's works work. *Nature,* 341, 397–404.

Jielof, R., Spoor, A., & de Vries, H. (1952). The microphonic activity of the lateral line. *Journal of Physiology,* 116, 137–157.

Kalmijn, A. J. (1988). Hydrodynamic and acoustic field detection. In J. Atema, R. R. Fay, A. N. Popper, & W. N. Tavolga (Eds.), *Sensory biology of aquatic animals* (pp. 83–130). New York: Springer.

Kalmijn, A. J. (1989). Functional evolution of lateral line and inner ear sensory systems. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line* (pp. 187–215). New York: Springer.

Kramer, G. (1933). Sinnesleistung und das Orientierungsverhalten von *Xenopus laevis*. Zoologische Jahrbücher, *Abteilung für Anatomie und Ontogenie der Tiere*, 52, 629–676.

Kroese, A. B. A., & van Netten, S. M. (1989). Sensory transduction in lateral line hair cells. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line* (pp. 265–284). New York: Springer.

Kroese, A. B. A., & Schellart, N. A. M. (1992). Velocity- and acceleration-sensitive units in the trunk lateral line of trout. *Journal of Neurophysiology*, 68, 2212–2221.

Kroese, A. B. A., van der Zalm, J. M., & van den Bercken, J. (1978). Frequency response of the lateral-line organ of *Xenopus laevis*. *Pfluegers Archiv*, 375, 167–175.

Kroese, A. B. A., Das, A., & Hudspeth, A. J. (1989). Blockage of the transduction channels of hair cells in the bullfrog's sacculus by aminoglycoside antibiotics. *Hearing Research*, 37, 203–217.

Kuiper, J. W. (1956). *The microphonic effect of the lateral line organ*. PhD thesis, University of Groningen, The Netherlands.

Lathi, B. (1998). *Signal processing and linear systems*. New York: Oxford University Press.

Liao, J. C. (2010). Organization and physiology of posterior lateral line afferent neurons in larval zebrafish. *Biology Letters*, 6, 402–405.

Marcotti, W., van Netten, S. M., & Kros, C. (2005). The aminoglycoside antibiotic dihydrostreptomycin rapidly enters mouse outer hair cells through the mechano-electrical transducer channels. *Journal of Physiology,* 567, 505–521.

McHenry, M. J., & van Netten, S. M. (2007). The flexural stiffness of superficial neuromasts in the zebrafish (*Danio rerio*) lateral line. *Journal of Experimental Biology*, 210, 4244–4253.

McHenry, M. J., Strother, J. A., & van Netten, S. M. (2008). Mechanical filtering by the boundary layer and fluid–structure interaction in the superficial neuromast of the fish lateral line system. *Journal of Comparative Physiology A,* 194, 795–810.

McHenry, M. J., Feitl, K. E., Strother, J. A., & Van Trump, W. J. (2009). Larval zebrafish rapidly sense the water flow of a predator's strike. *Biology Letters* 5, 477–497.

Montgomery, J. C. (1989). Lateral line detection of planktonic prey. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line* (pp. 561–574). New York: Springer.

Montgomery, J. C., Baker, C., & Carton, A. (1997). The lateral line can mediate rheotaxis in fish. *Nature,* 389, 960–963.

Montgomery, J. C., McDonald, F., Baker, C. F., Carton, A. G., & Ling, N. (2003). Sensory integration in the hydrodynamic world of rainbow trout. *Proceedings of the Royal Society B: Biological Sciences*, 270, S195–S197.

Münz, H. (1989) Functional organization of the lateral line periphery. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line* (pp. 285–297). New York: Springer.

Schlichting, H. (1979). *Boundary-layer theory*. New York: Springer-Verlag.

Song, J., Yan, H., & Popper, A. (1995). Damage and recovery of hair cells in fish canal (but not superficial) neuromasts after gentamicin exposure. *Hearing Research*, 91, 63–71.

Stewart, W. J., & McHenry, M. J. (2010). Sensing the strike of a predator fish depends on the specific gravity of a prey fish. *The Journal of Experimental Biology*, 213, 3769–3777.

Stewart, W. J., Cardenas, G. S., & McHenry, M. J. (2013) Zebrafish larvae evade predators by sensing water flow. *The Journal of Experimental Biology*, 216, 388–398.

Tsang, P. T. S. K. (1997). *Laser interferometric flow measurements in the lateral line organ*. Doctoral dissertation, University of Groningen.

van Netten, S. M. (1988). Laser interferometer microscope for the measurement of nanometer vibrational displacements of a light-scattering microscopic object. *The Journal of the Acoustical Society of America*, 83, 1667–1674.

van Netten, S. M. (1991). Hydrodynamics of the excitation of the cupula in the fish canal lateral line. *The Journal of the Acoustical Society of America*, 89, 310–319.

van Netten, S. M. (2006). Hydrodynamic detection by cupulae in a lateral line canal: Functional relations between physics and physiology. *Biological Cybernetics*, 94, 67–85.

van Netten, S. M., & Kroese, A. B. A. (1987). Laser interferometric measurements on the dynamic behavior of the cupula in the fish lateral line. *Hearing Research*, 29, 55–62.

van Netten, S. M., Dinklo, T., Marcotti, W., & Kros, C. J. (2003). Channel gating forces govern accuracy of mechano-electrical transduction in hair cells. *Proceedings of the National Academy of Sciences of the USA*, 100, 15510–15515.

Van Trump, W. J., & McHenry, M. J. (2008). The effect of morphological variation on the frequency response of superficial neuromasts in zebrafish (*Danio rerio*). *Journal of Experimental Biology*, 211, 2105–2115.

Watson, G., & Hessinger, D. (1989). Cnidocyte mechanoreceptors are tuned to the movements of swimming prey by chemoreceptors. *Science*, 243, 1589–1591.

Weber, D. D., & Schiewe, M. H. (1976). Morphology and function of the lateral line of juvenile steelhead trout in relation to gas-bubble disease. *Journal of Fish Biology*, 9, 217–233.

Wiersinga-Post, J. E. C., & van Netten, S. M. (2000). Temperature dependency of cupular mechanics and hair cell frequency selectivity in the fish canal lateral line organ, *Journal of Comparative Physiology A*, 186, 949–956.

Wubbels, R. J. (1992). Afferent response of a head canal neuromast of the ruff (*Acerina cernua*) lateral line. *Comparative Biochemistry and Physiology A*, 102, 19–26.

Sensory Ecology and Neuroethology of the Lateral Line

John Montgomery, Horst Bleckmann, and Sheryl Coombs

Keywords hydrodynamic sensors • surface waves • aquatic prey detection • aquatic predator avoidance • aquatic communication • fish schooling • sensory signals and noise • hydrodynamic imaging • control of swimming • rheotaxis

1 Introduction

The lateral line is found in all fish groups, and aquatic amphibians. Like hearing, it is a hair-cell based mechanoreceptor system. But in contrast to hearing, it is a distributed sensory system, with clusters of hair cells grouped into neuromasts dispersed over the head and trunk of the animal. The distributed nature of the lateral line sensors (see Webb, Chapter 2) provides some similarities with touch, and indeed the early description of the lateral line system as providing "touch at a distance" is still remarkably apt (Dijkgraaf, 1934). It is the dense, viscous nature of water interacting with the cupulae of the neuromasts that allows animals with lateral lines to 'feel' their immediate surroundings and to sense water movements

J. Montgomery (✉)
School of Biological Sciences and Institute of Marine Science, University of Auckland, Auckland 1142, New Zealand
e-mail: j.montgomery@auckland.ac.nz

H. Bleckmann
Universität Bonn, Institut für Zoologie, Poppelsdorfer Schloß, 53115 Bonn, Germany
e-mail: bleckmann@uni-bonn.de

S. Coombs
Department of Biological Sciences, JP Scott Center for Neuroscience, Mind and Behavior, Bowling Green State University, 434 Life Science Center, Bowling Green, OH 43403, USA
e-mail: scoombs@bgsu.edu

S. Coombs et al. (eds.), *The Lateral Line*, Springer Handbook of Auditory Research 48,
DOI 10.1007/2506_2013_17, © Springer Science+Business Media New York 2013,
Published online: 6 August 2013

relative to the body surface such as water currents or the water disturbances caused by other animals.

Like all major sensory systems, the lateral line makes an important contribution to the sensory capabilities of fish and aquatic amphibians and contributes to a wide range of core behaviors including: feeding, avoidance of predators, and communication. In these behaviors, the lateral line is detecting the hydrodynamic fields produced by other animals. Fluid dynamics determines that these source/receiver interactions are relatively short-range in comparison with hearing. Correspondingly, the lateral line provides a short range contribution to multimodal input for basic sensory abilities – namely, the ability to detect, localize, and at least in some respects, identify biological sources of interest. The close-range operation of the lateral line also means that in some instances the behavioral reactions and neural pathways need to be fast and somewhat stereotyped to be effective.

In addition to sensing biotic sources of interest, the lateral line also plays an important role in detecting abiotic or stationary features of the local environment. In blind Mexican cavefish (*Astyanax fasciatus*) though probably in other fish species as well, the fluid flows and pressure changes generated by the animal's own swimming movements get altered by surrounding stationary objects. This provides a stimulus to the lateral line that enables a fish to actively image its environment in a way that is somewhat analogous to active electroreception or echolocation. Large scale, ambient water flows created by wind and gravity are also of obvious importance to aquatic animals and the lateral line allows fish to sense, and orient, to flows, and then in turn, to use this information in combination with other senses to mediate a range of behaviors. Recent work on lateral line has moved into the complex domain of flow fluctuations generated by obstacles in the flow, the swimming activity of other animals including prey and schoolmates, and flows generated by the animal's own swimming.

This chapter will focus on the role of the lateral line in natural fish behavior, in effect, the sensory ecology of the lateral line. The approach is more conceptual than comprehensive, choosing representative behaviors and especially those that lend themselves to a neuroethological analysis. Understanding sensory and brain function in the context of natural behavior is the foundation for neuroethology. It provides a clear focus for the determination of the relevant parameters of the physical stimulus, the physical and physiological mediation of stimulus encoding, and a targeted approach as to how the central nervous system processes and transforms sensory inputs to behavioral action. A comprehensive neuroethological understanding of lateral-line behavior is still some way off, but the approach provides an organizing scaffold from which to work. Elements of this neuroethological framework are also covered in greater depth in other chapters, including those on the morphology and evolution of the lateral line (Webb, Chapter 2), and on information processing by the peripheral (Chagnaud & Coombs, Chapter 6) and central nervous system (Bleckmann & Mogdans, Chapter 8).

2 Surface Feeding (Source localization in 2D)

The water surface provides a nice example of source localization simplified to the case of two dimensions. The air-water interface provides an important food source for a number of fish and amphibian species. Particularly in forested areas, sunlight is captured by the forest canopy which limits the productivity of freshwater systems. In these, and similar, circumstances, insects falling onto the water surface, and struggling in the surface tension layer, provide an important food source (Lang, 1980). During the day, many visual-feeding fish utilize this resource but in addition, there are also some fish like the striped panchax (*Aplocheilus lineatus*) (Fig. 1) that use their lateral line to detect and locate prey on the water surface. Surface feeding fish (Schwartz, 1971), but also the African clawed frog (*Xenopus laevis*) (Görner, 1973), hunt predominantly at night, and can locate surface prey in complete darkness.

Typical wind generated surface waves contain only frequency components below 10 Hz. In contrast an insect struggling at the water surface creates concentric surface waves that have frequencies up to about 100 Hz (Lang, 1980; Bleckmann, 1994; and Fig. 2). Insect generated surface waves propagate out from the source in a series of concentric rings. At the source sizes and target distances relevant to the detection of small prey, the surface waves have a mix of capillary and gravity properties and propagate with well-defined characteristics (Bleckmann & Schwartz, 1982; Bleckmann, 1993). In addition to the concentric nature of the waves, higher frequency wave components travel faster than lower frequency components. Furthermore, higher frequency wave components are attenuated more strongly than lower frequency components during stimulus propagation (Bleckmann et al., 1989). Thus the water surface behaves like a low-pass filter. The depth impact of surface waves is very small. At a depth of one wavelength (e.g. 23.6 mm at 10 Hz and 2.9 mm at 140 Hz) the vertical movement of water particles is less than 1/500 of that observed at the water surface. Therefore whilst foraging in the dark, fish specialized in surface feeding sit with the dorsal surface of their head in the surface film (Fig. 1a). The behaviorally-measured threshold curve to single frequency wave stimuli shows that the surface feeding striped panchax is highly sensitive in the frequency range < 10 up to about 100 Hz (Fig. 3). Even if only a short lasting wave stimulus is presented, i.e. under open loop conditions, surface feeding fish accurately orient towards the source and then move towards it and stop with an accuracy of about 10%. These behavioral responses indicate that information on source direction and distance is encoded by the lateral line.

In the striped panchax the lateral line system across the top of its head consists of a steoeotyped array of 18 neuromasts situated in open grooves (half-formed canals) (Fig. 1b), the borders of which have been described as fleshy ridges (Schwarz et al., 2011). Each neuromast has a unique receptive field (Bleckmann et al., 1989), in part defined by the inherent directional sensitivity of the neuromast, which corresponds to the long axis of the open grooves in which it sits. The inherent directional sensitivity of the neuromast results from the directional properties of its hair cells

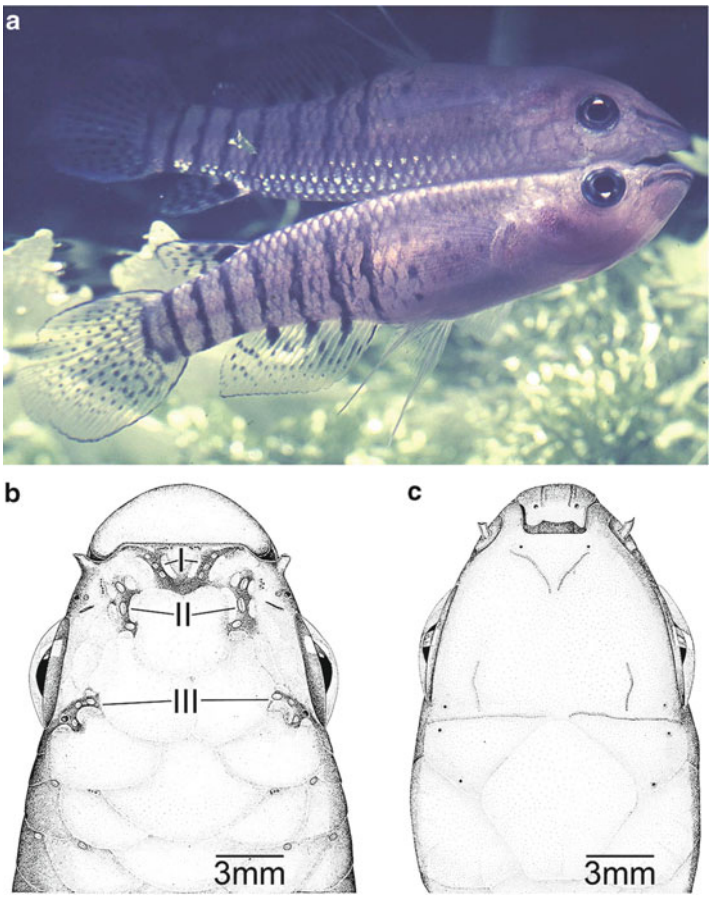

Fig. 1 (**a**-**c**). (**a**) The surface feeding striped panchax *Aplocheilus lineatus*. At night surface feeding fish hunt immediately below the water surface, maximizing their sensitivity to capillary surface waves. B. Dorsal view of the heads of the striped panchax (**b**) and the African butterfly fish *Pantodon bucholzi* (**c**) In striped panchax large dorsal head neuromasts are arranged in three groups (labeled I, II and III from rostral to caudal), each of which consists of three single organs all of which are bordered by fleshy ridges. In the African butterfly fish 6 rows of up to 70 very small (about 50 x 30 μm) superficial neuromasts are seen. The cephalic lateral line of the African butterfly fish in addition has 8 large banana shaped canal neuromasts (each of which has up to 3000 hair cells) situated below membranous coverings of widened head lateral line canals (Bleckmann et al., 1989). The drawings of both fish species were kindly provided by G. Tittel

and the fact that each hair cell responds maximally to displacement of the neuromast cupula in a single direction, producing a cosine response characteristic with respect to directional stimulation (Flock, 1965; Bleckmann et al., 1989; Chagnaud & Coombs, Chapter 7). As in other fish, there are two populations of hair cells within each neuromast, each aligned on the same axis, but with opposite polarities and directional sensitivities. The open canal grooves described above

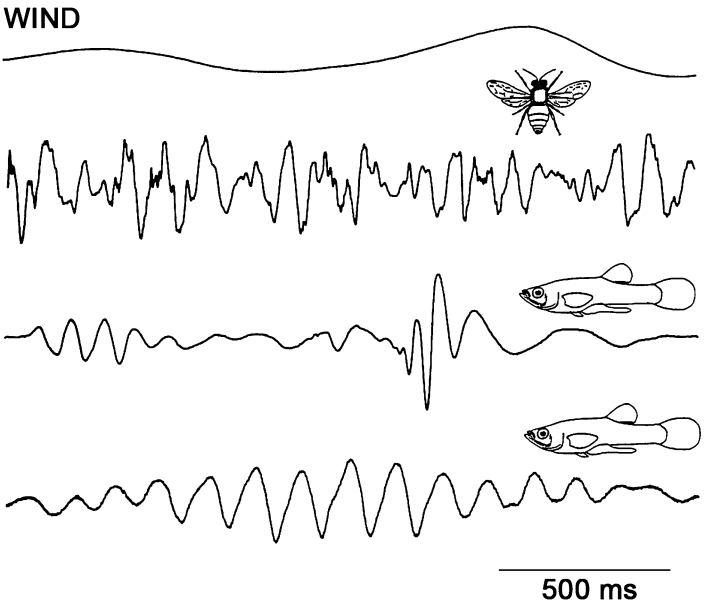

Fig. 2 Examples of water surface waves (displacement). From top to bottom: caused by wind, a struggling fly *Calliphora vicina*, and a guppy *Poecilia reticulate*. The guppy was contacting the water surface for breathing (top) and taking dry food from the water surface (bottom). Amplitudes are not to scale

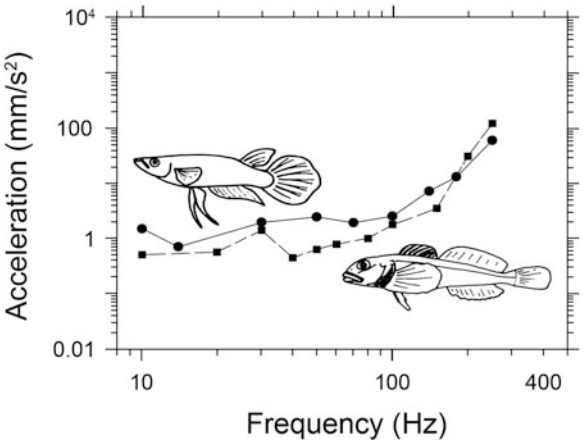

Fig. 3 Behavioral acceleration thresholds of the surface feeding striped panchaz (top curve) and the bottom dwelling mottled sculpin. Redrawn from Bleckmann (1980) and Coombs and Janssen (1990)

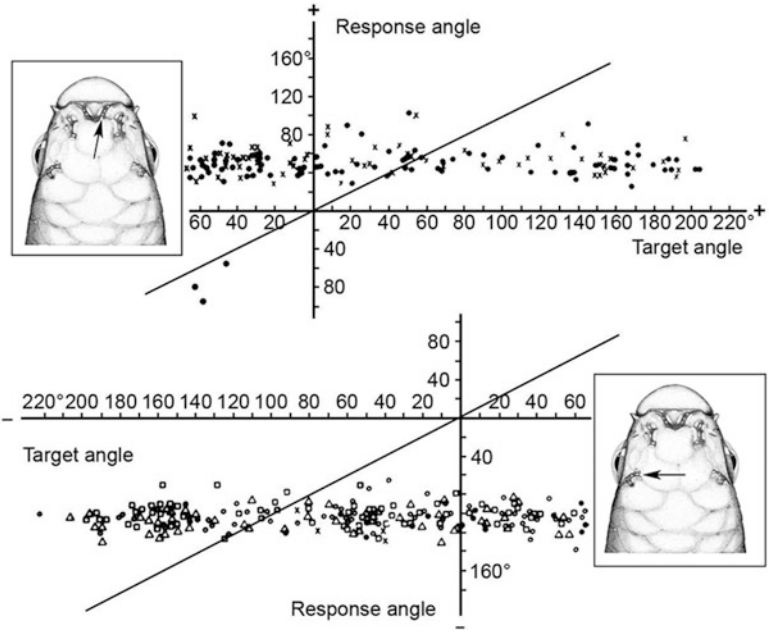

Fig. 4 Relationship between target- and response angle for striped panchax *Aplocheilus lineatus* with only one out of the 18 neuromasts located on the dorsal side of the head was left intact (arrows). Different symbols belong to different test series with the same animal (redrawn from Müller and Schwartz, 1982)

may alter the direction of water in the groove and over the neuromast relative to that outside of the groove. In short, the population of cephalic neuromasts provides intensity and spectral information that depends on target location, and hence can be decoded by the CNS to produce the orientation behavior. As the propagation speed of water surface waves is low (in the relevant frequency range of 10 to 100 Hz between 23 and 36 cm s^{-1}), the neuromasts most likely also provide temporal information that could contribute to directional orientation. Details of the CNS processing of the information from the spatial array of neuromasts, or how target direction is represented, are unknown. However, when all neuromasts except one are removed from the cephalic lateral line, striped panchax always turn in a particular direction regardless of target position (Fig. 4). Furthermore, the response angle correlates with the location of the neuromast: anterior neuromasts drive responses through small angles whereas posterior neuromasts elicit responses through large angles. This position code is consistent with direction estimation based on the relative timing of activity between neuromasts.

Having turned towards the stimulus, surface feeding fish glide towards the location of the target and stop. This provides direct behavioral evidence that target

distance is also estimated. Stopping close to the prey facilitates a final orientation and strike particularly if the prey is still moving. The question then becomes: how does the lateral line encode target distance? An elegant series of behavioral experiments using the prey-orienting behaviors of the striped panchax (Bleckmann & Schwartz, 1982) and the African butterfly fish (*Pantodon buchholzi*) (Hoin-Radkovski et al., 1984) shows that this ability taps into the way in which the shape, and frequency composition, of the passing waveform varies with target distance. Because higher frequency wave components travel at higher velocities and attenuate more strongly during propagation, prey waves have more high-frequency components close to the source, and the wave packet is relatively compressed. At longer distances from the source, the wave packet has fewer high-frequency components and is extended in time. The use of these complex patterns of the wave packet to estimate target distance is shown by producing a 'phantom' stimulus: synthetic patterns from a close target that mimic the wave patterns of a more distance source. Under these conditions, the fish acts as predicted by the use of wave pattern for distance estimation. It overshoots the closer source and approaches the 'phantom' target.

These experiments are a nice reminder of the hierarchy of evidence that relates to animal orientation and behavior. Firstly, characterization of the physical stimulus is important to be able to propose a specific orientation mechanism. Secondly, neurophysiology is then necessary to demonstrate that the sensory system in question responds to and encodes the requisite features of the stimulus. Finally, only behavioral experiments can provide evidence that the animal not only can, but indeed does, utilize the proposed orientation mechanism. The direct behavioral evidence becomes even stronger when the physical stimulus can be manipulated in such a way as to generate a 'phantom' stimulus to which the animal responds in the way predicted.

That surface feeding fish use not only the spectral cues in the complex wave pattern, but also other wave features for distance estimation is indicated by the following experiments. If single frequency wave stimuli are presented, distance determination still occurs, but is less effective. The fish now tend to underestimate the distance if it exceeds 6 to 8 cm. In general, the relative localization error at a given source distance increases with frequency and at a given frequency, increases with source distance. This indicates that the fish compute the curvature of the wave front and that spectral cues are also used for distance determination. In other words, if no other cues are available, a high-frequency wave train is interpreted to have travelled a shorter distance than a low frequency one (Bleckmann, 1988; Bleckmann et al., 1989). Thus surface feeding fish utilize redundant cues for wave source localization. That the curvature of a concentric wave stimulus is one of the cues used for distance estimation is supported by CNS recordings from midbrain cells in the African clawed toad which show curvature-dependent spike rates (Claas et al., 1989; Behrend et al., 2008).

3 Detecting Prey in Midwater

Below the surface, the physics of water disturbances produced by potential prey are quite different from surface waves (Kalmijn, 1988). In addition, the problem becomes one of locating, or tracking, a target in 3D space. The type of water disturbances and the effective lateral line stimulus depend on how the disturbances are created. The flows generated by the beating limbs of a small crustacean differ from the ventilation or filter feeding currents of a larger crab or bivalve, which differ again from the stimulus generated by a small but fast moving animal, or the complex flows generated by larger swimming or breathing fish (e.g. Bleckmann et al., 1991; Hanke et al., 2012). There have been extensive behavioral studies of lateral line mediated prey detection across a wide range of species. The physics of the flows mediating these predator prey interactions are complex and differ on a case-by-case basis. The general description is that local or near-field flows around a vibrating object will provide the stimulus to the lateral line. The simplest of these types of flows will be produced by a pulsating sphere (monopole) or by a constant volume sphere vibrating backwards and forwards (dipole). The latter of these two is a better representation for some common types of lateral line stimuli and hence has become one of the standard stimulus generators for lateral line studies. Some species of fish, most studied being the mottled sculpin (*Cottus bairdi*) show an unconditioned approach and strike at a small vibrating sphere (Hoekstra & Janssen, 1985). This behavior supports the use of the dipole stimulus as a reasonable proxy for the more complex fields of the small epibenthic prey on which these species feed.

The dipole field for a given sphere size, vibration frequency and amplitude is well defined and the oscillating flow can be specified for each point in space around the dipole (Kalmijn, 1988). Midwater and bottom dwelling fish like mottled sculpin are very sensitive to dipole stimuli, their behavioral threshold curve is similar to the threshold curve of a surface feeding fish (Fig. 3). One can, in principle, model the pattern of activation over the entire lateral line system as a function of dipole location, given some simplifying assumptions and knowledge about the number, sensitivity, orientation and spatial distribution of superficial and canal neuromasts. In practice, however, this is very difficult to do, and moreover, the precise location and number of neuromasts that mediate any given behavioral response is unknown, meaning that the underlying pattern of stimulation that evokes a behavioral response is difficult to determine.

A few examples of particular predator–prey interactions can serve to illustrate the complexity and diversity of the requirements for the detection and 3D localization of stationary targets, and the tracking and interception for a moving target. One of the best models for lateral line based detection and localization of stationary prey has been the mottled sculpin (e.g. Coombs et al., 2001). As noted above, this fish shows an initial, unconditioned orienting response, followed by a step-by-step approach and final strike at a small vibrating sphere that effectively mimics their natural prey (e.g. *Daphnia*; small water fleas that effectively hover in the water

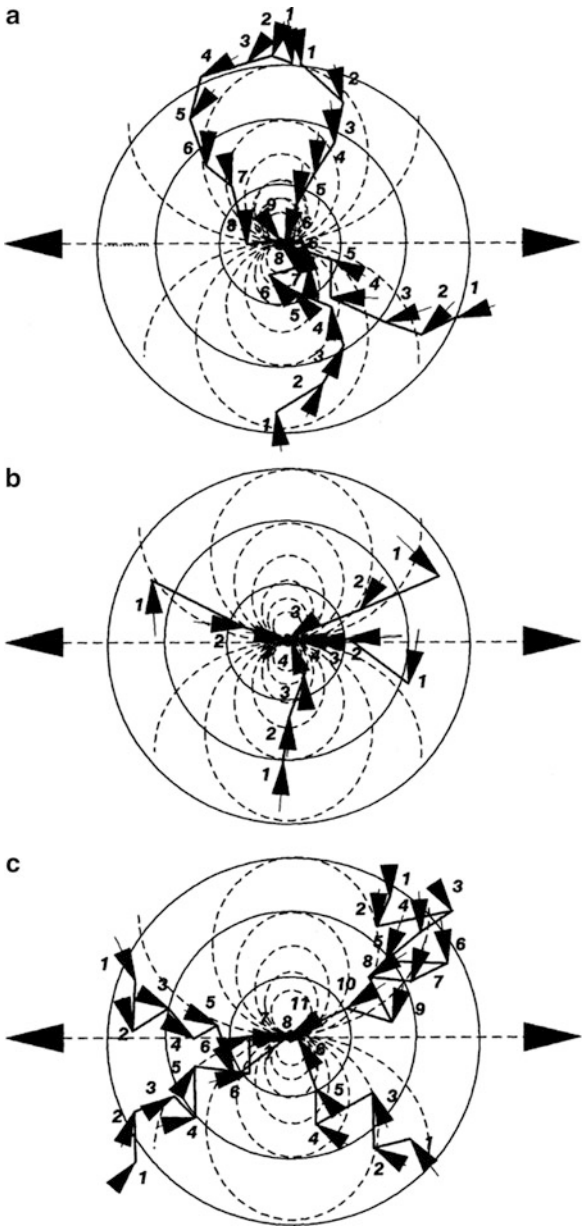

Fig. 5 (**a**-**c**) Examples of typical, unconditioned step-by-step approach patterns to an 'artificial' prey (a 50 Hz vibrating sphere). (**a**) smoothly arching approaches in which the fish keeps its head to one side of the source. (**b**) direct path in which the source is kept mainly in front of the fish's head. (**c**) zigzag approaches in which the fish alternates between being to the left and right of the source. Dashed lines indicate flow lines about the sphere (center of graph), whereas thin-lined circles represent fixed radial distances of 3, 6, and 9 cm from sphere center (from Coombs and Conley, 1997)

column). Prey localization, approach and strike are suited to a small, low-intensity target that is effectively stationary. Blind mottled sculpin approach the target in a series of movements (Fig. 5), and once the target is within a given range of the mouth, the strike is made. The interpretation of this step-like approach is that target direction and distance is estimated during the stationary phase of each step, after

which the sculpin then moves closer to the prey and stops to re-estimate target position. It is likely that the water flows generated by the mottled sculpin's own movements swamp the lateral line signal from the prey. This effect is well illustrated in the chronic recording from implanted electrodes in the anterior lateral line nerve of freely swimming oyster toadfish, *Opsanus tau* (Palmer et al., 2005). Afferent fibers experienced a dramatic increase in firing during predatory strikes caused by the movement of the animal itself as part of the strike. This issue of small signals and potentially large self-generated 'noise' is central to understanding the effective use of the lateral line system and will be considered in Section 6. It is also worth noting that the movement towards the prey must be programmed in a way that minimizes physical displacement of the prey away from the predator.

Information contained in the spatial excitation pattern along the arrayed sensors of the lateral line system of mottled sculpin, as well as other sub-surface feeding fish and amphibians, is thought to play a fundamental role in guiding prey-orienting behaviors. However, the way in which prey location is encoded by the excitation pattern of the peripheral lateral line and used by the central nervous system is still largely unknown. Coombs & Patton (2009) tested the hypothesis that mottled sculpin use excitation peaks (local 'hot spots') to determine the somatotopic location of an artificial prey (vibrating sphere/dipole source) along the body surface. Dipole orientation (axis of sphere vibration relative to the long axis of the fish) was manipulated to produce excitatory peaks in different body locations without changing the actual sphere location. The results show that orienting accuracy is largely independent of source orientation, but not source distance and that turning directions are not guided by local hot spots in the somatotopic activation pattern of the lateral line.

From a wide range of evidence in fish and other vertebrates (summarized in Coombs & Patton, 2009) it is likely that the optic tectum contains a map of the turning magnitudes and directions needed to orient to a lateral line stimulus source. As Coombs and Patton (2009) pointed out, however, it is also clear that this map cannot be a simple topographic map of the body surface because stimulus sources at the same somatotopic location, but at different distances away from the body, lie at different visual angles, and thus require different orienting movements. The fish must therefore combine somatotopic information about both source distance and source location to determine the direction of the source with respect to the head and eyes. To produce the map, information about these two stimulus parameters must be computationally transformed from a somatotopic to an egocentric coordinate system that is in register with other sensory direction maps in the midbrain.

Computed space maps have been found in the auditory system of barn owl (*Tyto alba*) (Knudsen 1987), but also in the lateral line system of the African clawed toad (Claas et al., 1989) and the axolotl (*Ambystoma mexicanum*) (Bartels et al., 1990). Since source localization by the lateral line relies on spatial (somatotopic) activation patterns rather than bilateral cues (Conley & Coombs, 1998), the computations will necessarily be different and will likely need to take source orientation into account as well. Theoretically, fish could use an array of neural filters tuned to

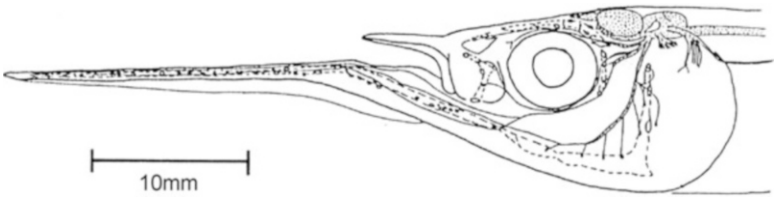

Fig. 6 The nocturnal planktivorous half beak *Hyporamphus ihi* showing the extended mandibular lateral line canal along the bill. These fish feed at night on fast moving mobile plankton using their lateral line. Laboratory feeding studies show that prey moving along the lateral line array in either direction are intercepted whereas prey moving across the array are missed (from Montgomery and Saunders, 1985)

particular combinations of source orientation, distance, and somatotopic location. Such a filter array could classify entire lateral line pressure gradient or velocity patterns rather than relying on a few key features, thereby increasing robustness against noise.

The description above applies to orientation towards and capture of a relatively small, low-intensity target that is effectively stationary within the receptive field of the lateral line array. Like the mottled sculpin, the half-beak (*Hyporamphus ihi*) is a planktivore. However, their prey are fast moving mobile plankton (Montgomery & Saunders, 1985; Saunders & Montgomery, 1985), and successful prey capture depends on the movement of the prey tracking along the sensory array of the lateral line (Montgomery, 1989). These fish have a distinctive lengthy lower jaw that gives them their common name of half-beaks (Fig. 6). The beak and extended mandibular lateral line canal provide an extended lateral line sensory array that allows for non-visual tracking and interception of small, but relatively fast moving, prey.

As shown above, the lateral line provides for target localization and tracking to enable successful prey capture, but successful predation also requires effective prey search. Under normal conditions in the wild, lateral line feeders, like visual predators, must sit and wait for prey to come to them, or actively search the environment for suitable prey. Sit-and-wait predation based on lateral line alone has been shown in the stargazer (*Leptoscopus macropygus)* (Montgomery & Coombs, 1998). Active search behavior has been well documented for visual feeders, but only recently explored from the standpoint of lateral-line mediated predation. The observation is that nocturnal predators like the dwarf scorpion fish (*Scorpaena papillosa*) (Fig. 7) adopt a saltatory search pattern consisting of alternating periods of time when the fish is stationary, and when it moves forward by a set distance. The stationary phase is the search period during which a prey may be detected inducing an orientation and attack. Prey capture occurs throughout the search space (Fig. 7). The dwarf scorpion fish feeds only on benthic prey (Montgomery & Hamilton, 1997) so like the surface feeding fish, the search space is essentially 2D. After a relatively set time with no detection, the fish moves forward to the edge of the previous search space, and pauses to ‘listen’ for

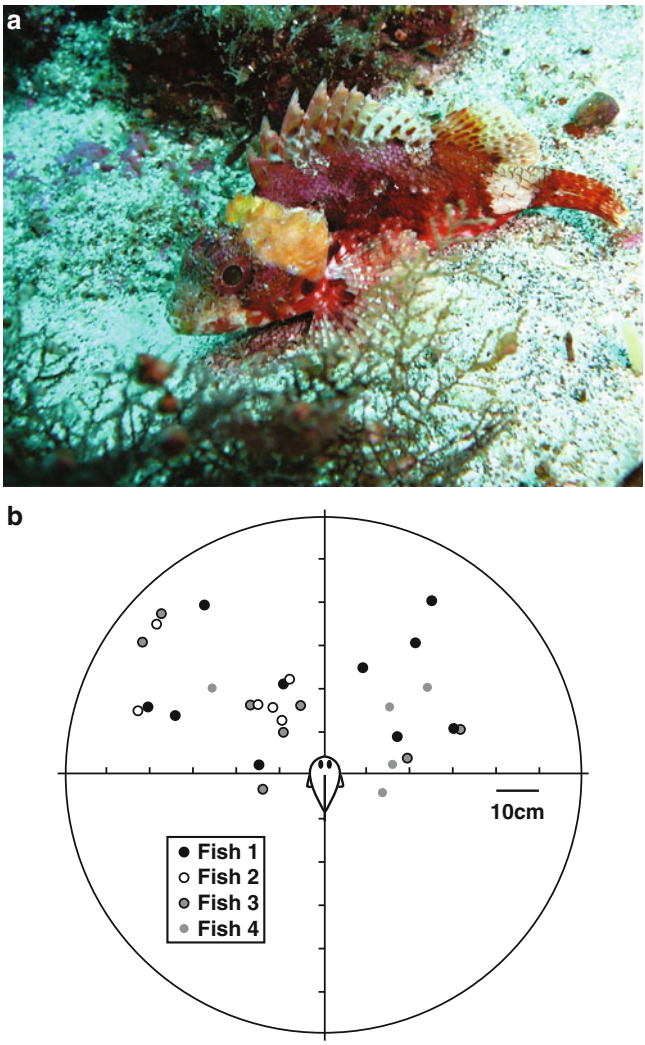

Fig. 7 A The dwarf scorpionfish *Scorpaena papillosa* detects the hydrodynamic signals produced by prey with the mechanosensory lateral line. This species hunts with a pause and move/search, or saltatory, pattern. The pause phase of the search cycle is used to detect prey and pauses often end early in order to initiate an approach at prey which are detected throughout the search space. B Polar plot showing the positions of prey relative to the fish at the time of prey detection. Note that most prey is found within a semicircular space. Data from different individual fish is represented by a different color circles (From Bassett et al. 2007)

prey in the new search space (Bassett et al., 2007). The spatial distribution of attacks relative to the fish's position defines the search space, and the time spent stationary, and the distance and direction of movement between the search phases, all contribute to the search efficiency.

Swimming fish leave a hydrodynamic trail consisting of vortices that provide information about the swimming direction and swimming velocity. In still water, the hydrodynamic trail of goldfish (*Carassius auratus*) could be visualized for up to 5 minutes (Hanke & Bleckmann, 2000). Hydrodynamic trails may provide hydrodynamic signatures associated with the swimming styles of different fish species (Hanke & Bleckmann, 2004). Behavioral evidence for hydrodynamic wake tracking of piscivorous fish has been provided by Pohlmann et al., (2001, 2004). Although the use of olfactory information could not be completely ruled out in these studies (Montgomery et al., 2002), they did show that predatory fish can intercept and follow the trail produced by prey fish using predominantly their lateral line system.

In many circumstances, the lateral line will also work alongside other senses in prey search. A number of studies explored these issues of multimodal sensory interactions, including: (1) the use of lateral line in chemosensory search (Baker et al., 2002; Carton & Montgomery, 2003; Jayne et al., 2007; and Section 9); (2) the use of lateral line in electrosensory search (von der Emde & Bleckmann, 1998); (3) the switch from visual search at a distance to lateral-line guided strike up close (New et al., 2001); (4) the comparison of information-processing demands for prey capture in lateral line and electrosensory systems (Coombs et al., 2002), and (5) the functional relationship between hearing and the lateral line in prey detection and localization (Braun et al., 2002; Braun & Coombs, 2010; Braun & Sand, Chapter 10). The relative role of the lateral line and other senses also changes with light conditions. As light levels decrease, the mechanosensory lateral line will increase in importance. The relative role of lateral line and other senses in predation also changes during development. Vision typically dominates, but in some species and some stages of development, the lateral line plays a more dominant role (Liao & Chang, 2003).

4 Predator avoidance

Predator/prey interactions are two-sided; as discussed above, predators can detect and attack prey based on lateral line information, but prey can also detect the approach or strike of a predator using the lateral line. It is particularly in this case that the speed of the strike and close range of operation of the lateral line dictates that the behavioral pathways and reactions for lateral line mediated predator avoidance must be fast to be effective. In this regard is has been known for a long time that the lateral line provides direct input onto the two Mauthner cells (e.g. Korn & Faber, 1975). The Mauthner cells are critical, decision-making neurons in the recticulospinal network of the hindbrain (Korn & Faber, 2005). They mediate an escape response (C start) that has a minimum latency of only 6.4 ms in goldfish (Eaton & Hackett, 1984). Recent research on the role of the lateral line in predator avoidance and escape response initiation has concentrated on developing a model system with zebrafish (*Danio rerio*) larvae showing that the

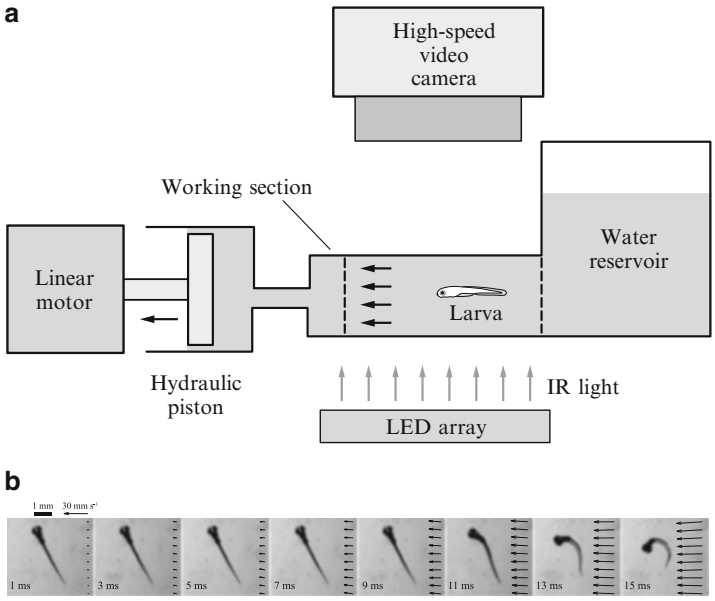

Fig. 8 Water flow stimulates an escape response in zebrafish *Danio rerio* larvae. (**a**) The impulse chamber used to generate flow includes a computer-controlled linear motor that actuates a hydraulic piston. The motion of the hydraulic piston (black arrow) creates flow through the working section. A high-speed video camera (250 frames sK1) recorded the responses of larvae that were backlit with an array of infrared LEDs in a darkened room. (**b**) Video stills of a representative fast start response for a single larva (5.90 dpf) from a dorsal view with velocity vectors from the representative flow stimulus ((i) 1 ms, (ii) 3 ms, (iii) 5 ms, (iv) 7 ms, (v) 9 ms, (vi) 11 ms, (vii) 13 ms and (viii) 15 ms) (From McHenry et al. 2009)

lateral line system plays a substantive role in predator evasion at this vulnerable stage of growth in this species (McHenry et al., 2009; Fig. 8). This research has also explored the effects of swimming and aspects of development on the lateral line stimulus. Swimming larvae are only half as likely as motionless larvae to respond to the flows produced by a suction predator (Feitl et al., 2010), and the reduction in fish density that follows the inflation of the swim bladder during development dramatically reduces the stimulus to the lateral line during a simulated strike (Stewart & McHenry, 2010).

The reduction in the effective stimulus to the lateral line after swim bladder inflation suggests a developmental change in the relative role of lateral line inputs to the Mauthner-mediated escape response. Indeed, lateral line inputs to the Mauthner cells are insufficient by themselves for initiating escape responses in adult fish and are thought to play more of a modulatory role (Casagrand et al., 1999). In contrast, either auditory or visual inputs alone are sufficient for this purpose (Eaton et al., 1977), but auditory inputs are particularly important in otophysan fishes, such as the goldfish and zebrafish (Canfield & Eaton, 1990; Casagrand et al, 1999). In these species, audition

involves the swim bladder, which functions as a sound pressure transducer and amplifier. Whereas visual or pressure-driven auditory inputs dominate the initiation of the escape response, lateral line inputs guide the direction of the response once it has begun so that fish don't collide with nearby obstacles (Mirjany et al., 2011).

5 Intraspecific communication – spawning, parenting, aggression and schooling

As a close range sensory system, the lateral line is an obvious candidate for close range communication. With external fertilization being the norm across fishes, spawning synchronization is an important element of fish behavior and communication. In addition to spawning synchronization, mating communication may also play a role in mate selection. Although a lateral line component to mating communication has only been studied in a few species such as salmon (*Oncorhynchus nerka*) (Satou et al., 1994) and cave-dwelling Atlantic mollies (*Poecilia mexicana*) (Plath et al., 2004) the likelihood exists that this is not uncommon in fishes. The evidence from the two studies cited above shows that the lateral line is involved in both spawning synchrony and mate selection.

Male Siamese fighting fish (*Betta splendens*) constantly guard their juveniles. If threatened the male adopts an oblique position below the water surface and starts to produce surface waves with the pectoral fins. Even without vision the juveniles approach the male. On reaching it they are sucked up and transported back by the male to the air bubble nest (Kaus & Schwartz, 1986).

Fire-bellied toads (*Bombina sp.*) produce large surface waves by strokes of the hind legs during mating behavior and these waves are used as signals that define the territory of the respective male (Walkowiak & Münz, 1985). In addition, some fishes produce hydrodynamic stimuli during aggressive interactions (e.g. Lamprecht, 1973). For instance, in the golden dwarf cichlid (*Nannacara anomala*) one animal, the actor, pushes water with its tailfin in the direction of the other fish (Enquist et al., 1990). The two animals often change role (from beater to recipient and vice versa) and usually orient laterally to each other. They thus ensure that the hydrodynamic stimulus can be perceived by the recipient fish. Although direct evidence is missing, the lateral line is most likely involved in this behavior.

Schooling behavior is another candidate for close range communication. Tight schooling coordination in response to predator threat is very demanding in terms of the high temporal and spatial resolution characteristics required for sensory coordination of the school (Ritz et al., 2011). Observations and studies of complex schooling behavior (Pitcher & Parrish, 1993) tend to evoke descriptions of the school as a 'super organism'. Discrete 'behaviors' of the school are observable such as 'splits, vacuoles and flash expansion'. The sensory basis of these school behaviors is hard to study, but is almost certainly due to the sensory detection of an attack by the fish on the 'front line' via the visual looming stimulus of the

predator, and/or the associated pressure pulse of a lunging strike. The behavior of the school will result from the way in which this information propagates into the school, both directly in response to the predator, and indirectly, in response to the propagated startle responses of the 'front line' fish. Thus, communication between neighbors is likely central to the schooling response when under attack, but it is also a key to understanding schooling behavior as a general evolutionary strategy for optimizing the transmission of threat information.

In this context, there is good experimental evidence and theoretical reasoning to support the interactive involvement of both vision and lateral line (Partridge & Pitcher 1980; Faucher et al., 2010) in the maintenance of school structure. Nearest-neighbor distance appears to be maintained by opposing forces of attraction (via visual feedback) and repulsion (via lateral line feedback). Whereas an individual's relative position and orientation with respect to neighboring fish appears to be maintained by vision, the relative velocity and direction of travel seems to be regulated by the lateral line (Partridge & Pitcher, 1980). Essentially, the lateral line enables individuals to maintain close associations with each other without colliding. The lateral line may also interact with hearing in schooling behavior, especially in clupeids (e.g. sprat, herring, shad), arguably 'champions' among schooling species. These fish have air filled cavities in their head that are mechanically linked to both the inner ear and a portion of the head lateral line system (Denton & Blaxter, 1976). Rapid schooling maneuvers of clupeids produce pressure pulses (Gray & Denton, 1991), which, like those produced by rapidly approaching predators, can be detected by the air bubble/inner ear/lateral-line system. In fact, this represents one of the rare cases in which the lateral line system responds to pressure, rather than to pressure-gradients or flow, although the precise nature of auditory/lateral line interactions in schooling behavior is still poorly understood.

Schooling behavior may also provide hydrodynamic benefits to fish, depending on an individual's position within the school relative to the hydrodynamic structures (trailing wakes of shed vortices) produced by other nearby fish, particularly those in front (Breder, 1965). Liao (2007; Fig. 9) provides an excellent review, as well as the theoretical rationale for a hydrodynamic basis to school structure. The prediction is that a fish located behind and in between two members of the school can take advantage of the average reduced flow velocity associated with the thrust wakes of those ahead. In effect, fish in schools can benefit from flow refuging (exploiting regions of reduced flow or reduced pressure) and vortex capture (harnessing the energy of environmental vortices). Direct experimental determination of vortex capture, associated energetic benefits and its sensory basis have not been done for schooling fish. However, as covered in Section 9, individual fish swimming in a flume use lateral line information to position themselves in an energetically favorable position behind a cylinder (Sutterlin & Waddy, 1975; Montgomery et al., 2003), and to entrain to shed vortices from a bluff, or non-streamlined, object in the flow (Liao et al., 2003a,b; Przybilla et al., 2010; Bleckmann et al., 2012).

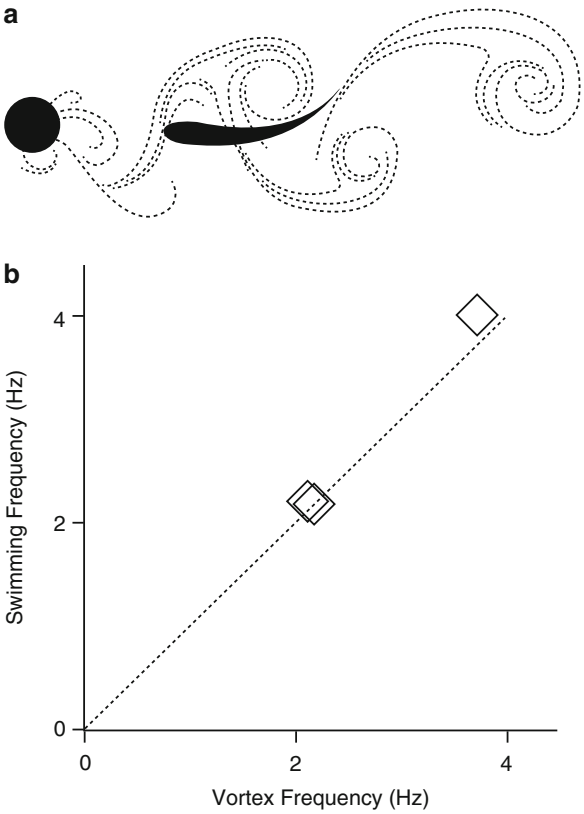

Fig. 9 (**a**) Schematic illustrating the hydrodynamic benefit gained by a fish swimming behind a bluff body, such as a cylinder, in the flow. Fish can exploit the energy of discrete vortices as well as the average reduced velocity in the Kármán street. In a two-dimensional fish school side-by-side thrust wakes generated by two individuals create an analogous Kármán street. (**b**) The graph of swimming frequency vs shed vortex frequency shows a strong match for 3 different combinations of cylinder size and flow velocity. This indicates that the fish are not just 'drafting' in the wake behind the cylinder, but tuning their swimming frequency to match that of the shed vortices. Dotted line is the line of equality. (Redrawn from Liao 2007)

6 Signals and Noise

Aquatic environments are often contaminated with hydrodynamic noise (broadband velocity and pressure fluctuations caused by unsteady flow or turbulences). Therefore the real challenge for the lateral line is not simply a sufficient sensitivity to detect water motions, but rather the ability to detect a signal in the presence of noise. Therefore, separating signals from noise is essential in understanding the sensory ecology and neuroethology of the lateral line. In this regard, the submodalities of the fish lateral line (superficial neuromasts on the skin surface and canal neuromasts located in subdermal canals) (Webb, Chapter 2) are relevant.

The simple description is that with respect to water displacement, superficial neuromasts are low-pass filters encoding low-frequency water motions of up to about 80 Hz. In comparison, canal neuromasts do not respond to DC flow, but are sensitive to higher oscillating flows up to approximately 250 Hz.

The essential idea is that superficial neuromast respond to unidirectional or low frequency AC flow (Coombs & Montgomery, 1994; Voigt et al., 2000), whereas canal neuromasts are less influenced by low frequency large scale flows (noise) such as those in a creek or river, or movements of the animal itself. The division of labor between superficial and canal neuromasts is well illustrated by the effects of background flow on the responses of these two submodalities to a small vibrating source (Engelmann et al., 2000). At zero back-ground flow (in still water), all afferent fibers phase-lock to a vibrating sphere stimulus; however, with increasing background flow rates the responses of one class of afferents is progressively masked whereas another class continues to encode the higher frequency source. It is likely that superficial neuromast input can be equated with the class of afferents masked by the flow "noise" and canal neuromasts as the unaffected class. This functional distinction between superficial and canal neuromasts is further reinforced by the behavioral findings that flowing water decreases hydrodynamic signal detection in a fish with an epidermal (superficial) lateral-line system (Bassett et al., 2006) to a greater extent than it does in a fish with a more typical lateral-line canal system (Kanter & Coombs, 2003). That superficial neuromasts are nevertheless important in a fluvial environment is supported by the behavioral findings that superficial neuromasts mediate rheotaxis (orientation to water flow; Montgomery et al. 1997), whereas canal neuromasts mediate prey detection (or orientation to a small vibrating source) (Coombs et al., 2001; Kanter & Coombs, 2003). For further details on the biomechanical and functional dichotomy between these two lateral line submodalities see McHenry and van Netten (Chapter 4) and Chagnaud and Coombs (Chapter 6).

7 Self-generated Flows as Noise

Even in still water, fish and aquatic amphibians may move around and thus generate hydrodynamic noise. Self-generated noise can be recognized as an issue for many sensory systems, but given the sensitivity of lateral line receptors and the observation that most fish are seldom motionless, self-generated noise may be a particular problem for the lateral line. The scale of the problem is under-recognized because almost all physiological studies have been made on immobilized animals. However, lateral line afferent activity has been recorded in freely swimming fish (Palmer et al., 2005), swimming tethered lampreys (*Petromyzon marinus*) (Ayali et al., 2009), and in restrained breathing fish (Montgomery et al., 1996). In all cases the movements generated by swimming and breathing produce strong modulation of the lateral line afferents. In the particular case of the breathing fish, self-stimulation of lateral line receptors occurs close to the head and respiratory flows.

One advantage self-generated noise has over other noise sources is that, at least to a certain degree, it is under the control of the animal. So the simplest strategy for noise reduction is to cease movement. As covered earlier in this chapter (section 3), complete motionlessness is a behavioral strategy adopted by sit-and-wait predators like the stargazer (Montgomery & Coombs, 1998). Cessation of gill movements during prey location by the oyster toadfish (Tricas and Highstein, 1991), and "the pause and then move search strategy" of dwarf scorpionfish (Bassett et al., 2007) are but two examples of how motionlessness can be controlled to suit the needs of the predator.

Another relatively simple approach to self-generated noise is to down regulate lateral line sensitivity during active movement (Russell & Roberts, 1972). This approach is appropriate to rapid movements where lateral line sensitivity can be reduced by activation of the efferent system (see Chagnaud & Coombs, Chapter 6 for further details on this system). However, efferent down-regulation of sensitivity need not be all-or-nothing or always in response to self-motion. Chronic nerve recording in active oyster toadfish showed incomplete inhibition during locomotion and selective action of the efferent system on one class of lateral line afferents in response to visual presentation of natural prey (Tricas & Highstein, 1991).

As a final noise-reduction strategy, the brain can use *a priori* knowledge to actively cancel afferent inputs that are linked to the animals own movements. Undulatory movements will provide a regular and predictable pattern of afferent input. Because the movements are generated by the animal itself, it has, in effect, an *a priori* knowledge of movement and the potential to predict and cancel the associated afferent inputs. Studies on both lateral line and electrosense, but particularly electrosense, show that the hindbrain processing centers for both of these senses form an adaptive filter that learns to cancel predictable input (Bodznick et al., 1999; Montgomery & Bodznick, 1999). The basis of this ability is the cerebellar-like structure of these hindbrain centers (see also Wulliman & Grothe, Chapter 7). The *crista cerebellaris*, that overlies these structures, has a molecular layer composed of parallel fibers that carry information about ongoing movements. This information comes as efference copy from motor centers, proprioceptive information about movement, and from a number of other sources. In effect, the molecular layer contains a rich matrix of information about movement. The principal cell type of the lateral line hindbrain center is the crest cell. Crest cells have dorsal spiny molecular layer dendrites that receive parallel fiber information, but also direct lateral-line afferent input on their ventral dendrites. A rather simple synaptic plasticity learning rule allows the input from the parallel fibers to generate a "negative image" of the re-afferent noise arriving at the ventral dendrites. In this way, the re-afferent noise is cancelled, yet the crest cells remain sensitive to external biologically important signals (Montgomery & Bodznick, 1994). Ventilation is one example of a movement that produces unwanted sensory re-afference. Recordings from lateral-line afferents, particularly in the area of the gills, show strong ventilation mediated responses. By comparison, the crest cells show greatly reduced responses to ventilation movement (Montgomery et al., 1996).

8 Self-generated Flows as Signal – Hydrodynamic Imaging and Control of Swimming

In low and zero light environments, the lateral line provides an alternative to vision. In addition to encoding abiotic flows and water movements produced by other animals, the lateral line senses self-generated flow to mediate collision avoidance and object detection. The flow field around a gliding fish is distorted by nearby objects, and these distortions can be sensed by the lateral line. This active use of self-generated flows has been termed "hydrodynamic imaging." The blind Mexican cavefish uses active flow sensing for a variety of spatial tasks, including obstacle avoidance (Teyke, 1985; Windsor et al., 2008), discrimination of spatial features that differ in their orientation (Campenhausen et al., 1981) or spacing (Hassan, 1986), and exploration of novel environments (Burt de Perera, 2004; Burt de Perera & Braithwaite, 2005; Braithwaite & Burt De Perera, 2006).

For a gliding fish, the information available for hydrodynamic imaging depends on the properties of its flow field and how this flow field is altered by the presence of objects. Particle image velocimetry has been used to measure the flow fields around gliding blind cave fish as they moved through open water and when heading towards a wall (Windsor et al., 2010a). These measurements, combined with computational fluid dynamics models, were used to estimate the stimulus to the lateral line. Results show that there is a high-pressure region around the nose of the fish, low-pressure regions corresponding to accelerated flow around the widest part of the body and a thick laminar boundary layer down the body. When approaching a wall head-on, the changes in the stimulus to the lateral line were confined to approximately the first 20% of the body. When swimming parallel to the wall, characteristic changes in the form of the flow field occur when the fish are within approximately 0.2 body lengths of the wall. The stimulus to the lateral line is estimated to be sufficient for fish to detect walls when they are 0.1 body lengths away (the mean distance at which they normally swim from a wall), but insufficient for the fish to detect a wall when 0.25 body lengths away. These fluid dynamics analyses of the nature of the flow fields surrounding the fish (Windsor et al., 2010b) reinforce the view from simpler potential flow models (Hassan 1992a, b) that hydrodynamic imaging can only be used by fish to detect surfaces and objects at short range.

Self-generated flows may also play a useful role in providing sensory feedback for swimming control. This suggestion has been made for many years, but experimental evidence in support of an active contribution of lateral line to swimming efficiency has been scarce. Two roles for lateral line feedback have been proposed. Lighthill (1993) suggested that the lateral line sensors in the subcerebral canal system of the herring provide an appropriate feedback signal into a possible system for controlling yaw by oscillatory neck deflections so as to minimize the effective pressure difference and any associated cross flow effects across the head of the fish. It was proposed that swimming clupeid fishes may use this as an 'active' mechanism for reduction of hydrodynamic resistance.

This theory was supported by an analysis of the mechanics of the subcerebral perilymph canal, which crosses the head between the lateral lines of clupeid fishes (Denton and Gray, 1993), and an analysis of the head turning movements in herring and other fishes (Rowe et al., 1993). However, direct evidence for a role of lateral line feedback in this behavior was not provided. In the golden shiner *Notemigonus crysoleucas* drag reduction was not adversely influenced by disabling the lateral line system (McHenry et al., 2010).

The second suggested role for lateral line feedback in the efficient control of swimming came from the measurements of the boundary layer in swimming fish (Anderson et al. 2001; see also McHenry & Liao, Chapter 3). This study observed inflected boundary layers that appeared to be stabilized during the later phases of the undulatory cycle, and suggested that these boundary layer profiles may provide evidence of a contribution of hydrodynamic sensing to the optimization of swimming performance. Again, this suggestion remains to be directly tested, however, Yanase et al. (2012) have recently found that unilateral disruption of the superficial neuromasts impairs hydrodynamic performance and increases the metabolic cost of swimming in the yellowtail kingfish (*Seriola lalandi*).

9 Orientation to Flows

In the aquatic environment of fish, orientation to flow (rheotaxis), finding refuge from flows, and reducing the costs of locomotion in turbulent flows are all important behaviors. It would seem obvious that flow sensing should play a useful role in all these behaviors. However, even the simplest of these, orientation to uniform flows, is not without complexity. To know that it is transported by the current, a fish needs an external reference frame. For many fish, this reference frame is the substrate and surrounding environment as sensed by the visual system. For example, station holding for a fish in midwater in a uniform current is largely mediated by optomotor responses to stabilize the image of the surroundings on the retina and to minimize 'optic flow'. Although a fish being swept downstream results in an optic flow stimulus to the visual system, little if any hydrodynamic flow stimulus to the lateral line is generated in this circumstance. For this reason, the long-held view was that the lateral line played little or no role in rheotaxis (e.g. Dijkgraaf, 1963). However, for fish sitting on the substrate in slow flows that are insufficient for displacing it downstream, the lateral line can sense the flow relative to the body surface, thus enabling the fish to orient into the flow (Montgomery et al., 1997; Montgomery et al., 2000; Fig. 10). In these circumstances, the threshold for positive rheotaxis (orientation into the flow) is markedly lower for a fish with the lateral line, and in particular, if the superficial neuromasts of the lateral line are intact.

This form of rheotaxis, using intermittent physical contact as the external reference frame, is also used by the Mexican blind cavefish. In this species, again, a low rheotactic threshold depends on an intact superficial neuromast system

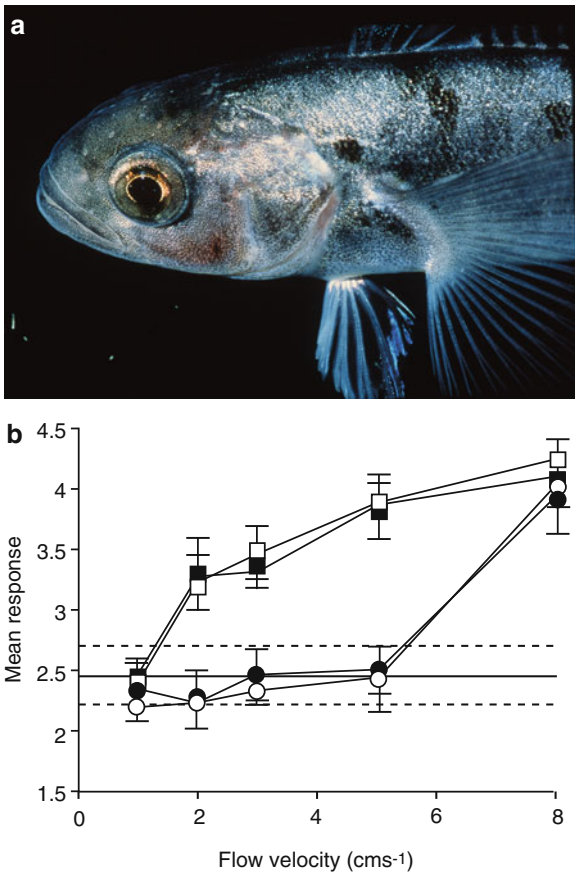

Fig. 10 Rheotactic responses of the antarctic fish *Pagothenia borchgrevinki*. Rheotactic responses; horizontal solid and broken lines indicate mean + 95% confidence intervals of the orientation response in the absence of current; filled squares, normal fish; open squares, gentamicin-treated fish; filled circles, streptomycin-treated fish; open circles, after physical ablation of the superficial neuromasts. Mean response, number of fish facing upstream

(Baker and Montgomery, 1999; Montgomery et al., 2001). Also of interest is that the normal threshold for rheotaxis is certainly not equal to the lowest current these fish can detect. The unconditioned rheotactic response to uniform flows was exhibited with a threshold of less than 3 cm s^{-1}. The effect of pairing an odor stimulant with water current dropped the rheotactic threshold to less than 0.4 cm s^{-1}. Olfactory released rheotaxis is likely to play an important part in tracking odor sources underwater and has been reported in a number of fish species (Baker et al., 2002; Carton and Montgomery, 2003; Jayne et al., 2007).

Understanding the contribution of the lateral line to rheotaxis has a number of potential practical applications ranging across a wide spectrum, from fish conservation to hair cell drug and toxicity testing (Coffin et al., Chapter 11). With respect to fish conservation, many, if not most of our inland waterways have been modified by dams or canals which impede or facilitate, the movement of fishes through these systems. Fish passage at these structures clearly has many implications for conservation, ranging from disruption of fish movement and migration during important

life-history phases, to unwanted spread of introduced and invasive species. Understanding the role of flow detection in shaping the behavior of fish around these structures provides an important contribution to the 'tool box' for effective design and management of modified waterways (Hasler et al., 2009). At the other end of the spectrum, in the zebrafish model unconditioned rheotaxis and superficial placement of hair cells in the lateral line system provide some interesting possibilities for hair cell toxicity and protection screening (Coffin et al., 2010; Coffin et al., Chapter 11).

Orientation to uniform flows may have its complexities, but clearly flow refuging and swimming in turbulent flows requires an altogether higher level of sophistication in flow sensing and control proficiency. Flow sensing has been shown to be involved in station holding behind an object in a flow (Sutterlin & Waddy, 1975; Montgomery et al., 2003), but perhaps more interesting is the way in fish can use their lateral line to track hydrodynamic trails left by prey (Pohlmann et al., 2004), and to surf vortex streets (Liao et al., 2003a, b; Liao, 2007). Liao (2003) showed that trout *Oncorhynchus mykiss* alter their body kinematics to synchronize with the shed vortices generated by a stationary object in the flow. These shed vortices are known as a Kármán street, and the tuning of the body movements to these vortices has been termed a Kármán gait. Subsequent work showed that using this gait, fish can capture the energy of environmental vortices and hence consume less oxygen in turbulent flows than would otherwise be expected (Taguchi & Liao, 2011).

10 Summary

The lateral line of fishes and amphibians has some unique characteristics and makes a few 'signature' contributions that will apply to a wide variety of behaviors and species. For example, the lateral-line mediated ability of fish to react rapidly to nearby obstacles or neighboring fish is important to the navigational and spatial orientation abilities of blind cavefish, to the abilities of fish to school and avoid predators with highly synchronized maneuvers, and the ability of solitary fish to escape predators in cluttered environments. Because the distance range of the lateral line in most cases is relatively short and avoidance reactions must be quick, it is reasonable to hypothesize that the Mauthner cells and/or other fast-response reticulospinal systems are involved in many, if not all of these fundamental abilities. The importance of the Mauthner cells to the lateral line system is underscored by the fact that afferent connections between the lateral line periphery and the Mauthner cells are some of the earliest to develop in larval zebrafish (Pujol-Marti et al., 2011). These afferent neurons are also some of the largest, meaning that the propagation of information to the brain will be very rapid.

Although it is well known that the lateral line system is involved in many behaviors, the exact role this sensory system plays in the various behaviors is often not well understood. There are several reasons for this. First, to design the

relevant behavioral experiments we need to know the temporal and spatial characteristics of the biologically meaningful stimuli for each species we are investigating. Unfortunately this knowledge is hard to get since it requires three-dimensional particle image velocimetry and/or other sophisticated measuring techniques. Second, sensory systems are to a degree matched filters designed to separate signals from noise. Therefore we also need to know the hydrodynamic noise to which the lateral line system of the species we are investigating is exposed to in its natural environment. Hydrodynamic measurements in the field are even more challenging than those in the lab. Third, the behavior of most fish and amphibian relies on multimodal (chemosensory, visual, somatosensory, acoustic, vestibular) input, thus blocking the lateral line often results in subtle modifications of the behavior under study. For instance, fish exposed to a stationary cylinder still Kármán gait, entrain, or swim in the bow wake when their lateral line is blocked (see above). However, if the vortex shedding cylinder is moved perpendicular to the bulk flow direction in the horizontal plane with a velocity of only 1 cm s^{-1}, they fail to perform the task in darkness (Bleckmann et al., 2012). Another example is surface-feeding fish and aquatic amphibians. If parts of their lateral line are blocked, they still orient to a surface wave source, but with a prolonged latency and, depending on the number of neuromasts ablated, with a reduced precision (Bleckmann et al., 1989; Görner & Mohr, 1989).

This chapter has summarized knowledge of the capabilities of the lateral line and its contribution to behavior, neuroethology, and sensory ecology. In particular, studies have been reviewed that provide examples of the role of the lateral line in prey detection, predator avoidance, communication, and orientation, and studies that illustrate the issues of signals and noise in this sensory system. Although much has been learned about the neuroethology of the lateral line in terms of its general function across fish and amphibians, there is still much to do in terms of studying the details of form and function of lateral lines across development, and across the huge diversity of species found in these groups. The understanding of such adaptations is especially intriguing in view of the peripheral diversity of the lateral line. For instance, more needs to be known about the hydrodynamic environment and the lateral line mediated behavior of fishes that have only superficial neuromasts, are dominated by canals with many pores, have canals without pores, or have multiple trunk and/or highly branched canals. Some of this diversity will be of adaptive significance and provide insight into the details of form and function in the lateral line. However, some of the diversity will also be related to retention of key functional attributes, such as filtering properties, in the face of structural changes driven by other evolutionary/developmental considerations (Montgomery et al., 1994; Montgomery and Clements, 2000). In addition, the observed variation in lateral line structure on the head of surface feeding fish remind us that different types of lateral lines may also serve identical behavioral functions (e.g. Bleckmann et al., 1989).

Acknowledgements We thank Joachim Mogdans and Vera Schlüssel for commenting on the manuscript.

References

Anderson, E. J., Mcgillis, W. R., & Grosenbaugh, M. A. (2001). The boundary layer of swimming fish. *Journal of Experimental Biology*, 204, 81–102.

Ayali, A., Gelman, S., Tytell, E. D., & Cohen, A. H. (2009). Lateral-line activity during undulatory body motions suggests a feedback link in closed-loop control of sea lamprey swimming. *Canadian Journal of Zoology*, 87, 671–683.

Baker, C. F., & Montgomery, J. C. (1999). The sensory basis of rheotaxis in the blind Mexican cave fish, *Astyanax fasciatus*. *Journal of Comparative Physiology A*, 184, 519–527.

Baker, C. F., Montgomery, J. C., & Dennis, T. E. (2002). The sensory basis of olfactory search behaviour in the banded kokopu (*Galaxias fasciatus*). *Journal of Comparative Physiology A*, 188, 553–560.

Bartels, M., Münz, H., & Claas, B. (1990). Representation of lateral line and electrosensory systems in the midbrain of the axolotl, *Ambystoma mexicanum*. *Journal of Comparative Physiology A*, 167, 347–356.

Bassett, D., Carton, A. G., & Montgomery, J. C. (2006). Flowing water decreases hydrodynamic signal detection in a fish with an epidermal lateral line-system. *Marine and Freshwater Research*, 57, 611–617.

Bassett, D., Carton, A. G., & Montgomery, J. C. (2007). Saltatory search in a lateral line predator. *Journal of Fish Biology*, 70, 1148–1160.

Behrend, O., Branoner, F., Ziehm, U., & Zhivkov, Z. (2008). Lateral line units in the amphibian brain could integrate wave curvatures. *Journal of Comparative Physiology A*, 194, 777–783.

Bleckmann, H. (1980). Reaction time and stimulus frequency in prey localization of the surface-feeding fish, *Aplocheilus lineatus*. *Journal of Comparative Physiology A*, 140, 163–172.

Bleckmann, H. (1988). Prey identification and prey localization in surface-feeding fish and fishing spiders. In J. Atema, R.R. Fay, A.N. Popper, W. Tavolga (eds.), Sensory Biology of Aquatic Animals (pp. 619–641). Springer: New York.

Bleckmann, H. (1993). Role of the lateral line in fish behaviour. In T. J. Pitcher (ed.), *Behaviour of Teleost Fishes* (pp. 177–202), London: Chapman and Hall.

Bleckmann, H. (1994). Perception of hydrodynamic stimuli in aquatic and semiaquatic animals. In W. Rathmayer (ed.), *Progress in Zoology. Vol 41* (pp. 1–115). Stuttgart: Gustav Fischer.

Bleckmann, H., & Schwartz, E. (1982). The functional significance of frequency modulation within a wave train for prey localization in the surface feeding *Aplocheilus lineatus* (Cyprinodontidae). *Journal of Comparative Physiology A*, 145, 331–339.

Bleckmann H., Tittel, G., & Blübaum-Gronau, E. (1989). The lateral line system of surface-feeding fish: Anatomy, physiology, and behavior. In S. Coombs, P. Görner, H. Münz (eds.), *The Mechnosensory Lateral Line. Neurobiology and Behavior* (pp. 501–526). New York: Springer.

Bleckmann, H., Breithaupt, T., Blickhan, R., & Tautz, J. (1991). The time course and frequency content of hydrodynamic events caused by moving fish, frogs, and crustaceans. *Journal of Comparative Physiology A*, 168, 749–757.

Bleckmann, H., Przybilla, A., Klein, A., Schmitz, A., Kunze, S., & Brücker, C. (2012). Station holding of Trout: Behavior, Physiology and Hydrodynamics. In C. Tropea, H. Bleckmann (eds.) *Nature-inspired fluid mechanics* (pp. 161–178). Heidelberg: Springer.

Bodznick, D., Montgomery, J. C., & Carey, M. (1999). Adaptive mechanisms in the elasmobranch hindbrain. *Journal of Experimental Biology*, 202, 1357–1364.

Braithwaite, V. A., & De Perera, T. B. (2006). Short-range orientation in fish: How fish map space. *Marine and Freshwater Behaviour and Physiology*, 39, 37–47.

Braun, C. B., & Coombs, S. (2010). Vibratory sources as compound stimuli for the octavolateralis systems: Dissection of specific stimulation channels using multiple behavioral approaches. *Journal of Experimental Psychology: Animal Behavioral Processes*, 36, 243–257.

Braun, C. B., Coombs, S., & Fay, R. R. (2002). What is the nature of multisensory interactions between octavolateralis sub-systems? *Brain Behavior and Evolution*, 59, 162–176.

Breder, C. M. (1965). Vortices and fish schools. *Zoologica*, *50*, 97–114.
Burt de Perera, T. (2004). Spatial parameters encoded in the spatial map of the blind Mexican cave fish, *Astyanax fasciatus*. *Animal Behavior*, 68, 291–295.
Burt de Perera, T., & Braithwaite, V. A. (2005). Laterality in a non-visual sensory modality - the lateral line of fish. *Current Biology, 15*, 241–242.
Campenhausen, C., Riess, I., & Weissert, R. (1981). Detection of stationary objects by the blind cave fish *Anoptichthys jordani* (Characidae). *Journal of Comparative Physiology A*, 143, 369–374.
Canfield, J. G., & Eaton, R. C. (1990). Swimbladder acoustic pressure transduction initiates mauthner-mediated escape. *Nature*, 347, 760–762.
Carton, A. G., & Montgomery, J. C. (2003). Evidence of rheotactic component in the odor search behaviour of freshwater eels. *Journal of Fish Biology*, 62, 501–516.
Casagrand, J. L., Guzik, A. L., & Eaton, R. C. (1999). Mauthner and reticulospinal responses to the onset of acoustic pressure and acceleration stimuli. *Journal of Neurophysiology*, 82, 1422–1437.
Claas B, Münz H, Zittlau E (1989) Direction coding in central parts of the lateral line system. In: S Coombs, P Görner, H Münz (eds) *The Mechnosensory Lateral Line. Neurobiology and Behavior* (pp. 409–420). New York: Springer
Coffin, A. B., Ou, H., Owens, K. N., Santos, F., Simon, J. A., Rubel, E. W., & Raible, D. W. (2010). Chemical screening for hair cell loss and protection in the zebrafish lateral line. *Zebrafish*, 7, 3–11.
Conley RA, Coombs S (1998) Dipole source localization by mottled sculpin. III. orientation after site-specific, unilateral blockage of the lateral line system. *Journal of Comparative Physiology A*, 183: 335–334
Coombs, S., & Janssen, J. (1990). Behavioral and neurophysiological assessment of lateral line sensitivity in the mottled sculpin, *Cottus bairdi*. *Journal of Comparative Physiology A*, 167, 557–567.
Coombs, S., & Conley, R. A. (1997). Dipole source localization by mottled sculpin. I. Approach strategies. *Journal of Comparative Physiology A*, 180, 387–399.
Coombs, S., & Montgomery, J. C. (1994). Structure and function of superficial neuromasts in the Antarctic fish, *Trematomus bernacchii*. *Brain Behavior and Evolution*, 44, 287–298.
Coombs, S., & Patton, P. (2009). Lateral line stimulation patterns and prey orienting behavior in the Lake Michigan mottled sculpin (*Cottus bairdi*). Journal of Comparative Physiology A, 195, 279–297.
Coombs, S., Braun, C. B., & Donovan, B. (2001). The orienting response of lake michigan mottled sculpin is mediated by canal neuromasts. *Journal of Experimental Biology*, 204, 337–348.
Coombs, S., New, J. G., & Nelson, M. (2002). Information-processing demands in electrosensory and mechanosensory lateral line systems. *Journal of Physiology - Paris*, 96, 341–354.
Denton, E. J., & Blaxter, J. H. S. (1976). The mechanical relationships between the clupeid swimbladder, inner ear and the lateral line. *Journal of the Marine Biology Association of the United Kingdom*, 56, 787–807.
Denton, E. J., & Gray, J. A. B. (1993). Stimulation of the acoustico-lateralis system of clupeid fish by external sources and their own movements. *Philosophical Transactions of the Royal Society B*, 341, 113–127.
Dijkgraaf. S. (1934). Untersuchungen über die Funktion der Seitenorgane an Fischen. *Zeitschrift für Vergleichende Physiology*, 20, 162–214.
Dijkgraaf, S. (1963). The functioning and significance of the lateral-line organs. *Biological Reviews*, 38, 51–105.
Eaton, R. C. & Hackett, J. T. (1984). The role of Mauthner cells in fast-starts involving escape in teleost fish. In R. C. Eaton (ed) *Neural Mechanisms of Startle Behavior* pp. 213–266. New York: Plenum Press.
Eaton, R. C., Bombardieri, R. A., & Meyer, D. L. (1977). The mauthner-initiated startle response in teleost fish. *Journal of Experimental Biology*, 66, 65–81.

Engelmann, J., Hanke, W., Mogdans, J., & Bleckmann, H. (2000). Hydrodynamic stimuli and the fish lateral line. *Nature*, 408, 51–52.

Enquist, M., Leimar, O., Ljunberg, T., Mallner, Y., & Segerdahl, N. (1990). A test of the sequential assessment game: fighting in the cichlid fish *Nannacara anomala*. *Animal Behaviour*, 40, 1–14.

Faucher, K., Parmentier, E., Becco, C., Vandewalle, N., & Vandewalle, P. (2010) Fish lateral system is required for accurate control of shoaling behaviour. *Animal Behaviour*, 79, 679–687.

Feitl, K. E., Ngo, V., & McHenry, M. J. (2010). Are fish less responsive to a flow stimulus when swimming? *Journal of Experimental Biology*, 213, 3131–3137.

Flock Å (1965). Electronmicroscopic and electrophysiological studies on the lateral line canal organ. *Acta Otolaryngology*, 199, 1–90.

Görner, P. (1973). The importance of the lateral line system for the perception of surface waves in the clawed toad *Xenopus laevis* Daudin. *Experientia* 29, 295.

Görner, G., & Mohr, C. (1989). Stimulus localization in *Xenopus*: Role of directional sensitivity of lateral line stitches. In S. Coombs, P. Görner, H. Münz (eds.), *The Mechnosensory Lateral Line. Neurobiology and Behavior* (pp. 543–560). New York: Springer.

Gray, J. A. B., & Denton, E. J. (1991). Fast pressure pulses and communication between fish. *Journal of the Marine Biology Association of the United Kingdom*, 71, 83–106.

Hanke, W., & Bleckmann, H. (2000). The ageing of the low frequency water disturbances caused by swimming goldfish and its possible relevance to prey detection. *Journal of Experimental Biology*, 203, 1193–1200.

Hanke, W., & Bleckmann, H. (2004). The hydrodynamic trails of *Lepomis gibbosus* (Centrarchidae), *Colomesus psittacus* (Tetraodontidae) and *Thysochromis ansorgii* (Cichlidae) investigated with scanning particle image velocimetry. *Journal of Experimental Biology*, 207, 1585–1596.

Hanke, W., Wieskotten, S., Niesterok, B., Miersch, L., Witte, M., Brede, M., Leder, A., & Dehnhard, D. (2012) Hydrodynamic perception in pinnipeds. In C. Tropea, H. Bleckmann (eds.) *Nature-inspired fluid mechanics* (pp. 255–270). Heidelberg: Springer,

Hassan, E.S. (1986). On the discrimination of spatial intervals by the blind cave fish (*Anoptichthys jordani*). *Journal of Comparative Physiology A*, 159, 701–710.

Hassan, E.S. (1992a). Mathematical-description of the stimuli to the lateral line system of fish derived from a 3-dimensional flow field analysis: I. The cases of moving in open water and of gliding towards a plane surface. *Biological Cybernetics*, 66, 443–452.

Hassan, E.S. (1992b). Mathematical-description of the stimuli to the lateral line system of fish derived from a 3-dimensional flow field analysis: II. The case of gliding alongside or above a plane surface. *Biological Cybernetics*, 66, 453–461.

Hasler, C. T., Pon, L. B., Roscoe, D. W., Mossop, B., Patterson, D. A., Hinch, S. G., & Cooke, S. J. (2009). Expanding the "toolbox" for studying the biological responses of individual fish to hydropower infrastructure and operating strategies. *Environmental Reviews*, 17, 179–197.

Hoekstra, D., & Janssen, J. (1985). Non-visual feeding behavior of the mottled sculpin, *Cottus bairdi*, in Lake Michigan. *Environmental Biology of Fishes*, 12, 111–117.

Hoin-Radkovski, I., Bleckmann, H., & Schwartz, E. (1984). Determination of source distance in the surface-feeding fish *Pantodon buchholzi* (Pantodontidae). *Animal Behaviour*, 32, 840–851.

Jayne, M., Gardiner, J. M., & Atema, J. (2007). Sharks need the lateral line to locate odor sources: rheotaxis and eddy chemotaxis. *Journal of Experimental Biology*, 210, 1925–1934.

Kalmijn, A. J. (1988). Hydrodynamic and acoustic field detection. In Sensory Biology of Aquatic Animals (J. Atema, R. R. Fay, A. N. Popper, and W. N. Tavolga, eds.), pp. 83–130. New York: Springer-Verlag.

Kanter, M. J. and Coombs, S. (2003). Rheotaxis and prey detection in uniform currents by Lake Michigan mottled sculpin (Cottus bairdi). *Journal of Experimental Biology*, 206, 59–70.

Kaus,, S., & Schwartz, E. (1986). Reaction of young *Betta splendens* to surface waves of the water. In F. G. Barth, E. A. Seyfarth (eds). Verhandlungen der Deutschen Zoologischen Gesellschaft (pp. 218–219). Stuttgart: Gustav Fischer.

Knudsen, E. I. (1987). Neural derivation of sound source location in the barn owl - an example of a computational map. *Annals of the New York Academy of Science*, 510, 33–38.

Korn, H., & Faber, D. S. (1975). Inputs from the posterior lateral line nerves upon the goldfish Mauthner cell. I. Properties and synaptic localization of the excitatory component. *Brain Research*, 17, 342–348.

Korn, H., & Faber, D. S. (2005). The Mauthner cell half a century later: A neurobiological model for decision-making? *Neuron*, 47, 13–28.

Lamprecht, J. (1973) Mechanismen des Paarzusammenhaltes beim Cichliden *Tilapia mariae* Boulenger 1899 (Cichlidae, Teleostei). *Zeitschrift für Tierpsychologie*, 32, 10–61.

Lang, H. H. (1980). Surface wave discrimination between prey and nonprey by the backswimmer *Notonecta glauca* L. (Hemiptera, Heteroptera). *Behavioral Ecology and Sociobiology*, 6, 233–246.

Liao, J. C. (2007). A review of fish swimming mechanics and behavior in altered flows. *Philosophical Transactions of the Royal Society Series B*, 362, 1973–1993.

Liao, J. C., & Chang, E. Y. (2003). Role of sensory mechanisms in predatory feeding behavior of juvenile red drum *Sciaenops ocellatus*. *Fisheries Science*, 69, 317–322.

Liao, J. C., Beal, D. N., Lauder, G. V., & Triantafyllou, M. S. (2003a). The Kármán gait: Novel kinematics of rainbow trout swimming in a vortex street. *Journal of Experimental Biology*, 206, 1059–1073.

Liao, J. C., Beal, D. N., Lauder, G. V., & Triantafyllou, M. S. (2003b). Fish exploiting vortices decrease muscle activity. *Science*, 302, 1566–1569.

Lighthill, J. (1993). Estimates of pressure differences across the head of a swimming clupeid fish. *Philosophical Transactions of the Royal Society Series B*, 341, 129–140.

McHenry, M. J., Feitl, K. E., Strother, J. A., & Van Trump, W. J. (2009). Larval zebrafish rapidly sense the water flow of a predator's strike. *Royal Society Biology Letters*, 5, 477–97.

McHenry, M. J., Michel, K. B., Stewart, W., & Müller, U. K. (2010). Hydrodynamic sensing does not facilitate active drag reduction in the golden shiner (*Notemigonus crysoleucas*). *Journal of Experimental Biology*, 213, 1309–1319.

Mirjany, M., Preuss, T., & Faber, D. S. (2011). Role of the lateral line mechanosensory system in directionality of goldfish auditory evoked escape response. *Journal of Experimental Biology*, 214, 3358–3367.

Montgomery, J. C. (1989) Lateral line detection of planktonic prey. In: Coombs, S., Gorner, P. & Munz, H. (eds) The Mechanosensory Lateral Line Neurobiology and Evolution. pp 561–574, Springer, New York.

Montgomery, J. C. & Saunders, A. J. (1985). Functional morphology of the piper Hyporhamphus ihi with reference to the role of the lateral line in feeding. *Proceedings of the Royal Society of London B*, 224, 197–208.

Montgomery, J. C., & Bodznick, D. (1994). An adaptive filter cancels self-induced noise in the electrosensory and lateral line mechanosensory systems of fish. *Neuroscience Letters*, 174, 145–148.

Montgomery, J. C, & Hamilton, A. R. (1997). The Sensory Biology of Prey Capture in the Dwarf Scorpion Fish (Scorpaena papillosus). *Marine and Freshwater Behaviour and Physiology,* 30: 209–223.

Montgomery, J. C., & Coombs, S. (1998). Peripheral encoding of moving sources by the lateral line system of a sit-and-wait predator. *Journal of Experimental Biology* 201, 91–102.

Montgomery, J. C., & Bodznick, D. (1999). Signals and noise in the elasmobranch electrosensory system. *Journal of Experimental Biology*, 202, 1349–1355.

Montgomery, J. C., Clements, K. (2000). Disaptation and recovery in the evolution of Antarctic fish. *Trends in Ecology and Evolution*, 15, 267–271.

Montgomery, J. C., Coombs, S., & Janssen, J. (1994). Form and function relationships in lateral-line systems - comparative data from 6 species of antarctic notothenioid fish. *Brain Behavior and Evolution*, 44, 299–306.

Montgomery, J. C., Bodznick, D., & Halstead, M. B. D. (1996). Hindbrain signal processing in the lateral line system of the dwarf scorpionfish, *Scorpeana papillosus*. *Journal of Experimental Biology*, 199, 893–899.

Montgomery, J. C., Baker, C. F., & Carton, A. G. (1997). The lateral line can mediate rheotaxis in fish. *Nature*, 389, 960–963.

Montgomery, J. C., Carton, A. G., Voigt, R., Baker, C. F., & Diebel, C. (2000). Sensory processing of water currents by fish. *Philosophical Transaction of the Royal Society B*, 355, 1325–1327.

Montgomery, J. C., Coombs, S., & Baker, C. F. (2001). The mechanosensory lateral line system of the hypogean form of *Astyanax fasciatus*. *Environmental Biology of Fishes*, 62, 87–96.

Montgomery, J. C., Macdonald, F., Baker, C. F., & Carton, A. G. (2002). Hydrodynamic contributions to multimodal guidance of prey capture behavior in fish. *Brain Behaviour and Evolution*, 59, 190–198.

Montgomery, J.C., Mcdonald, F., Baker, C.F. Carton, A.G.. & Ling, N. (2003). Sensory integration in the hydrodynamic world of rainbow trout. *Proceedings: Biological Sciences*, 270, Suppl. 2 195–197.

Müller, U., & Schwartz, E. (1982). Influence of single neuromasts on prey localizing behavior of the surface feeding fish, *Aplocheilus lineatus*. *Journal of Comparative Physiology A*, 149, 399–408.

New, J. G., Fewkes, L. A., & Khan, A. N. (2001). Strike feeding behavior in the muskellunge, *Esox masquinongy*: contributions of the lateral line and visual sensory systems. *Journal of Experimental Biology*, 204, 1207–1221.

Palmer, L. M., Deffenbaugh, M., & Mensinger, A. F. (2005). Sensitivity of the anterior lateral line to natural stimuli in the oyster toadfish, *Opsanus tau* (Linnaeus). *Journal of Experimental Biology*, 208, 3441–50.

Partridge, B. L., & Pitcher, T. J. (1980). The sensory basis of fish schools: Relative roles of lateral line and vision. *Journal of Comparative Physiology A*, 135, 315–325.

Pitcher, T. J., & Parrish, J. K. (1993). Function of shoaling behaviour in teleosts. In T. Pitcher (ed.). *Behaviour of Teleost Fishes* (pp. 363–439). London: Chapman and Hall.

Plath, M., Parzefall, J., Korner, K. E., & Schlupp, I. (2004). Sexual selection in darkness? Female mating preferences in surface- and cave-dwelling Atlantic mollies. *Behavioral Ecology and Sociobiology*, 55, 596–601.

Pohlmann, K., Grasso, F. W., & Breithaupt, T. (2001). Tracking wakes: The nocturnal predatory strategy of piscivorous catfish. *Proceedings of the National Academy of Science USA*, 98, 7371–7374.

Pohlmann, K., Atema, J., & Breithaupt, T. (2004). The importance of the lateral line in nocturnal predation of piscivorous catfish. *Journal of Experimental Biology*, 207, 2971–2978.

Przybilla, A., Kunze, S., Rudert, A., Bleckmann, H., & Brücker, C. (2010). Entraining in trout: A behavioural and hydrodynamic analysis. *Journal of Experimental Biology*, 213, 2976–2986.

Pujol-Marti, J., Zecca, A., Baudoin, J., Faucherre, A., Asakawa, K., Kawakami, K., & Lopez-Schier, H. (2011). Neuronal birth order identifies a dimorphic sensorineural map. *Journal of Neuroscience*, 32, 2976–2987.

Ritz, D. A., Hobday, A .J., Montgomery, J. C., & Wardy, A. J. W. (2011). Social aggregation in the pelagic zone with special reference to fish and invertebrates. *Advances in Marine Biology*, 60, 163–230.

Rowe, D. M., Denton, E. J., & Batty, R. S. (1993). Head turning in herring and some other fish. *Philosophical Transactions of the Royal Society London B*, 341, 141–148.

Russell, I. J., & Roberts, B. L. (1972). Inhibition of spontaneous lateral-line activity by efferent nerve stimulation. *Journal of Experimental Biology*, 57, 77–82.

Satou, M., Takeuchi, H.A., Tanabe, M., Kitamura, S., Okumoto, N., & Iwata, M. (1994). Behavioral and electrophysiological evidences that the lateral-line is involved in the inter-sexual vibrational communication of the hime salmon (landlocked red salmon, *Oncorhynchus nerka*). *Journal of Comparative Physiology A*, 174, 539–549.

Saunders, A. J., & Montgomery, J. C. (1985). Field and laboratory studies of the feeding behaviour of the piper *Hyporhamphus ihi* with reference to the role of the lateral line in feeding. *Proceedings of the Royal Society of London B*, 224, 209–221.

Schwartz, E. (1971). Die Ortung von Wasserwellen durch Oberflachenfische. *Zeitschrift für vergleichende Physiologie*, 74, 64–80.

Schwarz, J. S., Reichenbach, T., & Hudspeth, A. J. (2011). A hydrodynamic sensory antenna used by killifish for nocturnal hunting. *Journal of Experimental Biology*, 214, 1857–1866.

Stewart, W. J., & McHenry, M. J. (2010). Sensing the strike of a predator fish depends on the specific gravity of a prey fish. *Journal of Experimental Biology*, 213, 3769–3777.

Sutterlin, A. M., & Waddy, S. (1975). Possible role of the posterior lateral line in obstacle entrainment by brook trout (*Salvelinus fontinalis*). *Journal of the Fisheries Research Board of Canada*, 32, 2441–2446.

Taguchi, M., & Liao, J. C. (2011). Rainbow trout consume less oxygen in turbulence: the energetics of swimming behaviors at different speeds. *Journal of Experimental Biology*, 214, 1428–1436.

Teyke, T. (1985). Collision with and avoidance of obstacles by blind cave fish *Anoptichthys jordani* (Characidae). *Journal of Comparative Physiology A*, 157, 837–843.

Tricas, T. C., & Highstein, S. M. (1991). Action of the octavolateralis efferent system upon the lateral line of free-swimming toadfish, *Opsanus tau*. *Journal of Comparative Physiology A*, 169, 25–37.

Voigt, R., Carton, A. G., Montgomery, J. C. (2000). Responses of lateral line afferent neurones to water flow. *Journal of Experimental Biology*, 203, 2495–502.

von der Emde, G., & Bleckmann, H. (1998). Finding food: senses involved in foraging for insect larvae in the electric fish, *Gnathonemus petersii*. *Journal of Experimental Biology*, 20, 969–980.

Walkowiak, W., & Münz, H. (1985). The significance of water-surface waves in the communication of fire-bellied toads. *Naturwissenschaften*, 72, 49–50.

Windsor, S. P., Tan, D., & Montgomery, J. C. (2008). Swimming kinematics and hydrodynamic imaging in the blind Mexican cave fish (*Astyanax fasciatus*). *Journal of Experimental Biology*, 211, 2950–2959.

Windsor, S. P., Norris, S., Cameron, S. M., Mallinson, G. D., & Montgomery, J. C. (2010a) The flow fields involved in hydrodynamic imaging by blind Mexican cave fish (*Astyanax fasciatus*). Part I: open water and heading towards a wall. *Journal of Experimental Biology*, 213, 3819–31.

Windsor, S. P., Norris, S., Cameron, S. M., Mallinson, G. D., & Montgomery, J. C. (2010b) The flow fields involved in hydrodynamic imaging by blind Mexican cave fish (*Astyanax fasciatus*). Part II: gliding parallel to a wall. *Journal of Experimental Biology*, 213, 3832–42.

Yanase, K., Herbert, N. A., & Montgomery, J. C. (2012) Disrupted flow sensing impairs hydrodynamic performance and increases the metabolic cost of swimming in the yellowtail kingfish, Seriola lalandi. *Journal of Experimental Biology* (in press; published on-line doi:10.1242/jeb.073437)

Information Encoding and Processing by the Peripheral Lateral Line System

Boris Philippe Chagnaud and Sheryl Coombs

Keywords Aquatic vertebrates • Canal and superficial neuromast • Dipole • Frequency tuning • Hair cell • Information coding and processing • Natural and artificial hydrodynamic stimuli • Octavolateral efferent system • Peripheral organization • Receptive field

Abbreviations

ALLN	anterior lateral line nerve
CN	canal neuromast
CNS	central nervous system
MON	medial octavolateral nucleus
OEN	octavolateral efferent nucleus
PFT	potential flow theory
PIV	particle image velocimetry
PLLN	posterior lateral line nerve
SN	superficial neuromast

B.P. Chagnaud
Department of Biology II, Ludwig-Maximilians-University Munich,
Großhaderner Straße 2, D-82152 Planegg-Martinsried, Germany

S. Coombs (✉)
Department of Biological Sciences, Bowling Green State University and J. P. Scott Center for Neuroscience, Mind and Behavior, Bowling Green, OH 43403, USA
e-mail: scoombs@bgnet.bgsu.edu

S. Coombs et al. (eds.), *The Lateral Line*, Springer Handbook of Auditory Research 48,
DOI 10.1007/2506_2013_15, © Springer Science+Business Media New York 2013,
Published online: 29 June 2013

1 Introduction

As a hydrodynamic sensory system, the lateral line enables fish and some aquatic amphibians to detect wide-scale, ambient water motions created by wind and gravity, as well as local water disturbances, such as those created by animal movements or by the interactions between ambient water motions and aquascape features. Like all sensory systems, the lateral line system must extract biologically significant information from a welter of stimuli that bombard it in order to increase the probability of an animal's survival. Critically important stimulus features (e.g., those that permit determination of a predator's approach speed and direction) must be extracted, while irrelevant background noises that interfere with the detection and processing of important information must often be suppressed. Thus, lateral line sense organs have evolved not only to transduce fluid motion into neuronal signals, but also to act as critical first-stage filters that shape the information that the brain receives and reduce the amount of central processing that is required.

Although it is impossible to know if fish actually form hydrodynamic images of the environment in the same way that, for example, humans might form visual images, it is possible to describe how hydrodynamic information is represented by the peripheral nervous system and how this representation changes over time and in different behavioral contexts. Technological advances in our ability both to measure and model the spatial characteristics of flow fields have led to significant advances in our understanding of how flow patterns can be used to obtain information about flow-generating sources. Examples include how Mexican blind cavefish (*Astyanax mexicanus*) can avoid obstacles based on obstacle-created distortions in their self-generated flow field (Windsor et al., 2010a,b), how piscivorous predators can obtain information about a prey's whereabouts from the prey's hydrodynamic trail (Hanke et al., 2000; Hanke & Bleckmann, 2004), and how the location and distance of a small vibrating body can be encoded in the spatial pattern of water motion along arrayed flow sensors in the lateral line (Ćurčić-Blake & van Netten, 2006; Goulet et al., 2008; Rapo et al., 2009).

To understand fully the nature of hydrodynamic information available to fish, one must first understand how incoming water motions are transformed and represented in the peripheral nervous system. Information available to the brain in the form of spike activity in primary afferent fibers can be shaped by many factors, including (1) boundary layers at the interface between the fish's body and the surrounding water (see the chapter by McHenry & Liao); (2) the biophysical properties of the transduction elements (hair cells; Section 2) and the structures that surround them (see the chapter by van Netten & McHenry; and Section 5); (3) the spatial distribution, orientation and innervation of flow sensors (see chapter by Webb; and Section 3); and (4) descending influences of efferent innervation from the central nervous system (CNS; Section 6). This chapter examines how these factors influence stimulus encoding by primary afferent fibers, and in general, how

these and other features of the peripheral nervous system shape hydrodynamic information received by the brain.

2 Sensory Transduction and Response Characteristics of Hair Cells

The transduction of hydrodynamic events into a neuronal code in the lateral line system is mediated by hair cells, the same receptor cells found in the vestibular and auditory systems of all vertebrates. Much of what is known today about the basic functional properties of lateral line hair cells comes from the classic studies of Åke Flock and his colleagues in the 1960s and early 1970s on the lateral line canal system of the freshwater burbot (*Lota lota*) (Flock, 1965a,b; Harris et al., 1970). These studies revealed two important features of hair cells that directly impact how stimulus information is encoded by the lateral line system. One is the directional sensitivity of the hair cell and the other is the nonlinearity of hair cell responses to opposing stimulus directions.

The directional selectivity of the hair cell arises from the morphological polarization of the transduction apparatus, which consists of an apical bundle of stereovillae with one elongated kinocilium at the periphery (Fig. 1a). The stereovillae increase in length in a systematic fashion in the direction of the eccentrically placed kinocilium. Displacement of the hair bundle toward the kinocilium results in a depolarization of the hair cell membrane and an increase in the firing rate of the afferent fiber, whereas displacement in the opposite direction causes a hyperpolarizing response and a decrease in the firing rate (Fig. 1a). Displacements in directions orthogonal to the axis of morphologic polarization result in no response, and off-axis directions result in response magnitudes that are a cosine function of the stimulus direction (Fig. 1b) (Flock, 1965b).

A distinct, nonlinear feature of hair cells is that for equal displacements in opposite directions, the magnitude of the depolarizing response is greater than that of the hyperpolarizing response. Nevertheless, for a given direction of displacement, response magnitude increases linearly with displacement amplitude over several orders of magnitude (up to ~50 nm, RMS) (Kroese & van Netten, 1989).

Insofar as it has been investigated, lateral line hair cells do not appear to have any intrinsic electrical tuning (Kroese & van Netten, 1989), as has been reported for hair cells in other sensory systems (e.g., turtle cochlea). Rather, frequency tuning in the lateral line system appears to be dominated by biophysical factors associated with the number of hair cells per sense organ and structural features that are intrinsic (e.g., stereovillae length) or extrinsic (e.g., size and shape of surrounding structures) to the hair cell (see the chapter by McHenry & van Netten and Section 5). However, studies of hair cell physiology have involved only a few species, for example, the ruffe (*Acerina cernua*) and the burbot (*Lota lota*), with no direct

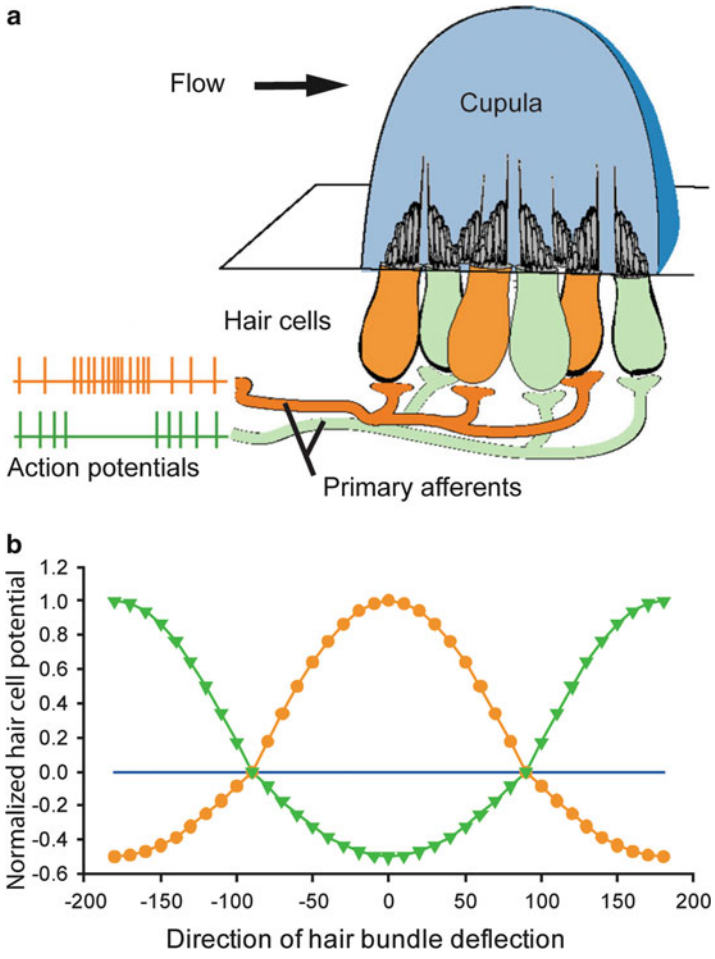

Fig. 1 Opponent organization of lateral line neuromasts. (**a**) Hair cells on any given neuromast are oriented in one of two opposing (orange and green) directions, resulting in a single axis of best sensitivity. (Courtesy of H. Bleckmann.) (**b**) Hair cell responsiveness, modeled as a cosine function of the direction of hair bundle deflection for the two oppositely oriented populations of hair cells

comparisons between hair cells in different submodalities (superficial or canal neuromast; see Section 5) (Flock, 1965a,b; Kroese & van Netten, 1987). Thus, it is difficult to make sweeping generalizations about the intrinsic response properties of hair cells, especially because several features, such as stereovillae length, are known to vary between submodalities and species (Flock, 1971; Russell & Sellick, 1976; Faucher et al., 2005). For further details on hair cell function, readers are referred to Kroese and van Netten (1989) (lateral line hair cells) and Ashmore (1991) and Eatock et al. (2006) (hair cells in other systems).

3 Functional Organization of the Peripheral Lateral Line System

Although the number, type, and distribution pattern of lateral line flow sensors may vary greatly between species (Coombs et al., 1988; see also the chapter by Webb), the peripheral lateral line system of both fish and amphibians has at least four basic organizational features in common: (1) an opponent organization of hair cells that gives rise to a single axis of best sensitivity for each sense organ, the neuromast (Section 3.1); (2) the arrangement of multiple neuromasts into linear arrays on the head and trunk, typically in rostrocaudal and dorsoventral directions (Section 3.2); (3) the coalescence of afferent fibers from the head and trunk into separate cranial nerves, each of which projects to a different region of the hindbrain; and (4) the formation of an orderly topographical map of rostrocaudal body location within each trunk or head region of the hindbrain (Section 3.3). In addition, the lateral line system of fishes can be subdivided into two submodalities: superficial neuromasts (SNs) that reside on the skin surface and canal neuromasts (CNs) that are enclosed in fluid-filled canals just below the skin surface (see Section 5 for further details).

3.1 Opponent Organization of Hair Cells

With rare exceptions (e.g., Shardo, 1996), hair cells in lateral line neuromasts exhibit an organization of oppositely oriented hair cells (Flock & Wersäll, 1962; López-Schier et al., 2004) (Fig. 1). Oppositely oriented hair cells, which are spatially intermingled throughout the neuromast, are innervated by separate populations of afferent nerve fibers, each of which synapses with hair cells of the same orientation during development (Faucherre et al., 2009). As a result, each neuromast has a single, bidirectional axis of best sensitivity (or responsiveness). This means that stimulation in one direction along this axis will result in an increase in firing rate for one fiber population and a decrease in the other and vice versa for stimulation in the opposite direction (Görner, 1963) (Fig. 1a). The functional ramifications of this highly conserved, opponent organization has yet to be fully understood, but Wiese (1984, 1988) has suggested that it helps to preserve responsiveness to AC (oscillatory) flows in the presence of sustained DC (unidirectional) flows (e.g., those in a stream or those created by forward swimming motions). If parallels to the vertebrate vestibular system can be drawn, the opponent organization may also serve to amplify the signal to the brain. The hair cells of the semicircular canals are also arranged in an opponent fashion, with hair cells of, for example, the horizontal canal on the left side having orientations that are opposite to those on the right side. Thus, a horizontal head rotation in one direction excites one population while inhibiting the other. Such an arrangement means that the difference in neuronal activity between left and right sides can be interpreted by

the brain as a head rotation in a given direction (Highstein et al., 2004) and that the amplitude of the difference signal will be greater than that of the signal from either side alone.

3.2 *Neuromast Distribution, Orientation, and Innervation Patterns*

The lateral line system most likely got its name from the highly visible line of scales running down the flanks of most fish. Within each scale is a short, open-ended tube (or canal) with a single canal neuromast inside. Although this "line" of CN scales represents only one of many not-so-visible CN and SN arrays in the lateral line system of bony fishes (Fig. 2) (see also the chapter by Webb), it nevertheless captures the hallmark features of the lateral line as a system of many flow sensors distributed over wide regions and organized (for the most part) into arrays. Although lateral line canals may exhibit some curvature, for example, to course above or below the eye, they generally follow a rostrocaudal (e.g., mandibular and trunk canals) or dorsoventral (e.g., pre-opercular canal) direction. In addition, there is a single (supratemporal) canal that runs across the top of the head in a lateromedial (left/right) direction. Thus, all three axes of a 3D-coordinate system are represented. SNs are also frequently organized into lines, some of which follow the course of canals as "accessory lines" (Coombs & Janssen, 1989; see also the chapter by Webb) and others that form rows that are independent of canals, for example, dorsoventrally oriented rows on trunk scales and rostrocaudally oriented rows along the caudal fin rays (Webb, 1989a; Schmitz et al., 2008) (Fig 2). Some species have large "fields" of SNs, but these typically consist of multiple, parallel lines of SNs. In addition, there is usually a line of SNs that form a ring around the nares.

Based on cases examined so far, the CN axis of best sensitivity is always parallel to the long axis of the canal (Flock & Wersäll, 1962; Janssen et al., 1987; Webb, 1989b) (Fig. 2). This no doubt follows from the fact that flow directions inside the canal are constrained to this axis. In contrast, SNs on fish are typically (but not always) free of surrounding structures that direct water motions. Experimental verification of SN orientations (axis of best sensitivity), based on SEM visualization of hair cell orientations, are limited to a few teleost species, including tilapia (*Oreochromis aureus*; Webb, 1989a), sea bass (*Dicentrarchus labrax*; Faucher et al., 2005), and goldfish (*Carassius auratus*; Schmitz et al., 2008). Although difficult to generalize to all 30,000+ species of fish, SNs in these few species have at least four features in common: (1) they maintain the same orientation within a given row, typically either parallel or orthogonal to the long axis of the row (Fig. 2); (2) they form rows that vary widely in their orientation on the head, but that are typically limited to rostrocaudal or dorsoventral directions on the trunk; (3) they form rows of rostrocaudally oriented SNs along the caudal fin rays (Fig. 2); and (4) they tend to have dorsoventral orientations when located near CNs on the trunk. In

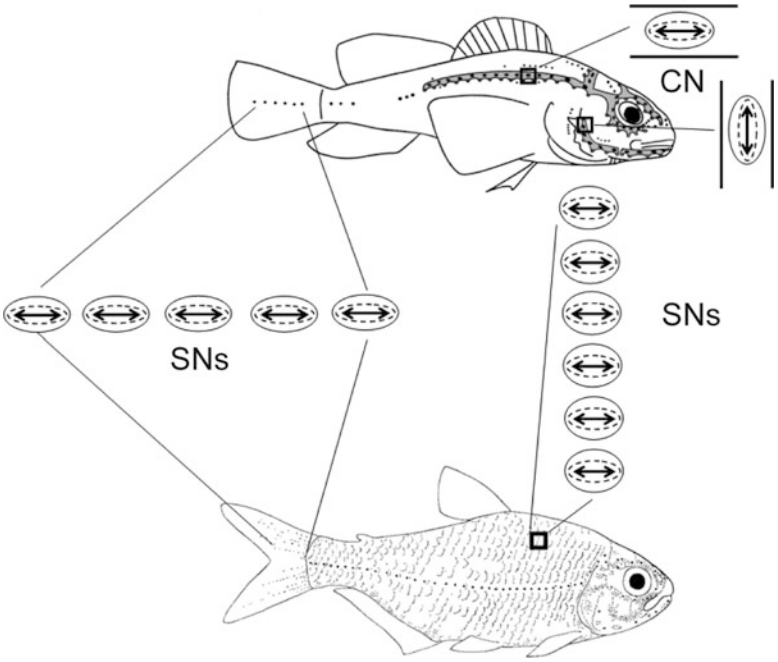

Fig. 2 General principles of neuromast distribution and orientation. The Lake Michigan mottled sculpin (*Cottus bairdi,* Scorpaeniformes) (top) and the Mexican tetra (*Astyanax mexicanus*, Characiformes) (bottom, adapted from Schemmel, 1967) differ dramatically in the number and spatial extent of SNs (small dots) on the body surface. Nevertheless, SNs in both species tend to form rows with axes of best sensitivity (double arrows) that are either parallel (e.g., SN rows on caudal fin rays, inset) or orthogonal (e.g., SN rows on trunk scales of the Mexican tetra, inset) to the row. CNs (large filled circles) are found in canals that run above (supraorbital) and below (infraorbital) the eye, down the cheek (preopercle), along the lower jaw (mandibular), across the top of the head (supratemporal), and down the trunk (trunk canal). The axis of best sensitivity of each CN is parallel to the long axis of the canal (top right insets)

goldfish, which have thousands of SNs all over the body surface (a row on nearly every trunk scale), only a small minority of those on the trunk have dorsoventral orientations and these are found on scales with CNs (Schmitz et al., 2008).

The spatial distribution and orientation of neuromasts in aquatic amphibians are similar to those in fish, but direct comparisons are difficult because amphibians lack canal neuromasts. In the clawed frog (*Xenopus laevis*), short lines of 2–15 SNs, called stitches, form rows or lines that generally follow the same distribution patterns as canals in fishes (e.g., along the trunk, above and below the eye, etc.). Moreover, the orientations of stitches, like SN rows on fish, are varied on the head, but restricted to either rostrocaudal or dorsoventral directions on the trunk. In *Xenopus*, skin papillae on both sides of each SN form a channel that likely directs water motions along the SN axis of best sensitivity, which is always orthogonal to the long axis of the stitch (Görner, 1963).

The lateral line system of the amphibian axolotl (*Ambystoma mexicanum*) is innervated by five distinct cranial nerves, each with its own ganglion (Northcutt, 1992; Northcutt et al., 2000). In fishes, there are at least three and as many as seven cranial nerves supplying the lateral line (Northcutt, 1989). Typically, neuromasts on the head are innervated by afferent fibers in the anterior lateral line nerve (ALLN), those on the trunk by fibers in the posterior lateral line nerve (PLLN), and those in the middle (post-otic region on the head) by yet a third (middle) lateral line nerve (Northcutt, 1989; Song & Northcutt, 1991). For a phylogenetic/evolutionary perspective on the spatial distribution and innervation of lateral line neuromasts, the readers are referred to Northcutt (1989), Song and Northcutt (1991), and the chapter by Webb.

Innervation patterns depend on submodality and hair cell polarity. In fish, afferent innervation of SNs and CNs differ in terms of the number of neuromasts that are contacted by a single fiber. SN fibers frequently innervate more than one SN (Münz, 1979; Nagiel et al., 2008; Faucherre et al., 2009). SNs innervated by the same fiber are typically part of the same row of SNs, as reported for tilapia (*Sarotherodon niloticus*) (Münz, 1985) and similarly, in the same stitch, as reported for the clawed frog (Mohr & Görner, 1996). Moreover, hair cells contacted by the same fiber appear to be of the same orientation (polarity) in all SNs, as indicated by both anatomical (Faucherre et al., 2009) and physiological (Montgomery & Coombs, 1992; Coombs et al., 1996) studies. In *Tilapia*, up to 10 superficial neuromasts on the same trunk scale may be innervated by a single fiber, but innervation of more than one CN by the same fiber is rare (<4%) (Münz, 1979, 1985). Most importantly, there is no evidence that single fibers innervate both SNs and CNs. In summary, SNs and CNs are innervated by separate nerve fibers, each of which integrates information from hair cells of the same orientation within a given SN or CN and in the case of SN fibers, also among SNs in the same row.

3.3 *Relationship between Peripheral Innervation Patterns and Termination Sites in the Brain*

Although it is beyond the scope of this chapter to discuss how information is processed by the CNS (see the chapter by Bleckmann & Mogdans), it is worth considering how or if organizational features of the peripheral nervous system (i.e., opponent organization of hair cells, spatial distribution of neuromasts, and subdivision of the system into two submodalities) are preserved centrally by the pattern of afferent termination sites in the brain. Tract-tracing neuroanatomical studies reveal that afferent fibers in bony fish project to four major regions of the brain (reviewed in McCormick, 1989; see also the chapter by Wullimann & Grothe): (1) the medial octavolateralis nucleus (MON) in the medulla, the only first-order nucleus that contributes to the ascending lemniscal pathway to the

forebrain; (2) the caudal nucleus, also in the medulla; (3) the eminentia granularis in the cerebellum, which feeds back down to the MON as part of an adaptive filter network for suppressing repeated and expected stimuli (e.g., the ones caused by the animal's own respiration) (Montgomery et al., 1995a); and (4) the Mauthner cell and reticulospinal network, which mediates rapid escape responses (Zottoli & Danielson, 1989) and other fast-start behaviors (e.g., Wöhl & Schuster, 2007). It is currently unknown whether individual afferent fibers terminate in all four areas of the brain, or whether different fibers project to different brain regions or some combination of both. Curiously, there is little anatomical evidence for a clear segregation of SN and CN inputs in the hindbrain (Puzdrowski, 1989), despite strong evidence for a functional dichotomy between the two submodalities (Section 5).

Nevertheless, response properties of central neurons in teleost fish indicate that information from the two submodalities, as well as that from oppositely oriented hair cells, are processed in separate, but parallel pathways—at least up to the level of the midbrain (Bleckmann, 2008; see also the chapter by Bleckman & Mogdans). A segregation of fibers from oppositely oriented hair cells is also likely in aquatic amphibians, based on the coalescence of primary afferent fibers into two distinct dorsomedial and ventrolateral fascicles as they enter the brain stem (Fritzsch, 1981; Altman & Dawes, 1983).

Recent anatomical and physiological studies on the development of trunk neuromast innervation in larval zebrafish are consistent with the idea that there may be two, functionally distinct, populations of developing afferent connections to the brain (Haehnel et al., 2012; Liao & Haehnel, 2012; Pujol-Martí et al., 2012). The first population consists of large, early-born and less excitable neurons that innervate multiple neuromasts and the second, of small, later-born and more sensitive neurons that innervate single neuromasts. The former projects to a more medial location in the hindbrain (consistent with the Mauthner cell location), while the latter projects to more lateral locations (consistent with the MON location). Based on these anatomical and physiological distinctions, the story that is beginning to emerge is that early-born cells mediate Mauthner-mediated escape responses to strong hydrodynamic stimuli that simultaneously stimulate wide regions of the body. In contrast, later-born cells are hypothesized to preserve the fine-grain resolution of spatial nonuniformities of hydrodynamic stimuli along the body surface—information that is presumably processed by the MON and the rest of the ascending lemniscal pathway.

Theories for how spatial patterns of flow activity along arrayed lateral line sensors contain information about, for example, the location of dipole sources or shed vortices in the wake of a swimming fish (Section 7) raise the question of whether or not information about instantaneous spatial patterns of activity is preserved and represented in the MON. Such a representation would seem to require that information from simultaneously activated neuromasts at different body locations (1) arrive at the MON at the same time and (2) form an orderly map of the body surface (i.e., a somatotopic map) in the MON. Evidence for the first

requirement comes from a single study on PLLN fibers in the trout (*Oncorhynchus mykiss*) (Schellart & Kroese, 2002). Conduction velocities were found to be slowest (~13 m s^{-1}) for fibers innervating neuromasts near the head and fastest (~33 m s^{-1}) for those near the tail, suggesting that longer travel distances to the brain were compensated for (at least, somewhat) by faster conduction velocities. Recent studies on developing innervation patterns in larval zebrafish, however, suggest an alternative interpretation of these data—that fast conducting fibers from the tail region form part of a dedicated pathway for Mauthner-mediated escape responses (Haehnel et al., 2012; Liao & Haehnel, 2012; Pujol-Martí et al., 2012).

Evidence for somatotopic mapping comes from studies on the zebrafish (*Danio rerio*), in which ALLN and PLLN fiber terminals were found to project to two separate regions of the MON—a ventromedial region that maps relative rostrocaudal location of head neuromasts and a dorsolateral region that maps relative rostrocaudal location of trunk neuromasts (Alexandre & Ghysen, 1999). Whether or not there are orderly maps of other body axes (e.g., dorsoventral or lateromedial) remains to be seen, but lateral line maps of the body surface do not appear to be as precise and as comprehensive as electrosensory maps in the hindbrain of weakly electric fish (Carr, 1990).

Interestingly, the zebrafish data indicate that there may be two separate maps (one for the head and one for the trunk), rather than a single, continuous map of body surface from head to tail, as seems to be the case for electrosensory maps. This arrangement—segregation of PLLN and ALLN terminals into dorsolateral and ventromedial regions of the MON—has been reported for several different species of fish (e.g., McCormick, 1983; Puzdrowski, 1989; New & Singh, 1994), as well as the African clawed frog (*Xenopus laevis*; Will et al., 1985). Unfortunately, little if any information is available on the termination sites of additional lateral line nerve fibers (e.g., in the middle nerve) relative to those of the PLLN and ALLN.

4 Neuronal Encoding of Information by Lateral Line Afferents

Lateral line afferent fibers, like other sensory afferents, rely on spike trains to represent stimulus information. The ability of lateral line fibers to respond to a sinusoidal signal at a given phase angle (i.e., to phase-lock) is robust over the entire range of low frequencies to which the system responds (Coombs et al., 1988; Engelmann et al., 2002; Chagnaud et al., 2007b) (Fig. 3). Thus, temporal codes that rely on the precise timing of individual spikes with respect to the stimulus are clearly available for encoding temporal dimensions of the stimulus. Similarly, rate codes, which rely on the number of spikes that occur in a relatively short time period, increase linearly with stimulus amplitude over a 20-dB range (Coombs et al., 1988; Bleckman et al., 1989), and thus are available for encoding stimulus

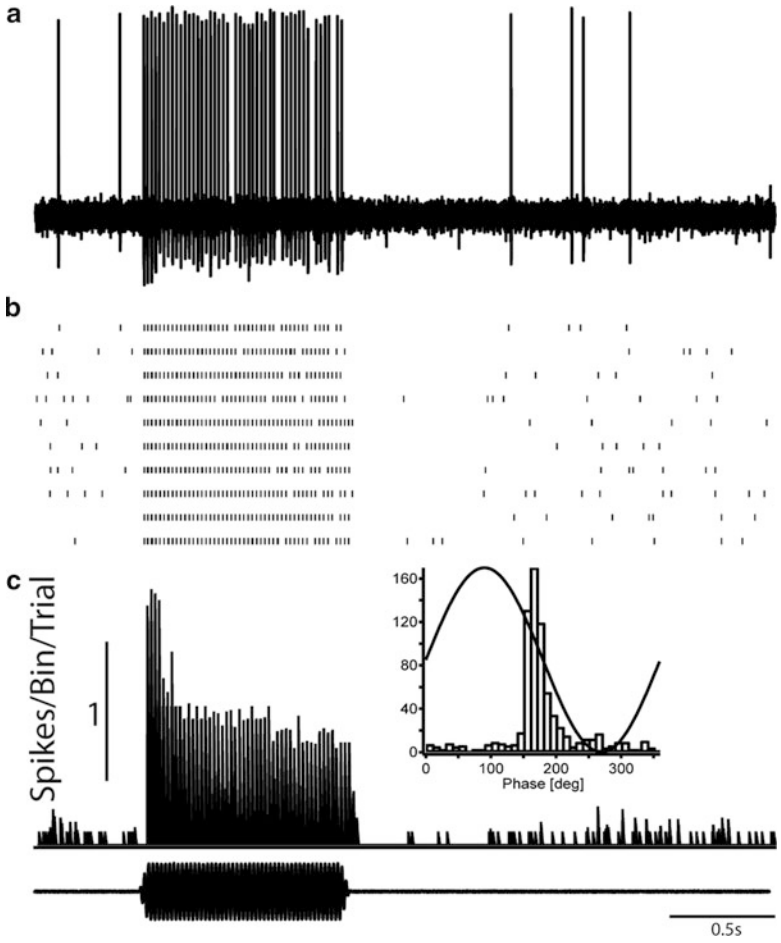

Fig. 3 (**a**) Spike train response of a lateral line afferent fiber to a sustained sinusoidal signal (stimulus trace at very bottom of fig.). (**b**) Dot-raster representation of spikes from the same fiber to 10 presentations of the same stimulus and (**c**) peristimulus-time (left) and period (right) histograms of the same data shown in (**b**)

amplitude. However, because the lateral line system responds to a vector quantity (flow) using directionally sensitive hair cells (Flock, 1965a, b) (Section 2), the firing rate of afferent fibers depends not only on stimulus magnitude but also on stimulus direction. Thus, an increase or decrease in afferent firing rate could signify a change in stimulus magnitude, direction, or both and the nervous system must sort this all out. Consequently, population codes, which rely on the pattern of activity across different fibers, are likely to be very important for encoding spatial patterns of activity along arrayed sensors, as discussed in Section 7.

5 Partitioning of Information by Lateral Line Submodalities

Most, if not all sensory systems consist of submodalities (e.g., rods and cones in the visual system) that respond to different stimulus dimensions and that partition incoming stimuli into parallel streams of information. The lateral line system partitions information not only according to spatial location along the body surface (Section 3.3), but also according to different flow dimensions, as encoded by SN and CN submodalities. SN and CN submodalities differ in many ways other than their location relative to the skin surface (Table 1). Most importantly, SNs and CNs differ in their response properties and the kind of information that they encode, as summarized in this section.

5.1 Relevant Stimulus Dimensions and Response Dynamics

In the mechanosensory lateral line, the response dynamics of afferent fibers depend heavily on fluid viscosity, as well as the mass and elasticity of structural elements in and around the neuromast (see the chapters by McHenry & Liao and van Netten & McHenry). Because SNs are superficially situated, they are directly exposed to flow along the body surface and their response is normally driven by flow velocity and boundary layer shear stress (spatial velocity gradients) along the overlying hydrogelatinous structure (the cupula), which couples the motions of the surrounding water to the underlying hair cells (Denton & Gray, 1983; Kalmijn, 1989; see also the chapter by van Netten & McHenry). When considering fluid motion inside the canal, typical CNs, like SNs, are driven by flow velocity over the cupula and neuromast. However, flow inside the canal is impeded by the boundary layer developing on the internal walls of small-diameter canals. Thus, inertial forces must come into play before fluids can move inside the canal. As a result,

Table 1 Summary of superficial and canal neuromast features

	Superficial neuromast	Canal neuromast
No. of hair cells	$< \sim 50$	~ 100–1000's
Size (diameter)	$< \sim 100$ µm	~100 µm–2 mm
Cupula shape	High aspect ratio (>2)	Low aspect ratio (<1)
No. of neuromasts/fiber	Several (as many as 10)	Rarely > 1
Relevant stimulus dimension	Flow velocity/sheer stress	Flow acceleration/pressure gradient
Frequency response (re: velocity)	Low pass (<0.1–10's of Hz)	Band pass (10's–100's of Hz)
Threshold sensitivity	$10^{-2} - 10^{-5}$ m s^{-1}	10^{-6} m s^{-2}/10^{-3} Pa/2 mm (2 mm relates to the canal interpore distance)

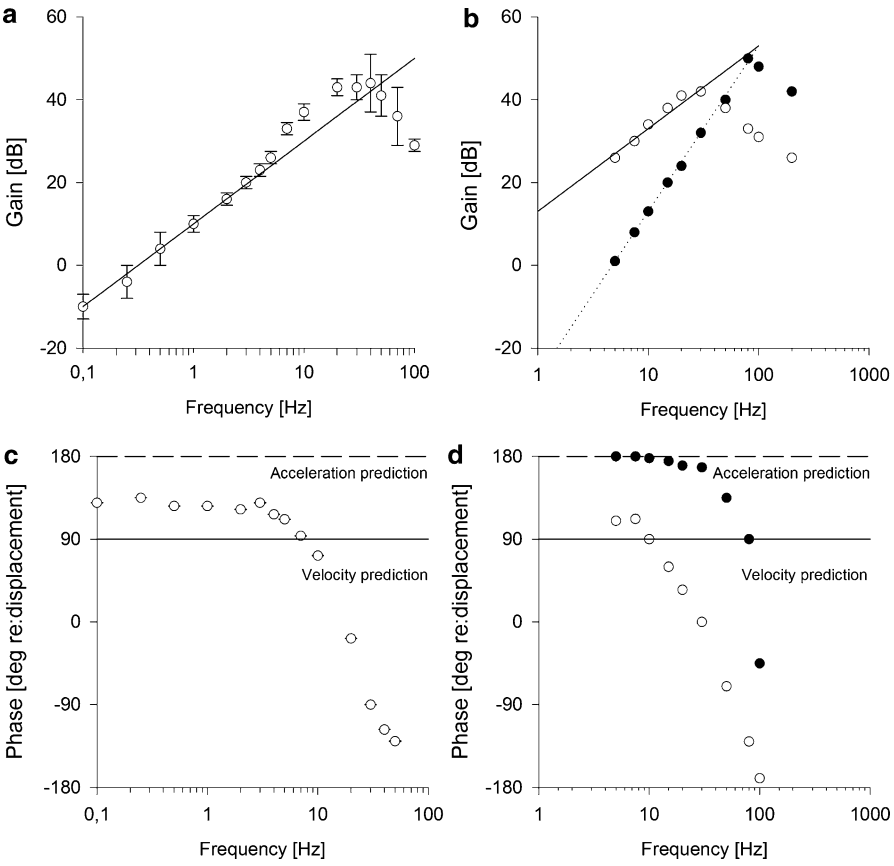

Fig. 4 Gain (% modulation of spontaneous activity) (**a**, **b**) and phase angle (deg re: sphere displacement) (**c**, **d**) responses of SN (open circles) and CN (filled circles) fibers in response to a small sphere oscillating at different frequencies. Data for *Xenopus* (**a**, **c**) and trout (**b**, **d**) are replotted from Kroese et al. (1978) and Kroese and Schellart (1992). Dashed lines indicate the gain (20 dB/decade slopes) and phase angle (90° re: sphere displacement) predictions for a velocity driven response, whereas solid lines indicate the gain (40 dB/decade slope) and phase angle (180° re: sphere displacement) predictions for an acceleration-driven response

inside fluid motion is proportional to the net acceleration between the fish and the surrounding water, which is also proportional to the pressure difference between the two adjacent canal pores (Denton & Gray, 1983, 1988; Kalmijn, 1988, 1989).

The clearest evidence for this functional dichotomy comes from a linear frequency-response analysis of afferent fibers in the African clawed frog (Kroese & van Netten, 1987) (Fig. 4a, c) and the trout (*Oncorhynchus mykiss*) (Kroese & Schellart, 1992) (Fig. 4b, d). In these studies, both the gain (% modulation of spontaneous activity) (Fig. 4a, b) and phase angle (preferred firing time during a sinusoidal cycle of stimulation) (Fig. 4c, d) of afferent fiber responses to a sinusoidally oscillating sphere (dipole stimulus) were measured. This analysis

revealed that fibers fell into two response categories in which responses of SN fibers (open circles, Fig. 4) conformed to predictions for a velocity-driven response (dashed lines, Fig. 4) and those of CN fibers (filled circles) conformed to predictions for an acceleration-driven response (solid lines, Fig. 4). Although several other species show evidence of a similar dichotomy (Section 5.2), there may be exceptions to this rule in some species. Indeed, species-specific morphological variations in lateral line structures (Coombs et al., 1989; see also the chapter by Webb), coupled with theoretical predictions based on physics (Denton & Gray, 1989), indicate that some lateral line neuromasts may respond to displacement and in rare cases, even pressure (e.g., in clupeids) (Denton & Gray, 1979). Nevertheless, response dynamics that fall outside of the flow velocity/acceleration dichotomy are likely to be the exceptions rather than the general rule.

Conspicuously absent from the lateral line system are any obvious signs of amplitude and time (phase)-encoding submodalities, as is found in the closely related electrosensory system of fish and in mammalian auditory systems (reviewed in Carr, 1993). Both SN and CN fibers exhibit tonic to slowly adapting responses to maintained stimuli (Coombs & Janssen, 1989; Voigt et al., 2000) and peripheral features commonly associated with phase-sensitive pathways (e.g., minimal branching in the axonal arbor of primary afferents, large afferent terminals or calyceal synapses) have not yet been found. This is probably not too surprising, given that the lateral line system generally operates at frequencies below 200 Hz, where phase-locking abilities are robust (Fig. 3). Thus, both amplitude and phase can be adequately represented in the same fiber.

5.2 Frequency Selectivity and Threshold Sensitivity

The peripheral auditory system of mammals is well known for its partitioning of information in the frequency domain (e.g., Kiang et al., 1969). A bank of differently tuned auditory fibers, which span the entire frequency range of hearing, preserves the frequency selectivity found along the basilar membrane of the cochlea. This arrangement is well suited for a spectral analysis of complex sounds. In addition, the tuning of individual auditory fibers to different frequency regions improves signal detection in the presence of noise, based on spectral differences between signal and noise. Although there is little evidence for a continuous "bank" of differently tuned fibers in the lateral line system, velocity-sensitive SNs and acceleration-sensitive CNs nevertheless divide the frequency range of detection into low- and high-frequency regions.

The "view" of how the two submodality partition frequency information, however, is heavily influenced by whether displacement, velocity, or acceleration is chosen as the frame of reference (Kalmijn, 1989). In the displacement frame used by Kroese and colleagues, relative responsiveness (gain) is plotted for a fixed displacement amplitude at different oscillation frequencies (Fig. 4a, b). This generates a picture of SN and CN fibers as having band pass characteristics with

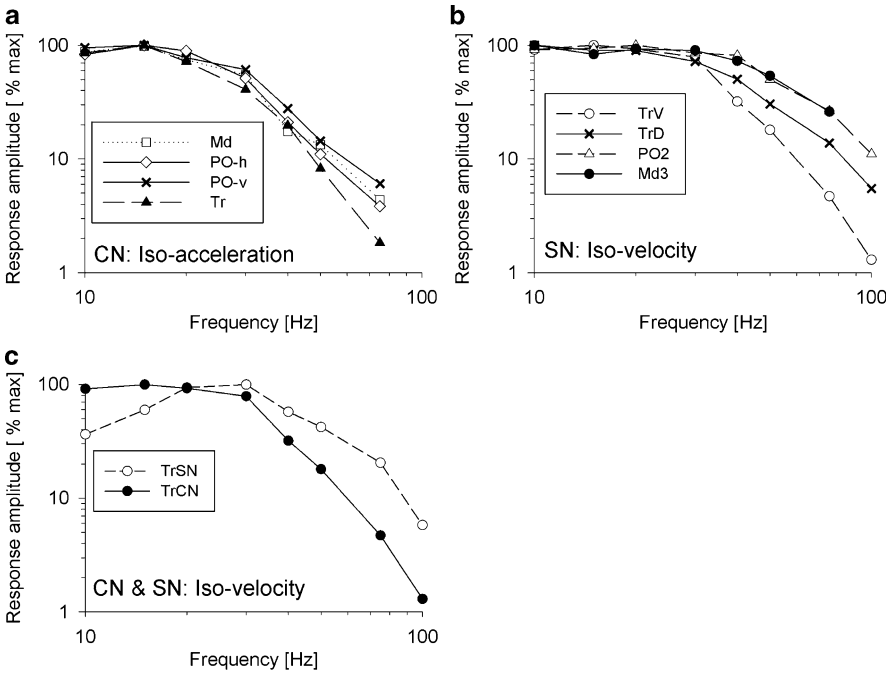

Fig. 5 Normalized response amplitude (% of maximum spike rate) of CN (**a**) and SN (**b**) fibers innervating neuromasts in different canals or body locations in *Trematomus bernachii*. Iso-acceleration stimuli were used to measure CN responsiveness in (**a**), whereas iso-velocity stimuli were used to measure SN responsiveness in (**b**). (**c**) Direct comparisons of a SN and CN fiber responding to iso-velocity stimuli. Md, mandible; PO-h, horizontal arm of preopercle; PO-v, vertical arm of preopercle; Tr, trunk. (Data replotted from Coombs and Montgomery, 1992, 1994)

a single best frequency that is typically lower for SNs than CNs for any given species (e.g., 30 and 80 Hz, respectively, for SN and CN fibers in the trout, as illustrated in Fig. 4b).

However, SN and CN responses are not proportional to displacement, but rather to velocity and acceleration, respectively. A different approach in which the frequency response properties of lateral line fibers are measured with stimuli of equal velocity or acceleration amplitudes reveals that both CN (Fig. 5a, c) and SN (Fig. 5b, c) fibers have low-pass characteristics when plotted in terms of their relevant stimulus dimension (Coombs & Montgomery, 1992, 1994; Montgomery & Coombs, 1992; Montgomery et al., 1994). That is, they respond maximally and equally well over a limited range of low frequencies, reinforcing the idea of SNs as flow velocity detectors and CNs as flow acceleration detectors.

The upper limit to this low-frequency range depends on a number of factors that govern the mechanical properties of the neuromast and surrounding structures (see the chapter by van Netten & McHenry). In the Antarctic fish *Trematomus bernachii*, the high-frequency cutoff (frequency at which responsiveness drops to 50% of maximum) varies according to neuromast size for SNs, but not CNs. That is,

the largest SNs on the ventral trunk line (TrV in Fig. 5b) have the lowest high-frequency cutoff (~30 Hz) and the smallest SNs on the head (Md3, PO2 in Fig. 5b) have the highest high-frequency cutoffs (~50 Hz). Although nonadaptive explanations for these small differences have been proposed (Coombs & Montgomery, 1994), it remains to be seen whether they are functionally significant or not. In contrast to SNs, the high-frequency cutoffs of CNs at different body locations are all very similar (~30 Hz) (Fig. 5a), despite a wide range of neuromast and canal diameters (100–600 μm) (Coombs & Montgomery, 1992). The absence of response variability across CN fibers provides evidence for the extent to which canal dimensions can vary without sacrificing essential canal functions (defined later in this section) and serves as a cautionary reminder that morphological variation does not always signify functional variation.

It is now generally accepted that canals function not only to protect neuromasts from damage, but also as mechanical filters to reduce low-frequency noise (Montgomery et al., 1994, 2009; see also the chapter by Montgomery et al.). When plotted in the same *velocity* frame of reference as SNs, it can be seen that the responsiveness of CN fibers to low frequency stimuli (< ~20 Hz) are reduced relative to that of SN fibers and may even be enhanced somewhat at higher frequencies (> ~30 Hz) (Fig. 5c). The reduction is due to the high-pass filtering action of canals, which reduce the amplitude of water velocity inside the canal relative to that outside the canal for low compared to high frequencies (Denton & Gray, 1983; Coombs & van Netten, 2005; see also the chapter by van Netten & McHenry). Enhancement, on the other hand, can happen if canal diameter decreases in the vicinity of the neuromast, resulting in increased flow speed in the narrow region relative to wide regions of the canal. From an information-processing point of view, canals can thus be seen to improve signal-to-noise ratios for the detection of high-frequency signals (e.g., from prey) in the presence of low-frequency noises, such as those present in ambient currents or currents produced by the fish's own swimming motions (see also the chapter by Montgomery et al.; and Section 7.1).

Tuning curve data from PLLN fibers in the Lake Michigan mottled sculpin (*Cottus bairdi*) confirm that afferent fibers can be divided into two populations of velocity- and acceleration-sensitive fibers, with the latter having greater sensitivity at higher frequencies than the former (Fig. 6a) (Coombs & Janssen, 1989). Further, compared to velocity-sensitive tuning curves, acceleration-sensitive tuning curves are a good match, both in terms of sensitivity and bandwidth, for behaviorally measured thresholds obtained under nearly identical stimulus conditions (same source, same source location). A similar story can be told for ALLN fibers innervating supraorbital CNs in the surface-feeding topminnow (*Aplocheilus lineatus*; Fig. 6b) (Bleckmann & Topp, 1981). In both cases, the broad tuning characteristics of a single population of acceleration-sensitive (CN) fibers are sufficient to account for the entire frequency range of behavioral detection. Thus, there is at present little evidence that the lateral line system uses differently tuned fibers for performing any kind of spectral analysis, as is done by the mammalian auditory system. In fact, a filter-bank representation of spectral characteristics is

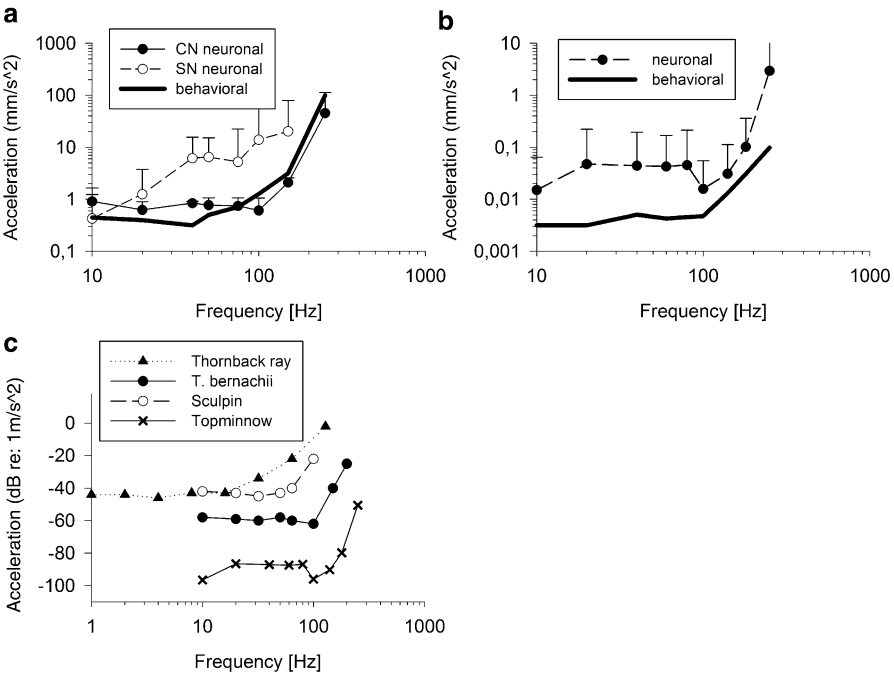

Fig. 6 Neuronal (thin dashed and solid lines) threshold curves for PLLN fibers in the mottled sculpin (**a**) and ALLN fibers in the surface-dwelling topminnow (**b**) compared to behavioral thresholds (thick solid lines) in each species. Neuronal tuning curves from four different species of cartilaginous and bony fish from very different environments and water temperatures are compared in (**c**): three benthic species, one from a temperate marine environment (thornback ray) (Görner & Kalmijn, 1989), one from a frigid (Antarctic) marine environment (*Trematomus bernachii*) (Montgomery & Coombs, 1992), and the third from a cool freshwater environment (Lake Michigan mottled sculpin) (Coombs & Janssen, 1990). The fourth species is the surface-dwelling, tropical water killifish (topminnow) (Topp, 1983)

unnecessary, given that frequency can be encoded temporally by the phase-locking abilities of afferent fibers.

From a comparative look at available tuning curve data, it can be seen that high-frequency cutoffs (frequency at which acceleration-sensitivity starts to decline) vary from ~30 Hz (thornback ray; *Platyrhinoidis triseriata*) to ~100 Hz (mottled sculpin and topminnow) (Fig. 6c). In this regard, it is worth noting that temperature also impacts the frequency responsiveness of lateral line fibers, as has been experimentally determined in the cold-water ruffe (*Acerina cernua*) and the warm-water African clown knifefish (*Notopterus chitala*; Wiersinga-Post & van Netten, 2000). An increase in temperature produces an upward shift in the frequency of maximum hair cell response, as measured by the amplitude of the summed extracellular potentials. In the cold-water ruffe, the frequency of maximum hair cell response (in a displacement frame of reference) for supraorbital CNs is 116 Hz at the normal habitat temperature of this species (4°C), but 290 Hz at 20°C.

By comparison, the frequency of maximum hair cell response in the warm-water clown knifefish is 460 Hz at its normal habitat temperature (28°C). This is the highest "best" frequency ever reported for the lateral line system in any species. Remarkably, the best frequency of the temperature-independent cupula response matches that of the hair cell response at the normal habitat temperature of each species. This suggests that structural features have coevolved to take advantage of the upper physiological limit dictated by the animals normal temperature (Wiersinga-Post & van Netten, 2000; van Netten, 2006).

Absolute sensitivity also depends on a number of factors, including structural features that produce mechanical resonances and the number of hair cells innervated by a single fiber. Tuning curve estimates of best acceleration sensitivity range from ~10^{-5} (ALLN fibers in topminnow) to ~10^{-2} m s^{-2} (PLLN fibers in thornback ray) for CNs responding to sinusoidal (AC) stimuli in the region of best sensitivity (Fig. 6c). In mottled sculpin, an acceleration sensitivity of 0.001 ms^{-2} corresponds to a pressure-gradient sensitivity of 0.002 Pa/2 mm, where 2 mm is the interpore spacing on the trunk canal of a 10-cm long fish. Estimates of velocity sensitivity in SNs depend on whether a DC (unidirectional flow) or AC (oscillating flow) is used. Velocity thresholds estimated from peak or peak–peak velocity levels in AC signals fall within 10^{-5}–10^{-4} m/s for both fish (Coombs & Janssen, 1989; Liao, 2010) and amphibians (Görner, 1963), and as a group are generally lower than estimates obtained with DC stimuli, which fall between 10^{-3} and 10^{-2} m/s (Engelmann et al., 2000, Voigt et al., 2000).

However, given that DC flow over the skin surface of a fish may result in microturbulence with AC components (Chagnaud et al., 2008a) (Section 7.1), it is difficult to interpret these measures. As such, experimental evidence for SN responses to "pure" DC stimuli is absent and difficult to obtain, but there is nevertheless good evidence that SNs respond extremely well to very low frequencies (i.e., 0.1 Hz) (Kroese et al., 1989) (Fig. 4a,c). One way to think about SNs is that they respond to low-frequency AC signals, but also to low-frequency modulations of DC stimuli. Finally, it should be pointed out that estimates of best displacement sensitivity (in the 10^{-9}–10^{-10} m range, as mathematically derived from velocity and acceleration thresholds) are on par with those from hair cells in other sensory systems, including the mammalian auditory system (Hudspeth & Markin, 1994).

5.3 Receptive Fields and Spatial Selectivity

Receptive field data obtained with unidirectional flow sources (e.g., water jet) are lacking and those obtained with bidirectional (dipole) sources are difficult to interpret owing to the spatial complexity of dipole flow fields, which are bilaterally but not radially symmetrical (Kalmijn, 1988, 1989). Receptive fields to dipole sources are complicated further by the fact that hair cells are directionally sensitive, meaning that the receptive field size and shape for any given neuromast/afferent

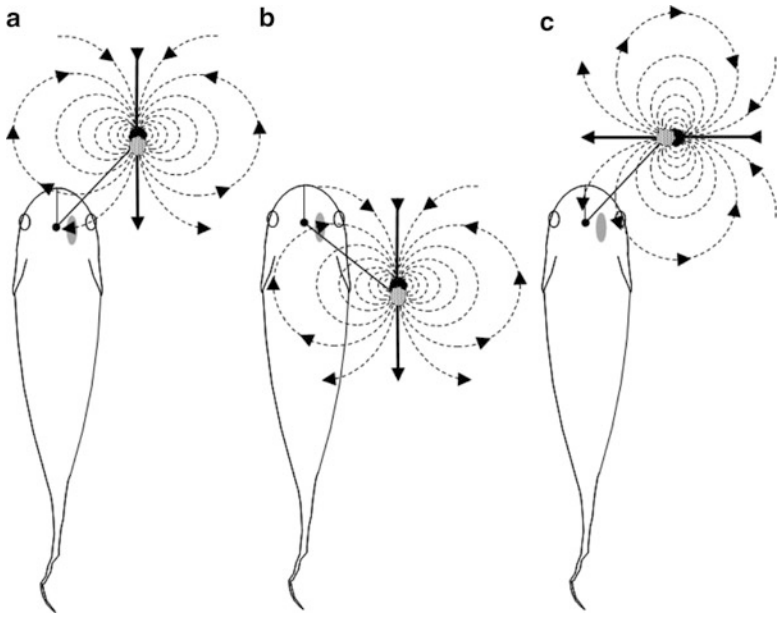

Fig. 7 Illustration of how flow direction over a given (e.g., supraorbital) neuromast (gray oval) varies with dipole source location when source orientation is fixed (**a, b**) and with source orientation when location is fixed (**a, c**). For this particular type of source, it is doubtful that flow direction over a single neuromast carries useful information about either source location or orientation

fiber will depend not only on source amplitude, but also on flow direction, which depends on both source location and orientation (Fig. 7). Nevertheless, two points about spatial selectivity and receptive fields can be made. First, the physics of lateral line stimulation by dipoles dictate that for any given source amplitude and orientation, responsiveness will decline steeply with distance from the neuromast (Fig. 10b). This is due to the fact that flow amplitude (whether measured in displacement, velocity or acceleration units) declines steeply with 1/distance^3 from a dipole source (Kalmijn, 1988). Given that the lateral line responds to the net motion (velocity or acceleration) between the fish and the surrounding water, the effective amplitude will decline even more steeply (1/distance^4). Second, based on response properties and peripheral innervation patterns, CNs are likely to preserve information about the spatial heterogeneities of a flow field, whereas SNs are more likely to smooth (average) them out. This is because SN fibers respond to flow velocity and integrate hair cell inputs from multiple neuromasts, whereas CN fibers respond to spatial differences in flow velocity (acceleration) and typically integrate hair cell inputs from within a single neuromast. How the receptive field size of a group of mutually innervated SNs compares to that of a single CN for stimuli of equal effectiveness (e.g., at the most effective frequency, orientation, etc.) remains to be seen. However, groups of mutually innervated SNs

can extend over large areas, for example, along the entire length of the caudal fin (Münz, 1979, 1985). The idea that each CN fiber is driven by local flow anomalies in a restricted region of space is further supported by the absence of any evidence for mechanical coupling between adjacent CNs (Denton & Gray, 1983; Coombs et al., 1996). Neuronal responses of CN fibers can be predicted solely by the pressure difference across the surrounding two canal pores (see Fig. 10e, f), indicating little if any influence from adjacent canal segments.

5.4 Directional Selectivity

The directional selectivity (or sensitivity) of the lateral line system can be described in terms of (1) the *direction of flow* over a given neuromast with respect to the *axis of hair cell polarization* or (2) the *location or orientation of a flow source* with respect to some *reference point on the fish* (Fig. 7). Source orientation may be described in terms of the direction of translational movement, or, in the case of oscillating sources, as the axis of bidirectional oscillation. Because flow fields around discrete sources (e.g., moving animals) are spatially complex, flow direction in the vicinity of a single SN will vary in complex ways with source location and orientation (Fig. 7). Further, even relatively uniform, unidirectional flow fields (e.g., a stream) can result in local perturbations of flow direction and amplitude along the body and lateral line system (Voigt et al., 2000; Chagnaud et al., 2008a; and Section 7.1). Therefore, the spatial distribution of local flow amplitudes and directions along arrayed neuromasts is likely to be an important source of information about either large-scale currents or discrete flow sources.

Given that hair cell responsiveness is a cosine function of the direction of hair bundle displacement (Flock, 1965a, b) (see Fig. 1b), it is tempting to assume that the firing rate of an afferent fiber varies in a similar fashion with the direction of flow over the neuromast. However, direct measures of this kind have rarely been made, and thus it is difficult to know how or if surrounding structures such as the cupula may further sharpen the inherent directional tuning of the neuromast hair cells. In any event, it is reasonable to assume that neuromasts respond best (if not exclusively) to flow directions along the axis of hair cell polarization (see Fig. 2), as has been confirmed experimentally in *Xenopus laevis* (Görner, 1963; Görner & Mohr, 1989).

For CNs, flow inside the canal is constrained to one of two directions along the canal axis, and thus flow direction inside the canal bears no simple relationship to flow direction outside the canal. For this and other reasons, CNs are not likely to be well suited for encoding information about flow direction. In contrast, flow around SNs is normally (but not always; see Schwarz et al., 2011) free from physical constraint. Thus, by comparing the response magnitude of dorsoventrally and rostrocaudally oriented neuromasts, it should theoretically be possible to compute the resulting flow direction along the skin surface. Moreover, the fact that individual fibers innervate multiple SNs in a row means that local deviations about the

mean overall flow direction will likely be averaged out. In support of these theoretical distinctions, SNs, but not CNs, appear to underlie rheotactic abilities of fish in slow currents (Montgomery et al., 1997).

The directional sensitivity of single neuromasts to different source angles has been measured for surface wave sources, which produce radially symmetrical, slowly propagating waves with dominant motions in the vertical plane (Bleckmann, 1985). In the surface-feeding African clawed frog, SN afferents innervating stitches on the head were found to be omnidirectional, responding to surface wave sources from all directions around the head (Zittlau et al., 1986). Indices of directional specificity (length of the mean vector) were quite low (0.26) compared to those obtained from optic tectum cells in the midbrain (>0.8) under identical stimulus conditions. In contrast, hair cell potentials from large CNs on the head of two species of surface-feeding fish (*Aplocheilus lineatus* and *Pantodon buchholzi*) exhibited strong directional preferences, most likely shaped by the orientation of canals and grooves (developmentally stunted, half-formed canals) on the head (Bleckmann et al., 1989a; Schwarz et al., 2011). Further, the unconditioned, prey-orienting responses of these surface-feeding fishes have been used to demonstrate high levels of orientation accuracy for a wide range (360°) of source angles. Nevertheless, sensory deprivation experiments point to time-of-arrival cues at different neuromasts, rather than directional tuning of individual neuromasts, as the likely mechanism of source localization abilities in these fish (reviewed in Bleckmann et al., 1985; Görner & Mohr, 1989; see also the chapter by Montgomery et al.).

6 Efferent Modulation of Peripheral Activity

Insofar as it is understood, the octavolateralis efferent system functions as a gain control system to modulate hair cell sensitivity in the vestibular and auditory systems of all vertebrates (Köppl, 2011), as well as in the lateral line system of fishes and aquatic amphibians (Roberts & Meredith, 1989). In each case, efferent neurons make synaptic contacts with both hair cells and the afferent fibers innervating them (Hama, 1978; Köppl, 2011). Lateral line efferent fibers are anatomically easy to identify, as they typically possess smaller diameters than afferent fibers (e.g., Münz, 1985; Northcutt, 1992), indicating that conduction velocities are relatively slow and temporal fidelity unimportant. This is in strong contrast to afferent fibers for which fiber diameters and thus conduction velocities are believed to increase with increasing distances from the brain (see Section 3.3). Efferent cell bodies reside in the bilaterally paired octavolateralis efferent nucleus (OEN), which straddles the midline and is in close association with the branchiomotor columns in the hindbrain medulla in both fish and amphibians (Roberts and Meredith, 1989; see also the chapter by Wullimann & Grothe). The OEN receives inputs from a variety of sources, including locomotor and sensory nuclei (Roberts & Meredith, 1989; see also the chapter by Wullimann & Grothe). In

fishes and amphibians there is no clear segregation of the OEN into distinct cell populations, according to whether their targets are auditory, vestibular, or lateral line (Roberts & Meredith, 1989). However, there is a tendency for a crude topographic segregation, with efferents innervating lateral line organs on the head region being more rostrally located than those supplying the trunk (reviewed in Wagner & Schwartz, 1996; Bricaud et al., 2001). This tendency appears to be species specific, with some species showing evidence of distinct rostral and caudal subdivisions whereas others do not (Wagner & Schwartz, 1996; Bricaud et al., 2001). However, evidence for a strict topographic map (an orderly representation of relative rostrocaudal position) is lacking. Moreover, rostral and caudal subdivisions seem to differ in terms of their topographic organization. In *Aplocheilus*, for example, approximately 66% of efferents from the rostral subdivision innervate lateral line organs on the head, whereas those in the caudal subdivision are evenly divided between those that supply the head and trunk (Wagner & Schwartz, 1996).

The total number of OEN neurons in most, if not all species studied so far, is far less than the total number of neuromasts, indicating a high degree of divergence and low spatial selectivity of OEN innervation (Bricaud et al., 2001). Thus, it is assumed that a single efferent neuron innervates more than one neuromast (Köppl, 2011). Further, in fish, a given efferent fiber can innervate all hair cells within a given neuromast, including those of opposite polarities (Faucherre et al., 2009), as well as hair cells in different lateral line submodalities (i.e., both SNs and CNs; Münz, 1985), on different sides of the body (Roberts & Meredith, 1989) and in other octavolateralis modalities (e.g., vestibular and auditory systems; Münz, 1985). Nevertheless, efferent fibers do show some degree of differential innervation of head and trunk regions of the lateral line, which likely relates to the rostrocaudal segregation of cell bodies in the OEN (Wagner & Schwartz, 1996) and separate rostral and caudal nerve rami (Song & Northcutt, 1991).

OEN neurons are predominantly cholinergic (Flock & Lam, 1974), reflecting their motoneuronal origin. However, other neuroactive peptides known to modulate hair cell sensitivity, including γ-aminobutyric acid (GABA), may be present in lateral line efferent synapses as well (Roberts & Meredith, 1989). The action of the efferent system on lateral line hair cells has been shown to reduce both spontaneous and evoked activity in afferent neurons (Russell, 1971; Tricas & Highstein, 1991). Despite the predominant inhibitory activity of OEN efferents, several reports have shown excitatory effects exemplified by an increase in discharge rate of afferents innervating vestibular (Highstein & Baker, 1985) and lateral line afferents (Flock & Russell, 1973).

The efferent system can be activated in one of two major ways: (1) by stimulation of different sensory modalities, including visual (Tricas & Highstein, 1990) and somatosensory (Roberts & Russell, 1972) systems or (2) by motor acts (e.g., vocalization, swimming motions) that self-stimulate the octavolateralis sense organs (Tricas & Highstein, 1991; Weeg et al., 2005). Clear evidence of self-stimulation of the lateral line comes from physiological recordings of afferent activity during respiratory gill (Montgomery et al., 1996) and swimming (Russell & Roberts, 1974; Ayali et al., 2009) movements of restrained fish, as well as from

freely swimming fish (Palmer et al., 2005). Although flows generated by self-movement can serve a useful function (e.g., in active flow-sensing of stationary objects by Mexican blind cavefish) (Teyke, 1985; Windsor et al., 2008, 2010a,b), they can also create noise interference and saturation problems for the detection of other flow sources (e.g., prey). Thus, one of the proposed functions of the efferent system is that it inhibits hair cell activity under circumstances when self-motion is expected to over swamp the system (Roberts & Meredith, 1989).

All in all, the function of the efferent system in the processing of lateral line information is somewhat complicated because OEN efferents exhibit different modes of activation (sensory or motor), different effects on hair cells (excitatory or inhibitory) and diffuse influences on hair cells of different polarities, different submodalities of the lateral line, and different octavolateralis modalities all together. The most parsimonious view of the efferent system is thus as a context-dependent, gain-control system that operates in both feedback and feed forward modes (Roberts & Meredith, 1989). This duality permits control over hair cell sensitivity in context-appropriate ways. In the case of continued strong stimulation (self-generated or otherwise), both modes of the efferent system can be used to turn down the gain so as to prevent overstimulation of hair cells and improve overall signal-to-noise ratios. In the feedback mode, the system responds to sensory inputs about overstimulation and in the feed forward mode, it responds to premotor inputs that inform the OEN about motor instructions for behavioral actions in anticipation of overstimulation. In the case of sensory-evoked states of arousal (Highstein & Baker, 1985; Tricas & Highstein, 1991), the efferent system could operate in a feed forward mode to turn up the gain in anticipation of either predator or prey. This might be particularly true in cases in which sensory systems such as vision, with long-range sensing abilities, can inform the OEN about anticipated stimulation of shorter-range systems, such as the lateral line.

It is conceivable that the rostral and caudal subdivisions of the OEN subserve feedback and feed forward circuits, respectively (Bricaud et al., 2001). This idea stems from the observation that sensorimotor areas of the brain for instructing C-start escape behaviors (i.e., the Mauthner cell and reticulospinal system) are in close proximity to caudal OEN cells in at least two species of fish (Metcalfe et al., 1985; Wagner & Schwartz, 1996). Not only does the Mauthner-mediated escape behavior produce strong hydrodynamic stimuli (Tytell & Lauder, 2008), but activation of the Mauthner cell also leads to activation of the efferent system. Thus, it is easy to see how feed forward inhibition of the lateral line to block overstimulation during this fast-start behavior could be advantageous in this circumstance (Zottoli & Danielson, 1989).

In addition to the efferent innervation by the OEN, the peripheral lateral line system also receives diencephalic efferent input in zebrafish (Metcalfe et al., 1985; Bricaud et al., 2001), goldfish (Zottoli & van Horne, 1983; Puzdrowski, 1989), and catfish (New & Singh, 1994). Contrary to the OEN neurons, diencephalic neurons appear to be catecholaminergic and excitatory (Bricaud et al., 2001), but their function remains elusive.

7 Peripheral Encoding of Hydrodynamic Stimuli

The hydrodynamic stimuli that can be detected and encoded by the lateral line system can be grouped into three broad categories: (1) large-scale ambient water motions (e.g., streams, tidal currents, ocean waves) created by wind, temperature gradients or gravity, and local flow perturbations created by (2) stationary or (3) moving sources. Whereas animate sources create local flows via whole-body or body part movements, inanimate (or immobile) sources act as bluff bodies to create nearby flow disturbances in the presence of large-scale water motions. Each type of hydrodynamic stimulus provides important information to fish. For example, the direction of ambient water motion can provide stream-dwelling fish with the information they need to conserve energy and prevent downstream displacement, to travel to an upstream natal spawning site or odorous prey, or to maximize their interception of downstream planktonic drift (see the chapter by Montgomery et al.). Likewise, the hydrodynamic signatures of animate sources theoretically contribute information about the identity of the source, how big it is, where it is with respect to self, how fast it is moving, and what direction it moves. Finally, local flow disturbances caused by inanimate sources are thought to provide fish with information about habitat structure, including the location of flow refuges or prime foraging sites. All of this information is likely extracted from the spatiotemporal pattern of flow along the arrayed sensors of the lateral line system.

Flow patterns around different animate and inanimate bodies can vary dramatically, as Fig. 8 illustrates. Flow patterns depend not only on body size and the relative speed of motion between the body and the surrounding water (as predicted

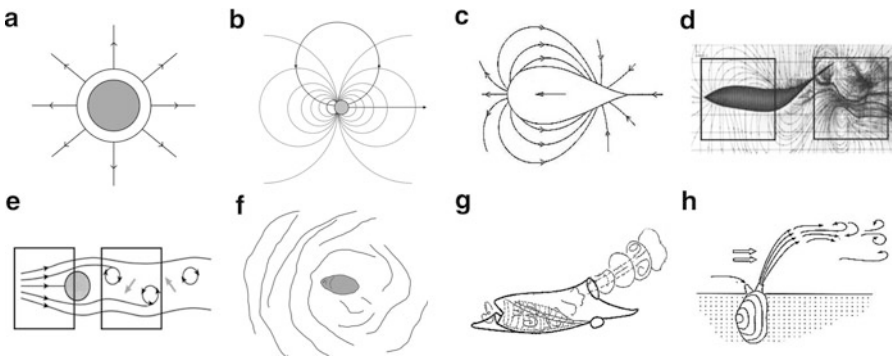

Fig. 8 Examples of water flow patterns around different flow-generating or flow-disrupting sources. (**a**) Pulsating bubble (monopole source). (**b**) Vibrating sphere (dipole source), frequently used as lateral line stimulus in experimental studies. (**c**) Gliding motions of a fish during the coast phase of burst and coast swimming, as modeled for Mexican blind cavefish by Hassan (1985). (**d**) Swimming motions (caudal body and fin undulations) of a giant *Danio*. (From Wolfgang et al., 1999.) (**e**) Bluff body in a stream generating a von Kármán vortex wake. (**f**) Surface waves produced by a whirlygig beetle. (**g**) Water jets produced by salp (Madin, 1990). (**h**) Exhalant siphon of a bivalve mollusc. (From Montgomery et al., 1995.) Boxes in (**d**) and (**e**) emphasize differences in flow patterns between leading and trailing edges of a moving (**d**) or stationary (**e**) body

by the Reynolds number) (see the chapter by McHenry & Liao), but also on location with respect to the leading or trailing edge of a moving body (Fig. 8d, e) or a stationary body in flow (Fig. 8e). The forward translational motion of a fish, for example, can arguably be modeled as a mechanical dipole, defined by the difference that exists between a positive (above ambient) pressure at the leading edge and negative (below ambient) pressure at the trailing edge (e.g., compare leading edge flow patterns in Fig. 8c, d). Movement along more than one axis, such as that produced by undulatory movements of the caudal body and fin during fish swimming, can result in more complex, multipole fields. Small, slow-moving bodies (or small bodies in slow flows) (Reynolds number <10) will produce laminar flows with more or less parallel streamlines, whereas large, fast-moving bodies (or large stationary bodies in fast flows) will in addition produce trailing vortices (intermediate Reynolds numbers) or fully turbulent wakes (high Reynolds numbers). All things considered, it is easy to see how flow patterns can provide fish with rich information about their natural environment, including habitat structure and animate sources of interest.

7.1 Encoding of Large-Scale Ambient Water Motions

Large-scale unidirectional flows (currents) are prevalent in many aquatic environments, including streams, rivers, and oceans. Aquatic animals show a strong orienting response (rheotaxis) to these large-scale flows in which they typically orient upstream (positive rheotaxis) to minimize drag, but sometimes also downstream (negative rheotaxis) (see also the chapter by Montgomery et al.). Because rheotaxis is a robust behavior that utilizes visual, vestibular, tactile, and lateral line cues (Arnold, 1974; Montgomery et al., 1997), the exact nature of lateral line contributions to this multisensory behavior is difficult to discern and likely to be context dependent. Nevertheless, behavioral experiments show that SNs but not CNs are necessary for rheotactic behaviors at low flow speeds (<~8 cm s^{-1})-a finding that has been replicated in several different fish species (Montgomery et al., 1997; Baker & Montgomery, 1999).

As might be expected from the different response properties of SN and CN fibers to AC (dipole) stimuli (Section 5), afferent fiber responses to unidirectional (DC) stimuli also fall into two categories (Engelmann et al., 2000, 2002; Voigt et al., 2000) (Fig. 9a). This dichotomy appears to hold for both rheophilic (e.g., stream-dwelling trout) and limnophilic (e.g., pond-dwelling goldfish) species. Fibers responding to unidirectional flows increased their firing rate in a linear fashion to increasing flow speed (Voigt et al., 2000; Carton & Montgomery, 2002; Chagnaud et al., 2008a). The most sensitive of these fibers (type I fibers presumably innervating velocity-sensitive SNs) are characterized by steep rate/level slopes and nonadapting (tonic) responses to a maintained stimulus, whereas insensitive or weakly sensitive fibers (type II fibers presumably innervating acceleration-sensitive CNs) have flat or shallow rate/level slopes and adapting responses (Voigt et al., 2000).

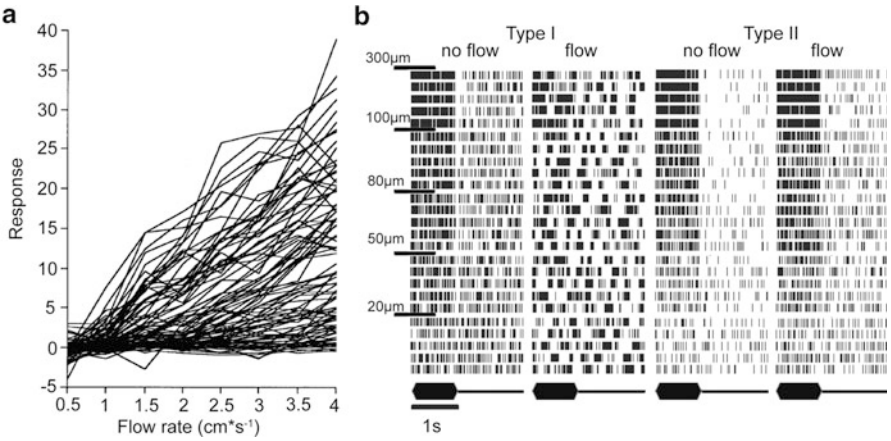

Fig. 9 Effect of unidirectional flow on primary lateral line afferent responses. (**a**) Relationship between flow velocity and mean discharge rate of primary afferents in the New Zealand long-fin eel *Anguilla dieffenbachii*. Note that the majority of fibers increased their discharge rate with increasing flow velocity. (Data adapted from Voigt et al., 2000.) (**b**) Raster plots of evoked spikes from a type I (likely innervating a SN) and type II (likely innervating a CN) afferent to a vibrating sphere (respective sphere displacement indicated at the left) under no-flow and unidirectional flow conditions. Note that both afferents respond similarly under still water conditions. Under flow conditions, however, the type I afferent (likely innervating a SN) response to the vibrating sphere is reduced. (Data adapted from Engelmann et al., 2000)

To determine if stream-like flows created noise-interference problems for fish, the responsiveness of type I and II fibers to a suprathreshold AC stimulus (50 Hz vibrating sphere) was investigated in the presence and absence of a stream-like flow (Engelmann et al., 2002; Chagnaud et al., 2007b) (Fig. 9b). In the absence of flow, the responses of type I and II fibers to the AC stimulus were similar. However, in the presence of a 10 cm s^{-1} flow, the responses of type I fibers to the AC stimulus were masked, whereas those of type II fibers were not. This finding underscores the functional utility of CNs for detecting AC signals in the presence of flow noise. Moreover, the physiological results are consistent with behavioral results from mottled sculpin showing that the CN-mediated ability of these fish to detect AC signals is little affected by DC flow noise (Coombs et al., 2001).

One surprising result of neurophysiological studies with stream-like stimuli is that reversals in flow direction do not produce the expected results, given that fibers innervate hair cells of one polarity only (Section 3.1). That is, a switch from, for example, rostrocaudal to caudorostral flow directions does not cause an increase in firing rate followed by a decrease in firing rate (or vice versa, depending on the orientation of the innervated hair cells with respect to the current direction). Rather, the vast majority of primary afferents were found to respond with increases in firing rate (Voigt et al., 2000), regardless of the flow direction (Chagnaud et al., 2008a). One explanation may be that under the conditions of these experiments there are micro and macroscopic turbulences along the fish's skin surface, as evidenced by the burst-like firing patterns of afferents to unidirectional flow (e.g., Engelmann et al., 2002).

In essence, the turbulence contributes an AC component to the otherwise DC flow, preventing complete saturation and adaptation of the afferent fiber response to maintained stimulation in one direction. An alternative explanation is that sampling biases (i.e., recording from a large population of CN fibers in addition to some SN fibers) could lead to the false conclusion that SN fibers respond to AC rather than DC components of the flow (Montgomery et al., 2009). Unfortunately, such a sampling bias is difficult to rule out when recording blindly from cranial nerves with mixed SN and CN fibers without using time-consuming procedures to distinguish between them (e.g., linear frequency-response analysis of Kroese et al., 1989) (Section 5.1).

The common turbulences in natural water flows may also provide usable cues for determining water flow direction and speed. As an individual packet of turbulence moves along the fish surface in the prevailing direction of bulk flow, it should lead to sequential activation of neighboring neuromasts (Chagnaud et al., 2008b). A comparison of activity in afferent fibers that innervate adjacent neuromasts could consequently be used to determine both flow velocity (from the time interval between sequentially activated neuromasts) and direction (from the sequence of activated neuromasts). Thus, the neuronal activity of closely spaced neuromasts can be correlated over time, demonstrating the potential to extract both flow velocity and flow direction via a cross correlation mechanism of lateral line afferent responses (Chagnaud et al., 2008b). Alternatively, given the directional tuning of neuromasts (Section 3.1) and their varying orientations on the body surface (Section 3.2), it is possible that flow direction and speed could be computed by vector addition of inputs from multiple neuromasts, a task that seems best suited to SNs (Section 5.4).

7.2 *Dipole Fields and Spatial Activity Patterns Along Lateral Line Arrays*

Dipole fields have played an important, but incomplete role in our understanding of how spatial patterns of activity along a linear array of sensors might encode information about flow sources, such as their location, distance, and orientation (Coombs et al., 1996, 2001) (Fig. 10). Dipole-like fields can be generated in different ways: by the translational or oscillatory movements of a solid body or by the presence of a stationary body in moving water. Under ideal (unbounded) conditions and with certain simplifying assumptions, the field around these bodies can be mathematically modelled with potential flow theory (PFT), an approach that has been used to model flow patterns around Mexican blind cavefish (*Astyanax mexicanus*) as they glide past stationary obstacles (Hassan, 1992; Windsor et al., 2010a), as well as those emanating from artificial prey vibrations in the context of prey-orienting behaviors of mottled sculpin (Coombs et al., 1996). One important assumption of PFT models, that is, freedom from vorticity, is violated in the boundary layer (solid–water interface) and other regions (e.g., in the trailing

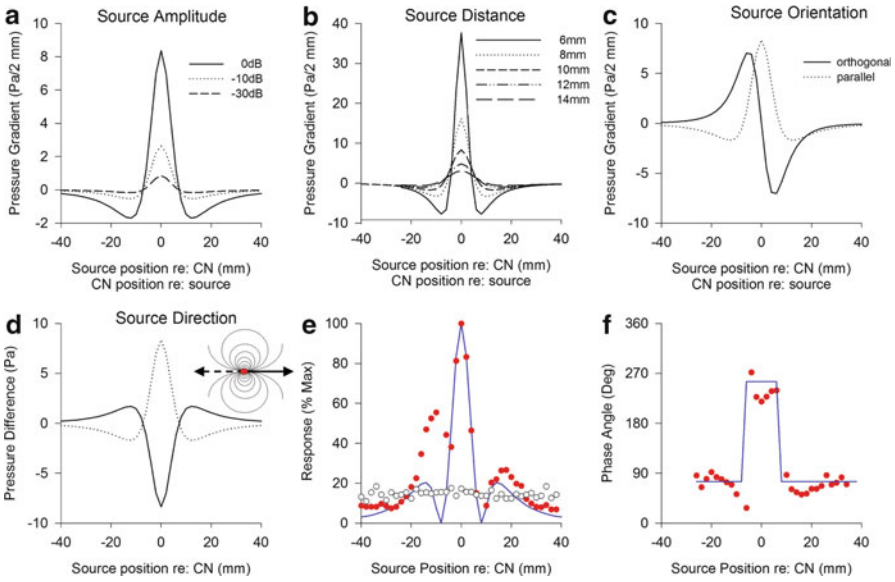

Fig. 10 Illustration of the *sequential pattern of activation* of a single CN (*x*-axis title = source position re: CN) when the source changes its location along a linear transect with respect to CN location ($x = 0$). The same figure also illustrates the *instantaneous spatial pattern of activation* across an array of CNs when the location of the source is fixed (at $x = 0$) (*x*-axis title = CN location re: source). Both sequential and instantaneous activation patterns vary with different source characteristics, including (**a**) source amplitude, (**b**) source distance, (**c**) source orientation, that is, the axis of source vibration is parallel or perpendicular to the long axis of the sensory array and (**d**) source direction, that is, whether the source is moving forward or backward along its axis of vibration. In (**a–c**), the pressure gradient across the surrounding two canal pores at each source position is plotted for the same phase of the sinusoidal cycle of source oscillation. In (**d**), the pressure gradient is plotted for two opposite phases of the sinusoidal cycle to show how the pressure-gradient direction (fore or aft along the canal axis as indicated by positive and negative values on the *y*-axis) oscillates over time at any given position. In (**e**) and (**f**), the magnitude (**e**) and phase angle (**f**) response of a PLLN fiber (red closed symbols) are plotted relative to spontaneous response rates (black open symbols) and modeled predictions for the pressure-gradient stimulus in blue. (Data from Coombs et al., 1996.) The slight mismatch between neuronal and modeled predictions are due to the fact that the fish's body was tilted slightly downward with respect to the axis of source translocation in these neurophysiological studies

wake of a swimming fish or an object in a stream) where shear stresses and vortices predominate. Thus, PFT is not adequate for modeling vortex structures and cannot adequately describe the stimulus to SNs responding to shear stresses in the boundary layer. Nevertheless, it is very useful for describing the pressure-gradient stimulus to CNs, which are impervious to boundary layer effects (Rapo et al., 2009; see also the chapter by van Netten & McHenry).

PFT models can be used to predict how various source parameters (e.g., amplitude, distance, and orientation) affect the *instantaneous spatial pattern* of stimulus amplitudes and directions (modeled as pressure gradients) along an array of CNs for

Table 2 Summary of spatial activation and their corresponding source features

Spatial Activation Feature	Source Feature
Location of peak amplitude on sensory array	Somatotopic location of source (X, Y)
Width or slope of excitatory peak	Source distance (Z)
Peak amplitude	Source distance, size, and amplitude
Sign (polarity)	Source direction (e.g., fore vs. aft)
Shape of activation pattern	Source orientation

a fixed source location (Fig. 10a–d, x-axis labeled CN position re: source). By the same token, they can also predict how the stimulus to a single sensor changes over time to the changing positions of a translocating source (Fig. 10a–f, x-axis labeled Source position re: CN). For an oscillating source at a fixed location and orientation, the pressure-gradient direction at any given CN location reverses its polarity over time (Fig. 10d) and the response magnitude and phase angle of each CN fiber faithfully represent the amplitude and direction (polarity) of the local pressure difference between surrounding canal pores (Fig. 10e, f). From modeling efforts like these, it can be seen that several prominent features in the spatial activation carry information about the source (Table 2). For example, the location of peak excitatory regions provides information about the somatotopic location of the source and the shape of the activation pattern carries information about source orientation (Fig. 10c). Because the peak amplitude in the pattern varies with several source parameters, including source distance, size, and amplitude, this simple feature is not a very useful piece of information in and of itself. However, when the bandwidth of the peak excitatory region and/or its spatial slope is normalized to peak amplitude, unambiguous information about source distance is provided (von der Emde et al., 1998; Coombs et al., 2002). The sign or the polarity of pressure gradients also carries information. The sign corresponds to the polarity of flow direction inside the canal (e.g., fore or aft), and in combination with the shape of the pattern, carries information about the relative direction of movement between source and fish. Precisely how this information is extracted and used by the CNS to guide behavior is unknown, but models such as these provide testable hypotheses of behavioral performance (e.g., Coombs & Patton, 2009). These will no doubt improve as the field progresses to more realistic and sophisticated models that use computational fluid dynamics to determine viscous effects and that also determine activation patterns over the entire lateral line system (e.g., Rapo et al., 2009), rather than just a single line of neuromasts along the trunk (e.g., Coombs et al., 1996).

Several signal-processing approaches have been used to extract information from dipole activation patterns, including the use of *prominent features* (e.g., location of minima, maxima and zero (polarity reversal) points (Franosch et al., 2005; Goulet et al., 2008), *template matching* using preobtained "banks" of patterns for known source parameters (Pandya et al., 2006), *wavelet transform* (Ćurčić-Blake & van Netten, 2006), *beamforming* (Yang et al., 2010), *model-based*

estimation (Abdulsadda & Xiaobo, 2011), and even *artificial neuronal networks* (Abdulsadda & Xiaobo, 2011). Some of these processing strategies are unlikely to be implemented by the CNS. Template-matching would seem to require a huge bank of templates to cover every scenario and thus unlikely to be very efficient. Feature-based approaches also have serious drawbacks since various source parameters interact in complex ways to affect prominent features in the activation pattern. For example, peak excitatory regions to signify source location (Fig. 10a) are confounded by changes in source orientation (Fig. 10c) (Coombs & Patton, 2009). In short, it is unknown at present how or if any of these algorithms are implemented by the CNS of fish and amphibians.

7.3 Flow Disturbances: Vortex Shedding

Vortex rings are highly sustained patterns of spiral motions that can occur in many different biological situations (e.g., Vogel, 1996; see also the chapter by Liao & McHenry) (Fig. 8d, e, g, h). Vortices are typically shed in the wake of swimming fish (Blickhan et al., 1992; Drucker & Lauder, 1999; Nauen & Lauder, 2002) and the wake contains information about fish size, swimming speed, and swimming direction (Blickhan et al., 1992; Hanke et al., 2000; Hanke & Bleckmann, 2004). In addition, objects placed in a unidirectional flow may generate an alternating (left, right) series of vortices behind it termed Kármán vortex streets (see the chapter by McHenry & Liao) (Fig. 8e). Behavioral experiments show that fish can detect vortex rings (Tou, 1991) and that piscivorous catfish can follow the vortex trails of their prey in the dark (Pohlmann et al., 2001, 2004). Further, fish exploit vortex streets behind bluff bodies for station holding (Sutterlin & Waddy, 1975; Przybilla et al., 2010) and to reduce the costs of locomotion (Liao et al., 2003a,b). Thus, vortices provide useful hydrodynamic information to fish about vortex-generating sources, whether animate or inanimate.

In response to a single vortex ring travelling along the fish's body, primary lateral line afferents of goldfish display highly reproducible changes in discharge rate as the vortex ring passes over the innervated neuromast (Chagnaud et al., 2006; Franosch et al., 2009) (Fig. 11). The pattern of response depends primarily on the direction of water motions in the vortex, re: the orientation of the innervated hair cells (e.g., compare Fig. 11a, b). Mathematical models of vortex encoding by the lateral line indicate that a single neuromast fiber could encode the orientation (spin direction) of the vortex ring, re: the neuromast's axis of best sensitivity, but not its radius, distance, or velocity (Franosch et al., 2009). Nevertheless, the spatiotemporal pattern of activity along fibers from differently oriented neuromasts could theoretically provide information about many if not all of these remaining parameters.

For stationary bluff bodies in a stream, the frequency of vortex shedding depends on the flow velocity and the diameter of the bluff body (Vogel, 1996; see also the chapter by McHenry & Liao). A Fourier analysis of the temporal firing pattern of

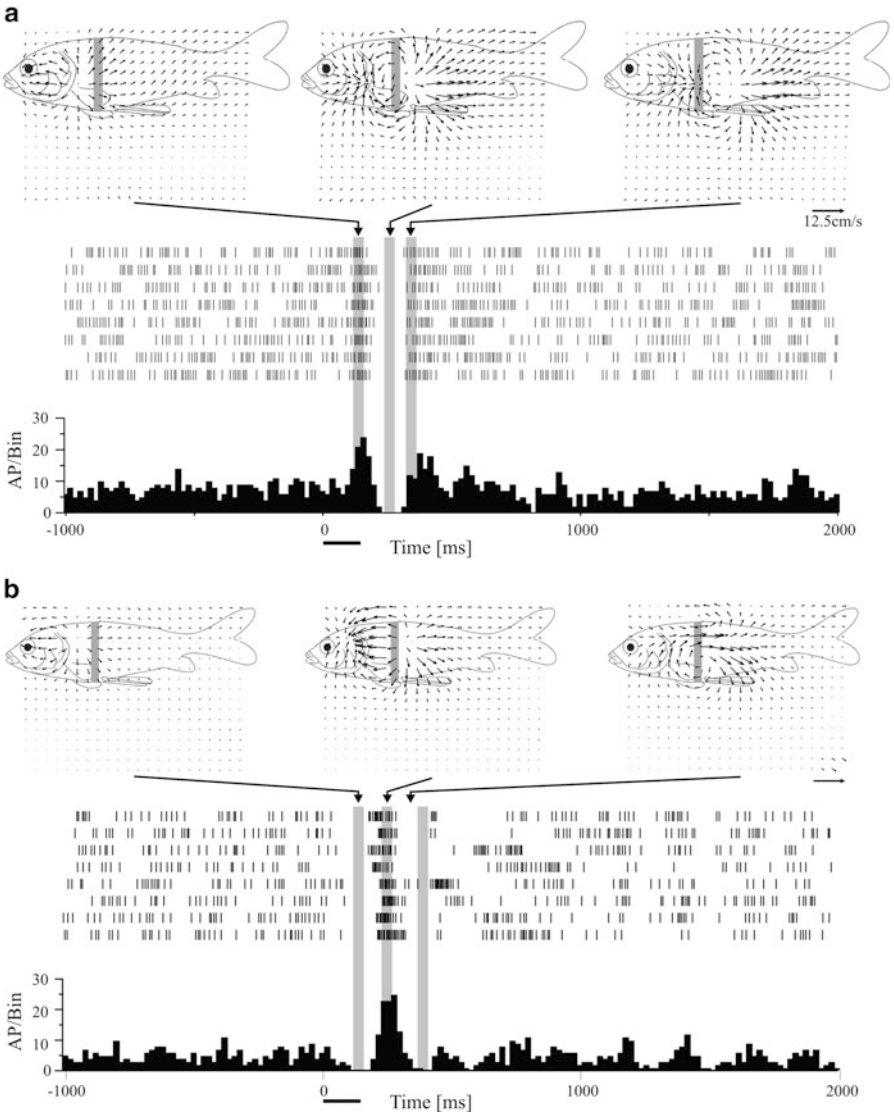

Fig. 11 Responses from a goldfish lateral line afferent to a single vortex travelling from head to tail (**a**) and from tail to head (**b**) along the fish's body. (**Top**) 2D plot of water particle motion. (**Middle**) Dot-raster plot of evoked spike activity during repeated stimulus presentations. (**Bottom**) Peri-stimulus time histogram based on dot-raster data shown in middle panel. (Adapted from Chagnaud et al., 2006)

lateral line afferents to a vortex street reveals that the vortex shedding frequency is indeed represented by the peak in the amplitude spectrum (Chagnaud et al., 2007a). Moreover, the "goodness" of the information about shedding frequency (i.e., the amplitude of the vortex-shedding peak) depends on the position of the fish relative to the bluff body (in this case, a cylinder). Lateral positions (behind, but to the left

or right of the cylinder) resulted in stronger representations of the shedding frequency than positions centered on the cylinder, as would be expected by the lateral positions of shed vortices (Fig. 8e). That fish position themselves to maximize vortex interception is evidenced by the lateral entrainment of stream-dwelling fish to bluff bodies (Sutterlin & Waddy, 1975; Przybilla et al., 2010) and by the lateral positions that piscivorous catfish hold with respect to the hydrodynamic trails that they follow (Pohlmann et al., 2001, 2004).

7.4 *Models of Unidirectional Body Movement: Translating Objects*

Within their environment fish are constantly exposed to moving bodies, such as prey or predators. Fish can readily detect the speed and direction of moving objects in behavioral experiments (Vogel & Bleckmann, 2001). The responses of peripheral lateral line fibers to an object moving at constant speed along the length of a fish show several distinct features, including highly reproducible patterns of response that are direction dependent (Bleckmann & Zelick, 1993; Mogdans & Bleckmann, 1998; Mogdans & Geisen, 2009) (Fig. 12a). The reproducible responses to the approaching and passing object are followed by less reproducible and more variable responses in the wake of the object (Mogdans & Bleckmann, 1998; Montgomery & Coombs, 1998). Nevertheless, the direction, speed, and translocation of the object

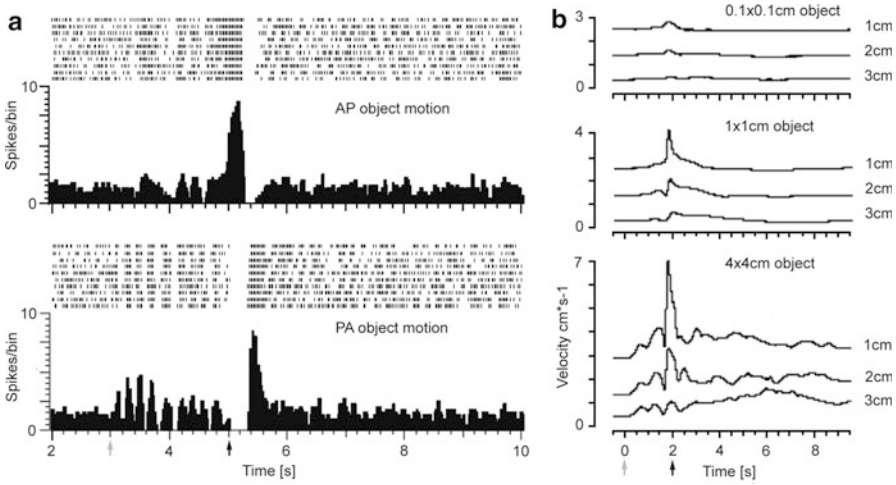

Fig. 12 (**a**) Responses from a single anterior lateral line nerve fiber in the goldfish to a translating object as a function of travel direction (tail to head in top set of graphs; head to tail in bottom set). Top trace in each set shows dot-raster plot of spikes over repeated stimulus presentations; bottom panel: Peri-stimulus time histograms of spike activity shown in dot-raster. (**b**) Single-point measurement of water velocity to a translating object of small (0.1 cm square, top), medium (1.0 cm square, middle), and large (4 cm square, bottom) size and at three distances from the sensor (1, 2, and 3 cm). [Data from **a** and **b** adapted from Mogdans & Geisen, 2009)

are represented in the temporal pattern of firing activity in a single neuromast fiber (Fig. 12). Response magnitude (peak firing rate), on the other hand, is likely to vary with multiple parameters, such as object speed, size, and distance (Fig. 12b) and thus, by itself, is not a very useful code for any of these parameters. In principle, the pressure-gradient pattern around a translating body (minus its wake features) can be modeled with PFT (Section 7.2). In this respect, the reproducible components of the response patterns to the approaching and passing object are a good match to modeled and measured pressure-gradient patterns (Montgomery & Coombs, 1998; Mogdans & Geisen, 2009). Finally, it should be noted that type II fibers presumed to innervate CNs exhibit robust responses to the passage of a translating object, even in the presence of a high (>10 cm s^{-1}) background flow (Engelmann et al., 2003).

7.5 Surface Waves

Surface waves, such as those created by terrestrial insects that have fallen into the water or aquatic insects that skim the water's surface (e.g., whirligig beetles) (see Fig. 8f) are potent lateral line stimuli. Not surprisingly, surface-feeding fish such as the topminnow (*Aplocheilus lineatus*) have several behavioral (see the chapter by Montgomery et al.) and anatomical adaptations for intercepting and detecting surface waves, including specializations of the lateral line (e.g., enlarged canal neuromasts in topless canals) on the flattened, dorsal surface of their heads (Bleckmann et al., 1989a). Unfortunately, there are very few data on the response properties of afferent fibers to surface waves, and the few data that do exist fail to characterize the spatiotemporal pattern of response to, for example, a spreading surface wave. Nevertheless, two important points can be made. One, surface waves and subsurface water disturbances (Sections 7.1–7.4) differ from one another in many significant ways, including propagation speed and how water disturbances change with distance from the source. Thus, peripheral codes for various source characteristics may be very different in each case. For example, hydrodynamic disturbances created by dipole sources propagate at the speed of sound (Kalmijn, 1989), whereas those in surface waves propagate very slowly (cm's/s) (Bleckmann et al., 1989a). Thus, instantaneous spatial patterns of activity may be more useful for representing various dipole source parameters, such as distance and location, than for surface wave sources. Indeed, behavioral experiments on prey-orienting responses of mottled sculpin to subsurface dipole sources and of topminnow to surface-wave sources indicate that for source location, spatial patterns are used in the former case (Conley & Coombs, 1998) and time of arrival cues are used in the latter (reviewed in Bleckmann, 1985; Görner & Mohr, 1989). As a second example, the amplitude of particle motion in a surface wave decreases in a frequency-dependent fashion, with high-frequency components attenuating more rapidly with distance than low-frequency components. In contrast, a frequency-dependent attenuation of water motion does not occur for subsurface sources in similar unbounded (free field) conditions. As a result, temporal (frequency-following)

codes, as reported for afferent fibers in the surface-feeding clawed frog (Zittlau et al., 1986; Elepfandt & Wiedemer, 1987), provide information about source distance, an idea that is supported by behavioral experiments.

As a second important point, lateral line afferents from neuromasts on the dorsal surface of some surface-feeding fishes respond to surface wave sources in a directionally selective manner with each neuromast being "tuned" to different directions, depending on its location and orientation on the head (Bleckmann et al., 1989a; Schwarz et al., 2011). Thus, the pattern of activity across different spatially tuned neuromasts could provide information about source location. Nevertheless, behavioral experiments indicate that time of arrival cues (for this slowly propagating wave) across spatially distributed neuromasts are used to determine source location, not directional tuning of neuromasts (Bleckmann et al., 1989).

8 Summary and Conclusions

The peripheral lateral line system is characterized by several hallmark features: (1) it consists of many (from <50 to >1000) individual flow sensors distributed all over the head and body; (2) each sensor has an opponent organization of hair cells that results in a single axis of bidirectional sensitivity; (3) flow sensors are subdivided into functionally distinct submodalities (CNs and SNs); and (4) sensors are arranged into discrete arrays. Despite many speculations about the functional ramifications of these features, even some of the most basic features have yet to be fully understood and appreciated—largely because so little is known about how information is processed in the brain, but also because well-designed behavioral and physiological tests of specific functions are lacking. A good example of a poorly understood feature that could benefit from this approach is the opponent organization of receptor cells (Section 3.1).

Another example involves the widely held belief that the spatially distributed nature of this system is ideally suited for encoding spatiotemporal features of complex flows and for forming hydrodynamic images of the environment. Recent technological advances in our ability to measure and model flow patterns have indeed led to a far richer appreciation of the kinds of information that these complex patterns hold (Sections 7.2–7.4). Nevertheless, we still know very little about how spatiotemporal information is processed and used by the CNS to direct actual behavior. In the case of spatiotemporal information about the location of discrete flow-generating sources (e.g., a stationary dipole; Section 7.2), the processing strategies for orienting behaviors must ultimately transform a 2-D, *somatotopic* representation of source parameters along the body surface into a 3-D *egocentric* representation with respect to a single, head-centered frame of reference (Coombs & Patton, 2009; see also the chapter by Montgomery et al.). This transformation undoubtedly involves the optic tectum of the midbrain, a highly conserved site of multisensory and motorsensory integration that subserves orienting behaviors in all vertebrates (Stein & Meredith, 1993). Thus, the many processing strategies and

algorithms put forward by engineering and computational modeling groups must ultimately be tested with respect to how or if these algorithms are implemented in the brain to direct *behavior*.

The functional dichotomy between SNs and CNs has come into much sharper focus in recent years—largely because of well-motivated behavioral and physiological experiments to test behaviorally and ecologically relevant hypotheses (see the chapter by Montgomery et al.). In particular, CNs have been identified as playing a key role in detecting and localizing (AC) signals from discrete sources and for being able to do so, even in the presence of flow noise (Sections 5.2 and 7.1). In contrast, SNs have been identified as playing a key role in detecting wide-scale, ambient currents and in mediating rheotaxis to slow currents (see the chapter by Montgomery et al.). Both behavioral and physiological lines of evidence suggest that superficial neuromasts (SNs) function in the spatiotemporal *integration* of information across multiple receptors (e.g., to compute the general direction of a uniform or large-scale current) and conversely, canal neuromasts (CNs) function in the spatiotemporal *segregation* of information for encoding the spatial heterogeneities associated with small, current-generating or current-distorting sources) (reviewed in Kanter & Coombs, 2003). Nonetheless, multiple studies have revealed that information from the different submodalities may be combined in different ways under different behavioral contexts. Whereas a single submodality (either SNs or CNs) may be used for relatively simple tasks, for example, rheotaxis at low current speeds (SN) or prey orientation in still water (CN), both submodalities are likely to work together in ways not yet understood for more demanding tasks (e.g., active flow sensing by Mexican blind cavefish).

Recent work on the developing lateral line system in zebrafish has also shed new light on the organization of the peripheral lateral line system, raising several interesting questions regarding the function of CNs and SNs and how they are wired up to the brain. This work indicates that there may be fast-conducting pathways from widely distributed, mutually innervated neuromasts to the Mauthner cell/reticulospinal escape network (Liao & Haehnel, 2012; Pujol-Martí et al., 2012; and Section 3.3). Clearly, this finding must be reconciled with the prevailing view that in adult fish a single CN fiber innervates a single neuromast and mutually innervated SNs are restricted to a small locale (e.g., to a single scale). Unfortunately, all neuromasts are superficial at larval stages, so the submodal destination of the mutually innervated, widely distributed neuromasts is in question—that is, it is not known whether they remain superficial or become enclosed in canals at later stages of development (see the chapter by Webb).

Further complicating the issue is the fact that the majority of neuromasts on the trunk remain superficial in adult zebrafish because canal formation has been developmentally arrested. In other words, this small fish has retained some of its larval characteristics through a process known as paedomorphosis. Thus, it is difficult to know if the mutually innervated neuromasts belong to the SN or presumptive CN categories (see the chapter by Webb). If SNs, then the larval zebrafish finding may be consistent with what is known about mutually innervated SNs in other adult fish, albeit at a somewhat larger scale of spatial integration than

currently believed. If CNs, then this may be evidence of a separate "pool" of CN fibers never before recognized. Such a pool would suggest that in addition to fiber populations being segregated according to hair cell orientation and submodality, they are also segregated into slow and fast conducting pathways according to fiber diameter and termination site (i.e., Mauthner cell vs. MON) in the brain. Indeed, there is evidence that thin and thick saccular (S1 and S2) afferents to goldfish auditory organs are segregated along these lines (Furukawa & Ishii, 1967). Further research is needed to address the question of whether the putative fast-conducting pathway in larval zebrafish persists in adult fish and if so, whether or not fast and slow afferent pathways represent a common organizational plan in other species.

Despite our advanced understanding of the physics that shape the SN/CN response dichotomy (see the chapter by van Netten & McHenry), there is still a prominent lack of data on the basic electrophysiological response properties of "naked" lateral line hair cells. Do lateral line hair cells, like vertebrate auditory hair cells (Eatock, 2000), adapt to a constant (DC) deflection? If they adapt, what is the time course of adaptation? Data on this question are needed to understand fully how neuromasts respond under conditions of constant exposure to unidirectional, ambient flow. Also lacking is detailed information on the intrinsic response properties of SN and CN hair cells. For example, given that SNs are presumably "designed" for responding to DC and low-frequency stimuli, do their hair cells show less adaptation than CN hair cells? Do hair cells in the two submodalities have other electrical or micromechanical properties that further differentiate their response properties? There is some anatomical (Song & Northcutt, 1991) and pharmacological (Song et al., 1995) evidence to suggest that hair cells in the two submodalities are fundamentally different. Comparative electrophysiological studies of hair cell responses coupled with pharmacological characterizations of hair cell ionic channels are needed to address potential differences in the intrinsic response properties of lateral line hair cells.

As a final note, our understanding of peripheral processing by the lateral line will undoubtedly improve as we gain more realistic, 3D "pictures" of complex flow fields using techniques like particle imaging velocimetry. Techniques like these, coupled with computational fluid dynamics to construct 3D models of spatiotemporal activation patterns along the lateral line system of a given species (e.g., Rapo et al., 2009), will be particularly instructive, especially if they incorporate both viscous and potential flow effects to model the effective stimulus to both SNs and CNs.

References

Abdulsadda, A. T., & Xiaobo, T. (2011). *Underwater source localization using an IPMC-based artificial lateral line* Paper presented at the IEEE International Conference on Robotics and Automation (ICRA), May 9–13, 2011, Shanghai.

Alexandre, D., & Ghysen, A. (1999). Somatotopy of the lateral line projection in larval zebrafish. *Proceedings of the National Academy of Sciences of the USA,* 96(13), 7558–7562.

Altman, J. S., & Dawes, E. A. (1983). A cobalt study of medullary sensory projections from lateral line nerves, associated cutaneous nerves, and the VIIIth nerve in adult *Xenopus*. *The Journal of Comparative Neurology,* 213(3), 310–326.

Arnold, G. (1974). Rheotropism in fishes. *Biological Reviews,* 49, 515–576.

Ashmore, J. F. (1991). The electrophysiology of hair cells. *Annual Review of Physiology,* 53(1), 465–476.

Ayali, A., Gelman, S., Tytell, E. D., & Cohen, A. H. (2009). Lateral-line activity during undulatory body motions suggests a feedback link in closed-loop control of sea lamprey swimming. *Canadian Journal of Zoology,* 87(8), 671–683.

Baker, C. F., & Montgomery, J. C. (1999). Lateral line mediated rheotaxis in the Antarctic fish *Pagothenia borchgrevinki*. *Polar Biology,* 21(5), 305–309.

Bleckmann, H. (1985). Perception of water surface waves: how surface waves are used for prey identification, prey localization, and intraspecific communication. In D. Ottoson (Ed.), *Progress in sensory physiology* (pp. 147–166). Heidelberg: Springer-Verlag.

Bleckmann, H. (2008). Peripheral and central processing of lateral line information. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 194 (2), 145–158.

Bleckmann, H., & Topp, G. (1981). Surface wave sensitivity of the lateral line organs of the topminnow *Aplocheilus lineatus*. *Naturwissenschaften,* 68(12), 624–625.

Bleckmann, H., & Zelick, R. (1993). The responses of peripheral and central mechanosensory lateral line units of weakly electric fish to moving objects. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 172(1), 115–128.

Bleckmann, H., Tittel, G., & Blübaum-Gronau, E. (1989a). The lateral line system of surface-feeding fish: Anatomy, physiology, and behavior. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 501–526). New York: Springer-Verlag.

Bleckmann, H., Weiss, O., & Bullock, T. H. (1989b). Physiology of lateral line mechanoreceptive regions in the elasmobranch brain. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 164(4), 459–474.

Blickhan, R., Krick, C., Breithaupt, T., Zehren, D., & Nachtigall, W. (1992). Generation of a vortex-chain in the wake of a subundulatory swimmer. *Naturwissenschaften,* 79, 220–221.

Bricaud, O., Chaar, V., Dambly-Chaudière, C., & Ghysen, A. (2001). Early efferent innervation of the zebrafish lateral line. *The Journal of Comparative Neurology,* 434(3), 253–261.

Carr, C. E. (1990). Neuroethology of electric fish. *Bioscience,* 40(4), 259–267.

Carr, C. E. (1993). Processing of temporal information in the brain. *Annual Review of Neuroscience,* 16(1), 223–243.

Carton, A., & Montgomery, J. (2002). Responses of lateral line receptors to water flow in the Antarctic notothenioid, *Trematomus bernacchii*. *Polar Biology,* 25(10), 789–793.

Chagnaud, B. P., Bleckmann, H., & Engelmann, J. (2006). Neural responses of goldfish lateral line afferents to vortex motions. *Journal of Experimental Biology,* 209(2), 327–342.

Chagnaud, B. P., Bleckmann, H., & Hofmann, M. H. (2007a). Kármán vortex street detection by the lateral line. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 193(7), 753–763.

Chagnaud, B. P., Hofmann, M. H., & Mogdans, J. (2007b). Responses to dipole stimuli of anterior lateral line nerve fibres in goldfish, *Carassius auratus*, under still and running water conditions. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 193(2), 249–263.

Chagnaud, B. P., Bleckmann, H., & Hofmann, M. H. (2008a). Lateral line nerve fibers do not code bulk water flow direction in turbulent flow. *Zoology* (Jena), 111(3), 204–217.

Chagnaud, B. P., Brücker, C., Hofmann, M. H., & Bleckmann, H. (2008b). Measuring flow velocity and flow direction by spatial and temporal analysis of flow fluctuations. *Journal of Neuroscience,* 28(17), 4479–4487.

Conley, R. A., & Coombs, S. (1998). Dipole source localization by mottled sculpin. III. Orientation after site-specific, unilateral denervation of the lateral line system. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 183(3), 335–344.

Coombs, S., & Janssen, J. (1989). Peripheral processing by the lateral line system of the mottled sculpin (*Cottus bairdi*). In S. Coombs, P. Görner & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 299–319). New York: Springer-Verlag.

Coombs, S., & Janssen, J. (1990). Behavioral and neurophysiological assessment of lateral line sensitivity in the mottled sculpin, *Cottus bairdi*. *Journal of Comparative Physiology A: Sensory Neural and Behavioral Physiology,* 167(4), 557–567.

Coombs, S., & Montgomery, J. (1992). Fibers innervating different parts of the lateral line system of an Antarctic notothenioid, *Trematomus bernacchii*, have similar frequency responses, despite large variation in the peripheral morphology. *Brain Behavior and Evolution,* 40(5), 217–233.

Coombs, S., & Montgomery, J. (1994). Function and evolution of superficial neuromasts in an Antarctic notothenioid fish. *Brain Behavior and Evolution,* 44(6), 287–298.

Coombs, S., & van Netten, S. (2005). The hydrodynamics and structural mechanics of the lateral line system. In E. S. Robert & V. L. George (Eds.), *Fish physiology*, Vol. 23 (pp. 103–139). San Diego: Academic Press.

Coombs, S., & Patton, P. (2009). Lateral line stimulation patterns and prey orienting behavior in the Lake Michigan mottled sculpin *Cottus bairdi*. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 195(3), 279–297.

Coombs, S., Janssen, J., & Webb, J. F. (1988). Diversity of lateral line systems: Evolutionary and functional considerations. In J. Atema, R. R. Fay, A. N. Popper, & W. N. Tavolga (Eds.), *Sensory biology of aquatic animals* (pp. 553–593). New York: Springer-Verlag.

Coombs, S., Fay, R. R., & Janssen, J. (1989). Hot-film anemometry for measuring lateral line stimuli. *Journal of the Acoustical Society of America,* 85(5), 2185–2193.

Coombs, S., Hastings, M., & Finneran, J. (1996). Modeling and measuring lateral line excitation patterns to changing dipole source locations. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 178(3), 359–371.

Coombs, S., Braun, C. B., & Donovan, B. (2001). The orienting response of Lake Michigan mottled sculpin is mediated by canal neuromasts. *Journal of Experimental Biology,* 204(2), 337–348.

Coombs, S., New, J. G., & Nelson, M. (2002). Information-processing demands in electrosensory and mechanosensory lateral line systems. *Journal of Physiology* (Paris), 96(5–6), 341–354.

Ćurčić-Blake, B., & van Netten, S. M. (2006). Source location encoding in the fish lateral line canal. *Journal of Experimental Biology,* 209(8), 1548–1559.

Denton, E. J., & Gray, J. A. B. (1979). The analysis of sound by the sprat ear. *Nature,* 282, 406–407.

Denton, E. J., & Gray, J. (1983). Mechanical factors in the excitation of clupeid lateral lines. *Proceedings of the Royal Society of London B: Biological Sciences,* 218(1210), 1–26.

Denton, E. J., & Gray, J. A. B. (1988). Mechanical factors in the excitation of the lateral lines of fishes (pp. 595–617). In J. Atema, R. R. Fay, A. N. Popper & W. N. Tavolga (Eds.), *Sensory biology of aquatic animals*. New York: Springer-Verlag.

Denton, E. J., & Gray, J. A. B. (1989). Some observations on the forces acting on neuromasts in fish lateral line canals. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 229–246). New York: Springer-Verlag.

Drucker, E. G., & Lauder, G. V. (1999). Locomotor forces on a swimming fish: Three-dimensional vortex wake dynamics quantified using digital particle image velocimetry. *Journal of Experimental Biology,* 202(18), 2393–2412.

Eatock, R. A. (2000). Adaptation in hair cells. *Annual Review of Neuroscience,* 23(1), 285–314.

Eatock, R. A., Fay, R. R., & Popper, A. N., Eds. (2006). *Vertebrate hair cells*. New York: Springer.

Elepfandt, A., & Wiedemer, L. (1987). Lateral-line responses to water surface waves in the clawed frog, *Xenopus laevis*. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 160(5), 667–682.

Engelmann, J., Hanke, W., Mogdans, J., & Bleckmann, H. (2000). Hydrodynamic stimuli and the fish lateral line. *Nature,* 408(6808), 51–52.

Engelmann, J., Hanke, W., & Bleckmann, H. (2002). Lateral line reception in still- and running water. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 188(7), 513–526.

Engelmann, J., Kröther, S., Bleckmann, H., & Mogdans, J. (2003). Effects of running water on lateral line responses to moving objects. *Brain Behavior and Evolution,* 61(4), 195–212.

Faucher, K., Lagardère, J.-P., & Aubert, A. (2005). Quantitative aspects of the spatial distribution and morphological characteristics of the sea bass (*Dicentrarchus labrax L.*; Teleostei, Serranidae) trunk lateral line neuromasts. *Brain Behavior and Evolution,* 65, 231–243.

Faucherre, A., Pujol-Martí, J., Kawakami, K., & López-Schier, H. (2009). Afferent neurons of the zebrafish lateral line are strict selectors of hair-cell orientation. *PLoS ONE,* 4(2), e4477.

Flock, Å. (1965a). Transducing mechanisms in the lateral line canal organ receptors. *Cold Spring Harbor Symposia on Quantitative Biology,* 30, 133–145.

Flock, Å. (1965b). Electron microscopic and electrophysiological studies on the lateral line canal organ. *Acta Oto-laryngologica Supplementum,* S199, 7–90.

Flock, Å. (1971). Sensory transduction in hair cells. In W. Loewenstein (Ed.), *Handbook of sensory physiology,* Vol. 1 (pp. 396–441). New York: Springer-Verlag.

Flock, Å., & Wersäll, J. (1962). A study of the orientation of the sensory hairs of the receptor cells in the lateral line organ of fish, with special reference to the function of the receptors. *The Journal of Cell Biology,* 15(1), 19–27.

Flock, Å., & Russell, I. J. (1973). The post-synaptic action of efferent fibres in the lateral line organ of the burbot *Lota lota*. *Journal of Physiology,* 235(3), 591–605.

Flock, Å. K. E., & Lam, D. M. K. (1974). Neurotransmitter synthesis in inner ear and lateral line sense organs. *Nature,* 249(5453), 142–144.

Franosch, J.-M., Sichert, A., Suttner, M., & Hemmen, J. (2005). Estimating position and velocity of a submerged moving object by the clawed frog *Xenopus* and by fish—A cybernetic approach. *Biological Cybernetics,* 93(4), 231–238.

Franosch, J.-M. P., Hagedorn, H. J. A., Goulet, J., Engelmann, J., & van Hemmen, J. L. (2009). Wake tracking and the detection of vortex rings by the canal lateral line of fish. *Physical Review Letters,* 103(7), 078102.

Fritzsch, B. (1981). The pattern of lateral-line afferents in urodeles: A horseradish-peroxidase study. *Cell & Tissue Research,* 218(3), 581–594.

Furukawa, T., & Ishii, Y. (1967). Neurophysiological studies on hearing in goldfish. *Journal of Neurophysiology,* 30, 1377–1403.

Görner, P. (1963). Untersuchungen zur Morphologie und Elektrophysiologie des Seitenlinienorgans vom Krallenfrosch (*Xenopus laevis* Daudin). *Zeitschrift für vergleichende Physiologie,* 47, 316–338.

Görner, P., & Kalmijn, A. J. (1989). Frequency response of lateral line neuromasts in the thornback ray (*Platyrhinoidis triseriata*). In J. Erber, R. Menzel, H.-J. Pflüger, & D. Todt (Eds.), *Proceedings of the 2nd international congress of neuroethology,* 1st ed. Stuttgart: Thieme.

Görner, P., & Mohr, C. (1989). Stimulus localization in *Xenopus*: Role of directional sensitivity of lateral line stitches. In S. Coombs, P. Görner & H. Münz (Eds.), *The mechanosensory lateral line. Neurobiology and evolution* (pp. 543–560).New York: Springer-Verlag.

Goulet, J., Engelmann, J., Chagnaud, B., Franosch, J.-M., Suttner, M., & van Hemmen, J. (2008). Object localization through the lateral line system of fish: Theory and experiment. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 194(1), 1–17.

Haehnel, M., Taguchi, M., & Liao, J. C. (2012). Heterogeneity and dynamics of lateral line afferent innervation during development in zebrafish (*Danio rerio*). *The Journal of Comparative Neurology,* 520(7), 1376–1386.

Hama, K. (1978). A study of the fine structure of the pit organ of the common Japanese sea eel *Conger myriaster*. *Cell and Tissue Research,* 189(3), 375–388.

Hanke, W., & Bleckmann, H. (2004). The hydrodynamic trails of *Lepomis gibbosus* (Centrarchidae), *Colomesus psittacus* (Tetraodontidae) and *Thysochromis ansorgii* (Cichlidae) investigated with scanning particle image velocimetry. *Journal of Experimental Biology,* 207(9), 1585–1596.

Hanke, W., Brücker, C., & Bleckmann, H. (2000). The ageing of the low-frequency water disturbances caused by swimming goldfish and its possible relevance to prey detection. *Journal of Experimental Biology,* 203(7), 1193–1200.

Harris, G. G., Frishkopf, L. S., & Flock, Å. (1970). Receptor potentials from hair cells of the lateral line. *Science,* 167(3914), 76–79.

Hassan, E. S. (1985). Mathematical analysis of the stimulus for the lateral line organ. *Biological Cybernetics,* 52(1), 23–36.

Hassan, E.-S. (1992). Mathematical description of the stimuli to the lateral line system of fish derived from a three-dimensional flow field analysis. *Biological Cybernetics,* 66(5), 443–452.

Highstein, S. M., & Baker, R. (1985). Action of the efferent vestibular system on primary afferents in the toadfish, *Opsanus tau*. *Journal of Neurophysiology,* 54(2), 370–384.

Highstein, S. M., Fay, R. R., & Popper, A. N. (2004). *The vestibular system* Springer Verlag.

Hudspeth, A. J., & Markin, V. S. (1994). The ear's gears: Mechanoelectrical transduction by hair cells. *Physics Today,* 47(2), 22–28.

Janssen, J., Coombs, S., Hoekstra, D., & Platt , C. (1987). Anatomy and differential growth of the lateral line system of the mottled sculpin, *Cottus bairdi* (Scorpaeniformes: Cottidae). *Brain, Behavior and Evolution,* 30(3–4), 220–229.

Kalmijn, A. J. (1988). Hydrodynamic and acoustic field detection. In J. Atema, R. R. Fay, A. N. Popper, & W. N. Tavolga (Eds.), *Sensory biology of aquatic animals*. New York: Springer-Verlag,.

Kalmijn, A. J. (1989). Functional evolution of lateral line and inner ear sensory systems. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 187–215). New York: Springer-Verlag.

Kanter, M. J., & Coombs, S. (2003). Rheotaxis and prey detection in uniform currents by Lake Michigan mottled sculpin (*Cottus bairdi*). *Journal of Experimental Biology,* 206(1), 59–70.

Kiang, N. Y. S., Baer, T., Marr, E. M., & Demont, D. (1969). Discharge rates of single auditory-nerve fibers as functions of tone level. *The Journal of the Acoustical Society of America,* 46 (1A), 106.

Köppl, C. (2011). Evolution of the octavolateral efferent system. In D. K. Ryugo, R. R. Fay, & A. N. Popper (Eds.), *Auditory and vestibular efferents* (pp. 217–259). New York: Springer-Verlag.

Kroese, A. B., & van Netten, S. M. (1987). The application of incident light polarization microscopy for the visualization of vertebrate sensory hair cells in vivo. *Journal of Microscopy,* 145(3), 309–317.

Kroese, A., & van Netten, S. (1989). Sensory transduction in lateral line hair cells. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution*. New York: Springer-Verlag.

Kroese, A. B., & Schellart, N. A. (1992). Velocity- and acceleration-sensitive units in the trunk lateral line of the trout. *Journal of Neurophysiology,* 68(6), 2212–2221.

Kroese, A. B., Van der Zalm, J. M., & Van den Bercken, J. (1978). Frequency response of the lateral-line organ of *Xenopus laevis*. *Pflügers Archive,* 375(2), 167–175.

Kroese, A. B. A., Prins, M., & Schellart, N. A. M. (1989). Regional differences in conduction velocity and fibre diameter in posterior lateral line afferent axons in the trout. *Journal of Physiology,* 418, 136.

Liao, J. C., & Haehnel, M. (2012). Physiology of afferent neurons in larval zebrafish provides a functional framework for lateral line somatotopy. *Journal of Neurophysiology,* 107(10), 2615–2623.

Liao, J. C., Beal, D. N., Lauder, G. V., & Triantafyllou, M. S. (2003a). Fish exploiting vortices decrease muscle activity. *Science,* 302(5650), 1566–1569.

Liao, J. C., Beal, D. N., Lauder, G. V., & Triantafyllou, M. S. (2003b). The Kármán gait: Novel body kinematics of rainbow trout swimming in a vortex street. *Journal of Experimental Biology,* 206(6), 1059–1073.

López-Schier, H., Starr, C. J., Kappler, J. A., Kollmar, R., & Hudspeth, A. J. (2004). Directional cell migration establishes the axes of planar polarity in the posterior lateral-line organ of the zebrafish. *Developmental Cell,* 7(3), 401–412.

Madin, L. P. (1990). Aspects of jet propulsion in salps. *Canadian Journal of Zoology,* 68(4), 765–777.

McCormick, C. A. (1983). Central connection of the octavolateralis nerves in the pike cichlid, *Crenicichla lepidota*. *Brain Research,* 265(2), 177–185.

McCormick, C. A. (1989). Central lateral line mechanosensory pathways in bony fish. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and volution* (pp. 79–97). New York: Springer-Verlag.

Metcalfe, W. K., Kimmel, C. B., & Schabtach, E. (1985). Anatomy of the posterior lateral line system in young larvae of the zebrafish. *The Journal of Comparative Neurology,* 233(3), 377–389.

Mogdans, J., & Bleckmann, H. (1998). Responses of the goldfish trunk lateral line to moving objects. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 182, 659–676.

Mogdans, J., & Geisen, S. (2009). Responses of the goldfish head lateral line to moving objects. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 195(2), 151–165.

Mohr, C., & Görner, P. (1996). Innervation patterns of the lateral line stitches of the clawed frog, *Xenopus laevis*, and their reorganization during metamorphosis. *Brain, Behavior and Evolution,* 48(2), 55–69.

Montgomery, J., & Coombs, S. (1992). Physiological characterization of lateral line function in the Antarctic fish *Trematomus bernacchii*. *Brain, Behavior and Evolution,* 40(5), 209–216.

Montgomery, J., & Coombs, S. L. (1998). Peripheral encoding of moving sources by the lateral line system of a sit-and-wait predator. *Journal of Experimental Biology,* 201(1), 91–102.

Montgomery, J., Coombs, S., & Janssen, J. (1994). Form and function relationships in lateral line systems: Comparative data from six species of Antarctic notothenioid fish. *Brain, Behavior and Evolution,* 44(6), 299–306.

Montgomery, J. C., Coombs, S., Conley, R. A., & Bodznick, D. (1995a). Hindbrain sensory processing in lateral line, electrosensory and auditory systems: A comparative overview of anatomical and functional similarities. *Auditory Neuroscience,* 1, 207–231.

Montgomery, J., Coombs, S., & Halstead, M. (1995b). Biology of the mechanosensory lateral line in fishes. *Reviews in Fish Biology and Fisheries,* 5(4), 399–416.

Montgomery, J., Bodznick, D., & Halstead, M. (1996). Hindbrain signal processing in the lateral line system of the dwarf scorpionfish *Scopeana papillosus*. *Journal of Experimental Biology,* 199(4), 893–899.

Montgomery, J., Baker, C. F., & Carton, A. G. (1997). The lateral line can mediate rheotaxis in fish. *Nature,* 389, 960–963.

Montgomery, J. C., Windsor, S., & Bassett, D. (2009). Behavior and physiology of mechanoreception: Separating signal and noise. *Integrative Zoology,* 4(1), 3–12.

Münz, H. (1979). Morphology and innervation of the lateral line system of *Sarotherodon niloticus L.* (Cichlidae, Teleostei). *Zoomorphology,* 93, 73–86.

Münz, H. (1985). Single unit activity in the peripheral lateral line system of the cichlid fish, *Sarotherodon niloticus L. Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 157, 555–568.

Nagiel, A., Andor-Ardó, D., & Hudspeth, A. J. (2008). Specificity of afferent synapses onto plane-polarized hair cells in the posterior lateral line of the zebrafish. *The Journal of Neuroscience,* 28(34), 8442–8453.

Nauen, J. C., & Lauder, G. V. (2002). Hydrodynamics of caudal fin locomotion by chub mackerel, *Scomber japonicus* (Scombridae). *Journal of Experimental Biology,* 205(Pt 12), 1709–1724.

New, J. G., & Singh, S. (1994). Central topography of anterior lateral line nerve projections in the channel catfish, *Ictalurus punctatus*. *Brain, Behavior and Evolution,* 43(1), 34–50.

Northcutt, G. (1989). The phylogenetic distribution and innervation of craniate mechanoreceptive lateral lines. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 17–78). New York: Springer-Verlag.

Northcutt, R. G. (1992). Distribution and innervation of lateral line organs in the axolotl. *Journal of Comparative Neurology,* 325(1), 95–123.

Northcutt, R. G., Holmes, P. H., & Albert, J. S. (2000). Distribution and innervation of lateral line organs in the channel catfish. *Journal of Comparative Neurology,* 421(4), 570–592.

Palmer, L. M., Deffenbaugh, M., & Mensinger, A. F. (2005). Sensitivity of the anterior lateral line to natural stimuli in the oyster toadfish, *Opsanus tau* (Linnaeus). *Journal of Experimental Biology,* 208(18), 3441–3450.

Pandya, S., Yang, Y., Jones, D. L., Engel, J., & Liu, C. (2006). Multisensor processing algorithms for underwater dipole localization and tracking using MEMS artificial lateral-line sensors. *EURASIP Journal on Applied Signal Processing,* 2006, 1–9.

Pohlmann, K., Grasso, F. W., & Breithaupt, T. (2001). Tracking wakes: The nocturnal predatory strategy of piscivorous catfish. *Proceedings of the National Academy of Sciences of the USA,* 98(13), 7371–7374.

Pohlmann, K., Atema, J., & Breithaupt, T. (2004). The importance of the lateral line in nocturnal predation of piscivorous catfish. *Journal of Experimental Biology,* 207(17), 2971–2978.

Przybilla, A., Kunze, S., Rudert, A., Bleckmann, H., & Brücker, C. (2010). Entraining in trout: A behavioural and hydrodynamic analysis. *Journal of Experimental Biology,* 213(17), 2976–2986.

Pujol-Martí, J., Zecca, A., Baudoin, J.-P., Faucherre, A., Asakawa, K., Kawakami, K., & López-Schier, H. (2012). Neuronal birth order identifies a dimorphic sensorineural map. *The Journal of Neuroscience,* 32(9), 2976–2987.

Puzdrowski, R. L. (1989). Peripheral distribution and central projections of the lateral-line nerves in goldfish, *Carassius auratus*. *Brain Behavior and Evolution,* 34(2), 110–131.

Rapo, M. A., Jiang, H., Grosenbaugh, M. A., & Coombs, S. (2009). Using computational fluid dynamics to calculate the stimulus to the lateral line of a fish in still water. *Journal of Experimental Biology,* 212(10), 1494–1505.

Roberts, B. L., & Russell, I. J. (1972). The activity of lateral-line efferent neurones in stationary and swimming dogfish. *Journal of Experimental Biology,* 57(2), 435–448.

Roberts, B. L., & Meredith, G. E. (1989). The efferent system. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 445–459). New York: Springer-Verlag.

Russell, I. J. (1971). The pharmacology of efferent synapses in the lateral-line system of *Xenopus laevis*. *Journal of Experimental Biology,* 54(3), 643–658.

Russell, I. J., & Roberts, B. L. (1974). Active reduction of lateral-line sensitivity in swimming dogfish. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 94(1), 7–15.

Russell, I. J., & Sellick, P. M. (1976). Measurement of potassium and chloride ion concentrations in the cupulae of the lateral lines of *Xenopus laevis*. *The Journal of Physiology,* 257(1), 245–255.

Schellart, N. S., & Kroese, A. K. (2002). Conduction velocity compensation for afferent fiber length in the trunk lateral line of the trout. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 188(7), 561–576.

Schemmel, C. (1967). Vergleichende Untersuchungen an den Hautsinnesorganen ober- und unterirdisch lebender *Astyanax*-Formen. *Zoomorphology,* 61(2), 255–316.

Schmitz, A., Bleckmann, H., & Mogdans, J. (2008). Organization of the superficial neuromast system in goldfish, *Carassius auratus*. *Journal of Morphology,* 269(6), 751–761.

Schwarz, J. S., Reichenbach, T., & Hudspeth, A. J. (2011). A hydrodynamic sensory antenna used by killifish for nocturnal hunting. *Journal of Experimental Biology,* 214(11), 1857–1866.

Shardo, J. (1996). Radial polarity of the first neuromast in embryonic American shad, *Alosa sapidissima* (Teleostei: Clupeomorpha). *Copeia*, 226–228.

Song, J., & Northcutt, R. G. (1991). Morphology, distribution and innervation of the lateral-line receptors of the florida gar, *Lepisosteus platyrhincus*. *Brain Behavior and Evolution,* 37, 10–37.

Song, J., Yan, H. Y., & Popper, A. N. (1995). Damage and recovery of hair cells in fish canal (but not superficial) neuromasts after gentamicin exposure. *Hearing Research,* 91(1–2), 63–71.

Stein, B. E., & Meredith, M. A. (1993). *The merging of the senses*. Cambridge, MA: The MIT Press.

Sutterlin, A. M., & Waddy, S. (1975). Possible role of the posterior lateral line in obstacle entrainment by brook trout (*Salvelinus fontinalis*). *Journal of the Fisheries Research Board of Canada,* 32, 2441–2446.

Teyke, T. (1985). Collision with and avoidance of obstacles by blind cave fish *Anoptichthys jordani*; (Characidae). *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 157(6), 837–843.

Topp, G. (1983). Primary lateral line response to water surface waves in the topminnow *Aplocheilus lineatus* (Pisces, Cyrinodontidae). *Pflügers Archive,* 397, 62–67.

Tou, S. K. W. (1991). A statistical and experimental study on fish response subject to vortex ring motion. *Journal of Environmental Science and Health A,* 26(5), 755–775.

Tricas, T. C., & Highstein, S. M. (1990). Visually mediated inhibition of lateral line primary afferent activity by the octavolateralis efferent system during predation in the free-swimming toadfish, *Opsanus tau*. *Experimental Brain Research,* 83(1), 233–236.

Tricas, T. C., & Highstein, S. M. (1991). Action of the octavolateralis efferent system upon the lateral line of free-swimming toadfish, *Opsanus tau*. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 169(1), 25–37.

Tytell, E. D., & Lauder, G. V. (2008). Hydrodynamics of the escape response in bluegill sunfish, *Lepomis macrochirus*. *Journal of Experimental Biology,* 211(21), 3359–3369.

van Netten, S. (2006). Hydrodynamic detection by cupulae in a lateral line canal: Functional relations between physics and physiology. *Biological Cybernetics,* 94(1), 67–85.

Vogel, D., & Bleckmann, H. (2001). Behavioral discrimination of water motions caused by moving objects. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 186(12), 1107–1117.

Vogel, S. (1996). *Life in moving fluids*. Princeton, NJ: Princeton University Press.

Voigt, R., Carton, A. G., & Montgomery, J. C. (2000). Responses of anterior lateral line afferent neurones to water flow. *Journal of Experimental Biology,* 203(16), 2495–2502.

von der Emde, G., Schwarz, S., Gomez, L., Budelli, R., & Grant, K. (1998). Electric fish measure distance in the dark. *Nature,* 395(6705), 890–894.

Wagner, T., & Schwartz, E. (1996). Efferent neurons of the lateral line system and their innervation of lateral line branches in a euteleost and an osteoglossomorph. *Anatomy and Embryology,* 194(3), 271–278.

Webb, J. F. (1989a). Neuromast morphology and lateral line trunk canal ontogeny in two species of cichlids: An SEM study. *Journal of Morphology,* 202(1), 53–68.

Webb, J. F. (1989b). Developmental constraints and evolution of the lateral line system in teleost fishes In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 79–97). New York: Springer-Verlag.

Weeg, M. S., Land, B. R., & Bass, A. H. (2005). Vocal pathways modulate efferent neurons to the inner ear and lateral line. *Journal of Neuroscience,* 25(25), 5967–5974.

Wiersinga-Post, J. E. C., & van Netten, S. M. (2000). Temperature dependency of cupular mechanics and hair cell frequency selectivity in the fish canal lateral line organ. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 186(10), 949–956.

Wiese, K. (1984). Neural enhancement of directionality in sensory pathways of two arthropods, the cricket and the crayfish. In D. Varju & H. U. Schnitzler (Eds.), *Localization and orientation in biology and engineering* (pp. 186–191). New York: Springer-Verlag.

Wiese, K. (1988). The representation of hydrodynamic parameters in the CNS of the crayfish, *Procambarus*. In J. Atema, R. R. Fay, A. N. Popper, & W. N. Tavolga (Eds.), *Sensory biology of aquatic animals* (pp. 665–686). New York: Springer-Verlag.

Will, U., Luhede, G., & Görner, P. (1985). The area octavo-lateralis in *Xenopus laevis*. *Cell and Tissue Research,* 239(1), 163–175.

Windsor, S. P., Tan, D., & Montgomery, J. C. (2008). Swimming kinematics and hydrodynamic imaging in the blind Mexican cave fish (*Astyanax fasciatus*). *Journal of Experimental Biology,* 211(18), 2950–2959.

Windsor, S. P., Norris, S. E., Cameron, S. M., Mallinson, G. D., & Montgomery, J. C. (2010a). The flow fields involved in hydrodynamic imaging by blind Mexican cave fish (*Astyanax fasciatus*). Part I: Open water and heading towards a wall. *Journal of Experimental Biology,* 213(22), 3819–3831.

Windsor, S. P., Norris, S. E., Cameron, S. M., Mallinson, G. D., & Montgomery, J. C. (2010b). The flow fields involved in hydrodynamic imaging by blind Mexican cave fish (*Astyanax fasciatus*). Part II: Gliding parallel to a wall. *Journal of Experimental Biology,* 213(22), 3832–3842.

Wöhl, S., & Schuster, S. (2007). The predictive start of hunting archer fish: A flexible and precise motor pattern performed with the kinematics of an escape C-start. *Journal of Experimental Biology,* 210(2), 311–324.

Wolfgang, M. J., Anderson, J. M., Grosenbaugh, M. A., Yue, D. K., & Triantafyllou, M. S. (1999). Near-body flow dynamics in swimming fish. *Journal of Experimental Biology,* 202(17), 2303–2327.

Yang, Y., Nguyen, N., Chen, N., Lockwood, M., Tucker, C., Hu, H., Bleckmann, H., Liu, C., & Jones, D. L. (2010). Artificial lateral line with biomimetic neuromasts to emulate fish sensing. *Bioinspiration & Biomimetics,* 5, 016001.

Zittlau, K. E., Claas, B., & Münz, H. (1986). Directional sensitivity of lateral line units in the clawed toad X*enopus laevis*; Daudin. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology,* 158(4), 469–477.

Zottoli, S. J., & Van Horne, C. (1983). Posterior lateral line afferent and efferent pathways within the central nervous system of the goldfish with special reference to the Mauthner cell. *The Journal of Comparative Neurology,* 219(1), 100–111.

Zottoli, S. J., & Danielson, P. D. (1989). Lateral line afferent and efferent systems of the goldfish with special reference to the Mauthner cell. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 461–478). New York: Springer-Verlag.

The Central Nervous Organization of the Lateral Line System

Mario F. Wullimann and Benedikt Grothe

Keywords Amphibian lateral line • Cartilaginous fish lateral line • Crest cells • Electrosensory centers • Hippocampus • Lamprey lateral line • Lateral line nerve projections • Medial octavolateralis nucleus • Octavolateralis area • Pallial amygdala • Posterior tuberculum • Preglomerular complex • Sensory maps • Sensory thalamus • Teleost lateral line • Torus semicircularis

Abbreviations often used in text:

ALLN	anterior lateral line nerves
CON	caudal octavolateralis nucleus
Dc/Dd/Dl/Dm	central/dorsal/lateral/medial zones of dorsal (pallial) telencephalon
DON	dorsal octavolateralis nucleus
ELL	electrosensory lateral line lobe
EOD	electric organ discharge
LMN	lateral mesencephalic nucleus
MON	medial octavolateralis nucleus
MV	medioventral toral nucleus (mormyrids)
NE	exterolateral toral nucleus (mormyrids)
NL	lateral toral nucleus (mormyrids)
PCT	posterior central thalamic nucleus
PEd	dorsal preeminential nucleus
PGLd	dorsal division of lateral preglomerular nucleus
PLLN	posterior lateral line nerves

M.F. Wullimann (✉) • B. Grothe
Graduate School of Systemic Neurosciences & Department Biology II,
Ludwig-Maximilians-Universität Munich, Biozentrum, 82152 Planegg, Germany
e-mail: wullimann@bio.lmu.de; grothe@bio.lmu.de

S. Coombs et al. (eds.), *The Lateral Line*, Springer Handbook of Auditory Research 48,
DOI 10.1007/2506_2013_18,
Published online: 6 August 2013

PLT	posterior lateral thalamic nucleus
TS(c,l)	torus semicircularis (central, lateral, etc)
VON	ventral octavolateralis nucleus

1 Introduction

In the present chapter, the central neuroanatomy of the mechanosensory and electrosensory lateral line system in craniates will be considered in each craniate/vertebrate taxon (Fig. 1). Both sensory systems will be dealt with because the neuroanatomy of the mechanosensory lateral line system can not be treated reasonably when ignoring that of the electrosensory system. These two sensory systems share commonalities to a degree that no other two sensory systems do (even including the octaval system of the inner ear). Among those commonalities are that (1) the developmental origin of peripheral receptors in the skin as well as that of the cranial nerve ganglion cells is from the same source, that is, the lateral line placodes (embryonic epidermal thickenings with neurogenic potential), (2) the primary sensory neurons (cranial nerve ganglion cells) may populate the same ganglia and their peripheral fibers may course in the same lateral line nerves, (3) the central fibers of lateral line ganglion cells all terminate in the anterior alar plate of the rhombencephalon, the so-called octavolateralis area.

The hierarchical synaptic chain of ascending pathways in the central nervous system - from the rhombencephalon to the telencephalon - further illustrates the close developmental and evolutionary relationship of these two functionally distinct sensory systems. As mentioned, primary lateral line centers always involve rhombencephalic nuclei in the octavolateralis area (dorsal octavolateralis nucleus for the electrosensory system; medial octavolateralis nucleus for the mechanosensory system) and projections from these nuclei reach a caudal part of the midbrain roof (torus semicircularis). In the diencephalon, two areas are involved, the posterior tuberculum (preglomerular area in teleosts) and/or the dorsal thalamus, and sometimes in addition hypothalamic centers. Projections to the telencephalic pallium (in particular the medial pallium, i.e., the hippocampus homologue) arise only from the posterior tubercular and/or dorsal thalamic lateral line related nuclei.

Additionally, some basic information on the octaval system will be given, mainly because the new concept of the octavolateralis area (see below) cannot be gathered without information on at least the location of the primary sensory octaval nuclei in the octavolateralis area, which are therefore also depicted in addition to lateral line centers in many figures. Also, cases of limited overlap of primary octaval and lateral line nerve projections in mechanosensory and octaval nuclei will be addressed (see also Chapter by Braun & Sand). However, the ascending octaval pathways will only be touched when they converge with lateral line pathways.

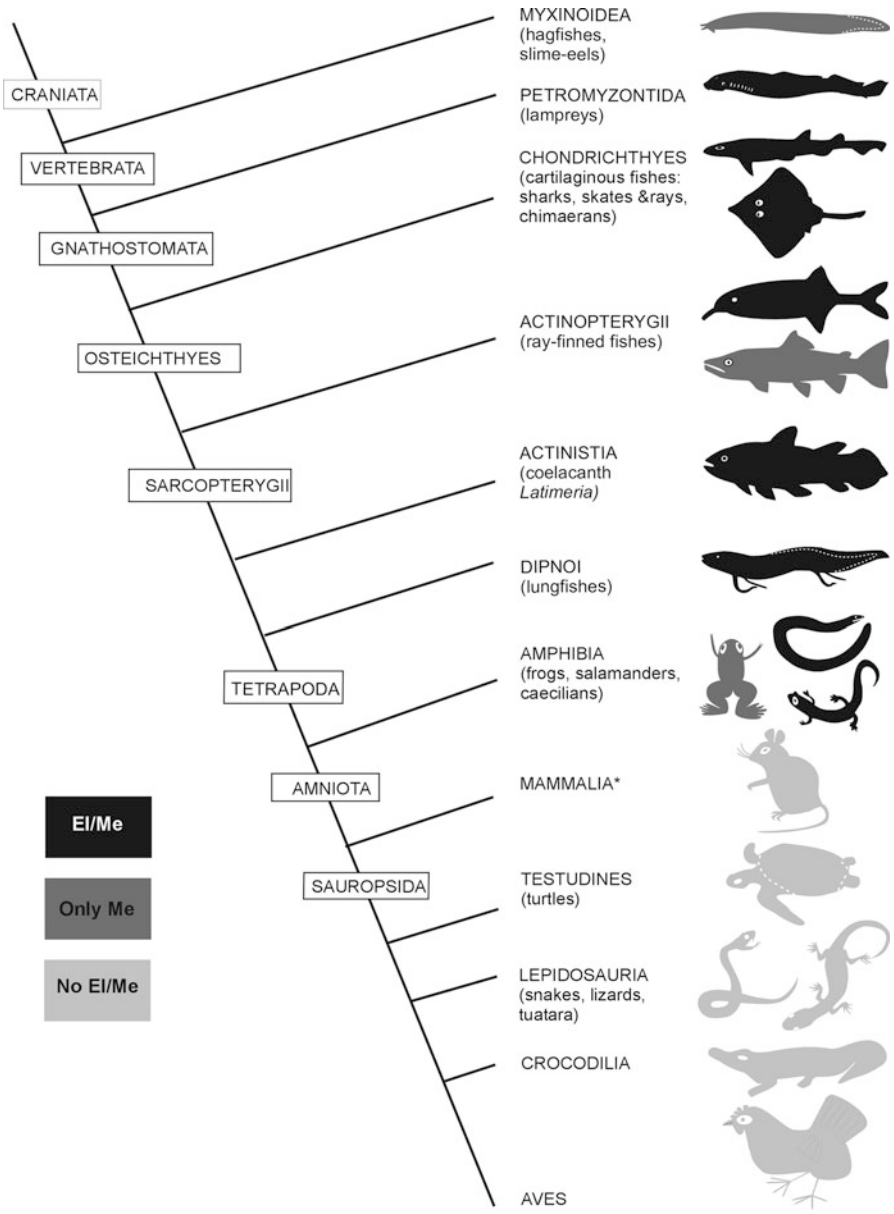

Fig. 1 Cladogram of extant craniate groups with distribution of lateral line mechano- (Me) and electroreception (El) indicated. All groups have inner ear vestibular systems. * Both monotremes (*Platypus*; Scheich et al., 1986) and some eutherians (Guiana dolphin; Czech-Damal et al., 2011) independently acquire trigeminal nerve innervated electroreception, which is convergent to electroreception described in this chapter

This detailed analyis of the lateral line system will start with agnathans and proceed to cartilaginous and ray-finned fishes. Some ecological and paleontological information is given, in particular for agnathans, in order to understand possible regressive phenomena in the lateral line system. From this, it may be concluded that the mechanosensory lateral line is ancestral for craniates, and electroreception is ancestral for vertebrates (Fig. 1). Basal ray-finned fishes share a lot of commonalities with cartilaginous fishes, whereas teleosts (derived ray-finned fishes) lose the electrosensory system, only to have it re-evolve various times. These electrosensory teleostean taxa (silurids, gymnotoids, mormyrids) will be treated separately and, thus, the reader may easily acquire the general phylogenetic story on the mechanosensory lateral line system by skipping these sections and directly proceed to lobe-finned fishes (which include amphibians).

As mentioned, the octavolateralis area is in receipt of lateral line and octaval (VIII) nerve projections. Ironically, it had been recognized historically that the octavolateral (or acousticolateral) area consists of dorsal, medial and ventral nuclei (for example: Larsell, 1967; see discussion in Northcutt, 1986a; McCormick, 1992). Nevertheless, the predominant view into the early 20th century, based on normal histology, has been that input from these nerves to the octavolateralis area is strongly overlapping. Modern tracing methods developed around 1980, in particular the use of horseradish peroxidase (HRP) as an *in vivo* neuronal tracer and its subsequent histochemical visualization (Mesulam, 1982), led to a revision of this view because antero- and retrogradely labeled axonal projections and terminal fields could now be demonstrated more reliably than for example with silver degeneration methods. Thus, largely non-overlapping primary projections of octaval and lateral line mechanosensory and electrosensory projections were shown to reach ventral, medial (intermediate) and dorsal nuclei, respectively (as will be detailed below). A closely related idea is that the inner ear arose phylogenetically as an internalization of part of the peripheral lateral line system (acousticolateralis or octavolateralis hypothesis; see Chapter by Braun & Sand). The phyletic distribution of these sensory organs in craniates together with developmental studies then indicated that the mechanosensory lateral line organs and the inner ear are equally old among craniates (Northcutt, 1986a). However, this is only part of a more fundamental change in how neurobiologists began to view the lateral line system, synthesizing information coming from neuronal tracing, electrophysiology and developmental studies, culminating in the recognition of the mechansensory (and electrosensory) lateral line system as a functionally distinct sensory system on all investigated levels: phylogeny, neuroanatomy, neurophysiology, and development (compare Coombs et al., 1989). Today it is widely accepted that the lateral line nerves are cranial nerves in their own right characterized by discrete embryonic origins (placodes different from the otic one), as well as by distinct adult sensory organs (i.e., neuromasts and electroreceptors) and sensory ganglia, as well as primary central projection areas, with all these characters being separate from those of other cranial nerves, such as the trigeminal, vagal or octaval nerves (McCormick, 1982; Northcutt, 1989).

2 The Agnathan Condition: Myxinoids and Petromyzontids

The current consensus based on phenotypic character analysis is that agnathans are not monophyletic (i.e., they do not share a single last common ancestor, but see discussion of conflicting molecular data in Janvier, 2008). Hagfishes are the sistergroup of vertebrates (lampreys and gnathostomes) and lampreys are the sistergroup of gnathostomes (jawed vertebrates; Fig. 1). Recent systematic accounts on fossil (†) and extant agnathan relationships (Janvier, 2008) propose lampreys and soft-bodied euphaneropids (†) as sistergroup to all other known fossil ostracoderms (e.g., osteostracans, heterostracans, anaspids; characterized by a heavy dermoskeleton) and all gnathostomes. Osteostracans (†) represent the sistergroup of gnathostomes, which makes fossil ostracoderms non-monophyletic. However, unlike in previous suggestions (Northcutt, 1996), lampreys are not closely related to anaspids (†). Consequently, the absence of a dermal armor (exoskeleton) and presence of a cartilaginous endoskeleton (cranium) in modern lampreys (and hagfishes) may not be interpreted as regressive, but represent the ancestral craniate condition. However, this does not preclude regressive processes in other organ systems in extant agnathans (see below).

Hagfishes (Myxinoids) are the only known extant non-vertebrate craniates. They are highly specialized to live on deep ocean shelfs (benthic/endobenthic) and have predominantly chemosensory orientation (Braun 1996, 1998). Their mode of life as scavengers on large bodied vertebrates (including whales) can obviously not be ancestral as fossil agnathans are the first craniates originating in the Paleozoic (Ordovician). In line with this, hagfish fossil record only dates back to the Carboniferous. Interestingly, newer reports indicate that hagfish predation on small invertebrates does occur (discussed in Braun & Northcutt, 1998), more likely representing the ancestral agnathan mode of life. Thus, hagfishes likely show a mixture of primitive and secondary simplified (regressive) characters (Braun, 1996; Northcutt, 1996; Braun & Northcutt, 1997). The lateral line system illustrates this nicely. Pacific (eptatretid) hagfishes have epidermal grooves in the lateral head that contain sensory cells with a kinocilium resembling vertebrate hair cells. However, hagfish hair cells do not show the vertebrate-typical graded (polarized) stereovilli (with the longest ones toward the kinocilium) and hair cells are not arranged into differently oriented populations with opposing polarization as in all vertebrate fish species examined (see below and chapter by Chagnaud & Coombs). Eptatretid hair cells also do not group into functional multicellular units (neuromasts) covered by a cupula and are, thus, not sensitive to displacement in one plane in opposing directions as is the case in vertebrates. These lateral line hair cells in pre- and postoptic epidermal grooves of the eptatretid hagfish head are innervated by two anterior lateral line nerves (Braun & Northcutt, 1997) which project centrally to the ipsilateral octavalateralis area (Kishida et al., 1987) in the rostrodorsal medulla oblongata where the lateral line nerve terminal field lies dorsal to the more ventral octaval nerve projection zone (Amemiya et al., 1985).

In contrast, Atlantic myxinid species do not have a lateral line system at all. They live at greater depths than eptatretids and are burrowers in sandy environments. The Pacific eptatretids may also burrow, but remain more often on the sea floor surface even in the resting state (discussed in Braun & Northcutt, 1998). Thus, the absence of a lateral line system in Atlantic myxinids correlates nicely with their burrowing lifestyles that likely interfere with lateral line function. Since Atlantic myxinids are generally interpreted to show more regressive characters than Pacific eptatretids (for example in the eyes; Fernholm & Holmberg, 1975), the presence of a lateral line system in eptatretids suggests that it is ancestral for craniates, whereas its absence in Atlantic myxinids might represent a secondary loss for this group. Moreover, developmental evidence and the high intraspecific variability of lateral line grooves suggest that the absence of true neuromasts in eptatredids may also be regressive (Braun & Northcutt, 1997). In any case, both the lateral line and octaval systems of hagfishes lack efferent octavolateralis cells (i.e., central medullary cholinergic cells synapsing on peripheral receptor cells). There is also no evidence for electroreception in hagfishes (Bullock et al., 1982, 1983). These two absences, together with the lack of lateral line canals, are likely ancestral for craniates. Information on ascending projections of the lateral line system in hagfishes is not available, although it is clear that the highly differentiated, cortically organized pallium (5 layers) of eptatretids receives in addition to extensive olfactory input also diencephalic input of unknown functional significance (Wicht & Northcutt, 1998).

Lampreys (Petromyzontids), the sole extant representatives of agnathan vertebrates (Fig. 1), are now regarded as outgroup of fossil ostracoderms and gnathostomes (see above; Janvier, 2008). Extant adult lampreys are parasitic on large bony fishes and, thus, are not benthic and generally more mobile than hagfishes. Similar to hagfishes, the parasitic lifestyle of lampreys is hardly feasible without large bony fish hosts. Consequently, the lamprey fossil record only dates back to the very late Devonian (during which large bony fishes first evolved) and not the Ordovician-Silurian-Early Devonian, when ostracoderm radiation peaked (Janvier, 2008). Thus, despite the fact that many lamprey characters, in particular regarding the skeleton, have newly been interpreted as being ancestral instead of regressive (see above), lampreys may still show derived features, in particular with regard to their parasitic mode of life.

Unlike hagfish, lampreys have mechanosensitive free (superficial) neuromasts containing polarized sensory cells with one kinocilium and size-graded stereovilli. Within a single neuromast, the kinocilium is either at the rostral or caudal rim of a given hair cell and all hair cells of a neuromast are unified by a cupula. Therefore, neuromasts form a functional unit that has a single axis of best sensitivity in opposite directions (Yamada, 1973; Jörgensen, 1989), a typical feature of the peripheral lateral line system (see below and Chapter by Chagnaud & Coombs). Lampreys furthermore have electrosensitive end buds (which are different from ampullary organs of gnathostomes, see below), and photosensitive multivillous cells (Ronan & Bodznick, 1986; Braun 1996). All of these sensory organs/cells are innervated by cranial nerves that are referred to as lateral line nerves. Neuronal tracing experiments revealed that three anterior lateral line nerve (ALLN) ganglia

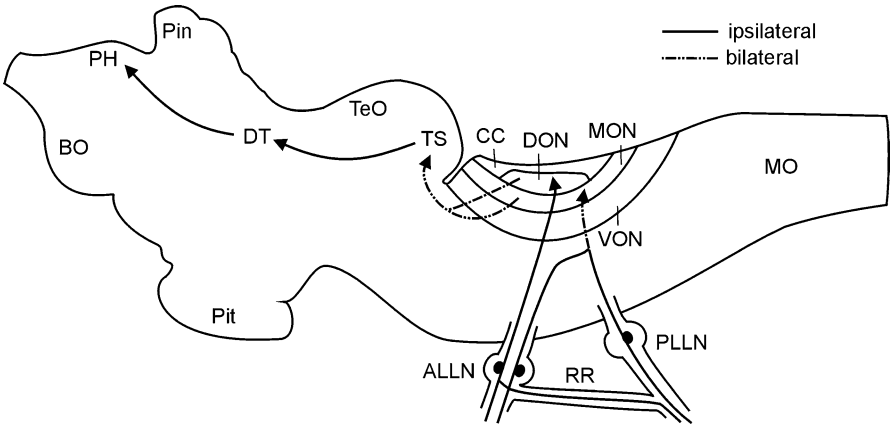

Fig. 2 Schematic lateral view of lamprey ascending lateral line pathways (modified after Northcutt, 1981, see text for more citations). Note that the ventral octaval column contains three octavomotor nuclei (not shown) with descending (spinal) efferent connections. Note that the posterior lateral line nerve ganglion contains only mechanosensory lateral line cells, whereas the anterior ganglia contain additionally electrosensory cells (see text for details). Abbreviations: ALLN anterior lateral line nerves, BO olfactory bulb, CC cerebellar crest, DON dorsal octavolateralis nucleus, DT dorsal thalamus, MO medulla oblongata, MON medial octavolateralis nucleus, PH primordium hippocampi, Pin pineal, Pit pituitary, PLLN posterior lateral line nerve, RR recurrent ramus, TeO optic tectum, TS torus semicircularis, VON ventral octavolateralis column

in lampreys contain primary electrosensory cell bodies (intracapsular and lateral ganglion) and mechanosensory cell bodies (medial ganglion) (Ronan & Northcutt, 1987; Koyama et al., 1990). Their peripheral fibers course in buccal and superficial ophthalmic (both modalities) and hyomandibular rami (only mechanosensory fibers) to reach sensory organs on the snout and around the eye. The single posterior lateral line nerve (PLLN) ganglion has only mechanosensory ganglion cells innervating the trunk neuromasts. However, electrosensory fibers join the PLLN via a recurrent ALLN ramus to innervate trunk electroreceptors (Fig. 2).

The anterior rhombencephalic alar plate of lampreys represents the octavolateralis area which is segregated into three subdivisions: the dorsal octavolateralis nucleus (DON) receiving electrosensory information, an intermediate or medial octavolateralis nucleus (MON) for mechanosensory lateral line information and a ventral octavolateralis nucleus (VON; Northcutt, 1980a, 1981) for octaval information (Fig. 2). The DON and MON are covered by a molecular layer which may correspond to the cerebellar crest of gnathostomes (see below). Contralateral primary mechanosensory lateral line projections to the MON are unique for lampreys. Upon crossing brain sides, mechanosensory fibers terminate also in the transverse ridge (traditionally erroneously recognized as cerebellar corpus) forming the anterior border of the rhomboid groove. This ridge may be comparable to a part of the vestibulo-lateral cerebellar lobe (auricles of cartilaginous fishes, eminentia granularis of bony fishes; see below). A peculiarity of the

lamprey electrosensory projection to the DON is that giant terminals are found in the rostral and caudal DON, but only small ones in between, which is possibly related to the processing of temporal or intensity features of the stimulus, respectively (Kishida et al., 1988; Koyama et al., 1993).

In addition to this general segregation of modalities in the lamprey primary sensory centers, there is some overlap of mechanosensory and octaval projections in the dorsal VON and ventrolateral MON (Koyama et al., 1989). The mechanosensory inputs are somatotopically organized in MON (for further details, see Chapters by Chagnaud & Coombs and Bleckmann & Mogdans). There are no efferent octavolateralis cells in the lamprey mechanosensory lateral line system, as opposed to the octaval system (Koyama et al., 1989). Also larval lampreys (ammocoetes) possess both a mechano- and electrosensory lateral line system - somewhat surprisingly in view of their burrowing, filter-feeding lifestyle (Ronan, 1988; González & Anadón, 1992; Gelman et al., 2007). According to the basal systematic position of lampreys (Janvier, 2008), the absence of lateral line canals may be ancestral for craniates. However, lateral line canals are clearly present in the heavy bony armors of most fossil ostracoderm groups and, thus, predate gnathostomes (Northcutt, 1989).

Modern tracing experiments furthermore established that the lamprey torus semicircularis, typically located in the ventroposterior division of the midbrain alar plate (Iwahori et al., 1996), receives bilateral input from the DON and MON (but none from VON) and has in turn strong ipsilateral projections to dorsal and ventral thalamus (Gonzàlez et al., 1999). However, projections from MON (mechanosensory lateral line) and DON (electrosensory) pathways have not been traced separately. Furthermore, thalamic nuclei project to the ipsilateral pallium (the so-called primordium hippocampi; Polenova & Vesselkin, 1993). Evoked potential and single unit electrophysiology revealed electrosensory responses from the DON, torus semicircularis, and optic tectum with increasing latencies (Bodznick & Northcutt, 1981), supporting the anatomical data on the synaptic organization of ascending lateral line pathways. However, comparable physiological information on lateral line mechanosensation is not available and, thus, the case for parallel processing of modalities in the lamprey lateral line system has not been fully made. Also, because physiological information does not exist for thalamic and telencephalic levels, it is not known for certain whether lateral line information reaches forebrain levels.

3 Cartilaginous Fishes: Basal Extant Gnathostomes

Chondrichthyans (cartilaginous fishes) comprise elasmobranchs, which include sharks as well as skates and rays (batoids), and holocephalans (chimaeras, e.g., ratfishes); together, these fishes represent the extant gnathostome outgroup to the remaining vertebrates (Fig. 1). The following findings are compiled from various shark, skate and ray species and are quite comparable between these groups at least

regarding the primary central lateral line nerve projection zones. The tracing data stem mostly from Fink-Heimer silver degeneration and HRP experiments.

Elasmobranchs have three anterior lateral line nerve (ALLN) ganglia giving rise to peripheral superficial ophthalmic, buccal and external mandibular rami. These rami innervate canal neuromasts, pit lines with free (superficial) neuromasts and ampullary electrosensory organs of the head (ampullae of Lorenzini). In addition, a PLLN ganglion gives rise to a single nerve that innervates only mechanoreceptors (neuromasts) on the trunk (McGready & Boord, 1976; Boord & Campbell, 1977; Koester, 1983). The central ALLN fibers segregate into a dorsal root containing the electrosensory fibers (Bodznick & Northcutt, 1980) and a ventral root with mechanosensory fibers; the PLLN root is solely mechanosensory (Koester, 1983; Puzdrowski & Leonard, 1993; Smeets 1998). The dorsal root projects to the DON, the ventral and posterior roots to the MON (Fig. 3). Single lateral line fibers typically bifurcate into an anterior and posterior branch within the MON and DON. Additional spatially segregated mechanosensory projections reach the vestibulo-cerebellum (the lateral granular mass and a more medial area of the auricular lower lip; Koester, 1983, Puzdrowski & Leonard, 1993). Both MON and DON are covered by a molecular layer, the crista cerebellaris (Fig. 3). Purkinje-like cells (also called multipolar or crest cells) in DON/MON are located at the periphery towards the cerebellar crest and their dendrites extend into both cerebellar crest and deep parts of DON/MON, where various other cell types are present. Furthermore, auricular granule cells project tangentially into the cerebellar crest of MON (from the lateral granular mass) and of DON (from the dorsal granular ridge; compare with Figs. 3, 4). The cerebellar crest also contains GABAergic stellate cells and, thus, resembles the cerebellar molecular layer (Koester, 1983; Smeets, 1998), although the Purkinje-like crest cells are not GABAergic (Duman & Bodznick, 1997). The noted parallel fiber input from cerebellar granule cells provides proprioceptive/electrosensory input to DON and proprioceptive/auditory/mechanosensory input to MON cerebellar crest (Bodznick and Boord, 1986; Boord & Montgomery, 1989; Conley & Bodznick, 1994) and likely acts in the context of eliminating self-generated (reafferent) signals from the relevant external sensory input (Montgomery et al., 1995; Bell et al., 1997). The elasmobranch ventral octavolateralis area is separated into five distinct nuclei, an anterior, a magnocellular, a descending, a periventricular and a posterior nucleus all of which receive octaval projections (Boord & Roberts, 1980; Northcutt, 1981; Barry, 1987).

Both electroreceptors and lateral line mechanoreceptors are topographically represented within the elasmobranch primary sensory nuclei. Anterior lateral line nerve mechanosensory fibers project into the medial, those from the PLLN into the lateral MON (Fig. 3; Koester, 1983; Puzdrowski & Leonard, 1993). Moreover, diverse ALLN branches (see above) and, therefore, the peripheral distributions of lateral line receptor organs, are somatotopically represented in primary sensory nuclei, in particular the electrosensory terminals in the entire DON, and to a less strict degree the mechanosensory terminals within the medial MON (Bodznick & Schmidt, 1984; Puzdrowski & Leonard, 1993). This somatotopy translates roughly

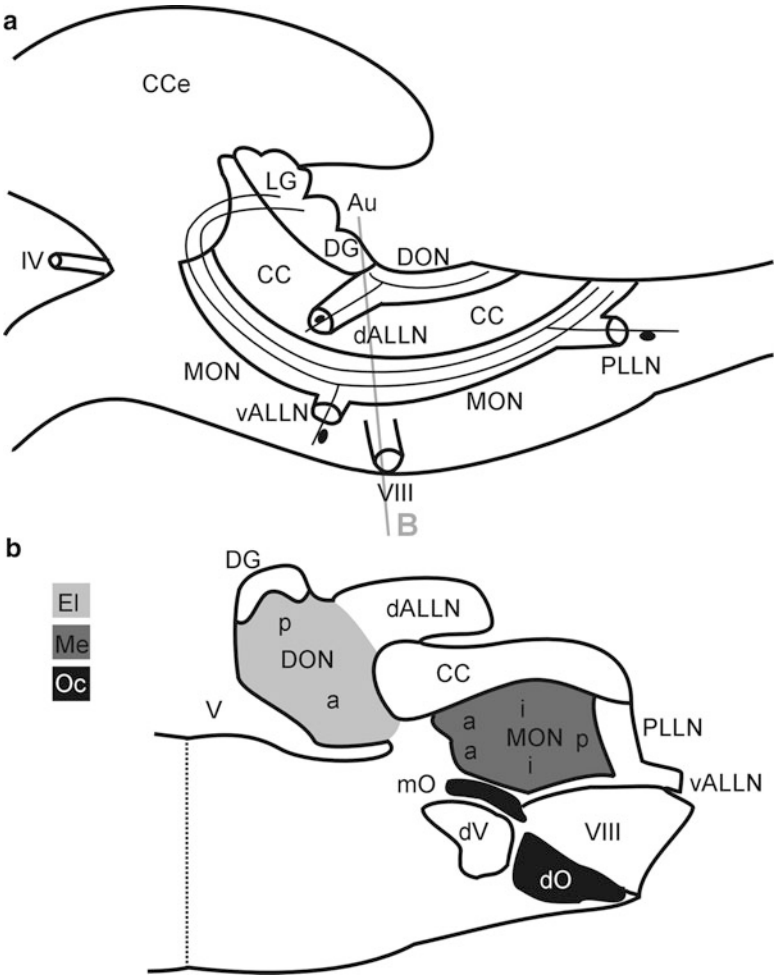

Fig. 3 Lateral line and octaval nerves and octavolateralis area in the medulla oblongata of the lesser-spotted dogfish *Scyliorhinus canicula* (modified after Boord & Roberts, 1980). (**a**) Schematic lateral view. Note bifurcation of incoming lateral line fibers and medial (vALLN) versus lateral (PLLN) segregation of mechanosensory lateral line fibers (see text). (**b**) Schematic transverse section through right side of dogfish octavolateralis area (section level indicated with gray line in **a**) showing segregation of electrosensory (El), mechanosensory (Me) and octaval (Oc) projections. Note that information on projection (other than octaval) sites and somatotopy is from additional elasmobranch species (see text). Abbreviations: a representation of receptors in anterior body periphery, Au auricle, CC crista cerebellaris, CCe corpus cerebelli, dALLN dorsal root of anterior lateral line nerve, DG dorsal granular ridge of auricle, dO descending octaval nucleus, DON dorsal octavolateralis nucleus, dV descending trigeminal root, i representation of receptors in intermediate body periphery, LG lateral granular mass of auricle, mO magnocellular octaval nucleus, MON medial octavolateralis nucleus, p representation of receptors in posterior body periphery, PLLN posterior lateral line nerve, vALLN ventral root of anterior lateral line nerve, V fourth ventricle IV trochlear nerve, VIII octaval nerve

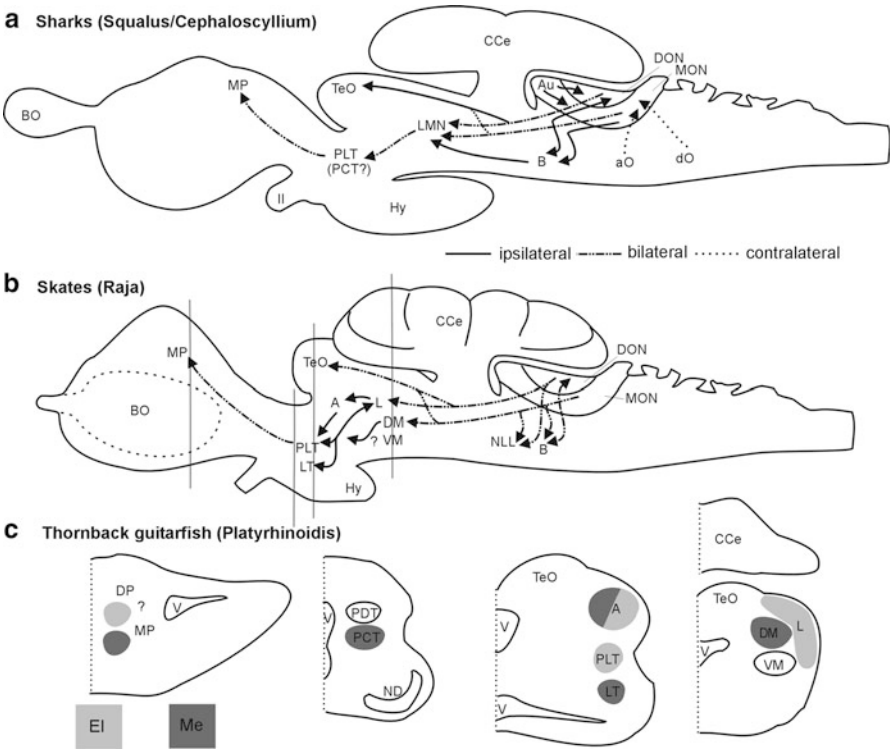

Fig. 4 Schematic lateral views of shark (**a**) and skate (**b**) lateral line ascending pathways. Note that additional strong commissural interconnections between primary sensory lateral line nuclei are not drawn in figures. Also, auricular inputs to batoid DON/MON, as well as DON's ipsilateral afferents from - and contralateral efferents to - a paralemniscal nucleus (Bodznick & Boord, 1986; see text for more citations) are not shown. Note also that *bilateral* means *predominantly contralateral*. (**c**) Schematic transverse views of right brain side of a ray (thornback guitarfish *Platyrhinoidis triseriata*) show electrophysiological identification of electrosensory (El) and mechanosensory (Me) lateral line brain structures (modified from Bleckmann et al., 1987, see text). For convenience, their approximate levels are indicated in the skate lateral view. Note that in *Platyrhinoidis* both PLT/PCT project to the medial pallium (see text for citations). Abbreviations: A anterior mesencephalic nucleus, aO anterior octaval nucleus, Au auricle, B nucleus B, BO olfactory bulb, CCe corpus cerebelli, DM dorsomedial mesencephalic nucleus, DP dorsal pallium, dO descending octaval nucleus, DON dorsal octavolateralis nucleus, Hy hypothalamus, L lateral mesencephalic nucleus of batoids, LMN lateral mesencephalic nucleus of sharks, LT lateral tuberal nucleus, MON medial octavolateralis nucleus, MP medial pallium, ND nucleus diffusus of hypothalamus, NLL lateral lemniscal nucleus, PCT posterior central thalamic nucleus, PDT posterior dorsal thalamic nucleus, PLT posterior lateral thalamic nucleus, TeO optic tectum, V ventricle, VM ventromedial mesencephalic nucleus, II optic nerve

into anteroposterior representations in MON and DON (Fig. 3b), with additional segregation of dorsal versus ventrally located electroreceptors in skates within DON, respectively (Bodznick & Schmidt, 1984). The medial octavolateralis nucleus contains dense cell plates in its center (C1/C2 or nucleus X; discussed in

Puzdrowski & Leonard, 1993) surrounded by mechanosensory terminals. These cell plates represent secondary projection cells of the MON (see below), which is corroborated by the fact that they can be driven by electrical stimulation of ALLN fibers, but not of octaval fibers (Puzdrowski and Leonard, 1993). Nevertheless, there are limited converging projections of octaval and lateral line fibers in the caudal part of the MON and in the magnocellular octaval nucleus, plus more extensive overlaps in the auricles of the vestibulocerebellum (Koester, 1983; Puzdrowski & Leonard, 1993). A very restricted octaval projection to DON (Barry, 1987) is doubtful. Cartilaginous fishes have a cholinergic octavolateralis efferent nucleus located rostral to the visceromotor column (of cranial nerves VII, IX and X) that innervates bilaterally both inner ear and lateral line hair cells, but not electroreceptors (Meredith & Roberts, 1986; Anadón et al., 2000).

Ascending projections arising in DON and MON in elasmobranchs differ somewhat between sharks and batoids and will be examined separately. Studies in sharks exist for a squalomorph shark, the spiny dogfish *Squalus acanthias* (Boord & Northcutt, 1988) and for a galeomorph shark, the carpet or draughtsboard shark (*Cephaloscyllium isabellum*; Boord & Montgomery, 1989). In sharks, both MON and DON have strong reciprocal commissural interconnections. Furthermore, fibers emanating from MON/DON anteriorly form bilateral lemnisci that give rise to the following interconnections. Ipsilateral reciprocal connections with a second order medullary nucleus B exist with DON, but the shark MON has only efferents to nucleus B. In addition, the MON receives contralateral input from both anterior and descending octaval nuclei.

Ascending projections from MON and DON reach bilaterally (predominantly contralaterally) a midbrain region ventral to the optic tectum called lateral mesencephalic nucleus (LMN). The LMN is subdivided into dorsolateral and ventromedial regions which receive electrosensory and lateral line mechanosensory fibers as corroborated with electrophysiology (Northcutt & Bodznick, 1983; Boord & Montgomery, 1989). Both DON and MON fibers also extend further into the ipsilateral or contralateral central zone of the optic tectum, respectively (Fig. 4; Boord & Northcutt, 1988; Boord & Montgomery, 1989). Retrograde tracing in *Cephaloscyllium* showed the origin of mechanosensory projections to LMN in cell plate X, plus in additional multipolar cells in MON (including crest cells, see above; Boord & Montgomery, 1989).

In *Cephaloscyllium*, the LMN projects bilaterally to a diencephalic nucleus termed posterior central thalamus (PCT; Boord & Montgomery, 1989). In *Squalus*, a more laterally located nucleus, the posterior lateral thalamic nucleus (PLT) projects mostly contralaterally to the telencephalic medial pallium (Smeets & Northcutt, 1987; Fig. 4a). Although an input from LMN to PLT remains undocumented in *Squalus*, it likely represents a diencephalic lateral line nucleus (see below). Thus, it is unclear whether sharks have one or two diencephalic nuclei that relay lateral line information from the midbrain to the telencephalon.

A more differentiated picture for lateral line midbrain and forebrain centers emerged for batoids, i.e., the thornback guitarfish, *Platyrhinoidis triseriata* and two skates of the genus *Raja*. While lateral line pathways have been examined in more

detail in skates (Boord & Northcutt, 1982, Bodznick & Northcutt, 1984, Bodznick & Boord, 1986; summarized in Fig. 4b), more electrophysiology exists for *Platyrhinoidis* (see below). In addition to strong reciprocal commissural interconnections, the skate MON and DON give rise to parallel lemniscal mechanosensory and electrosensory pathways, respectively, which course predominantly contralaterally (as in sharks), and reach a lateral lemniscal nucleus and nucleus B (the latter is reciprocally connected with DON). In all batoids, the lateral mesencephalic complex contains four nuclei, lateral (L), dorsomedial (DM), ventromedial (VM) and anterior (A) ones (Fig. 4). Lateral and dorsomedial nuclei are in receipt of electrosensory (DON) and lateral line mechanosensory (MON) inputs, respectively (Boord and Northcutt, 1982), whereas the anterior nucleus is postsynaptic to the lateral one (Bodznick & Boord, 1986). Retrograde tracing from mesencephalic lateral and dorsomedial nuclei reveal that cell plates C1/C2 are the major source of the mechanosensory projection to the dorsomedial nucleus, together with other cells in MON, and that electrosensory projections to the lateral nucleus arise from DON (*Raja*; Barry, 1987). Predominantly ipsilateral connections arise then from the mesencephalic lateral nucleus to the posterior lateral thalamic nucleus (PLT) and to the lateral tuberal nucleus (LT) in the hypothalamus. The posterior lateral thalamic nucleus has also input from the mesencephalic anterior nucleus and projects back to the mesencephalic lateral nucleus (Bodznick & Boord, 1986). The PLT in turn (but not LT) projects to the telencephalic medial pallium (predominantly contralaterally again, thus switching sides). The exact course of lateral line mechanosensory DM output to the diencephalon is unclear in skates. The midbrain area containing lateral line related nuclei of sharks (LMN) and anterior, lateral and dorsomedial/ ventromedial mesencephalic nuclei in batoids may be considered homologous to the torus semicircularis/inferior colliculus of other vertebrates. In batoids, projections from the rhombencephalic lateral lemniscal nucleus (not depicted) and also from MON and DON reach the central zone of the optic tectum (Fig. 4; Boord & Northcutt, 1982; Boord & Montgomery, 1989). Altogether this indicates that the pathways originating in the lateral line mechanosensory MON and the electrosensory DON ascend multisynaptically to the forebrain in cartilaginous fishes. Indeed, electrical stimulation of the DON elicits evoked potential responses in medial pallium and diencephalic PLT (and lateral tuberal nucleus) of the skate (Bodznick & Northcutt, 1984).

The central nervous system of the thornback guitarfish (*Platyrhinoidis*) is well investigated electrophysiologically using either vibrating sphere stimuli (Bleckmann et al., 1989) or PLLN shocks (Bleckmann et al., 1987) to stimulate the mechanosensory lateral line system or rectangular pulse field stimuli for the electrosensory system (Schweitzer, 1983; 1986). Electrosensory stimulation produced evoked responses in the lateral and anterior mesencephalic nuclei and the diencephalic PLT; electrosensory evoked responses were also seen in the dorsal or medial pallium (Fig. 4c; Bullock et al., 1993). Furthermore, omitted stimulus- (i.e., event-) related potentials (likely related to electrosensory expectation) were reported at DON, L and pallial levels. Mechanosensory stimulation resulted in evoked responses in the dorsomedial and anterior mesencephalic nuclei, in the

diencephalic posterior central thalamic (PCT) and lateral tuberal (LT) nuclei, and in a ventral medial pallial division (Fig. 4c). Interestingly, these data identify a mechanosensory diencephalic nucleus (PCT) different from the electrosensory PLT, both of which project to the telencephalon in *Platyrhinoidis* (Fiebig & Bleckmann, 1989). Furthermore, both the anterior (A) and lateral (L) mesencephalic nuclei were shown to project to the diencephalic PLT nucleus in this species (Schweitzer and Lowe, 1984). A recent dextran amine tracing study in *Platyrhinodis* confirmed strong PLT projections to the pallium, but did not identify a pallial projecting PCT (Hofmann & Northcutt, 2008). This study also reported a strong input to the mesencephalic lateral (electrosensory) and dorsomedial (mechanosensory) nuclei from a dorsal pallial division and hypothesized that this represents a higher order olfactory connection via the subpallium (area basalis superficialis) converging with lateral line information in the mesencephalon. However, basal forebrain inputs to the pallium may alternatively represent modulatory (non-sensory) input.

Thus, the overall situation speaks for parallel electrosensory and mechanosensory pathways up to telencephalic levels in *Platyrhinoidis*. However, as in skates, the efferents of the (mechanosensory) dorsomedial mesencephalic nucleus are unknown, although they likely reach the diencephalic PCT. In this context, the most pressing questions are whether a diencephalic mechanosensory PCT exists in all cartilaginous fishes separate from an electrosensory PLT and how exactly the two lateral line modalities are represented in the medial/dorsal pallium. Evoked potential and multi-unit responses in the skate medial pallium following either optic nerve, PLLN or DON stimulation revealed largely overlapping electrosensory (although these were slightly deeper) and visual responses, and completely overlapping visual and mechanosensory responses (Bodznick, 1991). In the telencephalic dorsal pallium (nucleus centralis) of the galeomorph nurse shark, visually and trigeminally elicited responses were spatially segregated, suggesting that there may have been an evolutionary switch from multimodal processing in the medial pallium to unimodal processing in the dorsal pallium of cartilaginous fishes (Bodznick, 1991). More focused functional neuroanatomical work in cartilaginous fishes is clearly needed to resolve these important issues.

4 Ray-Finned Fishes: the most Successful Aquatic Bony Fishes

Ray-finned fishes (actinopterygians) underwent a similarly extensive evolutionary radiation as their osteichthyan sistergroup, the sarcopterygians (lobe-finned fishes, including tetrapods; see Section 5). Thus, actino- and sarcopterygians are each comprised of around 25000 extant species. It is peculiar that most actinopterygian taxa, which include over 90% of all extant aquatic vertebrate species, possess only a mechanosensory lateral line system, without an electrosensory counterpart, a fact with no immediate adaptationist explanation. A seminal phyletic analysis of

electrophysiological results from the DON in parallel with neuroanatomical studies of the octavolateralis area in all major aquatic craniates has revealed the ancestry of the electrosense within vertebrates and its late phylogenetic loss in tetrapods (Bullock et al., 1982, 1983). However, within actinopterygian fishes, the correlated presence of a DON in the octavolateralis area and evoked potential responses to electric stimuli in DON is only seen in the two most basal actinopterygian groups, polypteriforms (bichirs, reedfish) and chondrosteans (sturgeons and paddlefishes), whereas gars (Lepisosteiformes) and bowfins (Amiiformes) - formerly together called holosteans - and the overwhelming majority of more derived (and highly speciose) teleosts lack both electroreceptors and the related central nervous structures, such as the DON. Thus, electroreception which was present in the earliest vertebrates, was lost before teleosts arose in actinopterygian phylogeny and subsequently re-evolved in only a few teleost taxa (see Fig. 1; and Section 4.3). Lateral line central anatomy of electrosensory and non-electrosensory basal ray-finned fishes will be discussed first, followed by consideration of major teleost groups.

4.1 Basal Ray-Finned Fishes

Although the number of discrete lateral line nerve ganglia differs between various ray-finned (actinopterygian) fish groups, there is always an anterior complex of ganglia giving rise to at least a superficial ophthalmic, a buccal and an external mandibular ramus innervating the head periphery and a posterior complex of lateral line ganglia giving rise to nerves innervating the trunk periphery (see review: Northcutt, 1989). For simplicity, only anterior (ALLN) and posterior (PLLN) lateral line nerves will be used below. Basal ray-finned fishes with electroreception (polypteriforms, chondrosteans) resemble cartilaginous fishes in that they carry electrosensory fibers innervating ampullary organs only in the ALLNs, and mechanosenory fibers innervating canal and free (superficial) neuromasts in both ALLN and PLLNs (New & Northcutt, 1984; McCormick, 1989; Piotrowski & Northcutt, 1996). The associated octavolateralis area consequently consists of a dorsal electrosensory column (DON), an intermediate mechanosensory column (MON/plus the caudal octavolateralis nucleus) and a ventral octaval column. The caudal octavolateralis nucleus (CON) lies at the caudal end of MON, is not covered by the cerebellar crest, and is actually present in all gnathostome fishes (McCormick, 1982), including cartilaginous fishes (Puzdrowski & Leonard, 1993). As in elasmobranchs, the actinopterygian MON and DON display Purkinje-like cells towards the cerebellar crest, and various additional, more deeply lying cell types (i.e., granular, fusiform, polygonal), whereas the CON only consists of granular cells (McCormick, 1982; New & Northcut, 1984). The electrosensory nature of the DON was furthermore physiologically confirmed in polypteriforms and chondrosteans (Bullock et al., 1982, 1983). The ventral octaval column in these

electrosensory basal actinopterygians contains anterior, magnocellular, descending and posterior octaval nuclei (McCormick, 1982).

The sturgeon ALLN has a dorsal root carrying only electrosensory fibers which terminate in DON and the dorsal granular area of the lateral eminentia granularis, with DON showing evoked responses to electrosensory stimulation (New & Northcutt, 1984; New and Bodznick, 1985). The solely mechanosensory ventral root of ALLN, plus the PLLN, project ipsilaterally to several locations: the MON and its caudal elongation the CON, to the dorsal and rostral eminentia granularis (the actinopterygian vestibulolateral lobe) as well as to the ventral cerebellar corpus (New & Northcutt, 1984). In all these projection sites of the sturgeon lateral line nerves, there is a clear segregation of ALLN/PLLN fibers, with PLLN terminals being dorsal to those of ALLN within each structure. Lateral line nerve projections to the eminentia granularis and corpus cerebelli are bilateral in the sturgeon. In these two cerebellar structures (but not in MON/CON), the most ventral area, presumably the site of octaval nerve terminals (as in bowfins, see below), is always free of lateral line projections. Also, an additional medial part of the ventrolateral granular part of the eminentia granularis receives overlapping ALLN/PLLN projections, and the magnocellular octaval nucleus receives also ALLN input. Sturgeons also have efferent octavolateralis neurons lying at the rostral tip of the visceromotor column. Paddlefishes also have clear anatomical and physiological segregation of an electrosensitive DON and mechanosensitive MON (New & Bodznick, 1985) and they use dense electroreceptors in their rostrum to detect small electric fields emanating from planktonic prey (Wilkens et al., 2002). Electrosensory projections arising from the DON reach the optic tectum, the torus semicircularis and a lateral mesencephalic nucleus (LMN; Hofmann et al., 2002). DON neurons have large receptive fields and - unlike sharks (Section 3) - are not topographically organized (Hofmann et al., 2005). Unlike neurons in DON, those of LMN are activated by electrosensory signals irrespective of orientation and direction, but they also have large receptive fields. Neurons of the optic tectum instead have small receptive fields and are topographically arranged (Chagnaud et al., 2008a, b). The behavioral significance may be that the LMN guides the longer-range orienting response, whereas the optic tectum is involved in the final prey capture.

Although degeneration studies in lampreys, elasmobranchs and teleosts had previously indicated a restriction of octaval projections to the ventral octavolateralis column nuclei (Northcutt, 1981), it was not until the seminal work of Catherine McCormick using modern tracing methodology in the Northcutt laboratory that a new conceptual framework emerged revealing three functional separate longitudinal columns in the vertebrate octavolateral area dedicated to functionally distinct sensory systems (McCormick, 1981a, b, 1982, 1989). Her work concentrated on a pivotal species, the bowfin, *Amia calva*, which is together with gars in a phylogenetic position between teleosts and electrosensory basal ray-finned fishes (i.e., polypteriforms/chondrosteans: see above). As *Amia* lacks an electrosensory system, both a dorsal root of the ALLN and a dorsal column (DON) are absent. Thus, it has only one ALLN root projecting to the intermediate

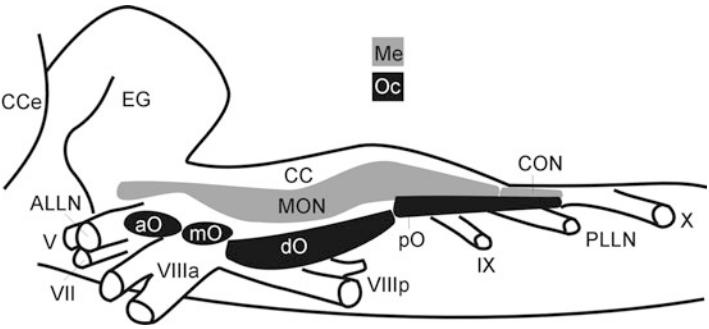

Fig. 5 Schematic lateral view of octavolateralis area in the bowfin *Amia calva* (redrawn after McCormick, 1981b). Abbreviations: ALLN anterior lateral line nerve, aO anterior octaval nucleus, CC crista cerebellaris, CCe corpus cerebelli, CON caudal octavolateralis nucleus, dO descending octaval nucleus, EG eminentia granularis, mO magnocellullar octaval nucleus, MON medial octavolateralis nucleus, PLLN posterior lateral line nerve, pO posterior octaval nucleus, V trigeminal nerve, VII facial nerve, VIIIa, p anterior, posterior parts of octaval nerve, IX glossopharyngeal nerve, X vagal nerve

(MON, CON) column. In addition, there is a ventral column that displays four octaval nuclei (anterior, magnocellular, descending and posterior ones; Fig. 5). These four nuclei are in receipt of octaval nerve projections in *Amia* (McCormick, 1981b), as is the most ventral division of the eminentia granularis. Additionally, sparse octaval nerve terminals were noted in the ventral MON, suggesting a small region of overlap between octaval and mechanosensory input. In contrast, the ALLN root projects heavily into the ventromedial parts of MON and CON, plus the intermediate division of the eminentia granularis, and the PLLN projects into the dorsolateral MON and dorsal eminentia granularis, and sparsely to the magnocellular octaval nucleus, very similar to the situation later reported in chondrosteans (see above; except for the absence of DON and lack of projections to the cerebellar corpus in *Amia*). The Florida gar (*Lepisosteus platyrhincus*) shows highly similar lateral line projections (Song & Northcutt, 1991). The octavolateralis region of *Amia* (Fig. 5) is illustrated because it serves as a blueprint for the teleostean situation and because the sturgeon/polypteriform octavolateral area highly resembles the elasmobranch situation (Fig. 3).

McCormick (1989) later reported MON connections in *Amia*. There are strong commissural interconnections between the two MONs arising from crest cells (McCormick, 1989). The peripheral dendrites of crest cells extend into the cerebellar crest, where they are contacted by parallel fibers issued by granular cells of the eminentia granularis whose axons enter the cerebellar crest tangentially and presumably provide processed lateral line and other higher order sensory inputs. Additionally, the crest cell ventral dendrites receive primary lateral line nerve input, as do deeper lying polygonal and granular cells. In contrast, the CON which receives only lateral line nerve input, consists exclusively of granular cells

and does not contribute to descending and ascending connections of the mechanosensory column (McCormick, 1989).

Ascending projections from MON arise in crest cells and deeper polygonal cells and run bilaterally (stronger contralaterally) within the lateral lemniscus (or lateral longitudinal fascicle) anteriorly. Reciprocal connections arise from the lateral lemniscus to the preeminential nucleus, a nucleus ventral to the eminentia granularis. Ascending lateral lemniscal fibers then terminate in a lateral division of the torus semicircularis, in the optic tectum and in a perilemniscal nucleus. Bulk tracer injections into the torus semicircularis show input from this perilemniscal nucleus and confirm MON input. In addition, these tracings reveal strong ipsilateral and weak contralateral ascending toral projections to the diencephalon, that is the central posterior thalamic nucleus (dorsal thalamus) and some divisions of the preglomerular area, in particular the lateral preglomerular nucleus (a migrated part of the posterior tuberculum; McCormick, 1989). These connections are very similar to those seen in non-electrosensory teleosts and their comparative and developmental significance will be discussed in the next section.

4.2 Non-Electrosensory Teleosts

Approximating 25000 species, teleost fishes display great variability in their central nervous systems (Meek & Nieuwenhuys, 1998; Wullimann, 1998; Wullimann and Vernier, 2009) and, thus, a general picture of teleostean central lateral line organization is not easy to give. The most basal teleost clade is that of the osteoglossomorphs which include for example osteoglossids (e.g., the South American Arapaima), as well as African mormyrids (elephantnose fishes) and notopterids (African knifefishes). Elopomorphs (e.g., anguilliform eels, tarpons, ladyfishes) are the next teleost clade, followed by the clupeomorphs (herrings and their relatives). The final clade is formed by the euteleosts which include very large radiations such as the ostaryophysines, for example cyprinids (carps and relatives), silurids (catfishes), or gymnotoids (South American knifefishes). Another huge euteleost clade, the acanthomorphs (perch-type fishes) include sticklebacks, flatfishes, seahorses, triggerfishes, cichlids, basses, and sunfishes, just to name a few. Euteleosts also include salmonids and esocids (pikes). As already pointed out, electroreception is lost in the closest outgroups of teleosts (Amiiformes, Lepisosteiformes) and an analysis within teleosts shows that the sole presence of the mechanosensory modality in the lateral line system becomes, thus, basal for this large group of vertebrates, with only some osteoglossomorphs and silurids/gymnotoids re-evolving electroreception (see next Section). Here, the focus will first be on a discussion of non-electrosensory cyprinid fishes, and information on other non-electrosensory teleosts will follow later.

Being ostaryophysines, cyprinids have a specialized auditory sense. This has drawn scientific attention amongst neurobiologists and the octavolateralis system is, thus, rather well investigated in cyprinids (Webster et al., 1992; Popper & Fay,

1993, 1999). The anterior portion of their swim bladder is mechanically linked to the inner ear via the Weberian ossicles - a series of bones and ligaments derived from most anterior vertebral and rib elements. The swim bladder, as a compressible gas cavity, acts as a sound pressure transducer and - together with the Weberian apparatus – as an amplifier transmitting sound pressure waves to the inner ear where in particular saccular (in goldfish apparently exclusively; Coombs et al., 2010), and maybe lagenar and utricular sensory epithelia are involved in sensing acoustic pressure signals (McCormick & Braford, 1994; Yamamoto & Ito, 2005). The information summarized here is from the common carp (*Cyprinus carpio*) and the goldfish (*Carassius auratus*). The cyprinid octaval nerve projects to the five nuclei comprising the octaval column, i.e., anterior, magnocellular, descending, tangential and posterior octaval nuclei (McCormick & Braford, 1994). The tangential nucleus is an additional solely vestibular nucleus present in teleosts which is absent in basal ray-finned fishes (see Section 4.1). In cyprinids, the dorsomedial part of the descending octaval nucleus has been identified as primary auditory center receiving saccular, as well as lagenar and utricular afferents (McCormick & Braford, 1994; Yamamoto & Ito, 2005). Notably, the large saccular input to this nucleus in the goldfish does not overlap with other inner ear inputs (McCormick & Braford, 1994). Also the dorsocaudal part of the anterior octaval nucleus receives saccular input, but mostly overlapping with all other inner ear inputs (McCormick & Braford, 1994). Descending spinal projections in cyprinids originate in all five octaval nuclei, with the exception of the said acoustically related dorsomedial part of the descending octaval nucleus (Prasada Rao et al., 1987; McCormick & Braford, 1994; Becker et al., 1997). The latter has instead ascending projections to the central nucleus of the torus semicircularis in cyprinids (Echteler, 1984, 1985b; McCormick & Hernandez, 1996), as does the anterior octaval nucleus in the carp in addition (Echteler, 1984, 1985a; Yamamoto & Ito, 2005). The zebrafish, another cyprinid species with relatively small primary chemosensory lobes compared to carp/goldfish, has an additional spinal projection descending from the MON (Becker et al., 1997), whereas in the goldfish, an additional spinal projection originates in the large (primary gustatory) facial lobe (Prasada Rao et al., 1987), indicating that different sensory systems are involved in the control of spinal circuits depending on species-specific sensory specialization. In this context, it is worth noticing that the pair of large Mauthner cells, which initiate hearing induced escape behavior, also receive lateral line input (for more citations and discussion, see Mirjany & Faber, 2011 and Chapter by Braun & Sand).

The cyprinid ALLN and PLLN roots enter the brain at the level of the octavolateralis area (Fig. 6a; Luiten, 1975; Zottoli & van Horne, 1983; Puzdrowski, 1989). Although there is an anterodorsal and anteroventral ALLN root in cyprinids, these together correspond to the ventral ALLN root of basal actinopterygians and, thus, solely contain mechanosensory fibers innervating canal and free (superficial) neuromasts, as does the PLLN (Puzdrowski, 1989; Schmitz et al., 2008). The lateral line nerves project ipsilaterally to the MON and CON, which lie anterior to the large gustatory facial and vagal lobes (Figs. 6a, b). Additional lateral line projections reach the cerebellar granular eminence and transgress even slightly into the

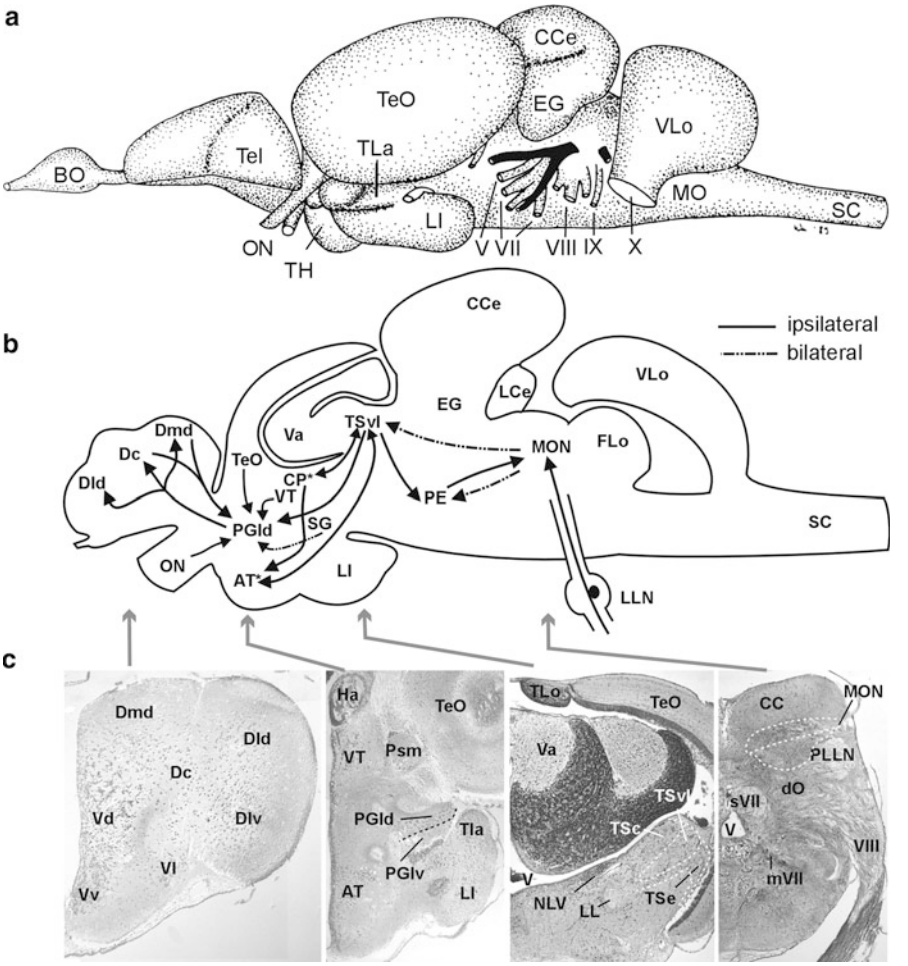

Fig. 6 Lateral line structures and pathways in cyprinids. (**a**) Lateral view of the goldfish (*Carassius auratus*) brain. Lateral line nerves are indicated in black. (**b**) Schematic lateral view of cyprinid brain showing mechanosensory lateral line pathways (for citations see text). * these two (central posterior thalamic and anterior tuberal) auditory nuclei project to the medial pallial zone (Dm; see text). The lateral line nerve (LLN) shown is meant to represent both anterior and posterior nerves. Commissural projections of MON and input from the eminentia granularis to MON are not shown (see text for details). (**c**) Four microphotographs show lateral line mechanosensory structures in transverse sections of goldfish brain stained with Bodian-silver procedure at telencephalic, diencephalic, mesencephalic, and rhombencephalic levels from left to right. Note that the dorsal crest cell area and the deep area of MON are indicated with stippled white lines. Abbrevations: AT anterior tuberal nucleus, BO bulbus olfactorius, CC crista cerebellaris, CCe corpus cerebelli, CP central posterior thalamic nucleus, Dc, Dld, Dlv, Dmd central, dorsolateral, ventrolateral, dosomedial zone of pallial area dorsalis telencephali, dO descending octaval nucleus, EG eminentia granularis, FLo facial lobe, Ha habenula, LCe lobus caudalis cerebelli, LI lobus inferior, LL lateral lemniscus (lateral longitudinal fascicle), LLN lateral line nerves, MO medulla oblongata, MON medial octavolateralis nucleus, mVII facial

cerebellar corpus (Puzdrowski, 1989). The anterior and posterior lateral line fiber terminations are segregated in MON and CON, with ALLN fibers lying anteroventrally and PLLN fibers posterodorsally. Within the eminentia granularis, ALLN fibers terminate anteriorly to those of the PLLN. A small zone of overlap between primary anterior lateral line and octaval nerve projections exists in the dorsal part of the magnocellular and descending octaval nuclei (Puzdrowski, 1989; McCormick & Braford, 1994). As in all gnathostome fishes, the cyprinid MON is covered by the cerebellar crest (Fig. 6c) which contains stellate and other cells. Large crest cells are located in an intermediate region between cerebellar crest and the deeper region of MON. The crest cells have peripheral dendrites extending into the cerebellar crest and either do or do not have basal dendrites into the deeper MON area where mostly granular cells were reported (New et al., 1996). The deeper MON area is recipient of primary lateral line input, whereas the cerebellar crest likely receives parallel fiber input from the eminentia granularis.

Both types of cyprinid MON crest cells give rise to commissural projections (not shown) and to second order lateral line projections ascending in the lateral lemniscus (Fig. 6b). These fibers terminate bilaterally, albeit with a stronger contralateral component, in the ventrolateral nucleus of the torus semicircularis (TSvl) and there are also reciprocal connections with the preeminential nucleus (McCormick & Hernandez, 1996; Fig. 6b). Furthermore, there are weaker projections from MON to the optic tectum and the principal sensory trigeminal nucleus (McCormick & Hernandez, 1996; both not drawn in Fig. 6b). The ventrolateral toral nucleus in turn has strong ipsilateral ascending projections to the dorsal division of the lateral preglomerular nucleus (PGld; Echteler, 1984; McCormick & Hernandez, 1996; Northcutt, 2006). This diencephalic nucleus in turn provides one of the strongest inputs to the dorsal telencephalic (pallial) area in cyprinids, in particular to the dorsal part of the lateral zone (Dld), but also weakly to the dorsal part of the medial zone (Dmd) and to the central zone (Dc) (Striedter, 1992; Northcutt, 2006; Yamamoto & Ito, 2008). Within the dorsolateral preglomerular nucleus (PGld), various sensory inputs are spatially segregated, with (2nd order visual) input from the optic tectum located dorsolaterally, retinal inputs dorsomedially, ventrolateral toral (lateral line) input ventrolaterally, and ventromedial thalamic (likely

Fig. 6 (continued) motor nucleus, NLV nucleus lateralis valvulae, ON optic nerve, PE preeminential nucleus, PGld dorsal part of lateral preglomerular nucleus, PGlv ventral part of lateral preglomerular nucleus, PLLN posterior lateral line nerve, PSm magnocellular superficial pretectal nucleus, SC spinal cord, SG subglomerular nucleus, sVII sensory root of facial nerve, Tel telencephalon, TeO tectum opticum, TH tuberal hypothalamus, TLa torus lateralis, TLo torus longitudinalis, TSc central nucleus of torus semicircularis, TSe external nucleus of torus semicircularis, TSvl ventrolateral nucleus of torus semicircularis, V ventricle, Vd, Vl, Vv dorsal, lateral, ventral nucleus of subpallial area ventralis telencephali, Va valvula cerebelli, VLo vagal lobe, VT ventral thalamus, V trigeminal nerve, VII facial nerve, VIII octaval nerve, IX glossopharyngeal nerve, X vagal nerve

somatosensory) inputs ventromedially. In contrast, the ventrolateral preglomerular nucleus (PGlv) receives auditory information from the medial pretoral nucleus (an additional midbrain toral nucleus in ostaryophysines that is postsynaptic to the auditory central toral nucleus; Striedter, 1991, 1992). Both the central posterior thalamic nucleus (the dorsal thalamic auditory "relay" nucleus that receives a main input from the central toral nucleus; Echteler, 1984; Lu & Fay, 1995; Yamamoto & Ito, 2005) and the hypothalamic anterior tuberal nucleus (a second diencephalic auditory target of the auditory central toral nucleus) have reciprocal connections with the (lateral line related) ventrolateral toral nucleus and project in turn to the medial (Dm), but not to the lateral pallial zone (Dl) (Northcutt, 2006). The dorsolateral preglomerular nucleus receives additional input from the subglomerular nucleus (Yamamoto & Ito, 2008). The central posterior thalamic nucleus (CP) also projects to the anterior tuberal nucleus (AT; Fig. 6; Striedter, 1991; Northcutt, 2006), but apparently not to PGld (Yamamoto & Ito, 2008). Thus, all these diencephalic nuclei may be involved in lateral line forebrain circuitry (Fig. 6b).

The descending connections within the cyprinid central lateral line mechanosensory system start out with the medial and central pallial zones projecting back onto the lateral preglomerular nucleus (Striedter, 1992; Northcutt, 2006; Yamamoto & Ito, 2008). However, there are no descending projections from the lateral preglomerular nucleus to the ventrolateral toral nucleus (Striedter, 1992). The ventrolateral toral nucleus projects in turn via a brain stem nucleus, the preeminential nucleus, to the primary sensory MON (McCormick & Hernandez, 1996). Finally, as in most teleosts investigated, the cyprinid mechanosensory system has two separate efferent octavolateralis neuronal populations in the region anterior to the visceromotor column and a third one in the diencephalic periventricular area of the posterior tuberculum, the latter seems special for cyprinids (Zottoli & van Horne, 1983; Puzdrowski, 1989). Thus, while the teleostean lateral line mechanosensory and octaval nerves do not have true somatomotor nuclei whose axons contact motor endplates of muscle fibers, they do have efferent cholinergic octavolateralis neurons that innervate their peripheral sensory organs (Danielson et al., 1988; Roberts & Meredith, 1989, 1992).

Results from neurophysiological studies on the peripheral (Fukuda, 1974; Chapter by Chagnaud & Coombs) and central (Bleckmann 2008; Chapter by Bleckmann & Mogdans) nervous system in cyprinids (and other teleosts) are consistent with the view that the lateral line neuronal network (outlined in Fig. 6b) detects and processes hydrodynamic stimuli which indicate relative movement between water and animal at low frequencies (up to 200 Hz) over relatively short distances (1 to 2 body lengths) to the fish (Mogdans et al., 1997; Mogdans & Kröther, 2001; Künzel et al., 2011; Chapter by Montgomery, Coombs & Bleckmann). This general information is relayed to the MON via lateral line fibers that encode for two submodalities. Lateral line fibers that innervate superficial neuromasts deal with low frequency stimuli (related to velocity/displacement) and appear to play a role in rheotaxis (orientation to water currents; Montgomery et al., 1997). In contrast, fibers innervating canal neuromasts (related to

acceleration) detect higher frequency hydrodynamic stimuli and appear to play a role in sensing and localizing discrete hydrodynamic sources, such as prey or predators – especially in the presence of background water flow noise (Engelmann et al., 2000; Kröther et al., 2002; Chapters by Montgomery, Coombs & Bleckmann; Chagnaud & Coombs). Physiological evidence further indicates that ventrolateral toral nucleus units at midbrain levels maintain the functional separation of these two submodalities.

In addition, the ventrolateral torus appears to preserve the anteroposterior topography of external moving objects (Wojtenek et al., 1998; Plachta et al., 2003; Engelmann & Bleckmann, 2004). However, it remains unclear if and where spatial maps based on lateral line information are present in the midbrain (Voges & Bleckmann, 2011).

The representation of mechanosensory lateral line stimuli in the cyprinid diencephalon remains unclear. After visual, acoustic or hydrodynamic stimulation, recordings in the goldfish diencephalon revealed multimodal unit responses in the anterior tuberal nucleus (AT) and unimodal ones (including lateral line stimuli) in the central posterior thalamic nucleus (CP; compare Fig. 6b; Kirsch et al., 2002). However, this study did not find evoked potential or unit responses after acoustic or lateral line stimulation in the lateral preglomerular nucleus. Knowing now the small extent of the lateral line input within the multisensory dorsolateral preglomerular nucleus (Northcutt, 2006; Yamamoto & Ito, 2008; see discussion above), this area might simply have been missed. Unfortunately, there are no physiological recordings in the cyprinid telencephalon related to hydrodynamic stimulation.

Finally, non-electrosensory teleosts other than cyprinids shall be considered. In elopomorph (European eel; Meredith et al., 1987), salmonid (rainbow trout; Schellart et al., 1992) and various acanthomorph teleosts (pike cichlid: McCormick, 1983; oscar: Meredith, 1984; O'Marra & McCormick, 1999; toadfish: Highstein et al., 1992; sleeper goby: Tomchick & Lu, 2005; damselfish: Maruska & Tricas, 2009) a similar picture has emerged regarding primary lateral line nerve projections to MON and CON, as well as to the granular eminence. Except for the trout, all investigated species receive such input to the dorsal part of the magnocellular octaval nucleus, with the oscar also receiving input to the dorsal part of the descending octaval nucleus. In a scorpaenid teleost, an ascending synaptic chain of connections has been reported from MON via the semicircular torus to a preglomerular nucleus and to a thalamic "ventromedial nucleus" (likely corresponding to the central posterior thalamic nucleus, see above); the latter two diencephalic lateral line targets in turn project to various dorsal pallial areas (Murakami et al., 1986). However, auditory and lateral line mechanosensory components have not been resolved anatomically, let alone physiologically, in this study. In the plainfin midshipman, ascending lateral line connections from MON via the midbrain ventrolateral torus (TSvl) reach the diencephalic posterior thalamic nucleus. However, midbrain projections to other diencephalic nuclei (e.g., the lateral preglomerular, central posterior thalamic and anterior tuberal nuclei) have not been demonstrated in this species, nor have descending projections

from the midbrain (TSvl) via 2nd order (preeminential nucleus) to 1st order (MON) hindbrain lateral line nuclei (Weeg & Bass, 2000).

Clupeiform fishes (e.g., herrings) represent a special case. Their swim bladder forms paired anterior diverticulae (auditory bullae) which are in close physical contact both with the utricle and cephalic lateral line canals. Sound pressure waves, thus, act on both hair cell systems. Centrally then, a large unique utricular projection area - fused in the midline - is present in the dorsomedial descending octaval nucleus which receives at the same time an extraordinarily extensive overlapping projection from the lateral line nerves (Meredith, 1985; McCormick, 1997), seemingly an adaptation to the peripheral specialization. Naturally, primary lateral line projections in clupeiforms also reach the MON/CON and the eminentia granularis.

A comparison of mechanosensory lateral line central neuroanatomy in ostaryophysines, other non-electrosensory teleosts and basal ray-finned fishes (see Section 4.1) indicates that the situation in cyprinids represents much of the ancestral evolutionary condition for teleosts. This applies in particular to the synaptic hierarchical chain of ascending lateral line connections from (1) the hindbrain MON, to (2) the ventrolateral toral nucleus in the midbrain, to (3) the dorsolateral preglomerular nucleus in the diencephalon to, finally, (4) the telencephalic pallium, as these connections have been found in other ray-finned fishes as well.

In contrast, specialized derived characters are seen in the lateral line nerve projections to the cerebellum. While such projections to the eminentia granularis are generally present in teleosts, lateral line nerve input to corpus and, in particular, valvula cerebelli is more rarely seen and has evolved several times independently (summarized in Wullimann et al., 1991).

Moreover, cyprinid ascending lateral line pathways were revealed to be more complex than previously known (Fig. 6b). There may be additional lateral line pathways via two predominantly auditory centers, the hypothalamic anterior tuberal nucleus and the central posterior thalamic nucleus (see above). Also, the dorsolateral preglomerular nucleus contains in addition to the small lateral line territory a mosaic of various sensory inputs, such as visual (tectum, retina) and somatosensory (ventral thalamus) inputs. It remains to be shown if and how these modalities are separately maintained at pallial levels. In any case, the dorsolateral (lateral line related) and ventrolateral (auditory related) preglomerular nuclei in the diencephalon have largely separate projection areas within the lateral pallial zone in the telencephalon (Yamamoto & Ito, 2008).

According to developmental (Wullimann, 2009; Mueller & Wullimann, 2009), connectional (Northcutt, 2006; Yamamoto & Ito, 2008) and behavioral data (Rodríguez et al., 2002; Salas et al., 2003), it is now widely accepted that the teleostean lateral pallial zone (Dl) is homologous to the medial pallium (hippocampus), whereas the medial pallial zone (Dm) would correspond to the ventral pallium (pallial amygdala). In this context it is interesting to point out that there is segregation of indirect auditory input from the medial pretoral nucleus via the ventrolateral preglomerular nucleus to the ventrolateral pallial zone (hippocampus homologue) and the more direct auditory input from the central toral nucleus via the anterior and

caudolateral preglomerular nuclei to the medial pallial zone (pallial amygdala homologue; Northcutt, 2006).

However, a simplistic interpretation of teleostean pallial functions based on the situation for the respective homologous pallial areas in mammals (i.e. Dl only for spatial memory based on sensory detail and Dm for fear conditioning/emotional processing) may lead astray. In reptiles and birds, the ventral pallium (pallial amygdala homologue/nidopallium), which would appear to be homologous to the teleostean Dm, is greatly enlarged in comparison to mammals and, unexpectedly, concerned with the processing of sensory detail (Bruce and Neary, 1995; Martínez-Garcia et al., 2009). Thus, an independent case of ventral pallial enlargement and functional specialization may have occurred in teleosts and birds/reptiles. The situation for the teleostean Dl (hippocampus homologue) corresponds closely to other anamniotes, as the medial pallium is always the target of diencephalic lateral line projections (see Sections 2; 3). Of note, Wullimann & Mueller (2004) have previously proposed that Dc and those portions of Dl/Dm directly surrounding Dc may be dorsal pallium. However, it appears now that all of Dm (ventral pallium), all of Dl (medial pallium; Northcutt, 2006; Yamamoto & Ito, 2008) and Dc (dorsal pallium; Mueller et al., 2011) might each represent separate major pallial divisions.

4.3 Electrosensory Teleosts

The extensive functional neuroanatomical literature on teleostean electroreception can not be completely summarized here. For example, the finer structure of the primary electrosensory lateral line lobes (ELL) or other central electrosensory structures, and in particular the central electromotor system are reviewed elsewhere (Chapters in Bullock & Heiligenberg, 1986; Bell et al., 1993; Bullock et al., 2005). In line with the present chapter's focus, the ascending central (lateral lemniscal) lateral line pathways in electrosensory teleosts will be discussed.

As noted above, the perception of weak electric fields (electroreception) using multicellular sensory organs (end buds in lampreys and ampullary organs in gnathostomes) innervated by lateral line nerves is ancestral for vertebrates. The signals perceived by ampullary organs with high sensitivity are DC or low frequency electric fields originating from prey, ocean currents, electrochemical sources, or locomotion of the animal in the earth magnetic field (Bodznick & Montogomery, 2005). However, electroreception was lost early in actinopterygian phylogeny (see Section 4.1 and Fig. 1), and re-appeared at least twice, if not four times, within teleosts (Bullock et al., 1982; 1983). Within the osteoglossomorphs, the African mormyrids/gymnarchids and the African knifefishes (i.e., *Xenomystus nigri*) - but not the Asian knifefishes - are electrosensory (Braford, 1986). Among the ostariophysans, both the gymnotoids (South-American knifefishes; Carr & Maler, 1986) and their sistergroup, the silurids (catfishes; Finger, 1986), are electrosensory. Whether xenomystines and silurids acquired electroreception independently of mormyrids and gymnotoids, respectively, is debatable. Although

silurids and xenomystines have ampullary organs for passive electroreception, they lack weakly electric organs (except for a unique weakly electric organ dorsal to the swim bladder in synodont catfishes; Hagedorn et al., 1990). In contrast, mormyrids (e.g., elephantnose fish, *Gnathonemus petersii*) and gymnotoids (e.g., chocolate ghost, *Apteronotus leptorhychus; glass knifefish, Eigenmannia virescens*) have active electroreception. A weakly electric organ (usually consisting of modified axial musculature; comprised of motor neurons in apteronotids) in the tail of these two distantly related groups emits low voltage electric signals (electric organ discharges, EODs) which are used in conjunction with specialized electroreceptors for electrolocation and electrocommunication (Bullock & Heiligenberg, 1986; Bell et al., 1993; Bullock et al., 2005). The degree of parallelism is striking. Besides the presence of electric organs, both mormyrids and gymnotoids exhibit three types of electroreceptors. One is specialized for low-frequency (passive) electroreception (ampullary organs, similar to those in other electrosensory teleosts), the other two are dedicated to high-frequency (active) electrolocation and electrocommunication (two types of tuberous organs exclusive for these teleosts).

4.3.1 Silurids

Given the phylogenetic relationship of cyprinids (the outgroup of characins, silurids and gymnotoids) and characins (outgroup of silurids and gymnotoids, the latter two being sister groups), the analysis of representatives from these families offers to reveal the evolutionary history of central nervous octavolateralis pathways in ostaryophysan teleosts. Thus, having already treated the soley mechanosensitive cyprinids, we shall now consider the central nervous lateral line centers in passive electrosensory silurids and active electrosensory gymnotoids.

The catfish rhombencephalic octavolateralis area displays in addition to five primary auditory nuclei (McCormick & Braford, 1993) and the primary mechanosensory MON, a very large, laterally situated electrosensory lateral line lobe (Figs. 7b, b'; ELL; Finger, 1986). Unlike in other electrosensory vertebrates discussed above (Figs. 2, 3), both the anterior and the posterior lateral line nerve ganglia (ALLN and PLLN) give rise to electrosensory fibers in addition to mechanosensory fibers (Fig. 7; Tong & Finger, 1983; Finger & Tong, 1984; Northcutt et al., 2000). The ALLN and PLLN projections are segregrated within the MON, the ELL and the eminentia granularis with the head represented medially and the trunk laterally in each structure. There is some very limited overlap between lateral line and octaval projections in the magnocellular and part of the descending octaval nuclei. Both MON and ELL are covered by a molecular layer (cerebellar crest) which receives tangential fibers originating in granule cells of the eminentia granularis and the caudal cerebellar lobe. However, the primary lateral line nerve fibers terminate in deeper layers of MON and ELL. Lateral lemniscal projections from the catfish MON and ELL arise from crest cells at the boundary between cerebellar crest and deeper layers of MON and ELL. The MON has bilateral projections through the lateral lemniscus to the midbrain ventral toral nucleus

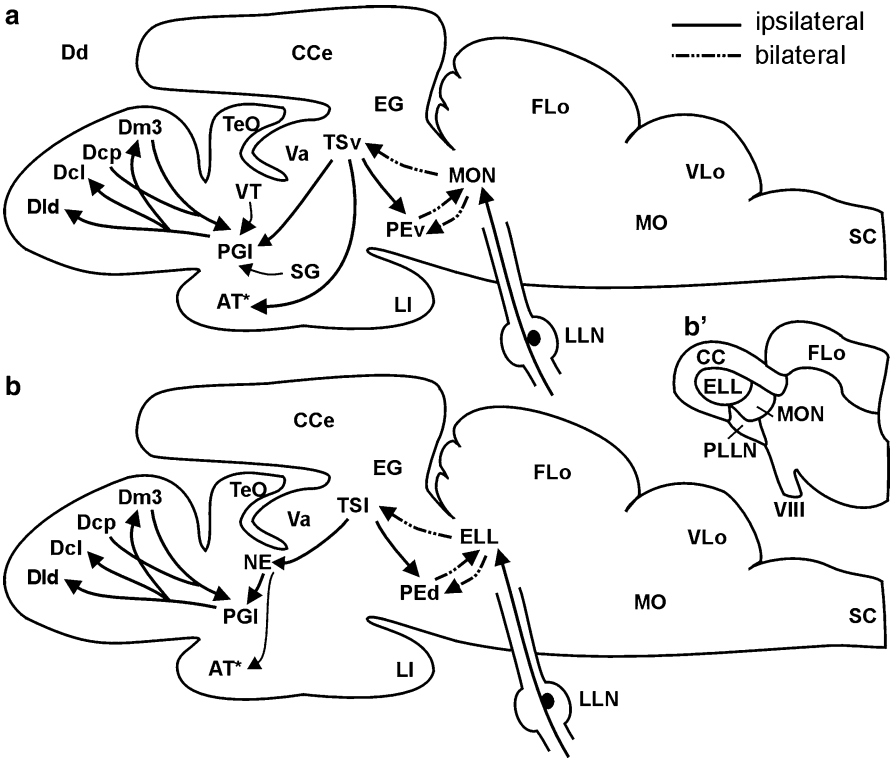

Fig. 7 Lateral line pathways in silurids. Schematic lateral views of catfish brain showing mechanosensory (**a**) and electrosensory (**b**) lateral line pathways (for citations see text). The hypothalamic auditory nucleus marked by an asterisk also receives mechano- (from TSv) and electrosensory (from NE) input and projects to different medial pallial subzones (Dm2/Dm4) than PGl does (see text). The illustrated lateral line nerve (LLN) represents both anterior and posterior nerves. Input from the eminentia granularis and caudal cerebellar lobe to MON and ELL is not shown (see text). (**b'**) is a transverse section through one side of catfish electrosensory lateral line lobe and medial octavolateralis nucleus. Abbrevations: AT anterior tuberal nucleus, CCe corpus cerebelli, Dcl, Dcp, Dld, Dm3 centrolateral, centroposterior, laterodorsal, medial zone 3 of pallial area dorsalis telencephali, EG eminentia granularis, ELL electrosensory lateral line lobe, FLo facial lobe, LI lobus inferior, LLN lateral line nerves, MO medulla oblongata, MON medial octavolateralis nucleus, NE nucleus electrosensorius (pretectum), PEd, PEv dorsal, ventral preeminential nucleus, PGl lateral preglomerular nucleus, PLLN posterior lateral line nerve, SC spinal cord, SG subglomerular nucleus, TeO tectum opticum, TSl, TSv lateral, ventral nucleus of torus semicircularis, Va valvula cerebelli, VT ventral thalamus, VLo vagal lobe, VIII octaval nerve

(TSv), ventral preeminential nucleus and optic tectum (the latter connection not shown in Fig. 7a). The silurid TSv, in turn, projects via the ventral preeminential nucleus back to MON (Finger & Tong, 1984).

Pioneering neuroanatomical and electrophysiological work (Knudsen, 1977; Tong, 1982; Tong & Finger, 1983) established that similar parallel electrosensory

pathways to the midbrain exist in catfishes. The silurid torus semicircularis has in addition to the central (TSc; auditory), medial pretoral (MPN; auditory) and ventral (TSv; mechanosensory) nuclei, which are also present in cyprinids, a large lateral toral nucleus (TSl; Knudsen, 1977; Finger, 1986; Striedter, 1991). The TSl receives the bulk of efferents from the ELL and projects via the dorsal preeminential nucleus back to ELL (Fig. 7b). The preeminential fibers enter the cerebellar crest of MON and ELL tangentially. Interestingly, New & He (1998) did not confirm a toral input to the catfish preeminential nucleus, but did report input to it from primary auditory nuclei. Early neuroethological studies also demonstrated that there is a lateral line mechanosensory pathway from TSv via the anterior tuberal nucleus (then interpreted as "thalamic") to the medial pallial zone (Finger, 1980; Finger & Bullock, 1982). Subsequent studies explored the auditory, mechanosensory and electrosensory pathways from midbrain to forebrain in silurids and other ostariophysan teleosts.

The catfish diencephalic lateral preglomerular nucleus receives its major input from the mechanosensory TSv (Striedter, 1992). Only a small ventral division of the catfish PGl receives input from the (auditory) MPN (Striedter, 1992), which is highly reminiscent of dorsal (multisensory) and ventral (auditory) PGl divisions in cyprinids (see Section 4.2). Also similar to cyprinids, PGl receives minor inputs from the ventral thalamus and subglomerular nucleus; however, tectal and retinal inputs to PGl have not been reported for catfish (Striedter, 1990). An additional dense input to the catfish PGl arises from the pretectal nucleus electrosensorius (NE; Fig. 7b; see below). Since a weak input from the central pretectal nucleus to PGl is also seen in goldfish (Striedter, 1992; although not confirmed by Yamamoto & Ito, 2008), NE might have evolved from a pretectal cell population that separated from the central pretectal nucleus in silurids (and gymnotoids). As seen in cyprinids, the silurid central posterior thalamic (CP) and anterior tuberal nuclei (AT) are targets of both the auditory TSc and MPN in the midbrain. The mechanosensory TSv additionally projects to AT in the catfish (Finger, 1986; Striedter, 1991), but an input of TSv to the catfish CP has not been reported. The AT in turn interconnects reciprocally with pallial zones Dm2 and Dm4, which are distinct from the PGl projection zones (Striedter, 1991). The latter are in the medial, central and lateral pallial zones (Dm3, Dcl, Dld), and projections back to PGl arise from the central (Dcp) and medial divisions (Dm3) (Striedter, 1991). Since doubts have been raised about whether the dorsal pallial division (Dd) is really a separate pallial division (Mueller et al., 2011), Dd is assumed here to be part of Dm.

Silurid electrosensory pathways run from the TSl to the (pretectal) nucleus electrosensorius, which then, via the PGl, reach the pallium (Dm3, Dcl, Dld). The NE also projects weakly to the anterior tuberal nucleus (AT; Striedter, 1991) indicating that auditory, mechanosensory and electrosensory information is processed there. Also at the level of the diencephalic PGl and telencephalic pallial zones, the mechanosensory and electrosensory pathways appear to converge (Fig. 7). Thus, it is not clear whether and how parallel processing is maintained between lateral line electro- and mechanosense (and audition) in the forebrain of catfishes.

4.3.2 Gymnotoids

The sistergroup of silurids, the weakly electric gymnotoids, possess in their skin from head to tail not only mechanosensory neuromasts and electrosensory ampullary organs, but also two types of electrosensory tuberous organs, called T-units (phase coders, which fire in synchrony with the EOD) and P-units (probality coders, which reflect EOD amplitude modulations in their discharge probability) (Heiligenberg, 1984; Carr & Maler, 1986; Bell & Maler, 2005). Only information on wave-type gymnotoids (which emit continuous EODs at highly regular, but individual, frequencies) will be discussed here, since far less is known on pulse-type species (which emit pulse-like EODs). Unlike in catfish, the peripheral electrosensory lateral line fibers in gymnotoids originate exclusively in the anterior lateral line nerve ganglia (with a recurrent lateral line ramus innervating the body trunk); the central fibers terminate in a gigantic electrosensory lateral line lobe (ELL, Figs. 8b, b"). The mechanosensory fibers from both ALLN and PLLN project topographically to the small MON (Fig. 8a; Maler et al., 1974; Vischer et al., 1989; Lannoo et al., 1989). Historically, the ELL and MON were named posterior and anterior lateral line lobe, respectively. Primary electrosensory fibers enter the deep neuropil layer of ELL, with T-unit fibers synapsing (electrotonically) on spherical cell bodies and P-unit fibers terminating (with chemical synapses) on basal dendrites of basilar pyramidal cells (E-cells which are excited by a rise in EOD amplitude) and, via (inhibitory) granular interneurons, on nonbasilar pyramidal cells (I-cells which are excited by a fall in EOD amplitude) (Heiligenberg, 1986; Bell & Maler, 2005). The medial segment of the ELL, where ampullary organ fibers terminate (see below), does not contain spherical cells (Maler, 1979). Cell bodies of basilar and nonbasilar pyramidal cells lie between molecular and deeper ELL layers (comparable to crest cells, see Sections 3; 4.2). Additional primary lateral line nerve projections reach the eminentia granularis, which, in turn, projects back to the contralateral superficial molecular layer of the ELL (Maler et al., 1974; Bell & Maler, 2005).

Neuroanatomical and electrophysiological studies revealed that the gymnotoid ELL exhibits four complete maps of the electrosensory body surface in medial, centromedial, centrolateral and lateral segments (Fig. 8b, b"), with the medial one receiving ampullary organ information and the remaining three segments receiving tuberous organ information (Heiligenberg & Dye, 1982; Carr & Maler, 1986; Lannoo et al., 1989). Thus, each electrosensory fiber that innervates a tuberous organ terminates in all three maps on pyramidal or spherical cells with varying degrees of convergence dependent on peripheral receptor density (the head is consistently overrepresented). The maps differ in size and, thus, in spatial resolution (Carr et al., 1982; Shumway, 1989). Furthermore, centromedial map lesions lead to deficits in the jamming avoidance response (JAR, see below), whereas lateral map lesions impair electrocommunication responses (Metzner & Juranek, 1997). While the head is always represented in the same orientation in each map, the dorsoventral axis is inverted in centromedial and lateral segments compared to the other two segments (v for ventral in Fig. 8b).

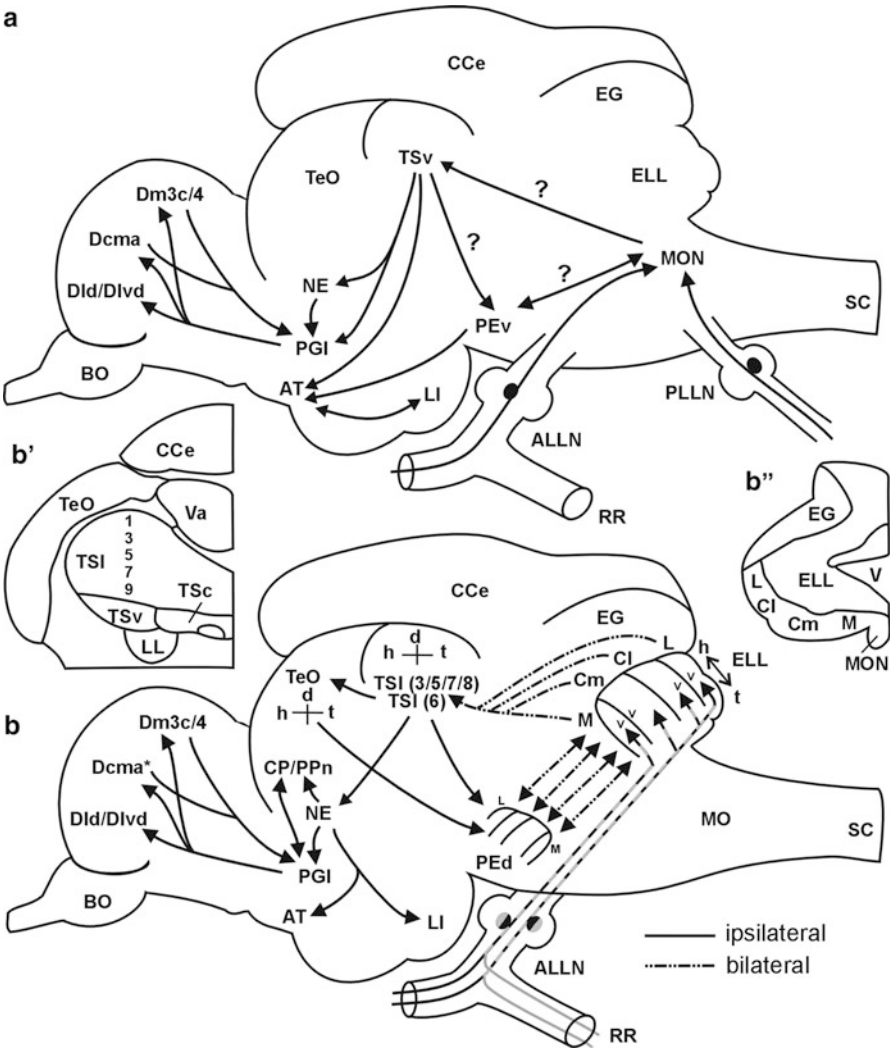

Fig. 8 Lateral line pathways in gymnotoids. Schematic lateral views of South-American knifefish brain showing (**a**) mechanosensory and (**b**) electrosensory lateral line pathways (for citations see text). Note that each of the four segments of electrosensory lateral line lobe and preeminential nucleus contains a map of the fish's entire electrosensory body surface (h: head, t: tail) with alternating dorsoventral orientation (v: ventral). ELL maps are shown as they appear in dorsal view on the right side of the body, whereas PEd maps are shown for the left body side. (**b**') is a transverse section through one side of the midbrain showing toral divisions. (**b**") is a transverse section through one side of ELL-EG, showing the arrangement of segments. Ampullary organs are represented in the medial segment and tuberous organs in the remaining segments. The lateral torus semicircularis and optic tectum each display a single, merged electrosensory map. *The central pallial zone (Dcma) projects to optic tectum and lateral torus semicircularis (not drawn, see text). Abbrevations: ALLN anterior lateral line nerve, AT anterior tuberal nucleus, BO bulbus

Pyramidal and spherical cells are the efferent cells of the ELL. They project bilaterally (mostly contralaterally) to the lateral torus semicircularis (TSl, also called TSd). Pyramidal cells (representing P-unit and ampullary organ information) also give off collaterals to the dorsal preeminential nucleus (PEd; Carr et al., 1981; Scheich & Ebbesson, 1981; Maler et al., 1982). Topographical information from several body maps (P-units, ampullary organ, but not T-units) is maintained in the efferent projections to the dorsal preeminential nucleus (Maler et al., 1982; Sas and Maler, 1983) and the maps are, thus, processed there in parallel (Fig. 8b). In contrast, the four ELL maps converge to a single map in the lateral torus semicircularis, with different electroreceptor type information segregated into different layers (Figs. 8b, b'; T-types in layer 6, P-types in layers 3/5/7/8, ampullary organs in 3 and 7; Carr et al., 1981; Rose & Heiligenberg, 1985; Carr & Maler, 1986; Carr et al., 1986). However, layer 6 neurons extend axons into layer 5/7 and also dendrites into adjacent layers. Thus, layer 6 neurons may receive information from and influence neurons dealing with P-type signals, indicating a first interaction of T- and P-systems. Both diffuse inhibitory and topographic excitatory (reciprocal) projections arise from the dorsal preeminential nucleus and terminate in the ELL. That is, inhibitory bipolar cells terminate on pyramidal cell bodies, while excitatory stellate cells synapse in the lower molecular layer of the ELL on pyramidal cell apical dendrites. Granular cells of the eminentia granularis also terminate in the ELL (upper molecular layer contralaterally/ventral molecular layer ipsilaterally), whereas eurydendroid cells (the teleostean homologous cells of efferent deep cerebellar nuclei) of the eminentia granularis project contralaterally to the TSl. The PEd furthermore connects reciprocally to the eminentia granularis (EG) bilaterally (connections with the latter not shown in Figure 8b; Sas & Maler, 1987; Bell & Maler, 2005). The TSl projects heavily back to the preeminential nucleus (topography unresolved). This descending TSd-PEd-EG pathway provides the ELL with electrosensory and proprioceptive feedback that helps to maintain sensitivity (gain control) in ELL. The topographical reciprocal connections between PEd and ELL may function as an attentional "searchlight" (Bastian, 1986a, b; Heiligenberg, 1990; Bell & Maler, 2005).

Fig. 8 (continued) olfactorius, Cl, Cm centrolateral, centromedial segment of ELL (tuberous organs), CCe corpus cerebelli, CP/PPn central posterior thalamic/prepacemaker nucleus, d dorsal, Dcma anterior part of centromedial zone of pallial area dorsalis telencephali, Dld, Dlvd, laterodorsal, dorsal part of lateroventral zone of pallial area dorsalis telencephali, Dm3c/4 two divisions of medial zone of pallial area dorsalis telencephali , EG eminentia granularis, ELL electrosensory lateral line lobe, h head, L lateral ELL segment (tuberous organs), LI lobus inferior, LL lateral lemniscus (lateral longitudinal fascicle), M medial ELL segment (ampullary organs), MO medulla oblongata, MON medial octavolateralis nucleus, NE nucleus electrosensorius (pretectum), PEd, PEv dorsal, ventral preeminential nucleus, PGl lateral preglomerular nucleus, PLLN posterior lateral line nerve, RR recurrent ramus of ALLN, SC spinal cord, t tail, TeO tectum opticum, TSc, TSl, TSv central, lateral, ventral nucleus of torus semicircularis, v ventral, V fourth ventricle, Va valvula cerebelli

The gymnotoid TSl also projects ipsilaterally and topographically to central layers of the optic tectum (Sas & Maler, 1986a, b; Heiligenberg & Rose, 1987; Carr & Maler, 1986). Retinal input to the tectum is located more superficially and is in register with electrosensory input (Bastian, 1982; Heiligenberg & Bastian, 1984). The optic tectum also feeds back into the PEd and has descending connections, via the brain stem reticular formation, to the spinal cord (not shown; Behrend & Donicht, 1990). The usual role of the optic tectum is object localization and control of orienting behaviors towards objects of interest (Stein and Rowland, 2011).

Further, the TSl – but not the optic tectum (Keller et al., 1990) - projects to a nucleus dorsal to the preglomerular nucleus, the pretectal nucleus electrosensorius (NE; Carr et al., 1981), probably without maintaining topography. The NE is a complex of four neuronal subpopulations and has a particularly important role in the jamming avoidance response (JAR) through its output to the prepacemaker nucleus (Keller et al., 1990; Bell & Maler, 2005). Through the JAR wave-type species move their EOD frequency slightly away from the frequency of conspecific EODs to minimize signal interference (Heiligenberg, 1986). One subpopulation of NE that processes electrosensory and one that processes acoustic/mechanosensory information also project to the hypothalamic anterior tuberal nucleus and inferior lobe (Keller et al., 1990).

There is controversy whether NE in gymnotoids also projects to the lateral preglomerular nucleus. This connection was found by Striedter in chocolate ghosts (*Apteronotus leptorhynchus*; Striedter; 1992), similar to the situation in silurids (see Section 4.3). Also retrograde tracing from the inferior lobe yielded no retrograde cells in the silurid NE (Striedter, 1991). However, the latter were seen in another gymnotoid (glass knifefish; *Eigenmannia virescens*; Keller et al., 1990) and, thus, NE efferents to the PGl were seen as misinterpreted interrupted fibers to the hypothalamic inferior lobe.

Because there are no direct telencephalic projections from NE (Keller et al., 1990; Wong, 1997), one may wonder how electrosensory information would reach the telencephalon in gymnotoids, if not through PGl, as the anterior tuberal nucleus has no pallial projections in gymnotoids (Giassi et al., 2007), unlike in silurids and cyprinids (see Sections 4.2; 4.3.1). Various gymnotoid pallial areas clearly take part in higher order memory processes related to recognition of conspecifics and are dependent on electrocommunication signals (Harvey-Girard et al. 2010). In any case, the gymnotoid PGl has heavy projections to the telencephalic pallium (Fig. 8b; Striedter, 1992; Zupanc, 1997; Corrêa et al., 1998). Interestingly, the central pallial zone not only projects to the optic tectum, but also to the TSl (not drawn; Corrêa et al., 1998).

The mechanosensory lateral line fibers coming from ALLN (head) and PLLN (trunk; Fig. 8a) terminate separately in MON and eminentia granularis (Maler et al., 1974). Unfortunately, the connections of the gymnotoid MON have not been investigated. However, gymnotoids possess a ventral preeminential nucleus (Sas & Maler, 1983) as do silurids, and a mechansensory division of the torus semicircularis (TSv; Matsubara et al., 1981; Scheich & Ebbesson, 1981; Carr & Maler, 1985). The TSv projects to PGl (Striedter, 1992), to the anterior tuberal

nucleus (Giassi et al., 2007) and to a division of the NE (Keller et al., 1990; see above). The anterior tuberal nucleus also receives input from the mechanosensory ventral preeminential nucleus and the hypothalamic inferior lobe (Giassi et al., 2007). Because of the convergences of mechanosensory and electrosensory input to PGl, their relative components within the ascending projections of PGl to the telencephalic pallium can not be discriminated from one another, similar to the situation in silurids.

4.3.3 Mormyrids

Finally, regarding the African mormyriforms, the focus will be on pulse-type EOD emitting mormyrids which are the majority of species - except for the wave-type EOD emitting Aba (*Gymnarchus niloticus*), the only gymnarchid. Like gymnotoids, mormyrids have mechanoreceptive neuromasts, ampullary organs, and two types of tuberous organs (knollenorgans, mormyromasts). However, mormyrid primary lateral line mechanosensory and electrosensory fibers are present in both anterior and posterior nerve ganglia (Fig. 9; Maler et al., 1973a, b; Bell & Russell, 1978; Bell, 1981a). Contrary to most other teleosts, octaval and lateral line nerves both project strongly to the medial octavolateralis nucleus (MON/anterior lobe of Bell, 1981a) and to the anterior octaval nucleus, but with limited overlap within these nuclei; additional minor overlapping projections are seen in the descending octaval nucleus and the eminentia granularis (Bell, 1981a). Therefore, the medial (auditory) part of the mormyrid MON has been interpreted as part of the descending octaval nucleus (McCormick (1992, 1999). Electrosensory fibers terminate in the ELL (posterior lobe of Bell, 1981a) which consists of a cortex and a nucleus of the ELL (Figs. 9c, d; 10a). Surprisingly, there is a small contingent of contralateral primary projections to both MON and ELL (only to cortex; Bell, 1981a).

The mormyrid ELL cortex consists of three zones, each with a somatotopic map of the electrosensory body periphery (note inversion of dorsoventral axis in two lateral zones compared to medial zone; Figs. 9c; 10a). Ampullary organs are represented in the ventrolateral zone and mormyromasts (tuberous receptors for active electrolocation) in the medial and dorsolateral zones (Bell & Russell, 1978; Bell & Szabo, 1986). Mormyromasts contain two sensory cell types, whereby A-type cells project through their innervating fibers to the medial ELL zone (concerned with resistive, dead objects), and B-type fibers project to the dorsolateral zone (concerned with capacitive, living objects; Bell et al., 1989; von der Emde, 1998). A critical difference to gymnotoids is that the fibers innervating the second tuberous receptor type, the knollenorgans (electrocommunication), project (electrotonically) to a separate structure within the ELL, but outside of the cortex, the nucleus of the ELL, which is located medially to the ventrolateral cortical zone (Fig. 10a). Its ascending connections are largely kept in parallel to those of the mormyromast/ampullary organ pathway at least up to the torus semicircularis (unlike in gymnotoids, where P and T-type information converges onto certain TSl cells; see Section 4.3.2).

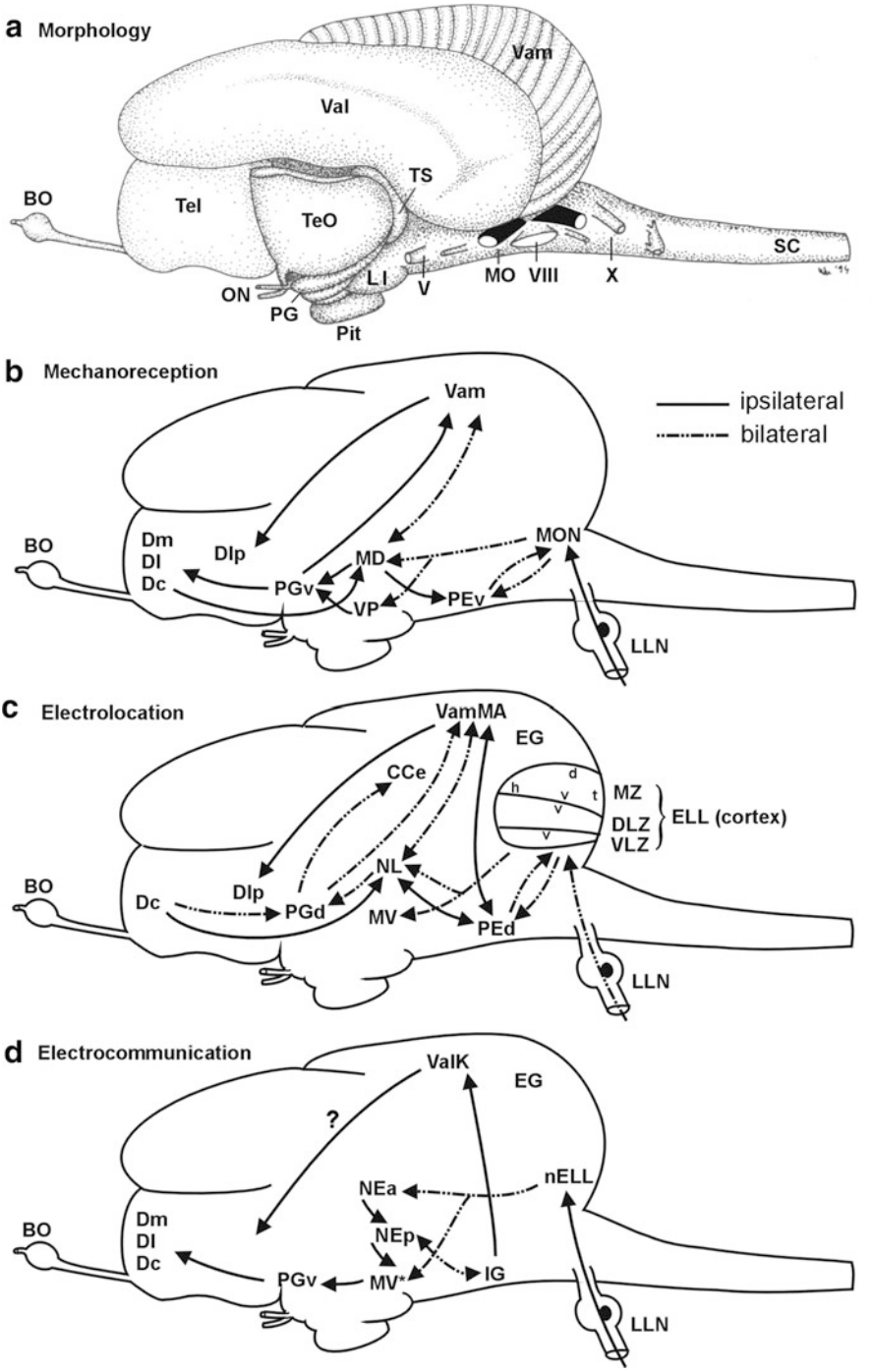

Fig. 9 Lateral line pathways in mormyrid fishes. (**a**) Lateral view of the mormyrid brain (*Gnathonemus petersii*; elephantnose fish). Anterior and posterior lateral line nerves are indicated

The circuitry within the mormyrid ELL is even more complex than in gymnotoids, but nevertheless similar in that it receives eminentia granularis (granular cell) input in its upper level of the superficial molecular layer and (dorsal) nucleus preeminentialis input more deeply. A ganglionic cell layer (Fig. 10a) follows more basally and includes one of the excitatory efferent ELL cell types, the large ganglionic (I- cells: inhibited by stimulation). The second efferent - large fusiform - cell type (E-cells: excited by stimulation) lies in the even deeper granular layer. Here, also granular cells (inhibitory and excitatory ones) are located. They are the exclusive recipients of primary afferent nerve fibers, which enter the ELL basally. The granular cells, in turn, synapse on the two efferent ELL cell types, but also involve loops via (inhibitory) medium ganglionic cells (again E-cells and I-cells) to the efferent cells (Grant et al., 1996; Meek et al., 1999; Bell & Maler, 2005).

The ascending mormyromast/ampullary organ (electrolocation) pathways (Fig. 9c) will now be considered. The mormyrid torus semicircularis contains five nuclei: a large lateral, and somewhat smaller exterolateral, mediodorsal, medioventral, and ventroposterior nuclei (Figs. 10 c-d). In addition to intrinsic commissural (intrazonal) and ispilateral interzonal (between MZ/DLZ) connections (not shown in Fig. 9), the ELL cortex has bilateral efferent projections to the lateral toral nucleus (NL), with collaterals to the medioventral toral nucleus (MV), as well as to the dorsal preeminential nucleus (PEd; Fig. 10b; Bell et al., 1981; Bell & Szabo, 1986; Grant et al., 1996). The heavy projection to NL and PEd is topographical. The three ELL cortical maps of mormyrids converge to one map in PEd (unlike in gymnotoids) and NL (as in gymnotoids). The ELL maps receive topographical reciprocal inputs from PEd medium sized core cells to the deep molecular layer, while small peripheral PEd cells project to the eminentia granularis, which in turn

Fig. 9 (continued) in black. The lateral line nerve (LLN) shown in (**b**) to (**c**) is meant to represent both nerves. Schematic lateral views of mormyrid brain showing (**b**) mechanosensory lateral line pathways, (**c**) mormyromast-ampullary organ electrosensory lateral line pathways (note that each of the three ELL zones contains a complete body map of the electrosensory skin periphery, with differing dorsoventral axes as indicated. Ampullary organs are represented in the ventrolateral zone and mormyromast A-type fibers in medial, and B-type fibers in dorsolateral zone), (**d**) knollenorgan electrosensory lateral line pathways (*MV also projects to ValK). For citations see text. Abbrevations: BO bulbus olfactorius, CCe corpus cerebelli, d dorsal, Dc, Dl, Dlp, Dm, central, lateral, lateroposterior, medial zone of pallial area dorsalis telencephali, DLZ dorsolateral zone of ELL, EG eminentia granularis, ELL electrosensory lateral line lobe, h head, LI lobus inferior, LLN lateral line nerves, MD mediodorsal nucleus of torus semicircularis, MO medulla oblongata, MON medial octavolateralis nucleus, MV medioventral nucleus of torus semicircularis, MZ medial zone of ELL, NEa, NEp anterior, posterior exterolateral nucleus of torus semicircularis, nELL nucleus of the ELL, NL lateral nucleus of torus semicircularis, ON optic nerve, PEd, PEv dorsal, ventral preeminential nucleus, PG preglomerular complex, PGd, PGv dorsal, ventral parts of preglomerular nucleus, Pit pituitary, SC spinal cord, t tail, Tel telencephalon, TeO tectum opticum, TS torus semicircularis, v ventral, ValK lateral leaf of valvula cerebelli (knollenorgan region), VamMA medial leaf of valvula cerebelli (mormyromast/ampullary region), VLZ ventrolateral, zone of ELL, VP ventroposterior nucleus of torus semicircularis, V trigeminal nerve, VIII octaval nerve, X vagal nerve

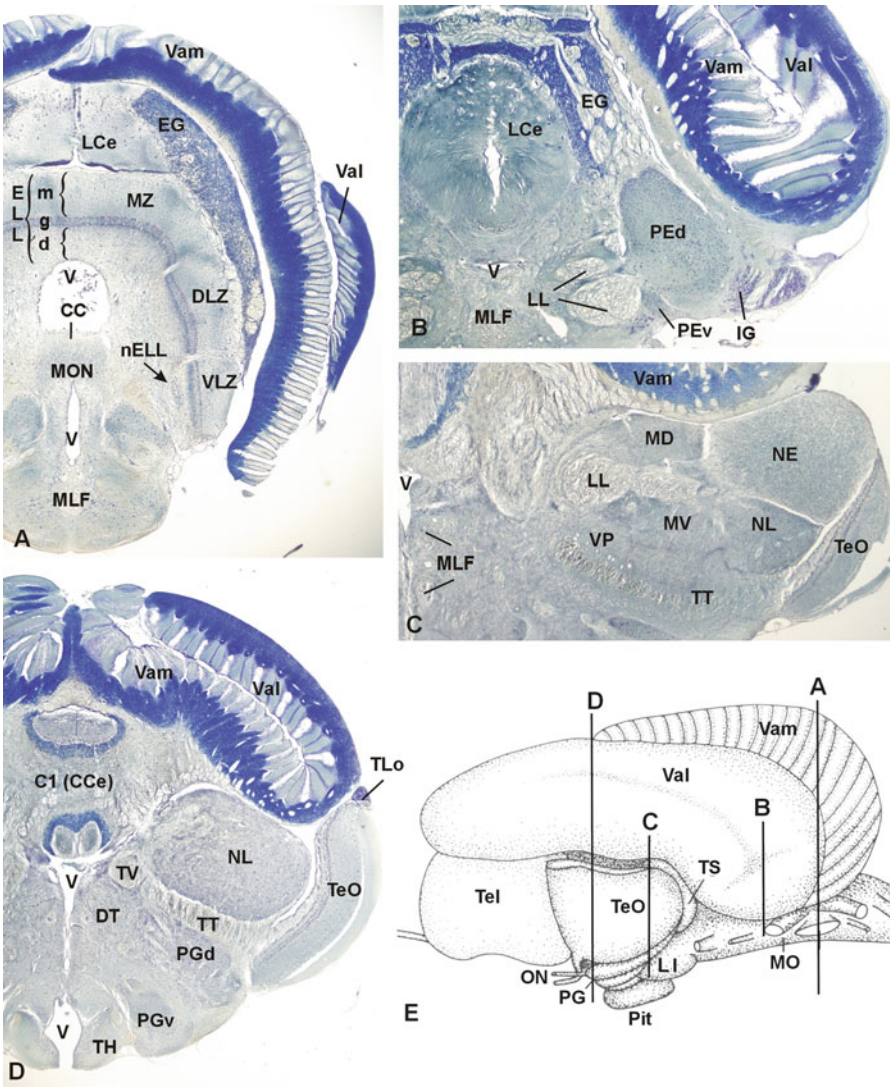

Fig. 10 Electrosensory and mechanosensory lateral line central nervous structures in a mormyrid fish, *Gnathonemus petersii*. Tranverse sections through (**a**) Electrosensory lateral line lobe (ELL) and mechanosensory medial octavolateralis nucleus (MON). Note dome-like structure of ELL below eminentia granularis/caudal cerebellar lobe and valvula cerebelli, as well as breaks between ELL cortex zones. (**b**) preeminential nucleus, (**c**) posterior level of torus semicircularis with all five toral nuclei. (**d**) anterior toral level showing diencephalic preglomerular complex and lateral toral nucleus (electrolocation). (**e**) Drawing of brain with section levels indicated. For citations see text. Abbrevations: CC crista cerebellaris, CCe corpus cerebelli, C1 lobe C1 of CCe, DLZ dorsolateral zone of ELL, d deep layers of ELL, DT dorsal thalamus, EG eminentia granularis, ELL electrosensory lateral line lobe, g ganglionic layer of ELL, IG isthmic granular population, LCe lobus caudalis cerebelli, LI lobus inferior, LL lateral lemniscus (lateral longitudinal fascicle), m molecular layer of ELL, MD, medial nucleus of torus semicircularis, MLF medial longitudinal

projects to the upper molecular ELL layer. The lateral toral nucleus is furthermore reciprocally and topographically connected with PEd (stronger input from PEd than output to PEd) and also has commissural projections (Finger et al., 1981; Bell & Szabo, 1986). The PEd, furthermore, acts - as in gymnotoids - via the eminentia granularis back on the ELL cortex (von der Emde & Bell, 1996; Meek et al., 1999) providing recurrent electrosensory feedback. Another such feedback circuit (similarly present in gymnotoids) runs from eminentia granularis (granular cells) via Purkinje and eurydendroid cells of the caudal cerebellar lobe to PEd and NL (Bell & Maler, 2005; Campbell et al., 2007; circuits involving the eminentia granularis and caudal cerebellar lobe are not shown in Fig. 9).

The NL also projects topographically to the optic tectum (not further considered) and to the diencephalon (dorsal preglomerular nucleus; PGd; Fig. 10d). Comparative considerations allowed for recognition of the preglomerular complex in mormyrids (Wullimann & Northcutt; 1990). Thus, the terms caudal, ventral, and dorsal preglomerular nuclei were introduced to replace formerly used names (posteroventral thalamic, anterior thalamic, and dorsal anterior pretectal nuclei, respectively) which is meanwhile widely accepted (von der Emde & Prechtl, 1999; Meek et al., 1999; Bell & Maler, 2005). Surprisingly however, the PGd does not project to the telencephalon as expected, but rather only receives an input from the central pallial zone (Dc; Wullimann & Northcutt, 1990). The PGd connects instead reciprocally with a particular area in the medial valvula cerebelli, as does the NL (with the valvula projecting additionally to PEd; Finger et al., 1981). Interconnections of NL (and likely also of PGd) with the valvula maintain topography. The medial valvula was recognized physiologically as related to mormyromast/ampullary organ information (VamMA; Russell & Bell, 1978). Unique among vertebrates is a direct connection of this electrolocation-related medial leaf of the valvula to the pallial telencephalon in mormyrids (lateroposterior pallial zone; Dlp; Wullimann & Rooney, 1990). Alternatively, ampullary organ/mormyromast information may reach the pallium via the medial toral nucleus (MV), since the latter receives ELL cortex input and projects to PGv, which, in turn has extensive projections to the pallium (Fig. 9c, d; Wullimann & Northcutt, 1990; von der Emde & Prechtl, 1999).

Regarding knollenorgan (electrocommunication) pathways (Fig. 9d), the nucleus of the ELL projects (non-topographically) to the anterior exterolateral toral nucleus (NEa), with collaterals to the MV (Enger et al., 1976;

Fig. 10 (continued) fascicle, MO medulla oblongata, MON medial octavolateralis nucleus, MV ventral nucleus of torus semicircularis, MZ medial zone of ELL, NE, NL, exterolateral, lateral nucleus of torus semicircularis, nELL nucleus of the ELL, ON optic nerve, PEd, PEv dorsal, ventral preeminential nucleus, PG preglomerular complex, PGd dorsal preglomerular nucleus, PGv ventral preglomerular nucleus, Pit pituitary, Tel telencephalon, TeO tectum opticum, TH tuberal hypothalamus, TLo torus longitudinalis, TS torus semicircularis, TT toro-preeminential tract, TV toro-valvular tract, V ventricle, Val, Vam lateral, medial leaf of valvula cerebelli, VLZ ventrolateral zone of ELL, VP ventroposterior nucleus of torus semicircularis

Szabo et al., 1983; Bell & Szabo, 1986). In MV, therefore, knollenorgan and mormyromast/ampullary organ information converges and both may reach via PGv the telencephalic pallium (see above; Fig. 9d). Moreover, the NEa synapses on neurons of the posterior exterolateral nucleus (NEp) which projects to an isthmic granular population (IG) ventral to PE and to MV. Interestingly, different from the medial valvular mormyromast/ampullary organ region (VamMA), a lateral valvular area has been shown physiologically to be knollenorgan related (ValK; Russel & Bell, 1978) and the latter receives differential input from the isthmic granular population and from MV (Haudegé-Carré, 1979; Finger et al., 1981; Bell & Szabo, 1986). Whether the ValK also projects directly to the telencephalon is unknown.

Critical for mormyrid descending motor pathways related to the generation of EODs (Carlson, 2002) are corollary discharge pathways which provide information on the reafference (the self-generated electric signal) to the ELL in addition to the primary sensory exafference (signals emitted by conspecifics). These corollary pathways filter out self-generated signals via inhibition in the nucleus of the ELL and also act in the ELL cortex in the discrimination of reafference versus exafference (Heiligenberg, 1984; Bell and Szabo, 1986; Meek & Grant 1994).

As mentioned above, the MON (Fig. 10a; previously anterior lateral line lobe; Bell, 1981a; Haugedé-Carré, 1983) receives primary octaval (medially) as well as lateral line mechanosensory projections (laterally) and its efferent connections thus, include auditory as well as mechanosensory pathways (Fig. 9b). However, these are segregated up into the mediodorsal toral nucleus (MD; Bell, 1981b; Haudegé-Carré, 1983; Kozloski & Crawford, 1998). The MON also has less massive collateral projections to the ventroposterior toral nucleus (VP) and reciprocal connections with the small ventral preeminential nucleus (PEv; Fig. 10b). The ascending connections of MD (both auditory and mechanosensory) and VP reach the ventral preglomerular nucleus (PGv; Bell, 1981b; von der Emde & Prechtl, 1999) which, in turn, projects to the pallium (Wullimann & Northcutt, 1990). Sensory evoked potentials and multiunit spike responses in extensive medial, central and lateral pallial areas (Dm, Dc, Dl) have demonstrated that the mormyrid telencephalic pallium displays largely unimodal sensory fields (visual, auditory, electrosensory and mechanosensory lateral line), with minor overlapping (multimodal) areas (Prechtl et al., 1998). Furthermore, nonoverlapping anterior auditory and posterior mechanosensory portions of the medial pallial area (Dm) both receive input from (presumably different cells within) PGv (von der Emde & Prechtl, 1999), leaving no doubt that mechanosensory lateral line, as well as auditory, information reaches the pallium via PGv. The MD and PGv have also efferents to the medial cerebellar valvula (Finger et al., 1981). With the exception of these valvular connections, the mechanosensory lateral line circuitry just described is highly comparable to such pathways seen in other (electrosensory and non-electrosensory) teleosts (compare Fig. 9 to Figs. 6–8). In summary, the mormyrid brain is highly consistently documented both physiologically and anatomically to display parallel lateral line (and octaval) sensory pathways ascending in parallel from brain stem to telencephalic pallium.

Beyond the remote phyletic distribution of weakly electric organs and multiple electroreceptor types in distantly related mormyrids and gymnotoids, various differences in their nervous systems reveal an independent evolutionary origin. In gymnotoids all electroreceptors (but not the mechanoreceptive neuromasts) are innervated exclusively by the anterior lateral line nerve root (Fig. 8), whereas in mormyrids (and ironically in silurids), the head electroreceptors are innervated by the anterior and those of the body trunk by the posterior lateral line nerve root (Figs. 7, 9). Whereas the electrosensory torus semicircularis (TSl) is laminated in gymnotoids (Fig. 8), it is subdivided into distinct nuclei in mormyrids (NL, NEa, NEp, MV; Fig. 10). An enlargement of the cerebellum occurs in both groups, involving the corpus cerebelli in gymnotoids (Fig. 8) and the valvula cerebelli in mormyrids (Figs. 9, 10).

Unique among electrosensory teleosts is that the cerebellar valvula (and corpus, i.e., C3) in mormyrids receives input from various centers of the ascending pathways of mechanosensation, electrolocation and electrocommunication (Figs. 9b, c, d; Finger et al., 1981; Meek et al., 1986). These interconnections with the cerebellum clearly represent a specialisation of mormyrids (Wullimann & Northcutt, 1990). This teleost family has extraordinarily large brains (Fig. 9a) and the major reason for it is the gigantic cerebellar valvula (Meek et al., 1992, 2008), half of which is involved with electrosensory processing (Finger et al., 1981, Bell & Szabo, 1986; see above).

Furthermore, the connections from midbrain to forebrain differ somewhat between gymnotoids and mormyrids. A diencephalic preglomerular nucleus (PGl, PGv) is always involved at the diencephalic level in the ascending mechanosensory lateral line pathways in teleosts (Figs. 6–9). This also seems to apply for electrosensory pathways in silurids and gymnotoids (PGl), although a (pretectal) nucleus electrosensorius is synaptically intermittent in these groups. In mormyrids, one (minor) electrosensory pathway runs via MV and PGv to pallium. However, the preglomerular nucleus recipient of the bulk of electrolocation information (PGd) does not project to the pallium, but instead seems to reach the telencephalon only via the medial cerebellar valvula (Fig. 8c). Thus, the mormyrid PGd/PGv may have arisen from an ancestral, soley mechanosensory population. These and many other differences corroborate the phylogenetic fact that mormyrids and gymnotoids do not share a common ancestor with the physical outfit necessary for active electrolocation.

5 Lobe -Finned Fishes: Coelacanths, Lungfishes, Amphibians

Lobe finned-fishes (sarcopterygians) include all fossil and extant lungfishes and actinistians (i.e., the coelacanth *Latimeria chalumnae*; Fig. 1), as well as all solely fossil lobe-finned fish taxa, for example the osteolepiforms. Among the latter fossils

are those most closely related to tetrapods which themselves are included in the sarcopterygians (Fig. 1). All non-tetrapod sarcopterygians possess both components of the ancestral lateral line system, i.e., electrosensitive ampullary organs as well as mechanosensitive canal and free neuromasts, clearly sharing common ancestry within vertebrates (Bemis & Hetherington, 1982; Jørgensen, 1991; Northcutt & Bemis, 1993). Among sarcopterygians, only lungfishes have ampullary organs on the trunk in addition to the head (Northcutt, 1986b). Among tetrapods, only amphibians display an electrosensory (ampullary organs) and mechanosensory (free neuromasts, but never lateral line canals) lateral line system (Fritzsch, 1989; Schlosser, 2002). Most larval and adult urodeles have both electro- and mechanosensory lateral line sensory modalities, with some notable exceptions in plethodontid salamanders (Fritzsch & Münz, 1986; Fritzsch, 1988a, 1989; Northcutt, 1992). Caecilians (gymnophionans) also have ampullary organs and neuromasts as larvae, but lose them as adults (Hetherington & Wake, 1979; Fritzsch et al., 1985; Fritzsch & Münz, 1986). Larval gymnophionans of the genus *Typhlonectes* only have ampullary organs, but no neuromasts (Fritzsch, 1989). Anurans never have ampullary organs, but anuran tadpoles retain a mechansosensory lateral line system. In various anuran taxa (mostly in pipids) the mechanosensory lateral line system is maintained into adulthood, for example in the African clawed frog *Xenopus laevis*. This retention is correlated with an adult aquatic lifestyle and is likely a secondary reversal within anurans (Fritzsch et al., 1987; Fritzsch, 1988b). Thus, an electrosensory and mechanosensory lateral line system is basally present in amphibians. In contrast, all amniotes lack any trace of lateral line peripheral and central nervous structures and these are believed to have been lost with the terrestrial life style (notably independently of similar losses in amphibians).

In all extant sarcopterygians, lateral line electroreceptors and mechanoreceptors coincide with the presence of a DON and a MON, respectively in the octavolateralis area dorsal to the octaval column (Northcutt, 1980b, 1986b; Fritzsch, 1988a, b; Will, 1989). However, almost nothing is known regarding the central anatomy of the lateral line system in non-tetrapod sarcopterygian and the focus will therefore be on (tetrapod) amphibians. As in the basal gnathostome pattern, larval and adult urodeles and larval gymnophionans have electrosensory ganglion cells only in the anterior lateral line nerve and these fibers enter the DON via the dorsal root (Fig. 11; Fritzsch, 1981; Fritzsch et al., 1985; Fritzsch, 1988a, b). Naturally, anurans lack this electrosensory projection, but anuran tadpoles and some adult forms (see above) share with gymnophionans and urodeles primary mechanosensory lateral line projections which reach via ALLN and PLLN the MON (usually called intermediate nucleus in amphibians), and the small eminentia granularis (Fig. 11; Fritzsch et al., 1984; Will et al., 1985a; Simpson et al., 1986). Octaval (saccular) projections reach also the most ventral zone of the intermediate nucleus. Overall, urodeles represent best the ancestral situation of the lateral line system in amphibians.

In adult *Xenopus laevis*, second order connections of the lateral line related intermediate nucleus, apart from commissural projections, consist of the main ascending lateral lemniscal projection to the ventrally located magnocellular

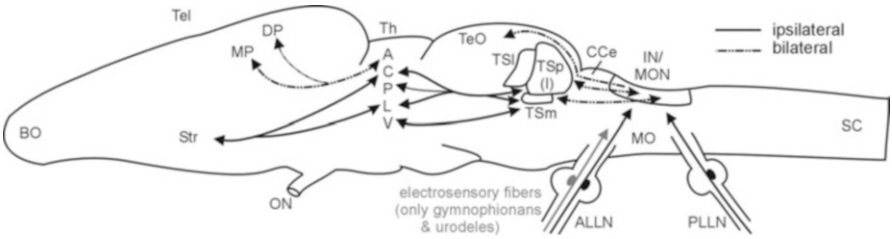

Fig. 11 Schematic lateral view of the brain of *Xenopus laevis* (after Edwards and Kelley, 2001) with mechanosensory lateral line pathways indicated (see text for citations). Grey arrow indicates primary electrosensory input in gymnophionans and urodeles from head ampullary organs to dorsal octavolateralis nucleus (not shown); its higher order connections are unknown. Note that MON (IN) has commissural connections (Will, 1988, 1989), that all parts of the torus semicircularis project to the optic tectum (Zittlau et al., 1988), and that the optic tectum projects to the lateral thalamus, all of which is not indicated in the figure. Primary projections after Lowe and Russell (1982) and Altman & Dawes (1983). Abbreviations: A, C, L, P anterior, central, lateral, posterior dorsal thalamic nucleus, ALLN anterior lateral line nerve, BO bulbus olfactorius, DP dorsal pallium, IN intermediate nucleus (=MON), MO medulla oblongata, MON medial octavolateralis nucleus, MP medial pallium, ON optic nerve, PLLN posterior lateral line nerve, SC spinal cord, Str striatum, Tel telencephalon, TeO tectum opticum, Th thalamus, TSl, TSm, TSp laminar, principal, magnocellular nucleus of torus semicircularis, V ventral thalamus

nucleus of the torus semicircularis (TSm) and, less extensively, to the optic tectum (Fig. 11; Will et al., 1985b; Zittlau et al., 1988; Will 1989). However, both neuroanatomy as well as neurophysiology in *Xenopus* indicates that, in addition to TSm, also the lateral part of the principal toral nucleus (TSp(l)) receives lateral line input from the intermediate nucleus (Lowe, 1986; Edwards & Kelley, 2001; Behrend et al., 2006). Both TSm and TSp have reciprocal connections with diencephalic nuclei, including strong ones with the central and lateral dorsal thalamic nuclei, and weak ones with the posterior dorsal thalamic nucleus, as well as with the ventral thalamus (Fig. 11; Edwards & Kelley, 2001). There are also efferent octavolateralis central cells innervating neuromasts in the amphibian lateral line system (Will, 1982; Münz & Claas, 1991).

In adult anuran species lacking a lateral line system, these midbrain toral and diencephalic thalamic divisions remain and serve auditory functions, with a central toral nucleus being the main recipient of ascending auditory brain stem projections (Feng & Lin, 1991; Luksch & Walkowiak, 1998) and a lateral toral nucleus (TSl) being the main auditory output to the central thalamic nucleus, but also to lateral, posterior and anterior thalamic nuclei and to the ventral thalamus (Hall & Feng, 1987; Wilczynski, 1988; Neary, 1988;). This indicates that none of the anuran toral nuclei are exclusively associated with lateral line processing. Finally, central and lateral dorsal thalamic nuclei project heavily to the anuran striatum (Wilczynski & Northcutt, 1983a), while the anterior dorsal thalamic nucleus projects to the medial and dorsal pallium (Neary, 1984; Laberge & Roth, 2007; Laberge et al., 2008), the latter most likely providing information of multisensory nature. These

telencephalo-thalamic connections are reciprocal (Wilczynski & Northcutt, 1983b; Westhoff & Roth, 2002). Thus, the telencephalic striatum may be reached through ascending connections of central and lateral thalamic nuclei also in *Xenopus* and convey lateral line information (Fig. 11). However, it remains unresolved if and where lateral line information is separately processed in the dorsal thalamus and striatum and, furthermore, how it would eventually reach pallial levels in anurans. In axolotls, mechano- and electrosensory stimuli lead to evoked potential or multiple unit responses only in the striatum, not in the medial pallium (Northcutt & Plassmann, 1989) which is consistent with the thalamo-telencephalic connections in anurans discussed above (see Fig. 11). The optic tectum in axolotls contains visual, as well as electrosensory and mechanosensory topographical maps (Bartels et al., 1990). Thus, it is also possible that lateral line information in amphibians reaches the striatum via a tecto-thalamic pathway. Overall, the situation in amphibians strongly contrasts with that in amniotes, where ascending sensory projections run via the thalamus to the dorsal pallium.

6 Conclusions and Summary

Despite variability in the craniate range of the mechanosensory and electrosensory lateral line periphery (see Chapter by Webb), there is a basal pattern of primary projections to the octavolataralis area. Generally, octaval (VIIIth nerve), mechanosensory and electrosensory fibers (lateral line nerves) terminate in a non-overlapping manner in their primary central nervous octavolateralis projection zones, i.e., ventral, intermediate and dorsal columns, respectively. Nevertheless, there are various cases of limited to more extensive overlap of mechanosensory and octaval projections both in the intermediate column and ventral column, as noted above for various taxa. The functional significance of these cases is discussed in a companion chapter (Braun & Sand).

The ancestral gnathostome pattern of how lateral line nerves enter the primary nuclei is that a dorsal root of the anterior lateral line nerve complex contains the electrosensory fibers (whose cell bodies are in anterior lateral line nerve ganglia), which terminate in the DON. This pattern is seen in cartilaginous fishes (Fig. 3), in non teleost ray-finned fishes (polypteriforms and chondrosteans) and, notably, in amphibians (urodeles and gymnophionans; Fig. 11). Teleost electroreception evolved newly after its loss in the ancestor of lepisosteiforms (gars) and amiiforms (bowfins; Fig. 5) and, not surprisingly, there is manifold deviation from the ancestral pattern just described. Teleostean electrosensory fibers may be in both anterior and posterior lateral line nerve ganglia (silurids, Fig. 7; mormyrids, Fig. 9), or only in the anterior lateral line nerve ganglion (gymnotoids, Fig. 8). The teleostean primary electrosensory lateral line lobe (ELL) is positionally and histologically different not only from the DON, but also between electrosensory teleosts, reflecting on convergent multiple evolutionary origins, which is also evident in differences of ascending pathways as discussed above. Lampreys too have electrosensory fibers only in the

anterior lateral line nerve ganglion complex (Fig. 2), strongly resembling the ancestral gnathostome pattern; their electrosensitive end buds, however, may or may not be homologous to ampullary organs.

Mechanosensory lateral line fibers always are contained both in anterior and posterior lateral line nerve ganglia in all craniates and project primarily to MON (Figs. 3–11). Myxinoids (eptatedrids), like most teleosts, have only a mechanosensory lateral line system, but no electrosensory system, indicating that the electrosense only evolved with the vertebrates, not the craniates (Fig. 1).

Regarding the functional neuroanatomy of ascending (lateral lemniscal) lateral line connections in craniates, the following may be said. Starting with the lateral line primary sensory nuclei (DON, MON), there is a parallel pattern of connectivity up to the midbrain in cartilaginous and ray-finned fishes. Predominant contralateral MON (and when present) DON projections reach the posterior alar midbrain (torus semicircularis). Ray-finned fishes have a feedback circuit via the preeminential nucleus, and nucleus B of cartilaginous fishes may be its homologue. While MON/DON projections to the torus semicircularis are also present in lampreys and amphibians, a feedback loop through a preeminential nucleus has not been desribed in either group. Since there is an uninterrupted anamniote evolutionary history of the mechanosensory lateral line system, its area of representation in the torus semicircularis may be concluded to be homologous among all (anamniote) craniates. The same may be said about the toral electrosensory centers with the exception of those in teleosts that arose newly.

More difficult is the situation in the diencephalon. Here three general areas are involved in lateral line processing: dorsal thalamus, posterior tuberculum and hypothalamus. In cartilaginous fishes – depending on the group – only one midbrain toral recipient nucleus, the posterior lateral thalamic nucleus (PLT; posterior tuberculum) has been described as (sharks and skates), while in rays, additionally to a PLT (electrosense), a posterior central thalamic nucleus (PCT; dorsal thalamus, mechanosense) has been noted (Fig. 4). The batoid hypothalamic lateral tuberal nucleus (mechanosense) does not have projections to the telencephalon. Thus, a key question remains whether and how parallel processing of lateral line electrosense and mechanosense does occur in the diencephalon of cartilaginous fishes.

Interestingly, in non-electrosensory teleosts and basal ray-finned fishes (as far as known), three diencephalic areas are also recipient of midbrain toral input, (1) the dorsal part of lateral preglomerular nucleus (PGld, posterior tuberculum), (2) the central posterior thalamic nucleus (dorsal thalamus) and (3) the anterior tuberal nucleus (hypothalamus). However, the major origin of lateral line projections to forebrain pallial areas (Dm: pallial amygdala; Dl: hippocampus homologue) is from the PGld. An unresolved question is whether the teleostean preglomerular area is of alar plate dorsal thalamic origin (Ishikawa et al., 2007) or of multiprosomeric alar and basal plate origin (Mueller & Wullimann, 2002), a question that will only be decided by fate studies. In silurids, gymnotoids and mormyrids, the lateral preglomerular area acquires a role as the main diencephalic projection area to the pallium which evolved independently for the electrosensory system in each taxon.

Lampreys and amphibians were reported to have a lateral line relay to the telencephalon in the dorsal thalamus only.

Finally, the major projection zones for electrosensory and mechanosensory lateral line information in the telencephalon would seem to be in the medial pallium (hippocampus homologue), at least in lampreys, cartilaginous fishes and ray-finned fishes (Dl). In teleosts, the pallial amygdala homologue (Dm) is an additional major projection zone. In contrast, lateral line information in amphibians relayed in the dorsal thalamus appears to reach the (subpallial) striatum only (although multimodal visual/auditory projections and maybe indirect lateral line projections via optic tectum do reach the medial pallium via the anterior thalamic nucleus).

Presently, our current state of knowledge on functional neuroanatomy of the craniate lateral line system does not allow for clearly establishing its ancestral pattern of ascending diencephalo-telencephalic connections. The medial pallium (hippocampus homologue) in all gnathostomes likely receives lateral line diencephalic input (mainly from posterior tuberculum and/or dorsal thalamus) ancestrally. However, tetrapods (amphibians) appear then to have lost diencephalo-pallial lateral line projections, but developed input to the subpallial striatum. Alternatively, lampreys, cartilaginous fishes, ray-finned fishes and lobe-finned fishes acquired mechano and electrosensory lateral line input to the telencephalon independently in evolution.

Acknowledgements We would like to thank Horst Bleckmann, Boris Chagnaud, Sheryl Coombs, Art Popper, Gerhard Schlosser and Georg Striedter for many helpful comments and suggestions for improvement. Both BG and MFW are supported by the Graduate School for Systemic Neurosciences (Ludwig-Maximilians-Universität Munich) and MFW by the DFG (SPP 1392, Project Wu/2-1 and 2–2).

References

Altman, J. S., & Dawes, E. A. (1983). A cobalt study of medullary sensory projections from lateral line nerves, associated cutaneous nerves, and he VIIIth nerve in adult *Xenopus*. *Journal of Comparative Neurology,* 213, 310–326.

Amemiya, F., Kisihida, R., Goris, R. C., Onishi, H., & Kusunoki, T. (1985). Primary vestibular projections in the hagfish, *Eptatretus burgeri*. *Brain Research,* 337: 73–93.

Anadón, R., Molist, P., Rodríguez-Moldes, I., López, J. M., Quintela, I., Cerviño, M. C., Barja, P., & González, A. (2000). Distribution of choline acetyltransferase immunoreactivity in the brain of an elasmobranch, the lesser spotted dogfish (*Scyliorhinus canicula*). *Journal of Comparative Neurology,* 420: 139–170.

Barry, M. A. (1987.) Afferent and efferent connections of the primary octaval nuclei in the clearnose skate, *Raja eglanteria*. *Journal of Comparative Neurology,* 266: 457–477.

Bartels, M., Münz. H., & Claas, B. (1990). Representation of lateral line and electrosensory systems in the midbrain of the axolotl, *Ambystoma mexicanum*. *Journal of Comparative Physiology A,* 167: 347–356.

Bastian, J. (1982). Vision and electroreception: integration of sensory information in the optic tectum of the weakly electric fish *Apteronotus albifrons*. *Journal of Comparative Physiology A*, 147: 287–297.

Bastian, J. (1986). Gain control in the electrosensory system mediated by descending inputs to the electrosensory lateral line lobe. *Journal of Neuroscience*, 6: 553–562.

Bastian, J. (1986). Electrolocation: behavior, anatomy, and physiology. In T. H. Bullock & W. Heiligenberg (Eds.), *Electroreception* (pp. 577–612). New York: John Wiley & Sons.

Becker, T., Wullimann, M. F., Becker, C., Bernhardt, R. R., & Schachner, M. (1997). Axonal regrowth after spinal cord transection in adult zebrafish. *Journal of Comparative Neurology*, 377: 577–595.

Behrend, K., & Donicht, M. (1990). Descending connections from the brainstem to the spinal cord in the electric fish *Eigenmannia*. *Brain, Behavior and Evolution*, 35: 227–239.

Behrend, O., Branoner, F., Zhikov, Z., & Ziehm, U. (2006). Neural responses to water surface waves in the midbrain of the aquatic predator *Xenopus laevis laevis*. *European Journal of Neuroscience*, 23: 729–744.

Bell, C. C. (1981a). Central distribution of octavolateral afferents and efferents in a teleost (Mormyridae). *Journal of Comparative Neurology*, 195: 391–414.

Bell, C. C. (1981b). Some central connections of medullary octavolateral centers in a mormyrid fish. In R. R. Fay, A. N. Popper & W. N. Tavolga (Eds.), *Hearing and Sound Communication in Fishes* (pp. 383–392). Berlin: Springer.

Bell, C. C., & Maler, L. (2005). Central neuroanatomy of electrosensory systems in fish. In T. H.Bullock, C. D. Hopkins, A. N. Popper & R. R. Fay (Eds.), *Electroreception* (pp. 68–111). New York: Springer.

Bell, C. C., & Russell, C. J. (1978). Termination of electroreceptor and mechanical lateral line afferents in the mormyrid acousticolateral area. *Journal of Comparative Neurology*, 182: 367–382.

Bell, C. C., & Szabo, T. S. (1986). Electroreception in mormyrid fish. In T. H. Bullock & W. Heiligenberg (Eds.), *Electroreception* (pp. 375–421). New York: John Wiley & Sons.

Bell, C. C., Finger, T. E., & Russell, C. J. (1981). Central connections of the posterior lateral line lobe in mormyrid fish. *Experimental Brain Research*,. 42: 9–22.

Bell, C. C., Zakon, H., & Finger, T. E. (1989). Mormyromast electroreceptor organs and their afferent fibers in mormyrid fish: I. Morphology. *Journal of Comparative Neurology*, 286: 391–407.

Bell, C. C., Hopkins C. D., & Grant, K. (1993). Contributions of electrosensory systems to neurobiology and neuroethology. *Journal of Comparative Physiology A*, 173: 657–763.

Bell, C. C., Bodznick, D., Montgomery, J., & Bastian, J. (1997). The generation and subtraction of sensory expectations within cerebellum-like structures. *Brain, Behavior and Evolution*, 50 (Suppl 1): 17–31.

Bemis, W. E., & Hetherington, T. E. (1982). The rostral organ of *Latimeria chalumnae*: morphological evidence of an electroreceptive function. *Copeia*, 1982: 467–471.

Bleckmann, H. (2008). Peripheral and central processing of lateral line information. *Journal of Comparative Physiology A*, 194: 145–158.

Bleckmann, H., Bullock, T. H., & J. M. Jørgensen J. M. (1987). The lateral line mechanoreceptive mesencephalic, diencephalic, and telencephalic regions in the thornback ray, *Platyrhinoidis triseriata* (Elasmobranchii). *Journal of Comparative Physiology A*, 161: 67–84.

Bleckmann, H., Weiss, O., & Bullock, T. H. (1989). Physiology of lateral line mechanoreceptive regions in the elasmobranch brain. *Journal of Comparative Physiology A*, 459–474.

Bodznick, D. (1991). Elasmobranch vision: multimodal integration in the brain. *Journal of Experimental Zoology, Supplement* 5: 108–116.

Bodznick, D., & Boord, R. L. (1986). Electroreception in Chondrichthyes. Central anatomy and physiology. In T. H. Bullock & W. Heiligenberg (Eds.), *Electroreception* (pp. 225–256). New York: John Wiley & Sons.

Bodznick, D., & Montgomery, J. C. (2005). The physiology of low-frequency electrosensory systems. In T. H.Bullock, C. D. Hopkins, A. N. Popper & R. R. Fay (Eds.), *Electroreception* (pp. 132–153). New York: Springer.

Bodznick, D., & Northcutt, R. G. (1980). Segregation of electro- and mechanoreceptive inputs to the elasmobranch medulla. *Brain Research*, 195: 313–321.

Bodznick, D., & Northcutt, R. G. (1981). Electroreception in lampreys: evidence that the earliest vertebrates were electroreceptive. *Science*, 212: 465–467.

Bodznick, D., & Northcutt, R. G. (1984). An electrosensory area in the telencephalon of the little skate, *Raja erinacea*. *Brain Research*, 298: 117–124.

Bodznick, D., & Schmidt, A. W. (1984). Somatotopy within the medullary electrosensory nucleus of the little skate, *Raja erinacea*. *Journal of Comparative Neurology*, 225: 581–590.

Boord, R. L., & Campbell, C. B. G. (1977). Structural and functional organization of the lateral line system of sharks. *American Zoologist*, 17: 431–441.

Boord, R. L., & Montgomery, J. C. (1989). Central mechanosensory lateral line centers and pathways among the elasmobranchs. In S. Coombs, P. Görner & P. Münz (Eds), *The Mechanosensory Lateral Line* (pp. 323–339). New York: Springer.

Boord, R L,, & Northcutt, R. G. (1982). Ascending lateral line pathways to the midbrain of the clearnose skate, *Raja eglanteria*. *Journal of Comparative Neurology*, 207: 274–282

Boord, R. L. & Northcutt, R. G. (1988). Medullary and mesencephalic pathways and connections of lateral line neurons of the spiny dogfish *Squalus acanthias*. *Brain, Behavior and Evolution*, 32: 76–88.

Boord, R. L., & Roberts, B. L. (1980). Medullary and cerebellar projectios of the statoacoustic nerve of the dogfish, *Scyliorhinus canicula*. *Journal of Comparative Neurology*, 193: 57–68.

Braford, M. R. Jr. (1986). African Knifefishes. In T. H. Bullock & W. Heiligenberg (Eds.), *Electroreception* (pp. 453–464). New York: John Wiley & Sons.

Braun, C. B. (1996). The sensory biology of lampreys and hagfishes: A phylogenetic assessment. *Brain, Behavior and Evolution*, 48: 262–276.

Braun, C. B. (1998). Schreiner organs: a new craniate chemosensory modality in hagfishes. *Journal of Comparative Neurology*, 392: 135–163.

Braun, C. B. & Northcutt, R. G. (1997). The lateral line system of hagfishes (Craniata: Myxinoidea). *Acta Zoologica Stockholm*, 78: 247–268.

Braun, C. B., & Northcutt, R. G. (1998). Cutaneous exteroreceptors and their innervation in hagfishes. In J. M. Jørgensen, J P., Lomholt, R. E. Weber & H. Halte H (Eds.), *The Biology of Hagfishes* (pp 512–532). London: Chapman & Hall.

Bruce LL, Neary TJ (1995) The limbic system of tetrapods: a comparative analysis of cortical amygdalar populations. *Brain, Behavior and Evolution*, 46: 224–234.

Bullock, T. H., & Heiligenberg, W. (1986). *Electroreception*. New York: John Wiley & Sons.

Bullock, T. H., Northcutt, R. G., & Bodznick, D. (1982) Evolution of electroreception. *Trends in Neurosciences*, 5:50–53.

Bullock, T. H., Bodznick, D. A.,& Northcutt, R. G. (1983). The phylogenetic distribution of electroreception: Evidence for convergent evolution of a primitive vertebrate sense modality. *Brain Research Reviews*, 6: 25–46.

Bullock, T. H., Karamürsel, S., & Hofmann, M. H. (1993). Interval-specific event related potentials to omitted stimuli in the electrosensory pathway in elasmobranchs: an elementary form of expectation. *Journal of Comparative Physiology A*, 172: 501–510.

Bullock, T. H., Hopkins, C. D., Popper, A. N., & Fay, R. R. (2005), *Electroreception*. New York: Springer.

Campbell, H. R., Meek, J., Zhang, J., & Bell, C. C. (2007). Anatomy of the posterior caudal lobe of the cerebellum and the eminentia granularis posterior in a mormyrid fish. *Journal of Comparative Neurology*, 502: 714–735.

Carlson, B. A. (2002). Neuroanatomy of the mormyrid electromotor control system. *Journal of Comparative Neurology*, 454: 440–455.

Carr, C. E., & Maler, L. (1985). A Golgi study of the cell types of the dorsal torus semicircularis of the electric fish *Eigenmannia* : functional and morphological diversity in the midbrain. *Journal of Comparative Neurology*, 235: 207–240.

Carr, C. E., & Maler, L. (1986). Electroreception in gymnotiform fish. In T. H. Bullock & W. Heiligenberg (Eds.), *Electroreception* (pp. 319–373). New York: John Wiley & Sons.

Carr, C. E., Maler, L., Heiligenberg, W,, & Sas, E. (1981). Laminar organization of the afferent and efferent systems of the torus semicircularis of gymnotiform fish: morphological substrates for parallel processing in the electrosensory system. *Journal of Comparative Neurology*, 203: 649–670.

Carr, C. E., Maler, L., & Sas, E. (1982). Peripheral organization and central projections of the electrosensory nerves in gymnotiform fish. *Journal of Comparative Neurology*, 211: 139–153.

Carr, C. E., Maler, L., & Taylor, B. (1986). A time-comparison circuit in the electric fish midbrain. I. Functional morphology. *Journal of Neuroscience*, 6: 1372–1383.

Chagnaud, B. P., Wilkens, L. A. & Hofmann, M. H. (2008a). Response properties of electrosensory neurons in the lateral mesencephalic nucleus of the paddlefish. *Journal of Comparative Physiology A*,194: 209–220.

Chagnaud, B. P., Wilkens, L. A., & Hofmann, M. H. (2008b). Receptive field organization of electrosensory neurons in the paddlefish (*Polyodon spathula*). *Journal of Physiology Paris*, 102: 246–255.

Conley, R. A., & Bodznick D. (1994). The cerebellar dorsal granular ridge in an elasmobranch has proprioceptive and electroreceptive representations and projects homotopically to the medullary electrosensory nucleus. *Journal of Comparative Physiology A*,: 174: 707–721.

Coombs, S., Görner, P., & Münz, H. (1989). *The Mechanosensory Lateral Line*. New York: Springer.

Coombs, S., Fay, R.R., & Elepfandt, A. (2010) Dipole source encoding and tracking by the goldfish auditory system. *The Journal of Experimental Biology*, 213: 3536–3547,

Corrêa, S. A. P., Grant, K., & Hoffmann, A. (1998). Afferent and efferent connections of the dorsocentral telencephalon in an electrosensory teleost, *Gymnotus carapo*. *Brain, Behavior and Evolution*, 52: 81–98.

Czech-Damal, N. U., Liebschner, A., Miersch, L., Klauer, G., Hanke, F. D., Marshall, C., Dehnhardt, G., & Hanke, W. (2011) Electroreception in the Guiana dolphin (Sotalia guianensis). *Proceedings of the Royal Society London B*, doi:10.1098/rspb.2011.1127

Danielson, P. D., Zottoli, S. J., Corrodi, J. G., Rhodes, K. J., & Mufson, E. J. (1988). Localization of choline acetyltransferase to somata of posterior lateral line efferents in the goldfish. *Brain Research*, 448: 158–161.

Duman, C.H. & Bodznick, D. (1997). Distinct but overlapping populations of commissural and GABAergic neurons in the dorsal nucleus of the little skate, *Raja erinacea*. *Brain, Behavior and Evolution*, 49: 63–120.

Echteler, S. M. (1984). Connections of the auditory midbrain in a teleost fish, *Cyprinus carpio*. *Journal of Comparative Neurology*, 230: 536–551.

Echteler, S. M. (1985a). Organization of central auditory pathways in a teleost fish, *Cyprinus carpio*. *Journal of Comparative Physiology A*, 156: 267–280.

Echteler, S. M. (1985b). Tonotopic organization in the midbrain of a teleost fish. *Brain Research*, 338: 387–391.

Edwards, C. J., & Kelley, D. B. (2001). Auditory and lateral line inputs to the midbrain of an aquatic anuran; neuroanatomic studies in *Xenopus laevis*. *Journal of Comparative Neurology*, 438: 148–162.

Engelmann, J., & Bleckmann, H. (2004). Coding of lateral line stimuli in the goldfish midbrain in still and running water. *Zoology*, 107: 135–151.

Engelmann, J., Hanke, W., Mogdans, J., & Bleckmann, H. (2000). Hydrodynamic stimuli and the fish lateral line. *Nature*, 408: 51–52.

Enger, P. S., Libouban, S., & Szabo, T. (1976). Rhombo-mesencephalic connections in the fast conducting electrosensory system of the mormyrid fish, *Gnathonemus petersii*. An HRP study. *Neuroscience Letters*, 3: 239–243.

Feng, A. S., & Lin, W. (1991). Differential innervation patterns of three divisions of frog auditory midbrain (torus semicircularis). *Journal of Comparative Neurology*, 306: 613–630.

Fernholm, B., & Holmberg, K. (1975). The eyes in three genera of hagfish (*Eptatretus*, *Paramyxine*, and *Myxine*). A case of degenerate evolution. *Vision Research*, 15: 253–259.

Fiebig, E. & Bleckmann, H. (1989) Cell groups afferent to the telencephalon in a cartilaginous fish (*Platyrhinoidis triseriata*). A WGA-HRP study. *Neuroscience Letters*, 105: 57–62.

Finger, T. E. (1980). Nonolfactory sensory pathway to the telencephalon in a teleost fish. *Science*, 210: 671–673.

Finger, T. E. (1986). Electroreception in catfish: behavior, anatomy and electrophysiology. In T. H. Bullock & W. Heiligenberg (Eds.), *Electroreception* (pp. 287-317). New York: Wiley,

Finger, T. E., & Bullock, T. H. (1982). Thalamic center for the lateral line system in the catfish *Ictalurus nebulosus*: evoked potential evidence. *Journal of Neurobiology*, 13: 39–47.

Finger, T. E., & Tong, S.-L. (1984). Central organization of eighth nerve and mechanosensory lateral line systems in the brainstem of ictalurid catfish. *Journal of Comparative Neurology*, 229: 129–151,

Finger, T. E., Bell, C. C., & Russell, C. J. (1981). Electrosensory pathways to the valvula cerebelli in mormyrid fish. *Experimental Brain Research*, 42: 23–33.

Fritzsch, B. (1981). The pattern of lateral-line afferents in urodeles. *Cell and Tissue Research*, 218: 581–594.

Fritzsch, B. (1988a). The lateral-line and inner-ear afferents in larval and adult urodeles. *Brain, Behavior and Evolution*, 31: 325–348.

Fritzsch, B. (1988b). Phylogenetic and ontogenetic origin of the dorsolateral auditory nucleus of anurans. In B. Fritzsch, M. J. Ryan, W. Wilczynski, T. E. Hetherington & W. Walkowiak (Eds.), *The evolution of the amphibian auditory system* (pp. 561–586). New York: John Wiley & Sons.

Fritzsch, B. (1989) Diversity and regression in the amphibian lateral line and electrosensory system. In S. Coombs, P. Görner, & P. Münz (Eds), *The Mechanosensory Lateral Line* (pp. 99–114). New York: Springer.

Fritzsch, B., & Münz, H. (1986). Electroreception in amphibians. In T. H. Bullock & W. Heiligenberg (Eds.), Electroreception (pp. 483–496). New York, John Wiley & Sons.

Fritzsch, B., Nikundiwe, A. M., & Will, U. (1984). Projection patterns of lateral-line afferent in anurans: a comparative HRP study. *Journal of Comparative Neurology*, 229: 451–469.

Fritzsch, B., Wahnschaffe, U., & Crapon de Caprona, M.-D. (1985). Anatomical evidence for electroreception in larval *Ichthyophis kohtaoensis*. *Naturwissenschaften*, 72: 102–104.

Fritzsch, B., Drewes, R. C., & Ruibal, R. (1987). The retention of the lateral line nuclei in adult anurans. *Copeia*, 1987: 127–155.

Fukuda, J. (1974). Fiber composition of the posterior lateral-line nerve of goldfish, investigated by electrophysiological and microscopical techniques. *Journal of Comparative Neurology*, 155: 203–218.

Gelman, S., Ayali, A., Tytell, E. D., & Cohen, A. H. (2007). Larval lampreys posses a functional lateral line system. *Journal of Comparative Physiology A*, 193: 271–277.

Giassi, A. C. C., Corrêa, S. A. L., & Hofmann, A. (2007). Fiber connections of the diencephalic nucleus tuberis anterior in the weakly electric fish, *Gymnotus* cf *carapo*: an in vivo tract-tracing stuy. *Journal of Comparative Neurology*, 503: 655–667.

González, J., & Anadón, R. (1992). Primary projections of the lateral line nerves in larval sea lamprey, *Petromyzon marinus* L. *Journal für Hirnforschung*, 33: 185–194.

González, M. .J, Yáñez, J., & Anadón, R. (1999). Afferent and efferent connections of the torus semicircularis in the sea lamprey: an experimental study. *Brain Research*, 826: 83–94.

Grant, K., Meek, J., Sugawara, Y., Veron, M., Denizot, J. P., Hafmans, T. G. M., Serrier, J., & Szabo, T. (1996). Projection neurons of the mormyrid electrosensory lateral line lobe: morphology, immunohistochemistry, and synaptology. *Journal of Comparative Neurology*, 375: 18–42.

Hagedorn, M., Womble, M., & Finger, T. E. (1990). Synodontid catfish: a new group of weakly electric fish. *Brain, Behavior and Evolution*, 35: 253–312.

Hall, J. C., & Feng, A. S. (1987). Evidence for parallel processing in the frog's auditory thalamus. *Journal of Comparative Neurology*, 258: 407–419.

Harvey-Girard, E., Tweedle, J., Ironstone, J., Cuddy, M., Ellis, W., & Maler. L. (2010). Long-term recognition memory of individual conspecifics is associated with telencephalic expression of Egr-1 in the electric fish *Apternonotus leptorhynchus*. *Journal of Comparative Neurology*, 518: 2666–2692.

Haugedé-Carré, F. (1979). The mesencephalic exterolateral posterior nucleus of the mormyrid fish *Bryenomyrus niger*: efferent connections studied by the HRP method. *Brain Research*, 178: 179–184.

Haugedé-Carré, F. (1983). The mormyrid mesencephalon. II. The medio-dorsal nucleus of the torus semicircularis: afferent and efferent connections studied with the HRP method. *Brain Research*, 268: 1–14.

Heiligenberg, W. (1984). The electric sense of weakly electric fish. *Annual Review of Physiology*, 46: 561–583.

Heiligenberg, W. (1986). Jamming avoidance responses. In T. H. Bullock & W. Heiligenberg (Eds.), *Electroreception* (pp. 613–649). New York: John Wiley & Sons.

Heiligenberg, W. (1990). Electrosensory systems in fish. *Synapse*, 6: 196–206.

Heiligenberg, W., & Bastian, J. (1984). The electric sense of weakly electric fish. *Annual Review of Physiology*, 46: 561–583.

Heiligenberg, W., & Dye, J. (1982). Labellin of electroreceptive afferents in a gymnotoid fish by intracellular injections of HRP: the mystery of multiple maps. *Journal of Comparative Physiology A*, 148: 287–296.

Heiligenberg, W., & Rose, G. J. (1987). The optic tectum of the gymnotiform electric fish, *Eigenmannia*: labeling of physiologically identified cells. *Neuroscience*, 22: 331–340.

Hetherington, T. E., & Wake, D. (1979). The lateral line system in larval Ichthyophis (Amphibia, Gymnophiona). *Zoomorphology*, 93: 209–225.

Highstein, S. M., Kitch, R., Carey, J., & Baker, R. (1992). Anatomical organization of the brainstem octavolateralis area of the oyster toadfish, *Opsanus tau*. *Journal of Comparative Neurology*, 319: 501–518.

Hofmann, M. H., & Northcutt, R. G. (2008). Organization of major telencephalic pathways in an elasmobranch, the thornback ray *Platyrhinoidis triseriata*. *Brain, Behavior and Evolution*, 72: 307–325.

Hofmann, M. H., Wojtenek, W., & Wilkens, L. A. (2002) Central organization of the electrosensory system in the paddlefish (*Polyodon spathula*). *Journal of Comparative Neurology*, 446: 25–36.

Hofmann, M. H., Chagnaud, B., & Wilkens, L. A. (2005). Response properties of electrosensory afferent fibers and secondary brain stem neurons in the paddlefish. *Journal of Experimental Biology*, 208: 4213–4333.

Ishikawa, Y., Yamamoto, N., Yoshimoto, M., Yasuda, T., Maruyama, K., Kage, T., Takeda, H., & Ito, H. (2007). Developmental origin of diencephalic sensory relay nuclei in teleosts. *Brain, Behavior and Evolution*, 69: 87–95.

Iwahori, N., Nakamura, K., & Tsuda, A. (1996). Neuronal organization of the optic tectum in the hagfish, *Eptatretus burgeri*: a Golgi study. *Anatomy and Embryology*, 193: 271–279.

Janvier, P. (2008). Early jawless vertebrates and cyclostome origins. *Zoological Science*, 25: 1045–1056.

Jørgensen, J. M. (1989). Evolution of octavolateralis sensory cells. In S. Coombs, P. Görner, & P. Münz (Eds.), *The Mechanosensory Lateral Line* (pp. 115–145). New York: Springer.

Jørgensen, J. M. (1991). Ciliated sensory cells in the rostral organ of the coelacanth *Latimeria chalumnae* (Smith 1939). *Acta Zoologica Stockholm*, 72: 121–124.

Keller, C. H., Maler, L., & Heiligenberg, W. (1990). Structural and functional organization of a diencephalic sensory-motor interface in the gymnotiform fish, *Eigenmannia*. *Journal of Comparative Neurology*, 293: 347–376.

Kirsch, J. A., Hofmann, M.H., Mogdans, J., & Bleckmann, H. (2002). Response properties of diencephalic neurons to visual, acoustic and hydrodynamic stimulation in the goldfish, *Carassius auratus*. *Zoology*, 105: 61–70.

Kishida, R., Goris, R. C., Nishizawa, H., Koyama, H., Kadota, T., & Amemiya, F. (1987). Primary neurons of the lateral line nerves and their central projections in hagfishes. *Journal of Comparative Neurology*, 264: 303–310.

Kishida, R., Koyama, H., & Goris, R. C. (1988). Giant lateral-line afferent terminals in the electroreceptive dorsal nucleus of lampreys. *Neuroscience Research*, 6: 83–87.

Knudsen, E. I. (1977). Distinct auditory and lateral line nuclei in the midbrain of catfishes. *Journal of Comparative Neurology*, 173: 417–432.

Koester, D. M. (1983). Central projections of the octavolateralis nerves of the clearnose skate, *Raja eglanteria*. *Journal of Comparative Neurology*, 221: 199–215.

Koyama, H., Kishida, R., Goris, R. C., & Kusunoki, T. (1989). Afferent and efferent projections of the VIIIth cranial nerve in the lamprey *Lampetra japonica*. *Journal of Comparative Neurology*, 280: 663–671.

Koyama, H., Kishida, R., Goris, R. C., & Kusunoki, T. (1990). Organization of the primary projections of the lateral line nerves in the lamprey *Lampetra japonica*. *Journal of Comparative Neurology*, 295: 277–289.

Koyama, H., Kishida, R., Goris, R., & Kusunoki, T. (1993). Giant terminals in the dorsal octavolateralis nucleus of lampreys. *Journal of Comparative Neurology*, 335: 245–251.

Kozloski, J., & Crawford, J. D. (1998). Functional neuroanatomy of auditory pathways in the sound-producing fish *Polli myrus*. *Journal of Comparative Neurology*, 401: 227–252.

Kröther S., Mogdans, J., & Bleckmann, H. (2002). Brainstem lateral line responses to sinusoidal wave stimuli in still and running water. *Journal of Experimental Biology*, 205: 1471–1484.

Künzel, S., Bleckmann, H., & Mogdans, J. (2011). Responses of brainstem lateral line units to different stimulus source locations and vibration directions. *Journal of Comparative Physiology A*, 197: 773–787.

Laberge, F., & Roth, G. (2007). Organization of the sensory input to the telencephalon in the fire-bellied toad, *Bombina orientalis*. *Journal of Comparative Neurology*, 502: 55–74.

Laberge, F., Mühlenbrock-Lenter, S., Dicke, U., & Roth, G. (2008). Thalamo-telencephalic pathways in the fire-bellied toad *Bombina orientalis*. *Journal of Comparative Neurology*, 508: 806–823.

Lannoo, M. J., Maler, L, & Tinner, B. (1989). Ganglion cell arrangement and axonal trajectories in the anterior lateral line nerve of the weakly electric fish *Apteronotus leptorhynchus* (Gymnotiformes). *Journal of Comparative Neurology*, 280: 331–342.

Larsell, O. (1967). *The comparative anatomy and histology of the cerebellum from myxinoids through birds*. Minneapolis: University of Minnesota Press.

Lowe, D. A. (1986). Organisation of lateral line and auditory areas in the midbrain of *Xenopus laevis*. *Journal of Comparative Neurology*, 245: 498–513.

Lowe, D. A., & Russell, I. J. (1982). The central projections of lateral line and cutanious sensory fibres (VII and X) in *Xenopus laevis*. Proceedings of the Royal Society London B, 216: 279–297.

Lu, Z., & Fay, R. R. (1995). Acoustic response properties of single neurons in the central posterior nucleus of the thalamus of the goldfish, *Carassius auratus*. *Journal of Comparative Physiology A*, 176: 747–760.

Luiten, P. G. M. (1975). The central projections of the trigeminal, facial and anterior lateral line nerves in the carp (*Cyprinus carpio* L.). *Journal of Comparative Neurology*, 160: 399–417.

Luksch, H., & Walkowiak, W. (1998). Morphology and axonal projection patterns of auditory neurons in the midbrain of the painted frog, *Discoglossus pictus*. *Hearing Research*, 122: 1–17.

Maler, L. (1979). The posterior lateral line lobe of certain gymnotid fish: quantitative light microscopy. *Journal of Comparative Neurology*, 183: 323–364.

Maler, L., Karten, H. J., & Bennett, M. V. L. (1973a). The central connections of the posterior lateral line nerve of *Gnathonemus petersii*. *Journal of Comparative Neurology*, 151: 57–66.

Maler, L., Karten, H. J., & Bennett, M. V. L. (1973b). The central connections of the anterior lateral line nerve of *Gnathonemus petersii*. *Journal of Comparative Neurology*, 151: 67–84.

Maler, L., Finger, T., & Karten, H. J. (1974). Differential projections of ordinary lateral line receptors and electroreceptors in the gymnotid fish, *Apteronotus* (*Sternarchus*) *albifrons*. *Journal of Comparative Neurology*, 158: 363–382.

Maler, L., Sas, E., Carr, C. E., & Matsubara, J. (1982). Efferent projections of the posterior lateral line lobe in gymnotiform fish. *Journal of Comparative Neurology*, 211: 154–164.

Martínez-Garcia, F., Novejarque, A., & Lanuza, E. (2009). The evolution of the amygdala in vertebrates. In JH Kaas (Ed.), *Evolutionary Neuroscience* (pp. 313–392). Amsterdam: Elsevier-Academic Press.

Maruska, K. P., & Tricas, T. C. (2009) Central projections of octavolateralis nerves in the brain of a soniferous damselfish (*Abudefduf abdominalis*). *Journal of Comparative Neurology*, 512: 628–650.

Matsubara, J., Finger, T. E., Maler, L., & Carr, C. E. (1981). Electrosensory, auditory and lateral line nuclei in the midbrain of a gymnotiform weakly electric fish, Sternopygidae. *Society for Neuroscience Abstracts*, 7: 84.

McCormick, C. A. (1981a) Comparative neuroanatomy of the octavolateralis area of fishes. In A. N. Popper & R. R. Fay (Eds.), *Hearing and sound communication in fishes* (pp. 375–381. New York: Springer.

McCormick, C. A. (1981b). Central projections of lateral line and eight nerves in the bowfin, *Amia calva*. *Journal of Comparative Neurology*, 197: 1–15.

McCormick, C. A. (1982). The organization of the octavolateralis area in actinopterygian fishes: a new interpretation. *Journal of Morphology*, 171: 159–181.

McCormick, C. A. (1983). Central connections of the octavolateralis nerves in the pike cichlid, *Crenicichla lepidota*. *Brain Research*, 265: 177–185.

McCormick, C. A. (1989). Central lateral line mechanosensory pathways in bony fish. In S. Coombs, P. Görner, & P. Münz (Eds.), *The Mechanosensory Lateral Line* (pp 341–365). New York: Springer.

McCormick, C. A. (1992). Evolution of central auditory pathways in anamniotes. In D. B. Webster, R. R. Fay & A. N. Popper (Eds.), *The Evolutionary Biology of Hearing* (pp. 323–350). New York: Springer.

McCormick, C. A. (1997). Organization and connections of octaval and lateral line centers in the medulla of a clupeid, *Dorosoma cepedianum*. *Hearing Research*, 110: 39–60.

McCormick, C. A. (1999). Anatomy of the central auditory pathways of fish and amphibians. In R. R. Fay & A. N. Popper (Eds.), *Comparative hearing: fish and amphibians* (pp. 155–217). New York: Springer.

McCormick, C. A., & Braford, M. R. Jr. (1993). The primary octaval nuclei and inner ear afferent projections in the otophysan *Ictalurus punctatus*. *Brain, Behavior and Evolution*, 42: 48–68.

McCormick, C. A., & Braford, M. R. Jr. (1994). Organization of inner ear endorgan projections in the goldfish, *Carassius auratus*. *Brain, Behavior and Evolution*, 43: 189–205.

McCormick, C. A., & Hernandez, D. V. (1996). Connections of the octaval and lateral line nuclei of the medulla in the goldfish, including the cytoarchitecture of the secondary octaval population in goldfish and catfish. *Brain, Behavior and. Evolution*, 47: 113–138.

McGready, P. J., & Boord, R. L. (1976). The topography of the superficial roots and ganglia of the anterior lateral line nerve of the smooth dogfish, *Mustelus canis*. *Journal of Morphology*, 150: 527–537.

Meek, J., & Grant, K. (1994). The role of motor command feedback in electrosensory processing. European Journal of Morphology 32: 225–234.Meek, J., & Nieuwenhuys, R. (1991). Palisade pattern of mormyrid Purkinje cells: a correlated light and electron microscopic study. *Journal of Comparative Neurology*, 306:156–192.

Meek, J, & Nieuwenhuys, R. (1998). Holosteans and teleosts. In R. Nieuwenhuys, H. J. ten Donkelaar, & C. Nicholson, (Eds.), *The central nervous system of vertebrates* (pp. 759–937). Berlin: Springer.

Meek, J., Nieuwenhuys, R., & Elsevier, D. (1986). Afferent and efferent connections of cerebellar lobe C3 of the mormyrid fish *Gnathonemus petersii*: an HRP study. *Journal of Comparative Neurology*, 245: 342–358.

Meek, J., Hafmans, T G., Maler, L., & Hawkes, R. (1992). Distribution of Zebrin II in the gigantocerebellum of the mormyrid fish Gnathonemus petersii compared with other teleosts. *Journal of Comparative Neurology*, 316: 17–31.

Meek, J., Grant, K., & Bell, C. (1999). Structural organization of the mormyrid electrosensory lateral line lobe. *Journal of Experimantal Biology*, 202: 1291–1300.

Meek, J., Jianji, Y., Han, V. Z., & Bell, C. C. (2008). Morphological analysis of the mormyrid cerebellum using immunohistochemistry, with emphasis on the unusual neuronal organization of the valvula. *Journal of Comparative Neurology*, 510: 396–421.

Meredith, G. E. (1984). Peripheral configuration and central projections of the lateral line system in *Astronotus ocellatus* (Cichlidae): a nonelectroreceptive teleost. *Journal of Comparative Neurology*, 228: 342–358.

Meredith, G. E. (1985). The distinctive central utricular projections in the herring. *Neuroscience Letters*, 55: 191–196.

Meredith, G. E., & Roberts, B. L. (1986). Central organization of the efferent supply to the labyrinthine and lateral line receptors of the dogfish. *Neuroscience*, 17: 225–233.

Meredith, G. E., Roberts, B. L., & Maslam, S. (1987). Distribution of afferent fibers in the brainstem from end organs in the ear and lateral line in the European eel. *Journal of Comparative Neurology*, 265: 507–520

Mesulam, M-M. (1982). *Tracing neural connections with horseradish peroxidase. IBRO Handbook series: Methods in the Neurosciences.* New York: John Wiley & Sons.

Metzner W., & Juranek, J. (1997). A sensory brain map for each behavior? *Proceedings of the National Academy of Sciences USA*, 94: 14798–14803.

Mirjany, M., & Faber, D. S. (2011). Characteristics of the anterior lateral line nerve input to the Mauthner cell. *Journal of Experimental Biology*, 214: 3368–3377.

Mogdans, J., & Kröther, S. (2001). Brainstem lateral line responses to sinusoidal wave stimuli in the goldfish, *Carassius auratus*. *Zoology*, 104: 153–166.

Mogdans, J., Bleckmann, H., & Menger, N. (1997). Sensitivity of central units in the goldfish, *Carassius auratus*, to transient hydrodynamic stimuli. *Brain, Behavior and Evolution*, 50: 261–283

Montgomery, J.C., Coombs, S., Conley, R.A., Bodznick, D.A. (1995). Hindbrain sensory processing in lateral line, electrosensory and auditory systems: A comparative overview of anatomical and functional similarities. *Auditory Neuroscience*, 1: 207–231.

Montgomery, J.C., Baker, C.F., & Carton, A.G. (1997). The lateral line can mediate rheotaxis in fish. *Nature*, 389: 960–963.

Mueller, T., & Wullimann, M. F. (2002). BrdU-, *neuroD*- and Hu-studies show unusual non-ventricular neurogenesis in the postembryonic zebrafish forebrain. *Mechanisms of Development*, 117: 123–135.

Mueller, T. & Wullimann, M. F. (2009). An evolutionary interpretation of teleostean forebrain anatomy. *Brain, Behavior and Evolution*, 74: 30–42.

Mueller, T., Dong, Z., Berberoglu, M. A., & Guo, S. (2011). The dorsal pallium in zebrafish, Danio rerio (Cyprinidae, Teleostei). *Brain Research*, 1381: 95–105.

Münz, H., & Claas, B. (1991). Activity of lateral line efferents in the axolotl (*Ambystoma mexicanum*). *Journal of Comparative Physiology A*, 169: 461–469.

Murakami, T., Fukuoka, T., & Ito, H. (1986). Telencephalic ascending acousticolateral system in a teleost, *Sebastiscus marmoratus*, with special reference to fiber connections of the nucleus preglomerulosus. *Journal of Comparative Neurology*, 247: 383–397.

Neary, T. (1984). Anterior thalamic nucleus projections to the dorsal pallium in ranid frogs. *Neuroscience Letters*, 51: 213–218.

Neary, T. J. (1988) Forebrain auditory pathways in ranid frogs.In B. Fritzsch, M. J. Ryan, W, Wilczynski , T. E. Hetherington & W. Walkowiak (Eds.), *The evolution of the amphibian auditory system* (pp. 233–252). New York: John Wiley & Sons.

New, J. G., & Bodznick, D. (1985). Segregation of electroreceptive and mechanoreceptive lateral line afferent in the hindbrain of chondrostean fishes. *Brain Rese*, 336: 89–98.

New, J. G., & He, J. (1998). Afferent and efferent connections of nucleus praeeminentialis in the channel catfish: a reevaluation. *Brain, Behavior and Evolution*, 51: 202–214.

New, J. G., & Northcutt, R. G. (1984). Central projections of the lateral line nerves in the shovelnose sturgeon. *Journal of Comparative Neurology*, 225: 129–140.

New, J.G., Coombs, S., McCormick, C. A., & Oshel, P. E. (1996). Cytoarchitecture of the medial octavolateralis nucleus in the goldfish, *Carassius auratus*. *Journal of Comparative Neurology*, 366: 534–546.

Northcutt, R. G. (1980a) Central auditory pathways in anamniotic vertebrates. In A. N. Popper & R. R. Fay (Eds.), Comparative studies of hearing in vertebrates (pp. 79–118). New York: Springer.

Northcutt, R. G. (1980b). Anatomical evidence of electroreception in the coelacanth (*Latimeria chalumnae*). *Zentralblatt für Veterinärmedizin C Histologie und Embryologie*, 9: 289–295.

Northcutt, R. G. (1981). Audition and the central nervous system of fishes. In W. N. Tavolga, A. N. Popper, & R. R. Fay (Eds.), *Hearing and Sound Communication in Fishes* (pp. 331–355). New York: Springer.

Northcutt, R. G. (1986a). Evolution of the octavolateralis system: evaluation and heuristic value of phylogenetic hypotheses. In R. W. Ruben et al. (Eds.), *The biology of change in otolaryngology* (pp. 3–14). Amsterdam: Elsevier.

Northcutt, R. G. (1986b). Electroreception in nonteleost bony fishes. In T. H. Bullock & W. Heiligenberg (Eds.), Electroreception (pp. 257–286). New York, John Wiley & Sons.

Northcutt, R. G. (1989). The phylogenetic distribution and innervation of craniate mechanoreceptive lateral lines. In S. Coombs, P. Görner & P. Münz (Eds.), *The Mechanosensory Lateral Line* (pp. 17–78). New York: Springer.

Northcutt, R. G. (1992). Distribution and innervation of lateral line organs in the axolotl. *Journal of Comparative Neurology*, 325: 95–123.

Northcutt, R. G. (1996). The agnathan ark: the origin of craniate brains. *Brain, Behavior and Evolution*, 48: 237–247.

Northcutt, R. G. (2006). Connections of the lateral and medial divisions of the goldfish telencephalic pallium. *Journal of Comparative Neurology*, 494 :903–943.

Northcutt, R. G., & Bemis, W. W. (1993). Cranial nerves of the coelacanth *Latimeria chalumnae* (Osteichthyes:Sarcopterygii: Actinistia) and comparison with other craniata. *Brain, Behavior and Evolution*, 42 (Suppl. 1): 1–76.

Northcutt, R. G., & Bodznick, D. (1983). Areas of electrosensory activity in the mesencephalon of the spiny dogfish, *Squalus acanthias*. *The Bulletin Mount Desert Island Biological Laboratory*, 23: 33–36.

Northcutt, R., G., & Plassmann, W. (1989). Electrosensory activity in the telencephalon of the axolotl. *Neuroscience Letters*, 99: 79–84.

Northcutt, R. G., Holmes, P. H., & Albert, J. S. (2000). Distribution and innervation of lateral line organs in the channel catfish. *Journal of Comparative Neurology*, 421: 570–592.

O'Marra, S., & McCormick, C. A. (1999). Organization and connections of the dorsal descending nucleus and other preseumed acoustic areas in the brainsem of the teleost fish, *Astronotus ocellatus*. *Hearing Research*, 129: 7–19.

Piotrowski, T., & Northcutt, R. G. (1996). The cranial nerves of the Senegal bichir, *Polypterus senegalus* (osteicthyes: actinopterygii: cladistia). *Brain, Behavior and Evolution*, 47: 55–102.

Plachta D. T. T., Hanke, W., & Bleckmann, H. (2003). A hydrodynamic topographic map in the midbrain of goldfish *Carassius auratus*. *Journal of Experimental Biology*, 206: 3479–3486.

Polenova, O. A., & Vesselkin, N. P. (1993). Olfactory and nonolfactory projections in the river lamprey (*Lampetra fluviatilis*) telencephalon. *Journal für Hirnforschung*, 34: 261–279.

Popper, A. N., & Fay, R. R. (1993). Sound detection and processing by fish: critical review and major research questions. *Brain, Behavior and Evolution*, 41: 14–38.

Popper, A. N. & Fay R. R. (1999). The auditory periphery in fishes. In R. R. Fay & A. N. Popper (Eds.), *Comparative hearing: fish and amphibians* (pp. 43–100). New York: Springer.

Prasada Rao, P. D., Jadhao, A. G., Sharma, S. C. (1987). Descending projection neurons to the spinal cord of the goldfish, *Carassius auratus*. *Journal of Comparative Neurology*, 265: 96–108.

Prechtl, J. C., von der Emde, G., Wolfart, J., Karamürsel, S., Akoev, G. N., Andrianov, Y. N., & Bullock, T. H. (1998). Sensory processing in the pallium of a mormyrid fish. *Journal of Neuroscience*, 18: 7381–7393.

Puzdrowski, R. L. (1989). Peripheral distribution and central projections of the lateral line nerves in goldfish, *Carassius auratus*. *Brain, Behavior and Evolution*, 34: 110–131.

Puzdrowski, R. L., & Leonard, R.B. (1993). The octavolateral systems in the stingray, *Dasyatis sabina*. I. Primary projections of the octaval and lateral line nerves. *Journal of Comparative Neurology*, 332: 21.37.

Roberts, B. L., & Meredith, G. E. (1989). The efferent system. In S. Coombs, P. Görner, P. & Münz (Eds.), *The Mechanosensory Lateral Line (*pp. 185–210). New York: Springer

Roberts, B. L., & Meredith, G. E. (1992). The efferent innervation of the ear: variations on an enigma. In D. B. Webster, R. R. Fay, & A. N. Popper (Eds.), *The Evolutionary Biology of Hearing* (pp. 185–210). New York: Springer.

Rodríguez, F., López, J. C., Vargas, J. .P, Broglio, C., Gómez, Y., & Salas, C. (2002). Spatial memory and hippocampal pallium through vertebrate evolution: insights from reptiles and teleost fish. *Brain Research Bulletin*, 57:499–503.

Ronan, M. (1988). Anatomical and physiological evidence for electroreception in larval lampreys. *Brain Research*, 448: 173–177.

Ronan, M., & Bodznick, D. (1986). End buds: non-ampullary electroreceptors in adult lampreys. *Journal of Comparative Physiology A*, 158: 9–15.

Ronan, M., & Northcutt, R. G. (1987). Primary projections of the lateral line nerves in adult lampreys. *Brain, Behavior and Evolution*, 30: 62–81.

Rose, G., & Heiligenberg, W. (1985). Structure and function of electrosensory neurons in the torus semicircularis of *Eigenmannia*: morphological correlates of phase and amplitude sensitivity. *Journal of Neuroscience*, 5: 2269–2280.

Russell, C J., & Bell, C. C. (1978). Neuronal responses to electrosensory input in mormyrid valvula cerebelli. *Journal of Neurophysiology*, 41: 1495–1510.

Salas, C., Broglio, C., Rodriguez, F. (2003). Evolution of forebrain spatial cognition in vertebrates: conservation across diversity. *Brain, Behavior and Evolution*, 62:72–82.

Sas, E., & Maler, L. (1983). The nucleus praeeminentialis: a Golgi study of a feedback center in the electrosensory system of gymnotid fish. *Journal of Comparative Neurology*, 221: 127–144.

Sas E., & Maler, L. (1986a). Retinofugal projections in a weakly electric gymnotid fish (*Apteronotus leptorhynchus*). *Neuroscience*, 18: 247–259.

Sas, E., & Maler, L. (1986b). The optic tectum of gymnotiform teleosts *Eigenmannia virescens* and *Apteronotus leptorhynchus*: a Golgi study. *Neuroscience*, 18: 215-

Sas, E., & Maler, L. (1987). The organization of afferent input to the caudal lobe of the cerebellum of the gymnotid fish *Apteronotus leptorhynchus*. *Anatomy and Embryology*, 177: 55–79.

Scheich, H., & Ebbesson, S. O. E. (1981). Inputs to the torus semicircularis in the electric fish *Eigenmannia virescens*. *Cell and Tissue Research*, 215: 531–536.

Scheich, H., Langner, G., Tidemann, C., Coles, R. B., & Guppy, A. (1986). Electroreception and electrolocation in platypus. *Nature*, 319: 401–402.

Schellart, N. A. M., Prins, M., & Kroese, A. B: A. (1992). The pattern of trunk lateral line afferents and efferents in the rainbow trout (Salmo gairdneri). *Brain, Behavior and Evolution*, 39: 371–380.

Schlosser, G. (2002) Development and evolution of lateral line placodes in amphibians. II. Evolutionary diversification. *Zoology*, 105: 177–193.

Schmitz, A., Bleckmann, H., & Mogdans, J. (2008). Organization of the superficial neuromast system in goldfish, *Carassius auratus*. *Journal of Morphology*, 269:751–761.

Schweitzer, J. (1983). The physiological and anatomical localization of two electroreceptive diencephalic nuclei in the thornback ray, *Platyrhinoidis triseriata*. *Journal of Comparative Neurology*, 153: 331–341.

Schweitzer, J. (1986). Functional organization of the electroreceptive midbrain in an elasmobranch (*Platyrhinoidis triseriata*). *Journal of Comparative Physiology A*, 158: 43–58.

Schweitzer, J., & Lowe, D. (1984). Mesencephalic and diencephalic cobalt-lysine injections in an elasmobranch: evidence for two parallel electrosensory pathways. *Neuroscience Letters,* 44: 317–322.

Shumway, C. (1989). Multiple electrosensory maps in the medulla of weakly electric gymnotiform fish. II. Anatomical differences. *Journal of Neuroscience*, 9: 4400–4415.

Simpson, H. B., Tobias, M. L., & Kelley, D. B. (1986). Origin and identification of fibers in the cranial nerve IX-X complex of *Xenopus laevis* : Lucifer Yellow backfills in vitro. *Journal of Comparative Neurology*, 244: 430–444.

Smeets, W. J. A. J. (1998). Cartilaginous fishes. In R. Nieuwenhuys, H. J. ten Donkelaar, & C. Nicholson, (Eds.), *The central nervous system of vertebrates* (pp. 551–654). Berlin: Springer.

Smeets, W. J. A. J., & Northcutt, R. G. (1987). At least one thalamotelencephalic pathway in cartilaginous fishes projects to the medial pallium. *Neuroscience Letters*, 78: 277–282.

Song, J., & Northcutt, R. G. (1991). The primary projections of the lateral-line nerves of the Florida gar, *Lepisosteus platyrhincus*. *Brain, Behavior and Evolution*, 37: 38–64.

Stein, B. E., & Rowland B. A. (2011). Organization and plasticity in multisensory integration: early and late experience affects its governing principles. *Progress in Brain Research*, 191: 145–163

Striedter, G. F. (1990). The diencephalon of the channel catfish, *Ictalurus punctatus*. II. Retinal, tectal, cerebellar and telencephalic connections. *Brain, Behavior and Evolution*, 36: 355–377.

Striedter, G. F. (1991). Auditory, electrosensory and mechanosensory lateral line pathways through the forebrain in channel catfishes. *Journal of Comparative Neurology*, 312: 311–331.

Striedter, G. F. (1992). Phylogenetic changes in the connection of the lateral preglomerular nucleus in ostariophysan teleosts: a pluralistic view of brain evolution. *Brain, Behavior and Evolution*, 39: 329–357.

Szabo, T., Ravaille, M., Libouban, S., & Enger, P. S. (1983). The mormyrid rhombencephalon: I. Light and EM investigations on the structure and connections of the lateral line lobe nucleus with HRP labelling. *Brain Research*, 266: 1–19.

Tomchik, S. M., & Lu, Z. (2005). Octavolateral projections and organization in the medulla of a teleost fish, the sleeper goby (*Dormitator latifrons*). *Journal of Comparative Neurology*, 481: 96–117.

Tong, S.-L. (1982) The nucleus praeeminentialis: an electro- and mechanoreceptive center in the brainstem of the catfish. *Journal of Comparative Physiology A*, 145: 299–309.

Tong, S.-L., & Finger, T. E. (1983). Central organization of the electrosensory lateral line system in bullhead catfish *Ictalurus nebulosus*. *Journal of Comparative Neurology*, 217: 1–16.

Vischer, H. A., Lannoo, M. J., & Heiligenberg, W. (1989). Development of the electrosensory nervous system in *Eigenmannia* (Gymnotiformes): I. The peripheral nervous system. *Journal of Comparative Neurology*, 290: 16–40.

Voges, K., & Bleckmann, H. (2011). Two-dimensional receptive fields of midbrain lateral line units in the goldfish, *Carassius auratus*. *Journal of Comparative Physiology A*, 197: 827–837.

von der Emde, G. (1998). Electroreception. In: D. H. Evans (Ed.), *Physiology of Fishes* (pp. 315–444). Boca Raton: CRC Press.

von der Emde, G., & Bell, C. C. (1996). Nucleus preeminentialis of mormyrid fish, a center for recurrent electrosensory feedback. I. Electrosensory and corollary discharge responses. *Journal of Neurophysiology*, 76: 1581–1596.

von der Emde, G., & Prechtl, J. C. (1999). Anatomical connections of auditory and lateral line areas of the dorsal telencephalon (Dm) in the osteoglossomorph teleost, *Gnathonemus petersii*. *Brain Research*, 818: 355–367.

Webster, D. B., Fay, R. R., & Popper, A. N. (1992). *The Evolutionary Biology of Hearing*. New York: Springer.

Weeg, M S., & Bass, A. H. (2000) Central lateral line pathways in a vocalizing fish. *Journal of Comparative Neurology*, 418: 41–64.

Westhoff, G., & Roth, G. (2002). Morphology and projection pattern of medial and dorsal pallial neurons in the frog *Discoglossus pictus* and the salamander *Plethodon jordani*. *Journal of Comparative Neurology*, 445: 97–121

Wicht H. Northcutt R.G. 1998. Telencephalic connections in the Pacific hagfish (*Eptatretus stouti*), with special reference to the thalamopallial system. *Journal of Comparative Neurology*, 395, 245–260.

Wilczynski, W. (1988). Brainstem auditory pathways in anuran amphibians. In B. Fritzsch, M. J. Ryan, W. Wilczynski, T. E. Hetherington & W, Walkowiak (Eds.), *The evolution of the amphibian auditory system* (pp. 209–232). New York: John Wiley & Sons.

Wilczynski, W., & Northcutt, R. G. (1983a). Connections of the bullfrog striatum: efferent projections. *Journal of Comparative Neurology*, 214: 333–343.

Wilczynski, W., & Northcutt, R. G. (1983b). Connections of the bullfrog striatum: afferent projections. *Journal of Comparative Neurology*, 214: 321–332.

Wilkens L. A., Hofmann, M. H., & Wojtenek, W. (2002). The electric sense of the paddlefish: a passive system for the detection and capture of zooplankton prey. *Journal of Physiology Paris*, 96: 363–377.

Will, U. (1982). Efferent neurons of the lateral-line system and the VIII cranial nerve in the brainstem of anurans. *Cell and Tissue Research*, 225: 673–685.

Will, U. (1988). Organization and projections of the area octavolateralis in amphibians. In B. Fritzsch, M. J. Ryan, W. Wilczynski, T. E. Hetherington & W. Walkowiak (Eds.), *The evolution of the amphibian auditory system* (pp. 185–208). New York: John Wiley & Sons.

Will, U. (1989). Central mechanosensory lateral line system in amphibians. In S. Coombs, P. Görner, & P. Münz (Eds), *The Mechanosensory Lateral Line* (pp. 365–386). New York: Springer.

Will, U., Luhede, G., & Görner, P. (1985a). The area octavo-lateralis in *Xenopus laevis*. I. The primary afferent projections. *Cell and Tissue Research*, 239: 147–161.

Will, U., Luhede, G., & Görner, P. (1985b). The area octavo-lateralis in *Xenopus laevis*. II. Second order projections and cytoarchitecture. *Cell and Tissue Research*, 239: 163–175.

Wojtenek, W., Mogdans, J., & Bleckmann, H. (1998). The response of midbrain lateral line units of the goldfish, *Carassius auratus*, to objects moving in the water. *Zoology*, 101: 69–82.

Wong, C. J. H. (1997). Connections of the basal forebrain of the weakly electric fish, *Eigenmannnia virescens*. *Journal of Comparative Neurology*, 389: 49–46.

Wullimann, M. F. 1998. The central nervous system. In: D. H. Evans (Ed.), *Physiology of Fishes* (pp. 245–282). Boca Raton: CRC Press.

Wullimann, M.F. (2009). Secondary neurogenesis and telencephalic organization in zebrafish and mouse. *Integrative Zoology*, 4: 123–133.

Wullimann, M. F., & Northcutt, R. G. (1990). Visual and electrosensory circuits of the diencephalon in mormyrids: an evolutionary perspective. *Journal of Comparative Neurology*, 297: 537–552.

Wullimann, M. F., & Rooney, D. J. (1990). A direct cerebello-telencephalic projection in an electrosensory mormyrid fish. *Brain Research*, 520: 354–357,

Wullimann, M. F., & Vernier, P. (2009). Evolution of the nervous system in fishes. In J. H. Kaas (Ed.), *Evolutionary Neuroscience* (pp. 147–168). Amsterdam: Elsevier-Academic Press.

Wullimann, M. F., & Mueller, T. (2004). Teleostean and mammalian forebrains contrasted: evidence from genes to behavior. *Journal of Comparative Neurology*, 475 : 143–162.

Wullimann, M. F., Hofmann, M. H., & Meyer, D. L. (1991). The valvula cerebelli of the spiny eel, Macrognathus aculeatus, receives primary lateral-line afferents from the rostrum of the upper jaw. *Cell and Tissue Research*, 266: 285–293.

Yamada, Y. (1973). Fine structure of the ordinary lateral line organ. I. The neuromast of lamprey, *Entosphenus japonicus*. *Journal of Ultrastructure Research*, 43: 1–17.

Yamamoto, N., & Ito, H. (2005). Fiber connections of the central nucleus of semicircular torus in cyprinids. *Journal of Comparative Neurology*, 491: 186–211.

Yamamoto, N., & Ito, H. (2008). Visual, lateral line, and auditory ascending pathways to the dorsal telencephalic area through the rostrolateral region of the lateral preglomerular nucleus in cyprinids. *Journal of Comparative Neurology*, 508: 615–647.

Zittlau, K. E., Claas, B., & Münz, H. (1988). Horseradish peroxidase study of tectal afferents in *Xenopus laevis* with spezial emphasis on their relationship to the lateral-line system. *Brain, Behavior and Evolution*, 32: 208–219.

Zottoli, S. J., & Van Horne, C. (1983). Posterior lateral line afferent and efferent pathways within the central nervous system of the goldfish with special reference to the Mauthner cell. *Journal of Comparative Neurology*, 219: 100–111.

Zupanc, G. K. H. (1997). The preglomerular nucleus of gymnotiform fish: relay station for conveying information between telencephalon and diencephalon. *Brain Research*, 761: 179–191.

Central Processing of Lateral Line Information

Horst Bleckmann and Joachim Mogdans

Keywords Fish • Dipole stimuli • Hydrodynamic reception • Medium flow • Moving sources • Receptive field • Running water • Vortices

Abbreviations

ALLN	anterior lateral line nerve
CN	canal neuromast
CNS	central nervous system
CON	caudal octavolateralis nucleus
MON	medial octavolateralis nucleus
PLLN	posterior lateral line nerve
PSTH	peristimulus time histogram
SN	superficial neuromast
RF	receptive field
TS	torus semicircularis

1 Introduction

With the lateral line system, fish and aquatic amphibians detect minute water motions. The response properties of the sense organs (neuromasts) and their primary afferent nerve fibers have been the subject of numerous studies (see the chapters by van Netten & McHenry and Chagnaud & Coombs). To determine the location and identity of a source of hydrodynamic disturbance, the brain must

H. Bleckmann (✉) • J. Mogdans
Institute of Zoology, University of Bonn, Poppelsdorfer Schloß 53115, Bonn, Germany
e-mail: Bleckmann@uni-bonn.de

S. Coombs et al. (eds.), *The Lateral Line*, Springer Handbook of Auditory Research 48,
DOI 10.1007/2506_2013_16,
Published online: 29 June 2013

analyze the hydrodynamic information that is received by the peripheral lateral line and represented by the activity of afferent lateral line nerve fibers. This chapter summarizes our current knowledge on the processing of various hydrodynamic stimuli at different levels of the ascending lateral line pathway.

2 The Ascending Lateral Line Pathway

Lateral line information is processed at all levels of the brain, from rhombencephalon to telencephalon (for detailed information on lateral line pathways, see McCormick, 1989 and the chapter by Wullimann & Grothe). In all fish examined so far, the lateral line nerves enter the ipsilateral brain stem and terminate in the medial octavolateralis nucleus (MON) and in the caudal octavolateralis nucleus (CON) in the medulla (Puzdrowski, 1989). Some primary lateral line projections may reach the ipsilateral cerebellar granular eminence and, in a few species, the cerebellar corpus. Primary lateral line afferents also project to the Mauthner cells, a pair of large and easily identifiable hindbrain neurons that mediate a fast escape response, the so-called C-start response (Zottoli & van Horne, 1983). The second-order projections from the MON terminate bilaterally, albeit with a stronger contralateral component, in the midbrain ventrolateral nucleus of the torus semicircularis (TS) and in the deep layers of the optic tectum. The final ascending pathway for the mechanosensory lateral line involves the relay of information from the midbrain to the forebrain through various diencephalic nuclei. Known telencephalic areas include the medial pallium in batoid elasmobranchs and the dorsal part of the telencephalon in teleosts (for a detailed review see the chapter by Wullimann & Grothe). Whereas we have a fairly good knowledge about the physiology of medullary and midbrain lateral line units (with the exception of the tectum opticum), very little is known about the response properties of cerebellar, diencephalic, and telencephalic lateral line areas.

3 General Physiology of the Central Lateral Line

To investigate the neural activity of central lateral line cells, averaged evoked potentials as well as multiunit and single unit responses have been recorded in response to a variety of stimuli, including electric lateral line nerve shocks, bulk flow, and water motions caused by a stationary vibrating sphere (dipole stimulus) or a moving (translating) object (e.g., a cylinder). A stationary vibrating sphere has the advantage that it causes local and predictable water motions (Coombs et al., 1989), whereas translating objects capture other features of biological relevance, including shed wakes. In this section, general features of spontaneous and evoked activity of central nervous system (CNS) units at different levels of the brain and in primary afferent fibers are compared to identify transformational trends along the ascending

pathway of the lateral line nervous system. Trends in evoked activity to different types of stimuli are considered in more detail in Section 4.

3.1 Spontaneous Activity and Evoked Response Latency

Like primary lateral line afferents, many central lateral line units show ongoing activity (Alnaes, 1973; Schellart & Kroese, 1989; Engelmann et al., 2002b). In general, the spike rates of ongoing and evoked activity decrease along the ascending central pathway whereas evoked response latencies increase. Ongoing activity in primary lateral line afferents (that may partly be due to artificially ventilating the gills of the experimental fish) can be as high as 108 impulses s^{-1} (Montgomery et al., 1996) but may be completely absent in midbrain and forebrain lateral line units (Bleckmann et al., 1989b; Kirsch et al., 2002a). If stimulated with a vibrating sphere, brain stem units have response latencies in the range of 12 up to about 28 ms, depending on stimulus frequency and amplitude (Bleckmann et al., 1989b). In contrast, latencies of forebrain lateral line responses may be as high as 80–270 ms (Bleckmann et al., 1989b; Kirsch et al., 2002b).

3.2 Primary-Like and Non-primary–Like Responses in the MON

Among those MON units that respond to a stationary dipole, typically two groups can be found: units with primary-like and units with non-primary–like responses (Coombs et al., 1998; Künzel et al., 2011). Primary-like responses are characterized by robust phase-locking and sustained increases in discharge rate. In general most medullary and midbrain lateral line units that phase couple respond to only one half of a full wave cycle (Bleckmann et al., 1989b; Bleckmann & Zelick, 1993; Montgomery et al., 1996), meaning that lateral line afferents with opposing directional sensitivities to, for example, tailward or headward movement, do not converge onto such neurons. In central lateral line units, the slopes of the level-response functions (response amplitude as function of stimulus amplitude) were generally lower than those of primary afferents.

3.3 Adaptation: Responses to Prolonged and Repetitive Stimuli

Another striking difference between lateral line afferents and central lateral line units are their responses to prolonged sinusoidal stimuli. Whereas primary afferents

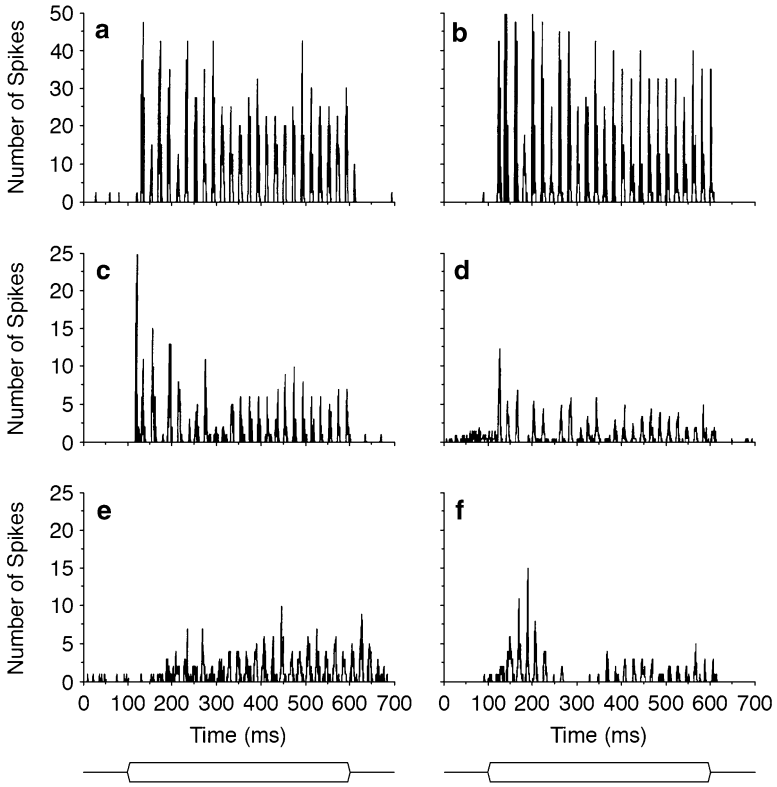

Fig. 1 Peristimulus time (PST) histograms of the responses to a 50-Hz vibrating sphere of two primary afferent nerve fibers and four MON units recorded in goldfish. Whereas primary afferents exhibited sustained responses (**a**, **b**), MON unit responses can be adapting (**c**, **d**), long-latency build-up (**e**), or phasic (**f**). (Adapted from Coombs et al., 1998)

show a tonic or phasic-tonic response to such stimuli, central lateral line units exhibit a variety of temporal response patterns. Non-primary–like responses were characterized by rather poor phase-locking and variable response patterns including increases or decreases in discharge rate. Responses were sustained, phasic, intermittent, or built-up (Wubbels et al. 1993; Montgomery et al. 1996) (Fig. 1).

Primary lateral line afferents of both fish and aquatic amphibians show no or only a weak response decrement to sequential stimuli. In contrast, responses recorded in the MON of fish already show a response decrement if the stimulus repetition rate exceeds 2 Hz. In the midbrain of the thornback guitarfish (*Platyrhinoidis triseriata*) and the African clawed frog (*Xenopus laevis*), a complete recovery of evoked potential or lateral line unit responses requires an interstimulus interval of more than 5 s (Zittlau et al., 1985; Bleckmann et al., 1987, b), whereas single-unit and/or evoked potentials recorded from diencephalic and telencephalic lateral line areas may still show a marked response decrement to sequential stimulus events that are

separated by intervals as long as 10 s (Bleckmann et al., 1987; Birkhofer et al., 1994). In one diencephalic lateral line area (posterior lateral tuberal nucleus) of the thornback guitarfish, a response decrement was manifest for interstimulus intervals of less than 55 s (Bleckmann et al., 1987). These findings suggest that higher-order lateral line areas are concerned mainly with the processing of novel hydrodynamic information.

3.4 Adequate Stimuli for Probing the CNS

With rare exceptions (Weeg & Bass, 2002), primary lateral line afferents are wideband (Münz, 1989; Bleckmann & Münz, 1990; Montgomery & Coombs, 1992) and extremely sensitive to the low-frequency sinusoidal water motions created by vibrating sources (e.g., at 100 Hz the peak-to-peak displacement threshold is about 0.1 μm) (Bleckmann & Topp, 1981; Münz, 1985; Bleckmann & Münz, 1990). Despite this, about 40% of all medullary and midbrain lateral line units do not respond to a vibrating sphere stimulus (Mogdans & Kröther, 2001; Plachta et al., 2003), even if the stimulus amplitudes are sufficient to drive primary lateral line afferents into saturation. Central lateral line units insensitive to a vibrating sphere stimulus may, however, readily respond to the water motions generated by a small object that passes the fish laterally. This indicates that many central lateral line units require more natural, that is, more complex temporal and/or spatial patterns of water motions in order to respond.

In this respect, it is interesting to note that natural hydrodynamic stimuli contain multiple frequencies and are modulated in frequency and/or amplitude (Montgomery & Macdonald, 1987; Bleckmann et al., 1991b). If stimulated with amplitude-modulated, constant-frequency water motions, MON and midbrain units respond to each modulation cycle even if these units exhibit phasic responses to an unmodulated sinusoidal stimulus (Plachta et al., 1999; Ali et al., 2010). Thus, the central lateral line appears to be adapted for the processing of amplitude- and/or frequency-modulated stimuli, and thus for the processing of more natural hydrodynamic stimuli.

If plotted as function of stimulus displacement, many medullary and midbrain lateral line units that are sensitive to a vibrating sphere stimulus are wideband, meaning that vibrating sphere stimuli cause neural responses in the frequency range from below 10 Hz up to at least 200 Hz (Bleckmann & Bullock, 1989). However, some central lateral line units may show a strong suppression of activity at higher (>50 Hz) frequencies (Montgomery et al., 1996). Displacement thresholds of medullary and midbrain lateral line units at 100 Hz may be as low as 0.01 μm (Bleckmann et al., 1989b). In contrast, the displacement thresholds of diencephalic and telenecephalic lateral line areas (evoked potentials and unit responses) are two to three orders of magnitude higher than the displacement thresholds of the most sensitive midbrain and hindbrain lateral line units (Bleckmann et al., 1989b).

3.5 *Frequency Selectivity and Sensitivity*

Midbrain lateral line units of trout yield two peaks of increased sensitivity that coincide with the best frequencies (in terms of displacement) of superficial neuromasts (SNs) and canal neuromasts (CNs) (Schellart & Kroese, 1989). If stimulated with iso-displacement stimuli (test range 33–200 Hz), MON and toral lateral line units of goldfish are low-frequency (33 Hz), mid-frequency (50–100 Hz), or high-frequency (>200 Hz) (Plachta et al., 1999; Ali et al., 2010). Some toral lateral line units of the catfish *Ancistrus* respond with a sustained firing rate to certain stimulus frequencies. If these frequencies are lowered or raised by as little as 2 Hz, only the phasic response component remains (Müller & Bleckmann, 1993). Given that afferent fibers are generally tuned to two frequency regions only, corresponding to the SN/CN dichotomy (see the chapter by Chaugnaud & Coombs), additional frequency selectivity observed in the CNS must arise through neural interactions (e.g., lateral inhibition). Frequency selectivity of central lateral line units is a prerequisite for the behavioral ability of fish (Bleckmann et al., 1981; Frühbeis, 1984; Vogel & Bleckmann, 1997) and aquatic amphibians (Elepfandt et al., 1985; Elepfandt, 1986) to discriminate water wave frequencies.

3.6 *Dynamic Amplitude Range*

In a few studies, the dynamic amplitude range of central lateral line units has been investigated. Although the highest stimulus intensities used were often not sufficient to saturate the neural responses, the dynamic amplitude range of central lateral line units may cover up to 90 dB (Bleckmann et al., 1989b). This is in contrast to a much narrower dynamic range (<40 dB) observed in primary afferent fibers in the mottled sculpin (*Cottus bairdi*) in response to dipole stimuli (Coombs & Janssen, 1990). In *Platyrhinoidis* some medullary units encode stimulus amplitudes of up to 150 μm, while other units already show saturation at a stimulus amplitude of 6 μm (Bleckmann et al., 1989b). Thus in terms of the upper stimulus amplitude that can be encoded, there is a range fractioning. In some central lateral line units, saturation is followed by a decrease of neural responses at higher intensities (Bleckmann et al., 1989b; Schellart & Kroese, 1989).

4 Lateral Line Maps

There are a number of organizational features of the peripheral lateral line system that might be preserved and mapped in the CNS, including the location and orientation (as defined by the axis of hair cell orientation) of neuromasts on the body. There is at present no indication that fibers from oppositely oriented hair cells

or from, for example, horizontally or vertically oriented hair cells in different SNs map separately in the brain (Fritzsch, 1989; Song & Northcutt, 1991b; Ivry & Baldo, 1992). However, a number of anatomical and physiological studies have demonstrated that body location of neuromasts is crudely mapped in the MON (Bleckmann et al., 1991a; Song & Northcutt, 1991b; Gompel et al., 2001). The best evidence is for a somatotopic mapping of the rostrocaudal body axis of the fish (Alexandre & Ghysen, 1999), although there may also be a crude somatotopic map of the dorsolateral and ventrolateral surfaces of the trunk in the MON of some fishes (Song & Northcutt, 1991b; Ivry & Baldo, 1992).

Missing from this overall picture, however, is any clear idea of the spatial precision with which information from either SN or CN fibers is mapped and if, in fact, both submodalities are somatotopically mapped. One anatomical study indicates that lateral line fibers innervating individual CNs terminate in a single well-defined field in the MON (New et al., 2000), suggesting that CNs might form high-resolution maps of the body surface. If so, this is consistent with the finding that mottled sculpin rely on CN information for localizing the precise position of artificial prey (Coombs et al., 2001). Moreover, this idea is supported by the observation that flow-insensitive toral neurons (those likely to be driven by flow-insensitive CNs via flow-insensitive relay neurons in the MON) encode the rostrocaudal location of a moving object (Plachta et al., 2003; Engelmann & Bleckmann, 2004). Indeed, anatomical studies indicate a crude topography of projections from the MON to the nucleus ventrolateralis of the torus semicircularis, and thus that somatotopic maps are preserved in the midbrain TS (Weeg & Bass, 2000).

In addition to hindbrain and midbrain somatotopic maps, physiological studies (Zittlau et al., 1986; Bartels et al., 1990; Behrend et al., 2006) have revealed lateral line maps in the midbrain tectum of the African clawed frog (*Xenopus laevis*) and the axolotl *Ambystoma mexicanum* that represent the direction of surface wave propagation (Fig. 2). Whether fish have similar computed maps of surface wave direction in the TO remains to be shown.

5 Responses of Central Lateral Line Units to Different Stimuli

As mentioned in Section 2, a number of different stimuli have been used in studies of lateral line central units. Because many of these have also been used to characterize the response properties of primary afferent fibers, this section examines in more detail the similarities and differences between peripheral and central responses to the same stimulus to show how information is transformed along the ascending lateral line pathway.

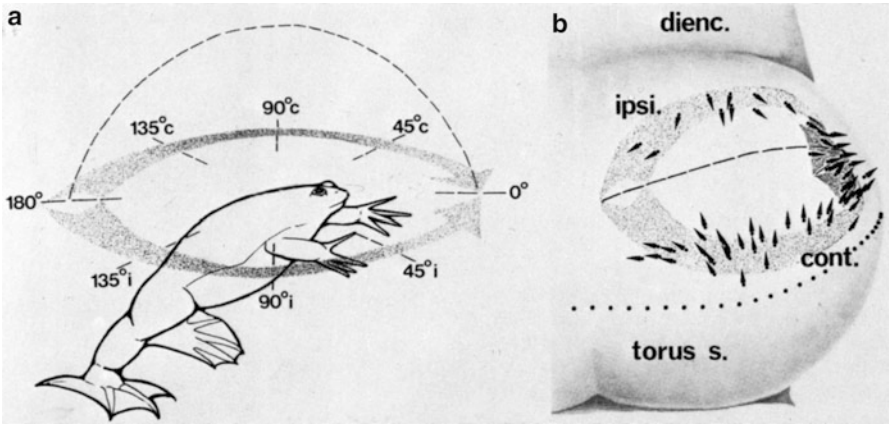

Fig. 2 (**a**, **b**) Best directions of tectal lateral line units in the African clawed frog (*Xenopus laevis*). Angles in (**a**) refer to the propagation direction of water surface waves with respect to the position of the animal. In (**b**), the surface of the TO and the TS is drawn as seen from above. Solid arrows indicate best directions of 60 units, which were recorded at the indicated locations. Broken line in (**a**): meridian, which divides the ipsilateral (ipsi.) from the contralateral (cont.) surroundings. Dotted line in (**b**): borderline between the TO and the TS. (Reproduced from Zittlau et al., 1986)

5.1 Using Dipole Sources to Map Receptive Fields

Dipole sources have been used to determine the frequency selectivity and sensitivity of peripheral and central lateral line cells (Section 5.5), but also in mapping their receptive fields (RFs). In response to the changing locations of a dipole source along the rostrocaudal axis of the fish, primary lateral line afferents and central lateral line units have diffuse and somewhat complex RFs that depend on a number of source parameters (Sand, 1981; Coombs et al., 1996; Coombs et al., 1998). This is because a dipole stimulus generates a complex spatial pattern of pressure gradients across the lateral line that depends in a predictable way on sphere location, distance, and angle of sphere vibration with respect to the axis of best sensitivity of a neuromast (Coombs et al., 1996; Ćurčić-Blake & van Netten, 2006; Coombs & Patton, 2009). When analyzed via a linear array of neuromasts, the spatial pressure gradient pattern along the body surface produced by a dipole at a fixed location matches the shape of the RF response function, which is described by spike activity as function of the changing locations of the dipole source (Fig. 3, upper row).

To determine if RFs are preserved or transformed by the CNS, RFs of medullary and midbrain lateral line units have been characterized in various studies (Coombs et al., 1998; Mogdans & Kröther, 2001; Künzel et al., 2011). These studies show that the RFs of most MON (Fig. 3, middle and lower) and toral (Fig. 4) lateral line units, in contrast to the RFs of primary lateral line afferents, do not encode the temporal changes in pressure gradients generated by a roving, vibrating sphere. One-dimensional RFs of medullary and midbrain lateral line units, determined

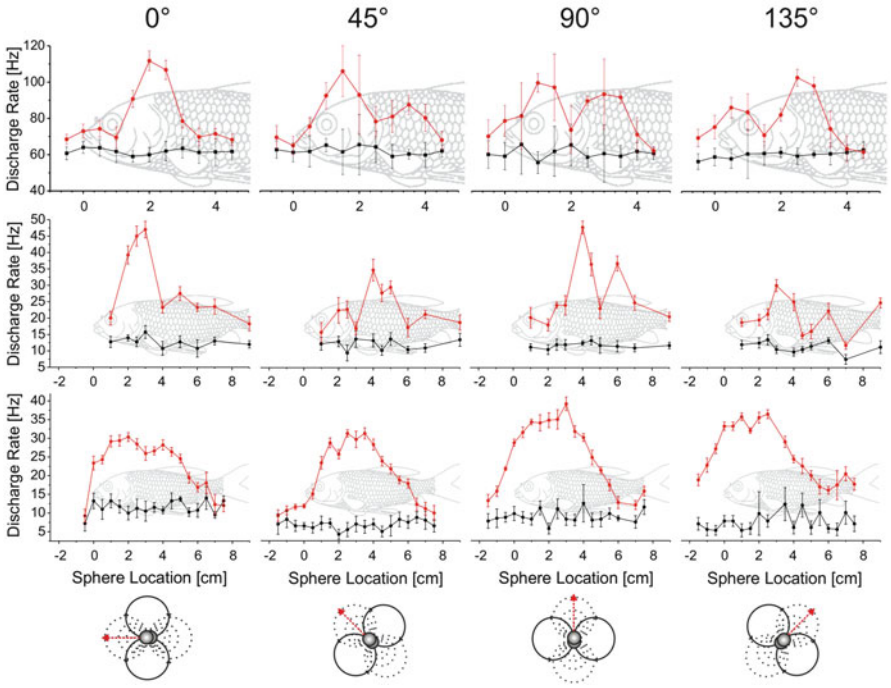

Fig. 3 RFs, determined with a vibrating sphere stimulus (frequency 50 Hz, peak-to-peak vibration amplitude were in the dynamic amplitude range of the units) of a primary lateral line afferent (upper) and two MON units (middle and lower). The dipole was placed at various locations alongside the fish and was vibrating at angles of 0° (parallel to the fish), 90° (toward the fish), 45° or 135° (intermediate). Bottom graphs: Iso-pressure contours (dashed lines) and flow lines (solid lines with arrows) around a dipole source (gray circle). Red arrows indicate angle of vibration relative to the fish. Black lines represent ongoing discharge rates and red lines represent evoked rates. Vertical bars represent one standard deviation. The fish symbol in each plot indicates the size and position of the fish relative to the position of the vibrating sphere. (Adapted from Künzel et al., 2011)

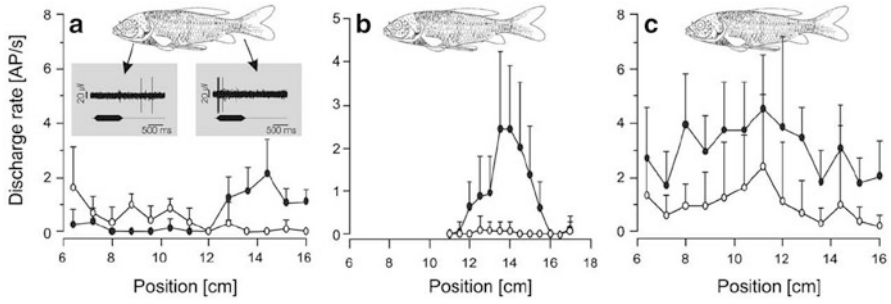

Fig. 4 RFs of three toral lateral line units, determined with a roving sphere vibrating at 50 Hz (600 µm p–p displacement) in still water. RFs were complex (**a**), small (**b**), or broad (**c**). The inset in (**a**) shows two original recordings obtained at the sphere positions indicated by arrows. Note that the rostral sphere position caused a decrease and the caudal sphere position a transient increase in discharge rate. Stimulus-evoked discharge rate (filled circles), ongoing discharge rates (open circles). Bars indicate the positive part of one standard deviation. The fish symbol above each plot indicates the size and position of the fish relative to the position of the vibrating sphere. (Adapted from Engelmann & Bleckmann, 2004)

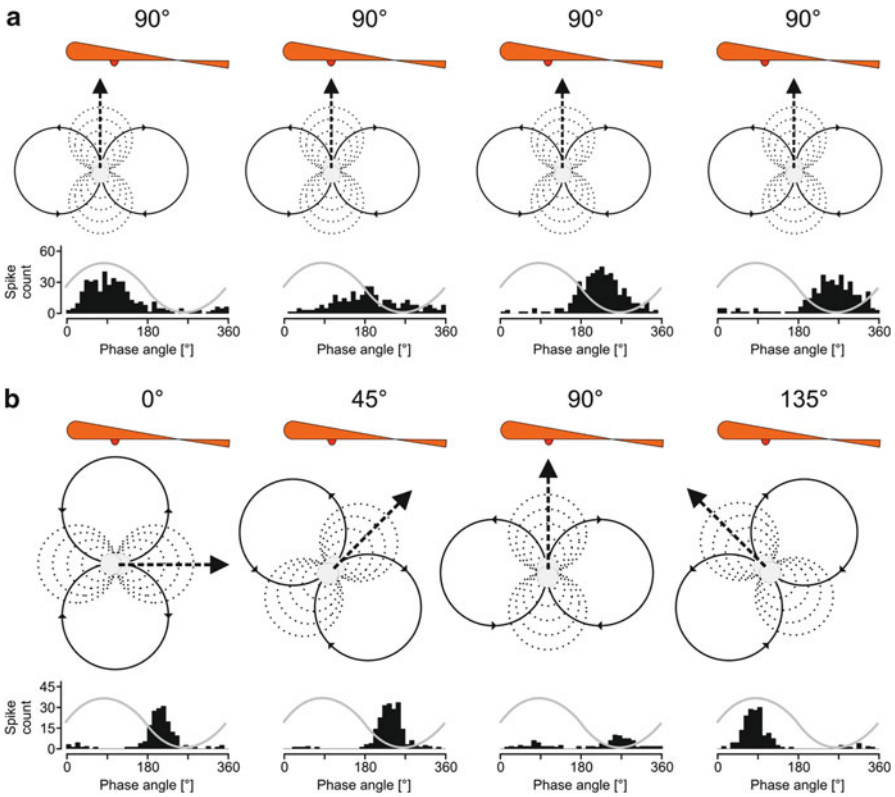

Fig. 5 (**a**, **b**) Phase histograms of the responses of midbrain lateral line units to a vibrating sphere (50 Hz). Iso-pressure contours (dashed lines) and flow lines (solid lines with arrowheads) around a dipole source. Iso-pressure contours are shown for the plane that bisects the source along its axis of oscillation, indicated by the large arrowheads. Note that for a given phase of sphere movement the flow direction on the surface of the fish depends on the direction of sphere vibration. Half circle on the left side of each fish symbol indicates the approximate center of the RF of the unit recorded from. (**a**) A change in the rostrocaudal position of the sphere by only 1 cm (sphere vibration direction 90°) caused a phase shift of about 180° in the neuronal response. (**b**) A change in the direction of sphere vibration from 45° to 135° also caused a 180° phase shift of the response. (Adapted with permission from Meyer, 2010)

along a single axis of space, range from small single or double peaked to large and multipeaked, covering most or even the whole surface of the fish (Coombs et al., 1998; Plachta et al., 1999; Kröther et al., 2004). This suggests that some central units receive input from a restricted portion of the lateral line periphery, whereas other units receive input from neuromasts that are widely distributed across the head and trunk of the fish.

Changes in the direction of sphere vibration may or may not cause changes in RF size and/or shape. In some units, small changes in sphere position and/or sphere vibration direction cause a 180° phase shift in the responses (Fig. 5). Thus, even

though many units have large RFs, these phase shifts may inform the animal about small changes in sphere position and/or sphere vibration direction.

Voges and Bleckmann (2011) characterized the two-dimensional extent of RFs in goldfish midbrain lateral line units. The RFs were round, horizontally or vertically stretched, or complex. Given the small RFs of primary afferents, the high convergence of lateral line input on central units is surprising. However, there are central units with a small RF. This indicates that at least up to the level of the midbrain, lateral line subsystems preserve high spatial resolution. The excitatory RFs of some MON and toral lateral line units include regions in which dipole stimulation leads to inhibition of ongoing activity (Fig. 4a). Whether dipole stimulation can also inhibit evoked activity is not known. Anatomical (New et al., 1996) and modeling data (Coombs et al., 1996; Montgomery & Coombs, 1998) suggest that primary-like RFs in central lateral line neurons are sharpened by neural mechanisms based on lateral inhibition. Physiological studies that confirm this are missing, however. Lateral line units in the TS of teleost fish receive input from a large but restricted portion of the contralateral body surface. The rostrocaudal position of the recording site corresponds to the rostrocaudal position of the RF on the body surface (Knudsen, 1977; Bleckmann & Zelick, 1993; Plachta et al., 2003). A similar somatotopic organization exists in the mesencephalic nuclear complex of the thornback ray (*Platyrhinoidis*; Bleckmann et al., 1989b).

In the corpus and valvula cerebelli of the goldfish (*Carassius auratus*), units that respond to ipsi- or contralateral stimulation of the lateral line in the tail or body region are found in a more posterior part than those that respond to stimulation of the head region. RFs are usually large, diffuse, and overlapping, and no pattern of specific topographic projection exists (Kotchabhakdi, 1976). The lateral line units recorded in the eminentia granularis of the catfish *Ictalurus* primarily respond to ipsilateral stimulation (Lee & Bullock, 1984). Again RFs are large and difficult to delimit. They overlap with one another and do not fall into any recognizable pattern. Units in the valvula, which may (or may not) be multimodal, have RFs that are confined to the head region (Lee & Bullock, 1984). Mapping of lateral line (mechanosensory) cerebellar RFs in *Platyrhinoidis* again revealed a complex somatotopy. The RFs are large and include ipsi- and contralateral body areas, such as the tail and anal fins, and are represented mostly in a relatively small region in the caudal tip of the posterior lobe of the cerebellar corpus; more rostral body areas (pectoral fins, trunk, and head area) are represented in the rest of the posterior lobe of the cerebellar corpus and the caudal part of the posterior lobe of the cerebellar corpus (Fiebig, 1988).

Almost no information is available on diencephalic lateral line RFs (Bleckmann et al., 1987). In the one case in which the RF was mapped in the lateral tuberal nucleus of *Platyrhonoidis*, the RF was large and complex, restricted to the anterior half of the body, and followed the course of the infraorbital and trunk lateral line canals. Telencephalic RFs, determined only with evoked potentials while the animal was stimulated with a vibrating sphere, are again large and may differ with respect to the number, polarities, and latencies of the peaks (Bleckmann et al., 1989b).

5.2 Responses to Moving Objects

A fish that is passed by another fish will experience a well-defined transient water motion and some ill-defined flow fluctuations that occur in the wake of the fish. A small object that is moved alongside a fish also generates transient water motions and a wake, both of which stimulate the entire lateral line (Mogdans & Bleckmann, 1998; Hanke & Bleckmann, 1999) (see Fig. 12 in the chapter by Chagnaud & Coombs). A moving object generates not only water motions, but also pressure changes. These changes are prominent only during the initial transient component of the stimulus and are negligible in the wake of an object.

Primary lateral line afferents respond to an object that passes the fish laterally with a discharge pattern that consists of excitation followed by inhibition or vice versa (Mogdans & Bleckmann, 1998; Montgomery & Coombs, 1998; Engelmann et al., 2003). This response sequence inverts when the direction of object motion is reversed, as predicted from the directional sensitivity of lateral line hair cells. Afferent fibers that presumably innervate SNs in addition respond with bursts of spikes to the object's wake (see also the chapter by Chagnaud & Coombs).

In contrast to primary lateral line afferents, the responses of central lateral line units to moving object stimuli are highly diverse (Fig. 6). In the MON, two response types can be distinguished (Mogdans et al., 1997; Mogdans & Goenechea, 2000). Similar to most primary afferents, many MON units respond to the transient water motions caused by a passing object and to the ill-defined water motions in the wake of the object. Other MON units, however, respond only to the transient water motions but not to the wake. In the midbrain TS, the same two main response types are found (Fig. 6), suggesting again that SN and CN input is processed in separate channels up to the level of the midbrain. A third type of toral lateral line units responds only to the wake but not to the transient water motions caused by the moving object (Müller, 1996). In these units the responses to the transient water motions must be suppressed.

The responses of both types of MON units may or may not differ for anterior–posterior and posterior–anterior object motion direction (Mogdans et al., 1997; Mogdans & Goenechea, 2000; Engelmann et al., 2003). This indicates that inputs from the oppositely oriented hair cells within a neuromast converge on these MON units.

Those TS units that respond to the passing object but not to its wake are organized systematically and form a hydrodynamic topographic map: Units that receive input from anterior body areas are located rostrally, and those that receive input from posterior body areas are located caudally in the TS. Moreover, units that respond only to a passing object are located more ventrally in the TS than units that respond exclusively to a stationary dipole (Plachta et al., 2003).

5.3 Responses to Bulk Water Flow

In their natural habitat, fish are rarely surrounded by still water. Instead, in rivers and creeks as well as along the ocean shoreline, the water constantly moves and

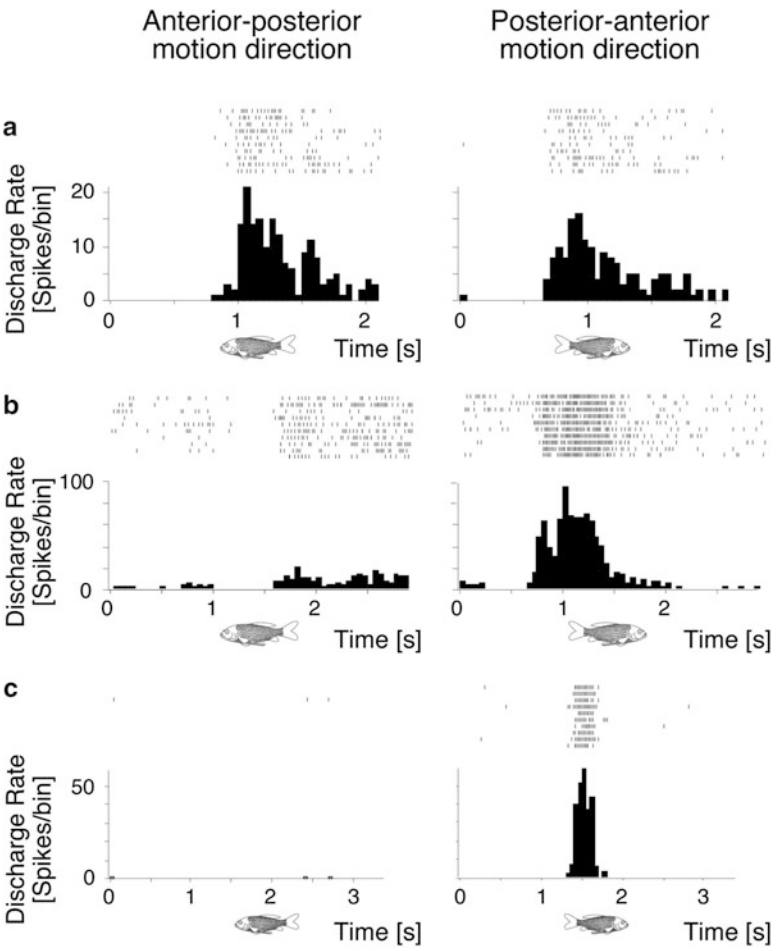

Fig. 6 (**a–c**) Responses of three midbrain lateral line units to an object that passes the fish from anterior-to-posterior (left) or from posterior-to-anterior (right). (**a**) A nondirectional sensitive unit that responded to both, the passing object and the wake caused by the passing object. (**b**) A highly directional sensitive unit that, in the preferred direction, also responded to the passing object and the wake of the object. (**c**) A highly directional sensitive unit that responded with a single burst while the object passed the fish but failed to respond to the wake. Object speed was between 15 and 20 cm s^{-1}; minimal object distance was 1 cm. The fish symbol below each plot indicates the size and position of the fish relative to the position of the moving object at the time indicated by the *x*-axis. (Reproduced from Wojtenek et al., 1998)

even in seemingly quiet ponds and lakes some gross water movements may occur. Further, the lateral line of many limnophilic fish may also be stimulated by gross water flow because fish tend to move constantly, at least during daytime. To better understand lateral line perception, researchers have investigated whether and how the peripheral and central lateral line responds to laminar and turbulent gross

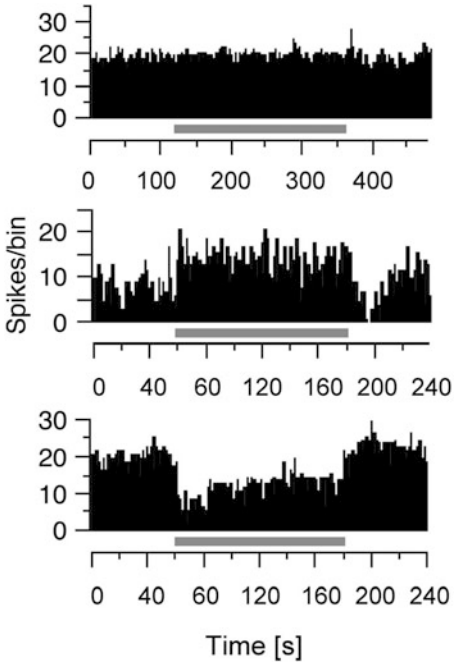

Fig. 7 Poststimulus time histograms (PSTHs, bin width 1 s) of the responses of three MON units to running water (15 cm s^{-1}). Gray bars indicate time of flow. Units are flow insensitive (**top**) or they respond to the flow with an increase (**middle**) or a decrease (**bottom**) of ongoing activity. (Adapted from Kröther et al., 2002)

water flow. In general the response profiles of MON and midbrain lateral line units to bulk water flow (test range 0–15 cm s^{-1}) are diverse. Flow sensitive units either increase or decrease their discharge rate in proportion to bulk flow velocity (Fig. 7).

Previous studies have shown that the peripheral lateral line of goldfish exposed to bulk water flow responds only to the flow fluctuations but not to the DC component of the flow (Chagnaud et al., 2007b). Because flow fluctuations travel with the flow, these studies have led to the hypothesis that the ability of fish to determine the velocity and direction of bulk water flow is based on neural circuits that function like a coincidence detector (see also the chapter by Chagnaud & Coombs). If so, it would be expected that coincidence-detecting units would be "tuned" to different bulk flow velocities and directions, while being relatively insensitive to the amplitude and frequency content of flow fluctuations. However, up to now, units that meet all three predictions have not been found. Instead, the discharge rate of most midbrain lateral line units simply increases with increasing bulk flow velocity (Fig. 8). The only central unit that was tuned to a certain bulk flow velocity was not directionally sensitive.

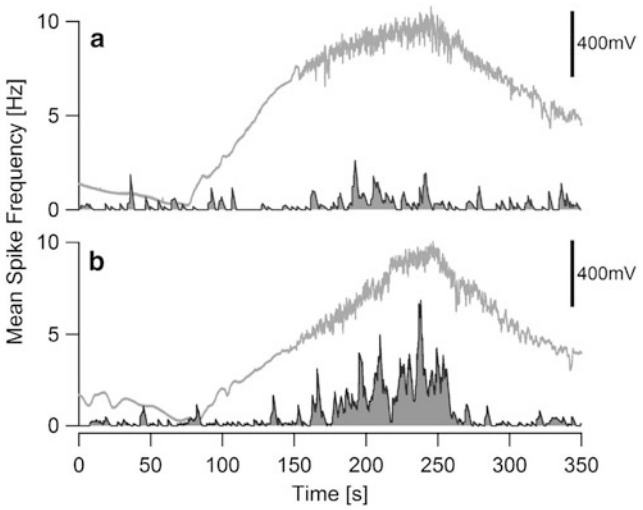

Fig. 8 A directionally sensitive lateral line unit recorded in the TS of the goldfish. PST histograms (bin width 3 s) of the neural responses (dark gray histogram) and superimposed hot-wire anemometer traces representing water velocity (light gray) for head-to-tail (**a**) and tail-to-head (**b**) water flow, respectively. Scale bars indicate that the water flow profiles were similar for both flow directions

5.4 Responses to Vortex Streets

Rheophilic fish prefer to hold station in disturbed flow regions, a behavior that has been systematically studied in flow tanks. Behind an obstacle in the flow, a so-called Kármán vortex street is generated, which is characterized by discrete, periodically shed, columnar vortices of alternating rotation direction. It has been shown that trout use the upstream water motions in a Kármán vortex streets to conserve energy (Liao, 2007). Fish may also use the lateral line for the detection of the vortices caused by the undulatory tail fin motions of another fish. Therefore, it is not surprising that primary lateral line afferents respond not only to single vortices (Chagnaud et al., 2006) but also to the vortices in a Kármán vortex street (Chagnaud et al., 2007a). Compared to still water conditions, both laminar water flow and flow contaminated with a Kármán vortex street cause an increase in the discharge rate of anterior lateral line nerve fibers. If exposed to a Kármán vortex street, the amplitude of spike train frequency spectra peaks at the vortex shedding frequency (Chagnaud et al., 2007a) (see also the chapter by Chagnaud & Coombs).

Some units in the MON of the rudd (*Scardinius erythrophthalmus*) are sensitive to the vortex streets generated by a cylinder positioned upstream. These units respond with short bursts to each vortex in a vortex street; consequently the burst frequency is identical with the vortex shedding frequency (Fig. 9).

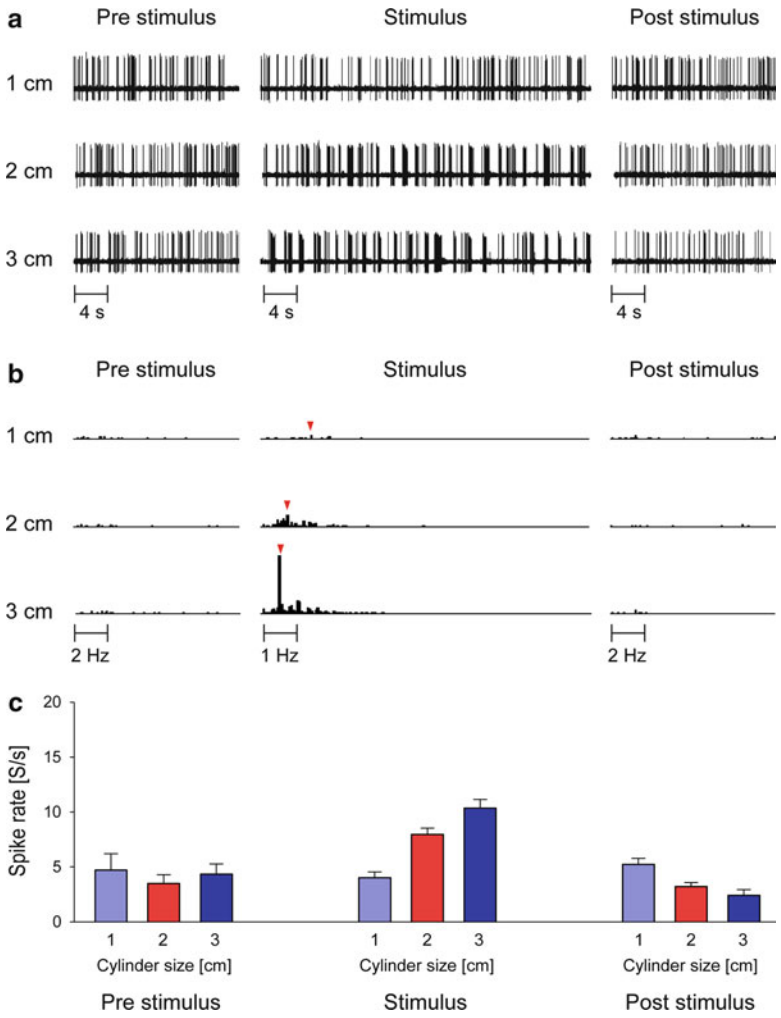

Fig. 9 Responses of a MON unit to uniform flow without a cylinder (left: prestimulus; right: poststimulus) and to the vortex motions (stimulus) caused by an upstream cylinder of 1, 2, and 3 cm diameter. Flow velocity varied between 6 and 7 cm s^{-1}. (**a**) Original recordings. Note the absence of bursts during the pre- and poststimulus conditions and the bursting activity during the stimulus condition. (**b**) Spectral composition of the neuronal responses. The spectra shown in the middle graphs (stimulus) peaked at frequencies close to the vortex shedding frequencies expected from the different cylinder sizes (red arrowheads). (**c**) Spike rates. With increasing cylinder diameter spikes rates increased during the stimulus condition but not during the pre- and poststimulus conditions. (Adapted from Bleckmann et al., 2012)

5.5 *Responses to Dipole and Moving Object Stimuli in Still and Running Water*

As has been pointed out (see the chapter by Webb) the lateral line of most fish consists of SNs and of CNs. In still water, afferent fibers from both types of neuromasts respond equally well to a vibrating sphere stimulus. In running water, however, responses of SNs to a vibrating sphere are masked. In contrast, at bulk flow velocities <10 cm s^{-1} responses of fibers innervating CNs are barely altered (Engelmann et al., 2000, 2002a). In the MON and TS of goldfish a similar dichotomy has been found (Kröther et al., 2002; Engelmann & Bleckmann, 2004). Many MON and TS units are flow sensitive. These units increase or decrease their discharge rates in running water. Consequently, their responses to a dipole stimulus are masked by bulk water flow. Other units are flow insensitive and their responses to the dipole stimulus are not masked in running water. This again suggests that the input from SNs and CNs is processed in separate channels and that the functional subdivision of the lateral line periphery is maintained to a large degree up to the level of the midbrain. However, there appears to be a third category of flow-insensitive MON units whose responses to the dipole are nevertheless reduced in running water. Perhaps the responses of these neurons are due to interactions between the SN and CN systems.

As with dipole stimuli, the effects of running water on the responses of central lateral line units to a moving object are more diverse than the effects of running water on primary afferent responses (Engelmann et al., 2003; Engelmann & Bleckmann, 2004). In general, both MON and midbrain units respond weaker when an object is moved with the flow. When the object is moved against the flow, MON responses are on average comparable to those in still water (Fig. 10). Thus, the masking effect depends not only on flow velocity, but also on the orientation of the fish with respect to the direction of bulk water flow. There are, however, differences between still and running water fish. In the limnophilic goldfish, most of the flow-sensitive MON units that respond to a moving object in still water do not respond or respond only weakly when the object is moved in running water alongside the fish. In contrast, in the rheophilic trout, the number of flow-sensitive MON units that respond to a moving object in still, but not running water, is smaller than in goldfish. That is, most flow-sensitive MON units in the trout respond to the moving object under both still and running water conditions. These physiological differences between goldfish and trout indicate that the central lateral line system of different fish species may be adapted to different hydrodynamic conditions.

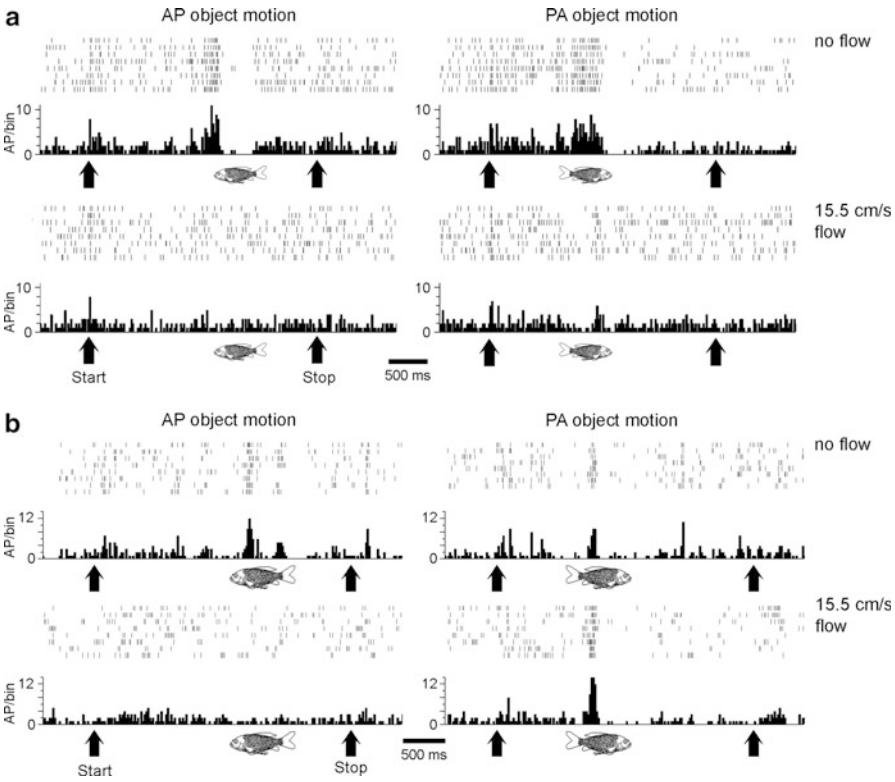

Fig. 10 (**a**, **b**) Responses of a flow-sensitive (**a**) and flow-insensitive (**b**) MON unit in goldfish to a moving object passing the fish laterally with a speed of 10 cm s^{-1}. Each graph shows a raster plot (each vertical line represents one action potential) of the responses to ten object presentations and the corresponding PSTHs (bin width 20 ms). Left: Anterior–posterior object motion. Right: Posterior–anterior object motion. Upper rows in (**a**) and (**b**): Still water conditions. Lower rows: running water conditions (flow velocity 15.5 cm s^{-1}). The fish symbol below each plot indicates the size and position of the fish relative to the position of the moving object as function of time. (Adapted from Engelmann et al., 2003) with permission of S. Karger AG, Basel)

6 Suppression of Common Mode Signals and Self-generated Noise

The mechanosensory lateral line is extremely sensitive to extrinsic water motions (see also the chapter by Chagnaud & Coombs). To maintain this sensitivity while the fish moves, the lateral line should be able to extract weak extrinsic stimuli from the large reafferent signals associated with the fish's own body movements. This is confirmed in a behavioral study that shows that the lateral line system of surface-feeding fish maintains its sensitivity while the fish is moving with a speed of up to 10 cm s^{-1} (1.5 body length) (Bleckmann, 1982).

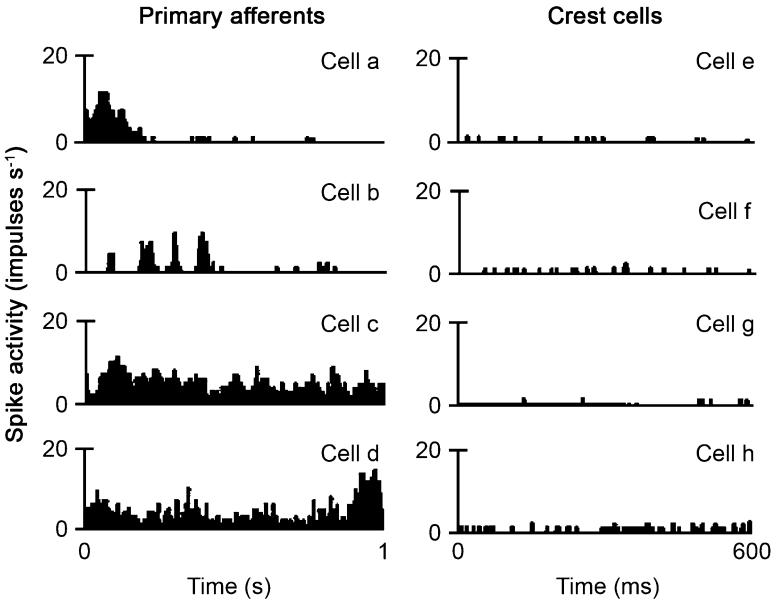

Fig. 11 Responses of four primary lateral line afferents (left-hand column) and 4 MON cells (right-hand column) to ventilation. Histograms of ongoing spike activity for 1 s in the case of primary afferents and 600 ms in the case of MON cells extend for most, but not all, of one ventilation cycle. Collection of spike activity to produce the histograms was initiated by the trigger generated from a strain gauge attached to the operculum, so the beginning of the histogram corresponds to opercular closure. The examples were chosen to show the range of responses observed. Note the much higher ongoing activity of the primary afferent units and their modulation by breathing activity. The RFs of crest cells (**e**) and (**f**) were on the operculum, those for cells (**g**) and (**h**) were on the lower jaw. (Reproduced from Montgomery et al., 1996) with permission of The Company of Biologists)

Gill motions strongly modulate the firing rates of primary lateral line afferents. This modulation is greatly suppressed in MON units (Fig. 11). Experimental data suggest that one neural mechanism of reafference suppression is common mode rejection (Montgomery & Bodznick, 1994; Nelson & Paulin, 1995). In addition to this mechanism, second-order neurons in the MON of teleost fish also "learn" to cancel the effects of stimuli that are coupled to the fish's gill movements (Montgomery & Bodznick, 1994).

7 Multimodal Integration

In general, multimodal integration of sensory information is crucial in organizing the behavior of animals. For instance, in the largemouth bass (*Micropterus salmoides*) and the pike (*Esox masquinongy*), lateral line and vision together determine the optimum distance and angular deviation for the initiation of a strike

(New, 2002). Weakly electric fish (*Gnathonemus petersii*) integrate electrosensory, mechanosensory, and visual information for prey detection and prey localization (von der Emde & Bleckmann, 1998). Both lateral line and chemosensory information play an important role in prey capture (Montgomery et al., 2002; Gardiner & Atema, 2007). In general, the few behavioral studies that have been performed with fish to address the question of multimodal integration demonstrate a hierarchy of the senses involved in predator/prey interactions, with different modalities playing different roles during certain phases of prey capture.

Despite these behavioral findings, most physiological studies of fish sensory biology have been restricted to a single modality. However, fish use not only the lateral line to detect and identify a stimulus source but also visual, acoustic, tactile, electrical (if they have an electrosensory system) and chemical cues (von der Emde & Bleckmann, 1992; Hara, 1993; Braun et al., 2002). Thus, to enable object detection, identification, and localization, inputs from different sensory modalities should converge in higher brain centers.

At least up to the level of the midbrain, the lateral line system of fishes maintains a largely separated central pathway. With possible exceptions (Andrianov & Ilynski, 1973), second-order lateral line units of the medulla are unimodal (Bleckmann & Bullock, 1989). However, midbrain and especially forebrain lateral line units may be bi-, tri-, or multimodal. In other words, higher-order lateral line units may also respond to visual, somatosensory, acoustic, vibratory, or electrosensory (ampullary or tuberous) input (Bleckmann & Bullock, 1989; Bartels et al., 1990; Kirsch et al., 2002a,b). Lateral line evoked discharges of central units may be suppressed by visual (Tricas & Highstein, 1990), acoustic, or ampullary input (Bleckmann et al., 1989b). In other cases, ampullary input facilitates lateral line responses (Müller & Bleckmann, 1993). In the thornback guitarfish *Platyrhinoidis* some diencephalic lateral line units respond only when the animal receives both lateral line and corresponding visual information (Bleckmann et al., 1987).

8 Physiology of Descending (Efferent) Lateral Line Pathways

In most teleosts investigated, the medial and central zones of the area dorsalis telencephali project back onto the lateral preglomerular nucleus in the diencephalon. The functional significance of these projections is not known. The MON receives descending input from parts of the cerebellum (Montgomery et al., 1995), from the nucleus preeminentialis, which receives input from the TS (Wullimann, 1998; Weeg & Bass, 2000) and - in some teleosts - from the ipsilateral sensory trigeminal nucleus (McCormick & Hernandez, 1996). Possible functions of descending recurrent inputs include gain control and the establishment of central representations of expected sensory input (Montgomery & Bodznick, 1994).

Lateral line neuromasts also receive descending (efferent) input (see the chapter by Chagnaud & Coombs). The somata of the efferent nerve fibers are located in the

octavolateralis efferent nucleus (Song & Northcutt, 1991a; Schellart et al., 1992; Wagner & Schwartz, 1992) and, in some euteleosts, in the diencephalon (Roberts & Meredith, 1989). Octavolateralis efferents respond to visual, somatosensory, vestibular, and lateral line stimuli (Roberts & Russell, 1972; Tricas & Highstein, 1990, 1991). The efferent system slightly modulates the overall sensitivity of the mechanosensory lateral line (Roberts & Meredith, 1989; Tricas & Highstein, 1990, 1991) but more studies are needed to uncover the biological function of descending lateral line pathways.

9 Conclusions and Open Questions

At present, we have a fairly good understanding of how single lateral line units in the brain stem MON and the midbrain TS respond to different lateral line stimuli, for example, a vibrating sphere, a moving object, or bulk water flow. In addition, we know whether and how the responses of MON and TS units to sinusoidal water motions or a moving object are affected by bulk water flow. However, despite all this knowledge, researchers still have not uncovered the computational rules and the circuit diagrams implemented in the central lateral line. There are several reasons for this. First, despite some progress (Montgomery & Macdonald, 1987; Bleckmann et al., 1991b; Hanke & Bleckmann, 2004) our knowledge about the temporal and spatial characteristics of biologically meaningful hydrodynamic stimuli is still sparse. Second, under natural conditions, the lateral line system constantly has to cope with self-generated and externally generated hydrodynamic noise. Peripheral (matched) filters may separate meaningful stimuli from hydrodynamic noise (Engelmann et al., 2000) but central mechanisms may also be involved. Recordings from central lateral line units of freely swimming fish may be particularly useful to uncover peripheral and central filters. Third, both biologically meaningful stimuli and natural noise conditions may be highly species specific, depending on the lifestyle and natural hydrodynamic environment of the respective species. As but one example, surface-feeding fish that live in small ponds have to cope with water surface waves and are probably less prone to hydrodynamic noise, whereas rheophilic fish often face turbulent hydrodynamic conditions and thus are constantly exposed to irregular water motions (Liao, 2007). The physiologist needs to know the natural stimuli and noise conditions a species is exposed to in order to increase the chance of finding highly selective lateral line units and thus to uncover central maps and computational rules.

The first gap in our knowledge is already apparent at the level of the medulla. In both aquatic amphibians and fish, primary lateral line afferents bifurcate after entering the MON and each of the two branches contacts many secondary cells (Claas & Münz, 1981; Blübaum-Gronau & Münz, 1987; Song & Northcutt, 1991b). Additional spatially segregated mechanosensory projections reach the vestibulocerebellum (Koester, 1983; Puzdrowski & Leonard, 1993). The functional significance of this bifurcation and divergence in the MON remains a mystery. Also, the

functional significance of having two brain stem nuclei, the MON and the CON, and the projections to the vestibulo-cerebellum, has never been investigated. We also do not know whether there are morphologically distinct subsystems that process SN and CN information separately. Furthermore we do not know whether the information of the two hair cell populations in a neuromast are processed in pathways that are morphologically separated. We also do not know whether and at which, respectively, level of the brain the different subsystems of the lateral line do converge.

Although we have some knowledge about the MON and TS, nearly nothing is known about the processing of lateral line information in the tectum opticum of fish. This is especially unfortunate because we know from studies in amphibians that a tectal lateral line map does exist, that it is in register with a visual and an electrosensory map (if the animal has electroreception), and that these maps represent the external space (Zittlau et al., 1986; Bartels et al., 1990). In addition, nearly nothing is known about the processing of lateral line information in the cerebellum, a brain structure that is involved not only in motor control (Denise & Darlot, 1993) but also in cognitive functions (Akshoomoff & Courchesne, 1992). Another gap in our knowledge refers to the function of the forebrain of fishes. Both the diencephalon and the telenecephalon, receive lateral line input but exhibit strong habituation (Bleckmann et al., 1987; Bleckmann et al., 1989b; Prechtl et al., 1998). Lateral line units (and evoked potentials) recorded from forebrain lateral line areas may require interstimulus intervals up to 50 s in order to respond in a repetitive stimulus regime (Bleckmann et al., 1989a). Thus finding a forebrain lateral line unit and testing the unit with various types of potentially meaningful biological stimuli is quite challenging. In general, researchers up to now barely have investigated adaptation and habituation in the central lateral line pathway. One intriguing question is whether the responses of units that require long interstimulus intervals can be dishabituated by the presentation of a novel stimulus.

Another major challenge for lateral line research is to establish a relationship between morphology and physiology at the cellular level. It is known that in a given nucleus various cell types are involved in the processing of hydrodynamic information. For instance, at least five MON cell types have been described (New et al., 1996). What is not known, however, are the functions and interconnections of the different cell types. Intracellular recording techniques with subsequent staining of the cell will help to reveal relationships between cell function and morphology. Knowing about these relationships will also help to develop central circuit diagrams. To date, the only comprehensive lateral line circuit diagram is that suggested by Montgomery & Bodznick (1994) for explaining the cancellation of self-generated noise caused by gill movements at the level of the MON.

Another huge gap in our knowledge refers to the function of the central efferent lateral line pathways. From the electrosensory lateral line it is known that the efferent pathway is involved in gain control and attention (Bastian, 1986), a finding that may apply to the mechanosensory lateral line as well. Finally, we have very limited knowledge about how information from different sensory modalities is integrated by central units. Although multimodal lateral line units have been recorded from the midbrain and forebrain of fishes (Kirsch et al., 2002a,b), little

is known about how one modality affects the other. Only if we investigate multimodal integration will we be able to understand fully how the fish brain integrates sensory input to adequately guide behavior.

Acknowledgments The authors are indebted to Sheryl Coombs and John Montgomery for carefully reading and commenting on the manuscript. They thank Vera Schlüssel and Sheryl Combs for stylistic help. The original research of the authors was generously supported by the Deutsche Forschungsgemeinschaft, the Bundesministerium für Bildung und Forschung, Defense Advances Research Project Agency, the Bundeanstalt für Gewässerkunde, Deutscher Akademischer Austauschdienst, and the Europäische Union.

References

Akshoomoff, N. A., & Courchesne, E. (1992). A new role for the cerebellum in cognitive operations. *Behavioral Neuroscience*, 106, 731–738.

Alexandre, D., & Ghysen, A. (1999). Somatotopy of the lateral line projection in larval zebrafish. *Proceedings of the National Academy of Sciences of the USA*, 96, 7558–7562.

Ali, R., Mogdans, J., & Bleckmann, H. (2010). Responses of medullary lateral line units of the goldfish, *Carassius auratus*, to amplitude-modulated sinusoidal wave stimuli. *International Journal of Zoology*, doi:10.1155/2010/762621.

Alnaes, E. (1973). Unit activity of ganglionic and medullary second order neurones in the eel lateral line system. *Acta Physiologica Scandinavia*, 88, 160–174.

Andrianov, G. N., & Ilynski, O. B. (1973). Some functional properties of central neurons connected with the lateral-line organs of the catfish (*Ictalurus nebulosus*). *Journal of Comparative Physiology A*, 86, 365–376.

Bartels, M., Münz, H., & Claas, B. (1990). Representation of lateral line and electrosensory systems in the midbrain of the axolotl, *Ambystoma mexicanum*. *Journal of Comparative Physiology A*, 167, 347–356.

Bastian, J. (1986). Gain control in the electrosensory system: A role for the descending projections to the electrosensory lateral line lobe. *Journal of Comparative Physiology A*, 158, 505–515.

Behrend, O., Branoner, F., Zhivko, Z., & Ziehm, U. (2006). Neural responses to water surface waves in the midbrain of the aquatic predator *Xenopus laevis*. *European Journal of Neuroscience*, 23, 729–744.

Birkhofer, M., Bleckmann, H., & Görner, P. (1994). Sensory activity in the telencephalon of the clawed toad, *Xenopus laevis*. *European Journal of Morphology*, 32, 262–266.

Bleckmann, H. (1982). Reaction time, threshold values and localization of prey in stationary and swimming surface feeding fish *Aplocheilus lineatus* (Cyprinodontidae). *Zoologisches Jahrbuch Abteilung Physiologie*, 86, 71–81.

Bleckmann, H., & Topp, G. (1981). Surface wave sensitivity of the lateral line organs of the topminnow *Aplocheilus lineatus*. *Naturwissenschaften*, 68, 624–625.

Bleckmann, H., & Bullock, T.H. (1989). Central nervous physiology of the lateral line system, with special reference to cartilaginous fishes. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 387–408). New York: Springer-Verlag.

Bleckmann, H., & Münz, H. (1990). Physiology of lateral-line mechanoreceptors in a teleost with highly branched, multiple lateral lines. *Brain, Behavior and Evolution*, 35, 240–250.

Bleckmann, H., & Zelick, R. (1993). The responses of peripheral and central mechanosensory lateral line units of weakly electric fish to moving objects. *Journal of Comparative Physiology A*, 172, 115–128.

Bleckmann, H., Waldner, I., & Schwartz, E. (1981). Frequency discrimination of the surface-feeding fish *Aplocheilus lineatus*—a prerequisite for prey localization? *Journal of Comparative Physiology A*, 143, 485–490.

Bleckmann, H., Bullock, T. H., & Jorgensen, J. M. (1987). The lateral line mechanoreceptive mesencephalic, diencephalic, and telencephalic regions in the thornback ray, *Platyrhinoidis triseriata* (Elasmobranchii). *Journal of Comparative Physiology A*, 161, 67–84.

Bleckmann, H., Tittel, G., & Blübaum-Gronau, E. (1989a). The lateral line system of surface-feeding fish: Anatomy, physiology, and behavior. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 501–526). New York: Springer-Verlag.

Bleckmann, H., Weiss, O., & Bullock, T. H. (1989b). Physiology of lateral line mechanoreceptive regions in the elasmobranch brain. *Journal of Comparative Physiology A*, 164, 459–474.

Bleckmann, H., Niemann, U., & Fritzsch, B. (1991a). Peripheral and central aspects of the acoustic and lateral line system of a bottom dwelling catfish, *Ancistrus* spec. *Journal of Comparative Neurology*, 314, 452–466.

Bleckmann, H., Breithaupt, T., Blickhan, R., & Tautz, J. (1991b). The time course and frequency content of hydrodynamic events caused by moving fish, frogs, and crustaceans. *Journal of Comparative Physiology A*, 168, 749–757.

Bleckmann, H., Przybilla, A., Klein, A., Schmitz, A., Kunze, S., & Brücker, C. (2012). Station holding in trout: Behavior, physiology and hydrodynamics. In T. Tropea & H. Bleckmann (Eds.), *Nature-inspired fluid mechanics* (pp. 161–177). New York: Springer.

Blübaum-Gronau, E., & Münz, H. (1987). Topological representation of primary afferents in various segments of the lateral line system in the butterflyfish, *Pantodon buchholzi Verhandlungen der Deutschen Zoologischen Gesellschaft* (pp. 268–269). Stuttgart: Gustav Fischer.

Braun, C. B., Coombs, S., & Fay, R. R. (2002). What is the nature of multisensory interaction between octavolateralis sub-systems? *Brain, Behavior and Evolution*, 59, 162–176.

Chagnaud, B. P., Bleckmann, H., & Engelmann, J. (2006). Neural responses of goldfish lateral line afferents to vortex motions. *Journal of Experimental Biology*, 209, 327–342.

Chagnaud, B. P., Bleckmann, H., & Hofmann, M. (2007a). Kármán vortex street detection by the lateral line. *Journal of Comparative Physiology A*, 193, 753–763.

Chagnaud, B. P., Bleckmann, H., & Hofmann, M. H. (2007b). Lateral line nerve fibers do not respond to bulk water flow direction. *Zoology*, 111, 204–207.

Claas, B., & Münz, H. (1981). Projection of lateral line afferents in a teleost brain. *Neuroscience Letters*, 23, 287–290.

Coombs, S., & Janssen, J. (1990). Behavioral and neurophysiological assessment of lateral line sensitivity in the mottled sculpin, *Cottus bairdi*. *Journal of Comparative Physiology A*, 167, 557–567.

Coombs, S., & Patton, P. (2009). Lateral line stimulation patterns and prey orieting behavior in the Lake Michigan mottled sculpin (*Cottus bairdi*). *Journal of Comparative Physiology A*, 195, 279–297.

Coombs, S., Fay, R. R., & Janssen, J. (1989). Hot-film anemometry for measuring lateral line stimuli. *Journal of the Acoustical Society of America*, 85, 2185–2193.

Coombs, S., Hastings, M., & Finneran, J. (1996). Modeling and measuring lateral line excitation patterns to changing dipole source locations. *Journal of Comparative Physiology A*, 178, 359–371.

Coombs, S., Mogdans, J., Halstead, M., & Montgomery, J. (1998). Transformation of peripheral inputs by the first-order lateral line brainstem nucleus. *Journal of Comparative Physiology A*, 182, 609–626.

Coombs, S., Braun, C. B. , & Donovan, B. (2001). The orienting response of Lake Michigan mottled sculpin is mediated by canal neuromasts. *Journal of Experimental Biology*, 204, 337–348.

Ćurčić-Blake, B., & van Netten, S. M. (2006). Source localization encoding in the fish lateral line. *Journal of Experimental Biology*, 209, 1548–1559.

Denise, P., & Darlot, C. (1993). The cerebellum as a predictor of neural messages II. Role in motor control and motion sickness. *Neuroscience*, 56, 647–655.

Elepfandt, A. (1986). Wave frequency recognition and absolute pitch for water waves in the clawed frog, *Xenopus laevis*. *Journal of Comparative Physiology A*, 158, 235–238.

Elepfandt, A., Seiler, B., & Aicher, B. (1985). Water wave frequency discrimination in the clawed frog, *Xenopus laevis*. *Journal of Comparative Physiology A*, 157, 255–261.

Engelmann, J., & Bleckmann, H. (2004). Coding of lateral line stimuli in the goldfish midbrain in still- and running water. *Zoology*, 107, 135–151.

Engelmann, J., Hanke, W., Mogdans, J., & Bleckmann, H. (2000). Hydrodynamic stimuli and the fish lateral line. *Nature*, 408, 51–52.

Engelmann, J., Hanke, W., & Bleckmann, H. (2002a). Lateral line reception in still- and running water. *Journal of Comparative Physiology A*, 188(7), 513–526.

Engelmann, J., Kröther, S., Mogdans, J., & Bleckmann, H. (2002b). Responses of primary and secondary lateral line units to dipole stimuli applied under still and running water conditions. *Bioacoustics*, 12, 158–160.

Engelmann, J., Kröther, S., Bleckmann, H., & Mogdans, J. (2003). Effects of running water on lateral line responses to moving objects. *Brain, Behavior and Evolution*, 61, 195–212.

Fiebig, E. (1988). Connections of the corpus cerebelli in the thornback guitarfish, *Platyrhinoidis triseriata* (Elasmobranchii): A study with WGA-HRP and extracellular granule cell recording. *Journal of Comparative Neurology*, 268, 567–583.

Fritzsch, B. (1989). Diversity and regression in the amphibian lateral line and electrosensory system. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 99–114). New York: Springer-Verlag.

Frühbeis, B. (1984). Verhaltensphysiologische Untersuchungen zur Frequenzunterscheidung und Empfindlichkeit durch das Seitenlinienorgan des blinden Höhlenfisches *Anoptichthys jordani*. Dissertation, Universität Mainz, 1–73.

Gardiner, J. M., & Atema, J. (2007). Sharks need the lateral line to locate odor sources: Rheotaxis and eddy chemotaxis. *Journal of Experimental Biology*, 210, 1925–1934.

Gompel, N., Dembly-Chaudière, C., & Ghysen, A. (2001). Neuronal differences prefigure somatotopy in the zebrafish lateral line. *Development*, 128, 387–393.

Hanke, W., & Bleckmann, H. (1999). Flow visualization and particle image velocimetry with a custom made inexpensive device. In D. Zissler (Ed.), *Verhandlungen der Deutschen Zoololgischen Gesellschaft*. Stuttgart: Gustav Fischer Verlag.

Hanke, W., & Bleckmann, H. (2004). The hydrodynamic trails of *Lepomis gibbosus* (Centrarchidae), *Colomesus psittacus* (Tetraodontidae) and *Thysochromis ansorgii* (Cichlidae) investigated with scanning particle image velocimetry. *Journal of Experimental Biology*, 207, 1585–1596.

Hara, O. (1993). Role of olfactation in fish behavior. In T. J. Pitcher (Ed.), *Behaviour of teleost fishes*, (2nd ed., pp. 171–199). London, New York: Chapman and Hall.

Ivry, R. B., & Baldo, J. V. (1992). Is the cerebellum involved in learning and cognition? *Current Opinion in Neurobiology*, 2, 212–216.

Kirsch, J. A., Hofman, M. A., Mogdans, J., & Bleckmann, H. (2002a). Responses of diencephalic neurons to sensory stimulation in the goldfish, *Carassius auratus*. *Brain Research Bulletin*, 57, 419–421.

Kirsch, J. A., Hofmann, M. H., Mogdans, J., & Bleckmann, H. (2002b). Response properties of diencephalic neurons to visual, acoustic and hydrodynamic stimulation in the goldfish, *Carassius auratus*. *Zoology*, 105, 61–70.

Knudsen, E. I. (1977). Distinct auditory and lateral line nuclei in the midbrain of catfishes. *Journal of Comparative Neurology*, 173, 417–432.

Koester, D. M. (1983). Central projections of the octavolateralis nerves of the clearnose skate, *Raja eglanteria*. *Journal of Comparative Neurology*, 221, 199–215.

Kotchabhakdi, N. (1976). Functional organization of the goldfish cerebellum: Information processing of input from peripheral sense organs. *Journal of Comparative Physiology A*, 112, 75–93.

Kröther, S., Mogdans, J., & Bleckmann, H. (2002). Brainstem lateral line responses to sinusoidal wave stimuli in still- and running water. *Journal of Experimental Biology*, 205, 1471–1484.

Kröther, S., Bleckmann, H., & Mogdans, J. (2004). Effects of running water on brainstem latetral line responses in trout, *Oncorhynchus mykiss*, to sinusoidal wave stimuli. *Journal of Comparative Physiology A*, 190, 437–448.

Künzel, S., Bleckmann, H., & Mogdans, J. (2011). Responses of brainstem lateral line units to different stimulus source locations and vibration directions. *Journal of Comparative Physiology A*, 197, 773–787.

Lee, L. T., & Bullock, T. H. (1984). Sensory representation in the cerebellum of the catfish. *Journal of Comparative Physiology A*, 13, 157–169.

Liao, J. C. (2007). A review of fish swimming mechanics and behaviour in altered flows. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 362, 1973–1993.

McCormick, C. A. (1989). Central lateral line mechanosensory pathways in bony fish. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution*. (pp. 341–364). New York: Springer-Verlag.

McCormick, C. A., & Hernandez, D. V. (1996). Connections of the octaval and lateral line nuclei of the medulla in the goldfish, including the cytoarchitecture of the secondary octaval population in goldfish and catfish. *Brain, Behavior and Evolution*, 47, 113–138.

Meyer G. (2010) Spatial sensitivity of midbrain lateral line units of the goldfish, *Carassius auratus*. PhD thesis, University of Bonn

Mogdans, J., & Bleckmann, H. (1998). Responses of the goldfish trunk lateral line to moving object. *Journal of Comparative Physiology A*, 182, 659–676.

Mogdans, J., & Goenechea, L. (2000). Responses of medullary lateral line units in the goldfish, *Carassius auratus*, to sinusoidal and complex wave stimuli. *Zoology*, 102, 227–237.

Mogdans, J., & Kröther, S. (2001). Brainstem lateral line responses to sinusoidal wave stimuli in the goldfish, *Carassius auratus*. *Zoology*, 104, 153–166.

Mogdans, J., Bleckmann, H., & Menger, N. (1997). Sensitivity of central units in the goldfish, *Carassius auratus*, to transient hydrodynamic stimuli. *Brain, Behavior and Evolution*, 50, 261–283.

Montgomery, J. C., & Macdonald, J. A. (1987). Sensory tuning of lateral line receptors in Antarctic fish to the movements of planctonic prey. *Science*, 235, 195–196.

Montgomery, J. C., & Coombs, S. (1992). Physiological characterization of lateral line function in the Antarctic fish *Trematomus bernacchii*. *Brain, Behavior and Evolution*, 40, 209–216.

Montgomery, J. C., & Bodznick, D. (1994). An adaptive filter that cancels self-induced noise in the electrosensory and lateral line mechanosensory systems of fish. *Neuroscience Letters*, 174, 145–148.

Montgomery, J. C., & Coombs, S. (1998). Peripheral encoding of moving sources by the lateral line system of a sit-and-wait predator. *Journal of Experimental Biology*, 201, 91–102.

Montgomery, J. C., Coombs, S., Conley, R. A., & Bodznick, D. (1995). Hindbrain sensory processing in lateral line, electrosensory, and auditory systems: A comparative overview of anatomical and functional similarities. *Auditory Neuroscience*, 1, 207–231.

Montgomery, J., Bodznick, D., & Halstead, M. (1996). Hindbrain signal processing in the lateral line system of the dwarf scorpionfish *Scopeana papillosus*. *Journal of Experimental Biology*, 199, 893–899.

Montgomery, J. C., Macdonald, F., Baker, C. F., & Carton, A. G. (2002). Hydrodynamic contributions to multimodal guidance of prey capture behavior in fish. *Brain, Behavior and Evolution*, 59, 190–198.

Müller, H. M. (1996). Indications for feature detection with the lateral line organ fish. *Comparative Biochemestry and Physiology*, 114, 257–263.

Müller, H. M., & Bleckmann, H. (1993). The responses of central octavolateralis cells to moving sources. *Journal of Comparative Physiology A*, 179, 455–471.

Münz, H. (1985). Single unit activity in the peripheral lateral line system of the cichlid fish *Sarotherodon niloticus* L. *Journal of Comparative Physiology A*, 157, 555–568.

Münz, H. (1989). Functional organization of the lateral line periphery. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 285–298). New York: Springer-Verlag.

Nelson, M. E., & Paulin, M. G. (1995). Neural stimulations of adaptive reafference suppression in the elasmobranch electrosensory system. *Journal of Comparative Physiology A*, 177, 723–736.

New, J. G. (2002). Multimodal integration in the feeding behaviors of predatory teleost fishes. *Brain, Behavior and Evolution*, 59, 177–189.

New, J. G., Coombs, S., McCormick, C. A., & Oshel, P. E. (1996). Cytoarchitecture of the medial octavolateralis nucleus in the goldfish, *Carassius auratus*. *Journal of Comparative Neurology*, 366, 534–546.

New, J. G., Braun, C. B., & Walter, K. (2000). Central projections of nerve fibers innervating individual canal neuromast organs in the muskellunge, *Esox masquinongy*. *Society of Neuroscience Abstracts*, 26, 146.

Plachta, D., Mogdans, J., & Bleckmann, H. (1999). Responses of midbrain lateral line units of the goldfish, *Carassius auratus*, to constant-amplitude and amplitude modulated water wave stimuli. *Journal of Comparative Physiology A*, 185, 405–417.

Plachta, D., Hanke, W., & Bleckmann, H. (2003). A hydrodynamic topographic map and two hydrodynamic subsystems in a vertebrate brain. *Journal of Experimental Biology*, 206, 3479–3486.

Prechtl, J. C., von der Emde, G., Wolfart, J., Karamürsel, S., Akoev, G. N., Andrianov, Y. N., & Bullock, T. H. (1998). Sensory processing in the pallium of a mormyrid fish. *Journal of Neuroscience*, 18, 7381–7393.

Puzdrowski, R. L. (1989). Peripheral distribution and central projections of the lateral-line nerves in goldfish, *Carassius auratus*. *Brain, Behavior and Evolution*, 34, 110–131.

Puzdrowski, R. L., & Leonard, R. B. (1993). The octavolateral systems in the stingray, *Dasyatis sabina*. I. Primary projections of the octaval and lateral line nerves. *Journal of Comparative Neurology*, 332, 21–37.

Roberts, B. L., & Russell, I. J. (1972). The activity of lateral-line efferent neurones in stationary and swimming dogfish. *Journal of Experimental Biology*, 57, 435–448.

Roberts, B. L., & Meredith, G. E. (1989). The efferent system. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 445–459). New York: Springer-Verlag.

Sand, O. (1981). The lateral line and sound reception. In W. N. Tavolga, A. N. Popper, & R. R. Fay (Eds.), *Hearing and sound communication in fishes* (pp. 459–480). New York: Springer-Verlag.

Schellart, N. A. M., & Kroese, A. B. A. (1989). Interrelationship of acousticolateral and visual systems in the teleost midbrain. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 421–443). New York: Springer-Verlag.

Schellart, N. A. M., Prins, M., & Kroese, A. B. A. (1992). The pattern of trunk lateral line afferents and efferents in the rainbow trout (*Salmo gairdneri*). *Brain, Behavior and Evolution*, 39, 371–380.

Song, J., & Northcutt, R. G. (1991a). Morphology, distribution and innervation of the lateral-line receptors of the Florida gar, *Lepisosteus platyrhincus*. *Brain, Behavior and Evolution*, 37, 10–37.

Song, J., & Northcutt, R. G. (1991b). The primary projections of the lateral-line nerves of the Florida gar, *Lepisosteus platyrhincus*. *Brain, Behavior and Evolution*, 37, 38–63.

Tricas, T. C., & Highstein, S. M. (1990). Visually mediated inhibition of lateral line primary afferent activity by the octavolateralis efferent system during predation in the free-swimming toadfish, *Opsanus tau*. *Experimental Brain Research*, 83, 233–236.

Tricas, T. C., & Highstein, S. M. (1991). Action of the octavolateralis efferent system upon the lateral line of free-swimming toadfish, *Opsanus tau*. *Journal of Comparative Physiology A*, 169, 25–37.

Vogel, D., & Bleckmann, H. (1997). Surface wave discrimination in the topminnow *Aplocheilus lineatus*. *Journal of Comparative Physiology A*, 180, 671–681.

Voges, K., & Bleckmann, H. (2011). Two-dimensional receptive fields of midbrain lateral line unitsin the goldfish, *Carassius auratus*. *Journal of Comparative Physiology A*, 197, 827–837.

von der Emde, G., & Bleckmann, H. (1992). Differential responses of two types of electroreceptive afferents to signal distortions may permit capacitance measurement in a weakly electric fish, *Gnathonemus petersii*. *Journal of Comparative Physiology A*, 171, 683–694.

von der Emde, G., & Bleckmann, H. (1998). Finding food: Senses involved in foraging for insect larvae in the electric fish *Gnathonemus petersii*. *Journal of Experimental Biology*, 201, 969–980.

Wagner, T., & Schwartz, E. (1992). Efferent lateral-line neurons of teleosts and their projection to lateral-line segments. In N. Elsner & W. D. Richter (Eds.), *Rhythmogenesis in neurons and networks*. *Proceedings of the* 20*th Göttingen neurobiology conference*. Stuttgart: Georg Thieme Verlag.

Weeg, M. S., & Bass, A. H. (2000). Central lateral line pathways in a vocalizing fish. *Journal of Comparative Neurology*, 418, 41–64.

Weeg, M. S., & Bass, A. (2002). Frequency response properties of lateral line superficial neuromasts in a vocal fish, with evidence for acoustic sensitivity. *Journal of Neurophysiology*, 88, 1252–1262.

Wojtenek, W., Mogdans, J., & Bleckmann, H. (1998). The responses of midbrain lateral line units of the goldfish *Carassius auratus* to moving objects. *Zoology*, 101, 69–82.

Wubbels, R. J., Kroese, A. B. A., & Schellart, N. A. M. (1993). Response properties of lateral line and auditory units in the medulla oblongata of the rainbow trout (*Oncorhynchus mykiss)*. *Journal of Experimental Biology*, 179, 77–92.

Wullimann, M. F. (1998). The central nervous system. In D. H. Evans (Ed.), *The physiology of fishes* (2nd ed., pp. 245–282). New York: CRC Press.

Zittlau, K. E., Claas, B., Münz, H., & Görner, P. (1985). Multisensory interaction in the torus semicircularis of the clawed toad *Xenopus laevis*. *Neuroscience Letters*, 60, 77–81.

Zittlau, K. E., Claas, B., & Münz, H. (1986). Directional sensitivity of lateral line units in the clawed toad *Xenopus laevis* Daudin. *Journal of Comparative Physiology A*, 158, 469–477.

Zottoli, S. J., & Horne, C. van. (1983). Posterior lateral line afferent and efferent pathways within the central nervous system of the goldfish with special reference to the Mauthner cell. *Journal of Comparative Neurology*, 219, 100–111.

Functional Overlap and Nonoverlap Between Lateral Line and Auditory Systems

Christopher B. Braun and Olav Sand

Keywords Differential water movement • Dipole source • Distant touch • Far field • Gas bladder • Hydrodynamic flow field • Mauthner neuron • Multisensory integration • Near field • Particle motion • Prey detection • Predator avoidance • Rheotaxis • Swim bladder • Wake tracking • Whole body acceleration

> "The mucous canals of the fishes are nothing else than an accessory hearing organ spread over the whole body surface. I am not wont to maintain that it elicits sensation of sound, but its function will be found to fall within the realm of this still imperfectly understood sense of hearing."
>
> Mayser (1882, cited and translated by Lowenstein, 1967, p. 5)

> ". . . the lateral line organ responds to near-field displacements of sound sources; there is no longer any reason for considering the lateral line as a non-acoustic receptor system."
>
> van Bergeijk (1964, p. 291)

> "They [lateral-line organs] serve mainly to detect and locate moving animals (prey, enemies, social partners) at short range on the basis of current-like water disturbances. . . They are not engaged in the detection of propagated sonic or infrasonic sound waves. . ."
>
> Dijkgraaf (1963, p. 95)

C.B. Braun (✉)
Department of Psychology, Hunter College (CUNY), Programs in Biopsychology & Behavioral Neuroscience and Ecology, Evolution and Behavior, City University of New York, 10021 New York, USA
e-mail: cbraun@hunter.cuny.edu

O. Sand
Department of Molecular Biosciences, University of Oslo, Oslo N-0316, Norway

S. Coombs et al. (eds.), *The Lateral Line*, Springer Handbook of Auditory Research 48,
DOI 10.1007/2506_2013_19, © Springer Science+Business Media New York 2013,
Published online: 15 August 2013

1 Introduction

The problem of functional overlap between fish auditory and lateral line systems is, at its root, a problem of understanding other minds. Do fish "hear" with their lateral lines? If a source stimulates both the lateral line and the ear simultaneously, does that give rise to a perception that is something other than hearing? The very definitions of hearing and sound are so hopelessly intertwined that all definitions of auditory function are inherently tautological or anthropomorphic (e.g., reflected in concepts of infra- or ultrasonic with respect to the human hearing range). Nonetheless, animals other than humans have ears and respond to sounds in the audible band with remarkable commonalities in acuity and perceptual properties (Fay, 1988). In fishes, the ear also responds to sound (particle acceleration) of very low frequency, well into the infrasonic bandwidth (Sand & Karlsen, 1986, 2000).

For the terrestrial human species it is certainly a difficult task to envisage the sensory world of aquatic animals, and the sensations and perceptions provided by the lateral line and the related electroreceptive organs are impossible for humans to appreciate fully. Throughout the history of comparative physiology, the prevailing view has been to consider the lateral line as an accessory hearing organ. This idea culminated with Willem van Bergeijk's (1964) erroneous arguments that the lateral line was the dominant hearing organ within the acoustic near field, and the only organ providing directional information about the sound source. Further, although he correctly stated that the inner ear also enables fish to detect sound in the acoustic far field, he also argued that this is possible only in species with a gas bladder that transforms sound pressure into particle motion. However, the extreme sensitivity of the inner ear to particle motion also enables fish lacking a gas bladder to detect far field sound (Chapman & Sand, 1974; Fay, 1984). The chapters by Coombs and Bleckmann in this volume provide a more thorough review of van Bergeijk's influence.

In the same era, Sven Dijkgraaf (1963) argued for a contrasting view and described the sensory quality of the lateral line as "touch-at-a-distance." He emphasized the very short detection range of the lateral line for both moving and stationary objects, arguing that the lateral line is able to detect vibratory sources only within a tiny fraction of the acoustic near field based on water movements relative to the surface of the fish. He also emphasized the role of the lateral line in detecting nearby objects by their distorting effects on the self-generated flow field around moving fish. This remarkable ability has now been studied extensively in the blind Mexican cavefish *Astyanax mexicanus* (e.g., von Campenhausen et al., 1981; Hassan, 1986; Windsor et al., 2008). Dijkgraaf's way of thinking was strikingly different from the prevailing ideas of the lateral line as an accessory hearing organ, and touch-at-a-distance is clearly distinct from any sense of "hearing." At a meeting in Bielefeldt, Germany, in 1987 on "The Mechanosensory Lateral Line," Dijkgraaf's vision of lateral line sensation representing a unique sensory modality separate from hearing was thoroughly addressed. To acknowledge and honor his scientific influence, the word "svenning" was suggested for this novel

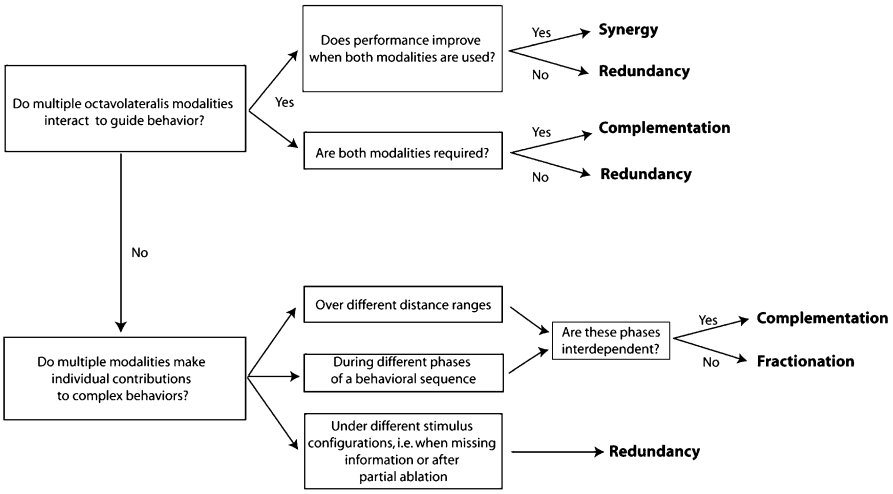

Fig. 1 A decision tree for evaluating multimodal interactions. The individual types of intermodal interactions are listed in boldface type

sensory modality (Platt et al., 1989). However, the deep commonalities in stimulus sources, physiological mechanisms, and ontogeny continue to require consideration of intersensory interactions between the inner ear and the lateral line.

The lateral line system has long been known to have both ontogenetic and phylogenetic ties to the inner ear. Like the ear, lateral line end organs also respond to water motions ranging from nearly DC up to 50–200 Hz (see Section 1.4.1), certainly overlapping with the inner ear bandwidth of fishes, if not humans. However, whereas the inner ear otolith organs are accelerometers responding to either linear acceleration of the fish in a sound field or local particle acceleration emanating from a pulsating gas bladder (for review, see Popper et al., 2003), the lateral line organs detect relative motions between the animal surface and the surrounding water. The historical persistence of the view that the lateral line is a subordinate hearing organ results from the fact that all vibrating and moving underwater objects produce both hydrodynamic flow fields in the form of water displacements caused by the moving source (near field particle motions), and sound pressure fields associated with far field particle motions (see Section 1.2). Thus, many sources that stimulate one sense contain energies that may stimulate the other as well, and it is a reasonable assumption that the two senses may often act in concert (Braun et al., 2002), in a number of possible modes of interaction (Fig. 1). However, the accumulation of neuroanatomical and behavioral evidence strongly supports a view of the lateral line as an independent sensory system with its own functions, distinct stimuli, neural pathways, and processing rules. The present chapter attempts to describe areas of functional overlap and nonoverlap between these two sensory systems related by common sources of proximal stimulation and a shared evolutionary history.

The question of functional overlap can be restated in a few specific ways, ranging from the highest levels of organization to the lowest. Are there specific behavioral tasks that require or are enhanced by the use of both channels? Are there functional connections between the neuronal pathways of each channel? Do bimodal neurons exist and how do they combine inputs from the two channels? Even more subtly, are there cross-modal interactions that might not relate to a single behavioral task, but rather a conflict between two or more? For example, when presented with female pheromones, male moths fail to take evasive action from bat echolocation calls (Skals et al., 2005). This is clearly an intersensory interaction, but one that arises from a conflict between motivational states. Thus, the animal behaves in a way that reflects contributions from two sensory systems, but not because their information is being combined in a meaningful way. This chapter surveys the literature on lateral line and inner ear function in an attempt to determine how information from these two systems might interact in natural behaviors.

1.1 Evolutionary and Developmental Relationships

Outside of any functional considerations, the lateral line system and the inner ear share intimate details of evolutionary history and development. The lateral line and inner ear capsule both develop from a series of ectodermal thickenings, the dorsolateral placodes (Northcutt, 1996), which are an important synapomorphy (a shared derived feature, generally used as diagnostic or definitive for a taxon) of the Craniata (see the chapter by Webb in this volume). The early conceptions of "hearing associated" functions for the lateral line system were tied to the acoustico-lateralis hypothesis (e.g., Ayers, 1892), the idea that the lateral line represents a primitive state from which the ear evolved (or vice versa). Studies of jawless fishes strongly suggest that the inner ear (including both linear and angular acceleration detectors) and the lateralis systems (including both mechanosensory and electrosensory systems) all arose at one moment in vertebrate history (Braun, 1996). Together, these are termed the octavolateralis systems because of their origin from the octaval and associated dorsolateral placodes. Instead of an "acoustico-lateralis theory," the common origin suggests that the two systems are (or were) intertwined, at least by developmental history, or perhaps by integrative functions (see also the chapter by Coombs & Bleckmann in this volume). The origin of this embryonic tissue was a key innovation in the origin of the vertebrates (Northcutt & Gans, 1983), and all living vertebrates today still possess some derivatives of dorsolateral placodes. These may include all end organs of the inner ear, the neuromasts of the mechanosensory lateral line, and the electrosensory lateral line system (Modrell et al., 2011).

The individual receptor mechanisms derived from octavolateralis systems are highly diverse and include both displacement-sensitive and voltage-sensitive sensory cells. A wide range of pre-receptor structures filter and channel environmental

stimuli to increase the functional diversity of these systems. All octavolateralis systems share features of gross organization (Coombs & Montgomery, 2005; Braun, 2009) that may reflect either common developmental mechanisms (Baker et al., 2008), similar processing strategies, or both. In the case of the electrosensory and mechanosensory lateral lines, the organs share a similar distribution across the body surface, as well as many sources that are likely to stimulate both systems (e.g., emit a voltage field and create water motions). Thus, there is a great commonality in the central processing strategies that might be used by both systems (Montgomery et al., 1995). There is also recent evidence that object motion, as detected by the mechanosensory lateral line, enhances electrosensory responsiveness (Pluta & Kawasaki, 2008), but such cross-modal interactions have only been hinted at otherwise (Nelson et al., 2002; Schuster, 2006) and deserve future investigations.

1.2 The Multidimensional Hydrodynamic Source and Proximate Stimulation of the Lateral Line and Inner Ear

One reason to consider the functions of the lateral line and ear together is that the proximate stimuli are related, both in terms of their underlying physics and in that they often issue from a single source. Historically, there has been little distinction between hydrodynamics and acoustics (Richardson, 1954), and acoustic phenomena are really a particular type of fluid motion (Harris, 1964; Kalmijn, 1988). Objects that move through a fluid medium push the medium away at the advancing edge (increased pressure) and draw fluid in behind the trailing edge (decreased pressure), thus creating a hydrodynamic flow field around itself. Consequently, at a fixed point close to a moving object (e.g., a gliding fish), low-frequency fluctuations in both pressure and fluid motion will occur as the object passes. A stationary vibrating object (e.g., an oscillating fin) also generates local fluid motions, in addition to pressure fluctuations that propagate as a pressure wave away from the source. The amplitude of the pressure waves emitted from dipole sources, that is, objects vibrating with constant volume, is maximum along the axis of vibration and zero in directions perpendicular to this axis, whereas monopole sources, which pulsate in volume, emit pressure waves omnidirectionally. The propagating pressure waves are associated with oscillatory particle motion, which can be expressed as particle displacement, particle velocity, or particle acceleration. However, propagating sound causes no net flow of fluid, as is the case for the hydrodynamic flow close to a moving source. The oscillatory particle motion associated with the pressure wave depends on the elastic properties of the medium, and the ratio between particle motion and sound pressure defines the acoustic impedance of the fluid. In contrast, the hydrodynamic flow close to the source is ruled by the incompressible nature of fluids, and source motions cause net flow of the surrounding medium. These hydrodynamic motions attenuate steeply with distance, such as at a rate of

1/distance^3 for a dipole source and 1/distance^2 for a monopole source. In contrast, the propagating pressure wave and the associated particle motions attenuate at a rate of only 1/distance (Harris, 1964; Kalmijn, 1988). Very close to the source, the hydrodynamic fluid motions are much greater than the particle motions associated with the pressure wave. The difference in attenuation with distance means that at some distance from the source, the particle motions associated with the pressure wave are of equal amplitude to the more steeply attenuating hydrodynamic motions caused by incompressible flow. This distance is dependent on wavelength and is greatest at low frequencies. For a monopole source, the distance at which hydrodynamic flow and acoustic pressure fluctuations are equal can be estimated as the wavelength divided by 2π (for a 20-Hz dipole, this corresponds to about 12 m). For a dipole, the distance depends on the angle between the direction to the source and the axis of vibration, and is always larger than for a monopole source. Along the axis of source vibration, this distance can be estimated as 1.4 times the wavelength divided by 2π (i.e., about 17 m for a 20-Hz source).

This boundary heuristically defines two regions generally termed the acoustic near and far field, respectively. Particle motions associated with incompressible flow are commonly called near field flow, whereas those that are proportionate with sound pressure are called far field particle motions. However, these different types of particle motions, which are 90^o out of phase, coexist in both the near and far field, but with very different magnitudes. Close to a moving source, incompressible motions of fluid predominate, and these near field components attenuate below relevant noise floors within a short distance from the source. Further from the source, particle motions associated with the propagating pressure wave attenuate less steeply and form a relatively spatially homogeneous acoustic far field. It should be noted that fish and other animals moving underwater mainly produce extremely low-frequency particle motions (Kalmijn, 1989; Bleckmann et al., 1991). The major components of the particle motions caused by swimming fish are even below 20 Hz. For biological sources generating such low frequencies, the near field may extend beyond the audible distance range, and far field detection is hardly biologically relevant. In addition, these ideal descriptions depend on an unbounded medium. In shallow water, sound propagation is severely impeded or prevented in a wavelength-dependent manner. The shallow water functions as a high-pass filter with a sharp cut-off frequency, which is dependent on both depth and substrate rigidity (Rogers & Cox, 1988; Forrest et al., 1993). For a perfectly rigid bottom, the wavelength of the cut-off frequency is four times the water depth. For a muddy bottom with high density of gas bubbles from decaying material, this figure is close to twice the depth. In nature, the wavelength of the cut-off frequency will usually be between these extremes, for example about three times the water depth for mixed bottom substrates. This implies that for a 20-Hz source, sound propagation requires a depth of more than about 25 m. Thus, in many natural circumstances, far field propagated pressure waves simply are not a relevant part of a fish's experience. For a more complete treatment of these hydroacoustic principles, the reader is referred to Harris (1964), van Bergeijk (1964), Kalmijn (1988, 1989), and the chapter by McHenry and Liao in this volume.

The lateral line and the inner ear both function to detect particle motions, but in different ways. The particle movements in the flow field close to the source (the near field component) are spatially complex (inhomogeneous) and independent of the elastic properties of the medium. Therefore, a fish will behave like a rigid body, with forced motions reflecting an integration of the particle motions in the surrounding flow field (Denton & Gray, 1982, 1983). This will cause relative movements between the fish surface and surrounding particle motions. The part of the fish closest to the source will move with smaller amplitude than the adjacent water particles, whereas the opposite is true for the part most distant from the source. The spatially dispersed neuromasts are stimulated by differential water movement across the body surface, and their positions at many points along the body surface make the lateral line system ideally suited to map local flow fields (Coombs et al., 1996).

The forced accelerations of the rigid fish caused by near field motions will also stimulate the inner ear. The otoliths have a mass density three times that of the surrounding liquid and soft tissue, and the otolith motions will thus lag behind, and have smaller amplitude than, the motions of the adjacent tissue (de Vries, 1950). The differential motion of the soft fish tissue and the denser otolith creates shearing forces on the macular hair cells, the first step in neuronal transduction of a sound field. In a conceptual sense, the inertial inner ear responds to whole body acceleration of the fish (a spatial integration of the hydrodynamic near field motions) and the lateral line responds to local, differential water motions along the body (the derivative of the hydrodynamic spatial pattern). Both the inner ear and individual lateral line organs also respond to temporal patterns of their respective stimuli, which is clearly important for signal analysis.

The soft tissues of fish are virtually acoustically transparent and behave as the surrounding water particles in the acoustic far field. Therefore, there will be no differential movements between the surface of the fish and the adjacent water. Dijkgraaf (1963) predicted that such homogeneous, vibrational movements of fish and surrounding water at the same phase and amplitude would fail to stimulate the lateral line, and this was later shown experimentally by Sand (1981, 1984). However, the inner ear is ideally suited to detect such movements. Whereas the incident sound makes the soft tissue vibrate with the same phase and amplitude as the adjacent water particles, the motions of the dense otoliths lag behind and display smaller amplitude owing to their inertia, thus stimulating the macular hair cells as described in the preceding text. The otolith organs function as accelerometers, with equal sensitivity to near field and far field motions (Chapman & Sand, 1974), but the presence of a gas bladder may still enhance the auditory sensitivity, particularly in the far field and at higher frequencies. In a sound field, the pressure oscillations will cause the gas bladder to pulsate in volume, and the radial motions of the bladder surface may exceed the particle motions of the incident sound. Thus, a gas bladder may enhance hearing sensitivity by acting as a pressure to motion transformer. It is still unclear if gas bladder enhancement requires some particular mechanical linkage or minimum distance between the bladder and the ear, and the relevant frequency range of such enhancement is uncertain. In Atlantic cod

(*Gadus morhua*), which has no direct bladder–ear connection, the gas bladder appears to enhance the auditory sensitivity mainly at higher frequencies, beginning around 50 Hz, with increasing enhancement at frequencies up to a few hundred Hertz (Sand & Enger, 1973). In other taxa, the degree of enhancement and relevant frequency range may differ based on bladder size and shape and the nature of linkage between the bladder and ear. In goldfish (*Carassius auratus*), gas bladder deflation decreased the sensitivity to a 40 Hz source by 17 dB (Fay & Popper, 1974; Dailey & Braun, 2009), so gas bladder enhancement may also be important for inner ear function in the near field and at low frequencies.

An obvious assumption would be that the two senses act together to interpret a single stimulus source. However, the more common situation seems to be that relevant sources at a given instant stimulate only one of these sensory systems. For example, a fairly large vibratory source may generate whole body accelerations of a nearby fish, thus stimulating the inner ear, and if the fish is sufficiently close to the source, lateral line organs may be simultaneously stimulated. However, the amplitude of the local water motions decline steeply with distance, such as $1/\text{distance}^3$ for a dipole source, and the relative movements between the fish and surrounding water falls off even more steeply (Denton & Gray, 1982, 1983). Therefore, the lateral line will be completely insensitive to such a source at distances of less than the body length of even rather small fish (see Section 1.4.2). On the other hand, a tiny vibratory source, like for instance a small planktonic crustacean, may cause local water movements that are sufficient to stimulate the lateral line at very close range (Montgomery, 1989), although such small water motions may fail to cause sufficient whole body acceleration to stimulate the inner ear. Interestingly, the very short detection range of lateral organs protects this sensory system against being masked by ambient noise (Denton & Gray, 1983).

During the last two decades, it has become evident that wake tracking is a major function of the lateral line (see the chapter by Montgomery, Bleckmann, & Coombs in this volume). The stimuli used in these scenarios may have very weak pressure components and provide little or no stimulation to the inner ear (see the chapter by McHenry & Liao in this volume). A swimming fish leaves a trail of spinning vortices that persist for up to several minutes (Hanke et al., 2000; Hanke & Bleckmann, 2004). Such a wake can be detected by the lateral line of an intersecting fish and tracked, but is less likely to stimulate the inner ear. Obviously, wake tracking is very important in prey–predator interactions (Pohlmann et al., 2001, 2004). It is interesting to note that several groups of secondary aquatic vertebrates have developed "lateral line analogs" that may enable similar wake tracking, for example, sensitive vibrissae in seals and otters (Miersch et al., 2011), manatees (Reep et al., 2011), and mechanosensitive, cephalic appendices in water snakes (Catania et al., 2010). "Svenning" must be a very important sense for an aquatic animal.

Nevertheless, the two senses can in many cases act together to interpret a single stimulus source. It is this thought that led Braun et al. (2002) to ask "What is the nature of multisensory integration between octavolateralis systems?" It seems reasonable to assume that the nervous system should use all available information

(meaning from multiple input channels) to form percepts of objects in the environment and that higher-order perception must result from various kinds of interactions between the relevant sensory pathways. Braun et al. (2002) suggested that because this assumption is not yet justified by evidence, one should assume the null hypothesis that animal nervous systems *do not* integrate multiple channels of inputs about a single source. Although it is quite clear that the lateral line system is independent of audition in many behavioral contexts, behavioral researchers are increasingly aware that a particular sense may or may not be important to a given task, depending on particular conditions or behavioral state. The examples that follow describe the relationships between the inner ear and the lateral line, but in many instances, it is clear that neither modality is truly independent. Vision, chemoreception, and touch are all important in many of the same behavioral contexts as audition and lateral line sensation and these senses will be mentioned where relevant data exist. Nonetheless, the interrelations of audition and lateral line systems specifically remain somewhat vague. These two systems are so closely related in many ways, yet it has been difficult to demonstrate that their behavioral uses overlap. There may be some cases where particular species use both senses in close concert (particularly during short-range communication and predation/predator avoidance), and these are given further scrutiny (see Section 2).

1.3 The Multichannel Octavolateralis System

A continually growing number of studies examining inner ear or lateral line responsiveness (or both) have been based on a common stimulus source: a vibratory dipole. This source is a reasonable approximation of biological sources (Kalmijn, 1989) for both the lateral line and multiple inner ear end organs and produces a simple sound field including well-defined patterns of hydrodynamic flow and acoustic pressure. In most experimental tanks and many natural environments, a propagating pressure wave is not produced because the water is too shallow or confined (Rogers & Cox, 1988), but this source is useful as a model of flapping fish tails, appendages, swimming animals, and other sound-producing natural objects. That this one source can provide stimulation to multiple octavolateralis systems is one of many reasons to expect some interaction between submodalities. However, the relative responsiveness of the different submodalities will depend on both source size and distance.

Experiments with dipole sources reveal several aspects of octavolateralis function. In Lake Michigan mottled sculpin (*Cottus bairdi*), the fairly large vibratory bead (5–8 mm diameter) used in many published studies is a potent stimulus to both the inner ear and the lateral line (Braun & Coombs, 2010). Behavioral and physiological studies of the lateral line in the sculpin (Coombs & Janssen, 1989, 1990), demonstrate that it is a sensor array detecting relative water velocity or acceleration (or a mixture of the two) at various points along the body, and provides the central

nervous system with the information needed to analyze the three-dimensional flow pattern over the body surface (Coombs et al., 1996; Coombs & Patton 2009).

There have yet been no studies of inner ear physiology in mottled sculpin, but Braun and Coombs (2010) showed that these animals can use their inner ear to respond to a vibratory source of 40 Hz when the lateral line is pharmacologically ablated. Further, the performance of mottled sculpin in various behavioral tasks was generally either unaffected by the loss of specific sensory channels or completely eliminated, depending on the behavioral task. Distinct behavioral tasks (conditioned and unconditioned responses) seemed to rely on a single sense channel. Orienting responses, an innate component of feeding responses, were observed only when the lateral line was intact, and earlier studies have shown that partial ablations lead to partial orienting deficits (Hoekstra & Janssen 1985, 1986; Conley & Coombs 1998). Conditioned respiratory responses, on the other hand, were unaffected by lateral line ablation (Coombs, 1994). Sculpin could also be conditioned to respond to substrate vibration cues via their inner ear or ignore them, depending on the conditioning regime (Braun & Coombs, 2010). Similarly, Nauroth and Mogdans (2009) showed that both goldfish and oscars (*Astronotus ocellatus*) can be conditioned to respond to a 50-Hz vibrating bead without using their lateral line systems.

In goldfish, saccular units respond to a 50-Hz vibratory bead in proportion to the pressure encountered at the anterior chamber of the gas bladder. That is, saccular units responded proportionately to the change in pressure at the gas bladder as a vibratory source was moved in space relative to the gas bladder (Coombs et al., 2010). Conditioned behavioral response magnitudes also changed with bead position relative to the gas bladder, but these patterns were more variable than physiological responses. These authors also showed lagenar responses to the same source, but they did not show a clear pressure-detector location near the gas bladder, nor were these responses attenuated by gas bladder deflation (as saccular responses were). Together with data from Dailey and Braun (2009, 2011) and Coombs (1994), these results indicate that goldfish use their pressure sensitive inner ear (saccular end organ) to detect and analyze vibrating beads. For pure kinetic stimuli using a vibrating table, lagenar and utricular units show the same vibration sensitivity as saccular units, with thresholds of about 0.1 nm at 140 Hz (Fay, 1984). Thus, it is likely that the lagena and utricle are also involved in responses to vibrating sources, particularly regarding the directional characteristics of the stimuli (Sand & Bleckmann, 2008).

Casper and Mann (2006a) also used a dipole source to investigate hearing thresholds in two species of elasmobranchs. Elasmobranch audition is a subject of considerable debate, as field observations do not easily reconcile with laboratory data on hearing thresholds, and there is little agreement over which end organs are important for audition, and the mechanism of sound conduction through the head (see Myrberg, 2001 for review). Casper and Mann (2006a) showed high sensitivity to low-frequency dipoles, with particle acceleration thresholds lower than those previously published. This discrepancy may be due to differences in ambient noise levels, but Casper and Mann also suggested that stimulus type and orientation may affect which end organs are stimulated. By recording auditory evoked potentials,

Casper and Mann (2006a) found that responses were greatest when the stimulus source was located close to the parietal fossa. This finding supports an old idea that elasmobranch hearing depends on stimulation of the macula neglecta, with a possible sound path through the parietal fossa (see also Fay et al., 1974; Bullock & Corwin, 1979; Casper & Mann, 2006b). Casper and Mann (2006a) speculate that earlier studies using more uniform sound fields produced by monopole speakers may be less effective at stimulating the macula neglecta, and that responses to such sounds may be mediated by the sacculus. This raises the possibility that elasmobranchs might use one end organ for far field sounds (or more spatially uniform fields) and another organ for local punctate sources such as dipoles, capable of local stimulation of the parietal fossa. Future investigations should focus on elasmobranch hearing using local sources and end-organ ablations to reveal more about the potential for multichannel inner ear function in these animals.

1.3.1 Multiple Modalities Within the Lateral Line System

In goldfish, extensive physiological studies also demonstrate that the lateral line responds as an array of differential water motion detectors capable of analyzing the three-dimensional flow pattern over the body surface (Bleckmann & Zelick, 2009). Both behavioral and physiological data suggest that the lateral line system contains two types of receptor systems, linked to canal organs and superficial neuromasts. Canal neuromasts (CNs) are sensitive mostly to acceleration of the surrounding water relative to the body surface and have high-pass frequency-response profiles. In contrast, superficial neuromasts (SNs) are sensitive to some combination of relative velocity and acceleration and show saturated responses to low-frequency stimulation (see the chapters by Bleckmann & Mogdans,Chagnaud & Coombs, and McHenry & van Netten in this volume).

Although there have been some studies of the differences in innervation of CNs and SNs (Münz, 1989; Bleckmann, 2007), very little is known of the organization of central projections or information processing streams within the central nervous system (cf. Plachta et al., 2003 and chapters by Bleckmann & Mogdans and Chagnaud & Coombs in this volume). Several studies suggest that CNs are used in localization tasks with point sources (e.g., dipoles), whereas SNs have been implicated in tasks involving more spatially diffuse and low-frequency currents, such as rheotaxis (orientation to currents) (Montgomery et al., 1997; Coombs et al., 2001). These studies used gentamicin treatment, which was thought to reversibly destroy CNs, but leave SNs unaffected (Song et al., 1995). Unfortunately, more recent studies (van Trump et al., 2010; Brown et al., 2012) have shown that gentamicin also inactivates SNs, probably through transduction channel inactivation, and thus cannot be used to dissect SN from CN function. These recent findings leave some confusion in the literature. Lake Michigan mottled sculpin deprived of their lateral line (full pharmacological ablation by Co^{2+} or by gentamicin) do not orient to dipole sources, but skin scraping (intended to damage only superficial neuromasts) does not affect orientation (Coombs et al., 2001). Thus, it seems

reasonable to conclude that SNs play a limited role in dipole detection or may not be involved at all. It remains to be determined if other senses (i.e., inner ear senses) are also needed for dipole detection.

In a series of rheotaxis studies on different species, Montgomery and colleagues (1997) showed that gentamicin treatment had no effects on orientation to currents, but skin scraping generally reduced or eliminated this behavior. If indeed gentamicin eliminated both CNs and SNs but had no effect on rheotaxis, these results conflict with results showing that elimination of SNs alone eliminates orientation to currents. These studies will need to be repeated with careful controls and direct measurements (physiological or using vital dyes) of the effect of gentamicin and similar treatments. Nonetheless, there is still a developing body of evidence that the two submodalities are used in different behavioral contexts, and it is a reasonable hypothesis that CNs are responsible for the detection of objects and point sources and SNs are responsible for detection of larger-scale currents and stimuli that are spatially more uniform (see Section 2).

1.3.2 Special Cases

The lateral line and inner ear systems are both phylogenetically quite diverse (Braun & Grande 2008; see also the chapter by Webb in this volume). Some taxa have evolutionary novelties that alter the role of the lateral line or inner ear–associated structures in ways that conceivably link the functions of the two systems. For instance, in Clupeiformes (shad and herring), the recessus lateralis is a branch of the cephalic lateral line canal system that abuts a perilymphatic space (Denton & Blaxter, 1976). Pressure changes in the prootic, gas-filled bulla are translated to volume changes causing movements that are transmitted to the flexible wall of the recessus lateralis and inducing fluid motion within the lateral line canal. The function of this pressure sensitive portion of the lateral line has been the subject of some speculation, including use in source distance calculations (e.g., Schuijf & Budwalda, 1980). Denton and Gray (1983) suggested that neuronal comparisons of the distribution of the differential water motions sensed by the main lateral line system and the pressure sense provided by the end organs in the recessus lateralis could be used to obtain highly accurate source resolution, which might be essential for collision avoidance during the tight schooling seen in these fish. As it became known that some clupeiforms were able to detect the ultrasonic sonar clicks of their mammalian predators, most authors suggested that the complex arrangement of the utricle could be responsible for ultrasonic sensitivity (see Popper et al., 2004 for review). More recently, Wilson et al. (2009) showed that destruction of the lateral line neuromasts adjacent to the recessus lateralis eliminated ultrasonic sensitivity in Gulf menhaden (*Brevoortia patronus*). It is unknown if ultrasonic sensitivity also depends on the utricle or if cross-modal computations are required in some way. Future studies should examine the innervations of those specific neuromasts and follow their central projections to

reveal differences with other neuromasts and possible points of convergence with auditory pathways.

A similar pressure-sensitive lateral line component is also present in butterfly fish (Chaetodontidae), and Webb (1998) termed this structure a laterophysic connection. The function of this specialization is still unknown, but many species of chaetodonitids exhibit elaborate communication displays that include tail slaps, low frequency sounds, and vocalizations within 100–500 Hz and above 3 kHz (Tricas et al., 2006). It is possible that specialized neuromasts adjacent to the laterophysic connection have a distinct function in pressure reception, particularly during communication displays. It is also possible that this specialization of the gas bladder imparts pressure sensitivity to the inner ear as well (Webb & Smith, 2000). Interestingly, inner ear anatomy suggests that the specialized gas bladder morphology in some species of chaetodontids is not associated with corresponding specializations of the otoliths or maculae, as is typical of pressure-sensitive fish (Popper, 1977; Webb et al., 2010). Hearing sensitivity tests before and after gas bladder deflation and anatomical and physiological studies of the neuromasts in question will resolve the auditory or lateral line functions of this gas bladder morphology and may uncover intermodal interactions.

Two other cases of potentially pressure-sensitive lateral line systems have also been reported: Mormyridae (Elephantnose fishes: Stipetić, 1939, cited by Bleckmann 1994), and loricariids (armored catfishes: Bleckmann et al., 1991; Aquino & Schaefer 2002). In these taxa, there is an association of some part of the lateral line system with a gas filled cavity, but the function of these linkages is not known. Even parts of the unspecialized trunk lateral line are in close proximity to a gas compartment in species possessing a gas bladder, being separated from the gas by only a relatively thin body wall. However, exceedingly high, unnatural sound pressures may be required to stimulate lateral line end organs through this route (Sand, 1981).

1.4 Specific Areas of Overlap and Nonoverlap in Sensitivity

Some summary of the specific sensitivities of octavolateralis channels can be made based on existing behavioral and physiological data (see Table 1).

1.4.1 Frequency

Functioning as accelerometers, it is likely that inner ear sensitivity extends down to DC, although responses have only been tested for frequencies down to 0.1 Hz (Sand & Karlsen, 1986; Karlsen, 1992a, b). Technical limitations, owing to the very large displacement amplitudes required to achieve a given acceleration at very low frequencies, makes it difficult to experimentally test responses to lower frequencies. However, no sign of a low frequency cut-off in acceleration sensitivity has been

Table 1 Overlap in frequency and distance ranges and functions between the lateral line and inertial audition

	Inertial audition	Lateral line sensing
Frequency band	<0.1 to $\times 10^2$ Hz	<0.1 to $\times 10^2$ Hz
Distance range	Near and far field	Stationary objects: Close range (~centimeters)
		Wake tracking: Variable, potentially wide, range (several meters)
Stimuli	Vibratory sources	Vibratory sources
	Currents	Currents
	Reafference?	Hydrodynamic structure
		Reafference
		Active sensing using reafferent carrier (damming flow)
Behavioral relevance	Orientation	Orientation
	Navigation?	Communication
	Inertial guidance?	Prey detection
	Soundscape detection	Predator avoidance
	Communication	Escape response
	Prey detection	Swimming kinematics
	Predator avoidance	
	Escape responses	

noted in the few species that have been tested and indeed, audiograms of these species display a fairly flat sensitivity function below approximately 100 Hz with thresholds close to 10^{-5} ms^{-2} in the infrasonic range. This represents a sensitivity to linear acceleration several orders of magnitude higher than in humans (Todd et al., 2008). The lateral line is also exquisitely sensitive to low-frequency stimulation (Bleckmann, 1994; see also the chapter by Chagnaud & Coombs). The high-frequency cut-offs of both inertial audition and the lateral line have been the subjects of some debate (Kalmijn, 1988), in part because the same auditory or lateral line function can look quite different when plotted in terms of pressure, particle displacement, velocity, or acceleration. For the inertial inner ear, this question is sometimes further complicated by the presence of pressure-displacement transformers associated with gas-filled structures, which offer limited hearing enhancement (e.g., Chapman & Hawkins, 1973; Chapman & Sand, 1974) above a certain frequency that depends on gas volume and depth (Sand & Enger, 1973; Sand & Hawkins, 1973). This transition frequency may typically be 50–100 Hz. In all studies to date of species without any gas bladder–associated hearing enhancement, inner ear sensitivity declines rapidly above a few hundred Hertz, and most of these species do not respond to sounds above 1000 Hz (for review, see Popper et al., 2003). The upper frequency cut-off of the lateral line system is also difficult to estimate precisely. As discussed in Section 1.3.1 and in Chagnaud and Coombs (this volume), CN responses are proportional to acceleration of the fluid at the body surface, but SN responses are more directly related to velocity. In terms of velocity, SNs typically have low-pass response curves,

with steep roll-offs in sensitivity somewhere in the tens of Hertz (Bleckmann, 1994; see also Chagnaud & Coombs, this volume). In terms of acceleration, CNs also have low-pass characteristics. The canal may act to filter very low frequency stimuli, but CN responsiveness is highest in the tens of Hertz, with sharp declines at 100 Hz or above (Kalmijn, 1988; see also the chapter by Chagnaud & Coombs, this volume).

Although there is some consensus that low-frequency hearing in the near field is mediated primarily via particle-motion detection by otolithic end organs, auxillary structures that enhance hearing (e.g., gas-filled structures such as the swim bladder) may also make important contributions at low frequency. As noted, such enhancements are most significant for pressure-sensitive high-frequency hearing (Braun & Grande, 2008). Thus, it seems logical that this derived, increased sensitivity is most behaviorally important at higher frequencies, where fish that lack such abilities become deaf. However, Dailey and Braun (2009) showed that behavioral detection of a 40-Hz vibrating bead, a relatively weak pressure source, relies primarily on the pressure sensitive hearing channel in goldfish, a finding that is consistent with evoked responses in goldfish saccular fibers to a 50-Hz dipole (Coombs et al., 2010). Moreover, both of these studies showed that behavioral as well as neural sensitivity was greatly decreased by deflation of the gas bladder. The function of pressure-sensitive hearing at low frequencies is relatively unexplored and deserves further study. Although the sensitivity at very low frequencies (below 40 Hz) may not be enhanced by derived pressure sensitivity (Sand & Hawkins, 1973), such sensitivity may still be behaviorally important at higher intensities, as Karlsen et al. (2004) have shown for the fast start escape responses induced by a 7-Hz stimulus in the cyprinid species roach (*Rutilus rutilus*).

In summary, the inner ear and the lateral line systems have nearly identical frequency bands, probably also overlapping with enhanced hearing systems. The lateral line may parcel frequency space between the two submodalities, but both inertial inner ear and the lateral line systems are low-frequency sensors, mostly sensitive to very low (approaching DC) frequencies, with drastically reduced sensitivity at greater than100 Hz. This overlap in frequency bandwidth is another factor favoring the assumption that the two systems could or should operate in concert, but evidence showing that they truly do is sparse.

1.4.2 Distance

One of the often-cited distinctions between lateral line and inner ear function has been distance range (e.g., Coombs & Montgomery, 1999). There are several reasons to conclude that the lateral line operates over a shorter distance range than inner ear senses. Most importantly, the different types of stimulus parameters discussed above (see Section 1.2) generated by a single source each differ in their attenuation with distance from the source. Within the acoustic near field, the particle motions important to the lateral line and inertial inner ear decline rapidly with source distance ($1/\text{distance}^3$ for a dipole), whereas acoustic pressure used by

pressure-sensitive inner ear systems declines much less steeply with distance (1/distance). Even when detecting incident particle acceleration, that is, the pressure gradient, the inner ear can be expected to have a larger active space than the lateral line. For the inertial ear, the relevant pressure difference that provides whole-body acceleration in the local flow field is relative to the fish's body dimensions (e.g., head-to-tail, because the fish behaves like a rigid body in the local flow field), whereas for the lateral line (particularly CNs), a suprathreshold pressure gradient must be of a scale smaller than a body length to set up flow-field patterns that differentially stimulate adjacent neuromasts (Denton & Gray, 1983). Thus, it has been argued that both inertial audition and lateral line sensitivity should be dependent on body size, or neuromast spacing (which appears to scale with body size; many teleost taxa have inter-neuromast spacing of approximately 0.01 × body length: Coombs, personal communication of unpublished observations). These two considerations (sensitivity as a function of size and biophysical differences in proximate stimuli) have led numerous authors to claim that the lateral line is sensitive within one to two body lengths (e.g., Dijkgraaf, 1963;Denton & Gray, 1988; Coombs et al., 1992), whereas the inner ear sensitivity extends into the far field (e.g., Popper et al., 2003). Also in the true far field, where the particle motions are associated with sound pressure and the fish behaves acoustically as the surrounding water and not as a rigid body, the inner ear is stimulated by the incident particle acceleration in fish lacking a gas bladder (as described in Section 1.2). The detection of pressure mediated by a gas bladder is independent of fish length and has the greatest potential distance range, especially in the case of sources that produce propagating waves. Far field particle motions are inversely related to the first power of distance (1/distance) and thus attenuate much more gently with distance than the local flow fields generated by monopole (1/distance^2) or dipole (1/distance^3) sources, and should be detectable at much longer distances from the source. As noted, hearing in the true far field is not strictly dependent on the presence of a gas bladder, and such structures will increase the detection distance only as much as they enhance auditory sensitivity.

Although this range fractionation appears to be in effect in feeding behaviors (see Section 2.2), there are serious problems with this simple characterization of lateral line and inner ear functions. In a sense, asking which sense has a greater distance range is analogous to asking which human sense has a greater range, vision or olfaction? The answer obviously depends on the stimulus configuration and amplitude, the path and signal loss between source and receiver, and the ambient noise levels. Given favorable wind conditions, olfaction may identify a bakery long before one might read the business' sign, but a simple change in lighting or wind directions can reverse that hierarchy. The lateral line is stimulated by pressure gradients along the body surface, but such gradients might be part of the wake of a fish that passed minutes earlier (Hanke et al., 2000; Hanke & Bleckmann, 2004). How can the distance range of that detection be meaningfully expressed? Similarly, some water currents produced by animals (e.g., respiratory jets) can extend over very large distances. If an animal swims through such a hydrodynamic structure, a buried mollusk (for instance) might be detected at several fish lengths.

For such sources, time may be even more significant than distance, as these structures have a finite period before they decay into the ambient noise. Whereas the speed of sound determines the extremely short time lag between generation and detection of an auditory stimulus, the lateral line enables a fish to track vortices in a wake that is several minutes old and whose creator has long since swum away.

When used for hydrodynamic imaging (reviewed by Dijkgraaf, 1963), the extent of the self-generated local flow field around the body (and hence detection limits) may depend on swimming speed and body size and shape. There is some evidence that the swimming speed dictates the effective distance range of hydrodynamic imaging (Janssen, 1997, but see Windsor et al., 2010). Interestingly, object detection in burst-glide swimming (see the chapter by Montgomery et al. in this volume) is usually within a range of a few centimeters, much shorter than a body length (0.1 body lengths in Windsor et al., 2010 [wall detection], < 0.5 body lengths in Janssen, 1997 [prey orientation]). Using implanted electrodes and free swimming oyster toadfish (*Opsanus tau*), Palmer et al. (2005) also found that prey-induced neural activity in lateral line afferents occurred only when prey fish (minnows, *Fundulus heteroclitus*) were within a few centimeters, generally 0.4 body lengths. It should be noted that in the case of object detection using the distortion of the damming field, the stimulus energy is provided by the receiving fish. Hence, detection range is determined by the receiver's swimming speed and the resultant size of the damming field. In the case of detecting a swimming minnow, the stimulus energy is provided by the source's tail beats (vortices in the wake and the local flow field caused by movement of the fish's body through the water), and detection range thus depends on various factors, including the stimulus fish's size, swim speed, and tail beat frequency and amplitude.

Although the ultimate source of lateral line stimulation may be quite far away (as in the case of a buried mollusk, a jet produced by a fin flap, or the wake of fish), the proximate stimulation, the pressure gradient, must always be felt at the surface of the fish. In that respect, the distance range of the lateral line is literally millimeters, but the sources themselves dictate the space over which they establish suprathreshold pressure gradients. By analogy to olfaction—chemicals must reach the receptor cell membranes within the nose—but the effective distance range depends on the spread of the stimulus, which may spread and attenuate, become mixed by turbulence or convective processes, be projected in a directed manner (jets and currents), or even be deposited in a specific location with particular decay patterns (vortices and wake structures).

2 Integration and Nonintegration in Specific Behavioral Contexts

Auditory and lateral line senses are well known to be individually important in several contexts, particularly communication, feeding, and predator avoidance. Although the role of the behavioral significance of the lateral line is covered by

many chapters in this volume (Coombs & Bleckmann; McHenry & Liao; Montgomery, Bleckmann, & Coombs), it is worthwhile to examine these specific cases and ask how these senses may or may not be used in together in each specific behavioral context.

2.1 Communication

It is widely appreciated that complex communication is often multimodal (Partan & Marler, 2005), but few studies have truly utilized this understanding experimentally (Coleman, 2009). Acoustic communication is well known in fishes (Bass & Ladich, 2008), but the role of lateral line in short range communication is less well studied. The best documented example is the vibrational spawning behavior of Himé salmon, *Oncorhynchus nerka* (Satou et al., 1994a,b). In this case, the lateral line system is necessary to detect the vibratory cues that pass between the sexes during spawning. Many other species include quivering, fin flaps, and close range swimming and fin movements in their courtship and agonistic displays (e.g., Tricas et al., 2006; see also Ladich & Myrberg, 2006), and these behaviors can be expected to generate strong lateral line signals. Experiments should be designed to test the idea that these signals are used as specific communication signals (e.g., in complementary or redundant interactions) or if they influence motivational states in an accessory way, increasing response probabilities or intensities. Himé salmon remains the only known example where the lateral line is essential in communication, but in this case, the role of audition is not known. Vision is important to salmon spawning (Satou et al., 1994b), and the integration between vision and lateral line should be investigated further in this and many other species (Coleman, 2009).

2.2 Feeding and Predator Avoidance

Feeding and predator avoidance are both essentially object localization and tracking tasks. The role of the lateral line in feeding has been well documented in many species (see the chapter by Montgomery, Bleckmann, & Coombs in this volume). Several experimental studies have investigated the interactions between vision and the lateral line system (e.g., Enger et al., 1989; New et al., 2001; Schwalbe et al., 2012). In most of these studies, lateral line ablation eliminated strikes or reduced accuracy particularly in the absence of vision. The lateral line appears to be essential for the final stages of prey capture, but initial stages of acquisition and tracking may be dependent on vision or audition (Liang et al., 1998; Montgomery et al., 2002). The role of inertial audition is difficult to study because it cannot be eliminated without major behavioral alterations. Given the role of inertial (and pressure-sensitive) hearing at short range and the low frequencies presented by predator and prey motions alike (generally below 25 Hz; Kalmijn, 1988), it is likely

that the inner ear is also important in prey recognition and detection. In fact, such low frequencies may be particularly effective in inducing behavioral responses in fish (Knudsen et al., 1994, 1997; Sonny et al., 2006).

Predator avoidance, particularly escape behaviors, may be dependent on multiple octavolateralis systems. Mauthner neuron decision-making processes may include lateral line information (see Section 3.3 and Mirjany & Faber 2011), and the infrasonic sensitivity of the inner ear is also ideally suited for detecting approaching predators (Karlsen et al., 2004). As reviewed in Section 3.3, the Mauthner neuron escape network is a likely source of synergistic and complementary interactions between the inner ear and lateral line system. However, it is problematic that many studies investigating the role of audition and lateral line in prey–predator interactions, for example, the fast start escape responses discussed in Section 3.3, have employed frequencies far higher than those that are most biologically relevant.

2.3 Orientation to Currents, Including Rheotaxis and Object Entrainment

A number of recent studies have shown the involvement of the lateral line in orienting to currents (see the chapters by McHenry & Liao and Montgomery et al. in this volume), and these have already been discussed in Section 1.3.1. Initial studies suggested that only superficial neuromasts were responsible for rheotaxic behavior, but these conclusions may have been weakened by false assumptions about some of the blocking techniques (van Trump et al., 2010). Further, Montgomery et al., (2003) had already shown that both superficial and canal neuromasts were required for object entrainment in a stream, a typical use of rheotaxic abilities in fishes. It should be noted that orientation to a homogeneous current requires a fixed external reference frame, provided by visual or tactile stimuli, as Dijkgraaf (1963) thoroughly discussed in his influential review. Only when such an external reference frame is established, can the lateral line provide information about speed and direction of homogeneous currents.

Infrasonic or very low frequency detection by the inner ear may also be important for detecting relative current velocities. When a fish is swimming in a current with constant swimming activity, its velocity will change if the current velocity changes, either due to temporal current fluctuations or the fish entering a water body with a different current velocity. Such a change in the velocity of the fish may be sensed by the exceedingly sensitive linear acceleration detectors in the inner ear, thus providing information about the change in current velocity (Sand & Karlsen, 2000). For example, the relative speed and direction of layered ocean currents may be detected in this manner by a fish cruising at constant swimming speed through the boundary zone from one layer to the next. During the passage through the boundary zone, the fish may then experience a detectable acceleration, conveying information about the differences in current velocity between the layers.

This hypothesis may be prohibitively difficult to test, but it may be worthwhile to attempt to determine the response of the ear in a fish gently shifting its position relative to an object in a flow field. The presence of the object will cause local regions of different current velocities, which might be detected by the inner ear. The ability of a fish swimming in an experimental "tread-mill current" to detect subtle changes in current velocity should also be tested, for instance with behavioral conditioning techniques. In such experiments, a possible role of the inner ear could be established by blocking the mechanosensitivity of the lateral line, for instance using the cobalt method (Karlsen & Sand, 1987).

2.4 Schooling and Swimming

The importance of the lateral line in swimming and schooling has also been more clearly demonstrated by recent experimental studies (see Faucher et al., 2010; see also the chapter by McHenry & Liao in this volume). These new studies have confirmed the seminal finding of Pitcher et al. (1976) that blinded fish can school, although their responses to their neighbors' motions were slower and less accurate. Animals deprived of both vision and the lateral line were unable to school (see also Partridge & Pitcher, 1980 for review). In the context of schooling, if the infrasonic sensitivity of the inner ear is used for inertial guidance or detection of local current inhomogeneities, inertial audition may also be important for detecting neighbor distances and changes in swimming direction (see also Denton & Gray, 1983). The relative roles of vision, lateral line and inertial audition in schooling await further investigations (Larsson, 2009).

3 Central Nervous System Processing

Another avenue of exploring the relationship between the lateral line and the auditory systems is found in electrophysiological and anatomical data on the central nervous pathways of the two systems (see the chapters by Wullimann & Grothe and Bleckmann & Mogdans in this volume). In general, the pathways of lateral line and auditory information processing within the brain are distinct. The organs are innervated by individually distinct cranial nerves and project to mostly nonoverlapping hindbrain centers. From there, the sensory information in these channels is passed up the neuraxis through essentially independent pathways. There are potential sites of cross-talk between processing centers at all levels of the nervous system, but the evidence for bimodal interactions or processing centers is scant. It is reasonable to assume that higher level perceptual interactions might be occurring only at the level of the forebrain, where the understanding of function remains primitive. As knowledge accumulates on forebrain processing in aquatic

vertebrates, a more clear understanding of perceptual mixing between senses will emerge in the future.

3.1 Hindbrain Projection Zones

Early descriptions of octavolateralis central projections (e.g., Larsell, 1967) reported a large degree of overlap between inner ear and lateral line hindbrain representations, but this was clearly mistaken (McCormick, 1992), and more recent studies have documented a highly structured set of principal projection nuclei within the dorsal medulla, with little overlap between inner ear and lateral line projections (McCormick, 1999; McCormick & Wallace, 2012). Each octavolateralis end-organ has a unique pattern of projections to the hindbrain, with multiple overlapping targets for the otolithic end organs and the cupular end organs of the semicircular canals (Tomchick & Lu, 2005; McCormick & Wallace, 2012), with very little overlap between inner ear and lateral line organs in their primary projection nuclei. Some primary recipient hindbrain nuclei do receive inputs from multiple modalities, including the eminentia granularis and the magnocellular octavolateralis nucleus (Tomchick & Lu, 2005; Maruska & Tricas, 2009). Both of these structures have intimate connections with hindbrain reticular nuclei (McCormick, 1999) and may be involved in the multisensory regulation of startle responses (see Section 3.3). Although the other octaval nuclei do not appear to receive heavy projections from both inner ear and lateral line afferents, projection overlap may be more subtle, occurring at the transitional zones or via laterally extended dendrites of postsynaptic neurons. Eighth nerve afferents also sometimes terminate ventrally in the nucleus medialis, but this is taxonomically variable and not common in teleost fishes (McCormick, 1999). In the absence of overlapping projection zones, multimodal neurons may exist by virtue of dendritic connections between hindbrain nuclei. For instance, Weeg and Bass (2000) have shown that neurons within the dorsolateral division of the descending octaval nucleus (an inner ear recipient) receive inputs from both VIIIth nerve fibers and anterior lateral line nerve ganglion cells. These dual-modality neurons were identified after tracer injection in the auditory midbrain. On this basis, they suggested that already the dorsolateral descending octaval nucleus performs integrative functions. More intriguingly, these authors also showed a previously underappreciated interconnection between hindbrain primary recipient nuclei. Nucleus medialis (the lateral line recipient zone) is reciprocally and bilaterally connected to the magnocelluar octavolateralis nucleus and the dorsolateral division of the descending octaval nucleus. Medialis also receives projections from the intermediate divison of the descending octaval nucleus (also an inner ear recipient zone). Weeg and Bass (2000) suggested that some intermodality processing must occur within each "modality-specific" zone already in the hindbrain. The functional nature of this reticulation is still unclear, but low-level integration in supposedly "single-modality" brain areas may be a common feature of brain organization used to subtly process information

based on descending influences from other modalities (Stoffregen & Bardy, 2001; Schroeder & Foxe, 2005). Descending influences, such as projections from the auditory torus to the medial pretoral nucleus and subsequently to the cerebellar crest (Yamamoto & Ito, 2005), also have potential to modify the responsiveness of one modality based on processing within another.

3.2 Midbrain and Higher Brain Centers

Central nervous processing of higher-order stimulus features for both modalities occurs at midbrain and forebrain levels. Any bimodal contribution to the control of complex behavior should rely most heavily on areas upstream from the hindbrain. But the crucial experiments to find these regions in the midbrain, the diencephalon or the forebrain have not yet been conducted. Anatomical and some physiological evidence points to possible locations of bimodal interactions, but careful physiological experiments using multiple stimulus types are still needed. Most existing studies used loudspeakers or vibrating dipoles only, rather than using both to uncover truly bimodal cells at higher levels of the neuraxis. As described elsewhere (Bass et al., 2001; see also the chapter by Bleckmann & Mogdans in this volume), lateral line information is conducted from nucleus medialis to the nucleus ventrolateralis (of the torus semicircularis), while inner ear lemniscal fibers ascend to the nucleus centralis (of the torus semicircularis). However, intrinisic connections between these two toral regions are not well documented, and each region could affect processing in the other via intermediary extrinsic connections. Some such interactions must exist, because multimodal physiological responses have been shown in nucleus ventrolateralis by Edds-Walton and Fay (2005). These authors also used anatomical tracers to show that bimodal cells in ventrolateralis receive inputs in some combination from nucleus medialis, the dorsal division of the descending octaval nucleus, the secondary octaval nucleus, and from perilemniscal neurons associated with the lateral lemniscus (Edds-Walton & Fay, 2005). Tracer injections within each toral region did not label the other, suggesting that intrinsic connections between ventrolateralis and centralis are minimal (see also Bass et al., 2000). The function of these bimodal ventrolateralis cells, recipients of both auditory and lateral line lemniscal inputs, is not yet known.

In contrast to these bimodal cells, Weeg and Bass (2000) described a series of intrinsic midbrain connections that could serve as points of functional integration with the midbrain nucleus preeminentialis, at least in the plainfin midshipman (*Porichthys notatus*). The organization of preeminentialis is poorly known, but the ventral portion typically receives inputs from both nucleus medialis and nucleus ventrolateralis of the torus, making this region a candidate center for mechanosensory processing (McCormick & Hernandez, 1996). Weeg and Bass (2000) showed that this region in midshipman also receives an extensive projection from nucleus centralis (an auditory region). The significance of this bimodal region

within preeminentialis is unknown, as is the phylogenetic distribution of overlapping projections from both toral regions.

Ascending from toral regions, both auditory and lateral line information is carried by distinct pathways to the dorsal thalamus and the preglomerular complex, an important relay zone in teleost brains (Yamamoto & Ito, 2008). The preglomerular complex has only recently become a major target of tract-tracing studies (e.g., Northcutt, 2006), but it is the primary corticofugal center in the teleost diencephalon. The preglomerular nuclei appear to be unimodal, with discrete auditory (ventrally) and lateral line (dorsally) subdivisions within the lateral preglomerular nucleus. Both of these subdivisions project axons to the medial and lateral divisions of the pallium, but the specific target regions are distinct (von der Emde & Prechtl, 1999; Yamamoto & Ito, 2008). Similarly, field potentials recorded in pallium are largely unimodal (Prechtl et al., 1998). Thus, it appears that both the diencephalon and the forebrain process lateral line and auditory information largely independently. This suggests that higher-order control of behavior is unlikely to be based on multimodal integrations. Therefore, there may be no part of the higher nervous system that is a major integrator of both lateral line and auditory stimuli.

3.3 Mauthner Neuron Integration Between Lateral Line and Inner Ear Inputs

One place where lateral line and inner ear inputs are clearly integrated (at least in some species) is the Mauthner neurons. Mauthner neurons are large, characteristic neurons within the hindbrain reticular formation and are responsible for C-start type escape responses (Korn & Faber, 2005). The sensory input to Mauthner neurons probably varies between species, but auditory stimuli are rapid and ideally suited for threat detection. Accordingly, the main input to the Mauthner neuron is from the inner ear, but lateral line inputs are also known in both fish and amphibians (Will, 1986; Mirjany & Faber, 2011). Each inner ear end organ projects in a highly specific manner to portions of the Mauthner neuron lateral dendrite (Szabo et al., 2007). Sound pressure is a trigger of Mauthner neuron-initiated escapes in pressure sensitive fishes (Eaton & Popper, 1995). However, the kinetic sound component (acceleration) is of decisive importance at the low frequencies that are biologically most significant during predator strikes (Karlsen et al., 2004). Using a directionally well-defined stimulus at 7 Hz, Karlsen et al. (2004) showed that the fast start escape responses in the cyprinid species roach were in the general direction of the initial acceleration, and that the directional response persisted after blocking of the lateral line. However, Mirjany et al. (2011) have recently shown that the directionality of the response to a relatively high frequency (200 Hz) signal from a submerged loud speaker in a small container is dependent on lateral line inputs. Submerged loud speakers in small containers produce very complex acoustic fields, which

may make it impossible for the fish to determine the direction to the source based on acceleration detection by the inner ear. On the other hand, detection of the local flow field by the lateral line might still give adequate directional information, and in the absence of lateral line function, goldfish escape directionality fell to chance levels. These authors also showed that lateral line information is used to provide context to the Mauthner neuron escape response and may influence the final stages of the escape sequence (coordinated by the rest of the hindbrain reticular formation). For example, if the goldfish was placed between the predator (a speaker) and a wall, the correct escape direction (away from the predator) would result in a collision. Intact fish rarely made such an ill-fated decision and generally modified their escape direction toward the predator or in an arc leading away from the wall; fewer than 10 % of subjects collided with the wall. After lateral line inactivation, however, collision rates significantly increased. Mirjany et al. (2011) also showed that this interaction is mediated by inhibitory connection of the anterior lateral line nerve with the Mauthner cell dendrite, proximal to the saccular inputs. Clearly, lateral line inputs to the Mauthner neuron may be taxonomically widespread and are worthy of future investigations.

The Mauthner neuron escape circuit is a site of functional integration between auditory and lateral line sensory inputs. Although the control of behavior dependent on this circuit is relatively simple, here, finally, is a part of the brain that is "listening" to multiple octavolateralis senses simultaneously. Mauthner neurons and the associated brain stem escape network may also be involved in more complex behaviors, particularly hunting and prey capture (Canfield & Rose, 1993; Saskia & Schuster, 2007). This raises the intriguing possibility that if sensory information from multiple octavolateralis channels is used together in a specific behavioral context, it may result from intersensory integration at very low levels in the neuraxis.

4 Summary and Outstanding Questions

Both physical considerations and experimental data suggest that there is amazingly little functional overlap between the inner ear and the lateral line, in spite of their common embryological origin and similar structure and physiology of the sensory cells. Evidence for interactions between these two sensory modalities in the central nervous system also seems to be scant. However, although higher level percepts informed by both lateral line and inner ear inputs may not be readily demonstrated, there are many situations in which both senses may guide behavior. Future studies of both senses should continue to question the importance of the other. Particularly in cases of object localization (including predator and prey detection, swimming in schools) and communication (particularly at short range), experiments should be designed to test the involvement of both senses.

The dichotomy between near- and far-field particle motions as stimuli for inertial hearing continues to erode (Popper & Fay, 2011), and it is clear that

Table 2 Potential neural correlates of the different modes of intermodal interactions

Type of intermodal interaction	Potential neural correlates
Synergy	Bimodal processing centers
Comparativelementation	Bimodal processing centers
	Integration at the level of the final common path
Accessory	Parallel processing pathways
	Integration at the level of motivation or behavioral state
Redundant	Parallel processing pathways
	Integration at the level of the final common path
Fractionation	Parallel processing pathways
	Integration at the level of the final common path
	Integration at higher levels of behavioral organization

sound pressure sensitivity in species with enhanced hearing lowers the auditory thresholds at higher frequencies and extends both the audible frequency range and the distance range for detection (Braun & Grande, 2008). However, the role of sound pressure sensitivity in close range detection of low-frequency sources has been little appreciated (Coombs 1994; Karlsen et al., 2004; Dailey & Braun, 2009) and should be further explored.

The distinction between canal and superficial neuromasts has been the subject of many recent studies, and the examples given above point to both unique roles and examples of complementation between the two subsystems. How is information from these two subtypes of end organs represented in the nervous system? Do separate projection paths exist or is information combined at low levels of the processing path? This same set of questions should be pursued in cases of specialized lateral line organs like those in butterflyfishes and Clupeiforms. Are there "special" neuromasts or groups of neuromasts whose information is processed separately?

As stated in the introduction, questions of overlap of sensory function can be posed in many ways, but ultimately these are questions about the umwelt of an animal. What information is used to guide behavior? Does information combine in ways that allow an animal to recognize a multidimensional source? These questions will ultimately be answered by a combination of psychophysical experiments and studies of the neurophysiology of central pathways (see Table 2), but always there remains the central question: Where in the processing stream does the percept of the multidimensional source arise?

References

Aquino, A. E., & Schaefer, S. A. (2002). The temporal region of the cranium of loricarioid catfishes (Teleostei: Siluriformes): Morphological diversity and phylogenetic significance. *Zoologische Anzeiger*, 241, 223–244.

Ayers, H. (1892). Vertebrate cephalogenesis. II. A contribution to the morphology of the vertebrate ear, with a reconsideration of its functions. *Journal of Morphology*, 6, 1–360.

Baker, C. V. H., O'Neill, P., & McCole, R.B. (2008). Lateral line, otic and epibranchial placodes: Developmental and evolutionary links? *Journal of Experimental Zoology*, 310B, 370–383.

Bass, A. H., & Ladich, F. (2008). Vocal-acoustic communication: From neurons to behavior. In J. F. Webb, A. N. Popper, & R. R. Fay (Eds.), *Fish bioacoustics* (pp. 253–278). New York: Springer.

Bass, A. H., Bodnar, D. A., & Marchaterre, M. A. (2000). Midbrain acoustic circuitry in a vocalizing fish. *Journal of Comparative Neurology*, 419, 505–531.

Bass, A. H., Bodnar, D. A., & Marchaterre, M. A. (2001). Acoustic nuclei in the medulla and midbrain of the vocalizing gulf toadfish (*Opsanus beta*). *Brain Behavior and Evolution*, 57, 63–79.

Bleckmann, H. (1994). *Reception of hydrodynamic stimuli in aquatic and semiaquatic animals*. Progress in Zoology, Vol. 41. Jena, Germany: Gustav Fischer Verlag.

Bleckmann H. (2007). The lateral line system of fish. In T. J. Hara & B. S. Zielinski (Eds.), *Sensory systems neuroscience* (Vol. 25, pp. 411–453), San Diego: Elsevier Academic Press.

Bleckmann, H., & Zelick, R. (2009). Lateral line system of fish. *International Journal of Zoology*, 4, 13–25.

Bleckmann, H., Niemann, U., & Fritzsch, B. (1991). Peripheral and central aspects of the acoustic and lateral line system of a bottom dwelling catfish, *Ancistrus* sp. *Journal of Comparative Neurology*, 314, 452– 466.

Braun, C. B. (1996). The sensory biology of the living jawless fishes: A phylogenetic assessment. *Brain Behavior and Evolution*, 48, 262–276.

Braun, C. B. (2009). Evolution of the mechanosensory and electrosensory lateral line systems. In M. Binder, N. Hirokawa, & U. Windhorst (Eds.), *Encyclopedia of neuroscience* (pp. 1367–1375). New York: Springer.

Braun, C. B., & Coombs, S. (2010). Vibratory sources as compound stimuli for the octavolateralis systems: Dissection of specific stimulation channels using multiple behavioral approaches. *Journal of Experimental Psychology-Animal Behavior Processes*, 36, 243–257.

Braun, C. B., & Grande, T. (2008). Evolution of peripheral mechanisms for the enhancement of sound reception. In J. F. Webb, A. N. Popper, & R. R. Fay (Eds.), *Fish bioacoustics* (pp. 99–144). New York: Springer.

Braun, C. B., Coombs, S. & Fay, R. R. (2002). What is the nature of multisensory interaction between octavolateralis sub-systems? *Brain*, *Behavior and Evolution*, 59, 162–176.

Brown, A. D., Mussen, T. D., Sisneros, J. A., & Coffin, A. B. (2012). Reevaluating the use of aminoglycoside antibiotics in behavioral studies of the lateral line. *Hearing Research*, 271, 1–4.

Bullock, T. H., & Corwin, J. T. (1979). Acoustic evoked activity in the brain in sharks. *Journal of Comparative Physiology A*, 129, 223–234.

Canfield, J., & Rose, G. (1993). Activation of Mauthner neurons during prey capture. *Journal of Comparative Physiology A*, 172, 611–618.

Casper, B. M., & Mann, D. A. (2006a). Dipole hearing measurements in elasmobranch fishes. *Journal of Experimental Biology*, 210, 75–81.

Casper, B. M., & Mann, D. A. (2006b). Evoked potential audiograms of the nurse shark (*Ginglymostoma cirratum*) and the yellow stingray (*Urobatis jamaicensis*). *Environmental Biology Fishes*, 76, 101–108.

Catania, K. C., Leitch, D. B., & Gauthier, D. (2010). Function of the appendages in tentacled snakes (*Erpeton tentaculatus*). *Journal of Experimental Biology*, 213, 359–367.

Chapman, C. J., & Hawkins, A. D. (1973). A field study of hearing in the cod, *Gadus morhua* L. *Journal of Comparative Physiology*, 85, 147–167.

Chapman, C. J., & Sand, O. (1974). Field studies of hearing in two species of flatfish *Pleuronectes platessa* (L.) and *Limanda limanda* (L.) (Family Pleuronectidae). *Comparative Biochemistry and Physiology A*, 47, 371–385.

Coleman, S. (2009). Taxonomic and sensory biases in the mate-choice literature: There are far too few studies of chemical and multimodal communication. *Acta Ethologica*, 12, 45–48.

Conley, R. A., & Coombs, S. (1998). Dipole source localization by mottled sculpin. III. Orientation after site-specific, unilateral denervation of the lateral line system. *Journal of Comparative Physiology a-Sensory Neural and Behavioral Physiology*, 183, 335–344. doi:10.1007/s003590050260

Coombs, S. (1994). Near field detection of dipole sources by the goldfish (*Carassius auratus*) and the mottled sculpin (*Cottus bairdi*). *Journal of Experimental Biology*, 190, 109–129.

Coombs, S., & Janssen, J. (1989). Peripheral processing by the lateral line system of the mottled sculpin (*Cottus bairdi*). In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and behavior* (pp. 299–322). New York: Springer.

Coombs, S., & Janssen, J. (1990). Behavioral and neurophysiological assessment of lateral line sensitivity in the mottled sculpin, *Cottus bairdi*. *Journal of Comparative Physiology A*, 167, 557–567.

Coombs, S., & Montgomery, J. C. (1999). The enigmatic lateral line system. In R. R. Fay & A. N. Popper (Eds.), *Comparative hearing: Fish and amphibians* (pp. 319–262). New York: Springer.

Coombs, S., & Montgomery, J. (2005). Comparing octavolateralis sensory systems: What can we learn? In T. H. Bullock, C. D. Hopkins, A. N. Popper, & R. R. Fay (Eds.), *Electroreception* (pp. 318–359). New York: Springer.

Coombs, S., & Patton, P. (2009). Lateral line stimulation patterns and prey orienting behavior in the Lake Michigan mottled sculpin (*Cottus bairdi*). *Journal of Comparative Physiology A*, 195, 279–297.

Coombs, S., Janssen, J., & Montgomery, J. (1992). Functional and evolutionary implications of peripheral diversity in lateral line systems. In R. R. Fay & A. N. Popper (Eds.), *Evolutionary biology of hearing* (pp. 267–294). New York: Springer.

Coombs, S., Hastings, M., & Finneran, J. (1996). Modeling and measuring lateral line excitation patterns to changing dipole source locations. *Journal of Comparative Physiology A*, 178, 359–371.

Coombs, S., Braun, C. B., & Donovan B. (2001). Orienting response of Lake Michigan mottled sculpin is mediated by canal neuromasts. *Journal of Experimental Biology*, 204, 337–348.

Coombs, S., Fay, R. R., & Elepfandt, A. (2010). Dipole source encoding and tracking by the goldfish auditory system. *Journal of Experimental Biology*, 213, 3536–3547.

Dailey, D. D., & Braun, C. B. (2009). The detection of pressure fluctuations, sonic audition, is the dominant mode of dipole-source detection in goldfish (*Carassius auratus*). *Journal of Experimental Psychology: Animal Behavior Processes*, 35, 212–223.

Dailey, D. D., & Braun, C. B. (2011). Perception of frequency, amplitude, and azimuth of a vibratory dipole source by the octavolateralis system of goldfish (*Carasssius auratus*). *Journal of Comparative Psychology*, 125, 286–295.

Denton, E. J., & Blaxter, J. H. S. (1976). The mechanical relationships between the clupeid swimbladder, inner ear and lateral line. *Journal of the Marine Biology Association UK*, 56, 787–807.

Denton, E. J., & Gray, J. A. B. (1982). The rigidity of fish and patterns of lateral line stimulation. *Nature*, 297, 679–681.

Denton, E. J., & Gray, J. A. B. (1983). Mechanical factors in the excitation of clupeid lateral lines. *Proceedings of the Royal Society of London B*: *Biological Sciences*, 218, 1–26.

Denton, E. J., & Gray, J. A. B. (1988). Mechanical factors in the excitation of the lateral line of fishes. In J. Atema, R. R. Fay, A. N. Popper & W. N. Tavolga (Eds.), *Sensory biology of aquatic animals* (pp. 595–618). New York: Springer-Verlag.

de Vries, H. L. (1950). The mechanics of labyrinth otoliths. *Acta Oto-Laryngologica*, 38, 262–273.

Dijkgraaf, S. (1963). The Functioning and significance of the lateral-line organs. *Biological Review*, 38, 51–105.

Eaton, R., & Popper, A. N. (1995). The octavolateralis system and Mauthner cell: Interactions and questions. *Brain Behavior and Evolution*, 46, 124–130.

Edds-Walton, P. L., & Fay, R. R. (2005). Projections to bimodal sites in the torus semicircularis of the toadfish, *Opsanus tau*. *Brain Behavior and Evolution*, 66, 73–87.

Enger, P. S., Kalmijn, A. J., & Sand, O. (1989). Behavioral identification of lateral line and inner ear function. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and behavior* (pp. 575–587). New York: Springer-Verlag.

Faucher, K., Parmentier, E., Becco, C., Vandewalle, N., & Vandewalle, P. (2010). Fish lateral system is required for accurate control of shoaling behaviour. *Animal Behaviour*, 79, 679–687.

Fay, R. R. (1984). The goldfish ear codes the axis of acoustic particle motion in three dimensions. *Science*, 225, 951–954.

Fay, R. R. (1988). *Hearing in vertebrates: A psychophysics databook*. Winnetka, IL: Hill-Fay Associates.

Fay, R. R., & Popper, A. N. (1974). Acoustic stimulation of the ear of goldfish (*Carrassius auratus*). *Journal of Experimental Biology*, 61, 243–260.

Fay, R. R., Kendall, J. I., Popper, A. N., & Tester, A. L. (1974). Vibration detection by the macula neglecta of sharks. *Comparative Biochemistry and Physiology*, 47A, 1235–1240.

Forrest, T. G., Miller, G. L., & Zagar, J. R. (1993). Sound propagation in shallow water: Implications for acoustic communication by aquatic animals. *Bioacoustics*, 4, 259–270.

Hanke, W., & Bleckmann, H. (2004). The hydrodynamic trails of *Lepomis gibbosus* (Centrarchidae), *Colomesus psittacus* (Tetraodontidae) and *Thysochromis ansorgii* (Cichlidae) investigated with scanning particle image velocimetry. *Journal of Experimental Biology*, 207, 1585–1596.

Hanke, W., Brücker, C., & Bleckmann, H. (2000). The ageing of the low frequency water disturbances caused by swimming goldfish and its possible relevance to prey detection. *Journal of Experimental Biology*, 203, 1193–1200.

Harris, G. G. (1964). Considerations on the physics of sound production by fishes. In W. N. Tavolga (Ed.), *Marine bio-acoustics* (pp. 233–247). Oxford: Pergamon Press.

Hassan, E. S. (1986). On the discrimination of spatial intervals by the blind cave fish (*Anoptichthys jordani*). *Journal of Comparative Physiology A*, 159, 701–710.

Hoekstra, D., & Janssen, J. (1985). Non-visual feeding behavior of the mottled sculpin, *Cottus bairdi*, in Lake Michigan. *Environmental Biology of Fishes*, 12, 111–117.

Hoekstra, D., & Janssen, J. (1986). Lateral line receptivity in the mottled sculpin (*Cottus bairdi*). *Copeia*, 1986, 91–96.

Janssen, J. (1997). Comparison of response distance to prey via the lateral line in the ruffe and yellow perch. *Journal of Fish Biology*, 51, 921–930.

Kalmijn, A. J. (1988). Hydrodynamic and acoustic field detection. In J. Atema, R. R. Fay, A. N. Popper & W. N. Tavolga (Eds.), *Sensory biology of aquatic animals* (pp. 83–130). New York: Springer-Verlag.

Kalmijn, A. J. (1989). Functional evolution of lateral line and inner ear sensory systems. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and behavior* (pp.187–216). New York: Springer-Verlag.

Karlsen, H. E. (1992a). The inner ear is responsible for detection of infrasound in the perch (*Perca fluviatilis*). *Journal of Experimental Biology*, 171, 163–172.

Karlsen, H. E. (1992b). Infrasound sensitivity in the plaice (*Pleuronectes platessa*). *Journal of Experimental Biology*, 171, 173–187.

Karlsen, H. E., & Sand, O. (1987). Selective and reversible blocking of the lateral line in freshwater fish. *Journal of Experimental Biology*, 133, 249–267.

Karlsen, H. E., Piddington, R. W., Enger, P. S., & Sand, O. (2004). Infrasound initiates directional fast-start escape responses in juvenile roach *Rutilus rutilus*. *Journal of Experimental Biology*, 207, 4185–4193.

Knudsen, F. R., Enger, P. S., & Sand, O. (1994). Avoidance responses to low frequency sound in downstream migrating Atlantic salmon smolt, *Salmo salar* L. *Journal of Fish Biology*, 45, 227–233.

Knudsen, F. R., Schreck, C. B., Knapp, S. M., Enger, P. S., & Sand, O. (1997). Infrasound produces flight and avoidance responses in Pacific juvenile salmonids. *Journal of Fish Biology*, 51, 824–829.

Korn, H., & Faber, D. S. (2005). The Mauthner cell half a century later: A neurobiological model for decision-making? *Neuron*, 47, 13–28.

Ladich, F., & Myrberg, A. (2006). Agonistic behavior and acoustic communication. In F. Ladich, S. Collin, P. Moller, & B. Kapoor (Eds.), *Communication in fishes* (pp. 121–148). Enfield, NH: Science Publishers.

Larsell, O. (1967). *The comparative anatomy and histology of the cerebellum from Myxinoids through birds*. Minneapolis, MN: University of Minnesota Press.

Larsson, M. (2009). Possible functions of the octavolateralis system in fish schooling. *Fish and Fisheries*, 10, 344–353.

Liang, X. F., Liu, J. K., & Huang, B. Y. (1998). The role of sense organs in the feeding behavior of Chinese perch. *Journal of Fish Biology*, 52, 1058–1067.

Maruska, K. P., & Tricas, T. C. (2009). Central projections of octavolateralis nerves in the brain of a soniferous damselfish (*Abudefduf abdominalis*). *Journal of Comparative Neurology*, 512, 628–650.

McCormick, C. A. (1992). Evolution of central auditory pathways in anamniotes. In D.B. Webster, R. R. Fay, & A. N. Popper (Eds.), *The evolutionary biology of hearing* (pp. 323–350). New York: Springer-Verlag.

McCormick, C. A. (1999). Anatomy of the central auditory pathways of fish and amphibians. In R. R. Fay & A. N. Popper (Eds.), *Comparative hearing: Fish and amphibians* (pp. 155–217). New York: Springer-Verlag.

McCormick, C. A., & Hernandez, D. V. (1996). Connections of octaval and lateral line nuclei of the medulla in the goldfish, including the cytoarchitecture of the secondary octaval population in goldfish and catfish. *Brain Behavior and Evolution*, 47, 113–137.

McCormick, C. A., & Wallace, A. C. (2012). Otolith end organ projections to auditory neurons in the descending octaval nucleus of the goldfish, *Carassius auratus*: A confocal analysis. *Brain Behavior and Evolution*, 80, 41–63.

Miersch, L, Hanke, W., Wieskotton, S., Hanke, F. D., Oeffner, J., Leder, A., Brede, M., Witte, M., & Dehnhardt, G. (2011). Flow sensing by pinniped whiskers. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 366, 3077–3084.

Mirjany, M., & Faber, D. S. (2011). Characteristics of the anterior lateral line nerve input to the Mauthner cell. *Journal of Experimental Biology*, 214, 3368–3377.

Mirjany, M., Preuss, T., & Faber, D. S. (2011). Role of the lateral line mechanosensory system in directionality of goldfish auditory evoked escape response. *Journal of Experimental Biology*, 214, 3358–3367.

Modrell, M., Bemis, W. E., Northcutt, R. G., Davis, M., & Baker, C. (2011). Electrosensory ampullary organs are derived from lateral line placodes in bony fishes. *Nature Communications*, 2, 496.

Montgomery, J. (1989). Lateral line detection of planktonic prey. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and behavior* (pp. 561–574). New York: Springer-Verlag.

Montgomery, J. C., Coombs, S., Conley, R. A. & Bodznick, D. (1995). Hindbrain sensory processing in lateral line, electrosensory and auditory systems: A comparative overview of anatomical and functional similarities. *Auditory Neuroscience*, 1, 207–231.

Montgomery, J. C., Baker, C. F., & Carton, A. G. (1997). The lateral line can mediate rheotaxis in fish. *Nature*, 389, 960–963.

Montgomery, J., MacDonald, F., Baker, C. F., & Carton, A. G. (2002). Hydrodynamic contributions to multimodal guidance of prey capture behavior in fish. *Brain Behavior and Evolution*, 29, 190–198.

Montgomery, J. C., McDonald, F., Baker, C. F., Carton, A. G., & Ling, N. (2003). Sensory integration in the hydrodynamic world of rainbow trout. *Proceedings of the Royal Society of London B: Biological Sciences*, 270, S195–S197.

Münz H. (1989). Functional organization of the lateral line periphery. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and evolution* (pp. 285–298). New York: Springer-Verlag.

Myrberg, A. (2001). The acoustical biology of elasmobranchs. *Environmental Biology Fishes*, 60, 31–45.

Nauroth, I. E., & Mogdans, J. (2009). Goldfish and oscars have comparable responsiveness to dipole stimuli. *Naturwissenschaften*, 96, 1401–1409.

Nelson, M. E., MacIver, M. A., & Coombs, S. (2002). Modeling electrosensory and mechanosensory images during the predatory behavior of weakly electric fish. *Brain Behavior and Evolution*, 59, 199–210.

New, J. G., Fewkes, L. A., & Khan, A. N. (2001). Strike-feeding behavior in the muskellunge Esox masquinongy: Contributions of lateral line and visual sensory systems. *Journal of Experimental Biology*, 204, 1207–1221.

Northcutt, R. G. (1996). The origin of craniates: Neural crest, neurogenic placodes, and homeobox genes. *Israeli Journal of Zoology*, 42, S273–S313.

Northcutt, R. G. (2006). Connections of the lateral and medial divisions of the goldfish telencephalic pallium. *Journal of Comparative Neurology*, 494, 903–943.

Northcutt, R. G., & Gans, C. (1983). The genesis of neural crest and epidermal placodes: A reinterpretation of vertebrate origins. *Quarterly Review of Biology*, 58, 1–28.

Palmer, L. M., Deffenbaugh, M., & Mensinger, A. F. (2005). Sensitivity of the anterior lateral line to natural stimuli in the oyster toadfish, *Opsanus tau* (Linnaeus). *Journal of Experimental Biology*, 208, 3441–3450.

Partan, S. R., & Marler, P. (2005). Issues in the classification of multimodal communication signals. *American Naturalist*, 166, 231–245.

Partridge, B. L., & Pitcher, T. J. (1980). The sensory basis of fish schools: Relative roles of lateral line and vision. *Journal of Comparative Physiology A*, 135, 315–325.

Pitcher, T. J., Partridge, B. L., & Wardle, C. S/ (1976). A blind fish can school. *Science*, 194, 963–965.

Plachta, D. T. T., Hanke, W., & Bleckmann, H. (2003). A hydrodynamic topographic map in the midbrain of goldfish *Carassius auratus*. *Journal of Experimental Biology*, 206, 3479–3486.

Platt, C., Popper, A. N., & Fay, R. R. (1989). The ear as part of the octavolateralis system. In S. Coombs, P. Görner, & H. Münz (Eds.), *The mechanosensory lateral line: Neurobiology and behavior* (pp. 633–651). New York: Springer-Verlag.

Pluta, S. R., & Kawasaki, M. (2008). Multisensory enhancement of electromotor responses to a single moving object. *Journal of Experimental Biology*, 211, 2919–2930.

Pohlmann K., Grasso, F. W., & Breithaupt, T. (2001). Tracking wakes: The nocturnal predatory strategy of piscivorous catfish. *Proceedings of the National Academy of Sciences of the USA*, 98, 7371–7374.

Pohlmann, K., Atema, J., & Breithaupt, T. (2004). The importance of the lateral line in nocturnal predation of piscivorous catfish. *Journal of Experimental Biology*, 207, 2971–2978.

Popper, A. N. (1977). A scanning electron microscopic study of the sacculus and lagena in the ears of fifteen species of teleost fishes. *Journal of Morphology*, 153, 397–417.

Popper, A. N., & Fay, R. R.(2011). Rethinking sound detection by fishes. *Hearing Research*, 273, 25–36.

Popper, A. N., Fay, R. R., Platt, C., & Sand, O. (2003). Sound detection mechanisms and capabilities of teleost fishes. In S. P. Collin & J. N. Marshall (Eds.), *Sensory processing in aquatic environments* (pp. 3–38). New York: Springer.

Popper, A. N., Plachta, D. T., Mann, D. A., & Higgs, D. (2004). Response of clupeid fish to ultrasound: A review. *Ices Journal of Marine Science*, 61, 1057–1061.

Prechtl, J. C., von Der Emde, G., Wolfart, J., Karamürsel, S., Akoev, G. N., & Andrianov, Y. N. (1998). Sensory processing in the pallium of a mormyrid fish. *Journal of Neuroscience*, 18, 7381–7393.

Reep, R. L., Gaspard, J. C., Sarko, D., Rice, F. L., Mann, D. A., & Bauer, G. B. (2011). Manatee vibrissae: Evidence for a "lateral line" function. *Annals of the New York Academy of Sciences*, 1225, 101–109.

Richardson, E. G. (1954). The relations between acoustics and hydrodynamics. *Journal of the Acoustical Society of America*, 26, 615–617.

Rogers, P. H., & Cox, M. (1988). Underwater sound as a biological stimulus. In J. Atema, R. R. Fay, A. N. Popper, & W. N. Tavolga (Eds.), *Sensory biology of aquatic animals* (pp. 131–149). New York: Springer-Verlag.

Sand, O. (1981). The lateral-line and sound reception. In W. N. Tavolga, A. N. Popper, & R. R. Fay (Eds.), *Hearing and sound communication in fishes* (pp. 459–480). New York: Springer-Verlag.

Sand, O. (1984). Lateral line systems. In L. Bolis, R. D. Keynes, & S. H. P. Maddrell (Eds.), *Comparative physiology of sensory systems* (pp. 3–32). Cambridge, U.K.: Cambridge University Press.

Sand, O., & Enger, P. S. (1973). Evidence for an auditory function of the swim bladder in the cod. *Journal of Experimental Biology*, 59, 405–414.

Sand, O., & Hawkins, A. D. (1973). Acoustic properties of the cod swim bladder. *Journal of Experimental Biology*, 58, 797–820.

Sand, O., & Karlsen, H. E. (1986). Detection of infrasound by the Atlantic cod. *Journal of Experimental Biology*, 125, 197–204.

Sand, O., & Karlsen, H. E. (2000). Detection of infrasound and linear acceleration in fishes. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 355, 1295–1298.

Sand, O., & Bleckmann, H. (2008). Orientation to auditory and lateral line stimuli. In J. F. Webb, A. N. Popper, & R. R. Fay (Eds.), *Fish bioacoustics* (pp. 183–231). New York: Springer.

Saskia, W., & Schuster, S. (2007). The predictive start of a hunting archer fish: A flexible and precise motor pattern performed with the kinematics of an escape C-start. *Journal of Experimental Biology*, 210, 311–324.

Satou, M., Takeuchi, H. A., Nishii, J., Tanabe, M., Kitamura, S., & Okumoto, N. (1994a). Behavioral and electrophysiological evidences that the lateral line is involved in the intersexual vibrational communication of the himé salmon (landlocked red salmon, *Oncorhynchus nerka*). *Journal of Comparative Physiology*, 174, 539–549.

Satou, M., Takeuchi, H. A., Takei, K., Hasegawa, T., Matsushima, T., & Okumoto, N. (1994b). Characterization of vibrational and visual signals which elicit spawning behavior in the male himé salmon (landlocked red salmon, *Oncorhynchus nerka*). *Journal of Comparative Physiology*, 174, 527–537.

Schroeder, C., & Foxe, J. (2005). Multisensory contributions to low-level, 'unisensory' processing. *Current Opinion in Neurobiology*, 15, 454–458.

Schuijf, A., & Buwalda, R. J. A. (1980). Sound localization: A major problem in fish acoustics. In A. N. Popper & R. R. Fay (Eds.), *Comparative studies of hearing in vertebrates* (pp. 43–78). New York: Springer-Verlag.

Schuster, S. (2006). Integration of the electrosense with other senses: Implications for communication. In F. Ladich, S. P. Collin, P. Moller, & B. G. Kapoor (Eds.), *Communication in fishes* (pp. 781–804). Enfield, NH: Science Publishers.

Schwalbe, M. A. B., Bassett, D. K., & Webb, J. F. (2012). Feeding in the dark: Lateral-line-mediated prey detection in the peacock cichlid *Aulonocara stuartgranti*. *Journal of Experimental Biology*, 215, 2060–2071.

Skals, N., Anderson, P., Kanneworff, M., Lofstedt, C., & Surlykke, A. (2005). Her odours make him deaf: Crossmodal modulation of olfaction and hearing in a male moth. *Journal of Experimental Biology*, 208, 595–601.

Song, J., Yan, H. Y., & Popper, A. N. (1995). Damage and recovery of hair cells in fish canal (but not superficial) neuromasts after gentamicin exposure. *Hearing Research*, 91, 63–71.

Sonny, D., Knudsen, F. R., Enger, P. S., Kvernstuen, T., & Sand, O. (2006). Reactions of cyprinids to infrasound in a lake and at the cooling water inlet of a nuclear power plant. *Journal of Fish Biology*, 69, 735–748.

Stoffregen, T. A., & Bardy, B. G. (2001). On specification and the senses. *Behavioral Brain Sciences*, 24, 195–261.

Szabo, T. M., McCormick, C. A., & Faber, D. S. (2007). Otolith endorgan input to the Mauthner neuron in the goldfish. *Journal of Comparative Neurology*, 505, 511–525.

Todd, N. P. M., Rosengren, S. M., & Colebatch, J. G. (2008). Tuning and sensitivity of the human vestibular system to low-frequency vibration. *Neuroscience Letters*, 444, 36–41.

Tomchik, S. M., & Lu, Z. M. (2005). Octavolateral projections and organization in the medulla of a teleost fish, the sleeper goby (*Dormitator latifrons*). *Journal of Comparative Neurology*, 481, 96–117.

Tricas, T. C., Kajiura, S. M., & Kosaki, R. K. (2006). Acoustic communication in territorial butterflyfish: Test of the sound production hypothesis. *Journal of Experimental Biology*, 209, 4994–5004.

van Bergeijk, W. A. (1964). Directional and non-directional hearing in fish. In W. N. Tavolga (Ed.), *Marine bio-acoustics* (pp. 185–204). Oxford: Pergamon Press.

van Trump, W. J., Coombs, S., Duncan, K., & McHenry, M. J. (2010). Gentamicin is ototoxic to all hair cells in the fish lateral line system. *Hearing Research*, 261, 42–50.

von Campenhausen, C., Riess, I., & Weissert, R. (1981). Detection of stationary objects by the blind cavefish *Anoptichthys jordani* (Characidae). *Journal of Comparative Physiology A*, 143, 369–374.

von der Emde, G., & Prechtl, J. C. (1999). Anatomical connection of auditory and lateral line areas of the dorsal telencephalon (Dm) in the osteoglossomorph teleost, *Gnathonemus petersii*. *Brain Research*, 818, 355–367.

Webb, J. F. (1998). The laterophysic connection: A unique link between the swim bladder and the lateral-line system in *Chaetodon* (Perciformes: Chaetodontidae). *Copeia*, 1998, 1032–1036.

Webb, J. F., & Smith, W. L. (2000). The laterophysic connection in chaetodontid butterflyfish: Morphological variation and speculations on sensory function. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 355, 1125–1129.

Webb, J. F., Herman, J. L., Woods, C. F., & Ketten, D. R. (2010). The ears of butterflyfishes (Chaetodontidae): 'Hearing generalists' on noisy coral reefs? *Journal of Fish Biology*, 77, 1406–1423.

Weeg, M. S. & Bass, A. H. (2000). Central lateral line pathways in a vocalizing fish. *The Journal of Comparative Neurology*, 418, 41–64.

Will, U. (1986). Organization and projections of the area octavolateralis in amphibians. In B. Fritzsch, M. Ryan, W. Wilczynski, T. Hetherington, & W. Walkowiak (Eds.), *The evolution of the amphibian auditory system* (pp. 185–208). New York: John Wiley & Sons.

Wilson, M., Montie, E. W., Mann, K. A., & Mann, D. A. (2009). Ultrasound detection in the Gulf menhaden requires gas-filled bullae and an intact lateral line. *Journal of Experimental Biology*, 212, 3422–3427.

Windsor, S. P., Tan, D., & Montgomery, J. C. (2008). Swimming kinematics and hydrodynamic imaging in the blind Mexican cavefish (*Astyanax fasciatus*). *Journal of Experimental Biology*, 211, 2950–2959.

Windsor, S. P., Norris, S. E., Cameron, S. M., Mallinson, G. D., & Montgomery, J. C. (2010). The flow fields involved in hydrodynamic imaging by blind Mexican cave fish (*Astyanax fasciatus*). Part I: Open water and heading towards a wall. *Journal of Experimental Biology*, 213, 3819–3831.

Yamamoto, N., & Ito, H. (2005). Fiber connections of the anterior preglomerular nucleus in cyprinids with notes on telencephalic connections of the preglomerular complex. *Journal of Comparative Neurology*, 491, 212–233.

Yamamoto, N., & Ito, H. (2008). Visual, lateral line, and auditory ascending pathways to the dorsal telencephalic area through the rostrolateral region of the lateral preglomerular nucleus in cyprinids. *Journal of Comparative Neurology*, 508, 615–647.

Hearing Loss, Protection, and Regeneration in the Larval Zebrafish Lateral Line

Allison B. Coffin, Heather Brignull, David W. Raible, and Edwin W. Rubel

Keywords Aminoglycoside • Cell death • Cisplatin • Deafness • Drug screen • Fucoidin • Gentamicin • Genetic screen • Hair cell • Neomycin • Ototoxicity • Synthetic glucocorticoids

1 Introduction

The goal for this chapter is to introduce the zebrafish (*Danio rerio*) lateral line as a model system for hearing habilitation studies and to survey the literature on sensory hair cell loss, protection, and regeneration in the lateral line, specifically of larval zebrafish. The chapter opens with a brief history of zebrafish research and introduces some of the techniques that help make zebrafish a valuable species for these studies (Section 1). Subsequent sections discuss lateral line studies of genetic deafness (Section 2), drug-induced hair cell damage and protection (Sections 3 and 4), and hair cell regeneration (Section 5).

A.B. Coffin (✉)
Neuroscience Program, Washington State University, Vancouver, WA 98686, USA
e-mail: Allison.coffin@wsu.edu

H. Brignull (✉) • D.W. Raible
Department of Biological Structure, University of Washington, Seattle, WA 98195, USA
e-mail: brignull@u.washington.edu; draible@u.washington.edu

E.W. Rubel
Virginia Merrill Bloedel Hearing Research Center, University of Washington,
Seattle, WA 98195, USA
e-mail: rubel@uw.edu

S. Coombs et al. (eds.), *The Lateral Line*, Springer Handbook of Auditory Research 48,
DOI 10.1007/2506_2013_20, © Springer Science+Business Media New York 2013,
Published online: 23 August 2013

1.1 Zebrafish in the Lab

Zebrafish (*Danio rerio*) are small, striped cyprinid fishes found in slow-moving streams and rice paddies in southern Asia (Engeszer et al., 2007). Although a hobby aquarist favorite for years, zebrafish have more recently found fame in studies of vertebrate development and neurobiology. Pioneering work was done by George Streisinger and his colleagues at the University of Oregon in the 1970s (see Grunwald & Eisen, 2002 for a historical review of the field). Although the main focus of this chapter is the use of the zebrafish lateral line as a model system for auditory research, the chapter begins with a brief overview of major technical advances in zebrafish research to familiarize readers with some of the techniques that are applied to the auditory work discussed later in the chapter.

Increasing popularity of zebrafish for laboratory experiments is attributable to several features. Adults are small (3–5 cm), hardy, and can be kept at relatively high densities in affordable, commercially available aquaculture systems. Given appropriate temperature, light cycle, and water conditions, adults will breed year-round in captivity, with a single pair capable of producing upwards of several hundred embryos per week from the time of reproductive maturity (around 3–4 months in the lab) until senescence at 18–24 months of age. The embryos are transparent and develop externally, making them an ideal organism in which to study vertebrate development *in vivo*. At optimal temperatures (24–28°C), development proceeds in a highly reproducible and stereotyped fashion, as described in detail by Kimmel et al. (1995).

1.2 Techniques for Zebrafish Studies

There are a number of techniques that facilitate the versatility of zebrafish larvae for developmental and applied biomedical studies. Unlike most vertebrate species, zebrafish are suited to high-throughput screens designed to identify genetic or pharmacological targets of interest. These screens can be subdivided into reverse or forward approaches. Reverse approaches start with a target, genetic or pharmacological, that holds promise based on available data. These studies are more directed and often limited to a specific category of genes or drugs that investigators are particularly interested in. In contrast to reverse-directed approaches, forward-screens are often referred to as unbiased because the researcher begins by isolating a phenotype of interest and then trace it back to the cause, genetic or pharmacological, without any "bias" as to the cause of the phenotype.

The first large-scale forward genetic screens in zebrafish were performed in the mid-1990s (Mullins et al., 1994). These screens identified mutations that alter vertebrate development, including development of the notochord, brain, inner ear, and lateral line (Schier et al., 1996; Stemple et al., 1996; Whitfield et al., 1996). Publication of the first zebrafish linkage map (Postlethwait et al., 1994), followed

by the sequencing of the zebrafish genome by the Sanger Institute, provided the tools to map and ultimately identify the genes underlying specific mutations of interest.

Complementing random mutagenesis methods are a suite of techniques for over- and underexpressing specific genes in zebrafish. Transgenic zebrafish lines (those that carry an inserted or "foreign" gene) can be generated using the tol2 transposon, allowing for tissue-specific overexpression of a gene of interest or of a fluorescent reporter such as green fluorescent protein (GFP) (Kawakami et al., 2004; Burket et al., 2008; Suster et al., 2009). Injection of antisense morpholino oligonucleotides (morpholinos) at the one-cell stage is a powerful method of globally reducing gene expression in developing embryos, although the knock-down effect is efficient only during the first few days post-fertilization owing to a dilution of the morpholino during subsequent rounds of cell division (Nasevicius & Ekker, 2000). Morpholino knockdown of specific mRNA transcripts has helped reveal a suite of genes necessary for lateral line and inner ear development (Whitfield et al., 2002; Kerstetter et al., 2004). More recently, zinc-finger nuclease (ZFN) technology has been applied to zebrafish, allowing researchers to create targeted mutations that are stably inherited (Doyon et al., 2008; Meng et al., 2008; Foley et al., 2009).

Screening of compound libraries, sometimes also referred to as "chemical genetics," is another major advance in zebrafish research, providing key insights into both fundamental biological processes and disease mechanisms. Larval zebrafish are exposed to a known drug, a small molecule, or other drug-like compound from a library of hundreds or thousands of molecules, and assayed for a specific phenotype (reviewed in Kaufman et al., 2009). Zebrafish small molecule screens have identified compounds that affect many processes including organ and tissue development, tissue regeneration, and behavior patterns (Peterson et al., 2000; Mathew et al., 2007; Rihel et al., 2010). One advantage of chemical genetics is that zebrafish can be exposed to small molecules for precisely controlled intervals, not usually available with traditional mutagenesis screens. However, a drawback to small molecule screens is that in many cases, the molecular targets of these compounds are unknown. Both traditional genetic and chemical genetic screens have been applied to studies of hair cell loss, protection, and regeneration in the zebrafish lateral line (Chiu et al., 2008; Owens et al., 2008; Namdaran et al., 2012).

1.3 Zebrafish Lateral Line

The larval zebrafish lateral line consists of a series of neuromasts on the head (anterior lateral line) and the body (posterior lateral line) (see the chapter by Webb in this volume and Fig. 1 for a comparison of the adult and larval neuromast distribution). Neuromasts are located in stereotyped positions on the developing animal (Metcalfe et al., 1985; Raible & Kruse, 2000). The posterior lateral line develops from a migrating primordium that deposits neuromasts along the trailing edge of the

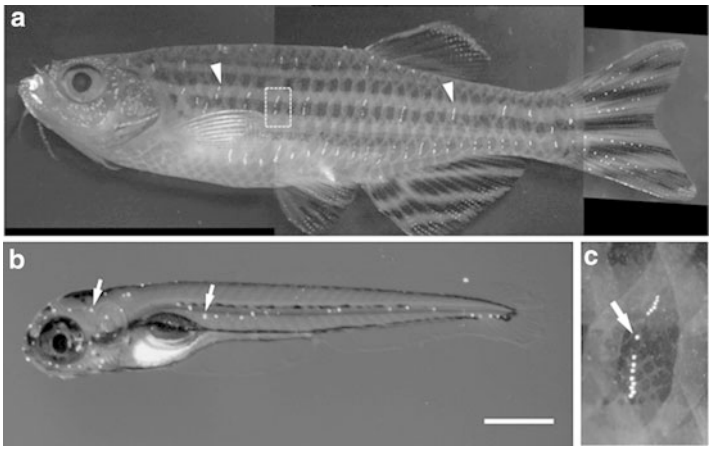

Fig. 1 Adult zebrafish (**a**) and 5 dpf larva (**b**), labeled with the vital dye DASPEI. In adults, neuromasts bud off and create stitches, the vertical lines of neuromasts (arrowheads). Example neuromasts are indicated by arrows and appear as white dots along the head and body of larva and as individual dots within stiches of adult (inset, **c**). Scale bar in b = 500 μm. (The image in **b** is from *Zebrafish*, 2010. Reprinted with permission of Mary Ann Liebert, New Rochelle, NY)

migratory body (David et al., 2002; reviewed in Ghysen & Dambly-Chaudiere, 2004). Each neuromast contains about 10–20 sensory hair cells and associated supporting cells and receives afferent and efferent innervation from the lateral line ganglia (Raible & Kruse, 2000; Ghysen & Dambly-Chaudiere, 2004). In zebrafish, the lateral line is already partially functional by 4 days post-fertilization (dpf), allowing for studies in relatively young larvae. As in other species (see the chapter by McHenry & Liao), it is thought that the zebrafish lateral line contributes to a variety of behaviors that involve detection of near-field water movements including prey detection, predator avoidance, orientation in current, and schooling.

Just like mammalian inner ear hair cells, zebrafish lateral line hair cells are susceptible to ototoxic drugs such as aminoglycoside antibiotics and platinum-based chemotherapy compounds (Harris et al., 2003; Ou et al., 2007; Owens et al., 2007). Moreover, homologs of several human deafness genes cause loss of hair cell function in the zebrafish lateral line (Ernest et al., 2000; Seiler et al., 2004). These genetic similarities in hair cell development and maintenance, combined with the similar responses to known ototoxic compounds, serve as the foundation for using the zebrafish lateral line as a model system for biomedical studies of hair cell loss and protection. Additional advantages include the external location of the hair cells that facilitates drug delivery and imaging for studies of dynamic events and hair cell viability, and the small size and high fecundity of the adults. Remarkably, zebrafish, as well as other fishes and most nonmammalian vertebrates, can regenerate lost hair cells and restore sensory function, making them an appealing model for hearing restoration and regenerative medicine (Corwin & Cotanche, 1988; Ryals & Rubel, 1988; Ma et al., 2008).

1.4 Hearing and Balance Disorders: What Is Being Modeled?

Hearing loss caused by damage to or death of sensory hair cells is the most common worldwide sensorineural disorder. As of 2004 the World Health Organization estimated that more than 275 million people live with moderate to profound hearing impairment, defined as a hearing loss that interferes with daily activities (WHO 2012). This can have a devastating impact on an individual with hearing loss, his or her family, and on the economy. Affected children often have delayed language development and impaired learning, while adults report feelings of isolation and reduced quality of life (Dalton et al., 2003; Kral & O'Donoghue, 2010). In the United States alone, the economic burden was estimated at $154–186 billion per year as of 2000, making hearing loss not only common but also exceedingly costly (Ruben, 2000).

Hearing loss can be caused by many factors including genetic mutations, workplace and recreational noise exposure, ototoxic drugs, and aging (see Keats et al., 2002 [SHAR Vol. 14]; Schacht et al., 2008 [SHAR Vol. 31]). Zebrafish provide a platform for study of individual factors and for analysis of epistatic interactions in hearing loss. Hair cells in the vestibular system can also be damaged by similar means, with equally devastating consequences (Zingler et al., 2007; Eppsteiner & Smith, 2011). Peripheral vestibular dysfunction causes dizziness and vertigo and is partially responsible for many of the falls experienced by the elderly (Barin & Dodson, 2011). Therefore, a better understanding of hair cell death, protection, and regeneration will facilitate habilitation of both auditory and vestibular function.

1.5 Tools of the Trade

1.5.1 Visualizing the Lateral Line

Several tools and techniques have been developed in recent years that facilitate studies of the lateral line in hair cell death, protection, and regeneration, particularly in the area of neuromast visualization. Figures 1 and 2 show representative examples of some of the labeling techniques available.

Vital dyes are arguably the easiest and most accessible way to label lateral line hair cells, with several dyes in widespread use. The mitochondrial potential dye DASPEI is a favorite, having been used to label the lateral line of many fish species, including both adult and larval zebrafish (Harris et al., 2003; Van Trump et al., 2010). Yo-Pro1 and related compounds are DNA-binding dyes that delineate hair cell nuclei, while FM1-43 is generally considered a marker for endocytosis and labels the hair cell cytoplasm (Meyers et al., 2003; Santos et al., 2006). All of these dyes are quickly taken up by hair cells when added to the embryo medium

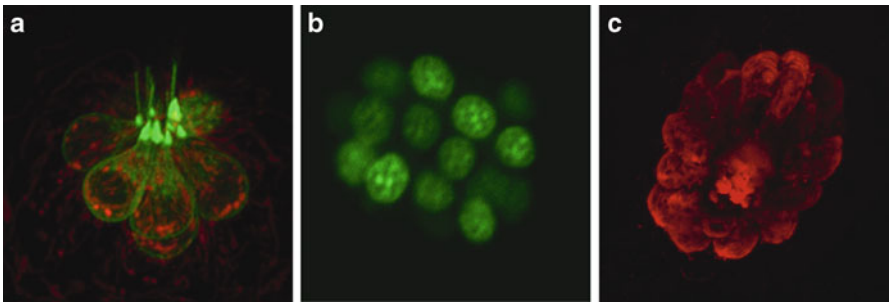

Fig. 2 Examples of different hair cell labeling techniques for lateral line visualization and quantification. (**a**) Hair cells in Brn3c:mGFP transgenic fish express GFP in the plasma membrane (green). This fish is also labeled with the vital dye MitoTracker Red to visualize mitochondria (red). (**b**) Hair cell nuclei labeled with the vial dye Yo-Pro1. Images in both **a** and **b** were collected in live, anesthetized larvae. In contrast, (**c**) shows an example of a post-fixation labeling technique, in this case labeling with an antibody to parvalbumin. (The image in **b** is from *Zebrafish*, 2010. Reprinted with permission of Mary Ann Liebert, New Rochelle, NY)

surrounding the fish. FM1-43 is additionally useful in that it is taken up in a transduction-dependent manner and is therefore considered a proxy for healthy hair cells (Meyers et al., 2003).

In addition to vital dye labeling, several groups have generated transgenic fish lines that express fluorescent proteins in hair cells, including Green Fluorescent Protein (GFP) driven by the Brn3c, parvalbumin3, or atp2b1a promoters (Parinov et al., 2004; Xiao et al., 2005; McDermott et al., 2010). These fish lines are useful for visualizing immature hair cells, as the promoters are often turned on early in hair cell development before some vital dyes can be internalized.

Finally, several classic post-fixation techniques are useful for visualizing zebrafish hair cells. Actin-rich stereocilia can be labeled with fluorescently tagged phalloidin (Williams & Holder, 2000; Harris et al., 2003), while antibodies to myosin VI, myosin VIIa, S100, and parvalbumin label hair cell bundles and soma (Germana et al., 2004; Lopez-Schier & Hudspeth, 2006; Coffin et al., 2007). Electron microscopy, although more labor-intensive than other techniques, also provides information on hair cell morphology and ultrastructure (Williams & Holder, 2000; Harris et al., 2003; Owens et al., 2007).

1.5.2 Assessing Lateral Line Function

Although most hearing habilitation studies in the zebrafish lateral line have relied heavily on imaging techniques, methods for electrophysiological and behavioral assessment of lateral line function have recently been developed. Work in Teresa Nicolson's laboratory has established protocols for recording hair cell microphonics and responses from individual lateral line afferents under both spontaneous and fluid jet-stimulated conditions in intact, immobilized larvae (Obholzer et al., 2008;

Trapani and Nicolson, 2011). These techniques have been useful in dissecting auditory pathways in zebrafish mutants to identify the physiological level of defects. Further behavioral assays include rheotaxis (orientation to water flow) (Suli et al., 2012) and flow-mediated startle responses (McHenry et al., 2009) for quantifying lateral line-mediated behavior. These techniques add to zebrafish lateral line research by facilitating comparisons of structure, function, and behavior under the same experimental conditions.

2 Genetic Deafness

There are many causes of deafness, but it is estimated that 60–70% of all deafness is the result of heterogeneous genetic factors (Raviv et al., 2010). There is a massive body of literature in this area, and an overview of clinical genetics is available in an earlier volume of the SHAR series, *Genetics of Auditory Disorders* (Keats et al., 2002). Although clinical genetics is an active area of research, there are difficulties inherent in human studies, such as geographical dispersion of family members, identification of families of appropriate size and genetic background, gaps in pedigrees, and obtaining approval to collect, transport, and process samples from patients that make the appeal of model organisms obvious. Model systems have been critical for identifying and understanding the function of genes linked to hearing and hearing loss, with mice in particular playing an important role. The following section examines the role of zebrafish in identifying novel deafness genes and elucidating the underlying causes of genetic deafness.

2.1 Mutagenesis Screens for Deafness Genes

The majority of genetic screens in zebrafish use the mutagen *N*-ethyl-*N*-nitrosurea (ENU) (Mullins et al., 1994; Solnica-Krezel et al., 1996). ENU introduces point mutations that can be later identified by traditional linkage mapping techniques. ENU mutagenesis screens have generated hundreds of mutant lines, many of which display morphological and/or functional defects in hearing and balance (reviewed in Whitfield, 2002; Nicolson, 2005).

Mutagenesis screens in zebrafish initially focused on isolating mutants exhibiting morphological defects visible under a dissecting microscope (Haffter et al., 1996; Malicki et al., 1996; Whitfield et al., 1996). The first major genetic screen for ear mutations produced 78 mutants with phenotypes such as very small or large ear size, abnormal position, size or number of otoliths, or malformation of internal structures such as the shape of the vestibular organs or changes in other aspects of development (Malicki et al., 1996; Whitfield et al., 1996). Secondary screening was performed to determine whether sensory patches in the auditory, vestibular, and lateral line systems developed normally in these ear-morphology mutants. Two of the mutants

displayed posterior lateral line abnormalities; *dog* mutants had fewer neuromasts than wild-type animals whereas *hypersensitive* mutants had nearly double the number of neuromasts (Whitfield et al., 1996).

Many of the mutants identified on the basis of morphological defects also displayed abnormal responses to noise and/or unusual swimming behaviors, as might be expected in animals with compromised function of the ear. Balance-defective swimming behaviors included swimming in circles, either horizontal or vertical, or swimming in a corkscrew path when stimulated. In the absence of stimulation, many of these mutants rested sideways or upside down on the bottom despite the presence of an inflated swim bladder, again suggesting compromised vestibular function. Behavioral phenotypes also revealed mutants that failed to respond to sound or vibrational stimuli, such as a tap on the dish, although they swam away from tactile stimulation (Malicki et al., 1996; Whitfield et al., 1996).

Genetic screening for motility in response to touch led to the identification of 15 additional mutants with balance-defective swim phenotypes in the absence of gross morphological defects of the ear (Granato et al., 1996). On further investigation, these "circler" mutants revealed more subtle defects such as decreased hair bundle integrity or defects in transduction (Nicolson et al., 1998).

Together, these morphological- and behavioral-genetic screens for ear-related abnormalities have isolated more than 90 mutant lines that have since been linked to at least 30 genes and the numbers continue to increase. The majority of genes isolated in these screens have been linked to mammalian orthologs, and more than a third are associated with human deafness syndromes including Usher syndrome and Waardenburg syndrome (reviewed in Whitfield, 2002; and Nicolson, 2005).

One such example of a zebrafish model of human deafness is the *mariner* mutant. M*ariner* was one of the mutants initially identified by its circler phenotype and further analysis revealed that *mariner* is also unresponsive to acoustic/vibrational stimuli (Granato et al., 1996; Nicolson et al., 1998). The mutation was later mapped to my*osin7a*, an unconventional myosin highly expressed in both zebrafish and mammalian hair cells (Ernest et al., 2000). A mouse model also exists for *myosin7a*. First described in 1929, *shaker* mice have progressive hearing loss and a tendency to walk in circles, a phenotype similar to the circular swimming pattern observed in *mariner* (Lord & Gates, 1929; Gibson et al., 1995). These models are also similar at the cellular level: lack of a robust electrophysiological response to stimuli and disorganized hair bundles are observed in *mariner* zebrafish (Nicolson et al., 1998; Ernest et al., 2000) and *shaker* mice (Richardson et al., 1997; Self et al., 1998). These models with mutations in *myosin7a* also contribute to the study of human deafness diseases. In patients, *MYOVIIA* has been linked to Usher1B syndrome (Weil et al., 1995) and both recessive and dominant forms of nonsyndromic deafness (Liu et al., 1997a,b).

Similar cases, where genetic mutations in zebrafish mutants act as models for human deafness, and often in parallel with other mammalian models, exist for many genes. Additional zebrafish mutants exist in structural genes such as *myosin6b* and *cadherin23* and developmental genes including *eyaI*, *sox10*, and *pax2*. These and additional zebrafish models of hearing disease are covered in more details in a wide

variety of reviews (Whitfield, 2002; Nicolson, 2005). The ability of zebrafish to phenocopy many of the major aspects of human hearing by single gene mutations provides strong support for the continued use of zebrafish as a model for the behavioral and molecular studies of deafness genes.

The majority of screens have been performed on larval zebrafish 5 dpf or younger. However, at least one screen was performed on adult zebrafish by testing their ability to respond to tone bursts at 400 Hz (Bang et al., 2001). In screening more than 6,500 adult animals roughly 1% had an abnormal response to the sound stimuli. The majority of the mutants isolated in this screen had defects limited to structures important for sound conduction, such as the swim bladder. Morphological defects were also detected in specialized hearing structures specific to Otophysan fishes, such as the Weberian ossicles. Although this particular screen did not identify any new genes important for hair cell development or function, it is the sole example of high-throughput, sound-based screening of adult zebrafish and introduced a technique that may have exciting future applications.

3 Ototoxicity

Certain therapeutic drugs can also cause sensorineural hearing loss. Aminoglycoside antibiotics (e.g., streptomycin, neomycin, gentamicin) and platinum-based chemotherapeutics (e.g., cisplatin) are the most well studied ototoxic drugs, both in terms of documented cases of deafness in human patients and in animal studies aimed at understanding mechanisms underlying ototoxic responses. Table 1 lists drugs known to cause hair cell loss in zebrafish.

3.1 Effects of Known Ototoxins on the Zebrafish Lateral Line

3.1.1 Aminoglycosides

Aminoglycoside ototoxicity was first discovered in the 1940s when reports of hearing loss cropped up in patients receiving streptomycin treatment (Schacht & Hawkins, 2006). The first lateral line experiment was performed in 1964, showing that streptomycin reduced lateral line microphonic potentials in the burbot *Lota lota*, a freshwater gadiform fish indigenous to parts of Europe and North America (Wersäll & Flock, 1964). Subsequent studies on the lateral line of other fish and amphibian species have confirmed the ototoxic effects of several aminoglycoside drugs (Kroese & van den Bercken, 1980, 1982; Kaus, 1987; Song et al., 1995). As a result, aminoglycoside treatment has become a standard tool for blocking sensory input in behavioral studies designed to investigate lateral line function (e.g., Montgomery et al., 1997; Coombs et al., 2001).

Table 1 Ototoxic drugs identified or confirmed in zebrafish lateral line

Drug name	Drug category/use	Reference
Neomycin	Aminoglycoside antibiotic	Williams & Holder, 2000; Harris et al., 2003
Gentamicin	Aminoglycoside antibiotic	Ton & Parng, 2005; Owens et al., 2009
Kanamycin	Aminoglycoside antibiotic	Owens et al., 2009
Cisplatin	Antineoplastic, DNA crosslinker	Ton & Parng, 2005; Ou et al., 2007
Chloramphenicol	Antibiotic	Chiu et al., 2008
Chlortetracycline HCl	Antibiotic	Chiu et al., 2008
Pentamidine isethionate	Antiprotozoal	Chiu et al., 2008
Spermadine	Ornithine decarboxylase inhibitor	Chiu et al., 2008
Tobramycin	Antibiotic	Chiu et al., 2008
Propantheline bromide	Anticholinergic	Chiu et al., 2008
Ethacrynic acid	Loop diuretic	Chiu et al., 2008
Pomiferin	Antioxidant	Chiu et al., 2008
Chlorophyllide	Antineoplastic	Chiu et al., 2008
Estradiol valerate	Estrogen	Chiu et al., 2008
Pentetrazole	CNS/respiratory/circulatory stimulant	Chiu et al., 2008
Guaiazulene	Antioxidant	Chiu et al., 2008
Rosolic acid	Diagnostic aid	Chiu et al., 2008
Vincamine	Vasodilator	Chiu et al., 2008
Demeclocycline HCl	Antibiotic	Chiu et al., 2008
Mefloquine	Antiprotozoal	Chiu et al., 2008
Candesartan	Angiotensin 1 receptor antagonist	Chiu et al., 2008
Simvastatin	HMGCoA reductase inhibitor, antihyperlipidemic	Chiu et al., 2008
Oxaliplatin	Antineoplastic, DNA cross linker	Hirose et al., 2011
Nitrogen mustard	Antineoplastic, alkylating agent	Hirose et al., 2011
Vincristine	Antineoplastic, microtubule inhibitor	Hirose et al., 2011
Vinorelbine	Antineoplastic, microtubule inhibitor	Hirose et al., 2011
Imatinib	Antineoplastic, receptor tyrosine kinase inhibitor	Hirose et al., 2011
Doxorubicin	Antineoplastic, topoisomerase poison	Hirose et al., 2011
Vinblastine	Antineoplastic, microtubule inhibitor	Ton & Parng, 2005; Hirose et al., 2011
Sunitinib	Antineoplastic, receptor tyrosine kinase inhibitor	Hirose et al., 2011
Raloxifene	Antineoplastic, estrogen receptor modulator	Hirose et al., 2011
Dactinomycin	Antineoplastic, transcription inhibitor	Hirose et al., 2011
Carmustine	Antineoplastic, alkylating agent	Hirose et al., 2011
Exemestane	Antineoplastic, steroidal aromatase inhibitor	Hirose et al., 2011
Quinine	Anti-malarial	Ton & Parng, 2005

At the beginning of the twenty-first century investigators began using the zebrafish lateral line as a model system to study hair cell toxicity due to therapeutic drugs. An initial study by Williams and Holder (2000) showed that neomycin robustly kills lateral line hair cells, and Harris et al. (2003) documented these effects more thoroughly by demonstrating that the response to neomycin is dose-dependent and similar in each neuromast. Hair cell susceptibility is dependent on both fish age and hair cell age, as hair cells in 4 dpf fish are significantly less sensitive to neomycin damage than those in 5 dpf or older animals (Murakami et al., 2003; Santos et al., 2006). These findings are consistent with mammalian studies that show a correlation between aminoglycoside sensitivity and hearing onset (Marot et al., 1980). Hair cells in adult zebrafish lateral line are also susceptible to aminoglycoside damage, suggesting that ototoxic responses of mature hair cells remain stable throughout the life of the animal (Van Trump et al., 2010).

More recent studies in the zebrafish lateral line seek to discover underlying cell death mechanism(s) responsible for aminoglycoside toxicity. Mitochondrial swelling, loss of mitochondrial membrane potential, and the necessity for mitochondrial-associated Bcl2 proteins all suggest that aminoglycosides activate mitochondrial-dependent cell death pathways (Owens et al., 2007; Coffin et al., 2013). Similar events have been demonstrated in rodent and chick inner ear, showing concordance between zebrafish and mammalian hair cell death responses (Hirose et al., 1999; Cunningham et al., 2004; Mangiardi et al., 2004; Matsui et al., 2004). Nuclear condensation and activation of classical caspase-dependent apoptosis may also occur, although the necessity of this class of proteases in hair cell death is debated (Williams & Holder 2000; Cunningham et al., 2002; Matsui et al., 2004; Jiang et al., 2006; Owens et al., 2007). Interestingly, recent research demonstrates that the time course of hair cell death differs dramatically for different aminoglycoside antibiotics, suggesting that these aminoglycosides may kill hair cells via different intracellular signaling cascades (Coffin et al., 2009; Owens et al., 2009). Further elucidation of hair cell death mechanisms is necessary to provide targeted therapy for patients who receive aminoglycoside treatment.

Although several studies agree that aminoglycosides cause dose-dependent hair cell death in the zebrafish lateral line, closer examination of these studies reveals interesting differences in concentration-dependent effects. Little hair cell death occurs with neomycin concentrations under 50 μM, and that at least 200 μM neomycin is required for virtually complete hair cell loss (Harris et al., 2003; Murakami et al., 2003; Owens et al., 2007). In contrast, concentrations as low as 10 μM were shown to cause significant hair cell loss by other groups, with complete hair cell death seen after treatment with just 16 μM neomycin (Williams & Holder, 2000; Ton & Parng, 2005). These dose-dependent differences are due to differences in ion composition in the embryo medium used by the different research groups (Coffin et al., 2009). Reducing the concentration of calcium or magnesium makes hair cells more sensitive to neomycin such that low concentrations become highly toxic (Kaus, 1992; Coffin et al., 2009). Divalent cations, specifically calcium, are thought to regulate the open probability of the hair cell transduction channel such that a greater fraction of channels are open at rest under low calcium conditions

(Corey & Hudspeth, 1983; Ricci & Fettiplace, 1998). Given that aminoglycoside uptake by hair cells is transduction-dependent and likely enters directly through the transduction channel itself (Steyger et al., 2003; Marcotti et al., 2005), the ability to shift the dose–response relationship of neomycin via modulation of divalent cation concentration is logical. Collectively, these findings underscore the need for careful documentation and appropriate controls so that lateral line ototoxicity data may be accurately compared between labs. They also lend additional support to recent evidence that post-treatment verification of hair cell loss is necessary when aminoglycosides are used as tools for blocking sensory input to the lateral line (Van Trump et al., 2010; Brown et al., 2011).

3.1.2 Cisplatin

Cisplatin is a highly toxic, platinum-based chemotherapeutic agent used in the treatment of a variety of solid tumors. Whereas aminoglycosides appear to kill lateral line hair cells with distinctly nonlinear time parameters, cisplatin has more or less predictable effects. There is a log-linear relationship between dose and time for loss of cisplatin-treated hair cells, suggesting that cisplatin damage is related to total intracellular cisplatin accumulation (Ou et al., 2007). There is little work to date on cell death signaling cascade activation in cisplatin-treated lateral line hair cells. Ton and Parng (2005) found that several antioxidants, including *N*-acetyl L-cysteine and D-methionine, protected hair cells in cisplatin-treated zebrafish, suggesting that cisplatin may induce oxidative stress pathways in damaged hair cells. Oxidative stress pathways have been implicated in both cisplatin and aminoglycoside ototoxicity, suggesting some conservation of cell death mechanisms between different classes of ototoxic drugs (Sha & Schacht, 2000; Rybak & Ramkumar, 2007).

Cisplatin-treated cells in the zebrafish lateral line also show signs of apoptotic cell death including nuclear condensation and mitochondrial swelling (Ou et al., 2007; Giari et al., 2011). Nuclear condensation and altered distribution of mitochondrial proteins such as cytochrome c are also evident in cochlear hair cells from cisplatin-treated guinea pigs, suggesting that these are conserved features of cisplatin-induced hair cell death in vertebrates (Wang et al., 2004). More studies are needed to dissect fully the contribution of specific cell death pathways to cisplatin ototoxicity.

3.1.3 Copper

Several studies have shown that copper is toxic to zebrafish lateral line hair cells (Hernandez et al., 2006; Linbo et al., 2006; Olivari et al., 2008). Copper concentrations from 1 to 50 μM rapidly kill hair cells, with the first signs of damage apparent within 5 minutes of exposure to 5 μM copper sulfate (Olivari et al., 2008). Copper-damaged hair cells show similar morphological changes to those seen in

hair cells damaged with other ototoxins, including signs of both apoptosis and necrosis (Hernandez et al., 2006; Olivari et al., 2008).

Copper is not considered an ototoxic threat in humans, so at first pass it appears that these studies are more important from a toxicology perspective than a biomedical one. However, evidence in mammalian inner ear suggests that cisplatin may be taken up by hair cells via a copper transporter (More et al., 2010). Therefore, some investigators have ironically suggested using copper as a competitive inhibitor of cisplatin entry into hair cells as a means of preventing cisplatin ototoxicity (More et al., 2010; Ding et al., 2011). These zebrafish studies highlight the potentially ototoxic nature of copper and suggest that copper is probably not a therapeutically viable protective strategy.

3.1.4 Discovery of Novel Ototoxins

Although there are incidental case reports of ototoxic side effects linked to several different drugs, as prescription drug use is greatest in older humans, ototoxic effects may be masked by or misdiagnosed as age-related hearing loss, or considered part of disease onset rather than an effect of treatment (Seligmann et al., 1996). Currently there are no systematic mechanisms in place to ensure identification of potential ototoxic side effects of therapeutic drugs. To tease out ototoxic effects that might have been overlooked, the zebrafish lateral line is now being used to screen for potential ototoxic drugs (Chiu et al., 2008; Hirose et al., 2011). The first screen was performed with the National Institute of Nervous Diseases and Stroke (NINDS) Custom Collection II library, which is composed of 1040 FDA-approved drugs and bioactive compounds (Chiu et al., 2008). Twenty-one potentially ototoxic compounds were identified in this screen, including known ototoxins such as neomycin and cisplatin, demonstrating that the screening paradigm is sensitive enough to pick up known toxins. Several novel candidate ototoxins were also detected from diverse drug classes, including multiple nonaminoglycoside antibiotics, antiprotozoal medications, and anticholinergic compounds. Two candidate ototoxins, propantheline and pentamidine, were tested for ototoxicity in mammals and both were found to kill hair cells in mouse utricle cultures, highlighting the utility of zebrafish lateral line as a first-pass screen for ototoxicity in other hair cell systems (Chiu et al., 2008).

Given the known ototoxicity of antineoplastic drugs such as cisplatin, an additional screen was performed of the 88 compounds in the National Cancer Institute (NCI) Approved Oncology Drugs Set to determine whether other anticancer drugs act as hair cell toxins (Hirose et al., 2011). As with the NINDS library screen described in the preceding paragraph, the NCI library screen detected several known ototoxins, demonstrating the robust nature of the screening paradigm. This NCI screen also identified four suspected ototoxins (those with hearing loss noted in occasional case reports) and five novel putative ototoxins, as well as ototoxic combinations of chemotherapy cocktails (see Table 1 for a complete list).

This study suggests that many neoplastic agents may have unrecognized ototoxic effects and that multidrug chemotherapy regimens are an area of concern.

There is currently no FDA requirement for ototoxicity testing during the drug development process, nor in the development of multidrug regimens. These drug screens demonstrate that many currently approved drugs may have unrecognized ototoxic potential and that the zebrafish lateral line is a powerful model system for discovery of novel ototoxins already in clinical use as well as for identifying the potential ototoxic effects of combinatorial drug regimens.

4 Protecting Hair Cells from Chemical Toxins

As discussed in Section 3, the larval zebrafish lateral line system has aided in the identification of potentially ototoxic drugs and the cell death mechanisms activated by these compounds. It is also well suited for screening for genes and small molecules that protect hair cells from ototoxic agents. Protective genes and compounds discovered in zebrafish are listed in Table 2.

Table 2 Hair cell protectants identified in zebrafish

(C) Compound/(G) gene	Target/gene ID	Protects against[a]	Reference
(C) PROTO1	unknown	Neomycin	Owens et al., 2008
(C) PROTO2	unknown	Neomycin	Owens et al., 2008
(G) Sentinel	Human CC2D2A gene	Neomycin	Owens et al., 2008
(G) Persephone	Chloride-bicarbonate exchanger	Neomycin	Owens et al., 2008
(G) Merovingian	unknown	Neomycin	Owens et al., 2008
(G) Bane	unknown	Neomycin	Owens et al., 2008
(G) Trainman	unknown	Neomycin	Owens et al., 2008
(C) Glutathione	Antioxidant	Cisplatin	Ton & Parng, 2005
(C) Allopurinol	xanthine oxidase inhibitor	Cisplatin	Ton & Parng, 2005
(C) *N*-acetyl-$_L$-cysteine	Antioxidant	Cisplatin	Ton & Parng, 2005
(C) 2-Oxothiazolidine-4-carboxylate	Antioxidant, cysteine precursor	Cisplatin	Ton & Parng, 2005
(C) D-Methionine	Antioxidant	Cisplatin	Ton & Parng, 2005
(C) Epicatechin	Antioxidant	Cisplatin	Kim et al., 2008
(C) Amsacrine	Topoisomerase 2 poison	Neomycin	Ou et al., 2009
(C) Carvedilol	Beta-2 adrenergic blocker	Neomycin	Ou et al., 2009
(C) Cepharanthine	Plasma membrane stabilizer	Neomycin	Ou et al., 2009
(C) Drofenine	Acetylcholinesterase inhibitor	Neomycin	Ou et al., 2009
(C) Hexamethyleneamiloride	Na/H exchange inhibitor	Neomycin	Ou et al., 2009
(C) Phenoxybenzamine	α-1 Adrenergic blocker	Neomycin	Ou et al., 2009
(C) Tacrine	Acetylcholinesterase inhibitor	Neomycin	Ou et al., 2009

[a]This indicates what ototoxin was used to identify the protective agent. Protection against other ototoxins has not yet been confirmed.

4.1 Uncovering Genes that Modulate Hair Cell Loss

Several kinds of evidence demonstrate that genetic differences can modulate responses to ototoxic challenges. For example, certain mitochondrial mutations increase patient susceptibly to aminoglycoside-induced hearing loss (Prezant et al., 1992; Guan et al., 2000). Another important example is the demonstration of a major genetic contribution to the age and severity of age related hearing loss (Gates et al., 1999). However, aside from the mitochondrial DNA mutations, few of these genetic modifiers have been identified. A zebrafish ENU mutagenesis screen (see Section 2) to identify genes that alter susceptibility to neomycin-induced hair cell death discovered five simple recessive mutations and five mutations with more complex genetics, each of which protected hair cells from neomycin damage (Owens et al., 2008). Linkage mapping and DNA sequencing in a protective mutant, known as *sentinel*, uncovered a premature stop codon in a novel gene of unknown function that was later linked to the human CC2D2A gene mutated in Joubert syndrome (Gorden et al., 2008). The *sentinel* mutation does not protect hair cells from cisplatin damage, further supporting the suggestion of segregation of cell death and protective pathways between ototoxic insults (Owens et al., 2008).

4.2 Discovery of Otoprotective Drugs

The zebrafish lateral line has been used to discover drugs and drug-like small molecules that protect hair cells from exposure to ototoxic conditions. Several research groups have undertaken targeted testing of candidate compounds based on a priori assumptions about hair cell death processes. For example, Ton and Parng (2005) showed that multiple antioxidants protected lateral line hair cells from cisplatin exposure (see Section 3.1.2). Kim et al. (2008) reported that the green tea extract epicatechin also protected lateral line hair cells from cisplatin-induced death.

The alternative approach of large- or medium-scale screening of known drugs or small, drug-like molecules offers the possibility for the discovery of novel protective drugs. The first such screen identified two novel protective compounds now named PROTO1 and PROTO2 (Owens et al., 2008). These PROTO compounds, both urea thiophene carboxamides, robustly protect zebrafish hair cells from neomycin damage but not cisplatin toxicity. Further experiments show that PROTO1 also provided robust protection of mammalian hair cells from aminoglycoside exposure (Owens et al., 2008). PROTO1 does not prevent uptake of fluorescently tagged aminoglycoside, suggesting that this compound may target specific intracellular processes activated after aminoglycoside entry into hair cells and further, that these processes are not acting in cisplatin-mediated hair cell death. Importantly, the PROTO compounds do not interfere with the antibacterial action of aminoglycosides.

Discovery of a novel small molecule compound is the first step in the clinical development of new otoprotective drugs. Additional steps include the development

and testing of alternative chemical formulations, assessment of pharmokinetics, and evaluation of cell-based actions of the drugs. However, development of a novel drug is an exceedingly long and expensive process, requiring several years and millions of dollars (Chong & Sullivan, 2007; Boguski et al., 2009). Therefore, repurposing of existing drugs for new uses offers an attractive alternative to *de novo* drug development. Using this logic, Ou et al. (2009) screened the NINDS Custom Collection II library (see Section 3.1.4) for new otoprotective compounds. Using the same drug library for multiple screen purposes (e.g., ototoxicity and otoprotection) further improves the efficiency and cost-effectiveness of the screening process.

Seven confirmed "hits" were obtained, with candidates belonging to multiple diverse drug classes including acetylcholinesterase inhibitors (Drofenine and Tacrine), diuretics (Hexamethyleneamiloride), and a plasma membrane stabilizer (Cepharanthine), all of which are currently in clinical use. All seven drugs provided dose-dependent protection against neomycin-induced hair cell loss (see Table 2). Tacrine also protected mouse utricular hair cells from neomycin damage in vitro, again suggesting that protective compounds discovered in zebrafish screens may be clinically useful (Ou et al., 2009). Collectively, these results offer robust proof-of-concept for the zebrafish lateral line system as a model for hearing-related drug discovery and highlight some important areas for future research on ototoxicity using drugs already approved for clinical use.

5 Hair Cell Regeneration

5.1 Hair Cell Regeneration in Diverse Vertebrate Taxa and Epithelia: A Brief Primer

Hair cell regeneration in amphibians was first documented in the 1930s as a component of larger studies on limb and tail regeneration. When tails are amputated from larval salamanders *(Amblystoma punctatum*), the regenerated tail contains a new lateral line, complete with neuromasts and hair cells (Stone, 1933, 1937). Since then, lateral line hair cell regeneration, in response to damage ranging from tail amputation to cell-specific ablation, has been routinely seen in a variety of larval amphibians, broadly including anurans (frogs and toads) and urodeles (salamanders) reviewed in Chapter 8 of *The Mechanosensory Lateral Line* (Coombs et al., 1989). Similarly, regeneration of lateral line hair cells has been well documented in the zebrafish (reviewed in Brignull et al., 2009). Many more studies have examined hair cell regeneration in the inner ear of anamniotes (fishes and amphibians). For example, the vestibular system of mature bullfrogs (*Rana catesbeiana*: Baird et. al., 1993), and the sensory epithelia of mature oscars (*Astronotus ocellatus*: Lombarte et. al, 1993), goldfish (*Carassius auratus*: Smith et al., 2006), and Atlantic cod (*Gadus morhua*: Faucher et al., 2009) all regenerate hair cells after damage. In cases where it has been examined, anamniotes combine

the ability to regenerate hair cells after damage with the continuous production of new hair cells in undamaged tissue in the ear (reviewed in Corwin, 1992; Lomarbte & Popper, 1994; Lanford et. al., 1996) or the lateral line (Jørgensen, 1991). The continued production of hair cells is generally thought to replace hair cells lost to aging and to maintain the density of hair cells in sensory epithelia that continue to grow throughout an animal's lifetime.

Regenerative capacity appears slightly more limited in nonmammalian amniotes such as birds and reptiles, in which studies on hair cells are, by necessity, limited to the ear. Hair cell regeneration occurs in the vestibular system of the lizard *Podaris sicula* (Avallone et al., 2003, 2008), and in the vestibular system of mature avian models in response to ototoxin-induced damage and as a part of normal cell turnover (reviewed in Stone & Cotanche, 2007). However, the distinction between regeneration and replacement as a result of turnover is important in avian models because the auditory and vestibular tissues behave differently. Whereas hair cell replacement is ongoing in the vestibular sensory epithelia (Jørgensen & Mathiesen, 1988; Weisleder & Rubel, 1993), there is no ongoing replacement of hair cells in the auditory epithelia and new hair cells are produced only during regeneration after sound- or ototoxin-induced damage (Corwin & Cotanche, 1988; Ryals & Rubel, 1988; Oesterle & Rubel, 1993). Despite the lack of regular turnover, regenerated hair cells in the auditory epithelia regain full morphological and functional maturity, even in adults. These and other studies in the extensive literature on regeneration in avian models are reviewed in Chapter 4 of *Hair Cell Regeneration*, *Repair, and Protection* (Salvi et al., 2008 {SHAR Vol. 33]). It remains to be determined whether the auditory epithelium in the lizard is similarly limited, with regeneration after damage but not ongoing hair cell production as a result of cell turnover.

Mammals, in contrast to other vertebrates, lack robust regeneration of inner ear hair cells, and hair cell production in mammals is typically limited to very early stages of life (reviewed in Warchol, 2011). In humans, the maximum number of hair cells found in the inner ear occurs during gestation (Ashmore, 2008). After birth, the number of hair cells in the inner ear begins a slow, steady decline that continues throughout life and the irreversible nature of human hearing loss indicated that hair cell replacement after damage is not possible. A more extensive overview of hair cell regeneration can be found in *Hair Cell Regeneration, Repair, and Protection* (Salvi et al., 2008 [SHAR Vol. 33]).

5.2 Understanding Regeneration

Hair cell regeneration has a rich history as part of tail and limb regeneration studies on amphibians (Stone, 1933; Speidel, 1947; Wright, 1947). These studies identified several stages in the process of limb regeneration that are conserved in fin regeneration studies in zebrafish (reviewed in Akimenko et al., 2003). The first two stages of limb or fin regeneration include wound healing and blastema formation. The blastema is a specialized tissue formed of de-differentiated cells that migrate

into the wound. Cells within the blastema proliferate and eventually migrate out again to form regenerating bone and muscle (Akimenko et al., 2003; Odelberg, 2005). Once the basic structure of the fin or limb has been reestablished, the lateral line begins the process of regenerating. Unlike in fin or limb regeneration, the blastema plays little to no role in replacing hair cells. Instead, cells in the last intact neuromast, closest to the plane of amputation, begin to proliferate and eventually a migrating primordium buds off (Stone, 1933; Dufourcq et al., 2006). In both zebrafish and axolotl salamanders, the primordium migrates along the length of the regenerated fin or limb and deposits new neuromasts. Although this process of regeneration closely mimics normal lateral line development, hair cell regeneration in neuromasts after hair cell-specific ablation follows a distinctly different regenerative process.

Initial studies of lateral line hair cell regeneration in zebrafish used the aminoglycoside antibiotic neomycin to kill hair cells simply by introducing it into water surrounding the fish (see Section 3.1.1) (Song et al., 1995; Harris et al., 2003). This is followed by an increase in the rate of proliferation in the surrounding supporting cells as determined by assaying for markers specific to phases of the cell cycle. Two markers commonly used in zebrafish studies are bromodeoxyuridine (BrdU), a thymidine analog that is taken up by cells in S-phase, and antibodies against phosphohistone3 (PH3) that identify cells in M-phase. High levels of reentry to the cell cycle, or proliferation, as indicated by either BrdU or PH3, persist for 18–20 hours after hair cell ablation and the majority of hair cells that develop are mitotically derived. By 48 hours, recovery is 80% complete and regenerated hair cells are able to take up FM1-43, indicating functional mechanotransduction. Recovery is complete within 72 hours of hair cell ablation, and regeneration was observed at all dosages of aminoglycoside antibiotics tested.

Importantly, studies utilizing aminoglycosides for regeneration experiments must take into account the developmental sensitivity of hair cells to the ototoxins. Studies have shown that immature hair cells, those hair cells that are unable to uptake mechanotransduction-dependent dyes, are largely insensitive to aminoglycosides (Murakami et al., 2003; Santos et al., 2006). Because there is some evidence for a constant, low level of turnover and hair cell replacement in larval neuromasts (Williams & Holder, 2000), this complicates analysis of the mechanism of hair cell regeneration. Studies in the lateral line clearly show that the majority of regenerated hair cells are mitotically derived from supporting cells (Hernandez et al., 2006; Ma et al., 2008; Wibowo et al., 2011). However, nearly all regeneration studies in the lateral line also show a few hair cells appearing during regeneration that are not labeled by indicators of mitosis. It is most likely that these cells are the now mature hair cells that were young enough to be insensitive to aminoglycosides during treatment. However, the possibility that these cells regenerated without undergoing mitosis cannot be ruled out.

The presence of nonmitotically labeled hair cells after regeneration in the zebrafish lateral line has been a matter of great interest because in mature chicken and amphibian models there are two distinct modes of hair cell regeneration (reviewed in Stone & Cotanche, 2007). In the chick auditory epithelia, initial phases

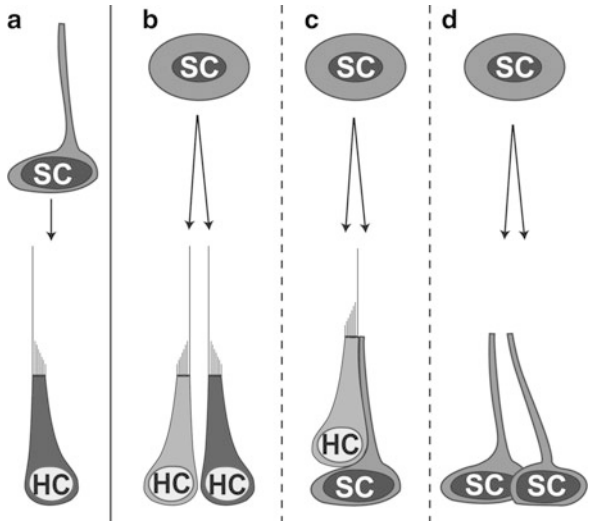

Fig. 3 Multiple mechanisms for hair cell (HC) regeneration have been observed. (**a**) Direct transdifferentiation, as seen in chicks, occurs when a fully differentiated support cell (SC) is converted into a HC without undergoing mitosis. (**b–d**) HC regeneration via mitosis of a de-differentiated SC is the major mode of regeneration in zebrafish and the second phase of HC regeneration in chicks. Live cell imaging in zebrafish indicates that the majority of SC division during regeneration is symmetric, producing two HCs and rapidly replenishing HCs while depleting SCs (**b**). Asymmetric SC division, producing one HC and one SC, occurs infrequently during the first 24 hours of HC regeneration but provides a mechanism for retaining the relative ratios of SCs to HCs (**c**). Symmetric division of SC into two SCs allows for the replenishment of the SC population following the rapid regeneration of HCs by symmetric division although it remains to be well documented

of hair cell regeneration occur by transdifferentiation in which supporting cells take on hair cell fates without undergoing mitosis (Fig. 3a). Direct transdifferentiation accounts for 30–50% of hair cell regeneration in the chick auditory organ. During later phases, the remainder of hair cells regeneration occurs via a mitotically-dependent mechanism (reviewed in Stone & Cotanche, 2007 and Fig. 3b–d). Hair cell production during development (Lopez-Schier et al., 2004) and regeneration (Lopez-Schier & Hudspeth, 2006) in the zebrafish lateral line is primarily symmetric: a single support cell becomes two hair cells (Fig. 3b). Currently, there is no evidence for nonsymmetric division of support cells during regeneration. However, the robust regenerative capacity of the lateral line neuromasts implies that some mechanism to replace support cells lost during regeneration exists. Candidate mechanisms for support cell replenishment may be via asymmetric cell division to produce one hair cell and one support cell (Fig. 3c), or via symmetric support cell division, resulting in two support cells (Fig. 3d).

Although there is no clear reason for the one-step process in zebrafish versus the two-step regeneration process in birds, it is tempting to speculate that it is related to the different time frames of regeneration in the respective model organisms.

Whereas zebrafish lateral line hair cells regenerate fully within 72 hours, regeneration in the avian inner ear takes several weeks. In starlings (*Sturnus vulgaris*), partial functional recovery appears at 3–4 weeks and is nearly complete at 2 months (Marean et al., 1993, 1998). Regeneration by transdifferentiation begins within 15 hours of gentamicin-induced hair cell ablation and typical hair cell morphology emerges after 2 days of recovery. The first evidence of supporting cells reentering the cell cycle begins 2–3 days after hair cell ablation. In addition to producing hair cells, mitotic division of supporting cells serves to replace the supporting cell population depleted during transdifferentiation (Fig. 3).

Copper, which is generally toxic to fish, is specifically toxic to the zebrafish lateral line (Hernandez et al., 2006; Linbo et al., 2006; Olivari et al., 2008) (see Section 3.1.3). Although copper kills hair cells of the lateral line in a dosage-dependent manner, at higher dosages copper also kills supporting cells. At concentrations where there is no apparent cell death in the supporting cells, hair cells regenerate within a few days. At high concentrations, however, hair cells fail to regenerate (Hernandez et al., 2006). These data further support the idea that the supporting cells may be the elusive stem-cell population that replaces lost hair cells.

Regardless of the cause of cell death, functional regeneration requires more than simply replacing lost cells. The organization and innervation of neuromasts must be reestablished as well. One important component of neuromast organization is the highly stereotyped organization of hair bundles. Each individual hair cell demonstrates planar polarity; cilia are arranged by height from the tallest kinocilium on one side to the shortest stereocilia on the other side (Fig. 4a). Each neuromast displays a specific internal organization with two populations of oppositely oriented hair cells aligned along a single, bidirectional axis (Fig. 4b) (see also the chapters by Webb and by Chagnaud & Coombs in this volume). The bidirectional axis of a neuromast is most clear in the 24 hours following regeneration, during which there is typically a clear, central demarcation in the neuromast with a strict mirror-image orientation of hair cells. However, as regeneration progresses, hair cells intermingle and the mirror-image organization is lost although organization relative to the bidirectional axis is maintained (Lopez-Schier & Hudspeth, 2006). Finally, the lateral line displays a specific organization in which subsets of neuromasts are oriented with hair cells aligned in parallel with, or perpendicular to, the lateral line of neuromasts down the trunk (Fig. 4c) (Flock & Wersäll, 1962; Lopez-Schier et al., 2004; Wibowo et al., 2011). All aspects of organization are maintained during regeneration.

Maintaining polarity during regeneration is critical for the sensory function of the lateral line, but also for the reestablishment of innervation. In the lateral line of larval zebrafish, a single afferent nerve makes contact with hair cells of the same polarity only, despite innervating multiple hair cells and in some cases, even multiple neuromasts (Lopez-Schier & Hudspeth, 2006; Nagiel et al., 2008). Therefore, during regeneration, neuromast polarity is reestablished before reinnervation (Lopez-Schier & Hudspeth, 2006). The mechanism by which a single neuron identifies and synapses with multiple hair cells of identical polarity in regenerating neuromasts remains unclear.

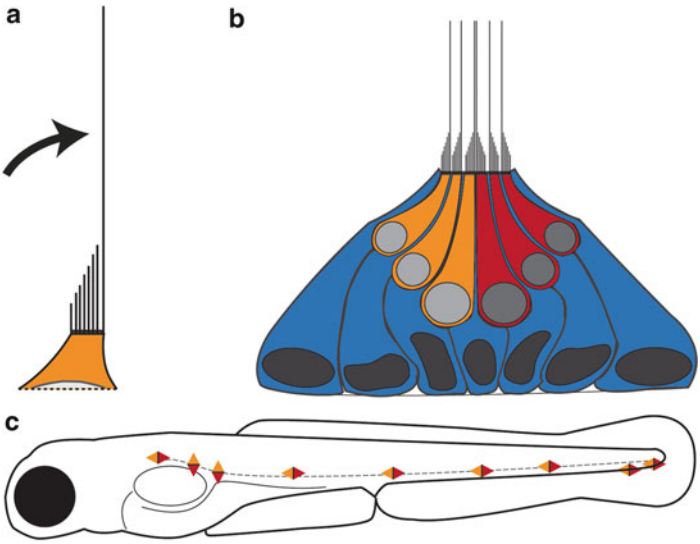

Fig. 4 (**a**) Polarity in a single hair cell is determined by the orientation of cilia in the classic stair-step fashion. Stimuli that move cilia in the direction indicated by the arrow, toward the large kinocilium, open mechanotransduction channels that initiate a signaling cascade. Stimuli out of alignment with hair cell polarity open fewer mechanotransduction channels, making the cell less responsive to those stimuli. (**b**) Neuromasts also have polarity, established by the organization of hair cells within each neuromast. In this simplified schematic, support cells (blue) surround two populations of hair cells depicting mirror image polarity, typical during the first few hours of hair cell regeneration. This organization defines a neuromast's sensitivity to stimuli along a single axis in early stages of development and regeneration. At later stages the two populations of oppositely oriented hair cells later become spatially intermingled such that the two populations are no longer segregated into two well-demarcated halves of the neuromast. (**c**) Neuromasts along the primary lateral line have specific placements with regard to their polarity. In a zebrafish at 4 dpf, the majority of neuromasts are aligned to respond to anterior-posterior stimuli (◀▶) while a subset located near the swim bladder respond to dorsal–ventral stimuli (▲▼). During the process of hair cell regeneration, the polarity must be reestablished at the level of individual cells (**a**), within a neuromast (**b**), and at the level of the entire animal (**c**). (Figure based on Nagiel et al., 2008)

Recent work has revealed that the mirror-symmetry of adjacent hair cells within a neuromast is the result of localized Notch signaling (Wibowo et al., 2011). In regenerating neuromasts, two areas of repressed Notch signaling, organized perpendicularly to the axis of planar polarity, allow for differentiation of supporting cells into hair cells. These two polar compartments essentially define the internal plane for mirror symmetry. Hair cell precursors in these low-Notch signaling compartments divide symmetrically and the sister cells consistently develop hair bundles with opposite polarities. The method by which the polar compartments are localized appropriately in relationship to the neuromast's planar polarity is an area of open investigation.

A second structural property of neuromasts that must be reestablished during regeneration is size. As described in Chapter 5 of *Fish Bioacoustics*

(Webb et al., 2008), neuromasts within the lateral line are highly stereotyped in both position and size. The number of hair cells per neuromast varies in relation to its position. For example, in animals at 4–5 dpf, the first supraorbital (SO1) neuromast of the anterior lateral line is small (7.4 ± 1.9 hair cells) compared to the second (SO2) neuromast (14.7 ± 4.0) (Harris et al., 2003). When neuromasts are ablated at 5 dpf, they regenerate to the appropriate size (Ma et al., 2008). Again, the Notch pathway seems a likely contributor to specification of neuromast size.

Notch signaling pathways are an appealing avenue for investigation owing to their extensive role in hair cell development (reviewed in Cotanche & Kaiser, 2010). Briefly stated, Notch is important in later stages of development for cell fate determination, leading to the specification of sensory versus nonsensory tissue within the inner ear. During development, cells expressing Notch adopt a sensory fate while signaling surrounding cells to adopt a nonsensory fate—a classic example of lateral inhibition. In these surrounding cells, pro-sensory genes are downregulated, notably *Atoh1*, a basic helix–loop–helix protein required for hair cell specification. Those cells expressing Notch become hair cells, while the neighboring cells that have down regulated pro-sensory genes become supporting cells.

During regeneration in the zebrafish lateral line, the same complement of genes is activated as in the developing inner ear. *Atoh1*, normally expressed at low levels in a few developing hair cells, is broadly upregulated in neuromasts undergoing regeneration for at least the first 24 hours and then returns to normal, low levels by 48 hours post-damage (Ma et al., 2008). This time frame is consistent with the observation that the highest levels of supporting cell proliferation in regenerating neuromasts occurs within the first 24 hours. Components of the Notch signaling pathway are similarly upregulated during regeneration of the damaged avian auditory epithelium (Cafaro et al., 2007; Daudet et al., 2009).

Conversely, the process of slowing down or stopping the production of new hair cells at the appropriate time is also regulated by Notch signaling. In the zebrafish lateral line, pharmacologically inhibiting Notch results in overproduction of hair cells during regeneration after hair cell ablation (Ma et al., 2008). These data are consistent with those from the mature chick auditory epithelium; pharmacological inhibition of Notch signaling pathways results in hair cell overproduction during damage-induced regeneration (Daudet et al., 2009). Significantly, downregulation of Notch signaling pathways in undamaged tissue, either in the developing lateral line or the avian auditory epithelia, has no effect (Ma et al., 2008; Daudet et al., 2009). These results contrast with those from mammalian models where repression of Notch signaling during normal development does result in the overproduction of hair cells in auditory epithelia (reviewed in Cotanche & Kaiser, 2010).

Although the overall effect of downregulating Notch signaling during damage-induced regeneration in avian or fish models is the overproduction of hair cells, it is important to note a potentially significant difference. In zebrafish, for which regeneration is primarily mitotic, repressing Notch signaling increases the rate and extends the duration of supporting cell proliferation causing the overproduction of hair cells (Ma et al., 2008). These data indicate that Notch signaling normally functions to halt mitotic activity in neuromasts at the appropriate time, thus acting

as a negative regulator of proliferation. This differs from the response of avian models to Notch repression in which hair cells are overproduced without increasing the rate of cell division. Increased production of hair cells in the absence of increased mitosis suggests that Notch signaling in avian models plays a role in regulating direct transdifferentiation of supporting cells into hair cells. These studies provide an example of how a similar outcomes, overproduction of hair cells during regeneration, in two model systems may be regulated differently at the molecular level, even via the same genes. Further, it highlights the importance of comparative studies in model organisms, especially in in the case of regeneration, where one of the fundamental goals is to understand how regenerative capacity has been lost en route to mammals.

5.3 Modulating Regeneration

Not surprisingly, there is great interest in screening for agents that stimulate hair cell regeneration and promising results are just beginning to emerge from such studies. Two complementary approaches to this end are chemical and genetic screens. In this section we review the outcomes of several screens, chemical and genetic, and discuss the implications and further directions for this area of research.

5.3.1 Chemical Screens for Regeneration

The same characteristics that make the zebrafish lateral line useful in screening for hair cell protectants (see Section 4.2) makes it an effective model in screening for modulators of hair cell regeneration. Following regeneration in the presence of candidate drugs, it is possible to rapidly assay lateral line hair cell regeneration by simple visual examination. Of more than 2000 drugs screened to date, several inhibitors and just three enhancers of hair cell regeneration have been identified.

Low molecular weight fucoidan (LMWF) was identified as an accelerant of hair cell regeneration in the lateral line (Moon et al., 2011). Following neomycin-induced hair cell ablation, the presence of LMWF significantly increases the rate of hair cell regeneration during the first 12 hours. However, this accelerated regeneration slows over the following 12 hours such that treated and untreated animals achieve similar hair cell numbers after 24 hours. BrdU labeling reveals that that increased hair cell regeneration is accompanied by increased rates of proliferation in supporting cells. Despite the increase in proliferation and regeneration, LMWF did not induce overproliferation of hair cells either during regeneration or during normal developmental addition of hair cells. It is important to note that there was no increase in the rate of cell death in regenerating neuromasts during the final 12 hours of regeneration. Therefore, LMWF accelerates the initial phases of regeneration, which results in a slower-than-normal rate of hair cell regeneration during the latter phases. This indicates that the activity of LMWF has a limited time

window in which to increase regeneration—perhaps as a result of habituation or to a limiting reagent, such as the number of stem cells or hair cell precursors available.

Fucoidan is a highly sulfated polysaccharide derived from brown seaweed that has a long history in traditional Asian medicine. More recent studies have revealed that fucoidans modulate immune system function and act as antitumor, anti-inflammatory, antibacterial, and antiviral agents, among other attributes (Kusaykin et al., 2008). Although the many known actions of fucoidan provide ample opportunity for speculation, the mechanism by which it stimulates hair cell production in regenerating, but not normally developing, neuromasts remains to be determined.

A larger screen examined a library of nearly 1700 FDA-approved drugs and bioactive compounds for modulation of hair cell regeneration in the lateral line of the brn3C transgenic line. This screen identified two enhancers and six inhibitors of regeneration (Namdaran et al., 2012). The enhancers of regeneration, prednisolone and dexamethasone, are both synthetic glucocorticoids (SGs) that act in a dosage-dependent manner to stimulate hair cell regeneration by increasing the rate of supporting cell proliferation. Interestingly, the SGs that enhance lateral line hair cell regeneration significantly inhibit fin regeneration. In the fin, the presence of exogenous glucocorticoids, via specific activation of the glucocorticoid receptors, decreases levels of proliferation in the plane of the amputation and inhibit formation of wound epithelium and blastema critical to fin regeneration (Mathew et al., 2007). These data suggest that enhanced lateral line hair cell regeneration in the presence of SGs is not a direct result of glucocorticoid-receptor activity. These data also highlight the importance of the cellular environment in regenerative processes. Neomycin induces hair cell– specific ablation that is enhanced by SGs. In contrast, hair cells lost as a result of fin amputation are dependent on multiple stages of tissue regeneration including wound healing, blastema formation, and finally redeposition of neuromasts (see Section 5.2).

It is interesting to note that both types of regeneration enhancing drugs that were identified in drug library screens stimulate excess proliferation by supporting cells. Despite this similarity, the outcomes of treatment with LMWF versus SGs are very different. LMWF accelerated initial stages of regeneration at the expense of later stages of regeneration without increasing the total number of hair cells. In contrast, SGs cause a sustained increase in the rate of supporting cell proliferation, leading to an increase in the total number of hair cells regenerated. Although the SGs provided a 10–25% increase in the total number of hair cells regenerated, it is a relatively modest increase in comparison to the doubling of hair cells regenerated when stimulated by DAPT, an inhibitor of the Notch signaling pathway (Ma et al., 2008). Clearly, neither the rate nor extent of proliferation-mediated hair cell regeneration is maximized by the introduction of SGs. It would be interesting to determine whether DAPT and SGs might be additive or synergistic as potential means of establishing the upper limits of hair cell regeneration in the lateral line.

A second significant difference between these hair cell regeneration enhancers is their effects on lateral line hair cell addition during normal development and hair cell turnover. DAPT treatment has little effect during 48 hours of treatment.

Similarly, LMWF does not increase the rate of hair cell development during the 24 hours tested. In contrast, SGs stimulate the rate of hair cell addition during both normal development and regeneration. The unique profile of each compound in regulating hair cell production during development and/or regeneration suggests at least partially distinct mechanisms of action for each of the drugs identified. Precisely what those mechanisms are remains to be determined.

Another open question arising from these studies is how altering the regenerative process, or the rate of development, affects the long-term survival of hair cells in these neuromasts with excess hair cells. Although in the short term (48–72 hours) DAPT and SGs result in neuromasts with unusually high numbers of hair cells, it is not known whether all the hair cells are appropriately innervated, have the correct polarity, or display altered rates of turnover or sensitivity. In essence, does the neuromast integrate additional hair cells into its overall organization or are they effectively ectopic? If they are fully integrated, does that change depend on whether extra hair cells are added during development or during regeneration? Studies in mammalian models have succeeded in inducing the production of ectopic hair cells, highlighting the exciting potential for initiating regeneration in mammals. However, the hair cells induced in these experiments were short lived, possibly owing to the absence of innervation and/or supporting cells. Examining the survival of lateral line hair cells resulting from drug-induced overproduction may provide suggestions of how the surrounding environment regulates hair cells survival and integration into functioning neuromasts that normally have well established size limits. This in turn may lead to a better understanding of the environmental cues required for hair cell survival in tissues that do not normally regenerate.

The recent screening study of FDA-approved drugs and bioactive compounds also identified several inhibitors of lateral line hair cell regeneration (Namdaran et al., 2012). The six inhibitors identified were those that provided a dosage-dependent inhibition of hair cell regeneration at concentrations that were not toxic to hair cells. The inhibitors fell into two general categories: those that slowed regeneration and those that completely blocked it. The two drugs that appeared to block regeneration also blocked proliferation of the supporting cells as indicated by a significant decrease in BrdU labeling.

The drugs identified as modulators of lateral line hair cell regeneration from drug screens may provide tools for a molecular dissection of hair cell growth and regeneration. Inhibitors in particular provide a method for isolating hair cells at various stages of regeneration in order to enrich the environment for analysis of stage-specific critical genes. Enhancers of regeneration provide molecular tools for understanding the process by which regeneration is halted when hair cells are at the appropriate density. Together, the drugs identified by large-scale screen provide new techniques for studying the basic biology of hair cells. They are also are attractive as candidate approaches to stimulating hair cell regeneration in the mammalian inner ear as we work toward the ability to assist hearing impaired patients.

5.3.2 Genetic Screens for Regeneration

A genetic approach to stimulating hair cell regeneration requires identifying and thoroughly characterizing target genes for manipulation. A variety of genetic approaches have been used to identify novel genes critical to hair cell regeneration. The *phoenix* mutant, with decreased hair cell regeneration, was identified in an insertional-mutagenesis screen where a modified retrovirus was randomly integrated into the zebrafish genome, disrupting the function of endogenous genes (Behra et al., 2009). The disrupted gene was identified by sequencing the region of the insertion based on the presence of the known retrovirus sequence. The gene identified in this mutant was a truly novel gene with no previously described function and no known homologs. The gene is expressed strongly in the supporting cells of neuromasts and discrete patches in the inner ear beginning around 2 dpf and persisting through at least 12 dpf. Based on conserved structures, the authors suggest *phoenix* is a structural protein with enzymatic ATPase activity.

Although much remains to be learned about the normal function of *phoenix*, when it is mutated in zebrafish, hair cell regeneration is impaired as a result of decreased proliferation in the supporting cell population. These data suggest that *phoenix* is active in regulating the ability of supporting cells to either recognize or respond to the loss of hair cells. *Phoenix* may play a role in allowing supporting cells to successfully enter or progress through the cell cycle and then differentiate either as supporting cells or as hair cells. This study provides an example of the potential use of zebrafish to identify novel genes that regulate hair cell regeneration independently of development. Although the lack of mammalian orthologs makes the analysis of *phoenix* challenging, it is also tempting to speculate that the absence of a gene in mammals, one that remains present in nonmammalian vertebrates, may account for differences in regenerative capacity.

6 Summary

The small size of the zebrafish and the large experimental toolbox available for zebrafish studies, combined with the external location and ease of manipulation of the lateral line, makes the zebrafish an ideal model for studies of hair cell death, protection, and regeneration. Targeted studies have uncovered some of the critical events that occur during the stages leading up to aminoglycoside- or cisplatin-induced hair cell death, and provide evidence that mitochondrial changes may be of central importance. More recently, studies in zebrafish that combine genetic and chemical screens have uncovered several genes and drugs that modulate hair cell death and regeneration.

It is important to note that, with few exceptions, regeneration studies utilizing the zebrafish lateral line have used larval animals. Although clear trends are

emerging in how regeneration occurs, it remains to be determined if they hold true in adult animals.

These studies land at the intersection of fundamental and applied research. Work using the zebrafish lateral line as a model is providing new insights into the molecular and genetic regulation of hair cell turnover and regeneration, and survival or death of hair cells in the face of stresses. In addition to contributing to our fundamental understanding of hair cell biology, the lateral line is providing a model for translational studies: drug screens to assay the impact of current and future pharmaceuticals in the zebrafish may provide hints as to their effect on mammalian hair cell survival and regeneration. Someday, the combination of basic and translational research available in the zebrafish could lead to therapies for humans struggling with hearing loss. Well before then, zebrafish lateral line research increases our fundamental understanding of basic cellular processes in such fields as intracellular signaling and stem cell biology. This junction between fundamental biology and translational studies lends additional power to the zebrafish lateral line as both a sensory system worthy of study in its own right and a model system for hearing habilitation.

References

Akimenko, M. A., Mari-Beffa, M., Becerra, J., & Geraudie, J. (2003). Old questions, new tools, and some answers to the mystery of fin regeneration. *Developmental Dynamics*, 226(2), 190–201.

Ashmore, J. (2008). Cochlear outer hair cell motility. *Physiological Reviews*, 88(1), 173–210.

Avallone, B., Fascio, U., Balsamo, G., & Marmo, F. (2008). Gentamicin ototoxicity in the saccule of the lizard *Podarcis sicula* induces hair cell recovery and regeneration. *Hearing Research*, 235(1–2), 15–22.

Avallone, B., Porritiello, M., Esposito, D., Mutone, R., Balsamo, G., & Marmo, F. (2003). Evidence for hair cell regeneration in the crista ampullaris of the lizard *Podarcis sicula*. *Hearing Research*, 178(1–2), 79–88.

Baird, R. A., Torres, M. A., & Schuff, N. R. (1993). Hair cell regeneration in the bullfrog vestibular otolith organs following aminoglycoside toxicity. *Hearing Research*, 65(1–2), 164–174.

Bang, P. I., Sewell, W. F., & Malicki, J. J. (2001). Morphology and cell type heterogeneities of the inner ear epithelia in adult and juvenile zebrafish (*Danio rerio*). *Journal of Comparative Neurology*, 438(2), 173–190.

Barin, K., & Dodson, E. E. (2011). Dizziness in the elderly. *Otolaryngologic Clinics of North America*, 44(2), 437–454.

Behra, M., Bradsher, J., Sougrat, R., Gallardo, V., Allende, M. L., & Burgess, S. M. (2009). Phoenix is required for mechanosensory hair cell regeneration in the zebrafish lateral line. *PLoS Genetics*, 5(4), e1000455.

Boguski, M. S., Mandl, K. D., & Sukhatme, V. P. (2009). Drug discovery: Repurposing with a difference. *Science*, 324(5933), 1394–1395.

Brignull, H. R., Raible, D. W., & Stone, J. S. (2009). Feathers and fins: Non-mammalian models for hair cell regeneration. *Brain Research*, 1277, 12–23.

Brown, A. D., Mussen, T. D., Sisneros, J. A., & Coffin, A. B. (2011) Reevaluating the use of aminoglycoside antibiotics in behavioral studies of the lateral line. *Hearing Research*, 272(1–2), 1–4.

Burket, C. T., Montgomery, J. E., Thummel, R., Kassen, S. C., LaFave, M. C., Langenau, D. M., Zon, L. I., & Hyde, D. R. (2008). Generation and characterization of transgenic zebrafish lines using different ubiquitous promoters. *Transgenic Research*, 17(2), 265–279.

Cafaro, J., Lee, G. S., & Stone, J. S. (2007). Atoh1 expression defines activated progenitors and differentiating hair cells during avian hair cell regeneration. *Developmental Dynamics*, 236(1), 156–170.

Chiu, L. L., Cunningham, L. L., Raible, D. W., Rubel, E. W., & Ou, H. C. (2008). Using the zebrafish lateral line to screen for ototoxicity. *Journal of the Association for Research in Otolaryngology*, 9(2), 178–190.

Chong, C. R., & Sullivan, D. J., Jr. (2007). New uses for old drugs. *Nature*, 448(7154), 645–646.

Coffin, A. B., Dabdoub, A., Kelley, M. W., & Popper, A. N. (2007). Myosin VI and VIIa distribution among inner ear epithelia in diverse fishes. *Hearing Research*, 224(1–2), 15–26.

Coffin, A. B., Reinhart, K. E., Owens, K. N., Raible, D. W., & Rubel, E. W. (2009). Extracellular divalent cations modulate aminoglycoside-induced hair cell death in the zebrafish lateral line. *Hearing Research*, 253(1–2), 42–51.

Coffin, A. B., Rubel, E. W, & Raible, D. W. (2013). Bax, Bcl2, and p53 differentially regulate neomycin- and gentamicin-induced hair cell death in the zebrafish lateral line. *Journal of the Association for Research in Otolaryngology*. doi: 10.1007/s10162-013-0404-1.

Coombs, S., Görner, P., & Münz, H. (1989). *The mechanosensory lateral line: Neurobiology and evolution*. New York: Springer-Verlag.

Coombs, S., Braun, C. B., & Donovan, B. (2001). The orienting response of Lake Michigan mottled sculpin is mediated by canal neuromasts. *Journal of Experimental Biology*, 204, 337–348.

Corey, D. P., & Hudspeth, A. J. (1983). Kinetics of the receptor current in bullfrog saccular hair cells. *Journal of Neuroscience*, 3(5), 962–976.

Corwin, J. T. (1992). Regeneration in the auditory system. *Experimental Neurology*, 115(1), 7–12.

Corwin, J. T., & Cotanche, D. A. (1988). Regeneration of sensory hair cells after acoustic trauma. *Science*, 240(4860), 1772–1774.

Cotanche, D. A., & Kaiser, C. L. (2010). Hair cell fate decisions in cochlear development and regeneration. *Hearing Research*, 266(1–2), 18–25.

Cunningham, L. L., Cheng, A. G., & Rubel, E. W. (2002). Caspase activation in hair cells of the mouse utricle exposed to neomycin. *Journal of Neuroscience*, 22(19), 8532–8540.

Cunningham, L. L., Matsui, J. I., Warchol, M. E., & Rubel, E. W. (2004). Overexpression of Bcl-2 prevents neomycin-induced hair cell death and caspase-9 activation in the adult mouse utricle in vitro. *Journal of Neurobiology*, 60(1), 89–100.

Dalton, D. S., Cruickshanks, K. J., Klein, B. E., Klein, R., Wiley, T. L., & Nondahl, D. M. (2003). The impact of hearing loss on quality of life in older adults. *Gerontologist*, 43(5), 661–668.

Daudet, N., Gibson, R., Shang, J., Bernard, A., Lewis, J., & Stone, J. (2009). Notch regulation of progenitor cell behavior in quiescent and regenerating auditory epithelium of mature birds. *Developmental Biology*, 326(1), 86–100.

David, N. B., Sapede, D., Saint-Etienne, L., Thisse, C., Thisse, B., Dambly-Chaudiere, C., Rosa, F. M., & Ghysen, A. (2002). Molecular basis of cell migration in the fish lateral line: Role of the chemokine receptor CXCR4 and of its ligand, SDF1. *Proceedings of the National Academy of Sciences of the USA*, 99(25), 16297–16302.

Ding, D., He, J., Allman, B. L., Yu, D., Jiang, H., Seigel, G. M., & Salvi, R. J. (2011). Cisplatin ototoxicity in rat cochlear organotypic cultures. *Hearing Research*.

Doyon, Y., McCammon, J. M., Miller, J. C., Faraji, F., Ngo, C., Katibah, G. E., Amora, R., Hocking, T. D., Zhang, L., Rebar, E. J., Gregory, P. D., Urnov, F. D., & Amacher, S. L. (2008). Heritable targeted gene disruption in zebrafish using designed zinc-finger nucleases. *Nature Biotechnology*, 26(6), 702–708.

Dufourcq, P., Roussigne, M., Blader, P., Rosa, F., Peyrieras, N., & Vriz, S. (2006). Mechanosensory organ regeneration in adults: The zebrafish lateral line as a model. *Molecular and Cellular Neurosciences*, 33(2), 180–187.

Engeszer, R. E., Patterson, L. B., Rao, A. A., & Parichy, D. M. (2007). Zebrafish in the wild: A review of natural history and new notes from the field. *Zebrafish*, 4(1), 21–40.

Eppsteiner, R. W., & Smith, R. J. (2011). Genetic disorders of the vestibular system. *Current Opinion in Otolaryngology & Head and Neck Surgery*, 19(5), 397–402.

Ernest, S., Rauch, G. J., Haffter, P., Geisler, R., Petit, C., & Nicolson, T. (2000). Mariner is defective in myosin VIIA: A zebrafish model for human hereditary deafness. *Human Molecular Genetics*, 9(14), 2189–2196.

Faucher, K., Aas-Hansen, O., Damsgard, B., Laukli, E., & Stenklev, N. C. (2009). Damage and functional recovery of the Atlantic cod (*Gadus morhua*) inner ear hair cells following local injection of gentamicin. *International Journal of Audiology*, 48(7), 456–464.

Flock, Å., & Wersäll, J. (1962). A study of the orientation of the sensory hairs of the receptor cells in the lateral line organ of fish, with special reference to the function of the receptors. *Journal of Cell Biology*, 15, 19–27.

Foley, J. E., Yeh, J. R., Maeder, M. L., Reyon, D., Sander, J. D., Peterson, R. T., & Joung, J. K. (2009). Rapid mutation of endogenous zebrafish genes using zinc finger nucleases made by Oligomerized Pool ENgineering (OPEN). *PLoS One*, 4(2), e4348.

Gates, G. A., Couropmitree, N. N., & Myers, R. H. (1999). Genetic associations in age-related hearing thresholds. *Archives of Otolaryngology - Head and Neck Surgery*, 125(6), 654–659.

Germana, A., Abbate, F., Gonzalez-Martinez, T., del Valle, M. E., de Carlos, F., Germana, G., & Vega, J. A. (2004). S100 protein is a useful and specific marker for hair cells of the lateral line system in postembryonic zebrafish. *Neuroscience Letters*, 365(3), 186–189.

Ghysen, A., & Dambly-Chaudiere, C. (2004). Development of the zebrafish lateral line. *Current Opinion in Neurobiology*, 14(1), 67–73.

Giari, L., Dezfuli, B. S., Astolfi, L., & Martini, A. (2011). Ultrastructural effects of cisplatin on the inner ear and lateral line system of zebrafish (*Danio rerio*) larvae. *Journal of Applied Toxicology*.

Gibson, F., Walsh, J., Mburu, P., Varela, A., Brown, K. A., Antonio, M., Beisel, K. W., Steel, K. P., & Brown, S. D. (1995). A type VII myosin encoded by the mouse deafness gene shaker-1. *Nature*, 374(6517), 62–64.

Gorden, N. T., Arts, H. H., Parisi, M. A., Coene, K. L., Letteboer, S. J., van Beersum, S. E., Mans, D. A., Hikida, A., Eckert, M., Knutzen, D., Alswaid, A. F., Ozyurek, H., Dibooglu, S., Otto, E. A., Liu, Y., Davis, E. E., Hutter, C. M., Bammler, T. K., Farin, F. M., Dorschner, M., Topcu, M., Zackai, E. H., Rosenthal, P., Owens, K. N., Katsanis, N., Vincent, J. B., Hildebrandt, F., Rubel, E. W., Raible, D. W., Knoers, N. V., Chance, P. F., Roepman, R., Moens, C. B., Glass, I. A., & Doherty, D. (2008). CC2D2A is mutated in Joubert syndrome and interacts with the ciliopathy-associated basal body protein CEP290. *American Journal of Human Genetics*, 83(5), 559–571.

Granato, M., van Eeden, F. J., Schach, U., Trowe, T., Brand, M., Furutani-Seiki, M., Haffter, P., Hammerschmidt, M., Heisenberg, C. P., Jiang, Y. J., Kane, D. A., Kelsh, R. N., Mullins, M. C., Odenthal, J., & Nusslein-Volhard, C. (1996). Genes controlling and mediating locomotion behavior of the zebrafish embryo and larva. *Development*, 123, 399–413.

Grunwald, D. J., & Eisen, J. S. (2002). Headwaters of the zebrafish – emergence of a new model vertebrate. *Nature Reviews: Genetics*, 3(9), 717–724.

Guan, M. X., Fischel-Ghodsian, N., & Attardi, G. (2000). A biochemical basis for the inherited susceptibility to aminoglycoside ototoxicity. *Human Molecular Genetics*, 9(12), 1787–1793.

Haffter, P., Granato, M., Brand, M., Mullins, M. C., Hammerschmidt, M., Kane, D. A., Odenthal, J., van Eeden, F. J., Jiang, Y. J., Heisenberg, C. P., Kelsh, R. N., Furutani-Seiki, M., Vogelsang, E., Beuchle, D., Schach, U., Fabian, C., & Nusslein-Volhard, C. (1996). The identification of genes with unique and essential functions in the development of the zebrafish, *Danio rerio*. *Development*, 123, 1–36.

Harris, J. A., Cheng, A. G., Cunningham, L. L., MacDonald, G., Raible, D. W., & Rubel, E. W. (2003). Neomycin-induced hair cell death and rapid regeneration in the lateral line of zebrafish (*Danio rerio*). *Journal of the Association for Research in Otolaryngology*, 4(2), 219–234.

Hernandez, P. P., Moreno, V., Olivari, F. A., & Allende, M. L. (2006). Sub-lethal concentrations of waterborne copper are toxic to lateral line neuromasts in zebrafish (*Danio rerio*). *Hearing Research*, 213(1–2), 1–10.

Hirose, K., Westrum, L. E., Stone, J. S., Zirpel, L., & Rubel, E. W. (1999). Dynamic studies of ototoxicity in mature avian auditory epithelium. *Annals of the New York Academy of Sciences*, 884, 389–409.

Hirose, Y., Simon, J. A., & Ou, H. C. (2011). Hair cell toxicity in anti-cancer drugs: Evaluating an anti-cancer drug library for independent and synergistic toxic effects on hair cells using the zebrafish lateral line. *Journal of the Association for Research in Otolaryngology*, 12(6), 719–728.

Jiang, H., Sha, S. H., Forge, A., & Schacht, J. (2006). Caspase-independent pathways of hair cell death induced by kanamycin in vivo. *Cell Death and Differentiation*, 13(1), 20–30.

Jørgensen, J. M. (1991). Regeneration of lateral line and inner ear vestibular cells. *Ciba Foundation Symposium*, 160, 151–163.

Jørgensen, J. M., & Mathiesen, C. (1988). The avian inner ear. Continuous production of hair cells in vestibular sensory organs, but not in the auditory papilla. *Naturwissenschaften*, 75(6), 319–320.

Kaufman, C. K., White, R. M., & Zon, L. (2009). Chemical genetic screening in the zebrafish embryo. *Nature Protocols*, 4(10), 1422–1432.

Kaus, S. (1987). The effect of aminoglycoside antibiotics on the lateral line organ of *Aplocheilus lineatus* (Cyprinodontidae). *Acta Oto-Laryngologica*, 103(5–6), 291–298.

Kaus, S. (1992). The influence of calcium on the ototoxicity of aminoglycosides. *Acta Oto-Laryngologica*, 112(1), 83–87.

Kawakami, K., Takeda, H., Kawakami, N., Kobayashi, M., Matsuda, N., & Mishina, M. (2004). A transposon-mediated gene trap approach identifies developmentally regulated genes in zebrafish. *Developmental Cell*, 7(1), 133–144.

Keats, B. J. B., Fay, R. R., & Popper, A. N. (2002). *Genetics of Auditory Disorders*. New York: Springer-Verlag.

Kerstetter, A. E., Azodi, E., Marrs, J. A., & Liu, Q. (2004). Cadherin-2 function in the cranial ganglia and lateral line system of developing zebrafish. *Developmental Dynamics*, 230(1), 137–143.

Kim, C. H., Kang, S. U., Pyun, J., Lee, M. H., Hwang, H. S., & Lee, H. (2008). Epicatechin protects auditory cells against cisplatin-induced death. *Apoptosis*, 13(9), 1184–1194.

Kimmel, C. B., Ballard, W. W., Kimmel, S. R., Ullmann, B., & Schilling, T. F. (1995). Stages of embryonic development of the zebrafish. *Developmental Dynamics*, 203(3), 253–310.

Kral, A., & O'Donoghue, G. M. (2010). Profound deafness in childhood. *New England Journal of Medicine*, 363(15), 1438–1450.

Kroese, A., & van den Bercken, J. (1980). Dual action of ototoxic antibiotics on sensory hair cells. *Nature*, 283(5745), 395–397.

Kroese, A., & van den Bercken, J. (1982). Effects of ototoxic antibiotics on sensory hair cell functioning. *Hearing Research*, 6(2), 183–197.

Kusaykin, M., Bakunina, I., Sova, V., Ermakova, S., Kuznetsova, T., Besednova, N., Zaporozhets, T., & Zvyagintseva, T. (2008). Structure, biological activity, and enzymatic transformation of fucoidans from the brown seaweeds. *Biotechnology Journal*, 3(7), 904–915.

Lanford, P. J., Presson, J. C., & Popper, A. N. (1996). Cell proliferation and hair cell addition in the ear of the goldfish, *Carassius auratus*. *Hearing Research*, 100(1–2), 1–9.

Linbo, T. L., Stehr, C. M., Incardona, J. P., & Scholz, N. L. (2006). Dissolved copper triggers cell death in the peripheral mechanosensory system of larval fish. *Environmental Toxicology and Chemistry*, 25(2), 597–603.

Liu, X. Z., Walsh, J., Mburu, P., Kendrick-Jones, J., Cope, M. J., Steel, K. P., & Brown, S. D. (1997a). Mutations in the myosin VIIA gene cause non-syndromic recessive deafness. *Nature Genetics*, 16(2), 188–190.

Liu, X. Z., Walsh, J., Tamagawa, Y., Kitamura, K., Nishizawa, M., Steel, K. P., & Brown, S. D. (1997b). Autosomal dominant non-syndromic deafness caused by a mutation in the myosin VIIA gene. *Nature Genetics*, 17(3), 268–269.

Lombarte, A., & Popper, A. N. (1994). Quantitative analyses of postembryonic hair cell addition in the otolithic endorgans of the inner ear of the European hake, *Merluccius merluccius* (Gadiformes, Teleostei). *Journal of Comparative Neurology*, 345(3), 419–428.

Lombarte, A., Yan, H. Y., Popper, A. N., Chang, J. S., & Platt, C. (1993). Damage and regeneration of hair cell ciliary bundles in a fish ear following treatment with gentamicin. *Hearing Research*, 64(2), 166–174.

Lopez-Schier, H., & Hudspeth, A. J. (2006). A two-step mechanism underlies the planar polarization of regenerating sensory hair cells. *Proceedings of the National Academy of Sciences of the USA*, 103(49), 18615–18620.

Lopez-Schier, H., Starr, C. J., Kappler, J. A., Kollmar, R., & Hudspeth, A. J. (2004). Directional cell migration establishes the axes of planar polarity in the posterior lateral-line organ of the zebrafish. *Developmental Cell*, 7(3), 401–412.

Lord, E. M., & Gates, W. H. (1929). Shaker, a new mutation of the house mouse. . *American Naturalist*, 63(688), 435–442.

Ma, E. Y., Rubel, E. W., & Raible, D. W. (2008). Notch signaling regulates the extent of hair cell regeneration in the zebrafish lateral line. *Journal of Neuroscience*, 28(9), 2261–2273.

Malicki, J., Schier, A. F., Solnica-Krezel, L., Stemple, D. L., Neuhauss, S. C., Stainier, D. Y., Abdelilah, S., Rangini, Z., Zwartkruis, F., & Driever, W. (1996). Mutations affecting development of the zebrafish ear. *Development*, 123, 275–283.

Mangiardi, D. A., McLaughlin-Williamson, K., May, K. E., Messana, E. P., Mountain, D. C., & Cotanche, D. A. (2004). Progression of hair cell ejection and molecular markers of apoptosis in the avian cochlea following gentamicin treatment. *Journal of Comparative Neurology*, 475(1), 1–18.

Marcotti, W., van Netten, S. M., & Kros, C. J. (2005). The aminoglycoside antibiotic dihydrostreptomycin rapidly enters mouse outer hair cells through the mechano-electrical transducer channels. *Journal of Physiology*, 567(Pt 2), 505–521.

Marean, G. C., Burt, J. M., Beecher, M. D., & Rubel, E. W. (1993). Hair cell regeneration in the European starling (*Sturnus vulgaris*): Recovery of pure-tone detection thresholds. *Hearing Research*, 71(1–2), 125–136.

Marean, G. C., Burt, J. M., Beecher, M. D., & Rubel, E. W. (1998). Auditory perception following hair cell regeneration in European starling (*Sturnus vulgaris*): Frequency and temporal resolution. *Journal of the Acoustical Society of America*, 103(6), 3567–3580.

Marot, M., Uziel, A., & Romand, R. (1980). Ototoxicity of kanamycin in developing rats: Relationship with the onset of the auditory function. *Hearing Research*, 2(2), 111–113.

Mathew, L. K., Sengupta, S., Kawakami, A., Andreasen, E. A., Lohr, C. V., Loynes, C. A., Renshaw, S. A., Peterson, R. T., & Tanguay, R. L. (2007). Unraveling tissue regeneration pathways using chemical genetics. *Journal of Biological Chemistry*, 282(48), 35202–35210.

Matsui, J. I., Gale, J. E., & Warchol, M. E. (2004). Critical signaling events during the aminoglycoside-induced death of sensory hair cells in vitro. *Journal of Neurobiology*, 61(2), 250–266.

McDermott, B. M., Jr., Asai, Y., Baucom, J. M., Jani, S. D., Castellanos, Y., Gomez, G., McClintock, J. M., Starr, C. J., & Hudspeth, A. J. (2010). Transgenic labeling of hair cells in the zebrafish acousticolateralis system. *Gene Expression Patterns*, 10(2–3), 113–118.

McHenry, M. J., Feitl, K. E., Strother, J. A., & Van Trump, W. J. (2009). Larval zebrafish rapidly sense the water flow of a predator's strike. *Biology Letters*, 5(4), 477–479.

Meng, X., Noyes, M. B., Zhu, L. J., Lawson, N. D., & Wolfe, S. A. (2008). Targeted gene inactivation in zebrafish using engineered zinc-finger nucleases. *Nature Biotechnology*, 26(6), 695–701.

Metcalfe, W. K., Kimmel, C. B., & Schabtach, E. (1985). Anatomy of the posterior lateral line system in young larvae of the zebrafish. *Journal of Comparative Neurology*, 233(3), 377–389.

Meyers, J. R., MacDonald, R. B., Duggan, A., Lenzi, D., Standaert, D. G., Corwin, J. T., & Corey, D. P. (2003). Lighting up the senses: FM1-43 loading of sensory cells through nonselective ion channels. *Journal of Neuroscience*, 23(10), 4054–4065.

Montgomery, J. C., Baker, C. F., & Carton, A. G. (1997). The lateral line can mediate rheotaxis in fish. *Nature*, 389, 960–963.

Moon, I. S., So, J. H., Jung, Y. M., Lee, W. S., Kim, E. Y., Choi, J. H., Kim, C. H., & Choi, J. Y. (2011). Fucoidan promotes mechanosensory hair cell regeneration following amino glycoside-induced cell death. *Hearing Research*, 282(1–2), 236–42.

More, S. S., Akil, O., Ianculescu, A. G., Geier, E. G., Lustig, L. R., & Giacomini, K. M. (2010). Role of the copper transporter, CTR1, in platinum-induced ototoxicity. *Journal of Neuroscience*, 30(28), 9500–9509.

Mullins, M. C., Hammerschmidt, M., Haffter, P., & Nusslein-Volhard, C. (1994). Large-scale mutagenesis in the zebrafish: In search of genes controlling development in a vertebrate. *Current Biology*, 4(3), 189–202.

Murakami, S. L., Cunningham, L. L., Werner, L. A., Bauer, E., Pujol, R., Raible, D. W., & Rubel, E. W. (2003). Developmental differences in susceptibility to neomycin-induced hair cell death in the lateral line neuromasts of zebrafish (*Danio rerio*). *Hearing Research*, 186(1–2), 47–56.

Nagiel, A., Andor-Ardo, D., & Hudspeth, A. J. (2008). Specificity of afferent synapses onto plane-polarized hair cells in the posterior lateral line of the zebrafish. *Journal of Neuroscience*, 28(34), 8442–8453.

Namdaran, P., Reinhart, K. E., Owens, K. N., Raible, D. W., & Rubel, E. W. (2012). Identification of modulators of hair cell regeneration in the zebrafish lateral line. *Journal of Neuroscience*, 32(10), 3516–3528.

Nasevicius, A., & Ekker, S. C. (2000). Effective targeted gene 'knockdown' in zebrafish. *Nature Genetics*, 26(2), 216–220.

Nicolson, T. (2005). The genetics of hearing and balance in zebrafish. *Annual Review of Genetics*, 39, 9–22.

Nicolson, T., Rusch, A., Friedrich, R. W., Granato, M., Ruppersberg, J. P., & Nusslein-Volhard, C. (1998). Genetic analysis of vertebrate sensory hair cell mechanosensation: The zebrafish circler mutants. *Neuron*, 20(2), 271–283.

Obholzer, N., Wolfson, S., Trapani, J. G., Mo, W., Nechiporuk, A., Busch-Nentwich, E., Seiler, C., Sidi, S., Sollner, C., Duncan, R. N., Boehland, A., Nicolson, T. (2008). Vesicular glutamate transporter 3 is required for synaptic transmission in zebrafish hair cells. *Journal of Neuroscience*, 28(9), 2110–2118.

Odelberg, S. J. (2005). Cellular plasticity in vertebrate regeneration. *Anatomical Record. Part B, New anatomist.*, 287(1), 25–35.

Oesterle, E.C., & Rubel, E.W (1993). Postnatal production of supporting cells in the chick cochlea. *Hearing Research* 66(2), 213–224

Olivari, F. A., Hernandez, P. P., & Allende, M. L. (2008). Acute copper exposure induces oxidative stress and cell death in lateral line hair cells of zebrafish larvae. *Brain Research*, 1244, 1–12.

Ou, H. C., Raible, D. W., & Rubel, E. W. (2007). Cisplatin-induced hair cell loss in zebrafish (*Danio rerio*) lateral line. *Hearing Research*, 233(1–2), 46–53.

Ou, H. C., Cunningham, L. L., Francis, S. P., Brandon, C. S., Simon, J. A., Raible, D. W., & Rubel, E. W. (2009). Identification of FDA-approved drugs and bioactives that protect hair cells in the zebrafish (Danio rerio) lateral line and mouse (*Mus musculus*) utricle. *Journal of the Association for Research in Otolaryngology*, 10(2), 191–203.

Owens, K. N., Cunningham, D. E., MacDonald, G., Rubel, E. W., Raible, D. W., & Pujol, R. (2007). Ultrastructural analysis of aminoglycoside-induced hair cell death in the zebrafish lateral line reveals an early mitochondrial response. *Journal of Comparative Neurology*, 502 (4), 522–543.

Owens, K. N., Santos, F., Roberts, B., Linbo, T., Coffin, A. B., Knisely, A. J., Simon, J. A., Rubel, E. W., & Raible, D. W. (2008). Identification of genetic and chemical modulators of zebrafish mechanosensory hair cell death. *PLoS Genetics*, 4(2), e1000020.

Owens, K. N., Coffin, A. B., Hong, L. S., Bennett, K. O., Rubel, E. W., & Raible, D. W. (2009). Response of mechanosensory hair cells of the zebrafish lateral line to aminoglycosides reveals distinct cell death pathways. *Hearing Research*, 253(1–2), 32–41.

Parinov, S., Kondrichin, I., Korzh, V., & Emelyanov, A. (2004). Tol2 transposon-mediated enhancer trap to identify developmentally regulated zebrafish genes in vivo. *Developmental Dynamics*, 231(2), 449–459.

Peterson, R. T., Link, B. A., Dowling, J. E., & Schreiber, S. L. (2000). Small molecule developmental screens reveal the logic and timing of vertebrate development. *Proceedings of the National Academy of Sciences of the USA*, 97(24), 12965–12969.

Postlethwait, J. H., Johnson, S. L., Midson, C. N., Talbot, W. S., Gates, M., Ballinger, E. W., Africa, D., Andrews, R., Carl, T., Eisen, J. S., Horne, S., Kimmel, C. B., Mutchinson, M., Johnson, M., & Rodriguez, A. (1994). A genetic linkage map for the zebrafish. *Science*, 264(5159), 699–703.

Prezant, R. T., Shohat, M., Jaber, L., Pressman, S., & Fischel-Ghodsian, N. (1992). Biochemical characterization of a pedigree with mitochondrially inherited deafness. *American Journal of Medical Genetics*, 44(4), 465–472.

Raible, D. W., & Kruse, G. J. (2000). Organization of the lateral line system in embryonic zebrafish. *Journal of Comparative Neurology*, 421(2), 189–198.

Raviv, D., Dror, A. A., & Avraham, K. B. (2010). Hearing loss: A common disorder caused by many rare alleles. *Annals of the New York Academy of Sciences*, 1214, 168–179.

Ricci, A. J., & Fettiplace, R. (1998). Calcium permeation of the turtle hair cell mechanotransducer channel and its relation to the composition of endolymph. *Journal of Physiology*, 506 (Pt 1), 159–173.

Richardson, G. P., Forge, A., Kros, C. J., Fleming, J., Brown, S. D., & Steel, K. P. (1997). Myosin VIIA is required for aminoglycoside accumulation in cochlear hair cells. *Journal of Neuroscience*, 17(24), 9506–9519.

Rihel, J., Prober, D. A., Arvanites, A., Lam, K., Zimmerman, S., Jang, S., Haggarty, S. J., Kokel, D., Rubin, L. L., Peterson, R. T., & Schier, A. F. (2010). Zebrafish behavioral profiling links drugs to biological targets and rest/wake regulation. *Science*, 327(5963), 348–351.

Ruben, R. J. (2000). Redefining the survival of the fittest: Communication disorders in the 21st century. *Laryngoscope*, 110(2 Pt 1), 241–245.

Ryals, B. M., & Rubel, E. W. (1988). Hair cell regeneration after acoustic trauma in adult Coturnix quail. *Science*, 240(4860), 1774–1776.

Rybak, L. P., & Ramkumar, V. (2007). Ototoxicity. *Kidney International*, 72(8), 931–935.

Salvi, R. J., Popper, A. N., & Fay, R. R. (2008). Hair Cell Regeneration, Repair, and Protection. New York: Springer.

Santos, F., MacDonald, G., Rubel, E. W., & Raible, D. W. (2006). Lateral line hair cell maturation is a determinant of aminoglycoside susceptibility in zebrafish (*Danio rerio*). *Hearing Research*, 213(1–2), 25–33.

Schacht, J., & Hawkins, J. E. (2006). Sketches of otohistory. Part 11: Ototoxicity: Drug-induced hearing loss. *Audiology and Neuro-Otology*, 11(1), 1–6.

Schacht, J., Popper, A. N., & Fay, R. R. (2008). Auditory Trauma, Protection, and Repair. New York: Springer.

Schier, A. F., Neuhauss, S. C., Harvey, M., Malicki, J., Solnica-Krezel, L., Stainier, D. Y., Zwartkruis, F., Abdelilah, S., Stemple, D. L., Rangini, Z., Yang, H., & Driever, W. (1996). Mutations affecting the development of the embryonic zebrafish brain. *Development*, 123, 165–178.

Seiler, C., Ben-David, O., Sidi, S., Hendrich, O., Rusch, A., Burnside, B., Avraham, K. B., & Nicolson, T. (2004). Myosin VI is required for structural integrity of the apical surface of sensory hair cells in zebrafish. *Developmental Biology*, 272(2), 328–338.

Self, T., Mahony, M., Fleming, J., Walsh, J., Brown, S. D., & Steel, K. P. (1998). Shaker-1 mutations reveal roles for myosin VIIA in both development and function of cochlear hair cells. *Development*, 125(4), 557–566.

Seligmann, H., Podoshin, L., Ben-David, J., Fradis, M., & Goldsher, M. (1996). Drug-induced tinnitus and other hearing disorders. *Drug Safety*, 14(3), 198–212.

Sha, S. H., & Schacht, J. (2000). Antioxidants attenuate gentamicin-induced free radical formation in vitro and ototoxicity in vivo D-Methionine is a potential protectant. *Hearing Research*, 142(1–2), 34–40.

Smith, M. E., Coffin, A. B., Miller, D. L., & Popper, A. N. (2006). Anatomical and functional recovery of the goldfish (*Carassius auratus*) ear following noise exposure. *Journal of Experimental Biology*, 209(Pt 21), 4193–4202.

Solnica-Krezel, L., Stemple, D. L., Mountcastle-Shah, E., Rangini, Z., Neuhauss, S. C., Malicki, J., Schier, A. F., Stainier, D. Y., Zwartkruis, F., Abdelilah, S., & Driever, W. (1996). Mutations affecting cell fates and cellular rearrangements during gastrulation in zebrafish. *Development*, 123, 67–80.

Song, J., Yan, H. Y., & Popper, A. N. (1995). Damage and recovery of hair cells in fish canal (but not superficial) neuromasts after gentamicin exposure. *Hearing Research*, 91(1–2), 63–71.

Speidel, C. C. (1947). Correlated studies of sense organs and nerves of the lateral-line in living frog tadpoles. *Journal of Comparative Neurology*, 87, 29–55.

Stemple, D. L., Solnica-Krezel, L., Zwartkruis, F., Neuhauss, S. C., Schier, A. F., Malicki, J., Stainier, D. Y., Abdelilah, S., Rangini, Z., Mountcastle-Shah, E., & Driever, W. (1996). Mutations affecting development of the notochord in zebrafish. *Development*, 123, 117–128.

Steyger, P. S., Peters, S. L., Rehling, J., Hordichok, A., & Dai, C. F. (2003). Uptake of gentamicin by bullfrog saccular hair cells in vitro. *Journal of the Association for Research in Otolaryngology*, 4(4), 565–578.

Stone, J. S., & Cotanche, D. A. (2007). Hair cell regeneration in the avian auditory epithelium. *International Journal of Developmental Biology*, 51(6–7), 633–647.

Stone, L. (1933). The development of lateral-line sense organs in amphibians observed in living and vital-stained preparations. *Journal of Comparative Neurology*, 57, 507–540.

Stone, L. (1937). Further experimental studies of the development of lateral-line sense organs in amphibians observed in living preparations. *Journal of Comparative Neurology*, 68, 83–115.

Suli, A., Watson, G. M., Rubel, E. W., & Raible, D. W. (2012). Rheotaxis in larval zebrafish is mediated by lateral line mechanosensory hair cells. *PLoS One*, 7(2), e29727.

Suster, M. L., Kikuta, H., Urasaki, A., Asakawa, K., & Kawakami, K. (2009). Transgenesis in zebrafish with the tol2 transposon system. *Methods in Molecular Biology*, 561, 41–63.

Ton, C., & Parng, C. (2005). The use of zebrafish for assessing ototoxic and otoprotective agents. *Hearing Research*, 208(1–2), 79–88.

Trapani, J. G., & Nicolson, T. (2011). Mechanism of spontaneous activity in afferent neurons of the zebrafish lateral-line organ. *Journal of Neuroscience*, 31(5), 1614–1623.

Van Trump, W. J., Coombs, S., Duncan, K., & McHenry, M. J. (2010). Gentamicin is ototoxic to all hair cells in the fish lateral line system. *Hearing Research*, 261 (1–2), 42–50.

Wang, J., Ladrech, S., Pujol, R., Brabet, P., Van De Water, T. R., & Puel, J. L. (2004). Caspase inhibitors, but not c-Jun NH2–terminal kinase inhibitor treatment, prevent cisplatin-induced hearing loss. *Cancer Research*, 64(24), 9217–9224.

Warchol, M. E. (2011). Sensory regeneration in the vertebrate inner ear: Differences at the levels of cells and species. *Hearing Research*, 273(1–2), 72–79.

Webb, J. F., Montgomery, J. C., & Mogdans, J. (2008). Bioacoustics and the lateral line system of fishes. In J. F. Webb, R. R. Fay, & A. N. Popper (Eds.), *Fish bioacoustics* (pp. 145–182). New York: Springer.

Weil, D., Blanchard, S., Kaplan, J., Guilford, P., Gibson, F., Walsh, J., Mburu, P., Varela, A., Levilliers, J., Weston, M. D., Kelley, P. M., Kimberling, W. J., Wagenaar, M., Levi-Acobas, F., Larget-Piet, D., Munnich, A., Steel, K. P., Brown, S. D. M., & Petit, C. (1995). Defective myosin VIIA gene responsible for Usher syndrome type 1B. *Nature*, 374(6517), 60–61.

Weisleder, P., & Rubel, E. W. (1993). Hair cell regeneration after streptomycin toxocity in the avian vestibular epithelium. *Journal of Comparative Neurology*, 331(1), 97–110.

Wersäll, J., & Flock, Å. (1964). Suppression and restoration of the microphonic output from the lateral line organ after local application of streptomycin. *Life Sciences*, 3, 1151–1155.

Whitfield, T. T. (2002). Zebrafish as a model for hearing and deafness. *Journal of Neurobiology*, 53(2), 157–171.

Whitfield, T. T., Granato, M., van Eeden, F. J., Schach, U., Brand, M., Furutani-Seiki, M., Haffter, P., Hammerschmidt, M., Heisenberg, C. P., Jiang, Y. J., Kane, D. A., Kelsh, R. N., Mullins, M. C., Odenthal, J., & Nusslein-Volhard, C. (1996). Mutations affecting development of the zebrafish inner ear and lateral line. *Development*, 123, 241–254.

Whitfield, T. T., Riley, B. B., Chiang, M. Y., & Phillips, B. (2002). Development of the zebrafish inner ear. *Developmental Dynamics*, 223(4), 427–458.

Wibowo, I., Pinto-Teixeira, F., Satou, C., Higashijima, S., & Lopez-Schier, H. (2011). Compartmentalized Notch signaling sustains epithelial mirror symmetry. *Development*, 138(6), 1143–1152.

Williams, J. A., & Holder, N. (2000). Cell turnover in neuromasts of zebrafish larvae. *Hearing Research*, 143(1–2), 171–181.

World Health Organization (2012). Deafness and Hearing Impairment Fact Sheet, 2012. Retrieved from http://www.who.int/mediacentre/factsheets/fs300/en/ (Accessed March 15, 2012).

Wright, M. R. (1947). Regeneration and degeneration experiments on lateral line nerves and sense organs in anurans. *Journal of Experimental Zoology*, 105, 221–257.

Xiao, T., Roeser, T., Staub, W., & Baier, H. (2005). A GFP-based genetic screen reveals mutations that disrupt the architecture of the zebrafish retinotectal projection. *Development*, 132(13), 2955–2967.

Zingler, V. C., Cnyrim, C., Jahn, K., Weintz, E., Fernbacher, J., Frenzel, C., Brandt, T., & Strupp, M. (2007). Causative factors and epidemiology of bilateral vestibulopathy in 255 patients. *Annals of Neurology*, 61(6), 524–532.