CULTURE, MIND, AND SOCIETY

A Cognitive Ethnography of Knowledge and Material Culture

Cognition, Experiment, and the Science of Salmon Lice

Mads Solberg

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Culture, Mind, and Society

Series Editor
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Series Editor's Foreword

Mads Solberg's ethnography invites readers to a journey into the world of the science of salmon and their parasites. At the same time it explores the cultural production and transfer of knowledge as carried out through the materiality of scientific work. Such work means that human knowledge is not merely a representation of nature but intimately part of it. The ethnography examines in particular how materials and interactions in the lab produce knowledge; how scientific practices combine the discursive, material and the social, and how implicit cognitive processes are sorted out through this work.

The book is a contribution to the anthropology of knowledge—following on the ground the work of experimental biologists with an emphasis on the cognitive processes embedded in their work. Solberg is interested in developing the concept of "distributed cognition" and in following how "materiality" plays out in the lab. These concepts allow for following scientists' work not just as individuals and not just by analyzing their sociality as such. The book is about understanding the

broader experimental system of a lab—the physical, social, and conceptual spaces in which scientists work. Solberg then asks how such a system is pragmatically shaped, and how cognitions are formed in such spaces.

Solberg explores these analytical questions in the concrete world of Norwegian scientists (at the Sea Lice Research Centre) who interrogate salmon lice, and situates this site within the larger world of aquaculture and its history. The ethnography delves into new technologies of RNA-interference and how they are used in "reverse vaccinology". Solberg demonstrates how cognition is pragmatically worked out by following collective and interspecies collaborations in the lab. He follows "choreographies" of enacted understanding in which scientists and technicians transform isolated, meaningless materials into meaningful wholes.

Understanding how scientists repress gene expression in the lice genome means following the epistemological work in which researchers, materials (like lice tissues or microscopes), techniques, perceptions and various representations thereof (including imaging, semiotics, and note taking) are all put together and interact. This collaborative work forms what Solberg calls "ecological assemblies." Analyzing them allows for understanding how "thinking through things" is worked out. Finally, Solberg draws attention to the ways distributed cognitive ecological systems are laden with values, emotions and political interests, which, Solberg suggests, should invite further inquiry and reflection.

Jerusalem, Israel Yehuda C. Goodman

Acknowledgments

This book should not have come to fruition without generous assistance from the clever people at the Sea Lice Research Centre. Director Frank Nilsen and Ingunn Wergeland made this study possible, after I showed up at their door in May 2012, asking whether they would mind an anthropologist spending a few years alongside their crew, observing their work. With kindness they provided a workspace, access to the lab, and let me tag along on events big and small. No small favor to accord a stranger, and more than I could have hoped for. Your hospitality is deeply appreciated, and I remain impressed by the community you have built. A big thanks to Lars Hamre and Per-Gunnar Espedal for showing me the ropes in the wet lab, teaching me about the secrets of salmon lice, and for many laughs. Rune Male kindly let me attend his lectures on the structure and function of genes, and offered enlightening conversations about the past, present, and future of molecular biology. The hard-working Ph.D.-students and postdocs at the Centre kindly answered my childlike questions about their work over the years, while they *really* had more important things to do. I owe them much. Christiane Eichner, Sussie Dalvin, and Sindre Grotmol gave generously from their time to

satisfy my curiosity about their work. Collaborating with Sussie on a conference paper on how salmon lice were framed in online resources for SeaLice 2014 in Portland (Maine), offered a great learning opportunity. Heidi Kongshaug and Wenche Telle explained the minutiae of work in the DNA lab to a fledging observer. Michael Dondrup and Inge Jonassen helped me understand basic principles about the digitization of life, and the bioinformatics of salmon lice. I would also like to thank other members of the community who kindly answered my questions, big and small. Various members of the SLRC have offered close readings of various parts of the manuscript and given valuable feedback. For this I am eternally grateful.

Grants from the Meltzer Foundation, the Mobility Fund at the University of Bergen's Faculty of Social Sciences, and the Mobility Fund for the Norwegian Research School in Anthropology, made it possible to spend the winter quarter 2014 at the Department of Cognitive Science, University of California—San Diego. Edwin Hutchins kindly sponsored my stay and thought me how to better think about cognitive anthropology. Hutchins and co-director Jim Hollan offered me a desk in the DCOG-HCI lab, and let me attend their research seminars, as well as many excellent lectures. My gratitude goes to faculty and graduate students affiliated with the lab for teaching me about their work, critically shaping this book in its infancy. Morana Alač deeply influenced my thoughts about how to respecify cognitive studies of science from an interactional perspective, offering perceptive and invaluable comments on later versions of this text. Thanks to Beverly Walton for getting critical paperwork in order.

I am grateful to John McNeil, who convinced me about the need to situate the science of salmon lice in the bigger context of parasitism and the evolution of human domestication of other species.

Much of this research was completed during my employment at the University of Bergen's Department of Social Anthropology, which provided resources and intellectual freedom. I also learned much from productive colleagues at the Centre for the Study of the Sciences and Humanities, an affiliation made possible through Matthias Kaiser, who weighed in with valuable perspectives as the project took shape. Andrea

Bender, and the late Sieghard Beller, invigorated the debate about anthropology's place in cognitive science and were remarkably supportive of this work, inviting me to present ideas in sessions at the Annual Meeting of the Society for Anthropological Sciences in Vancouver 2016, and at the Annual Meeting of the Cognitive Science Society in London 2017. Also, thanks to Radu Umbres who joined a stranger to host a panel on cognitive anthropology and cultural transmission at the conference for the European Association of Social Anthropology in Milan 2016. Michael Vina has been a great sparring partner, collaborator, and good friend since his arrival in Bergen in 2013.

In December 2015, I relocated to my native city, Ålesund. Møreforskning kindly provided an office space in a welcoming, interdisciplinary environment for applied research. A big thanks to director Agnes C. Gundersen, who generously offered a desk to a homeless anthropologist.

A huge intellectual debt is owed to Ståle Knudsen, who supported my project from early on and into maturity. He relentlessly commented on drafts and brought clarity. Thanks for giving me freedom to roam different intellectual avenues, and for helping me find a way back to the important anthropological questions.

More recently, my colleagues at the Department of Health Science at NTNU's campus in Ålesund, have provided an excellent working environment to finalize this manuscript. It has also been a pleasure to work with the editorial team at Palgrave Macmillan.

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The biggest debt of all is owed to my beloved wife Solfrid, our daughter Liv, and our son Dag. These delightful human beings, whom I sojourn together with, have pushed me when I needed a kick in the pants, and offered endless comfort when things were hard.

All remaining errors are my own responsibility. I am sure readers will help point them out.

About This Book

This book asks how scientists create and transform meaning about biological objects in the laboratory and gives a frontline perspective on how research materials and ideas come to life through experimentation. An exercise in the anthropology of knowledge, the study integrates recent advances in cognitive anthropology on distributed, extended, and embodied aspects of thought and action, with historical and philosophical perspectives on scientific experimentation. To account for acts of scientific meaning-making I argue for an integration of cognitive and social approaches through cognitive ethnography of biologists at work.

As a fundamental relationship in the evolutionary process, parasitism poses a challenge for all domestication projects. It inevitably shapes this precarious dynamic, whether it takes place on land or in water. One persistent problem for salmon farmers in the past five decades has been a small crustacean parasite by the name of *Lepeoptheirus salmonis*, colloquially known as "salmon lice" or "sea lice." Copepods like the salmon louse are at the center of fierce controversies about the future of salmon farming, in Norway and elsewhere. In marine aquaculture, a fast-growing

sector of the global food supply, scientific knowledge has become indispensable for handling parasitism and other fish health problems. Consequentially, insights derived from biosciences are fundamentally shaping the industry's trajectory.

This monograph presents an ethnographic study of a community of biologists in Western Norway, who have created a novel environment for conducting experimental research on *L. salmonis* and its relatives. Drawing on a range of techniques from molecular biology and other areas of the life sciences, the group creates new insight about the organism's genomic constitution. Their hope is that knowledge from molecular parasitology can lead to novel pest management tools, such as vaccines and other efficacious biomolecules, that may help bring this resilient parasite under control, before it causes more mischief.

Progress in scientific sensemaking is sustained by a complex material culture, which the research community describes as their "pipeline" for research. Here, I investigate this infrastructure through the concept of "experimental systems," a notion that draws attention to material, cognitive, practical, and social aspects of experimentation as a distinct family of epistemic activities. Through the framework of distributed cognition, the ethnography offers a window on the making of an experimental system, showing how biological phenomena and their representations are skillfully transformed and propagated to become meaningful entities through epistemic actions in the lab. To account for the operation of experimental systems in cognitive terms, I must widen the unit of analysis beyond the level of the individual scientist and the making of scientific theory, to encompass a larger system of interaction. Through this move, I show how the lab is a "cognitive ecology" that sets up divisions of labor, and distributes cognitive tasks in time, space, through artifacts, and between collaborators engaged in creating new knowledge.

Conventional accounts of experiments suggest that their purpose is auxiliary, as "handmaiden" to theory. By looking closely at laboratory action, the book instead shows how experimentation not simply tests theory but contributes to knowledge production through a set of broader epistemic strategies that rely on exploratory activities. In cognitive terms, such experimental practices fundamentally rely on a process of representation and re-representation. Through many epistemic iterations, the

objects of scientific interest, in this case aspects of the molecular biology of a small ectoparasite, are transformed and brought into focus.

A case is made for the value of video-supported cognitive ethnography to capture these distributed aspects of scientific practice, so that the minutiae of multimodal engagements between scientists and their cognitive ecology can be subjected to careful interactional analysis. A methodological implication of the book's approach to culture and cognition, is that the unit of ethnographic analysis must be constantly shifted, depending on what kind of phenomena is being explored. This requires a story that intermittently zooms in and out from different levels of activity, sometimes bringing into focus the "biological skin-bag" of the situated individual, and sometimes widening the frame to capture more long-term interactions between human actors and an immersive material culture of scientific instruments and artifacts.

Reconciling cognitive and social accounts of science has been difficult in the past. The first chapter sets the stage for my integrative project and describes how I approached the field. It also introduces conceptual problems in psychological anthropology, and tools for integrating cultural, social, and cognitive perspectives on science in a conciliatory spirit, to respecify the anthropology of knowledge from an interactional perspective. Chapter 2 tells the environmental history of salmon lice, and chronicles how biological science came to play an important function in fish health work and pest management in salmon aquaculture. Chapters 3 and 4 describes the creation of a new molecular paradigm for salmon lice research, emphasizing the domestication and cultivation of lice-strains in the laboratory, the emergence of a new system for experimentation, as well as the adoption of RNA interference technology for learning about the function of genes, and identify vaccine candidates alongside other therapeutic interventions.

Chapter 5 launches the book's second part, centered around a cognitive ethnography of the fine micro-structures of epistemic activity. It is based on video-supported interactional analyzes of RNA-interference experiments, measurements of gene expression, and microanatomical work with the microscope. Each of the activity-complexes described in Chapters 5, 6, and 7 involves the composition of "ecological assemblies" within the lab's cultural-cognitive ecosystems. These support embodied

agents as they execute epistemic tasks using a wide collection of material resources. In sum, these chapters draw out the cultural practices of cognition in experimental life science. Chapter 8 brings together threads from preceding chapters and sketches recent developments in the science of salmon lice. I spell out implications of this ethnographic study for future work on distributed cognition, cultural transmission, and the contribution of material culture to the evolution of scientific knowledge.

Contents

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List of Figures

List of Tables

1

Tools for the Study of Scientific Practice

Scientific knowledge production aims to make sense of a chaotic, unruly world. Fundamentally, it is a cultural elaboration of a process that cognitive scientists and anthropologists alike casually refer to as "meaning construction," or "meaning-making." Communities engaged in experimental science are situated within complex environments that support a myriad of tasks and goals. Inquiry about how meaning and insight arise from these interactive systems should prove fruitful for what Bourdieu once called "the science of science" (2004: 5). This study is both an ethnographic and theoretical contribution to such a project. It is the product of a two-year-long ethnographic engagement, starting August 2013, with a group of life scientists at the Sea Lice Research Centre (SLRC) in Bergen, Western Norway. The main associates in my story were instrumental in developing a novel experimental system for researching a fish parasite with the scientific name *Lepeoptheirus salmonis*, commonly known as "salmon louse" or "sea louse." Using a wide range of techniques from the molecular life sciences, my interlocutors hope to harness new biological knowledge about the organism's roughly 13,000 genes, to bring this resilient parasite under control before it causes more problems for salmonid mariculture. While the community is working

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toward such applications, they are also producing fundamental insights about the molecular parasitology of this remarkable organism (Fig. 1.1).

On one level, this case study of experimental science can be read as a contribution to the comparative anthropology of knowledge (Barth, 1992, 2002; Cohen, 2010; Crick, 1982). This is an anthropological project in the broad sense, seeking to understand humans as a knowledge-making species, a product of an "indissoluble" relation between minds, bodies, and environment (Marchand, 2010). According to Fredrik Barth, the task of an anthropologist of knowledge is to analyze "the content of an aggregate tradition of knowledge: the variety of ideas it contains, and how they are expressed; the pattern of their distribution, within communities and between communities; the processes of (re)production in this tradition of knowledge, and how they may explain its content and pattern of distribution; thus the processes of creativity, transmission and change" (1990: 1).

Knowledge, as Michael Lambek once remarked, is a productive focal point for anthropologists because the concept bridges a chasm between the ideal and material, subjective, and objective (1993). Knowledge has material effects in the world, is embodied in artifacts and actions, and distributed unequally in groups. The topic also intersects with that ill-defined complex known as the "problem of meaning," how meanings arise, develop, its transmission and reconstruction. Shore noted that the problem of meaning arises because meanings are "twice-born": they are publicly instituted as the meaning *of* something, but also have a parallel life as idiosyncratic meanings *for* particular individuals in specific contexts (Shore, 1995). Solving the problem of meaning through a naturalistic account of culture thus requires a story about the *interactive* nature of public and private representations.

Barth made the observation that knowledge always comes in three modalities: "a substantive corpus of assertions, a range of media of representation, and a social organization" (2002: 1). But while the Barthian approach to knowledge was productively wedded to a naturalistic attitude toward culture and society (1992), it did not cross-fertilize much with developments in psychological and cognitive anthropology, which takes the acquisition and use of implicit and explicit knowledges as its main subject matter. More recently, anthropologists have

Fig. 1.1 Gravid female adult lice, 8–18 mm long, with egg-strings clustering on salmon specimens (photos courtesy of Lars Hamre)

offered programmatic statements arguing for a closer engagement with neighboring disciplines that share the subject of human knowledge, by rethinking psychological and cognitive anthropology (Astuti & Bloch, 2012; Beller et al., 2012; Bender et al., 2010; Maurice Bloch, 2012). This book imagines itself as belonging to this venerable lineage of ethnographic research on human lifeworlds, a vast terrain of scholarship that has cast light on the interplay between institutional structures, enculturated minds, and embodied action by defiantly crossing disciplinary boundaries wherever necessary to answer analytical questions (Quinn, 2018). As such, this work on the anthropology of knowledge should be read as a contribution toward interdisciplinary rapprochement.

Throughout this ethnography, I approach knowledge production in experimental parasitology as fundamentally *cognitive* practices, involving the transformation and propagation of different kinds of representations. At the same time, I want to avoid a prematurely "internalist," or "mentalist" account of knowledge, that omits social and material dimensions which are central for understanding the growth of science. This challenge has been articulated by Alač and Hutchins (2004: 630). They consider cognitive processes playing out between human agents and their social and material environment to be an underappreciated domain of phenomena, ripe for exploration through a new kind of cognitive anthropology. Observing that such epistemic actions are always embedded in culturally constructed environments of practice, they are both fundamentally cognitive and amenable to ethnographic analyzes, such that "*careful examination of these interactions reveals action as cognition*" (ibid., emphasis by authors).

A primary objective is to show how analytical strands within this new kind of cognitive anthropology, specifically the framework of "distributed cognition" and its companion method "cognitive ethnography," can be deployed to make sense of how systems of experimentation become the real working units of the contemporary life sciences. This connects real time, ethnographic snapshots from the lab with work on the history, philosophy, and social aspects of experimental practice. My analysis builds on two working assumptions. The first being that scientific knowledge is a historical product of communities of interacting people and various material artifacts. Secondly, I assume that knowledge production

involve cognitive processes such as memory, decision-making, learning, problem-solving, communication, and language. These are culturally constituted activities where production, transformation, and distribution of representations are central.

Reconciling cognitive and social accounts of science has been controversial and is a risky project that is likely to come under critique from at least three sides (Heintz, 2004: 392). From the perspective of rationalists, who want to imbue science with a special ontological status as a truth-seeking enterprise, isolated from other spheres of influence, reconciliating the social and cognitive should raise strong objections, simply because what constitutes scientific thinking and sensemaking is likely too complex to productively analyze. Representatives from certain schools of thought within science studies are also likely to object. The gist of this objection can be identified in the work of Latour and Woolgar, who famously issued a ten-year moratorium on cognitive explanations in their 1986 postscript to *Laboratory Life*: "If our French epistemologist colleagues are sufficiently confident in the paramount importance of cognitive phenomena for understanding science, they will accept the challenge. We hereby promise that if anything remains to be explained at the end of this period, we too will turn to the mind!" (1986: 286). The fact that Latour "lifted" the moratorium a decade later (see J. D. Keller et al., 1996), might ease some skeptics.

Integrating cognitive and social studies should also raise objections from scholars who disdain talk about cognition as a relic of positivist epistemology, one magically transposing normative rationalist and positivist models into the heads of scientists a priori. But it is fallacious to equate cognition with rationality. Rather than presume rationality it is, as Heintz has spelled out, possible to restate the question of scientific cognition anew by analyzing it as the mechanisms and properties that underpin and sustain diverse scientific cultures, and not as patterns of thought that automatically results in true beliefs (2004: 394). The aim, then, is not to discover "the essence of science," but to investigate how the cognitive and social apparatus of science are together situated in various contexts and produce those cultural phenomena that appear throughout the history of science (ibid.). The untapped potential that lies in combining the explanatory powers of cognitive and social approaches

to scientific knowledge production, and thus helps navigate the pitfalls of cognitive and sociocultural reductionism (Nersessian, 2005), is simply too promising to ignore.

Unpacking this compound lens for analyzing scientific practice occupies the remainder of this chapter. Here, I show how a new kind of cognitive anthropology emerged, and how this body of work help account for the intricate dynamics of epistemic actions by connecting cognition and culture. Still, recent debates about the role of anthropology in interdisciplinary cognitive science have underscored how cognitive and psychological approaches have alienated many anthropologists (Beller et al., 2012; Bender et al., 2010; Maurice Bloch, 2012). Some propose that this alienation of anthropologists from the cognitive enterprise is due to its overreliance on experimental and quantitative approaches, at the expense of naturalistic, long-term ethnographic participant observation in everyday settings (Astuti & Bloch, 2012; Gatewood, 2012). Others suggest that cognitive approaches neglected the constitutive role of material culture, social relations, politics, and power structures in the making of human communities (Strauss & Quinn, 1997; Vike, 2011). Whatever merits or misconceptions that inform these concerns, there are still valuable opportunities for rapprochement between the social and cognitive (Quinn, 2018). Importantly, ethnographers can contribute to a larger scientific conversation on the nature of cognition and knowledge, around the theoretically central concept of "cultural transmission." Emerging from psychologically informed anthropology, this field is preoccupied with "the emergence, acquisition, storage, and communication of ideas and practices" (Cohen, 2010: 194). While disciplines differ in emphasis on their respective contributions to cultural transmission, "researchers across the human and social sciences are recognizing that the bodily, cognitive, neural, and social mechanisms that permit and constrain knowledge transmission are conjointly operative and mutually contingent" (ibid.). As a naturalistic project, these studies specify relationships between cognitive processes and cultural practice by integrating studies on localized actions, events, and contexts with explanatory models that account for the large-scale evolutionary trajectories of cultural productions (Ellen & Fischer, 2013). In the following chapters, my task is to explore, ethnographically, how such dynamics unfold in the laboratories

of biologists who strive toward new knowledge about a pesky parasite that is troublesome for salmon mariculture.

Approaching the Field

My analysis is based on ethnographic fieldwork from August 2013 to July 2015, with more intermittent observations in the time afterward. The SLRC drew my interest as a field site in early 2012, when I came across the first press releases from the Centre. There were several reasons why it struck me as an apt case study. Earlier, I had done fieldwork on political and social dimensions of forest management and environmental knowledge in the Shouf Mountains of Lebanon, which was subtly informed by insights from cognitive anthropology. Planning my next research project, I decided to explore the interface between scientific knowledge, cognition, and materiality in more detail.

Generously funded by The Research Council of Norway as a Centre for Research-based Innovation, the SLRC combined basic biological research with an applied angle, constituting a vibrant space involving a wide cast of different actors and epistemic interests. As I further engaged with the project, it also became clear that the SLRC offered an occasion to examine both the material cultures of science, and its role in the cultural transmission of knowledge, as it represented the genesis of an entirely novel experimental system. As a scientific institution, there was a stable membership of experts, routines for introducing newcomers into the epistemic community, and systematic documentations of the community's changing material and ideational culture through time. Of anthropological interest, the laboratory also presented a task-oriented, spatially bounded setting for the articulation of knowledge, guided by a diverse set of implicit and explicit rules.

A more personal motive for selecting this field site came from growing up in the coastal city of Ålesund in Western Norway. Here, I went through vocational training and entered the food industry, working some years in fine restaurants as a *chef de parti*e, before gradually transitioning into the academy. Trained in the culinary arts, I was attuned to the importance of embodied skills in gastronomy, and the necessity

of augmenting and distributing tasks to one's work environment. This insight is captured in what professional cooks refer to as *mise en place* (literally "putting in place"), the act of setting up one's workstation properly, as a curated environment for culinary action. This experience piqued my interest in questions about how the material cultures of experimental scientists influence the production of knowledge. As a chemist friend once brought to my attention; experimental science at the workbench can be remarkably similar to what goes on in a kitchen. Having grown up in an affluent coastal region built on seafood, I also appreciated the massive transformation brought about by the ascent of marine domestication. The case of SLRC provided an opportunity to peak behind the curtain to see how cutting-edge bioscience gets applied in aquaculture and contributes to a knowledge-intensive industry of great importance to our food system.

The possibility of carrying out "proper" anthropology in such familiar contexts has caused much debate. While this issue has become less of a concern in ethnographic studies of science, it was not uncommon for the first laboratory studies to use rhetorical devices that exotified and made the assumed familiar strange. By conjuring imagery of the anthropologist as a visitor among an alien "tribe" of scientists in the strange lands of the lab, early ethnographies of science attempted to demonstrate that decades of history and philosophy of science had failed to offer a realistic appraisal of what happened in these spaces (see Doing, 2008 for a critical assessment).

Still, when anthropology takes place "at home," in the investigator's own cultural milieu, it is unavoidable that research subjects organize their knowledge about the world in ways that overlap with the anthropologist's. It is fair to say that I shared with my informants both a naturalistic ontology about what entities exist in the world, a belief in the merits of empiricism as a guiding theory of knowledge, and a subscription to those loosely knit norms of argumentation and reasoning often called "rationalism." There are two common assumptions about such ontological overlaps. They can either positively contribute to an enriched understanding, or negatively affect the study by adding only "unnecessary mystifications" that render the commonplace complex (Strathern, 1987: 17). While I recognize the worry that ethnography risks losing

its unique characteristics in such homely projects, I think that whether such concerns are warranted greatly depends on the phenomena being examined and the study's execution. Skepticism toward insufficient exoticism and distance is motivated by a concern that the ethnography will become interview-driven, rather than observation-based. But far from it, cognitive ethnography as a discursive practice involves a *sharpening* of the observational focus, through an emphasis on micro events and disciplined reflexivity about the theoretical import of interactional phenomena.

Furthermore, scientific practices and laboratories are now so specialized and alien, compared to folk-knowledge, that the exotic and unknown can still act as guiding principles. Like in other field sites, an ethnographer of a molecular biology lab must enter a long period of communal socialization to acquire new ways of seeing and articulating the world (Rabinow, 1996: 2). As we account for the "particularity of practice" in these settings, my goal has been neither "glorification or unmasking" (ibid.: 17). Arguably, the strength of cognitive ethnography lies in the interactional data it obtains from long-term, systematic field observations. When we zoom in closely on these situations, even the textures of mundane things may offer surprises. Here, familiarity with the larger cultural domain where practices take place becomes a key asset for grasping the phenomena in question.

To build rapport, I first approached the Centre's director in spring 2013, via my academic supervisor, since they were professional acquaintances. The two of us were then cordially invited to present a research proposal at a staff meeting in May 2013. Here, I explained my approach to studying interaction in the laboratory and sketched some suggestions for topics to explore ethnographically. Fortunately, the Centre administration and research community found my proposal sufficiently intriguing to let me accompany them over their next years of work. In early August, I was generously provided with access keys to a shared office space at the Centre's facility, hosted by the University of Bergen's Department of Biology. My identity was negotiated around a dual status as a social scientist studying scientific reasoning and a doctoral student within the same University. Sharing an office space with other doctoral students and postdoctoral candidates, and establishing rapport with them through

"legitimate-peripheral participation," I could access interpretations of practices and perspectives on the field that were not necessarily shared by more established scientists (Mody & Kaiser, 2008). During my research, I participated in laboratory work, social events, attended lab meetings, and audited lectures on topics in molecular biology, aquaculture, and fish health biology. To become conversant about details on the ethical, legal, and epistemological principles behind the experimental use of fish, I also passed an exam on laboratory animal science.

In addition to learning about scientific practices through participant observation, I carried out formal interviews and informal conversations with members from the community, as well as industrial representatives and public administrators to learn about the economic, political, and ecological context of salmon lice. The parasite also made regular appearances in media, which provided an additional source of information. Numerous conferences, internal and public meetings attended to by SLRC staff, provided access to events that gave insight into how research findings were disseminated, and the paradigmatic problems that were on the agenda.[1]

During my participation in daily life as an ethnographer, I was invited to present my own work to the scientific community on several occasions. One forum were the internal lab meetings, where all members of the SLRC were expected to present their work each semester. These were occasions where I could raise topics and questions of my own interest, based on my observations, gauge my understanding of issues, and spawn discussions with the larger lab collective. I was also invited to present my work on the cognitive anthropology of science to three cohorts of Ph.D. students at the annual Molecular and Computational Biology Research School. While some of the concepts I used were alien to my interlocutors, they willingly engaged in stimulating discussions to correct misunderstandings and sharpen my perspectives. I also collaborated with one of the SLRC's senior scientists, Sussie Dalvin, on a presentation at the tenth International Sea Lice Conference in Portland (Maine), August 2014. Named "Communicating and framing salmon lice on the web," our talk

[1]As in all fieldwork there were occasions, like board meetings and other events with special-status participants, were I found it inappropriate to intervene or ask to attend, due to my status as a guest at the Centre.

offered a content analysis of how salmon lice and their associated risks are framed by different actors in the aquaculture landscape by surveying discourse in online materials.

For someone deeply interested in biology, but without formal training in molecular life science, acquiring sufficient knowledge about the parasitology of salmon lice and high-tech laboratory work implied a steep learning curve. There is no clear-cut answer to the question about what level of competence on a subject matter that an ethnographer of science must acquire, since this depends on the problems being investigated. As Philip Kitcher points out, the important thing is to have the necessary information that is pertinent for understanding the scientific activities in question (1998: 34). I was therefore aiming to acquire "interactional expertise" (Collins, 2004). Lodged between propositional knowledge, and embodied skills, interactional expertise makes it possible to converse with experts to learn about their practice but stands in contrast to the "contributory expertise" necessary to carry out experiments, publish papers in the field, and so on. This meant getting familiar with relevant topics and being able to sufficiently describe these in ways recognized as sensible by members of the scientific community.

No method that science has at its current disposal allows us a privileged, direct view of cognitive processes inside people's heads in the wild. It is even dubious to assume that we actually have *direct measurements of cognition*, even in the laboratory. Brain imaging technologies do not directly picture cognitive processes but detect physiological states that are used as proxies for inferring about higher order cognitive states. The distributed view on cognition tells us that scientists create and augment their cognitive powers partly by building the problem-solving environments whereby they exercise their powers (Hutchins, 1995: xvi). Cognitive ethnography, which I capitalize on here, assumes that the ethnographer can literally step into such sociocultural cognitive ecosystems and observe cognition in action. In total, I collected around 30 hours of high-definition digital video of different events with a handheld video camera. These data are mainly explored in Chapters 5, 6, and 7. As there is a potentially infinite stream of parallel events to record, video-assisted cognitive ethnography entails the risk of a kind of data deluge. Analyzes of video-recorded interactions are also very time consuming,

which adds to the urgency of sampling relevant episodes for detailed examination.

Decisions about what to record were based on background knowledge about the relevance of various practices to the Centre's overall mission. When filming sessions in the lab I positioned the camera to capture the broadest view of the action possible. Sometimes, if the interaction unfolded over a larger area, e.g., multiple rooms, I would use an additional audio recorder, or an iPhone camera as a supplement. When scientists were busy on a specific area on the lab bench, I would position myself behind them with the camera, or place the camera to record the scene from a sideways angle to capture as much of the situated interaction as possible. Since the camera was small, I could move it around to follow the action.

Salient events were then indexed and transcribed to capture fine-grained details of human interaction, using a simplified transcription scheme.[2] This was an iterative process where I moved between other resources, such as notes, documents, pictures, scientific reports, etc., looking for connections between phenomena of interest. Here, video recordings made it possible to "save the phenomena," and a resource for resisting the tendency to *decontextualize* ethnographic observations prematurely (Sormani et al., 2016: 126).

In *Handling Digital Brains*, Alač writes that she initially planned to study the fMRI center at the heart of her ethnography qua its organization as a research center (2011: 12–13). However, her work gradually centered on smaller units of practice, such as the collaborative sense-making routines that occur between colleagues doing situated work to make and interpret scientific visuals. In this study, I zoom in and out from collaborative micro-interactions to capture different levels of activity in the lab. The goal is to understand how representations propagate within a "pipeline" for research, where epistemic activities were organized around problem-solving in a local experimental system.

According to the Norwegian Personal Data Act, the use of video makes the project subject to the "duty to notify" the Norwegian Centre for Research Data, which recommended the project on the condition of

[2]Alač adopts a variation on Jeffersonian notation (2011). I use a simplified version here.

informed consent. While I use the names of prominent researchers in the field in the historical narrative, I have anonymized the identity of my informants, for their convenience, in the more intimate setting of micro-analyzes. I asked for permission to film on occasions where video offered a relevant aid for my inquiry. Other than a few joking remarks about the camera's presence ("surveillance!"), I did not receive complaints about the camera's intrusiveness. Interlocutors were usually filmed while performing familiar tasks. As these were attention demanding, my experience was that they quickly lost interest in the camera's presence and got on with their work. I was fortunate not to have the same experience as Nersessian, who had to discard the camera as a research tool, since her participants found it intrusive (2009: 733–734).

When selecting events for further inquiry, I was guided by Hasok Chang's "Checklist for Activity-Based Analysis," or what he humorously refers to as a "Recipe for the Transformation of Boring Philosophical Issues" (2014). Chang starts his methodical recipe with a rather indisputable premise; namely, that "a serious study of science must be concerned with what it is that we actually do in scientific work" (ibid.: 67). This requires a shift of emphasis from proposition to actions; who is doing what, why, how, and in what context? Chang's checklist suggests that the first thing is to characterize the activity; what is being done? Secondly, we should look at its purpose and external function; what are its aims? The third element is the systematic context of activity; is it singular, or routinized and thus part of something extensive? Studying systems of practice, we must always keep in mind that systems have goals beyond the purpose of the activities constituting the system (ibid.: 74). We must also attend to the agents; who do things to, and with, whom? And by which resources and capabilities do they do it? How free are the agents to make epistemic choices, and what constraints are in place? Finally, there is, like Barth reminded anthropologists (2002), always a set of metaphysical principles at play; what kind of world does it take for the activity to make sense, and who decides about its sensibility?

In this book I use cognitive ethnography to flesh out how these questions pertain to SLRC's experimental system, its history, and some everyday operations. Like all exegesis from the native's point of view, this requires strenuous balancing between doing justice to the world of

insider conceptions through which my informants think, know, and act in the world, and using a meaningful vocabulary for lay readers. I have tried to avoid flooding readers with technical terms used by my interlocutors, but in a Malinowskian spirit I do consider *some* insider language to be essential when accounting for meaning-making from their point of view.[3] I apologize for any nuisances this may cause.

Outline

This book is organized into two complementary parts. This chapter sets the stage in terms of what the case study is about, my approach to the field, and the scope of an anthropology of knowledge that takes cognitive and social dimensions seriously. It introduces a handful of conceptual issues in cognitive anthropology, elaborates on the framework of distributed cognition, and shows its relevance for the study of experimental practices. Grasping the cultural and material dimensions of scientific cognition and meaning-making in experimental bioscience requires a larger unit of analysis than the individual agent. I show how an emphasis on experimental systems enables us to take seriously the materiality of science, and clarify epistemological questions raised by this project, like the issue of "cognitive bloat" and the nature of epistemic agency.

The next three chapters situate the Sea Lice Research Centre and its experimental system through an ethnographically and historically informed account. Examining the Centre through the lens of distributed cognition, requires undertaking several journeys: through historical time, through physical and social space, and through conceptual space. I begin my story at the macro level in Chapter 2, with a wide shot that situates the science in the larger world of salmon aquaculture and lice management. Here, I examine the deep history of Norwegian salmon farming, looking at parasitism as a wicked management problem in

[3]This is not to be conflated with the contentious distinction between internal and external exposition in science studies, which has been treated with much dubiety (see Chang, 2016 for a recent discussion).

animal domestication, not only on land, but also in the sea. Management of pathogens has become a hot-button issue, profusely shaping the trajectory of salmon domestication, and will be a decisive factor determining its future path. A meaningful analysis of experimental science in the laboratories at the SLRC necessitates an appreciation of how scientific management of fish health through parasitology came to indirectly shape the coevolutionary, interspecies process that is marine salmon farming.

Chapter 3 tackles the historical background for the Research Centre and describes its social organization and scientific goals, by moving through physical, social, and conceptual spaces. I focus on the emergence of a novel system for probing the biology of salmon lice, how new technologies changed the nature of the experimental practice, and look at the division of epistemic labor. Critical for this story is how the parasite was domesticated in the lab, and the development of robust technologies for experimentation, such as a novel system for maintaining lice and hosts. My analysis of these "technologies of the mind" is informed by distributed cognition, along with historical and philosophical work on experimentation.

Expanding on this topic, Chapter 4 examines the conceptual space of central biotechnology in SLRC's experimental pipeline, namely, RNA interference (RNAi). Here, I show how RNAi was adapted as a key tool for screening the salmon lice genome for potential therapeutic targets. I draw on recent work on regulatory RNA research and related biotechnologies, which exemplify distinct modes of epistemic practices at play in the life sciences. It is shown how experimentation is not just for testing hypothesis but may serve other important epistemic goals as well. I capitalize on the ideas of the "New Experimentalists," who began rethinking experimentation as practice in the 1980s, and subsequent work on "exploratory experimentation" to discuss the epistemic role of RNAi in the science of salmon lice.

Chapters 5, 6, and 7 offer a series of situated micro-analyzes of everyday practices in the lab that shows how the extended experimental system constitutes a vehicle for thought and action. Here, I track different laboratory events and map the traffic of representations within the Centre's pipeline for research. By framing experimental systems as *cognitive ecosystems*, we see how small-scale practices link up into larger

interactive elements that constrain how, where, when, and in what form information travels, and gets interpreted by cognitive agents. I show how cultural practices within the experimental system link up cognitive resources, and how the sources of organization for ordered scientific practices originate outside of the individual performer. Depending on the epistemic phenomena in question, the most suitable unit of analysis can occasionally be found at the level of a situated, individual agent, while at other times the analysis must be expanded further beyond the individual skin and skull into the social and material environment.

In Chapter 5, I examine events sampled from the initiation and termination of RNAi experiments. These functional screenings probe the effects of specific genes on salmon lice biology. RNAi initiation and termination are socially and cognitively complex affairs, whose execution require the choreography of a collective of researchers. I look at how these situations set up epistemically rewarding relationships between samples of lice, instruments, and various representational artifacts.

How are valuable tissues from RNAi trials cared for, and endowed with biological meanings within the experimental pipeline? Chapter 6 addresses these questions by examining how patterns of gene expression become visible using a technology known as *real-time quantitative polymerase chain reaction*. Here, I follow the downstream benchwork of one particular researcher and examine how her situatedness within the lab's cognitive ecosystem makes such measurements possible. Through everyday operations, scientists opportunistically use artifacts to execute various creative actions that render patterns of gene expression visible. I analyze these epistemic activities as "ecological assemblies," cultural practices that orchestrate arrays of resources in the agent's environment to house and extend cognitive processes beyond the individual agent. By changing the arrangement of her external surroundings, the agent creates novel opportunities for knowledge and insight.

As icons of science, microscopes occupy a prominent place in epistemological debates about scientific realism and that which is invisible for the naked eye. Tapping into some of these, Chapter 7 examines how the anatomical structure, distribution, and development of salmon lice exocrine glands are collaboratively described through explorative microanatomy. Offering an ethnography of the microscopical study of

tissue samples (histology), this chapter shows how mundane artifacts and sophisticated imaging techniques help practitioners create spatial reference and thus biological meaning from microscopic phenomena. Spatial language, and a range of other semiotic resources, are intricately deployed to reason and achieve consensus about such biological entities. I show some of the cognitive practices that microscopists use to establish spatial reference to salient phenomena, and how representational states are propagated through embodied interactions in front of the microscope, via transformations to scribbled notes on paper, and eventually through the systematization and dissemination of findings in scientific publications.

In conclusion, Chapter 8 draws together threads from preceding chapters and sketches some recent developments in the science of salmon lice, both as it pertains to SLRC's experimental system and to the general trajectory of salmon aquaculture and lice management. I also spell out some implications of my study for future work on distributed cognition, cultural transmission in science, and the contribution of material culture to the evolution of scientific knowledge.

Primer on Cognitive Anthropology

Before presenting my roadmap for integrating cognitive and social studies of scientific meaning-making, I offer a brief primer on cognitive anthropology. After probing some limitations in how this field has conventionally approached cognition, I introduce "distributed cognition" as an alternative framework for rethinking the fundamentally cultural nature of cognition and action. Understanding scientific cognition in fields like molecular biology requires a larger unit of analysis than the individual agent. Works by historians and philosophers have identified "experimental systems" as a critical working unit for understanding contemporary science. This label describes heterogeneous arrangements of apparatus, material infrastructure, technical expertise, conceptual models, theoretical constructs, and cultural assumptions that govern research fields. The concept draws attention to the fact that knowledge in experimental science is a collective, cumulative endeavor. It is governed by a stream of activity that explores the phenomena in question

from many angles, rather than single, "decisive" experiments for hypothesis testing, performed by individuals working in solitude. I argue that this approach productively dovetails with the framework of distributed cognition, and other research on the situated, embodied, and extended character of mind and knowledge. Attending to material and distributed aspects of scientific reasoning raises questions about the locus of agency in distributed cognitive systems. I clarify these toward the end.

Distributed cognition, as an analytical framework, was introduced by the anthropologist Edwin Hutchins in *Cognition in the Wild* (*CiTW*), a landmark ethnographic study centered on large-ship navigation aboard a US Navy vessel (1995). Among other things, this work compared the representational assumptions of modern navigational culture in the US Navy with those of traditional Micronesian navigation. Based on a detailed ethnography of a hierarchical military culture, Hutchins specifies how cognition situated naturally is thoroughly distributed, socially and materially. A big idea was that cognitive scientists had attributed to the individual person many computational processes that are better understood as being performed by larger, heterogeneous systems. According to Hutchins, the computations that cognitive science had assumed were occurring inside people's heads frequently crisscrosses the boundary of the skin in ways that bestow humans with many cognitive powers. *CiTW* then argues for a perspectival shift and a new unit of analysis of cognition that carves out space for the role of cultural practices and materiality. Hutchins had trained in the tradition of cognitive anthropology, sometimes known as "the New Ethnography" or "ethnoscience", which emerged from the linguistic and cultural branch of American anthropology in the 1960s. But his case study represented a radical conceptual flip from conventional approaches to intelligible action within psychological anthropology and cognitive science. Why was this flip necessary?

Studies on the relation between mind, behavior, and language have a long-checkered history in anthropology and adjacent disciplines. In nineteenth-century Europe, German romanticists like Wilhelm von Humboldt explored the connections between languages and worldviews. Humboldt, and his contemporaries, believed that languages differed in

how suitable they were for describing how the world was (which, incidentally, explained the superiority of Indo-Europeans). In early American anthropology, Boas, Sapir, and Whorf pursued similar topics, and introduced the concept of linguistic relativity based on field research in Native American communities. While linguistically minded anthropologists agreed with the romanticists that structural aspects of different languages could uncover the roots of cultural differences, they proposed both weaker and stronger versions of the relativity hypothesis. Furthermore, the anthropologists disagreed about ranking languages in terms of their suitability for intellectual pursuits.

In the late 1950s, Claude Lévi-Strauss famously launched structuralism as a naturalistic program to compare the cultural products of the mind. Inspired by Roman Jakobson's structural linguistics, Lévi-Strauss claimed that human thought organizes information primarily as binary contrasts that form combinatory, abstract patterns that generate the concrete cultural variations found in the ethnographic and historical record. Lévi-Strauss' universalist approach to the production of cultural forms such as myths, exercised a huge influence across the humanities and parts of the social sciences, not only due to its positive contributions, but also because of strong reactions *against* the structuralist program.

As Lévi-Strauss developed his elaborate schema, the so-called "cognitive revolution" swept across the behavioral sciences, in disciplines such as psychology, linguistics, and philosophy, along with the nascent field of computer science. Many in this new vanguard also considered anthropology to be a crucial piece of the puzzle (Boden, 2008: 516). But although structuralism had been a "proto-cognitive" approach in some respects, few proponents engaged thoroughly with these developments (Sperber, 1985). Structural linguistics and particularly phoneme theory, a theory about the smallest units of significance which Levi-Strauss based his reasoning on, soon faced heavy criticisms from Noam Chomsky and others's generative grammar (Bloch, 2012: 54–59).[4] Through the

[4]While Lévi-Strauss proposed a comparative and naturalistic approach to culture, he did not, for various reasons, engage deeply with the cognitive program, instead aligning his project with Piaget's developmental psychology. Some anthropologists abandoned the enterprise as it offered no method beyond intuition to identify the minimal contrastive symbolic elements of cultural productions.

argument from the "poverty of the stimulus," for example, Chomskyan generativists claimed that structural linguists did not tell a plausible developmental story about how children learned languages at the speed they did. Instead, they hypothesized a biologically specialized mental faculty disposing humans to language acquisition, and that this innate module enabled the development of a universal grammar constraining language variation.

Early American cognitive anthropologists approached cognition from a rather different vantage point than such nativist, generative deep structures. Instead, they first tried to wed the anthropology of cultural particulars with formal linguistics by looking for semantic equivalents of the finite phonemes that were widely believed to characterize natural languages. Kinship terms, for instance, were assumed to have a paradigmatic structure that could be deduced by extracting semantic features from genealogies (see D'Andrade, 1995a). Such native mental categories and structures could not be observed directly. Instead, they had to be discovered through elicitation methods. This led to the development of stringent procedures for studying lexical items, known as componential analysis.

The resulting "ethnoscience", which equated culture with knowledge and its organization, was quite productive empirically. But there were major concerns about the psychological reality of formally elicited semantic structures. Keesing, a specialist on Melanesia sympathetic to the project of a science of culture, offered a harsh verdict of "messianic promises" to identify this "heart of cultural structure": "The new ethnographers have been unable to move beyond the analysis of artificially simplified and delineated (and usually trivial) semantic domains, and this has discouraged many of the originally faithful. Ethnoscience has almost bored itself to death" (1972: 307–308). Cognitive anthropologists had borrowed their conceptual framework from linguistics, but Keesing asserted that Chomsky's generative grammar had literally "destroyed" the foundational paradigm of ethnoscience, such that it "no longer made sense."

By this point some cognitive anthropologists, disillusioned with the old framework, had begun novel research on the formal properties of

taxonomic and classificatory models. And soon, topics like the universality of color terms and the structure of ethnobiological knowledge became matters of intense debate. Among ethnobiologists, for example, a pervasive disagreement ensued over the relative importance of utilitarian versus innate drivers of environmental knowledge and natural classification (see Hunn, 1982). Evidence indicated that most lexical domains were not organized taxonomically, with a few special exceptions in ethnoscientific folk knowledge. Nor could culture be conceptualized analogous to an integrated "grammar" or "code". The proposals from cognitive anthropologists had "failed to gel into a comprehensive, agreed upon new theory of cultural meaning" (Quinn, 2011: 34).

Eventually, the "new ethnographers" developed elicitation techniques, imported new methods like multidimensional scaling from psychology, and co-opted theoretical tools of greater sophistication. But it was still clear that a comprehensive understanding of how cultural knowledge and meaning was organized, required a rethink of fundamental issues: "In short, it cannot simply be assumed that distinct semantic domains are structured in the same way. Until independently assessed domains can be shown similar, meaning should be assumed to be a motley, not monolith" (Atran, 1993: 57).

Soon, new theoretical accounts from experimental psychology, including prototype models and schema theory, led to the emergence of the "cultural models school." In this approach, meanings were considered not as the product of simple checklists of features but determined by a complex organization of different mental representations. The notion of schemas was introduced to account for meaning construction in general. These cognitive–semantic structures were built up from experience, both conscious and unconscious, as well as from sensation and emotion. As experientially derived constructs, schemas could also give structure to future, novel experiences. Both individual meanings and shared, public representations could be understood in these schematic terms, hence the notions of "cultural schema" and "cultural model."[5] Later, research

[5]These concepts are used somewhat interchangeably in the literature, with some using "cultural schema" as the generic term, and "cultural model" for describing more general mental structures. Shore introduced the term "foundational schema" for widely shared and abstract conceptual structures, and reserve "models" for particular instantiations (1995: 53).

suggested that these schemas and models had directive force, created motivations, and oriented people toward certain outcomes and meanings, providing evaluative standards of what is good or bad, thereby driving behavior in culturally specific ways (Quinn, 2011). This work was further refined throughout the 1990s, with a wave of studies on the dynamic nature of cultural models and cultural representations. These indicated that the first wave of cognitive anthropologists had subscribed to an overtly ideational, language-like concept of culture.

Critically, the old paradigm had failed to address cultural transmission as *process* (Bloch, 1998; C. M. Keller & Keller, 1996; Lave & Wenger, 1991; Shore, 1995; Strauss & Quinn, 1997). In addition to growing dissatisfaction with the theoretical impasses of cognitive anthropology, failures to engage mainstream sociocultural anthropologists in the ongoing interdisciplinary conversation provided additional impetus for rethinking the "cognition and culture" field. In European social anthropology, structural-functionalist accounts had reigned supreme well into the 1960s, and the various approaches to social phenomena that followed, marginalized the space for cognitive perspectives even more than in American anthropology. One exception to the European trend was a small but influential group of scholars who began thinking about the distribution of cultural phenomena in terms of domain-specific, evolved cognitive mechanisms. These works developed around Dan Sperber's notion of an "epidemiology of representations" (1985, 1996). Sperber took a lead from Gabriel Tarde, one of Durkheim's detractors, by marrying Tarde's diffusionist approach to cultural diversity with theories about evolved cognitive dispositions. For Sperber, a naturalistic approach to culture should investigate the regulation, acquisition, variability, and use of mental and public representations and performances. Similar to medical epidemiology, an anti-reductionist discipline in search of mechanisms involved in distributing health and disease, anthropological studies of culture and society should attend to the irreducible *ecological* patterns of psychological phenomena (Sperber, 1996: 31).

In a landmark study, Scott Atran cashed in on Sperber's proposal, demonstrating how traditional precursors to modern biological science, like natural history and natural philosophy, were institutionalized byproducts of an innate, pan-human cognitive propensity for reasoning

about living kinds (1990). "Folk-biology" is an evolved disposition, he argued, that afford people across cultures the ability to reason about living entities by intuitively attributing them with essences, and by structuring representations of living kinds in terms of species-like groups organized in hierarchical relations. Building on comparative analyzes on ethnobiological classification, Atran suggests that this leads to a naïve, essentialist notion of species that conforms to a particular "generic" rank in folk taxonomies (like the generic label "tree"). These conceptions sometimes come into conflict with Darwinian and scientific species concepts (such as interbreeding). But intriguingly, adoption of a Darwinian species concept does not eliminate everyday intuitions about the generic level and an essentialist bias. Instead, such intuitions provide a cognitive resource for meta-representational reflections on biological information in ways that allow scientists and others to go beyond spontaneous, naïve intuitions, and reach new conclusions.

This work culminated in a series of comparative field investigations that productively combined experimental and ethnographic approaches in a variety of societies to understand environmental reasoning among different groups (Atran & Medin, 2008). Similar to what Chomsky had proposed for language, there were evolved special-purpose tools of the mind adapted for reasoning about natural kinds. Varieties of cultural knowledge emerge from these domain-specific, pan-human cognitive mechanisms when they get implemented in different ecological contexts. Details about how exactly such habits of the mind develop, and their relation to perennial anthropological issues like essentialist social categories, are still debated among specialists (Regnier & Astuti, 2015).

Interpretative anthropologists committed to *sui generis* views of culture criticized this agenda. A narrow focus on a few select domains of social life, a commitment to methodological formalism, and hubristic ambitions to *causally* explain social phenomena, was misguided as it simply failed to grasp what was special about human culture. David Schneider, for example, had early on criticized the application of cognitive and formal approaches to kinship studies (1965). Clifford Geertz also took issue with the mentalistic and individualist notions of culture proposed by the cognitivist program (1973), which he believed married

"extreme subjectivism" with "extreme formalism." In this view, the epistemic goal of ethnography and anthropology was not an explanation of social phenomena per se. Instead, the anthropologist's aim was interpretations of shared, public meanings; the Weberian webs of significance spun by humans. The goal of ethnography was "thick descriptions" of the social; an approach which could not be formally articulated and left little room for systematic data elicitation using other methods. Later, as evolutionary-informed analyzes gained traction in cognitive circles, these were seen to advocate a troublesome reductionist agenda. This also coincided with a displacement of epistemic virtues in parts of anthropology, like searching for objective models, favoring instead what D'Andrade called "moral models" (1995b). As Bloch describes, cognitive approaches fell on the wrong side of a spurious epistemological and ontological nature–culture divide, where sociocultural anthropology "declared itself the champion of 'culture' against a 'nature' which includes a consideration of the working of the mind" (2012: 6).

The social-reductionist alternative of Geertz and his followers effectively culturalized the mind, but simultaneously resisted any form of cognitively nuanced apprehension of culture (Shore, 1995: 35). In a mutual gesture, many cognitivists dismissed mainstream anthropology as succumbing to an untenable holism lacking methodical and theoretical rigor, effectively being incompatible with naturalistic accounts of culture. As Margaret Boden shows in her history of cognitive science, these internal disagreements about fundamental questions, sidelined the analysis of generative cognitive mechanisms that could account for both diversity and pan-human patterns of culture (2008). Consequently, anthropology became the "missing discipline" in debates about the mind.

Critiquing this development, Strauss and Quinn argued that Geertz's and other interpretivists' insistence that cultural meanings were only interesting *qua* their status as *publicly* shared representations, built on an inadequate "fax model of internalization" (1997: 23). The Geertzian claim that "culture is public *because meaning is*" (my emphasis), assumed that culture was an integrated, shared, and coherent symbolic system (1973: 315). But the notion of a unified symbolic system, an idea that was shared by early cognitive anthropologists, was notoriously ambiguous and lacked empirical warrant. People did not always attend

to publicly accessible symbols in the same way, and symbols did not straightforwardly determine how people understood and attributed meanings to things and events. Strauss and Quinn also took issue with poststructuralist attempts to explain away cultural meanings as "constructed." Neither were historical-materialist accounts of exploitative "hegemonies" of meaning plausible, they argued, in light of knowledge about the properties and organization of human mental faculties (see also Vike, 2011). Foucauldian concepts, such as *discourse* and *episteme*, appeared to dissolve any boundary between people's inner workings and their social world in ways that lacked empirical warrant (Strauss & Quinn, 1997: 26–41). Rather than dissolving the culture concept altogether and replacing it with more opaque terminology (see Shore, 1995: 45), there was a need to refine cognitive theory and accommodate more holistic analyzes of local meanings.

Strauss and Quinn found practice theory, a widely adopted approach to social phenomena which emphasized the implicit character of knowledge (Bourdieu, 1977), as somewhat compatible with the kind of cognitive approach to cultural meaning they proposed. But while practice theory offered a step in the right direction, it was nonetheless flawed since it refused to specify the cognitive mechanisms involved in the internalization processes of cultural learning. As Bloch has observed more recently: "By stressing the need to understand individual motivation and the processes that lead to action in living people, Bourdieu takes us to a point where we cannot do without the work of cognitive scientists, but he himself seems unwilling to take the further necessary step" (2004: 152). In conclusion, these objections implied that metaphors commonly used to make sense of the culture concept, and its role in the production of meaning, had not only been misleading, making anthropologists look in the wrong places for the wrong things, but lacked empirical justification. Culture could no longer be conceptualized as something transferred between humans like bodies warm to rays of sunshine. People were not sponges soaking up cultural stuff, and the notion that culture is like a pair of glasses through which we view the world, was at best misleading. New frameworks were called for.

Distributed Cognition

The culturalist position minimized the role of innate human dispositions and strategically overstated cognitive variance. But neither could the cognitivists hope to understand human nature by "factoring out dimensions of local variation" to expose a stripped-down, essentially *acultural* being (Shore, 2011: 148). The challenge was to articulate an approach that accommodated anthropological sensitivities to detect and understand local meanings and practices, with a view toward human meta-culture, the cognitive conditions that make observable cultural variation possible.

Being deeply committed to methodological individualism, cognitive anthropologists had long considered the enculturated agent as a natural unit of analysis. But treating cultural knowledge as a mind-internal and language-based phenomenon, had some unfortunate implications. Roy D'Andrade, for example, once suggested a division of labor between cognitive scientists, who study the general mechanisms by which the mind operates, and anthropologists, who study the range of cultural content of minds across social worlds: "Cognitive anthropology and cognitive psychology are both concerned with the interaction between processing and information, except that the cognitive anthropologist wants to know how cultural information is constrained and shaped by the way the brain processes such information, while the cognitive psychologist wants to know how the machinery of the brain works on all types of information, including cultural information" (1981: 183). While this was a nuanced proposal at the time, the separation between "cultural" and other forms of information, along with the distinction between content and process, is problematic in retrospect (Bender et al., 2010: 377). Not only does recent evidence suggest that even basic domains of perception are culturally malleable (Henrich et al., 2010), but an a priori separation of content and process also seems to ignore the material dimensions of culture, along with non-declarative knowledge like skills and practices. Cognitive anthropologists could no longer pursue their project by cramming everything cultural inside the native's head.

Hutchins' *Cognition in the Wild* offered a conceptual flip in this intellectual landscape by respecifying action as cognition, pleading for an anthropological reexamination of the enculturated mind as an emergent product of interactions between material artifacts, cultural practices, and cognition as the computation and propagation of representational states (1995). Building a case against reigning internalist models of the mind, Hutchins describes how early cognitive science defined bodies (sensory motor systems), emotion (affect), and social context as too difficult problems to tackle with standard computational approaches. Pioneers in the field accepted that these phenomena instead would have to be integrated later, when the field had matured. But even three decades after the cognitive revolution, Hutchins could still observe that much more was known about cognition "in the captivity of the laboratory" than cognition in "culturally constituted settings" (ibid.: 370–371). This was not simply a critique of the dominant cognitive paradigm, but also a critical commentary on cultural theories that had failed to engage with the naturalistic study of the mind.

Hutchins identified the malaise in cognitive science as a set of problematic and unexamined assumptions about minds as "physical symbol systems" (PSS). Basically, a PSS consists of a set of physical patterns that can be attached to each other to make a structure (an expression), and a set of processes that operate upon these symbols according to specific instructions (creating, altering, copying, destroying), and which is located in a world of real objects that include more than just symbolic expressions alone. Cognitive science was built on the assumption that symbolic representations, a class of things that exists in the world around us, could be located inside people's heads as constituent elements of the mind. In his original formulation of how an intelligent system could work, the mathematician-logician Alan Turing proposed an abstract model system, a Turing machine that manipulates a strip of tape according to rules, using the image of a mathematician at work, busy manipulating symbols in order to solve formal problems. Hutchins reminded us that this idealization actually interacts with a material world, using hands and eyes to manipulate symbols and perform computations: "The heart of Turing's great discovery was that the embodied actions of the mathematician and the world in which the mathematician

acted could be idealized and abstracted in such a way that the mathematician could be eliminated. What remained was the essence of the application of rules to strings of symbols. For the purposes of producing the computation, the way the mathematician actually interacted with the world is no more than an implementational detail" (ibid.: 362).

The first digital computers were based upon this metaphor and proved that it was possible to build "universal" or "Turing equivalent" machines that could formally manipulate symbols to compute any exactly specified function via a set of rules. Such a formal system would encode phenomena in the world as symbols put together into symbolic expressions. By manipulating a string of symbols following syntactic rules, it was possible to create newly formed strings that entailed some particular meanings about the world. Hutchins considered these formal systems to be so powerful that they were "the key to modern civilization" (ibid.: 360). Eventually, abstract symbol manipulation became a model for human thinking and was eventually refined into what today is recognizable as the computational theory of mind. The PSS hypothesis suggested that the mind–brain was best understood as an information-processing system operating on abstract symbols to perform computations. The computer, a mechanical system for rule-based symbol manipulation modelled on an idealized human agent, was replaced with the brain, which effectively placed the symbols Turing identified in the external environment into the head, the locus of brain-internal information processing.[6] As Wilson and Clark observe, this individualistic conception of thought and action resulted in a sandwich model of the mind, where cognition is "wedged between perception (on the input side) and action (on the output side)" (2009: 56).

While this was an extremely productive guiding idea when the field of cognitive science coalesced, elevating it as a central dogma had some unfortunate consequences. Internal symbol processing came to carry the entire explanatory burden in accounts of the mind. In his ethnographic study, Hutchins lays out the case of ship navigation on a large US navy

[6]The term 'computer' used to describe a person performing calculations in fields which required joint work teams to solve complex problems. Each participant usually worked on a subset of the problem.

vessel, which involves taking bearing readings and turning these observations into formal manipulations of numbers, symbols, and lines drawn on a chart to satisfy the constraining principles of nautics. He shows that many representations that are being manipulated to answer navigational questions are not in the head of any individual navigator, but out in the environment; being operated upon by human beings engaged in practical tasks, acting and communicating with each other to answer the general navigational question of "where are we?" How could these cultural activities, which were so evidently computational in nature, become invisible for cognitive science, and how could they be made visible again? Hutchins suggests that this requires a conceptual figure-ground reversal of a Kuhnian sort. Due to their incommensurability with the standard paradigm of cognitive science, Hutchins even finds his own words unruly (1995: 356). So, before his words can assume its intended meaning, he must reverse engineer the assumptions behind the computational metaphor of mind to expose its limitations.

We saw that when machines capable of manipulating symbols were created, these soon became model exemplars of intelligent systems. But the model that Turing had in mind when he first conceived the idea of the universal machine was an actual physical human being interacting with the world, manually manipulating symbols with a writing instrument, paper, and other tools. Turing's universal machine was based on abstracting away the human agent, her body, equipment, and the rules, which were all parts of a distributed system. This move would be unproblematic if the goal was simply to push the boundaries of humanity's cognitive accomplishments. But it offered an impoverished model for describing how flesh and blood human beings engaged with cognitive tasks in natural contexts. The cognitive properties of a human agent equipped with only the bare brain, according to Hutchins, did decidedly not have the same properties as those of the same agent equipped with a suite of tools, material symbols, and an external medium in which computations can be implemented. As with bare-handed carpentry, bare-brained thinking simply does not get us very far (Dennett, 2000). The physical symbol system hypothesis, Hutchins radically suggested, had reproduced the properties of the wrong system, and was no fitting model for individual cognition: *"It is a model of the operation of a sociocultural*

system from which the human actor has been removed" (1995: 363, italics in original).

A skewed view on the nature of information processing was the result of inappropriate conceptual surgery that replaced the biological brain with a computer. Unfortunately, says Hutchins, while the procedure seemed remarkably successful from a computational perspective, the role of body and environment to cognitive processes was forgotten in the operation's aftermath. Cognitive science then reshaped the image of the human mind on basis of a new but impoverished model; putting symbols, manipulation, implementation, and everything else into an abstraction, insulated by the skull's hard boundary. The provocative conclusion to Hutchins' line of reasoning is that the computer was *not* made in the image of a human agent, but rather in the image of what for Turing was a sociocultural system to begin with, one developed to solve certain kinds of problems; a human agent, the mathematician-logician, immersed in an actual environment seeded with physical symbols and the tools to manipulate them. An enskilled agent participating in a material culture emerging from a long chain of cultural evolution and selection in the mathematical domain.

The framework of distributed cognition proposed that the intracranial boundary was no longer a tenable demarcation for truly "cognitive" phenomena. While these boundaries were put up mainly for reasons of tractability, Hutchins proposed that the implementational details of symbolic manipulation, mattered a lot more for our understanding of cognitive systems than previously recognized. Think about the now-classic example of performing "long multiplication" using pen and paper to multiply two three-digit numbers (Magnus, 2007: 277). Some gifted individuals can solve such multiplication tasks by relying on mental imagery alone, without externally representing the problem. But most of us either have to use a tool, such as a calculator, or orchestrate our hands in other specific ways by manipulating a writing instrument to make inscriptions on paper or some other medium. In the latter cases, only some parts of the task are performed by the individual brain, while other major parts, such as representation and memory, are outsourced to external media that can be manipulated using specific rules. Clearly, the cognitive properties of an agent calculating three-digit numbers with just

the naked mind are different than those of an individual equipped with pen, paper, and the procedural rules for manipulating symbols by hand to construct an external representation of the problem. Although the output, the solution, remains the same, information is being processed in different ways in the two systems. This is also the case for many other familiar tools that litter our environments and which we frequently use to solve analytical problems large and small. Structure in the world does more than simply augment our memory capacities; it also changes the nature of the tasks we try to accomplish by facilitating coordination between the inside and outside of the agent.

Hutchins suggests we can rectify this erroneous conception of the mind by extending the unit of analysis beyond individual heads, to include the enculturated functional environment, or "cognitive ecology," where processes of cognition take place in the wild (Hutchins, 2010). In the above example, the *cognitive system* which performs the pen and paper computation is actually the person with its internal resources *plus* the inherited tools used to accomplish the task externally. But while this example indicates that we must broaden our unit of analysis, Hutchins maintains that we can *use the same language* that was previously reserved for describing internal mental events to account for the cognitive accomplishments of larger sociocultural systems. This means "computation" in the wide meaning of the word, realized through creating, transforming, and propagating representational states. The difference is that the media where this process unfolds is no longer restricted to a hundred billion neurons that are wired together in the human brain. For Hutchins, talking about cognition and computation in the case of extracranial events is therefore not an unwarranted metaphorical extension, as sceptics might object (see Adams & Aizawa, 2001).[7] Instead, this conception follows from the original source model that gave rise to the physical symbol system hypothesis; a wider information-processing

[7]Adams and Aizawa suggests that Hutchins only studies "naturally occurring computation" rather than true cognition (2001: 58–59). Their argument hinges on the importance of "non-derived meanings" for what they see as truly, intracranial cognitive processes, as opposed to "derived meanings" of external computations (meanings that we attribute to things). This is a technical argument that I cannot pursue here. See Clark (2008: 93–99) for a refutation of these objections.

system where human individuals are just one (special) component among several constituent parts. So, whatever turns out to be true about the implementational details of computational processing inside the head, Hutchins suggests we at least can be sure there are physical symbol systems, out in the world that is used by enculturated agents. Our use of these representations must certainly be accounted for.

In justifying his conceptual flip, Hutchins appeals to David Marr's classic levels of description for any information-processing system. A neuroscientist working on visual processing, Marr was concerned with how physical systems could accomplish computation. While there were many possible levels of description for any system, he identified three salient ones. Marr's dubbed his first level the computational level; a specification of what problem the system solves, and why it does it. This account must specify the constraints satisfied by the system's operation. Marr's second level, the representational or algorithmic, specifies the representations that are used and the algorithm by which representations are transformed; it must account for "logical organization of the structures that encode the information and the transformations by which the information is propagated through the system from input to output" (Hutchins, 1995: 50). The third level is the *implementational level*; the material substrate or architecture in which the algorithm and representational level is physically realized.

In the pen and paper example of long multiplication above, we see these three levels clearly coming into play (Magnus, 2007: 298–299). Computationally there are normative answers defined for the input of natural numbers during multiplication, the algorithm is specified by the stepwise transformations to be performed on the input and output, and the implementation is carried out using pen and paper (although exceptional individuals can execute the steps using only mental simulations). In the context of scientific practice, however, we can often simplify the scheme into a distinction between task, an abstract description of the computational goals the cognitive system must satisfy, and process, which specifies how this is accomplished and implemented (ibid.).

Studying these different levels of cognitive distribution in the wild required a descriptive enterprise for investigating the natural history of cognitive systems, to paraphrase Hutchins (1995: 371). He proposed

that ethnography was uniquely positioned to attend this new unit of analysis, which spanned beyond individual minds to the propagation of representational states through various representational media in larger interactive social systems, and even through historical time. A companion method to distributed cognition was therefore proposed. This "cognitive ethnography" would track, in the naturalistic contexts where cognition takes place, how events unfold in different communities of practice. Conceptualized this way, the ethnographer could literally "step into" cognitive systems to observe them in action.

The novelty of Hutchins' ethnographic project was using the *same* computational language that was usually reserved to describe internal, individual cognitive processes to account for what the anthropologist observed in the external world. Particularly, his own case study examined Western navigational practices in the US Navy as it was implemented in *pilotage*, determination of a ship's position relative to known geographic locations close to shore. He also compared such practices with the representational and algorithmic assumptions of Micronesian navigation, like celestial maps and other cultural resources and frames of reference employed in the famous *etak*-system. As a test case, navigation was well suited for analysis as these traditions. Despite variations on a common theme, all basically try to answer questions like "where am I, and how do I get to where I want to go?" In his comparison, Hutchins shows that even if two navigational systems basically solve the same computational problem, traditions can diverge profoundly in the representational assumptions that they bring to the problem-solving table. With respect to Marr's three levels of analysis *CitW* offered an ethnographic account of the second (representational) and third (implementational) levels of distributed cognitive systems. The reason for this is that any computational-level account is a formalized abstraction that is near impossible to convey in meaningful terms to an audience unfamiliar with the technical domain in question. So, while a computational-level account could theoretically be formalized for practices like navigation, many cognitive activities like those unfolding in the laboratory, are not sufficiently well-defined to be formally abstracted. In the ethnography of experimental science that follows, I will also keep the representational and implementational level centered.

This reconceptualization allows a reassessing of core assumptions about the minds and activities of enculturated agents, and to rethink what the source of this organization might be. Hutchins refers to this as "the attribution problem" (ibid.: 355). A byproduct of neglecting the cultural nature of cognition, the attribution problem may lead to an erroneous identification of boundaries in whatever intelligent system we are observing. Consequently, we may attribute the correct properties to the wrong system or, in the worst case, invent erroneous properties and spuriously attribute them to the wrong system. Distributed cognition therefore asks analysts to suspend judgment about the individual agent, and avoid over-attributing cognition to internal processes, so that one ends up with the wrong unit of analysis for explaining phenomena. Instead, we should first ensure that the phenomena under investigation are not caused by sociocultural practices which orchestrate interactions of brain, body, and culturally organized environments to produce higher level cognition (Hutchins, 2008).

Applying this externalist perspective to cultural systems, three features about cognitive processes come into view. First, cognition can be distributed across a social group. Secondly, cognitive processes may extend beyond the skin into the world so that internal and external structures, including materials like cultural artifacts and bodies, co-produce cognitive outcomes. Third, cognitive tasks can be distributed through time so that earlier events may transform later events (such as by propagation of media that encode representations). Consequentially, even a complete theory of internal processes cannot give us a complete account of many cognitive phenomena, since their dynamics are historically and socially contingent.

These three features have consequences for how we define the unit of analysis and the range of phenomena that can legitimately be invoked in accounts of cognitive processes. When applied to the cognitive life of experimental systems in laboratory science, as I do in the following, they also reveal intriguing features about the role of epistemic resources like artifacts and instruments in the production of knowledge. Hutchins calls such instances of material culture "cognitive artifacts" (1999), and in the laboratory they play a critical role in mediating scientific cognition by improving the informational environment of agents using them.

Cognitive artifacts are instances of material culture that are engineered to function as representational media, not simply by amplifying the cognitive powers of users, but often by transforming how tasks get accomplished. By crystallizing cultural knowledge and practices in physical structure, cognitive artifacts constrain action and embody invariant features of the world. Such artifacts range from a simple string tied around the finger for remembering, to lists tables and formulae, as well as specialized scientific diagrams and other tools. Even structures assembled for entirely different purposes may acquire cognitive functionality when humans interact with their environments and other agents in opportunistic ways. In subsequent chapters, we shall encounter a range of ethnographic examples that highlight the epistemic functions of diverse cognitive artifacts in the laboratory.

Related Germinations

The intellectual roots of distributed cognition are diverse. Hutchins points out that *Mind in Society*, a work spelling out the cultural-historical activity theory of Russian psychologist Lev Vygotsky, was published for an English audience in 1978 (Hutchins, 2001). Seven years later, American computer-scientist Marvin Minsky published his *Society of Mind*, a book title mirroring Vygotsky's. While Minsky used the language of social groups to account for what happens in the mind, Vygotsky's used the language of mind to account for the properties of social groups. For Hutchins, the timing of these two works suggested that "something special might be happening in systems of distributed processing" (ibid.: 2068).

There were other precursors, too. In 1964, the anthropologist John Milton Roberts published an essay on "The self-management of cultures," comparing patterns of informational management among four Native American groups. Roberts suggested that political and social organization in these groups could be conceptualized as information economies, where information could be received, created, stored, retrieved, transmitted, utilized, and lost (1964). Another precursor to the distributed view can be found in Gregory Bateson's notion of an

"ecology of mind," who saw informational loops extending from the mind, through the body and the environment, informed by the nascent field of cybernetics (1972).

Other germinations are found in "connectionism"; an influential approach to modelling intelligent systems in terms of artificial neural networks, developed by the UC San Diego-based Parallel Distributed Processing Research Group beginning around 1980. Here, simplified models of natural neural systems were constructed from the weighted interconnections among units (analogous with neurons and synapses). By using weighted connections, it was possible to study the effects of synapses that link up neurons through differentiated activation patterns across processing units. In *Culture and Inference: A Trobriand Case Study*, Hutchins applied connectionist concepts to analyze land litigation among Trobriand Islanders (1980). Drawing on fieldwork data, Hutchins showed how reasoning in land litigation was derived from propositions about land tenure. Natives used these propositions to make inferences to new disputes via a set of transfer formulas. Comparing these reasoning strategies with Western thought styles Hutchins found that similar logical principles governed both. Connectionism was also embraced by the Cultural Models school in psychological anthropology, as a basis for how cognitive schemas could be constructed, operated, and interrelated (see Quinn, 2011). These ideas were also adopted by Maurice Bloch, in an influential critique of conflations between language and culture among anthropologists, and a failure to adequately distinguish between implicit and explicit knowledge in accounts of social behavior (1991).

Also foreshadowing a distributed approach, were the ideas of experimental psychologist James Gibson (2014), who developed an idiosyncratic "ecological" approach to a vision where perception was considered a form of action, rather than a passive process (see Shapiro, 2011 for an assessment). Human perceptual systems, in Gibson's view, derived all necessary information from invariants in the agent's environment, which could be utilized directly as a sufficient basis for action, without internal representations. This approach of "direct realism" clashed with foundational ideas about information processing in early cognitive science. Gibson's embodied account complemented that of philosopher-scientist Michael Polanyi, who popularized the importance of tacit, implicit

knowledge in human experience, in contrast to propositional, explicit knowledge (Polanyi, 2005). In a telling example, Polanyi invokes the image of a junior physician learning to read x-ray pictures. A competent reader of x-ray imagery possesses perceptual and conceptual skills that are difficult to articulate verbally, but which afford the ability to see phenomena that others cannot (ibid.: 106). Elaborating on this theme, Pierre Bourdieu later developed his theory of practice around the idea that tacit competencies were unevenly distributed among members of various strata of society (1977).

Classical computationalism was also challenged by embodied accounts of knowledge emerging from phenomenological philosophy, which gained some prominence in anthropology (Csordas, 1990). Maurice Merleau-Ponty's phenomenology, for instance, inspired an influential critique of "standard" cognitive science based on the observation that cognition happens in the intersection between body and world, where bodies are both lived experiential structures and the milieu of cognitive processes (Varela et al., 1993: xvi). Like Gibson's, this body of work stressed the entanglements between perception and action through "enaction," motor activity and a suite of structural couplings and emergent dynamics between organisms and environment. Combining Gibson's ecological approach, phenomenology, and theories on embodiment, Tim Ingold further developed an "anti-representational" anthropology of knowledge (2000). In contrast to standard accounts in psychological anthropology, Ingold suggested that perception and action should not be seen as *culturally mediated*. Instead, he argued that humans perceive the world in a direct relationship, by moving about and making use of its many affordances through active, situated, and skilled engagement. This placed Ingold in the odd position of being both an "anti-cognitivist" and an "anti-culturalist."[8]

Hutchins' work on distributed cognition also developed in parallel with an influential "embodiment" thesis about language use and meaning construction, as a response to Chomsky's generative program (see Fauconnier, 2006 for an overview). This work in "cognitive linguistics"

[8]Tim Ingold's dismissal of representations makes his framework ill-suited for more detailed interactional analyzes of action. In science there is abundant interplay between internal and external representations.

tackled a diverse range of representational phenomena, based on the view that cultural meanings arise from, and are conceptually constrained by, the kind of bodies we possess as corporeal human beings. I return to the relationship between distributed cognition and embodied meaning construction in Chapters 6 and 7.

Other scholars turned to material culture. Drawing out the implications of Gibson's notion of affordance in new directions, cognitive scientist and designer Donald A. Norman investigated the cognitive consequences of artifacts, and the role of representational technologies in social systems (1992).[9] In opposition to the intracranialist orthodoxy, the philosopher Daniel Dennett also articulated an influential "transcranialist" position (1996). Minds, as he writes, are "composed of tools for thinking that we not only obtain from the wider social world, but largely leave in the world, instead of cluttering up our brains with them" (Dennett, 2000).

Another widely discussed conjecture on the constitutive role of external resources for cognition was offered by Andy Clark and David Chalmers in "The Extended Mind" (1998). Rather than empirical demonstration, Clark and Chalmers provided a thought experiment involving Inga, a woman with normal cognitive function, and the Alzheimer-impaired Otto, who meticulously kept his memories in a notebook. Here, they argued for dissolving artificial boundaries between internal and external cognitive processes, based on a principle of parity: "If, as we confront some task, a part of the world functions as a process which, *were it done in the head*, we would have no hesitation in recognizing as part of the cognitive process, then that part of the world *is* (so we claim), part of the cognitive process" (1998: 8).

Later, Clark introduced the "principle of ecological assembly" (PEA). The PEA, which we will revisit later, says that when cognitive agents are facing a task, they will recruit problem-solving resources eclectically and indiscriminately to achieve an acceptable result, with minimal effort (Clark, 2008: 13). It does not really matter whether these resources are neural, bodily, social, or environmental. The important thing is that our

[9]Norman founded the Department of Cognitive Science at UCSD, an intellectual ground zero for several key works in this tradition.

inner environment aligns with designed portions of our external environments. A tool-using cognizer must be sufficiently intelligent to recognize and use different tools, which in turn endow users with powers that were unavailable before the tools came into use.

Here, it should be noted that Hutchins' idea of distributed cognition and Clark's notion of extended mind significantly overlap, but that some differences in emphasis are worthwhile to unpack here. First of all, distributed cognition *is not a theory of a special type of cognition*, but a *framework for the study of all kinds of cognitive processes*. These may span from low-level neural processes, up to entire sociocultural assemblages that develop over large timespans, such as languages, writing systems, or other representational technologies. It tackles questions about the elements involved in producing cognition, in addition to developing hypotheses about the relation and interactions between elements. Distinctions between distributed cognition and the extended mind primarily concern the emphasis placed on the role of cultural transmission for the constitution of cognition, as well as demarcations of the scale and units of analysis (Hutchins, 2011). Hutchins suggests we may consider "extended mind" as a specific hypothesis nested within distributed cognition, with the latter being a more overarching framework for dissecting cognitive phenomena. Accordingly, the extended mind picks out "a particular class of distributed cognitive systems that operate on a spatial scale somewhat larger than an individual person," and on a "temporal scale typically completing operational cycles on the order of seconds or minutes" (2014: 37). At this mid-level scale, resources internal to an individual are coordinated and coupled with external elements in an agent's close social and material environment to produce certain cognitive outcomes. Clark calls these proximate interactions "ecological assemblies," while Hutchins prefers the term "functional system". However, distributed cognition does not only aim to account for cognitive events in an individual's immediate surroundings, but also to characterize cultural ecosystems at larger spatial and temporal scales. While extended mind hypothesize that there is usually a center for cognitive activity, distributed cognition does not presume a focal point in the traffic of representations a priori. The distributed view simply states that questions about the legitimate boundaries for cognitive systems must

be determined empirically, based on the density in the propagation of representations between elements that make up the system.

Differences in explanatory scope notwithstanding, both frameworks remain agnostic about the constitutive role of internal representations (i.e., sequences of abstract symbols) in human cognition, or whether our faculties are better described as products of connectionist networks and other dynamical systems (Rupert, 2009). For example, Hutchins considers the thesis on "modularity of mind," which emphasizes certain types of cognition as products of evolved biological structures with specific functional circuits dedicated to information processing for particular domains, to be a "clear example of taking the distributed cognition perspective" (2014: 37). Likewise, the architects of extended mind consider the hypothesis to be "compatible with both connectionist and classical views, with computational and non-computational approaches, and even with internalism and externalism in the traditional debates over mental content" (Clark, 2008: xv–xvi). But while Hutchins is explicitly convinced that "humans actually process internal representations of symbols," he does not accept that "symbol manipulation is *the* architecture of human cognition" (Hutchins, 1995: 370, my emphasis). This agnosticism about the implementational-level details is partly methodological. Cognitive ethnography is based on the principle that it is difficult to infer lower level constituent processes from higher level, emergent phenomena by observing cognition in the wild. Rather, the framework redresses an artifact of intellectual history, where symbol processing was assumed to be inside because "we took the computer as our model of mentality" (ibid.).

To summarize, the works surveyed here make up a diverse research agenda for exploring cognitive phenomena, guided by far broader ontological commitments than classical approaches (Shapiro, 2011). Drawing on a helpful typology by Robbins (2009), the gist of these claims can be outlined as follows. First, cognition does not just depend on the brain, but also the body in terms of causality and constitution (*embodiment*). Secondly, cognition routinely recruits structures in the environment (*embedding*). And third, cognition extends beyond the individual organism (*extension*). The goal of extending computational

processes into the material and cultural environment, is not to establish a *unified* theory of cognition. Rather, the hope that we can "sift the wheat of computation from the chaff of individualism" (Wilson & Clark, 2009: 61). Let us now see how this is relevant for the ethnographic study of scientific practices.

Connecting Cognition, Materiality, and the Social in Studies of Scientific Practice

Inquiry into the nature of scientific knowledge obviously has deep philosophical roots. In cognitive science, the study of scientific reasoning was launched by Herbert Simon, an early pioneer who envisioned that artificial intelligence could help explore the process of scientific discovery as a model for understanding human reasoning in general (see: Giere, 2008). But although Simon's ambitions to unveil the true nature of scientific reasoning through AI was unsuccessful, it spawned numerous studies on the cognitive dimensions of science, spanning topics like models and visual representations, reasoning, judgment, and conceptual change. These efforts resonated with Willard O. Quine's program of "naturalized epistemology," an attempt to bring philosophy and the empirical sciences into a close dialogue about the nature of human knowledge (Godfrey-Smith, 2009: 150–151). A similar ambition was visible in Kuhn's work on the nature of conceptual change in science (2012), which also grappled with the interplay between conceptual representation and perception (Kaiser, 2016; Nersessian, 2003).

One challenge for realizing Quine's program today is that cognitive and social studies of science is regularly conducted in relative isolation from each other. As Nersessian observes, such studies tend to "line up on either side of a perceived divide between cultural factors and cognitive factors in knowledge construction, evaluation, and transmission" (2006: 125). On one hand, cultural explanations of scientific development seem to black box cognitive dimensions. One the other, cognitive studies seldom make cultural factors an integrated part of the analysis, despite paying lip service to their importance. But any incongruity between these perspectives is illusionary and artificial.

One promising route to productively integrate cognitive and social studies of scientific practice, lies in the application of distributed cognition. This is not a new proposal. Ronald Giere, for example, has clarified the epistemological basis of a distributed account of science (see Giere, 2010 for a summary), while Nersessian and colleagues have operationalized the framework in historical case studies of physics and long-term ethnographic engagements with biological laboratories (see Chandrasekharan & Nersessian, 2015 for a recent interpretation). Additionally, there have been productive exchanges about the explanatory value of such applications (Brown, 2011; Magnus, 2007; Magnus & McClamrock, 2014; Toon, 2013; Vaesen, 2011). Approaching this subject matter from the view of anthropological linguistics and interactional analysis, Charles Goodwin has also studied the multimodal, communal character of scientific practices (Goodwin, 1994, 1995). Pushing this sort of interactional analysis in novel directions, Morana Alač mobilized distributed cognition for a series of ethnographic laboratory studies that show how works on fMRI scans acquire meaning in the hands of experts through embodied, social, and material interaction with scientific visuals (2011).

In addition to these attempts at respecifying cognition as action, there have also been efforts to carve out an anthropologically informed account of scientific practice that synthesizes the distributed framework with theories about evolved cognitive faculties (Heintz, 2004, 2007). Through case studies from the history of mathematics, Heintz develops an "integrated causal model" that combine theoretical tools from cognitive science with a naturalistic approach adopted from the Strong Program in the sociology of science. To move beyond the impasses of past debates about rationality, Heintz points to the human ability to engage in meta-representation. The production and use of *representations of representations*, he argues, is central for creating new scientific knowledge and conceptual change. Being an evolved disposition that all humans share, he proposes that meta-representations are critical for the evolution of distributed cognitive systems in science, as they enable humans to assess the epistemic status of the output from any innate cognitive dispositions. In this view, scientific culture is predicated on vigilant reasoning about one's intuitions and beliefs about phenomena. Scientists accomplish such

reasoning by propagating representations that arise from modular minds across diverse social and material loops. This distributes and transforms information beyond what Clark calls the "biological skin-bag" (2003: 5).

For Heintz, a satisfying description of science must consider both its social embeddedness and other cognitive constraints. Advocating a strong version of the "continuity hypothesis" about the relation between everyday thought and scientific reasoning, Heintz suggests that it is not possible to identify an absolute criterion for demarcation (2004: 396). Science in this respect, builds and depends on "common sense" or "human meta-culture," which is "innately grounded, and species-specific, apprehensions of the spatiotemporal, geometrical, chromatic, chemical and organic world in which we, and all other human beings, live our usual lives" (Atran, 1990: 2). Still, as underscored by ethnobiologist Roy Ellen, scientific knowledge is nonetheless both more efficacious than common sense, and enjoys a very different status, so that the assertion that it is "no more than common sense in a specialized institutional setting" comes close to saying nothing at all (2004: 432). Clearly, science is different from common sense. But how? From an anthropological perspective, the answer is twofold. First, the transformational powers of science are derived from institutionalized mechanisms for meaning-making through the "establishment, shaping and maintenance of intersubjectivity" in a community of practice (ibid.: 433). Secondly, scientific cultures do not only belong to the realm of ideas but encompass a range of material practices. The significance of materiality for scientific cognition is especially visible when we enter the experimental laboratory.

Beginning in the 1980s the field of science studies, broadly construed, underwent a "post-Kuhnian move away from the hegemony of theory" (Rheinberger, 1997: 1). One contribution was Ian Hacking's "Taxonomy of elements," a conjecture about the interplay between ideas, things, and marks in laboratory practice (1992). In this context, Hacking refers to fields that partially create the very phenomena they scrutinize, which "seldom or never occur in a pure state" and whose interference require isolated instruments (ibid.: 32) (Table 1.1).

Two aspects of Hacking's typology deserve brief comment. First, his elements do not include people, nor the building the experiment takes place in, and institutions. Neither does it account for authors

Table 1.1 Elements of laboratory practice, summarized after Ian Hacking (1992)

IDEAS	
1. Questions	Research questions of all kinds
2. Background knowledge	Seldom systematized but taken for granted both in the experimental process and in the write-up of results. Fuzzy boundary with 4 and 5
3. Systematic theory	High-level theory does not have direct experimental consequences and is seldomly revised on basis of experimental outcomes
4. Topical hypotheses	What physicists call "phenomenology." Connects systematic theories to observations within the experiment. More open to revision than systematic theory
5. Modelling of apparatus	Theories and background knowledge about instruments and equipment. Seldom equivalent to what is being pursued in the experiment
THINGS	
6. Target	Preparations and modification of the object of investigation; a tissue section, modification of cell with a foreign substance, and so forth
7. Source of modification	The apparatus that interacts with a target, such as a biological molecule delivered by microinjection
8. Detectors	The thing that measures the interference or modification of the target, like a DNA sequencing machine or similar instrument
9. Tools	"Humble things" that experimenters rely upon; off-the-shelf devices like micropipettes, test tubes, et cetera. Context-dependent and overlaps with 8
10. Data generators	The thing that counts; generators transfer representations of one kind into a different medium. May overlap with 8
MARKS	
11. Data	Outputs from detectors and data generators; not yet interpreted inscriptions. Some call this "raw data"; others say these are already interpreted and perspectival

(continued)

Table 1.1 (continued)

12. Data assessment	The first of three kinds of data processing; calculations of probable errors and other supposedly theory-neutral statistical techniques
13. Data reduction	Large quantities of unintelligible data requiring transformations to be meaningful
14. Data analysis	Events under scrutiny can be chosen, analyzed, and presented computationally. These are not theory-neutral statistical techniques, but relate to 1, 4, and 5
15. Data interpretation	Requires background knowledge combined with 3, 4, and 5

and audiences of scientific works, and issues of power. It is simply a typology over the "internal" epistemic resources found in experimental practices. External resources used to promote experimental results, or those involved in the politics of funding and allocating research priorities, have no place in the typology. Hacking thus defends the "conservative" internal–external heuristic in science studies (ibid.: 51). He does so against those who would argue that *stabilization* of a given result only becomes fact when the internal resources of experiment and laboratory get recruited into an alliance with external ones. Secondly, although Hacking considers these configurations to be epistemically "self-vindicating," the scheme does not deny the possibility of mission-oriented science, where techniques and devices developed in the laboratory move outside its boundaries for practical applications. Self-vindication simply implies that laboratory sciences become epistemically stable and consistently true to phenomena as theories and instruments become mutually adjusted to each other.

A problem with Hacking's inventory is that it does not tell us much about the structure of how these fifteen elements interact in a vibrant laboratory environment. In Hasok Chang's words: "It is as if he gave us the vocabulary of scientific practice, without a grammar to go with it" (2014: 69). Aspects of this grammar can be found in Hans-Jörg Rheinberger's work, who invoked the concept of "experimental systems," the basic unit of activity that propels the growth of knowledge in bioscience (1997, 2010). Here, experimental systems are driven forward by the

interplay between two elements. The elusive, unknown objects of scientific inquiry are "epistemic things," which result from a choreography of "technical things," the stable context of experimental work that includes instruments, laboratory techniques, concepts, and social resources.

An emphasis on experimental systems as the prime loci of epistemic action presents us with a view on scientific practice that deeply resonates with a distributed account of science and its attention to the role of material culture in cognitive processes (see Rheinberger, 2010: XVI). In this book, my goal is *to explicitly flesh out the implications of taking the distributed view on these units of knowledge production*. By looking ethnographically at how experimental systems, as complex cultural-cognitive ecologies, come to life, we may truly integrate social and cognitive understandings of science. Since no discipline has yet taken full ownership of the cognitive life of epistemic things, their character remains relatively unknown, with ample room for novel contributions. While historiographic accounts of experimental systems must contend with mapping the epistemic properties of a given system in retrospect based on written source materials (Rheinberger, 1997: 223), cognitive ethnographies of scientific practice allow us to collect data on the epistemic character of embodied interactions and material engagements in approximately real time.

We can now see more clearly that the gap between the social, cognitive, and material is not insurmountable. This task is also greatly helped by the fact that historian-philosophers like Rheinberger and Hacking have *implicitly* framed their descriptions of experimental science in accordance with principles from distributed cognition, thereby facilitating an integrative project. Hacking, as we saw, conceptualized laboratories as input–output devices which transform, reconfigure, and coordinate ideas, things, and marks. Similarly, Rheinberger emphasizes the constraining power of experimental systems. Rather than seeing experimental outcomes as byproducts of internal cognitive processes at work in the experimenter's brain, experimental systems provide a "space of representation," which scientists can use to "think with" (1997: 105). Giere's notion of "scientific perspectivism," which takes the outputs of scientific instruments to be fundamentally perspectival, further extends this line of reasoning (Giere, 2010). Accordingly, much scientific observation and

reasoning is only possible due to the support of material and conceptual aids, like models and theories. These afford scientists with an ability to manipulate phenomena of interest. Such a "laminated picture" of an intercalation between theory, experiment, and instrumentation also stand out from Galison's work on subcultures in physics (1997: 138).

Conceptualizations of scientific knowledge production as a kind of distributed cognition also appears elsewhere in science studies. In *Epistemic Cultures*, for example, Knorr-Cetina explicitly invokes a vocabulary similar to Hutchins' at least six times in her account of knowledge-making in high-energy physics and molecular biology (1999: 25, 165, 174, 179, 180, 242). On two occasions she employs the qualifiers "sort of," and "something like" to convey how material artifacts aid scientific work. Additionally, she introduces the concept of the "laboratope" (ibid.: 278), an artificial environment where knowledge evolves. This analytical unit is similar to what Hutchins' later described as "cognitive-cultural ecosystems," systems of constraint satisfaction that settle into a subset of possible configurations through stable, coherent practices (Hutchins, 2014).

It is, however, hard to assess whether Knorr-Cetina considers knowledge production in these fields to be *literally* distributed and extended, or whether she intends a deflated, *metaphorical* reading (Giere, 2002). Her interpretation is also problematic from the perspective of distributed cognition. For instance, Knorr-Cetina appears to claim that epistemic processes in molecular biology primarily occur at the level of individual subjects, while reserving truly distributed knowledge-making to what happens in the large experiments of high-energy physicists at CERN. However, an analysis in terms of distributed cognition would consider a single molecular biologist interacting with spreadsheets or pen and paper to calculate reagents, just as much a product of a distributed cultural-cognitive ecosystem as the epistemic labor of thousands of physicists around the globe, collaborating on a particle detector. The difference lies in the *density* of connections between elements in the distributed system, which must be specified by asking what information goes where, when, and in what form. Distributed cognition, in other words, implies that cognitive resources are *literally* distributed among the elements in a

cultural-cognitive ecosystem. Instead of specifying the traffic of representations involved, Knorr-Cetina instead invokes Durkheim's notion of "collective consciousness" to carry the explanatory burden of how knowledge comes to life.

Cognitive Bloat and the Question of Agency

If the cognitive anthropology of scientific knowledge must be widened to include material culture and situated practice, as I have proposed, what does this imply for our conception of individual agents as knowing subjects? There is no shortage of studies on technoscience that propose a rethink of rationalist intuitions about the loci of agency, by radically moving beyond anthropocentric analyzes and achieve analytical symmetry by equally weighing contributions from human and nonhuman entities in shaping epistemic outcomes. Andrew Pickering, for example, has articulated a position "where science and technology are contexts in which human agents conspicuously do not call all the shots" (1993: 562). His account seeks to move away from an understanding of science as primarily a *representational* activity. Instead, Pickering encourages us to think about the world encountered by scientists as one filled with agency, and not primarily littered with representations like facts and observations. In this view, our world is continuously doing things (he invokes weather as an analogy), and science extends how humans cope with this agency, by enlisting a wide variety of tools and other resources.

Pickering sketches two main positions on how to conceptualize agency for science studies. One is the fundamentally *asymmetrical* position that considers scientists to be agents who provide accounts of material agency in the world, like physical laws, biological mechanisms and so forth. These scientific accounts can then be studied as products of human activity. Alternatively, it is possible to tackle material agency itself. But this puts scholars of science studies in a position where they must defer analytic authority to the natural sciences to explain how material agency *really* works. These are the stock positions of traditional humanist approaches, both pragmatist and symbolic interactionist, as well as

interest theories, including certain flavors of the "Strong Program" in the sociology of science.

Alternatively, Pickering suggests a more semiotically performative conception of agency that may engender analytical symmetry between human and nonhumans, that could help us move beyond representationalism. But this is problematic. Although it would take material agency seriously by factoring in the performance of technical apparatuses in the material world, it risks a retreat to an image of "science-as-representation." This can be avoided, says Pickering, by looking at material agency as being "temporally emergent" in practice. Scientists cannot know how the material agency will behave and must develop devices to probe it by "tuning" into signals that cannot be known in advance. Also, to avoid "whiggish" accounts of science we should only draw on those epistemic resources that are available to the scientists themselves. Here, Pickering appears to make the strong claim that those who aim for a real-time understanding of science as practice, are on an equal footing with respect to the material agency of nature, like the scientists we study. According to Pickering, the latter does not (when working in the present), have the benefit of hindsight about what will, after all, be established as facts by future research (1993: 563). A second problem with the performative semiotic conception of agency, is the sticking point of intentionality. While humans have intentionality, most nonhumans, apart from some higher animals, do not. There is no material counterpart to intentionality, notes Pickering, but the intentional structure of human agency is always, like material agency, emergent from real-time activity where a dialectic of resistance and accommodation between the material and human creates a "mangle of practice."

Scientists cannot know in advance whether their attempts at intervening and understanding the world will succeed or fail, and it is only through trial and error, unfolding over time, that the "contours" of this agency can be known. For Pickering, this is not a technological determinist view of science, where material agency "forces itself upon scientists" (1993: 577). Instead, such resistances co-exist alongside human goals and plans. Resistances in science thus have a hybrid quality, irreducible to neither material agency nor human agency. This

"mangle" pulls material agency into the pathway of human agency, structuring it so that in effect neither material nor human agency has "its own pure dynamics" in the co-production of knowledge. According to Pickering, scientific activities link up existing cultural practice with future goals, but he does not want to say the relation is mechanical or causal. When human scientists accommodate material agency, they must revise intentions, plans, and goals. This becomes, in Pickering's terminology, a "dance of agency" between the materiality of nature, apparatuses, theories, models, and techniques. Similar conceptions of agency can, with differences in emphasis, be found in the works of Bruno Latour (1999b). Also here is agency considered a network effect of heterogenous associations between humans and nonhumans, one that is very different from the kind of "causal agency" that gets exercised when a physical entity affects the scientist's sense organs by refracting light through a microscope, for example (see, for instance, the exchange by Bloor, 1999a, 1999b; Latour, 1999a).

From the perspective of distributed cognition, these radical attempts at destabilizing the human agent operate on a level of abstraction that leaves out critical information about the sociology of interaction, microstructures of representational cascades, and the relevant cognitive divisions of labor among scientists. Details about these matters would be necessary to flesh out true examples of nonhuman agency in science. Latour, for example, argues against separating the mental from the material environment in ways that *appears* to harmonize with a distributed perspective (see J. D. Keller et al., 1996). But for Latour, it seems that if cognitive processes can somehow be identified outside of the embodied brain, then they cannot be inside at all. So rather than reconsidering the boundaries of the unit for cognitive analysis, Latour wants to sweep clean the psychological agency of human actors in its entirety. From the perspective of distributed cognition, such a radical, "mind-blind" conclusion about the loci of agency does not follow. Human cognition certainly moves across the boundary of the skull, but this does not mean that what occurs on the inside is of no importance to understand the traffic outside. Neither Pickering nor Latour offers the reader detailed empirical descriptions of how artifacts and other nonhuman entities can exercise "agential" behaviors in the absence of human interaction. For instance, nowhere in

their accounts do nonhuman entities appear to intentionally change the informational character of the environment, like epistemically minded flesh-and-blood scientists try to do. In fact, even Pickering and Latour's analyzes appear to accommodate minor roles for human representational agency in their performative accounts, by acknowledging scientists as intentional agents that use language, plan, model, theorize, write, and so on. Humans therefore still appear to play a special role in the case studies of scientific knowledge production we are confronted with, since only humans appear to have a capacity for instigating certain classes of action.

In the debate on distributed and extended cognition the problem of locating agency outside the boundary of the human has primarily been framed around the issue known as "cognitive bloat." Cognitive bloat is an imagined consequence of the two-way coupling between brains and environment, in which everything people interact with somewhat absurdly becomes part of their mind. Bloat raises the challenge of identifying and demarcating functional relationships between human agents and their environment that imply true instances of cognitive extension. Fortunately, this challenge has been addressed by outlining a set of "trust and glue" conditions for what constitutes genuine examples of extended cognitive systems (Clark, 2008). These state that the resources in question must be reliably available and typically invoked (*availability*). Furthermore, retrieved information must be endorsed by default (*trust*), and easily accessible, as and when required (*accessibility*).

Distributed and extended cognition views humans as biological agents with a natural and cultural history that has endowed us with capacities for interaction with our environment that fulfill these conditions. Humans and other organisms have not just evolved through natural selection so they are better adapted to their environments, they also engineer their environments through a process of "niche construction" that can transform the effects of natural selection (Sterelny, 2004). Beaver dams provide a telling example of this process, as the environmental transformations carried out by beavers may have fitness consequences on their descendants. One form of agency that is intimately related to niche construction is *epistemic agency*; the capacity of certain biological agents to engineer their own environments to acquire information

that is not ready at hand. A predator that moves into elevated terrain to have a better view of its prey, while remaining partly hidden in the bushes, can be said to exercise a low-level form of epistemic agency (other animals may demonstrate more sophisticated forms). A human that writes down a shopping list on a post-it, and sticks it on the fridge as a reminder, exercises a higher level epistemic agency involving the use of an epistemic artifact as a mnemonic aid. Experimental systems in the laboratory scaffold more complex cases of such agency, as we shall see. While low-tech epistemic agency is ubiquitous among animals, humans rely on higher level epistemic agency, whereby they attempt to improve their informational environments and create meaningful representations by using sophisticated epistemic artifacts to represent the world in ways nonhumans do not (Sterelny, 2004: 240).

Here, another asymmetry between humans and nonhumans come into view, namely, our ability to engage in trusting relationships with both conspecifics and nonhuman entities. In accordance with Clark's "trust and glue" conditions for cognitive extension, Heintz points out that trust is the "cement" of distributed cognitive systems in science (2007: 319). Representations about what are trustworthy components in an open-ended endeavor like scientific research is what keeps these extended cognitive systems together (Miller & Freiman, 2020). Changes in representations about who or what is trustworthy with respect to knowledge acquisition, what Wagenknecht dubs "epistemic trust" (2015: 162), can subsequently change the division of labor in the cognitive system. Such trusting relations with nonhumans are expressed through everyday statements like "the qPCR-machine gave accurate readings," and "the electrophoresis yielded positive results." In Chapters 3 and 4, we shall see how a gradual development of a new experimental system depended on the research community learning to trust the epistemic outcomes of new apparatus and techniques, while cultivating epistemic vigilance as good scientists.

By prematurely extending agency to all kinds of nonhuman entities we risk obscuring fundamental cognitive asymmetries between humans and other entities, such as the capacity to engage in representational activities for epistemic reasons, and to form trusting relations. Instead, we should refine our accounts of how the material cultures of situated practice

support the propagation and transformation of representations. Cognitive ethnography is uniquely suitable for this task, and can help us go beyond the limitations of framing of science through social-reductionist categories (Creager, 2002: 319–320). The view I advocate here thus acknowledges the contributions of nonhuman entities to scientific practice, as the difference between human and material agency is surely one of degree, not kind. But I reject a more radical metaphysical interpretation, to maintain human exceptionalism for certain representational activities (which humans, as far as we know, alone are capable of). The proposal to build an entirely new metaphysics of agency is simply unattractive, and a gambit for which there is little empirical support. It entails adopting metaphysical commitments whose epistemic costs for science studies are simply too great to justify (Giere, 2004, 2007).

Instead, I argue that humans are central as semiotic and epistemic agents in distributed cognitive systems. A true understanding of what is internal to the epistemic agent hinges on first specifying the computational and representational work that is being performed on the outside. Scientific knowledge production, then, should be considered a continuous process of representation and re-representation, where material artifacts participate in the traffic of cognitive representations across various material media in an open-ended process of meaning-making. By focusing on how scientists use tools and social structures outside the epidermis of skin and skull, we may, to paraphrase historian Jürgen Renn, avoid playing off against each other the cognitive, social, and material dimensions of science (2015: 39).

Justification for adopting a distributed perspective on experimental systems comes from its empirical and theoretical productivity, and not from pressing metaphysical needs to revise what we mean by an agent. If necessary, we can carve a space for material agency as a relational property by following the tempered advice of Malafouris, who advises us to not insist on asking *what* an agent is, but rather *when* an agent is (2013: 147–148). By viewing the world as activity-centered and not intrinsically human-centered, we can see scientific practices as projects for material engagement between people and things, without losing sight of cognitive accomplishments. In this view, agency becomes a "relational and emergent" product of material engagement with the world (ibid.).

This is supported by a simple fact. Ours is a species that scaffold its own thinking and meaning construction in unimaginably ingenious and recursive ways. As astutely observed by Andy Clark, we are not only self-engineering better worlds to think in, but also design worlds in which to build better environments in which to think, filling them with ever better-thinking tools, using these to fine-tune our utensils even more, educate ourselves in their use, and further refine our cognitive tools by building even better environments to cultivate them even more (1998: 59).

Perhaps nowhere are such instances of cognitive and epistemic scaffolding through engagements with our material world more ubiquitous than in scientific laboratories. To make sense of the cultural practices of cognition in the molecular science of salmon lice the first step will be to examine the context from which these thinking tools emerged. We must ask why and how such organisms were domesticated in the laboratory as objects of research for experimental biologists.

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2

Salmon Lice: The Environmental History of a Troubled Relationship

In October 2013, the Sea Lice Research Centre at the University of Bergen received a batch of *Lepeoptheirus salmonis* (Krøyer) from a site in Northwestern Norway.[1] A salmon producer had shipped the ectoparasites to the wet laboratory at the Centre, fearing that the local lice population had developed reduced sensitivity to a chemical known as hydrogen peroxide (H_2O_2). The farmer wanted the Centre to experimentally verify observations made by the salmon pen by performing a controlled bioassay that compared the sampled strains against strains verified as H_2O_2-sensitive.

L. salmonis belongs among the copepods, a diverse subclass of crustaceans. The salmon louse is considered a menace to salmon welfare as it is specialized to feed on blood and mucus. When large numbers of lice feed on the same fish, its protective skin is weakened, which can

[1] In this text, "salmon louse" refers to *L. salmonis*. The term "sea lice" is occasionally confused with the thimble jellyfish (*Linuche unguiculata*), causing "sea bather's eruption." Colloquially, "sea lice" also refers to related copepod parasites infecting a variety of fish, such as *Caligus elongatus* ("skottelus," or "fiskelus"), *Caligus curtus* ("torskelus"), and *Caligus rogercresseyii*.

M. Solberg, *A Cognitive Ethnography of Knowledge and Material Culture*, Culture, Mind, and Society, https://doi.org/10.1007/978-3-030-72511-2_2

cause secondary infections and problems with osmoregulation. High lice levels are also considered a threat to migrating stocks of wild salmon in the fjords where these farms are located. Furthermore, salmon lice management is extremely costly, and many interventions have unwanted environmental consequences. In 2018, it was estimated that the price tag for treatments and prevention in Norway was around 5.2 billion NOK, making *L. salmonis* a contentious topic in public debates about the future of salmon farming.

In 2013, chemical delousing with hydrogen peroxide was one of the few tools sea farmers had at their disposal for emergency interventions when lice levels rose above the legal threshold of 0.5 adult female lice per fish on average. To the public, this substance is better known for its industrial applications as an antiseptic and bleaching agent, than its role in food production. Salmons are treated with this highly oxidative compound by being pumped into enclosed tanks in specially designed well boats from their marine pens. Here, the fish swims around in a H_2O_2 solution for a few minutes depending on the strength of the liquid, causing lice to fall off, before the fish is pumped back into its enclosure. Although the operation is costly, labor-intensive, and stressful for the fish, it would indeed be grave news for the industry, and for future fish health work, if the parasite had become resistant to yet another compound. Unfortunately, the bioassays performed by scientists at the Centre confirmed the farmer's suspicions about hydrogen peroxide resistance, and their conclusions were later independently verified by other researchers. There was conclusive evidence that natural selection had, again, caught up with human attempts at controlling the lice population, which now resisted another treatment in a rapidly depleting arsenal of therapeutics. While deeply concerning for salmon farmers, this was also an exciting opportunity for the biologists to better understand the genetics of drug resistance. The lice that arrived in the laboratory were therefore used to cultivate a new H_2O_2-resistant strain of salmon lice for experimental uses.

This chapter tells the story of how salmon lice ended up as an object of intense experimental scrutiny in the laboratory. To make sense of this we must situate the parasite within the environmental history of salmon domestication, and how the management of *L. salmonis* emerged as a

most critical challenge. In what follows, I first conceptualize parasitism, domestication, and the great acceleration of marine domestication. I then narrate some of the early experiments in Norwegian aquaculture, and the trajectory of its fish-farming industry in the postwar period. We then turn to the context of fish health biology as a subject for scientific management in Norway, and how salmon lice emerged as a critical issue for the farming industry. I end by outlining how scientific fish health management contributes to a deeply coevolutionary, interspecies process of domestication that takes place both in the sea and in the lab.

Parasites

The 6th Edition of the *Oxford Dictionary of Biology* defines parasitism as "an association in which one organism (*the parasite*) lives on (*exoparasitism*), or in (*endoparasitism*), the body of another (the *host*), from which it obtains its nutrients" (Martin & Hine, 2008). This non-mutual, antagonistic relationship is a driving force in the evolution of life's diversity on Earth. Estimates of biodiversity suggest that more of the planet's existing organisms have a parasitic, rather than non-parasitic, lifestyle.

Biological anthropologists consider parasitism to be a central feature in our species' past, and phylogenetic studies of primate parasitism provide indirect evidence to track the evolutionary and behavioral history of our hominem ancestors (Perry, 2014). Humanity most likely acquired most of our parasite interlocutors from close primate relatives, or from animals frequently accompanying us. But the agricultural revolution likely influenced the coevolution between humans and our parasite guests more than any proceeding event. Every domestication project undertaken by humans since has entailed the creation and maintenance of new precarious relationships with parasites. Globalization has further contributed to the exchange of parasites between people and places, with the Columbian Exchange being the most familiar example. The colonization of the Americas involved massive movements of parasitic organisms from east to west (McNeill, 2003). With increased mobility today, parasites frequently become our fellow travelers.

Husbandry changed human lifestyles in fundamental ways, introducing unparalleled proximity to animals, with ample opportunities for transmission of animal infections to human bodies, a process called *zoonosis*. Today, we are afflicted by hundreds of parasitic species, not counting behavioral parasites, commensals like rats, obligate parasites without metabolism (viruses), and bacteria. These range from relatively innocent everyday endoparasites, like the nematode helminth pinworm (*Enterobius vermicularis*) which is widespread in nursery schools around the world, to more mischievous creatures. One is the human botfly *Dermatobia hominis*, whose nauseating effects on human bodies can be seen in many YouTube videos. Not to mention the four species from the microscopic, malaria-causing *Plasmodium*-genus, and exoparasitic arachnids, such as ticks, carriers of Lyme disease. History also tells us that our primordial relationship with parasites has even affected the rise and fall of world empires (McNeill, 1976).

Here it is useful to draw a distinction between parasites that directly interferes with our bodies, neutral parasites that cause little nuisance, and those giving us trouble by infecting *other* species under our care, and whose welfare we are held morally accountable for. All domestication projects, including the taming of fish, inevitably means coping with parasitic interlocutors of some kind. Given that this is a story about the latter of these relationships, we will not be concerned with parasites that fulfil their energetic and reproductive requirements by tapping directly into human bodies. Rather, this is an account of parasitism "by proxy." It concerns the unforeseen challenges that arose when we attempted to master the Atlantic salmon along with its parasitic interlocutors, and how modern bioscience, with its potential to domesticate other life forms in the laboratory, was enrolled to solve a major problem with one of our most prized farm animals.

Domesticating Fish

What does it mean to say that a fish is domesticated? In her widely celebrated *The Natural History of Domesticated Animals*, Julie Clutton-Brock recalls Francis Galton's historical summary of "man's domination

and manipulation of the animal kingdom" (1999: 15–16). Writing in 1865, Galton offered six conditions for any species to qualify as "domesticable." First, young animals of the species must survive when reared away from the parents. Secondly, the animal must be adaptable to a dominance hierarchy that is compatible with human co-existence. Third, the animal must not be adapted for instant flight, so that it may feed and breed in confinement. Fourth, the animal must be useful for its human domesticators. Fifth, the animal must breed freely in captivity. Galton's sixth and final condition bundles several social traits: the animal must possess a reasonable temper and versatile feeding habits, prefer the company of conspecifics, and be amenable to human communication. Galton's list forcefully demonstrates that domestication, a process our species has been engaged in for over millennia (well over thirty thousand years in the case of dogs), is a profoundly biocultural process.

Although the inhabitants of Norway have intervened in salmonid life histories for hundreds of years, much older fish domesticates can be found in world history. In a survey of the existing archeological evidence, Nash suggests that Egyptians in the New Kingdom reared tilapia, a paraphyletic tribe of *Cichlidae*, in cultivation around 2500 BC, perhaps earlier (Nash, 2010). Chinese common carp culture, a major fraction of farmed fish today, dates to at least 2070 BC. Although Egyptian practices might precede Chinese carp production, others suggest this was a rudimentary form of "proto-aquaculture" since tilapia may not primarily have been used as a food source (Beveridge & Little, 2002). Other ancient precursors include pond culture with ceremonial and commercial functions for Sumerian temples, dating back to 2500 BC. Roman fish culture, known as *vivariae piscinae*, developed from Egyptian and Assyrian practices. European cultivation of freshwater fish, such as carp, can be traced back to at least thirteenth-century France (Hoffman, 1995).

When do human intervention by feeding, hatching of fertilized eggs, and enhancement of fish habitats constitute domestication proper? The deep history of fish domestication is contentious. Balon suggests that fish, like other animals, should fulfill five criteria to qualify as fully domesticated (2004). The fish must be valued and purposively kept, and breeding must be subject to human control. It must also display different

behaviors and phenotypic variations not found among wild conspecifics. Finally, the fish should not be able to survive without human intervention. Most cultured fish do not fulfil the fourth and fifth criteria, meaning that not even a purportedly "ancient" species like the Chinese carp qualify as true domesticates (ibid.: 4). Balon's conclusion is therefore that besides the common carp (*Cyprinus carpio*), only guppies (*Carassius auratus*) and neon tetra (*Paracheirodon innesi*) of modern aquarium culture are fully domesticated, arguably making "exploited captives" a more fitting term for encultured fish (ibid.: 21).

Although these conceptual distinctions offer clarity about the natural and cultural history of aquaculture, I remain agnostic about the value of defining strict criteria for qualifying salmon and other marine animals as *truly* domesticated. In a pragmatic spirit, I therefore frame salmon as "domesticated" in this book, seeing this as a dynamic process of mutual interaction and coordination between humans, cultured salmon, and parasites, unfolding over evolutionary time. This recognizes Darwin's key insight that the attributes and boundaries of species are never fixed essences. As with modern, enculturated humans, a wealth of selection pressures acts on the biology of farmed salmon, and the emergent outcomes of these interspecies dynamics cannot always be attributed to human intentions. As Lien has argued, telling "co-species histories" like that of salmon domestication through an anthropocentric master frame of human control is problematic when dealing with complex, non-linear human-environment systems (2015: 3). She suggests that rather than redefining or sharpening our definition of domestication, we should recognize that we are dealing with a perpetual process of interspecies interactions, better understood in terms like mutuality, uncertainty, and tinkering. As we shall see, the industrial adventure of Norwegian salmon farming is also a co-species story about the unintentional proliferation of parasites.

The Great Acceleration of Marine Domestication

London, 1883. Although the first signs of a pending impoverishment in marine fisheries were appearing, overfishing was not yet an immediate concern. It certainly did not stop visitors from around the world to convene for the International Fisheries Exhibition. Here, those with a vested interest in marine resources could marvel at the latest technologies for harvesting the oceans. Among the spectacles people could admire were also state-of-the-art systems to enculture fish. However, many prominent intellectuals, the notable Thomas Huxley included, considered farming the seas to be a waste of time. After all, oceanic fisheries knew no limits at this point (Nash, 2010: 70). The prediction that aquaculture would potentially outgrow the outputs of conventional fisheries about a century later would strike the audience at the Exhibition as delusional.

Aquaculture takes place both in freshwater on land, and in salty oceans. While there has been a doubling of production every ten years for the past five decades, the growth of domesticated aquatic species first became a planetary force of reckoning in the 1980s, as production of a limited number of species greatly intensified (McNeill, 2001). This trajectory coincided with the overexploitation of conventional fisheries which, although once considered virtually inexhaustible, are now producing near their maximum sustainable capacity (Naylor & Burke, 2005). Shrimp aquaculture offers a telling example of this story. Its growth has been so rapid that it serves as a proxy for coastal zone development in a collection of statistical trends showcasing the "Great Acceleration" of major Earth-systems in the Anthropocene, a geological epoch recognizing humanity's planetary impact (Steffen et al., 2015).

In their *State of World Fisheries and Aquaculture*, the FAO report that aquaculture continues to grow faster than any other sector of food production, although the growth rate is slower than in the 1990s (2019). In 2018, the share of aquaculture in the global production of capture fisheries and aquaculture, reached 46.8%, a profound growth from 25.7% in the year 2000. Some researchers even project that "the development of aquaculture is bound to replace fisheries as animal husbandry

replaced hunting on land" (Duarte et al., 2007: 383). Two millennia ago, humans domesticated roughly 90% of the total number of currently domesticized terrestrial species, with a modest 3% increase since the Industrial Revolution. In comparison, large-scale aquaculture is knowledge and technology intensive, and coincides with the industrial age. 97% of all aquatic species currently domesticated were cultivated after the twentieth century began, with over 100 new species being domesticized in the past two decades. This rate is approximately a hundred times faster than for terrestrial species, and aquaculture has seen greater success when considering the fraction of known species under domestication.

Due to slow growth, long lifespans, specialized diets, and unsuitable behavioral traits, few remaining terrestrial species have the potential for domestication. Many marine species, however, have evolutionary affordances that makes them salient, as they can be bred for greater yield, with shorter generation times than terrestrial domesticates. Many fish, for example, have low levels of parental investment in their offspring after eggs have hatched. Additionally, there is a variety of taxa and species to domesticate, adapted to a broader range of habitats. New species are therefore brought under human stewardship each year, with estimates suggesting that a new marine species now require around ten years of intensive research to be commercially exploitable. Given the significant challenges faced by land-based operations, such as competition for limited resources like territory and freshwater, forecasts predict that coastal and offshore mariculture will expand the most in coming decades (Gentry et al., 2017).

Salmon Farming and Salmon Lice

In Norway, where farming of high-value anadromous salmonid finfish has dominated, there have been heated public disputes about the costs of aquaculture. Sticking points include the potentially negative effects of salmon aquaculture on wild salmon stocks; disputes with conventional fisheries over coastal zone management; environmental pollutants and the challenge of sustainable feed production; and concerns about fish welfare (Aasetre & Vik, 2013; Lien, 2015; Rosenberg, 2008; Torrissen

et al., 2013). Disputes about the great acceleration of salmon aquaculture hinge on fundamental disagreements about the past and future distribution of environmental costs. Some believe diversification of domesticated marine species represents a positive contribution by ensuring heterogeneity in habitat and resource consumption compared to other kinds of husbandry (Duarte et al., 2009). Others argue that raising carnivorous finfish like salmonids, which consume nutrients that could be refined for human consumption, is akin to raising "tigers of the sea" (Naylor & Burke, 2005). Other again, see feed resources as well-managed, and argues that farmed salmon utilizes plant and animal resources so efficiently that it should be positively framed as a "super-chicken of the sea", given the increased global demand for animal protein (Torrissen et al., 2011).

On the assumption that Peak Oil is imminent before long, industrial fish farming in Norway has been rhetorically framed as the "New Oil" a pillar of the future economy of an expansive, oil-fueled welfare state. In one event, the Norwegian prime minister described salmon farming as "the Norwegian IKEA"; applying the frame of a successful industrial adventure based on mass-produced commodities to highlight its potential (NTB, 2015). Others have framed salmon as "the Norwegian Tesla"; a luxury, high-tech food product, that disrupts conventional food production (Berge, 2014). Given that increased levels of affluence have led to an increased protein demand, farmed salmon is also regularly framed as a contributor to the planet's food supply. Critics, however, counter that Norwegian salmon is a luxury commodity mainly targeting the affluent middle class. In this view, the expansion of aquaculture should prioritize more sustainable species, requiring less technological scaffolding and operating at a lower level in the food chain.

However, fish health problems caused by parasitic infections are arguably the most pressing challenge for Norwegian salmon aquaculture today. From a human health perspective, domestication of new aquatic species is relatively harmless compared to novel terrestrial animals; there are few concerns over potential zoonosis from aquatic animals due to the evolutionary distance that separates humans and aquatic organisms. But these new human–animal relationships present major challenges with

respect to the management of parasites in livestock production. Parasitic organisms threaten the welfare of animals in human custody, and parasites may also act as vectors for other pathogens. With the intensification of aquaculture, there is also a rise in the level of parasite infections, accompanied by increased expenditures on infection management and prophylaxis (Shinn et al., 2015). Although many kinds of pathogens have proven troublesome for the development of salmon aquaculture, the crustacean ectoparasite *Lepeoptheirus salmonis* has been an unrivalled cost driver. Anti-lice interventions, which require labor-intensive monitoring, prevention, and treatment have become exorbitant. Bath treatments with hydrogen peroxide, for example, involve high-risk operations with well boats, chemicals, manpower, and heavy machinery at sea.

Medicinal feeds, like SLICE, are simple to administer, but costly and vulnerable to evolutionary adaptations for reduced sensitivity. Cleaner fish (wrasse and lump suckers), which are added to pens to eat lice from fish, must be tended and cared for on their own terms, and an entire professional field of cleaner-fish services has emerged as market demands for new solutions have soared. Many mechanical delousing options are also available: from simple external physical shields ("skirts") that protect pens from free-floating lice in the water stream, to high-tech equipment like truck-sized mechanical devices that removes lice using lukewarm water, as well as laser-based automated delousing machines. Rotational fallowing of farming sites is also costly and time-consuming. Estimates suggest that around 10% of production costs are now allocated to mediating this parasitic relationship, and costs are rising.

While lice have become entangled with every imaginable aspect of salmon domestication in recent years, the parasite was historically seen as a quality hallmark on wild salmon. Since lice are not well-adapted to freshwater, the presence of lice suggested that a salmon specimen had recently come upriver from the ocean to spawn. A Danish-Norwegian bishop and naturalist, Erik Pontoppidan (1698–1763), provided one of the first accounts (see Berland & Margolis, 1983): "great schools of salmon moving from the sea into fresh water, partly to refresh themselves, and partly to rid themselves by rubbing and washing in the swift currents and waterfalls, of a kind of greenish vermin called 'Laxe-Luus,' attached between the fins, plaguing it in the heat of spring." *L. salmonis*

was scientifically described by the zoologist Henrik Nikolai Krøyer in 1837. Although known to cause damage if present in great numbers, salmon lice were not considered a major pest on wild fish before the dawn of salmon aquaculture. With highly host-specific preferences, the parasite is specialized to exploit salmonids. Since these are non-schooling fish out at sea, any potential host specimens would be few and far between. But when higher densities of salmon farms became commonplace along the Norwegian coastline in the 1970s, the availability of host salmonids changed fundamentally. The parasite became more abundant, and antiparasitic interventions of farmers changed its population dynamics.

Ectoparasites on fish face a range of challenges. As other parasites, they must locate a host, attach, stay in place over time, acquire nutrients, and reproduce. Parasitic lifecycles are complex, and understanding their developmental pathways is central for coping with parasitic relationships. Salmon lice belong to the copepods, a group of small crustaceans found in most aquatic habitats and is currently believed to have an eight-stage life cycle. The first three life stages, known as nauplius I, II, and the copepodid-stage, are planktonic, and spent searching for a host in the sea. During the third stage, the parasite, now roughly 0.7 mm long, infects salmonid fish. The five subsequent life stages are spent in a parasitic relationship with the host. During the fourth and fifth life stages, the parasite attaches to fish by employing a protein filament, and in the remaining three stages (preadult I, II, and as a fully adult lice) the parasite moves about on the host's surface, inflicting damage on the fish by feeding on mucus and blood. Female specimens produce egg-strings containing several hundred eggs at a rapid pace. At 10 °C it generally takes a female around 50 days to mature from an egg into an adult specimen (40 days for males). Sexually dimorphic, adult males average around 5–6 mm, and females between 8 and 18 mm. At this point, the parasite may cause skin wounds, thereby exposing the fish to bacterial and fungal infections. These lesions may, in turn, disturb the osmotic salt balance of the fish, and if the infection pressure become sufficient, the stress caused by pathogen loads may cause weight loss, reduced health and death.

L. salmonis has become a recurring matter of concern in public debates about the future of salmon farming, although the effects of this negative media coverage on market demand have likely been negligible (Liu et al., 2016). Some frames in these arguments reflect the normative expansion of our moral circle to include non-humans like farmed fish, including health and welfare concerns (Lund et al., 2007). Does the fish suffer, and what is an acceptable amount of suffering in livestock production? Other frames question the sustainability of using chemotherapeutants against pathogens and their side effects on marine ecosystems (Aasetre & Vik, 2013). Yet other conservation-laden frames emphasize the impact of lice on wild salmon due to the densities of current stocks of farmed salmon. Since the number of wild salmonids that migrate upriver along the Norwegian coast annually is minuscule in comparison with the millions of captive fish in pens, these frames highlight farms as pathogen reservoirs that can devastate wild stocks.

All these frames make assertions about how the costs of lice should be allocated. Consequentially, public debates about lice have become polarized around the question of how environmental externalities ought to be handled. Therefore, they also engender different solutions. Techno-optimistic and economizing frames, stressing the economic costs of lice as an unresolved, but a tractable problem, draws other implications for regulatory management than risk frames that conceptualizes lice as an environmental concern, or an animal welfare issue. Despite disagreements over the solutions, there is consensus across different frames that the "lice-problem" must be solved to realize the potential of a blue, post-oil national economy.

Early Experiments in Norwegian Aquaculture

To understand how lice profoundly shaped Norwegian salmon aquaculture, and became an intriguing object of experimental science, we must look at the origins of salmon farming. Where land-based animal husbandry could draw on thousands of years of cumulative knowledge, those who brought this newcomer to the farm had to start from scratch.

Atlantic salmon (*Salmo salar*) and trout (*Salmo trutto*) were prized resources along the Norwegian coastline and rivers, and were traded as smoked, cured, or freshly iced. Humans have long affected fish populations unintentionally, through fishery-driven selection pressures for the evolution of early sexual maturation and other life-history characteristics. In the case of salmonids, intentional interventions in their river lives began in 1853, after a royal decree by the Danish king in a period of dispute about rights and entitlement to river fisheries. The Norwegian ichthyologist Halvor H. Rasch (1805–1883) led the first hatchery efforts, practicing what we today recognize as applied biological research on the process of stroking fish for gametes and fertilizing the ova with sperm (Solhaug, 1976: 548). By fertilizing and caring for the eggs until hatching, and rearing the resulting alevins, fish fry could be transplanted to enrich watersheds.

In his work *On the Artificial Propagation of Fish*, Rasch outlined new methods and identified several challenges in hatching and transplanting of freshwater fish, like the sensitive period from fertilization to the first feed uptake, which remain a critical bottleneck in salmon farming today. Rasch's vision was not purely scientific, although he won considerable recognition for his work, including a gold medal from the International Exposition in Paris 1867. He strongly believed that fish culture had unrealized commercial potential, by increasing important yields of anadromous fish species (Møller & Haaland, 2014a). With his assistant, Marius G. Hetting, who became Norway's first fisheries inspector in 1868, Rasch promoted hatcheries to boost freshwater fisheries, and proposed regulatory measures to prevent overharvesting. While small-scale hatching efforts were practiced in Norway before Rasch and Hetting started touting its benefits, they successfully mobilized political support for experimental research on large-scale rearing of fish in both freshwater and seawater, where salmon and trout were known to grow quickly.

Others saw the potential in the artificial breeding of fish. Attuned to international trends, Rasch acquired knowledge from hatcheries abroad, such as in Scotland and France, at a time when naturalists across the continent saw potential in fish culture as a method to increase fisheries outputs by releasing fry into the oceans for sea ranching (Nash, 2010).

Rasch was inspired by a Dane by the name of Heinz Kolding, who argued for the economic value of hatcheries in a letter to Norwegian authorities in 1851, the year when the first national salmon law (*Lakseloven*) came into effect. But despite valiant efforts by its advocates, large-scale pond culture in Norway was commercially unsuccessful at first. Among the Scandinavian countries, only Denmark developed a significant industry with organized feed provisioning and a sales organization. This loss of momentum could be ascribed to a variety of biological and technical problems. One tremendous challenge that any cultivation project must cope with is the problem of parasite-induced disease. The dynamics are relatively simple, as the main idea behind aquaculture is to confine large volumes of fish in a relatively small space. But high fish densities tend to intensify pathogen virulence and worsen disease outbreaks, in ways that are notoriously hard to mitigate. Without preventive measures and pharmaceutical intervention, populations of fish reared together are endangered by an assortment of microbes.

The nineteenth-century farmers who experimented with pond culture experienced the debilitating effects of these pathogens, and due to production challenges related to poor feed uptake and slow growth, pond culture eventually went dormant around the 1880s. This fiasco paved the way for imports of Danish roe and fry from allegedly superior disease-resistant Californian rainbow trout (*Oncorhynchus mykiss*), roughly two decades later (Møller & Haaland, 2014a). Initiating a period known as the "rainbow fever," several new trout facilities were established with the hope of making good money around 1906 and 1907. But the fever passed, as these experiments with trout failed to meet expectations, possibly due to a lack of basic understanding of fish behavior, reproductive biology, nutrition, and disease. After these scattered attempts, Norwegian pond farming entered a period of stasis lasting throughout the Second World War.

While most fish-farming efforts failed to mature into a large-scale commercial success in the late nineteenth century, it nonetheless appears that the many experiments in pond culture across Europe provided key technological scaffolding that was instrumental for scaling up this niche half a century later (Nash, 2010: 80). In this period, marine

biology expanded as a scientific discipline, and new professional organizations and infrastructures dedicated to pursuing knowledge about aquatic ecosystems were created. For example, many hatchery laboratories established in Norway and elsewhere on the continent, under the auspice of Rasch and his likeminded peers, were gradually converted into facilities for marine biological science.

From Rural Sideline to Industrial Production

In the wake of the war, commercial pond culture again saw a revival, as a few faithful entrepreneurs started tinkering with the practice, once more by modelling the pattern of Danish trout farming. Some of these individuals became instrumental in turning Norwegian fish culture from a marginal sideline, basically an outgrowth of the composite subsistence strategy known as the "fisher-farmer" (*fiskerbonde*), into a massive commercial and technological success.

In 1962, there were only twenty to thirty active small-scale farms, when excluding those preoccupied with hatching and rearing fish for watershed management (Møller & Haaland, 2014b: 57). Producing an estimated thousand metric tons in 1969, their total output was commercially insignificant. While Norwegian farmers were endowed with suitable terrain and plenty of freshwater for their ponds, they were in the periphery of major continental markets. Furthermore, the produce was a pale, portion-sized trout of variable quality, in low demand both domestically and abroad.

Two radical shifts in farming practices in the late 1960s and early 1970s were pivotal for subsequent developments (Berge, 2000). The first critical turning point was the decision to move the anadromous fish from freshwater to marine habitat, to deal with disease, slow growth, and poor feed uptake. The second transformation came when farmers switched from trout to Atlantic salmon, a species fetching much higher market value.

Past efforts to enculturate trout and salmon in saltwater had failed, but in the rural town of Sykkylven on the northwestern coast of Norway, two industrious brothers named Karstein and Olav Vik built a productive

experimental facility where they demonstrated the feasibility of saltwater farming. Taking inspiration from Denmark and determined to learn from past failures, this architect and farmer systematically studied critical bottlenecks, including salinity tolerance, feed uptake, and feeding regimens. Their first achievement was to establish brood fish that survived after spawning. Another breakthrough came when they demonstrated that rainbow trout and later, salmon, could be easily acclimatized to life in saltwater *polls* (enclosed inlets and creeks), even thriving in these environments. In 1959, the brothers placed young salmon in wooden floating cages and reared them to maturity over a three-year period. This story of success spread along the coast and stimulated new efforts at fish culture by industrious risk-takers. Two prominent examples were the owners of Mowi, a company that began raising salmon in saltwater polls on the island Sotra outside of Bergen, and the Grøndtvedt-brothers, based on the island Hitra. Many of these innovators saw great difficulties in acquiring wild roe from salmon fishermen, who reasonably considered farmed fish as competition to their own business. However, by the late 1960s, the demand for smolt had grown so large that hatcheries dedicated to smolt production were established outside of Bergen, which increased the availability of younglings to farmers (Nash, 2010: 123).

While freshwater cultivators could draw on the accumulated knowledge from pond culture and watershed management, the trailblazers who moved trout and salmon into marine environments had to rely on trial and error heuristics. The Vik brothers, for instance, meticulously documented their experiments over a six-year period to make sense of various critical dimensions, formulating an idiosyncratic "research program" (Osland, 1990). Apart from generic know-how concerning practical tasks like hatching and nursing, there was little in the way of scientific theory to guide them beyond the fry's initial life cycle.[2]

In the 1960s there was little evidence that large-scale salmon farming was feasible and could make a significant contribution to rural coastal economies, so at first, there was scant assistance to be had from the

[2]Salmon mariculture began almost in parallel on both sides of the Atlantic in the late 1950s (Nash, 2010). Attempts with Pacific salmon in the US around the Puget Sound to boost fisheries were plagued by disease and saw little success in comparison.

Norwegian public sector and its knowledge organizations. Marine biologists doubted the salmon's ability to develop roe in saltwater, and the fisheries inspector at the time, Joakim Harstad, was known for his pessimism. Even the Rural Development Fund, the only public funding source supporting these startups, cautioned against investments in this new enterprise (Osland, 1990). Despite an urgent need for more reliable knowledge on the biology, production technology and economics of salmon farming, there were no formal organizations that could disseminate the necessary knowledge.

Faced with skeptical state representatives, early farmers therefore relied on horizontal, decentralized, and informal peer networks to exchange practical knowledge. The Vik brothers, for instance, developed a clever system with three dirt ponds with fresh water, brackish water, and saltwater for gradual acclimatization of their fish. This contraption caught foreign interest, and even attracted the attention of British-Dutch consumer goods giant Unilever, who paid the brothers 20,000 GBP for rights to copy their design and build a similar facility (Møller & Haaland, 2014b: 67; Osland, 1990). A condition set by Unilever for this transaction was that the brothers would keep their design a trade secret. However, the duo later admitted that they happily shared their specifications with anyone who showed interest in their work. Further south, in the Bergen area, another group of farmers would entertain weekly meetings in a café to share their latest insight, since they lacked institutions of learning that could help distribute knowledge. It has been suggested that these egalitarian structures for peer-to-peer knowledge transmission were key to explain the success of Norwegian salmon farmers early on, in comparison with countries like Scotland, which quickly privatized research and kept trade secrets strictly within the boundary of firms (although the details here remain disputed, see Berge, 2000; Møller & Haaland, 2014b: 77).

The Norwegian Fish Farmers Association was established in 1970, as commercial success was on the horizon. Faced with growing popularity, the need for state support, and control, became pressing, and the authorities began to develop services that could provision for these emerging enterprises. But due to the institutional and administrative framework that regulated saltwater and freshwater fisheries in Norway,

central authorities and established scientific institutions came to support the industry relatively late (Chutko, 2011; Hovland, 2014; Osland, 1990). At the time, the saltwater and freshwater domain were managed by two different institutions, and there was little consensus about which administrative body fish culture should sort under. Should the new enterprise be categorized as a part of the fisheries, or as livestock production? The fisheries were, after all, specialized domains of managerial expertise, and the Norwegian Directorate of Fisheries (*Fiskeridirektoratet*) had grown into an important public agency overseeing the increasingly scientific management of Norway's fishing fleet after WWII.[3] One account even suggests that the growth of aquaculture in the 1970s was indirectly financed in part by the over-taxation of fishing stocks in the preceding decade (Berge, 2000: 162).

Aquaculture did, in some ways, resemble agriculture and livestock production more than "fish-hunting." Thus, the Department of Freshwater Fisheries (*Fiskeetaten*), sorting under the Ministry of Agriculture, could be a suitable body for oversight, although outputs from fish farms were dwarfed in size by marine fisheries. Established as early as 1855, over three decades before the authority for marine fisheries, the agency for freshwater affairs had been an official research and management institution since 1910, divided into a practical administrative and a scientific branch populated by university-trained biologists. It had also merged with *Statens Forsøksvirksomhet for Ferskvannsfiskeriene*, a public experimental facility for freshwater fish in 1945. The freshwater agency wielded biological expertise on the early lifecycle of anadromous fish, and managed commercial and recreational freshwater fisheries of economic and cultural value. In postwar Norway, watersheds had been targets for expanding hydroelectric power infrastructure, and licenses for these constructions required developers to guarantee the health of riverine fish populations. But despite being competently staffed, *Fiskeetaten* was no clear candidate for managing the growing numbers of fish farms. Agricultural authorities, the freshwater bureau included, had displayed little interest in marine aquaculture at first, and when they got interested,

[3]This effort was supported Michael Sars, his son Georg Sars, and Johan Hjort, who made substantial contributions to the fields of marine science and fisheries management.

they had few resources to support the farming communities. Furthermore, the pioneering fish farmers sought political independence from the agricultural establishment, which they considered conservative and stagnant.

One consequence of this institutional schism was a delay in a concise scientific research program for salmonid aquaculture in the early days of industrial expansion. Researchers from the Norwegian Agricultural College, for instance, were primarily interested in the breeding properties of fish from a genetic perspective, and failed to collaborate on a joint research station for aquaculture with scientists at the Institute for Marine Research, who were curious about the industrial potential of aquaculture (Møller & Haaland, 2014c). Fortuitously for the farmers, the disagreement led to the establishment of two independent, but highly productive, research stations for aquaculture science.

While a parliamentary interpellation from 1961 proposed that the Institute of Marine Research should take responsibility for the field in the early phase, it was still nearly a decade before scientific institutions got seriously involved. Historian Nils Kolle suggests that biologists first became interested in the topic after fish farmers approached them directly for science-based advice (2014c: 147). However, it soon became clear that research on aquaculture offered individual scientists, academic departments, and research institutions an opportunity to position themselves in an exciting, future-oriented field, with promising commercial applications. And while the managerial and research infrastructure for aquaculture lagged half a century behind those of agriculture, they grew fast once established in the early 70s, as those in leadership positions saw benefits in constructively engaging with the fish-farming community. Soon, research groups and even entire departments dedicated to salmonid aquaculture were established.

A shift in science policy was also imminent, as the research had to benefit the growing industry. New research stations were needed to run controlled experiments on breeding, disease, physiology, and production technology. Furthermore, national scientific organizations and institutions of higher learning had to address an increasing knowledge gap. A state commission led by Nils Lysø, a former fisheries minister and county governor, was therefore convened in 1972. Their mandate was

to investigate the prospects of aquaculture and suggest policies to help develop these businesses. Surprisingly, this work took five years and was not finished before 1977. In part, this was caused by the commission's failure to keep up with rapid developments in the field, and partly due to tensions between agricultural and fisheries interests that delayed the outcome (Kolle, 2014b). Farming practices were even expanding so profusely that a temporary regulation had to be put in place in 1973, to gain *some* control.

One of the commission's main legacies was the institutionalization of salmon as two different entities under the Norwegian management regime: a *wild* salmon managed by the freshwater authorities (now sorting under the Ministry of Environment's Environmental Directorate), and a *farmed* salmon to be managed by the saltwater authorities, sorting under the Ministry of Fisheries. The Lysø-commission also discussed the need for guidance services, educational institutions, scientific research on fish health, breeding and production technology. In their 1977 report, the commission also formulated an explicit policy objective: to retain local ownership through decentralized, smaller firms, and maintain fish farming as a sideline for people in coastal areas. The reigning political consensus was based on a social contract that saw individual farms mainly as self-sustaining economic units, contributing to rural development. Capital investments were therefore actively discouraged by regulating who could own farms, and the size of ownership. All market exchange was also recommended to proceed via a centralized sales organization. Clearly, Norwegian salmon farming was never intended to be a global industry based on foreign capital investments.

Although some of these recommendations were controversial, the commission deeply influenced the sector's development in the next years, and key principles from their proposal were formalized in the Aquaculture Act of 1981. However, since salmon farming grew faster than the commission predicted, industrial liberalization followed before long. A legal revision in 1985, for example, removed the owner-farmer principle. Then, as production tripled between 1987 and 1990 without a similar increase in market demand, massive overproduction became a reality. This was partly a consequence of a regulatory regime that disincentivized farmers to pace their production according to market demand. The result

was a total collapse of the salmon market in 1990–1991, and a major crisis in the industry. Soon, a national restructuring of the entire salmon industry followed. Through a series of bankruptcies and mergers, farm ownership was suddenly concentrated in significantly fewer companies than before. More deregulations followed in 1991, before the industry again faced a period of re-regulation in 1996, as a new feed-quota system was introduced to prevent overproduction from happening again. This quota system was abolished in 2005 in favor of a new management protocol based on a principle of maximally allowed biomass (*maksimalt tillatt biomasse, MTB*), instead of feed quotas. It is a version of this principle, which determines how much biomass of living fish is allowed in the sea per concession, that regulates the industry today.

Foregrounding Fish Health

Rapid growth of salmon production in the late 80s and early 90s was not a result of Norwegian authorities handing out an abundance of farming concessions. Instead, it was enabled by improvements in production technology. Backed by intense research to optimize the production process, salmon mariculture was launched on the path toward industrial triumph, with a landed value of roughly 64.5 billion NOKs in 2018.

At first, farming pens were makeshift rectangular wooden structures, with seines attached to them. Eventually, these were replaced by more versatile octagonal pens, where the fish could swim in circles, demonstrating formidable growth (Berge, 2000).[4] Then, in 1974, the production of a polyethylene construction known as the Polar Circle-pen began in Northern Norway. This novel design, which replaced wood, was soon exported to fish farmers abroad. Based on modern materials, these new contraptions were less capital intensive than land-based ponds or fenced-off saltwater inlets, which required elaborate technical arrangements. Plausibly, innovation in pen technology was based on knowledge transfer from the saltwater fisheries (purse-seiners, in particular), which

[4]The design was called "Grøndtvedt-pens," after two pioneering brothers on the island Hitra in Trøndelag County (Osland, 1990).

had accumulated experience about keeping fish in nets and transferring live fish into well boats. New plastic technologies also appeared, and lightweight materials such as polyethylene, PVC, and fiberglass revolutionized the production and design of life-support systems, not just for marine fish culture, but also for wet laboratories and hatcheries (Nash, 2010: 170). The growing supply industry became important translators of scientific insights produced by research institutions and universities.

Meanwhile, public research institutes invested heavily in national breeding programs based on the population genetics of salmon stocks. This effort enabled farmers to select brood fish for attractive traits such as growth rate, sexual maturation, meat quality, and other heritable attributes affecting production and quality. Additional biological research uncovered the environmental parameters that made the fish grow healthily, while maintaining high quality and an attractive appearance for consumers. New hand-held measurement devices also became available for analyses that before required entire laboratories to perform.

The logistics of fish feeding, which had become a massive bottleneck, exemplify this progress. Initially, farmers experimented with manually grinding and mixing fish with nutritional additives, sometimes using cement blenders. One widespread approach included freezing the resulting dough in chunks that could be hand-fed to the pens. Later, dry-feed pellets, developed by the agricultural company Skretting in 1963, significantly eased the logistics of feeding. Automatic feeding systems became reality a decade later. This technology also spurred research on nutritionally enriched feed components which reduced the salmon's "feed conversion ratio"; a measurement of how effectively animals convert feed mass into productive output. Lien suggests that this humble feed pellet offered farmers a kind of "time machine," whose transformative powers made salmon farming into a scalable enterprise (2015: 120). By detaching water from the marine feed resources, decay was halted, which enabled shipments and storage of marine resources across vast distances in concert with new trade agreements and value chains.

The entrepreneurs who switched their production habitat from freshwater to marine cultivation faced less complications with fish diseases than in freshwater, at first. But any illusions about the ocean being a

disease-free environment were soon shattered. These first farmers usually lived near the ocean, and often positioned their pens so that they could literally monitor their facilities from their own living rooms. And due to this pragmatic choice, pens tended to cluster together in areas where water circulation was poor, with low flowrates and in close proximity. In itself, fish farming at sea does not create new diseases, but pathogens can move over large distances in the marine environment, and high concentrations of animals in a small area, combined with lax hygiene, can lead to horizontal outbreaks from infectious agents that cause little mischief in the wild. Farming pens use nets to contain fish, and these containers can freely exchange their contents with the surrounding water mass. When the industrial expansion was scaffolded by new technology that increased fish densities per unit of volume, the risks of epizootic transmissions also escalated. In turn, new technologies of governance, area planning, and work on preventive fish health with new vaccines, became crucial to tackle the inevitable disease problems that followed. These developments exerted strong pressures to streamline and standardize production.

Although salmon lice had become a nuisance for farmers, it was other fast-acting and lethal infectious diseases that first caught their immediate attention (Kolle, 2014a). Since other production factors were insignificant if the produce perished from disease before it was sold, fish health quickly became a key determinant for economic success. The Fish Disease Act from 1968 legislated the protection of wild fish against diseases by placing restrictions on imports and provided veterinarians with a monopoly to prescribe medicines. But this regulation was soon inadequate, and some stakeholders worried that impressions about poor hygiene could jeopardize the reputation of farmed fish among consumers. Mortality rates in the freshwater phase of the life cycle, for instance, fluctuated between 10 and 70% as late as in 1987 (ibid.). We saw that the Lysø-commission received support for an intermediary Concession Act in 1973, until a permanent law was worked out. Besides offering a regulatory mechanism in accordance with the commission's political vision, this concession schema also provided a legal basis for fish health and hygiene. This intermediary act was an instrument that

public administrators could wield to regulate and plan new farming facilities, by establishing minimum distances between neighboring facilities to prevent disease transmission, for instance.

Since pathogen dynamics are determined by factors like water current, temperature, farm densities, and other "local" characteristics, salmon production was a context-sensitive operation from the beginning. In 1974, as much as 90% of cultured fish suffered bacterial infections of *Vibrio salmonicida*, manifesting in the form of pale gills and skin lesions. Then, in 1976, the eponymous Hitra-disease erupted on an island outside of Trøndelag county, in Central Norway. Also caused by *V. salmonicida*, later known as "cold-water vibriosis," these outbreaks decimated several farms in 1979. Affecting as many as half of all Norwegian farms, the disease left a trail of bankruptcies.[5] Antibiotic remedies became the only viable solution to these problems, and its consumption skyrocketed in the late 1980s, as a tremendous growth in production volume brought these biological vulnerabilities into the light. By the end of the decade, fish health emerged as a paramount concern, as bacterial infections like furunculosis, vibriosis, and viral diseases such as infectious salmon anemia and infectious pancreatic necrosis, threatened the industry with extinction (Kolle, 2014a).

Out of this precarious situation, a new cultural consensus soon emerged. To build a viable industry, medicinal treatments had to become the last resort. Prophylaxis, based around the science of fish health, immunology, and vaccination schemes, was institutionalized as a foundational management principle. In 1983, a major initiative to harmonize efforts, called Healthy Fish (*Frisk Fisk*), was launched by an association of farmers in collaboration with the national sales cooperative. Lasting until 1996, several vaccines against the most prevalent diseases were developed under the umbrella of this initiative. In 1990, a new law for coordinating and regulating fish disease management (*Fiskesykdomsloven*) in marine captives was also put in place, expanding on the old law of 1968, which only covered freshwater fish. R&D investments in this phase were also significant, as funding increased from 50 million NOK in 1984 to

[5]A costly two-year battle ensued over the approval of a vaccine against *Vibrio salmonicida* between the University of Tromsø, who developed it, and the Veterinary Institute in Oslo, who was mandated with approving the treatment.

300 million in 1989 (Kolle, 2014a: 186). The University of Bergen and the University of Tromsø also created new professional degrees in "fish health biology" ("aquatic medicine," *fiskehelsebiologi*), in dialogue with the industry. A protected title only granted to those with a five-year specialization, the fiskehelsebiolog complemented the work of regular veterinarians, and soon occupied key managerial positions in hatcheries and farms. Established in 1989, it took 18 years and a long professional struggle with veterinary authorities, before these so-called "fish doctors" were given prescription rights for fish medicines.[6]

The transformative effect of this concerted cultural and technological change on fish health should not be underestimated and is illustrated by the following numbers. In 1987, farmers spent almost 50 metric tons of antibiotics on roughly 54,800 tons of total production, less than 5% of today's annual production. In comparison, the use of antibiotics in the period between 2013 and 2017 hovered between 201 and 860 kilograms, on an annual volume of produce averaging over 1.2 million tons.

The threat posed by salmon lice to the welfare of fish reared in captivity, along with its possible negative effects on wild stocks, also came under increased public scrutiny in the 1990s. While obviously afflicting the fish kept in pens, the parasite was also suspected to be a major cause behind an observed decline in wild salmon populations. Smaller fish seemed particularly vulnerable to lice attacks. Now spread in clusters along the coast, salmon farms were suspected to cause an increase in infection pressure on wild salmon, by functioning as host reservoirs. Here, large amounts of parasites could proliferate and potentially exacerbate the mortality of smolts during their migration from the rivers to the ocean.

As part of a cultural shift toward a preventive approach to pest management, a National Action Plan Against Lice (*Nasjonal Handlingsplan mot Lus på Laksefisk*) was launched in 1996, with support from The Research Council of Norway. The plan was designed by a commission of representatives from farming companies, governmental agencies, as well as scientific and other professional organizations. Eventually, this strategy

[6]The Norwegian seafood industry had long pushed for a closer integration with the European Single Market. Paradoxically, prescription rights for fish health biologists were partly delayed due to European Economic Area regulations (Hersoug et al., 2012).

was codified, and a series of regional administrative regulations were introduced. These placed upper limits on the average amount of lice per fish that were allowed in farms, before antiparasitic treatment would have to be initiated. In 2000, these regional regulations were unified under a national law aimed at reducing lice infections (*Forskrift om bekjempelse av lakselus*). When the public food-hygiene regimen was reorganized as the Norwegian Food Safety Authority in 2004, fish health work in general, and the lice issue in particular, was placed high on the agenda with highly detailed and mandatory reporting schemes.

Increased focus on salmon lice as a management problem also coincided with a strong push to revitalize aquaculture science toward the end of the millennium, as funding opportunities for scientific research began to wane. Some stakeholders even worried that a lack of public R&D support could engender a chasm between practitioners in the industry, and the relevant scientific communities (Hersoug, 2014a). This call for more funding was answered and aquaculture was increasingly prioritized in national research policies and strategies around the turn of the millennium. Sophisticated biotechnological research, in particular, such as the mapping of the salmon genome, was considered essential for keeping *Lakse-Norge* economically competitive, and to seize national control over a valuable commodity in the emerging "bioeconomy." Between 1999 and 2003, funding for marine R&D was higher than any other scientific domains, with public funds representing 76% of total R&D investments in the field (Hersoug, 2014b: 307). These numbers tripled over the next years, seeing up to 7% annual growth, thereby exceeding the relative growth of the Norwegian GDP, and funding for other scientific fields in the same period.

But although marine aquaculture was prioritized in national research programs, the industry's growth ambitions called for even more problem-solving. Knowledge to accomplish this would be derived through scientific means, but instead of academically focused on epistemic virtues like research publications in prestigious journals, it would primarily be oriented toward practical applications (ibid.: 308). So, although farming companies differed in their levels of commitment to R&D investments, the Norwegian Seafood Federation eventually called for the establishment of a research fund to be financed by a tax of 0.3% on all seafood

exports. Organized as a limited company, owned and supervised by the Ministry of Trade, Industry and Fisheries in 2001, the Norwegian Seafood Research Fund would complement public funds, based on value-adding priorities set by a board of representatives from three industry advisory groups.

Managing Salmon Lice: Coevolution and Resistance

Salmon lice were likely among the first major pests that salmon farmers could directly observe on their livestock, after transitioning from freshwater to saltwater culture. At first, they were at a loss about how to cope with the infections, but a solution eventually presented itself in the form of a compound known as trichlorfon, sold under the brand-name *Neguvon*. The organic compound, which belong among the so-called organophosphates, was originally used for antiparasitic treatments of pigs and was dissolvable in water. A citation from a correspondence on treatment regimens for *Neguvon* in the journal *Aquaculture* from 1977, illustrates the urgency: "In sea farms, however, where large numbers of salmonids are kept under confined conditions, the parasite has every possibility for mass infection. Attacks with several hundred parasites per fish have been recorded, and over 2000 parasites have been counted on a single Atlantic salmon" (Brandal & Egidius, 1977: 177).

Over the years, a stream of new remedies against the parasite were deployed under veterinary auspices (Aaen et al., 2015). The majority of these worked by disrupting neural signaling or chitin synthesis, crucial for the development of arthropod exoskeletons during molting. *Neguvon* was first administered orally, but farmers later switched to bath treatments due to difficulties with controlling the intake through feeding. Then came natural pyrethrin-baths (*Py-Sal*), using an oily substance as an impractical "top dressing" on the fish pen (Torrissen et al., 2013). Next, dichlorvos was used, an organophosphate first introduced among Scottish farmers as *Nuvan*. Baths of hydrogen peroxide followed, a powerful oxidant that disrupts cell membranes, with narrow safety margins. In the late 1980s, lice infestations intensified, and farmers

turned to ivermectin. The compound showed a prolonged effect but also had low safety margins. Diflubenzuron (*Lepsidon*, *Releeze*) entered the scene in the early 90s, while its relative teflubenzuron (*Ektobann*) appeared a decade later. The drawback of this drug was that the effect was exclusively restricted to the early developmental stages of lice. Another organophosphate, azamethipos (sold as *Salmosan*), was introduced in 1994. Then bath treatments with synthetic pyrethroids such as cypermethrin (*Excis*, *Betamax*) and deltamethrin (*Alpha Max*) followed suit, showing better effects and safety margins than many other drugs.

The compounds deployed against salmon lice all had their pros and cons: some were easy to administer, while others only worked on specific stages of the lifecycle. A few were highly toxic, with low safety margins both for the livestock and for the humans tending them. But common for these therapeutics was the fact that salmon lice would eventually develop reduced sensitivity toward all the drugs after prolonged use. Organophosphates, for example, lost their efficacy already in the mid-90s, while the class known as pyrethroids lasted roughly a half decade longer. Many farmers, weary of the constant struggles against their parasitic interlocutor, hoped they had a silver bullet when a compound named emamectin benzoate appeared in 1999. Sold under the brand SLICE, and belonging to a class of insecticides called avermectins, which are fermentation products from the bacteria Streptomyces avermitilis, the substance disrupts mechanisms involved in transmitting nerve impulses, causing paralysis and death.

At first, SLICE was a godsend for farmers, but between 2002 and 2006, a trend suggesting gradually reduced efficacy was evident, and finally, the parasite forcefully demonstrated resistance against all the chemotherapeutic treatments maintained by farmers in their arsenal. And despite efforts to bring a new chitin-synthesis inhibitor called Imvixa (lufenuron) to market, no new drugs have entered the Norwegian market after SLICE as of yet.

A Mutual Causation Process

The story of salmon lice in modern aquaculture is one of coevolution: "Intensive farming creates conditions for parasite growth and transmission drastically different from what parasites experience in wild host populations and may therefore alter selection on various traits, such as life-history traits and virulence" (Mennerat et al., 2010: 59). Drug resistance is an extension of this process, as human interventions exert strong selection pressures on certain genotypes in a naturally abundant parasite population through ever more technology- and knowledge-intensive farming practices.

The evolutionary mechanisms at play here are similar to those propelling the familiar case of antibiotics resistance in human medicine. Individuals in a given salmon lice population vary in their sensitivity to chemicals. When interventions are made with chemotherapeutants to reduce infections in pens, as farmers must abide by current regulations, they never successfully eradicate all the lice in single a location. Often, some specimens survive because they possess mutations that reduces their sensitivity to the administered treatment. Such genetically based resistance mechanisms work by point mutations in the genetic pathway that is targeted by the antiparasitic chemical. This, in turn, results in either protein insensitivity, up-regulation of genes for detoxifying metabolism, biochemical modifications of cellular pumps that reduce uptake of medicinal compounds in feeds, or by modifying the organisms' cuticle thickness, which physically shields the animal against chemicals (Aaen et al., 2015: 73). Lice that possess such traits will display increased fitness in an environment where antiparasiticides are frequently used. Their offspring may then inherit genotypes that on average are less drug sensitive than those carried by the ancestral population. As such, multiple rounds of selection may breed a new population of "super-lice" over time, ever more resistant to the treatments they are exposed to.

These dynamics, which severely complicates lice management, are in part driven by cultural practices meant to ensure fish welfare, as regulations change rapidly to keep up with the biological complexities of farming pens. For example, between the summer of 2008 and January 2013, the law was revised five times in four and a half years, ushering

in a new regulation every 10 months. Taking an evolutionary point of view, this sets up a culturally driven feedback mechanism that is likely to reinforce resistance to key therapeutics, as fish farmers have no other recourse than to deal with the short-term logic dictated by various legal instruments that requires them to maintain lice numbers under a fixed threshold.

The fight against drug-resistant lice thereby becomes a race against millions of mutagenic events that occur every time the population of salmon lice reproduces. Adding to the challenge, the many hundred fish farmers along the Norwegian coast also rely on a collection of idiosyncratic practices used to conform with lice regulations and pest management, which makes coordination of pesticide use challenging. As one fish health biologist explained, it is not uncommon that farmers develop local drug regimens that deviate from the guidelines of the drug manufacturers and those who prescribe the medicine. Doubtlessly, the aqueous environment adds a layer of complexity to pest management (Nash, 2010). As farming takes place in open nets along the coast, lice strains can, in some conditions, quickly spread from one area to other sites. Therapeutic actions taken by a farmer in one area may therefore have cascading effects on the population dynamics of lice in neighboring farms. Resistance against emamectin benzoate, for instance, likely originated from a single progenitor, and then swept across the entire Atlantic lice population in a period between 1999 and 2010 (Besnier et al., 2014).

The idea of "coevolution" offers a conceptual frame to articulate inseparable relations between the cultural transmission of knowledge among human actors, and the expansion of drug resistance in lice. In its traditional formulation, coevolution is defined as "the evolution of complementary adaptations in two species caused by the selection pressures that each exerts on the other" (Martin & Hine, 2015). More recently, anthropologists have stressed the importance of cultural practices in transforming environments where biological selection takes place, introducing the notion of "gene-culture co-evolution" or "dual inheritance theory." This framework suggests that cultural transmission of socially learned information plays an active part in driving natural selection, a familiar example from our history of animal domestication being a culturally induced selection for lactose tolerance ("lactase persistence")

in groups that took up herding and milking (see Henrich, 2015 for a catalogue of examples). Drug-resistant salmon lice presents a variation on this theme of culturally induced coevolution, with drug resistance occurring in a parasite that torments another species under our care. In this case, the lice population responded to novel human interventions in the farming pen with an alternate biological constitution. The human response, on the other hand, was delivered through a shift in institutional reality, that introduced novel interventions that were often derived from the best available scientific knowledge.

These enduring interactions between people, lice, and salmon give rise to what Merrill Singer describes as a "mutual causation process" (2014: 1280). This is a situation where species A engages in some novel behavior, like human farmers attempting to domesticate salmon. In turn, this facilitates responsive changes in species B, as vast amounts of salmon are concentrated in densely populated pens. This affords species C with new opportunities, such as rapid proliferation due to an unprecedented abundance of salmon hosts. New actions are then elicited from species A, like the intensive use of parasiticides. Consequentially, species C responds by evolving genetic adaptations making certain individuals highly resistant to the compounds. In retaliation, species A then takes new epistemic and pragmatic actions, entering a mutual causation process that may extend ad infinitum.

Just as many fish diseases mutate in ways that require modifications in the design of vaccines to overcome new biological adaptations, salmon lice management provides fish health experts with an "eternal market" due to its remarkable ability to adapt to antiparasitic interventions. In this case, cultural responses to the lice problem, such as political decision-making, laws and animal ethics occasionally informed by scientific knowledge, become driving factors for the biological selection of resistant salmon lice, because they impel farmers to take mitigating actions that propel the mutual causation process forward. The precarious nature of this dynamic was described in frank terms by an entrepreneur from a major fish health consultancy in an article from a Norwegian business daily, aptly named "Loaded on a lousy salary": "I make money out of every new lice-legislation the authorities enforce, but I don't know why we should make money on this. More control does not result in less

lice and does not help wild salmon. The only people making money from this are those who are selling lice-therapeutics. Salmon lice has created a whole industry" (Ytreberg, 2015).

The entrepreneur's ambivalence stems from the fact that Norwegian salmon farmers have been subjected to a host of new regulatory regimes since the turn of the millennium that have significantly reduced local decision-making power. This includes a comprehensive audit culture. One study found that a fairly typical farming company filled out approximately 1300 official forms in a single year (Normann et al., 2005: 1). Under the current legal regimen, farmers are obliged to conduct weekly assessments of lice levels, and therapeutic interventions are prescribed where lice counts exceed an average threshold of 0.5 adult female lice per fish. National monitoring and reporting schemes, administrated by the Norwegian Food Safety Authority, also work to ensure that farmers along the coastline comply with these management systems, and every week the latest data is made publicly available online (see: http://lusedata.no).

Given that technical progress has enabled massive increases in production volume by shortening the period from fish egg to finished product, despite current caps on maximally allowed biomass, one could argue that the present concession system offers a rather weak management mechanism. However, in the absence of efficient therapeutics against lice, Norwegian authorities will not allow salmon farmers to expand production beyond current numbers, despite political imaginaries projecting a fivefold increase in the future to capitalize on the soaring global demand for fresh fish.

In response to this grave situation, new interventions by farmers, based on an abundance of scientific research, aim to augment management practices in ways that minimize or circumvent the problem of therapeutic resistance. Consequentially, there are scores of inventive solutions in progress, ranging from anti-lice-attachment feeds to cleaner fish, as well as novel chemotherapeutic regimens and various mechanical delousing systems. For instance, significant investments have been made into closed containment systems for use at sea, while some have proposed to move the entire production process onto land in special plants. On the more technology-intensive side, one company has even developed

an "optical delousing technique" based on an apparatus that combines machine vision and a laser beam to identify and directly incapacitate louse individuals on salmonids swimming in the pen.

Others have proposed a solution where genomic selection is used to identify more lice-resistant brood fish for cutting-edge breeding programs. Some biologists, however, advise caution due to the differential rates of reproduction between the two species (Jensen, 2010). According to this line of reasoning, farmed salmon has a generation time that lasts roughly three to four years, while that of lice is between seven and ten generations per year. This means that the parasite has a generation time up to forty times faster than its host, so that for every five salmon generation there could possibly be hundreds of lice generations subjected to strong selection pressures. Introducing a new breed of lice-resistant fish to the pen can therefore drive the lice population toward a new class of "super-lice," impervious to the salmon's immunological defenses. If this occurs, it is unknown whether farmers can rely on artificial breeding to keep up with the evolutionary arms race. And while this may not constitute a major hazard for farmed salmon, since their lifecycle and reproduction are controlled in captivity, the resulting "super-lice" could jeopardize wild salmon stocks. As with antiparasitic compounds, and other delousing methods where resistance is a probable outcome, breeding is likely no silver bullet.

As summarized by the frank entrepreneur we encountered earlier: "Fantasy has no limits. There's hardly a week without someone calling me about some snake oil-thing against salmon lice. God knows we've tested a lot of weird stuff against lice. We've tested, tested and tested. We flush, we clean, we use lasers, we use skirts and I don't know what the fuck we don't do" (Ytreberg, 2015). This constant struggle against parasitic encroachment in salmon farming demonstrates the open-ended nature of domestication processes (Lien, 2015). Relationships of this kind are even more peculiar given that in nature, even parasites are beset by other parasitic organisms. Salmon lice themselves have been proven to carry an assortment of bacteria, fungal agents known as microsporidia (Nylund et al., 2010), and viruses (Økland et al., 2014). These hyperparasites make their living by parasitizing other parasites. Ironically, some scientists have even proposed that such viruses could, given the right

biotechnological advances, even become potential sources for lice control in the distant future (Nordland, 2015).

Given the convoluted nature of these relationships, human mastery and control seem at best to be ideals that domesticators strive toward, rather than a fixed property of human relationships with livestock. Such precarious exchanges are likely to forever characterize those sites of enactment that Lien describes as a *domus*: "fragile assemblages of beings and things that, as long as they hold together, constitute the conditions of growth and reproduction of humans as well as of nonhuman beings" (2015: 5). The trajectory of salmon farming from an extensive to an intensive mode of production also highlights how humans and our companion species will continue to face new crises, made more acute by the very success of our own projects. Here, I have offered a "naturalistic contextualization" of the feedback and feed-forward mechanisms acting on biological and social systems in this perpetuating mutual causation process (Singer, 2014: 1281).

Antagonistic relationships with parasites have evolved in trajectory with human societies and will likely take part in any future domestication adventures that our species embark on. Such relationships also call for new epistemic projects on a grand scale. Fredrik Barth suggested that the key concern of an anthropology of knowledge should be to analyze the contents of aggregate traditions of ideas, their expression, patterns of distribution and how they come to life through creativity, transmission, and exchange (1990: 1). With respect to the epistemic work that accompanies a phenomenon like drug-resistant salmon lice, we must also attend to the effects of knowledge, and how content, distribution patterns, creativity, transmission, and change extend back into the biological realm. In this case, scientific insights have acted both as a driver of interventions in the farming pen that cause unintended biological complications, but also offers its means of detection, and a source of future solutions. These feedback loops between the actions of socially positioned agents and evolving biological phenomena are shaped by the representations of knowledge that human agents construct (Barth, 2002: 10).

Applications of parasitological knowledge to animals, and eventually marine domesticates, began as offshoots from medical specialties like

infectious disease and human parasitology. This field emerged through descriptions of specific infections, identification of disease-causing parasites, accounts of species' lifecycles, and ascriptions of causal links between disease outbreaks and vector transmission. For a long time, the science of parasitology was a subfield of tropical medicine, which sought to understand and control the effects of pathogens in European colonies, and where possible, eradicate their transmission routes through public health work and other interventions. But as part of a general trend where more domains of biological science are increasingly "molecularized," so have parasitology "gone molecular" through the application of cutting-edge genomics research. The science of salmon lice is no exception. Like the parasite's host, the lice genome has been thoroughly mapped (see Treimo, 2007).

The fall of 2016 saw widespread media coverage of heavy lice infestations on a salmon farm located on the northwestern coast of Norway. Reports also suggested that the owners of the farm had failed to take appropriate measures, despite facing a very critical situation. In the media, images of fish with severe skin lesions circulated widely, and commentators decried the event as deeply troubling from an animal welfare perspective. Interviewed about the case in November 2016, Professor Frank Nilsen, one of the world's foremost experts on the parasite, explained that he had not seen lice-related injuries of this magnitude since the end of the 1980s. Finding more effective measures against lice was urgent. In what follows, I situate the reader in the laboratories of the Sea Lice Research Centre, where a group of molecular parasitologists under Nilsen's directorship strive to respond to these urgencies.

Environmental historian Stephen Bocking shows how ecological studies of salmon lice in the Broughton archipelago on Canada's Pacific coast, generated considerable political frictions over the future of salmon farming (2012). But in contrast to situated ecological science of this kind, the experimental laboratory of the SLRC operates according to a different, more universalizing logic, which Robert Kohler has described as "placelessness" (2002: 9). This concept stresses the laboratory's ascribed status as a neutral site, an epistemic virtue, which effectively guarantees the robust credibility of scientific outcomes. When tracing the production of novel scientific meanings in the laboratory,

instead of the salmon pen, we are offered with a quite different perspective on the *domus* of salmon aquaculture, or how humans and farmed animals learn to live well together (Lien, 2015: 165). Here, I offer a cognitive ethnography of fundamental epistemic activities involved in this kind of experimental knowledge production. Vigilant about potential industrial applications of their scientific insights, this research community uses state-of-the-art methods to probe the salmon louse and its genome sequence for molecular mechanisms and pathways of target genes that can be mobilized for novel interventions. The hope is to circumvent the pitfalls of past failures to sustainably manage parasitic adaptation in domesticated salmon. Solving these problems of lice management requires further acts of domestication in the laboratory.

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3

Making a Cognitive Ecology for Experimental Practice

In reviewing the history of salmon lice in Norwegian aquaculture, I highlighted key challenges that arose when farms expanded, and widespread drug resistance developed in lice populations along the coast. Even though the scientific community caught interest relatively late, scientific knowledge deeply influenced the trajectory of marine farming. Enjoying generous funding opportunities compared to many other fields, scientists shaped salmon mariculture through new organizations for research and development that emerged in lockstep with industrial expansion. Challenges associated with this development also called for the institutionalization of new vocations, such as the fish health biologist (*fiskehelsebiolog*), and scientific practices aimed at hands-on problem-solving.

In this chapter, I examine how this burdensome parasite was approached by a group that eventually formed the Sea Lice Research Centre (SLRC), an ambitious project devised to tackle the lice problem. Heeding Hacking's advice that "the philosopher of experiment must descend from semantics and think about things and actions instead of ideas and expectations" (1992: 61), I tell the story about the birth and development of the experimental system at the center of this community.

M. Solberg, *A Cognitive Ethnography of Knowledge and Material Culture*, Culture, Mind, and Society, https://doi.org/10.1007/978-3-030-72511-2_3

By supplementing what Nersessian calls a "cognitive-historical analysis" (2009) with observations and insights from long-term ethnographic research, I track the course of this evolving experimental system through time, as well as social, physical, and conceptual space. To describe mutually dependent elements of this culturally organized environment for thought and action, what Hutchins dubs a "cognitive ecology" (2010), I relate the development of novel scientific tools to the evolving problem-space faced by the research collective. Attention is on the origin, transmission, and change of practices in the laboratory over time. I end with observations on the epistemological features of *L. salmonis* as an experimental organism.

An intellectual division of labor through massive research endeavors, today recognizable as "Big Science", became increasingly institutionalized after the surge in scientific enterprise during the arms races of the Second World War and the Cold War. As Peter Galison reminds us: "Big Science is not just big relative to what scientists knew before, it is big relative to all science" (1992: 2). While Big Science is a heterogenous category, enterprises like CERN's Large Hadron Collider and the International Space Station offer iconic prototypes of such ventures. In the former case, thousands of scientists and engineers, distributed across the face of the planet, work jointly on a technical infrastructure of such enormity that the facility straddles national borders.

After biology entered an era of high-throughput genomics after the Human Genome Project, there is now also Big Biology: a field producing massive amounts of data that no single human could possibly analyze on their own, without assistance from tremendous computational power, and production lines housed in factory-like laboratories (Stevens, 2013). Like its counterpart in physics, Big Biology involves new research practices and novel arrangements in terms of funding, facilities and technology, interdisciplinary collaboration, and management, cutting across traditional boundaries, both institutionally and nationally. Resembling "Big Biology" proper in some ways, but definitively smaller in scope and scale, the Sea Lice Research Centre counted over thirty-five members at the height of its activity in 2015. Possessing different kinds of technical expertise and disciplinary backgrounds, these worked across several collaborating Norwegian research institutions. This

collective work contributed to a burgeoning, eclectic field, best characterized as "marine molecular parasitology." An ill-defined but highly active research area situated in the junction between molecular biology, marine science and applied fish health biology, parasitology, molecular genomics, and veterinary science. As an "intersection" defined by a particular problem-space located between disciplines, the field constitutes a "trading zone" between scientific cultures, to invoke two salient metaphors (Galison, 1997, 2010: see Chapter 9).[1] Members of the community opportunistically co-opted scientific tools they found useful for making sense of lice biology. Attending a variety of professional meetings, their venues spanned from the biannual International Sea Lice Conference on copepod biology in wild and farmed environments, to fish health conferences and marine parasitology more generally, to meetings on specialized topics in molecular biology. The group would also publish in an assortment of journals, ranging from specialist periodicals like *The International Journal of Parasitology* and *Parasitology International*, *Experimental Parasitology*, and *Journal of Fish Diseases*, to outlets targeting a broader audience, like *Marine Genomics*, *BMC Genomics*, and *PLOS One*.

Galison's metaphor of an intersection suggests sufficient, but not necessarily complete and mutual, coordination between research fields that partially share discursive and material practices. Such coordination unfolds through boundary objects and practices on the levels of experimentation, theorizing, and instrumentation. What matters in these spaces is primarily participatory coordination, and not *full-fledged* agreement about epistemic signification. As with traffic intersections of a more familiar kind, the metaphor also indicates that participating agents can have slightly diverging goals from each other, without compromising the smooth, pragmatic operation of the intersection itself.

The Nature of Experimental Systems

Epistemic actions refer to operations people make to improve their informational environment to simplify problem-solving, rather than move closer to a physical goal (Kirsh, 1995; Kirsh & Maglio, 1994; Kirsh

& Robbins, 2013). In the anthropology of knowledge and scientific practice, one may also talk about systems for epistemic activity: "a more-or-less coherent set of mental or physical operations that are intended to contribute to the production or improvement of knowledge in a particular way, in accordance with some discernible rules (though the rules may be unarticulated)" (Chang, 2014: 72). Together, these concepts suggest that material culture plays an important role in thinking, and by extension, laboratory science. How has this relationship between materiality and knowledge been construed?

An early precursor to studies on the material aspects of scientific knowledge production can be found in Ludwig Fleck's work on the genesis of scientific facts (1979). Fleck launched a pioneering sociological study on the Wassermann reaction for detecting syphilis. *Genesis* introduced the idea that scientific research is a distributed phenomenon, constituted by "thought-collectives" (*Denkkollektiv*) working through particular "thought-styles" (*Denkstil*), the material and conceptual resources used by different communities of epistemic practice. More recent work on the materiality of scientific reasoning elaborates upon Fleck's insights. The interface between cognition, practice, and materiality has been explored through analyses of how physical and conceptual models support scientific reasoning (Alač & Hutchins, 2004; Giere & Moffatt, 2003; Myers, 2015; Nersessian, 2010; Weisberg, 2012). These analyses suggest that scientific deliberation not only occurs through induction or deduction, as traditional philosophical models presuppose, but that scientific reasoning relies heavily on abductive inference, inferences to the best explanation. Scientists engage in such reasoning through manipulation and intensive tweaking of both physical materials and conceptual structure to represent and solve problems. Nersessian, for example, demonstrated through a series of longitudinal ethnographic studies how such constructive manipulations, which she terms "model-based simulation," have emergent cognitive properties that produce novel insights in biomedical engineering (2009). She echoes Hutchins' adage that scientists, like other humans, partly create their own cognitive powers by creating the problem-solving environments in which they exercise those powers. In this perspective, interactions with the material environment are not just *aids for* reasoning but instantiate productive

forms *of* reasoning. These material engagements can drive conceptual change through cyclical processes of constraint satisfaction and bootstrapping that includes selective construction, simulation, evaluation, and adaptation of different intermediary models, often through the creative use of analogy. In turn, these manipulations of material structure support novel understanding of the target problems. This approach breaks with the exclusive emphasis on scientific activity as primarily theory-driven, in favor of a broader range of representational practices (Giere, 2010). In this case, the ontologically diverse category of "models" becomes a productive interface between sociocultural and cognitive approaches to knowledge. Roy Ellen, for instance, has argued that attention to models and modelling is necessary to understand the configurations of technical, material, and social features that enable predictive knowledge about the world across knowledge traditions (2004: 409, 422).

The life of representational practices in lab science is also underscored by work on so-called "experimental systems," which stresses the interplay between material *and* conceptual resources. In *Towards a History of Epistemic Things*, Hans-Jörg Rheinberger quotes the Nobel Laureate biologist François Jacob, who poignantly summarized the epistemic utility of such constructs: "In analysing a problem, the biologist is constrained to focus on a fragment of reality, on a piece of the universe which he arbitrarily isolates to define certain of its parameters. In biology, any study thus begins with the choice of a 'system'. On this choice depends the experimenter's freedom to manoeuvre, the nature of the questions he is free to ask, and even, often, the type of answer he can obtain" (François Jacob, quoted in Rheinberger, 1997: 25).

In this seminal account of the experimental history of protein-synthesis, how biological cells translate RNA into protein via the adaptor molecule known as "transfer-RNA," Rheinberger argues that an adequate account of scientific knowledge production requires a description of how epistemic agents interact with instruments, apparatus and other "objects of manipulation" (ibid.: 91). In this view, many scientific concepts are embodied by technologies in practice, and not primarily theoretical propositions, with experimental systems being the real "working units" of

modern life science. As hybrid entities, experimental systems are simultaneously material, local, social, institutionalized, technical, instrumental, and epistemic. To be productive they must generate "surprise"; unforeseen results that feed back into the system and generate opportunities that can propel the experimental machinery forward. Importantly, experimental systems are units of signification. As models of entities and processes in the world, they are meaningful, *representational* systems that scientists think and tinker with. They also have a hybrid nature, as bifurcations of material, technical, and conceptual elements that act together with unpredictable consequences.

As devices for producing events that result in new insight, experimental systems are composed of two categories of elements that work in interplay. First, there are *epistemic things*. These are objects under investigation, the targets that experimental systems seek to understand and control; that which is not yet known. The second is *technical objects*, unknown elements that used to be epistemic things in the past but have been domesticated in the laboratory. Well-understood entities that have become standardized, black-boxed, and operationalized through technology, these technical objects are the bulk of a laboratory's material culture.

To be productive, epistemic and technical objects must be organized to "display their dynamics in a space of representation […] in which material graphemes are articulated and disconnected, placed, displaced and replaced" (ibid.: 3). Through "conjuncture, bifurcation and hybridization," experimental systems can aggregate into larger experimental cultures. Productive alignments between such elements create cognitive and spatiotemporal singularities; phenomena and events that have never occurred before, but which the scientist can meaningfully unify by formulating principles and patterns. According to Rheinberger, a single experimental result rarely proves or disproves hypotheses. Instead, scientists acquire knowledge when such systems reliably and repeatedly produce similar effects under the same conditions, as epistemic and technical things interact to constrain the possible space of the system's representational states.

When previously unknown, epistemic things get sufficiently stabilized, they may become part of the technical arrangement and join the scientific community's search for new resonances between technical things and the unknown. DNA sequencing, RNA interference, and the polymerase chain reaction, which are all everyday technologies that will be encountered in this ethnography, were once epistemic things in the molecular life sciences, unknown entities which only emerged from the efficaciousness of *other* experimental systems. Today these are ubiquitous, standardized, off-the-shelf, technical things.

Taming *Lepeoptheirus salmonis*

The Sea Lice Research Centre was the brainchild of Frank Nilsen, a merited professor of fish health biology, who served as its director and principal investigator. The Centre came to life at a moment when many conventional lice therapeutics had lost their efficacy due to evolutionary adaptations conferring resistance against parasiticides. As fish farmers ran out of treatment options, the relative management costs of salmon lice escalated to unprecedented levels, and new knowledge for lice control was sorely needed. Although the SLRC formally opened its laboratories in 2011, many critical features of its central experimental system date back to challenges that Nilsen grappled with after finishing his doctorate in 1998. As such, the trajectory of the Centre's "pipeline" was the outcome of a decade-long, interdisciplinary research program.

Nilsen was brought up in Sveio on the western coast of Norway, in a family with the first-hand experience in salmon farming, and was among the earliest graduates from the fish health program at the University of Bergen. His doctoral dissertation was on the parasitology of *microsporidians*, a group of unicellular organisms infecting a variety of fish species, at the former Institute for Fisheries and Marine Biology, now a part of the Department of Biology. Having applied novel molecular methods to evolutionary genetics of the microsporidian phylum, Nilsen was soon offered a research position at the Institute of Marine Research (IMR) at Nordnes, about two kilometers from the university campus in Bergen.

At the turn of the millennium, Norwegian salmon farmers, scientists, and the authorities were increasingly worried about lice as a major pathogen in salmon aquaculture. In an interview, Nilsen recalled that the only condition from his new employers was that his research had to address salmon lice in one way or another. So, despite that his real expertise was in molecular techniques, Nilsen was first engaged in field research collecting evidence on ecological interactions between wild salmon and lice, and infection pressure from lice in Norwegian fjords. Nilsen remembered the situation as quite dramatic, and it was not uncommon to find young salmonids infected with hundreds of lice on field trips. But although critics at that point voiced public concerns about the lice issue, farmers still had well-functioning therapeutics at their disposal, and regimented use of pharmaceuticals curbed the worst outbreaks. Still, worrisome reports about heavy lice infestations underlined the need for more research on basic and applied salmon lice biology to ensure long-term sustainability, and significant funding was soon made available for researchers.

In Chapter 2, we saw that farmers had become dependent on an efficient drug known as SLICE (emamectin benzoate), as other treatments lost their efficacy. But in 2005, reports of the first treatment failures with SLICE appeared in Ireland, and by 2007, Norwegian farmers also reported reduced efficacy. In an environment of polarized debate between stakeholders, Nilsen proved an adept at cumulatively advancing an applied research agenda. In 2000, he was awarded a significant five-year early-career grant from the National Research Council's Strategic Institute Program for a proposal to apply new molecular methods to study lice biology, and he also acquired additional funds from other funding schemes.

Later, when the IMR reorganized, Nilsen reconfigured his research group to focus more heavily on marine genomics, extending their scope to include commercially important species like Atlantic cod (*Gadus morhua*). At this time, cod was a prospective new species for domestication, modelled after the salmon success, and research on the species was lavishly funded for a period. Nilsen also acquired grants from The Research Council of Norway's program on Functional Genomics ("FUGE"), a 1.5 billion NOK funding scheme running between 2001

and 2011, to boost national biotechnology platforms. Launched in the wake of reports about Norwegian life science being fragmented and uncompetitive, the goal was to consolidate marine affairs as a fundamentally important pillar for the nation's future bioeconomy.

Given its economic importance, *L. salmonis* had been the subject of multiple studies before Nilsen started working on the parasite, including detailed accounts of its lifecycle and developmental stages. The fish health community at the University of Bergen, from which Nilsen was a graduate, began conducting seminal investigations in the early 1990s. A fish disease research group spearheaded by Nilsen's former teacher Are Nylund, which Nilsen later joined as a professor, had examined the parasite's role as a disease vector. Additionally, several grey papers and conference proceedings discussed aspects of salmon lice biology. But while these materials offered a critical base, the literature mainly centered on the parasite's gross morphology, its population dynamics, and therapeutics. So even though there had been considerable investments into the science of salmon lice broadly construed, there was an absence of infrastructure adapted to the kind of molecular research Nilsen advocated.

To address this problem, Nilsen assembled a team of technicians, researchers, and students to devise a productive infrastructure for molecular investigations. One challenge soon manifested, namely the practicalities involved in securing a sufficiently large and stable supply of salmon lice to the laboratory. Until 2002, specimens of *L. salmonis* had only been maintained on the fish host under laboratory conditions for one or two generations at best. Sometimes the female specimens would simply disappear from the fish; on other occasions, all the eggs and copepodites would perish because the rudimentary incubator systems being used only had stagnant water. This made it near impossible to produce stable, inbred lineages for molecular research. Initially, Nilsen's group therefore had no other recourse than to harvest specimens from the wild.

While this seemed like a feasible strategy, harvesting salmon lice turned out to be cumbersome, as one cannot, with any reasonable likelihood of success, simply cast buckets into the ocean and hope to catch an adequate number of *L. salmonis* specimens ready for experimentation. Fish farms, on the other hand, had thousands of hosts working as

breeding reactors, so it was possible to sample lice directly from these sites. But this too proved inconvenient. To harvest lice from live salmon, the fish had to be drawn from the pens under rough conditions, so that any lice still attached could be carefully removed from the sedated host using forceps. But this messy procedure could easily injure both fish and louse, so even though farmers were required by law to keep and report weekly lice counts, it was challenging to secure a stable lice supply, as infection numbers varied considerably through the year. For Nilsen's group, a provisional solution was to sample specimens from salmon processing plants, where fish are brought from farms by well boats.

But this routine was problematic as well. For one thing, lice specimens had to be kept alive until they reached the lab, which posed formidable logistical challenges. Additionally, an unstable lice supply introduced many epistemic risks. Nilsen had proposed to use novel molecular methods to study the parasite. But since the gene-expression profiles of many important genes were sex specific and sometimes unique for different life stages of the organism, lice specimens had to be controlled for sex and synchronized to similar stages in their lifecycle. Quality research also necessitated the identification and separation of different experimental strains by some form of genetic or phenotypical marker. Without a steady lice supply they could not develop strains with identifiable baseline markers, and it was not possible to plan more advanced experiments. The amount of residual nucleic acids in a single salmon louse was also relatively small due to the organism's physical dimensions (especially for specimens in the earlier life stages). To isolate genetic matter for comparative experiments, the group needed stable access to lice tissue. An unpredictable louse supply made long-term planning of assays difficult, and without being able to anticipate future supplies of experimental animals, it was hard to design experiments and pursue promising ideas in the lab, spontaneously.

In fact, dependency on wild lice practically ruled out whole classes of experimental designs, such as "common-garden experiments" which can be productively used to tests environmental effects. Common-garden designs would be critical for examining the influence of genes (the genotype) on the animal's development (its phenotype and ontogeny),

by comparing the developmental trajectories of two genetically distinct strains or populations of a species under identical environmental conditions. Additionally, any specimens used for gene-expression studies should have well-known baseline genetic properties. As the genetic variation in wild salmon lice was considerable, uncharted variations could introduce confounds in genomics-oriented studies. To fully utilize powerful comparative tools for analyzing gene expression, the research group therefore needed a stabile provision of lice of consistent quality, and with a familiar degree of reduced genomic variation, preferably. In sum, scientific progress on topics from host susceptibility to the effects of parasiticides and functional genomics depended on establishing a thriving culture of salmon lice.

Incubators

Nilsen and the team had to find a way to domesticate the parasite in the laboratory. Starting in 2002, the group began experimenting on a more sophisticated incubator and culturing system for *L. salmonis*. At the time, Lars Hamre, a researcher-technician who became one of Nilsen's close associates, was busy mapping the lifecycle of *Caligus curtus* ("cod-lice," *torskelus*), another copepod ectoparasite whose research also depended on solving the challenge of securing a steady supply of experimental animals. Hamre was able to devise a prototype hatchery with a continuous water flow that could also be used for cultivating *L. salmonis* and maintain generation after generation of lice in the lab, despite previous attempts seeing meagre success. These, in turn, could be used to make inbred strains, and by establishing these lineages in the lab, frequent field expeditions for harvesting lice were no longer necessary.

A series of experiments published in 2009 provides us with a template for understanding the system's general paradigm and its performance. Here, my account is based on conversations with the system designers, ethnographic observation of more recent versions, as well as scientific documentation. Building a viable infrastructure to domesticate lice required the group to strike a balance between practical constraints and the pursuit of scientifically ambitious questions. Since there were no

similar systems for comparison, it was difficult to converge on an optimal design of a life-support system for lice in their earliest life stage. At first, specimens had been temporarily kept in containers like modified plastic soda bottles, but the group began tinkering with other plastic materials such as tubing, casings, and plastic sheets to make contraptions for storing and breeding the parasites. These designs were then tested out iteratively, and eventually, a solution was found that satisfied practical, epistemic, and aesthetic constraints.

According to Hamre, the system's main architect, the main challenge was to establish an environment where the embryos in the fertilized egg-strings could thrive until hatching. Then, after hatching, the scientists had to maintain the vulnerable larvae through two pelagic stages until the infective copepodite stage, a fourteen-day process under normal lab temperatures. To ensure that the parasite developed in captivity, two important artifacts were created: a small incubator designed to rear pairs of egg strings in isolation (making it possible to track its development), and a larger incubator for hatching batches of lice, with up to fifty egg-strings. Both these devices relied on a continuous water flow to optimize water quality.

The first specimens of gravid females that went into this culturing system were collected from slaughterhouses, and their eggs were incubated and hatched in the new culturing system. Infective copepodids were then transplanted to small fish between 250 and 1500 grams, which were kept in water tanks ranging between 160 and 1500 liters. After successfully infecting these juveniles with lice, the salmon were then raised in the tanks, while the parasite matured on the fish. By rearing female and male lice together, the group could harvest the resulting egg-strings and incubate them, thereby propagating the next generation of experimental animals. Biologists conventionally dub founding members of such inbred and outbred lineages "generation zero" (F0), and the next generations F2, F3, and so on. By branching off lineages, by mating individuals with mutations of scientific interest, it was now possible to systematically create new strains.

One constraint on this design was the need to optimize the flow-through rate of water, the rate by which old water is replaced by fresh, so that specimens were kept in a suitable environment. Another related to

the properties of different plastic materials, and whether these could be assembled easily and durably on a mass scale without leakages, allowing for easy cleaning and maintenance. The group also invested considerable efforts into optimizing practical routines for handling lice. Since a salmon out of water twists about violently, thereby making an approach with sharp forceps in hand risky for scientists and fish alike, the hosts had to be sedated before sampling. But as sedation for lice-picking is stressful for the animal, and time-consuming, animal welfare considerations were pressing. As the system's designer explained: "The sedation procedure was optimized by adding a hypnoticum (metomidat) to the general anesthetic (benzocaine) to reduce stress responses and lower the induction time (time required for the fish to fall asleep). On other occasions, for instance when few lice were required, lice were collected directly with forceps from fish that were somewhat arrested by a lowered water level [in the tank]." After harvesting, new egg strings could then be placed back into the incubators and left to hatch and grow until they reached the copepod life stage.

In establishing the louse as a "living instrument" in the lab (Kohler, 1994), even mundane tasks could have deep epistemic consequences. For instance, handling and moving batches of lice in daily laboratory work had to be standardized for the group to obtain reliable experimental data without introducing systematic errors. One reoccurring problem concerned the identification of a method to estimate the required number of copepodites for infecting salmon hosts and get useful data from the process. Too large infections would needlessly stress the fish, but too small infections yielded insufficient specimens for subsequent experimentation. To gauge infection levels for each fish, the researchers also had to estimate the density of copepods in each water column without damaging them (Fig. 3.1).

Although there was no obvious way to do this, the group converged on a solution where a beaker was filled with seawater and then adding whatever available copepodids they had bred for the experiment. Commenting on an early draft of this written account, the architect explained the reasoning behind these choices as follows: "Since copepodids swim towards the dominant light source, they are not homogeneously distributed in a container. They also actively avoid a sucking

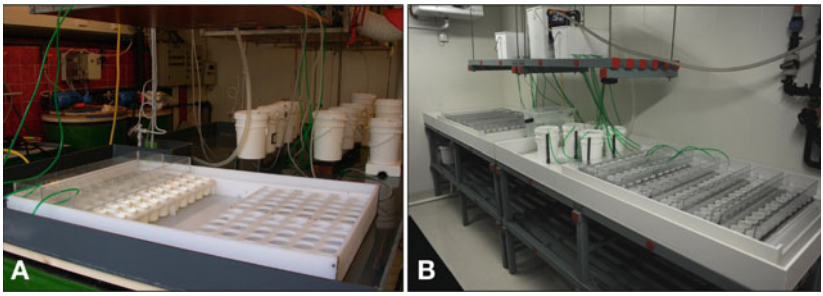

Fig. 3.1 A new material culture for the science of salmon lice. **A** Hatching system from 2003, known as the "multi-hatcher," bucket-hatchers in the background. **B** Reworked version of hatchery and "wet-table." Photos courtesy of Lars Hamre

action [by a pipette]. Thus, to estimate the total number of available copepodids, a transparent plastic tube (10 milliliter pipettes, with ends removed) was plunged to the bottom of the container after gently stirring it in a non-systematic fashion. With a thumb over the upper opening, the tube was lifted out of the water and emptied into a measuring beaker. This was repeated several times until a sample containing about 200 specimens was collected. The diameter of the transparent plastic tube was determined by a trade-off between having as big a diameter as possible to sample sufficient water (and avoid copepodids from escaping the moving tube), and a small enough diameter to retain the water within when lifted out of the water with a thumb over the upper opening."

Subsequently, the volume of water could be measured by reading off the value stamped on the container and inscribing it on a piece of paper. Afterward, the parasites could be placed in a strainer and flushed with *saltsprit* (a solution containing 70% alcohol and 9.2 grams of salt per liter), to stop the parasite from swimming when counting the specimens in the stereomicroscope, where they could be tallied using a special counting vessel. With the number of normal and healthy-looking copepods per unit of water at hand, this value could then be used to infer the overall copepodid density in the beaker.

The group also found a way to estimate the number of infectious copepods, which made it possible to learn about future correlations with adult stage lice. Hoping to create a simple infection model for gauging this

relationship, despite significant variations between the batches, Hamre decided to use a model based on a simple premise, namely the number of copepodites per fish that had to be added to the fish tank to get a required number of adult lice on a fish. This was calculated based on a standardized infection procedure that involved lowering the tank's water column to two or three times the fish's height, then adding copepodites, adding air to the tank for one hour, and subsequently returning the system to a normal water flow.

From experience, the group knew that roughly a third of the copepodids used to infect the fish remained after maturation into adulthood. This invariance was captured in an equation for calculating the relation between relevant experimental variables: the number of copepods necessary to infect x amount of fish equaled to the number of fish to be infected, multiplied by the number of desired adult lice, multiplied by 3 (summarized as $\text{copINFECTION} = \text{fish} \times \frac{\text{LICEPRADULT}}{\text{ADULT}} \times 3$). Through an iterative process of trial and error, the group devised a simple conceptual tool that could easily be applied by any lab member to compute infection numbers during experiments.

Laboratory Bricolage

The design of this incubator system exemplifies the kind of cognitive practice that Claude Lévi-Strauss described as *bricolage*, or simply "tinkering." In *The Savage Mind*, he proposed that scientist-engineers in complex, modern societies primarily deal with concepts, precision tools, and specialized materials, which are all carefully orchestrated and executed on basis of a master plan (1966). Lévi-Strauss contrasted this ideal type of "tamed" thought, with the "untamed" thinking of the *bricoleur*. In his view, the *bricoleur* is the common cognitive style in non-literate societies that rely on improvisators who can deal with the concrete resources at hand, with little to no concern about the intentions behind the original design and function of the available materials. Levi-Strauss invoked this contrast to highlight differences between modern and pre-modern human societies in how resources are used for cumulative knowledge production.

However, Lévi-Strauss' dichotomy between these two ideal types does not hold up to scrutiny, as this schema glosses over the multimodal complexities of scientific meaning-making and fails to capture the craft aspects involved in much scientific experimentation. In crafting a new experimental system for the molecular biology of lice, the scientists involved had to work through a trial-and-error process involving iterative, adaptive changes to their material culture. These, in turn, transformed mundane materials such as plastic tubes and sheets, glue, and other commercial off-the-shelf products (including discarded sour cream and ice cream containers), into a bespoke infrastructure for parasitological research. By 2009, the lab had cultivated sixteen laboratory strains of lice in the system, based on founding generations collected from different locations along the Norwegian coast. But while the resulting incubator system was successful, the experimental design itself was never conceptualized as *finalized*. On the contrary, parasites like *L. salmonis* offer experimentalists with specific biological challenges in comparison with non-parasitic life forms, and there were always possible improvements that could be made, as more was learned about how the component parts of the setup interacted with each other.

In the time that followed, many minute details pertaining to the incubators were tweaked to satisfy new epistemic needs that arose as the system matured to fully display its affordances under various conditions. One example was new quantifications of infection and survival success of lice attached on salmon. Other insights came from addressing more perennial problems with parasites on parasites, so-called "hyperparasites," that came to the group's attention when they brought the lifecycle under human control. This meant that the presence of ciliates (protozoans), and a range of bacterial and viral agents had to be carefully monitored. For instance, colleagues of Nilsen's team demonstrated that lice hosted a new microsporodium, a spore-forming unicellular parasite baptized *Paranucleospora theridion*, "little beast" (Nylund et al., 2010). Later, this research group published on the discovery of two novel viruses from the *Rhabdoviridae* family, together with members of the Sea Lice Research Centre (Økland et al., 2014). These findings would in turn spawn new lines for research, such as the effect of pathogens on host–parasite relations, providing fertile grounds for inquiry about whether

pathogens could be used for therapeutic applications. Weaponization of hyperparasites was theoretically possible, either by engineering the virus to be harmful by manipulating its genome to knock out genes that lice use when adapting to the host immune system; by engineering it to be more virulent and harmful, or by using viral agents to immunize the fish, thereby making it harder for infected lice to attach to salmon. From a commercial perspective, however, such interventions were infeasible due to prevalent consumer attitudes toward anything that resembled GMOs.

As part of this ever-evolving system, laboratory staff also devised new routines for book-keeping, such as adapting Excel spreadsheets to systematically track a wealth of details about relevant experimental events. These spreadsheets became devices for organizing and integrating critical information of different kinds, such as the pedigrees of lice strains, movements of lice and hosts between containers, hatching rates and the life stages of strains maintained in incubators; balance sheets marking deposits and withdrawals of lice; historical records of water quality, temperature, and salinity; and other relevant information.

With standardized lice at hand, Nilssen's group could now quantify differences between the various strains according to morphological factors like body size, and reproductive success (fitness, a measurement of successful offspring). It was also feasible to measure amounts of genetic variation, as a function of differences in specific micro-satellite loci.[2] This way, the group procured genomic insights about various lice strains. By creating so-called "pedigree diagrams," tables representing different variables for each inbred and outbred strain, the group showed that inbred strains exhibited less variation than outbred strains. This was important baseline knowledge for further genomic research.

Later, as this basic design was in place, the system would continue to evolve through novel iterations. New metrics were also devised to assess its performance. One key metric was the "developmental success" ratio, calculated as a function of the number of copepodite specimens divided by the total number of eggs. Assessments of comparable systems for lice breeding had shown that developmental success, measured as the ratio between eggs and successfully matured copepods, was 0.35 for stagnant water systems and 0.28 for those with running water. In the new experimental system, the success rate was a staggering 0.73, more than

twice as good as previous designs. In sum, the new incubators proved far more efficient than other solutions, opening a multitude of productive directions for research in the next years.

There were, however, some challenges on the horizon. When the Institute of Marine Research was scheduled for a major reorganization in 2007, Nilsen had been employed there for close to a decade. Taking stock of his career, he decided that it was time to change pastures and was soon offered a professorate at the University of Bergen's Department of Biology, while retaining an affiliate position at IMR. This new department was a merger between several smaller institutes and there were exciting opportunities to shape its future direction.

As a professor in the Fish Disease Research Group at his alma mater, Nilsen was awarded additional grants and soon his portfolio covered a multitude of different projects split between the two institutions. Recalling this period of his career, Nilsen found this joint affiliation to be crucial for his research program, since it allowed him to finalize ongoing work and maintain close collaborations with IMR scientists to develop future projects. Additionally, the university did not yet have in place laboratory facilities designed for the kind of experimental work on lice genomics that Nilsen and his peers pursued. By retaining this affiliation, he could continuously develop the infrastructure in close collaboration with his old partners. Furthermore, with a well-functioning wet lab in place at the IMR for producing a steady supply of data and lice, Nilsen could also establish a second facility at the University that complemented and improved upon the old experimental system. This would greatly improve capacity, and widen the potential scope for molecular lice research in new directions.

Nersessian notes that participation in a laboratory community goes beyond the exchange of theoretical propositions, but is based on expertise about its material fabric, and how different artifacts relate to each other, and to the overarching research agenda (2006a). In these epistemic cultures, knowledge about the history and development of instruments and apparatus become critical cognitive resources for the experimental system. This includes not just the expertise to narrate what different instruments can do, but also skills for using them properly in productive ways. The ability to articulate and perform efficient epistemic actions in

these contexts involves "cognitive partnerships," where specific artifacts become legitimate co-participants in the production of new insights. Since experimental systems are works in progress, those who participate in their development must be able to historicize the laboratory space as something more than a sequence of events to be recalled. History is a resource for novel design solutions, and for realizing the experimental system's epistemic potential.

Cognitive partnerships require extensive training and deep familiarity with the laboratory's history and operational constraints. In Hacking's taxonomy of the laboratory sciences, this competence relates to "modelling of apparatus"; theories and background knowledge about instrumentation that is seldom equivalent to what is pursued in a given experiment, but critical for its success (1992). Modelling of apparatus is often the providence of a few select staff and seldom uniformly distributed within a community. Given that such competencies cannot be easily reproduced, Nilsen mobilized the considerable assets from his project funds to recruit technicians, postdoctoral candidates, and other staff who were familiar with the experimental system as it was initially developed. Having ensured that operations of the lice-cultivating system were adequately reproduced at the Institute of Marine Research, Nilsen could then bring skilled staff with intimate knowledge about this infrastructure to his new laboratory at the University. Here, they harnessed the power of established cognitive partnerships to propagate and further refine the design of the experimental system.

The Single-Tank System

Vaccine development had long been a holy grail of applied salmon lice research, together with other effective therapeutics, ever since de-lousing agents began to lose their efficacy. Although it was unlikely to be 100% effective, meaning there still was a small chance that resistant lice strains could proliferate, a vaccine would nonetheless have many benefits when used in an integrated pest management system, alongside chemical therapeutics, mechanical interventions, and biological delousing methods like cleaner fish. Primarily, it would lower the infection pressure in salmon

pens, prolong the longevity of existing therapeutics, and reduce costly delousing treatments by changing the selection patterns in lice populations. As Nilsen explained during one of many conference presentations on the Centre's efforts to identify new therapeutics, antiparasitical treatments like vaccines needed to demonstrate at least a 50% reduction in lice infections to be of good use. On the other hand, less specific control measures like immuno-stimulants added to fish feed could positively influence pest management with significantly lower effects.

In the early 2000s, Nilsen launched a vaccine collaboration, with other IMR scientists and the fish health company Intervet Norbio (now a subsidiary of Intervet/Schering-Plough Animal Health), knowing that making vaccines for ectoparasites was notoriously difficult. Host–parasite relationships are often modelled on the metaphor of an arms race between two belligerents, with vaccines as weapons for managing this conflict. On one side is the host's immune system, which sets in motion defensive countermeasures to fend off parasitic infections. On the other is an operative that has evolved aggressive measures and biological tricks over millions of years to extract resources from the host and breach its immunological defenses. Since the host is normally both the parasite's main food resource *and* its habitat, the interloper spends its life in hostile territory, and the ability to survive and reproduce in this inhospitable environment require special adaptations.

A gene-centered view of parasitic evolution predicts that parasites evolve strategies that carefully balance tradeoffs between costs and benefits of *virulence*, a parasite's ability to inflict damage on the host. Virulence levels are determined by a variety of factors relating to two fundamentals of the parasitic lifestyle. First, parasitic behaviors should not kill the host *too* quickly, since this can induce costs like lower reproductive rates (there are cases where the pathogen fails to reproduce or transfer to alternative hosts before the original host perishes). Secondly, natural selection will work against *too much* moderation on the individual level, since reproducing individuals can then lose out in competition with more aggressive individuals who willingly extract more resources from the host to fast-track their own reproductive success. While there are different hypotheses about the evolution of virulence,[3] equilibrium points for different environments have evolved through

natural selection that navigate these major tradeoffs. These biological boundaries on the parasitic lifestyle suggest that the host–parasite complex is deeply intertwined, which in turn makes experimental manipulations highly challenging. If scientists manipulate one variable, like the parasite's feeding system or the host immune system, they may introduce confounding factors, which can inadvertently alter other aspects of parasite–host relationships in ways that cannot be adequately observed and controlled.

In contrast to internal parasites (*endoparasites*), ectoparasites spend their lives on the outside of the host, and in the case of lice with little physical contact except for a relatively small area on the outer skin from which the parasite feeds. Millions of years of evolution have honed the parasite's biological arsenal to exploit this niche by modulation of the host immune system to ensure that no effective host response is elicited by exposure to the interlocutor. This effectively creates a biological constraint for vaccine developers, making it very difficult to target ectoparasites in the same way as other pathogens. Additionally, special considerations apply when working on ectoparasites in the lab. Since *L. salmonis* spends its life on fish skin, it is extremely vulnerable to the conditions of the host's external environment.

While these constraints explain the lack of exoparasitic model systems in biology, Nilsen's collaboration sought a way to work productively around them to develop a vaccine. One inspiration came from breakthroughs in research on another blood-eating (hematophagous) ectoparasite, namely the cattle tick *Rhipicephalus (Boophilus) microplus*, which poses a formidable challenge for livestock farmers. In the late 1980s, a team of Australian livestock researchers developed a tick vaccine that relied on so-called "hidden" or "concealed" antigens to circumvent the tick's specialized capacities to circumvent the host defensive system (Willadsen, 2006). This group developed their vaccine around a protein known as BM86, found in the tick's digestive system. A "concealed" antigen, BM86 does not usually run into the host's immune system during a normal infection. Concealed antigens are efficacious because the parasite has not yet evolved a sophisticated immune counter-response against their antibodies, since the molecules have never been encountered through natural contact with the host.[4] Upon vaccination with

BM86, the host's immune system could thereby be "trained" to react to the antigen by producing antibodies that slowly attack the tick as it consumes its blood meal. Such concealed antigens can be either purified from the parasite or manufactured using recombinant technology in the laboratory.

As this was the only known ectoparasitic vaccine, Nilsen and his peers scrutinized the tick literature, and began searching for salmon antibodies in lice. Through immunohistochemistry they were able to show that host antibodies were, indeed, found in the lice intestine. They also found positive staining of salmon antibodies outside of the intestine, which indicated that the antibodies could cross the intestinal body (where the blood meal passes), and that it was theoretically possible that they could be delivered to critical organs. Eventually, the collaboration managed to procure a test vaccine, based on a protein purified from the yolks of unfertilized lice eggs, but evaluating the effects of these therapeutic interventions proved challenging.

In the starting phase of vaccine development, after establishing the incubator and breeding system, the scientist would rear their experimental salmon in large communal tanks at the Institute of Marine Research. But when the group experimented with the vaccine candidates, they detected variations in lice loss between the tanks, which could not be causally specified, and their experimental design suffered from unknown confounds. Complicating matters even more, there was precious little antibody available for experimentation, since purification of an "optimal" amount would take years. Therefore, the trials made compromises with respect to the number of immunized fish. A scarcity of inoculated salmon, which ran the risk of statistically under-powering their sample, also synergized with the materiality of the communal fish tanks in unexpected ways, as the experiment saw a surprisingly large variable lice loss. When controlling different parameters, there seemed to be interactive effects between salmon and lice, which exacerbated the analytical challenge. Apparently, some lice would "jump" between the hosts, and some cohabiting salmon would occasionally eat lice from other conspecifics in the tanks. In sum, the classical challenge paradigm they were using for their experiments made it hard to calculate solid statistics for answering whether the new interventions were truly effective.[5]

Feasibility of vaccine research thus hinged on whether the group could devise a system that mitigated a flurry of interactional effects between salmon, lice, and their shared environment. As the ambitions for molecular lice research grew, so did the limitations of the experimental system become more apparent. Another revolution in experimental design was therefore necessary, beyond culturing novel strains of salmon lice and setting up productive incubators. Specifically, the group needed a design that let them meticulously record the loss of any preadult and adult lice leaving the salmon host after infection. Such metrics could then be used to calculate precise mortality curves to gauge the effect of an intervention.

With no such system at hand, how could they tease apart and isolate these confounding factors? Recalling this formative period, the senior wet lab engineer Lars Hamre explained how the next extension of the system solved the issue of variable lice loss in vaccine experiments, while supporting efforts to domesticate a related parasite known as "cod-lice" (*Caligus curtus*). To tackle both these problems, Hamre proposed an intricate system based around smaller tanks where individual fish could be carefully monitored, instead of using standard communal fish tanks with inadequate experimental control. Shortly after building a proof-of-concept, a small trial with satisfactory results was conducted in mid-March 2008. By June the same year, their first iteration of the new system was up and running, providing infrastructure for experimental studies on parasitic virulence.

Reflecting on these historical events, the lab director emphasized how studies on ticks influenced his own thinking about the single-tank system and its epistemic potential. Scientists working on ticks with sheep face confounds like those bedeviling salmon lice researchers, when they are probing the efficacy of potential drugs. As with lice in water, there are many things that cause ticks to fall off livestock during experiments. Like with salmon, sheep have interactions with the external environment in the form of rubbing and scraping behavior, so researchers must ensure that observed tick loss during experiments can really be attributed to immune reactions stemming from a test vaccine and rule out other causes.

On sheep, this attribution problem was solved by shaving wool from the animal on specific locations, and glue metal rings onto the animal's skin. A specific number of ticks would then be placed within the rings. By stretching a fine mesh fabric across the opening, it was then possible to seal off the circumscribed area with the ticks secured inside. Next, the ticks and the host animal would be observed for the experimental period, and the number of parasites still attached could be quantified at the end, without researchers worrying about the ticks being lost for other reasons than the targeted intervention.

Nilsen drew analogies between this procedure and their own experimental designs for salmon lice. As Nersessian observes, this sort of problem-solving by analogy is a form of "model-based reasoning" that involves shifting the character of representations in subtle ways so that one representation can be seen in terms of the other, for instance, by changing the representational format or by externalizing the representation in another medium, such as a physical model (Nersessian, 2006b). Analogical problem-solving is used when there are recognized similarities between a problem situation (the target) and something familiar and better understood (the source domain). Analogical reasoning then unfolds through a cross-mapping between the source and target, where relevant constraints from both input domains are projected onto a second-order representation that maintains crucial isomorphic relations. Sometimes, several "bootstrapping" iterations are required to converge on a hybrid re-representation, or model, that satisfies multiple constraints to support problem-solving. The bootstrapping metaphor suggests that constraints, whether material or theoretical, are like bootstraps and that each crossing of the straps elaborates the scientific model and facilitates understandings of the target system.

In this case, the possibility of isolating each fish as separate and independent experimental units ordered in arrays of single tanks sharing a joint water supply bore similarities to how the use of mesh-clad rings placed on livestock provided a bounded unit of analysis for detecting the effects of a tick vaccine. Compared to communal tanks, where the infection level of any one fish depended on the behavior of other fish, which could not be controlled for, the single-tank environment provided a

bounded microcosm where host–parasite interactions could be explored in detail under controlled circumstances.

While the first iterations were rudimentary and built to demonstrate whether the principle of isolating experimental units was a reliable one, subsequent designs added sophistication. Envisioning a more ideal system, Hamre suggested that the salmonids also would have to be positioned in a sufficiently strong water current to thrive in the tank. This would also ensure that debris and "biofilm" did not accumulate too quickly. Other design constraints included easy access for feeding the fish, easy cleaning and maintenance, as well as an arrangement for detecting and counting lost lice, such as small nets to cover the water outlets. Similar to how the incubator system was assembled through trial and error, the group eventually converged on an entirely new design, using an array of 55-L commercial PE-grade, transparent plastic containers. These were perforated and fitted with a water supply and an outlet that were carefully aligned to create a powerful counter-current where the salmon could position itself (a strong current invites salmon to "stand" calm in the water, swimming against the current). This system would later be redesigned when its use displayed new opportunities for improvement. One example of a practical improvement that added experimental functionality was the retrofitting of tanks with a new custom-designed, individualized water supply to make it easier to infect salmon with lice (Fig. 3.2).

To compare the merits between their old and new system, Nilsen and Hamre ran a series of trials between 2008 and 2009 (2011). Here, they outlined four experiments that assessed the feasibility of cultivating small salmon infected with *L. salmonis* in arrays of single tanks, in a manner that became paradigmatic for subsequent lice challenges. In summary, these trials were conducted by first removing a particular laboratory strain of lice from their hosts, which were kept in large tanks at the Institute. Sets of eight males and females were then placed onto twenty new host fish, carefully allocated to individual tanks. Additionally, twenty fish were also infected and placed in 200-liter communal tanks. All fish were measured for length and weighed before and after the trial to evaluate their growth. Individual fish tanks were also fitted with a fine mesh net that was inspected daily to catalogue and collect any lice that fell off.

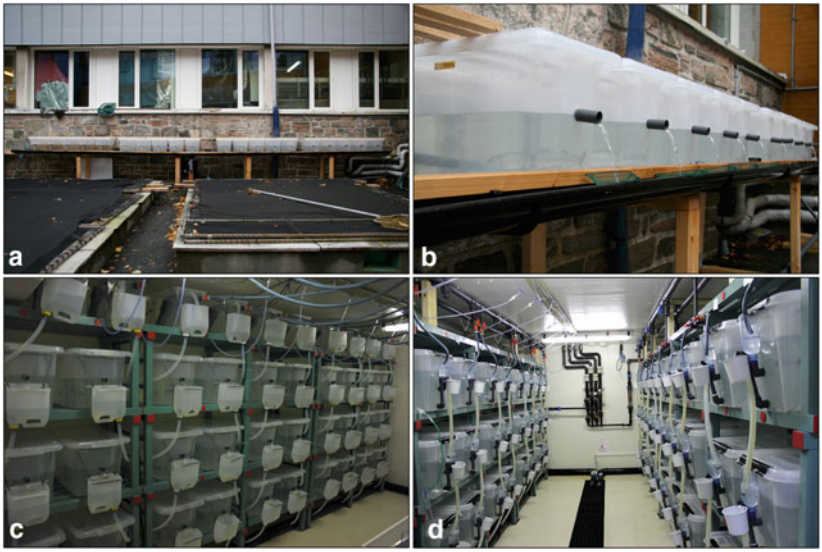

Fig. 3.2 Three iterations of the single-tank system. **a** and **b** was a proof of concept in the courtyard at the Institute for Marine Research, used in two vaccine trials. **c–d** displays single-tank system in shelfs. Notice the customized windshield washer-fluid canisters in **c**. In **d**, a recent iteration, fish are better positioned in the water current, and tanks are less susceptible to fouling. All photos with permission from Lars Hamre.

As with other experiments, the fish were hand-fed in the tanks using commercial fish feeds. When the four experiments were terminated, after 24, 40, 40, and 48 days, respectively, lice and their egg-strings were carefully counted and photographed. Afterward, these were subjected to a morphometric analysis using ImageJ, an open software used to measure pixel-value statistics, distances, and angles in micrographs.

Several aspects of this design were epistemically productive. Besides offering the researchers a precise count of lice loss, making it easier to identify causal relations between variables, the group could also estimate between-host variability and assess growth rates. Other experimental potentials were also revealed. For example, the new design made it possible to estimate lice abundance daily, by subtracting the cumulative number of lice collected in the nets from the number initially placed on the fish. This rate was captured in the formula: $R =$

$-\ln(N_{T1}/N_{T2})/\Delta T$. Here, the R represents the "daily instantaneous loss rate," while N stands for the number of lice, and ΔT ("delta" T) the difference between the days passed between $Time_1$ and $Time_2$, the start and endpoint of the experiment.

Another important insight gained from these trials was a new power analysis indicating that future experimental designs would require between three and six fish groups to detect an above 50% effect on lice loss. Such mathematical constructs would later be deployed in other contexts, where knowing the rate of loss, or the required power for statistical inferences, was critical. The latter was crucial since Norwegian animal welfare regulations demand that experimenters reduce the number of animals to the minimum necessary for sound statistical analysis.

With their new measurements in hand, the group could systematically deploy a range of statistical tools for calculating data about lice dynamics. This included analyses of morphometric features and infection-values, correlations in lice loss between specimens (to rule out differences in genetic susceptibility and individual variations in host immune response), as well as correlations in loss of salmon lice between female and male lice (using statistics like Spearman's rank correlation). It was also possible to estimate differences in lice loss across different trials, using variations on a statistical method known as "analysis of variance" (ANOVA), which estimates the probability by which different samples and variables are related to each other. Relations between lice loss and host size could also be characterized, using simple regression analysis. Now, it was feasible to investigate new relationships, such as those between the length of the louse cephalothorax and the size of male and female lice within each trial (lice loss turned out to be much greater in larger individuals, for example). The new system also afforded calculations of the specific growth rate, which measures the growth after a particular time interval, and the surface area for the host fish, since bigger hosts tended to have larger infections. As Hamre, the architect, concluded in an interview: "In sum, the system offered far better experimental control; the host–parasite relationship could now be studied in detail since there was no jumping of lice between hosts and filters allowed monitoring the exact life loss patterns from each individual host."

These trials also gave opportunities to develop new metrics for assessing the well-being of individual hosts, a major benefit from an animal welfare perspective. Since manhandling during experiments was stressful, the specimens required considerable time to readjust afterward. And while it seemingly took longer for individual fish to adjust to the single-tank environment compared to those kept in communal tanks, the single-tank specimens nonetheless appeared to adjust remarkably well. Most specimens lined up in the water current at day two after treatment, and some started eating again at day three, with most fish resuming feeding habits after roughly one week. All these were indications that the fish thrived.

The transparent plastics used in the new system also allowed for other observations. For example, it soon became clear that salmon had an easier time collecting feed pellets from the bottom of the new tanks, after delivery through the water inlet. Particles from excess food were also quickly flushed out, which significantly improved water quality. Furthermore, since salmon are adapted to avoid avian predators, lab workers would occasionally elicit stress responses from the fish when approaching the large, communal tanks for inspection. With the new system, the fish appeared to be calmer under these circumstances, possibly due to the increased visibility of the transparent walls in their new environment.

In summary, the single-tank system afforded many new conceptual insights, and its material properties captured key invariances which could be put to good use in future refinements of experimental design. With respect to the vaccine trials, these developments were promising, although no conclusive differences could be detected between the experimental condition and the control groups. More antigens were therefore purified, and new formal trials were conducted in different labs in the years that followed, using smaller fish, which required less antigens for injection. Still, results remained inconclusive. Although the trials showed that a vaccine was somewhat efficacious and technically feasible, it was not clear which of the vaccine components had an effect, and whether they could be scaled up commercially.

As with the incubators, the single-tank system had transformed from an elusive epistemic thing to a "technical object," to invoke Rheinberger's terminology. The more that was learned about this arrangement and its

elaborations, the more its intrinsic capacities could be played out. Since the new system demonstrated that only a few hosts were necessary for statistical detection of abnormal lice loss, one of its most important functions was to enable the use of new molecular technologies for screening the parasite's genome in search of potential vaccine candidates. Accumulation of such robust invariances also provided grounds for trusting the system in later experimental contexts, since insights about how the system behaved under conditions X and Y supported inferences about the state of the system under condition Z.

Extending the System

In addition to building a new generation of incubators and calibrating a novel tank system for future vaccine trials, Nilsen's group also expanded their research infrastructure for marine genomics. Among other things, the lab invested in a robotized high-throughput assembly for genomic sequencing, with the goal of accomplishing "as much large-scale sequencing as the group could afford," as Nilsen later described it. This technology also extended the group's collaborations with computational biologists and bioinformaticians.

Crafting a commercially viable vaccine required detailed insights about fundamental biological cascades in the louse, and identification of suitable vaccine targets among the many genes underpinning these mechanisms. Since a "brute search" strategy, where every single gene in the louse genome was tested, would be prohibitively costly and time-consuming, a sustained effort was made to use genomic methods to identify over 7000 Expressed Sequence Tags (ESTs). These are short and unique stretches of DNA derived from cDNA libraries, which can be used as a landmark for mapping active genes in the genome at the time of sampling. By searching the ESTs against bioinformatic databases containing gene libraries from many other organisms, it was theoretically possible to identify the functional characteristics of many louse genes. Additionally, Nilsen's group designed several DNA microarrays for salmon lice (and codfish, as well), through collaborations with the Norwegian Microarray Consortium to obtain expression profiles for the

ESTs. In turn, these profiles showed that distinct clusters of genes were turned on and off during certain critical phases of the lifecycle, such as during maturation and egg production, including genes coding for the antigens that were used to devise the first test vaccines.

Although these developments held some promise, identification of candidates using microarray studies was not feasible in the long run, since the list of recognized candidates surpassed the experimental system's capacity for clinical trials. As technically complex arrangements, clinical trials required large amounts of antigens from salmon lice, either isolated directly or manufactured using recombinant technology. Securing these resources was not only time-consuming, but necessitated the enlistment of other actors, like pharmaceutical companies with access to facilities for recombinant methods and the capacity to assess the commercial prospects of a potential vaccine. Furthermore, even using a very narrow search that resulted in full-fledged clinical trials for the roughly 20–100 candidate genes, which was the number of screens that Nilsen considered necessary for identifying a well-functioning treatment, would take unacceptably long and come at a tremendous cost. In the early 2000s, Nilsen's group was therefore searching for alternative screening methods based on new genomic technologies, which were undergoing rapid development at a moment when costs plummeted with the advent of "next-generation sequencing."

While Nilsen's group made multiple advances with respect to the experimental system in this period, they also faced setbacks. Lars Hamre, the designer of the incubator and single-tank system, worked to introduce Green Fluorescent Protein (GFP) into a retrovirus that would act as a vector when infecting salmon lice for his doctoral project. The idea was to use GFP as a reporter gene to learn more about patterns of gene expression in the louse, since this protein exhibits a strong fluorescence when illuminated by an ultraviolet light source. While GFP was available as an off-the-shelf technology, the project was risky and after some attempts, the data proved too messy to productively analyze, and the approach was abandoned. But what appeared to be an epistemic failure for an individual researcher turned out, rather fortuitously, to be a productive moment and critical branching point at the level of the experimental system. Having discarded GFP, the group remained on the

lookout for other clever methods they could use to further probe the biology of salmon lice. And coincidentally, another group of molecular biologists at the University of Bergen, had applied a novel, promising technology called RNA interference (RNAi) in a series of experiments on zebrafish some years before (Wargelius et al., 1999).

Nilsen and colleagues caught interest in this new and exciting method. RNAi's main advantage was that it offered an out-of-the-box technology for swiftly conducting functional screenings of the lice genome by "downregulating" the expression of specific target genes in living lice and observe their effects. The molecular mechanism of RNAi "interferes" with the translation of the protein that a particular sequence of nucleic acids codes for. By observing the development of RNAi-treated parasites in the incubators or on the host in the single-tank system, the group could get detailed insights into the biological functions of each target gene. Since RNAi "simulates" what happens when production of a specific protein is blocked (through vaccines, for instance), it would be possible to test hundreds of genes without costly and time-consuming clinical trials for each candidate. Clinical testing with actual vaccines could then be reserved only for the most promising targets.

In 2006, the Nilsen group was awarded funding from the Functional Genomics program to develop RNAi for salmon lice. Getting RNAi to work productively, however, required further tinkering in the lab. Although standardized RNAi kits were commercially available, the technology also had to be adapted to the specificities of salmon lice biology. In particular, the group had to find a robust way of injecting the parasite and adjust the composition of reagents used in the process. Augmenting the incubator and single-tank system with RNAi afforded Nilsen and his collaborators with entirely new epistemic options. We return to RNAi, and the messy process of adapting this pillar of the experimental system, in the next chapter.

Scaling up: The Sea Lice Research Centre

The idea to establish a specialized center of research dedicated to salmon lice came about two years later, when Nilsen was encouraged to submit

a proposal to The Research Council of Norway's second round of announcements for a funding scheme known as Centers for Research-based Innovation (CRI, *Senter for Forskningsbasert Innovasjon, SFI*) in 2010.[6] These were attractive funding opportunities for scientists who straddled the boundary between basic and applied research. It would give Nilsen's network a clear institutional identity, and long-term financial stability.

The CRI scheme first surfaced in a report to the Norwegian Parliament in 2004. *Commitment to Research* proposed a new instrument to strengthen the innovation capacity in publicly funded research, and make Norway competitive in the global knowledge economy by long-term investments in research collaborations with R&D-intensive businesses (MER, 2004). CRIs were inspired by so-called "Competence Centers," established across Europe to facilitate technology transfer between academia and industry. CRIs would be funded by the Research Council for five years, with the possibility of a three-year extension *if* successfully passing a mid-term evaluation. After the funding expired, the Centers would dissolve, or maintain their activity by other means. A fundamental principle for the scheme was joint funding between academic institutions and industrial partners, with the latter actively participating in the governing of appointed centers.[7] Here, the willingness for industry stakeholders to get involved to capitalize on research findings would be clear evidence for the societal *relevance* of the proposed science. Selection criteria for CRIs were thus much broader than demonstrations of cutting-edge science alone and included considerations about whether there was a strong potential for value-creation.

As such, the CRI scheme follows the patterns of "Mode 2 knowledge-production." Here, "[…] the old paradigm of scientific discovery ('Mode 1') – characterized by the hegemony of theoretical or, at any rate, experimental science; by an internally-driven taxonomy of disciplines; and by the autonomy of scientists and their host institutions, the universities – was being superseded by a new paradigm of knowledge production ('Mode 2'), which was socially distributed, application-oriented, trans-disciplinary, and subject to multiple accountabilities" (Nowotny et al., 2003: 179). In Centers for Research-Driven Innovation, research priorities were articulated in collaboration with external actors and

aimed toward commercializing intellectual property wherever possible. The funding model also made the recipients accountable toward non-academic partners, and subject to quality control by actors quite different from those usually considered to make up the scientific peer community.[8]

After reassurances that he had the full support of his faculty and department in spearheading the venture, Nilsen began a process he later described as basically "knocking on doors," searching for potential collaborators who could bring critical skills and expertise on board for the proposal. The first external senior scientist who signed on was Tor-Einar Horsberg, a pharmacology professor at the Norwegian University of Life Science (formerly the Norwegian School of Veterinary Science). Horsberg was tasked with running Work Package 1, focusing on new drugs (chemotherapeutants), resistance monitoring and control methods for lice. Coincidentally, scientists at a major feed company EWOS were also working on a separate grant proposal, and when Nilsen approached them, they joined forces with a project on anti-attachment feed components. This work package on "anti-attachment"-diets and immunology would be supervised by Simon Wadsworth, a senior researcher at the company.

The project would also benefit from insights about basic mechanisms involved in regulating host–parasite interactions, specifically, the domain known as "immuno-modulation" from the host animal's perspective. Øystein Evensen, another professor of veterinary science specializing in aqua-medicine, disease mechanisms, and vaccine development, was recruited to lead this work as head of Work Package 3 on immune controls, microarrays, and other molecular tools. Professor Rune Male, Nilsen's colleague in the Department of Molecular Biology, had previously worked extensively on the molecular biology of salmon. He joined to lead Work Package 4 on molecular parasitology as a basis for novel treatment methods focusing on RNAi techniques, the biology of growth, reproduction, and the endocrine system. Male also brought along an experienced laboratory technician to bolster the benchwork, and their efforts were strengthened by contributions from Sindre Grotmol, a professor of veterinary medicine.

A fifth work package, called LiceBase, aimed to build a novel digital infrastructure for the project. Envisioned as an integrated database and information repository for the louse genome, LiceBase would build a "genome-browser" where sequence information could be visualized through a regular web browser. These are bundles of software that make information about genes and their organization searchable and visualizable on a personal computer. The core idea is to make it possible to "see" biological entities by managing relationships between different representations of biological data in databases, as images projected to the user's computer screen (Stevens, 2013). As the amount of genetic sequence data about life on Earth has grown, the need for data-management systems has become pressing, as researchers in the era of Big Data are potentially facing a "data deluge," "data flood," or "overload" (see Strasser, 2012 for a critical appraisal). In data-driven biology, the objects of investigation "undergoes a series of transformations: the genome morphs from a text of As, Gs, Ts and Cs to a set of one-dimensional position coordinates in a database, to an array in a piece of code, to a picture on the screen" (Stevens, 2013: 186). The bioinformatician's task is to represent the genome's molecular arrangement based on partial information about sequence structure and function. Genome browsers transform the counterintuitive ontological status of these building blocks to human scale, as meaningful, interactive biological objects and localized, patterned events.

Sequencing had already been completed through other ventures, including the Salmon Louse Genome Project and Salmon Louse Prevention & Treatment ("Prevent," a project addressing lice management using cutting-edge molecular tools).[9] These involved partnerships between major research institutions and industrial players. Unfortunately, resources ran short before the genome was properly curated and annotated with biological information. LiceBase would build on these cumulated insights and disseminate the genome for open access. To lead this work, Nilsen brought onboard Inge Jonassen, a professor of bioinformatics, and they hired a postdoc to build and curate LiceBase. As such, the Center adopted a set of practices identified by Sabina Leonelli as "data-centric"; an approach where "efforts to mobilize integrate, and visualize data are valued as contributions to discovery in their own

right and not as mere by-product of efforts to create and test scientific theories" (2016: 2).

Well-organized and validated genomic data also made it possible for SLRC to embrace novel strategies for vaccine development. Conventional, "forward" development of vaccines is based on isolating different proteins, and then carefully describing the functionality of each. The most efficacious candidates are then vetted through full-fledged vaccine trials, which are costly and time-consuming, taking up to a decade or more. A "reverse" approach, on the other hand, starts with a partially or fully sequenced genome, and then uses *in silico* methods to identify promising candidates based on computer analyses of protein structures encoded by the sequence information. Computers can then be used to simulate the biological importance of each protein, and to search databases for known protein sequences that have been used successfully against similar pathogens. As costs for genomic sequencing have plummeted, this "reverse" approach can significantly shorten the timeframe of vaccine screenings. The Sea Lice Research Centre adopted a hybrid approach to vaccine development that incorporated elements of both strategies. While some therapeutic targets built on past vaccine research and were selected based on conventional "forward" approaches, other genetic pathways were identified and targeted using bioinformatic methods.

When Nilsen moved to the university from IMR, he brought along his trusted dry-lab technician Heidi Kongshaug. But to build a strong community, he needed additional researchers who were familiar with the experimental paradigm. Hamre, the engineer who devised the incubator and single-tank system, was recruited to develop the wet lab and its lice strains. He was soon joined by Per-Gunnar Espedal, a biologist who had worked on the experimental system and made critical discoveries that were instrumental for patenting molecular markers of pyrethroid drug-resistant populations of salmon lice. Generously funded as a CRI, Nilsen could also employ some of his former postdoctoral candidates as research scientists. Among these were Sussie Dalvin, a molecular biologist who began working with Nilsen after the first RNAi trials, as well as Christiane Eichner, who had worked extensively on salmon lice microarrays and other genomic tools. Together, Hamre and Dalvin

would jointly manage and develop the sixth work package, known as LiceLab, focusing on maintenance of host salmon, lice stocks, incubators, hatcheries, and the single-tank system. Needing administrative support, the Centre also recruited Ingunn Wergeland who had a background in biomedical research administration to run the business side of the operation.

Later, the Centre added dozens of doctoral students, postdocs, and other researchers to the line-up. However, to succeed with his proposal in accordance with the funding logic of CRIs, Nilsen needed to mobilize the patronage of strong industrial players. In Norway, fish health biology had an "applied" profile from the onset, as the field matured from a minor academic subfield to a professional education that supplied the farming industry with highly skilled workers (Hersoug et al., 2012). As a rising star in this field, Nilsen had cultivated relationships with a range of companies who could be approached as potential partners, and among those who joined the consortium were Marine Harvest (the world's largest aquaculture company), Lerøy Seafood Group, pharmaceutical company Novartis Animal Health (later Elanco), feed supplier EWOS (later Cargill), and the fish health consultancy PatoGen.[10] The latter was a small, successful biotech company founded by Vidar Asphaug and Magnus Devold, two Ph.D. alumni from the University of Bergen's fish health community, who had trained in molecular virology. From their main offices in Ålesund (a city north of Bergen), PatoGen offered farmers analytical tools for detecting infection and preventing disease outbreaks through novel use of diagnostic methods.[11] Except for EWOS (who had their own experimental facilities), these partners would not lead specific work packages themselves, but participate with funding, grant access to data and networks, and offer know-how on critical issues in salmon lice management, including guidance about what would be practically feasible outside the lab, and what sort of knowledge they believed was worth investing in.

After an intense period of negotiations about patent rights, a consortium agreement was finally signed between the parties. Importantly, the agreement between the academic and industrial partners spelled out "first rights of refusal" to intellectual property rights and contained declarations of commercial interests in different areas such as development of

new drugs, resistance monitoring, anti-attachment remedies, vaccines, and other non-specific immune therapeutics. Conforming with the social logic of CRI, the partners also devised a plan outlining the research progression of the Centre in terms of milestones and deliverables, as per the jargon of contemporary funding schemas. For instance, one of the early goals for the project was to screen around 60 RNAi targets annually, and at least 300 genetic targets within the lifetime of the Centre. The hope was that some of these could be matured into vaccine candidates or other kinds of therapeutic biomolecules for clinical testing. On the 9th of September 2011, the SLRC was ceremoniously opened by the Minister of Fisheries and Coastal Affairs, Lisbeth Berg-Hansen.

Material and Physical Space: Sites and Settings

Members of the consortium were spread across several institutions, employing a broad range of methods in their research. In the following, I focus mainly on the epistemic life of the experimental system located at the University of Bergen and the Institute of Marine Research, as these two sites hosted major activities sitting at the intersection between Work Package 4 (Molecular Parasitology), 5 (LiceBase), and 6 (LiceLab). In this cognitive ecology, functional screens of candidate genes for lice therapeutics were made possible through four core technologies, or "technical things," to adopt Rheinberger's vocabulary. These were: the incubator and hatching system for cultivating salmon lice strains; the single-tank system which provided an unprecedented degree of experimental control over host and parasite; a procedure for intervening on gene expression known as RNA interference; and LiceBase, a bioinformatic resource that embodied the research community's collective memory with an annotated louse genome, and vast amounts of experimental data.

In the age of Big Science, experimental systems tend to expand their reach through time and space, across national borders, and into cyberspace. So, while these resources were mainly operated by the Centre's staff in Bergen, there was also a lively exchange of people,

materials, data, and experimental resources between the partnering institutions, and other collaborators. Incubators, single-tank designs, and strains of specimens from LiceLab were often shared with other labs. Scientists from partner institutions would also regularly travel to Bergen to conduct joint RNAi experiments, and researchers based in Bergen occasionally visited other facilities to acquire new analytical methods, exchange insights, or use instrumentation that was unavailable in their home institutions.[12] Information was also disseminated to other scientific communities via LiceBase. Furthermore, the Centre relied on partners like the pharmaceutical giant Elanco to develop antigens for experimental testing. Producing potential therapeutics required advanced laboratory "pipelines" that the academic institutions did not have at their disposal. On the other hand, the specialized testing of compounds through efficacy trials on live salmon lice necessitated other experimental facilities than those maintained by Elanco. By mutually exchanging resources through the consortium, both organizations could progress in their knowledge. These encounters between epistemic cultures were, however, not entirely frictionless. Not only did they require academic scientists to articulate their tacit knowledge about LiceLab in detail, but they also meant that experimental designs and work routines had to be adapted in new ways to satisfy the audit culture of a multinational corporation.

The story so far shows how the experimental system at the SLRC emerged from an extended network of expertise crosscutting a variety of scientific fields, and an array of epistemic artifacts, which had cumulated insights and materialized solutions to a variety of challenging problems in the marine parasitology of salmon lice. Despite yielding ambiguous results regarding efficacy and commercial scalability, previous vaccine trials also led to many new insights that were ripe for further development. Nilsen believed that despite the timeliness and scientific quality of their research, it was precisely this demonstration of long-term commitment to expand the science of salmon lice to new areas that really persuaded The Research Council to fund their proposal. By orchestrating these resources, the Centre would "facilitate development of new methods for lice control and shorten the time from basic research to new products and tools for parasite control in the aquaculture sector to

achieve a true integrated pest management in the future." This would realize the ambition of becoming "world leading" in the field.

The framework of distributed cognition suggests that physical, social, and conceptual space is hugely important for human accomplishments like science. Let us now step into this cognitive ecology and observe more directly how everyday affairs in the laboratory supported specific forms of knowledge production to elucidate the secrets of *Lepeoptheirus salmonis*. I have mentioned that this experimental system was situated in the specific social setting of the University of Bergen, a public research university in Western Norway. More specifically, the Centre administration and its main contingent of researchers were hosted at the High-technology Centre (*Høyteknologisenteret*) at Marineholmen. An earlier iteration of the wet lab design, was located a few kilometers away, at the Institute of Marine Research at Nordnes. Scientists from Work Package 4, 5, and 6 did most of their experimental work in these two locations. The High-technology Centre opened in 1989, as Norway's first official "science park." As the main tenants included academic institutes for marine biology and computer science, it did not take long before the facility was known as "Fish & Chips" among locals. From a historical perspective, it is hardly surprising that the facility became a locus of cutting-edge marine biology. Close to downtown Bergen, the High-technology Centre is located at the same site as Norway's first biological field-research station, founded in 1891 as a part of Bergen Museum. Having advocated for establishing the station in 1887, the museum's most famous employee, zoologist-explorer, and Nobel laureate Fridtjof Nansen, resigned a few years before it materialized.

Popular among both naturalists and the public, the station sported novel attractions such as a seal park and an aquarium until it was dissolved in 1917, due to an increase in naval activity in the area. In 1922, the station was moved to Herdla outside of Bergen. Some years later, a new biochemical laboratory was built on the old site, which became the Department of Chemistry when the Museum received status as a university in 1946. Almost five decades later, four smaller departments specializing in marine biology, botany, zoology, and microbiology merged into the new Department of Biology in 2004. In a technology-driven move toward increased interdisciplinarity and molecularization

of the life sciences, the biology department was soon co-located with the molecular biologists, who had migrated to the building some years before.[13] Today, Bergen entertains Europe's largest concentration of marine scientists, and Marineholmen has become a central node in the regional innovation network as an interface between academia and industry. Under the promissory note of becoming "tomorrow's marine powerhouse," the research cluster is also scheduled for a massive expansion in the next decades, to host new facilities for "the Holy trinity" of marine affairs: industry, science, and a sizeable public administration (Bergstrøm, 2013).

At the High-technology Centre, SRLC's experimental system occupies several interconnected spaces for knowledge production. Our tour starts at the top, in the area occupied by SLRC at the Department of Molecular Biology on the fifth floor, before moving down through the Biology Department on the third floor, and finally the basement, where LiceLab is located alongside other infrastructure for marine research.

Accessible only by using a small keychain-sized chip, the basic floor patterns in both departments are similar. Like so many other laboratories, both have their hallways adorned with colorful scientific posters, showcasing recent studies by the research groups. Locked glass cabinets packed with spare micropipette tips, plastic tubes, and other disposable, off-the-shelf necessities, line the walls between posters and messenger boards projecting announcements about upcoming events. Some doors have windows, where passersby can observe the action on the benchtops. Small signs specify which group of researchers the space belongs to, or the main function of shared lab facilities. Throughout the workday, scientists, technicians, and students at the SLRC usually split their time between the wet lab, dry lab, conference rooms, and their offices. On both floors, people of different nationalities strike up lively chats in the hallways around coffee makers and water coolers. In front of the workbenches, aspiring and accomplished scientists alike carefully wield their micropipettes between test tubes and reagents to produce new, precious data, using detailed procedures scribbled down in notebooks and tomes detailing the laboratory methods of molecular biology.

For an untrained eye, there is not much conspicuous difference between the third and fifth floor facilities, although the probability of

encountering whole animal specimens in the Department of Biology is higher than coming across one in the Department of Molecular Biology. Thirty years ago, the differences would have been more noticeable, but the past decades have seen a gradual convergence in analytical methods and concepts, as bioscience has honed in on the molecular level as the most epistemically and financially rewarding scale of inquiry (Rheinberger, 2011). Fish health biology is no exception; the level of genes and proteins hold the greatest promise for groundbreaking revelations, and syntheses between the ecological, population, and evolutionary level of analysis are well on the way. If forced to describe the difference somewhat simplistically, one could say that the molecular biologists on the fifth floor, still *mainly* worry about what happens *inside* the cell, while the biologists' two stories below, *predominately* focus on biological processes at a higher organismic level. Still, this would be an oversimplification, and no hard distinction between the two fields is satisfactory, as the structure and function of genes and proteins are now of perennial interest to both fields. Consequentially, many departments of a similar kind have also merged in other universities, becoming huge departments of bioscience or life science.

On both floors, samples of DNA, RNA, protein, and more complex tissues, are processed by diligent caretakers with gloved fingers and (sometimes) white coats. Such protections are especially important during tasks that are sensitive to contamination or involve handling of noxious substances. These "dry" labs consist of a series of interconnected rooms where macromolecules such as DNA, RNA, and proteins are extracted, purified, manipulated, and analyzed, using a combination of well-established and new techniques and instruments. On benchtops sit microscopes, machines for varieties on the polymerase chain reaction (PCR), electrophoresis, micro-centrifuges, water baths, blotting tools, and other essential instruments. We also find necessary tools like micropipettes, disposable tubes, and pipette tips, which are all choreographed along with the contents of a seemingly endless supply of different cardboard boxes. These contain commercial "kits," reagents for carrying out experiments, big and small, according to standardized protocols described in the accompanying leaflets. Lab space on both floors contains dedicated chambers for sample preparation, DNA extraction,

amplification, and post-PCR analysis, and activities in these locations are supervised by laboratory technicians who ensure safe, orderly, and scientifically sound use of the facilities by students, post-docs, and other researchers alike. In later chapters, we look more closely at these choreographies and how they become epistemically productive.

As workspace comes at a premium, some benches are shared between research groups, and must therefore be kept meticulously clean and tidy, with equipment and reagents neatly labelled with the names of their owners. Members of this community, including visiting ethnographers, must attend to many physical and conceptual boundaries that govern conduct here. One such boundary regulates the flow of people and materials between separate spaces used in different stages of the polymerase chain reaction (PCR). Here, special restrictions on movement must apply to prevent contamination of biological samples. Equipment, reagents, and samples are always prepared separately, by gloved fingers, and should only move through physical space unidirectionally, from DNA extraction to amplification. This ensures that samples are not contaminated by nucleotides or other enzymes, like ribonucleases (RNases) and deoxyribonucleases (DNases). Ubiquitous on skin, hair, and other human debris, these enzymes defend against bacteria and viruses. But their chemical properties also make them susceptible to degrade precious samples upon contact, which is why they are resentfully referred to as "fingerases."

Researchers in experimental bioscience make progress by literally putting thoughts "into the benchtop and seeing whether it works or not" (Nersessian, 2010: 119). While the lab bench offers a key workspace for many epistemic activities, staff at the Centre must also attend to scientific inscriptions and graphic representations on their computer screens and interact with other media, including printed or handwritten text, as well as other scientific visuals, often at the same time. So, although scientists spend a lot of time facing their computers, this does not suggest idle, passive gazing at LCD monitors. Rather, working with computers entails an active, embodied, material engagement, where different media are coordinated and manipulated so that new understandings can take place. Scientists do not just think *about* scientific visuals, but also think *with* and *through* them (Alač, 2011).

Like so many other scientific phenomena, biological macromolecules are not available at "the human scale" by default (Turner, 2003: 23). As we shall see later, they only become tractable when they enter into meaningful relationships known as "blends," where material and conceptual structures mutually support each other (Hutchins, 2005). In other words, the genetic characteristics of salmon lice, such as sequence data, must be mediated by other means than direct engagement, and usually this means working with a computer and other specialized tools that can visualize complex biological interactions on the molecular level. In his historical ethnography of bioinformatics, Hallam Stevens shows how molecular biology in the digital era is an enterprise concerned with identifying solutions to the problem of representing macromolecules like nucleic acids, amino acids, and protein, in tractable and meaningful ways (2013). Since only computer-based instruments can render certain representations of biological phenomena legible, it is often in front of a monitor that scientific data acquires new meanings. But not all data are digital, and they can materialize in many ways, as stained or histochemically treated microscopy slides from louse tissue, paper-drawn diagrams, micrographs, as slabs of electrophoresis gel (or as pictures of said slabs), as handwritten entries in lab journals, or a variety of other forms. The office is an environment for coordinating bodies, data, and digital and non-digital artefacts in ways that render inscriptions and visuals meaningful.

Scientists and students also regularly discuss, plan, and teach in seminar rooms and lecture halls scattered throughout the High-technology Centre, hand off samples of nucleotides at the Sequencing Centre on the fifth floor, or travel to other university buildings to use shared facilities, such as the electron microscopy lab. Our guided tour of the facility, however, ends in the basement. It is here we find LiceLab, an epistemic infrastructure that is at the heart of the SLRC's experimental system. To access LiceLab we must pass through a long corridor, intermittently spaced with anonymous doors. Some of these hide large storage halls with small and large tanks containing a variety of fish species and other organisms like sponges, some exotic, others more familiar. The basement atmosphere is cool, due to the many thousands of liters of sea water that flows through the facility at any moment.

A faint smell of sulfur, fish feed, salt water, and detergent fill the brightly lit hallway. Another code-protected door takes us into the "wet" laboratory, made up of five interconnected rooms totaling roughly 80 square meters. This marks another physical and conceptual boundary, and visitors are asked to slip on plastic clogs and lab coats before entering. Inside, there are benchtops and shelves, arrays of plastic containers of different sizes, fiberglass tanks, garden-hose adaptors, modified food canisters, water pipers, and not least, salmon with lice attached to them. Although each separate component in LiceLab may seem mundane alone, the assemblage is an exotic epistemic artifact, indispensable for learning new things about the molecular foundations of salmon lice (Fig. 3.3).

LiceLab was powered by a temperature-controlled water supply provisioned by ILAB, a research foundation managing the state-owned facility of interconnected pumps transporting sea water from a depth of 105 meters outside of Nordnes. Freshwater, on the other hand, originates from Svartediket, an artificial lake comprising Bergen's main water reservoir. With the help of an intricate system of seven different physical filters, along with UV treatment, ILAB ensured 120 water qualities for different experimental applications. As Star and Ruhleder observed, these infrastructures are never just "things," but rather vital relationships for contemporary technoscience (1996: 253). Like a brain requires a steady blood supply, LiceLab depends on a stable, continuous flow of water for its operations. Staff therefore closely monitored the facility for variations in temperature, salinity, and impurities, with a suite of automated detectors and alarms.

At the time of my ethnographic fieldwork, LiceLab housed nine lice strains, and many experimental outcomes at the Centre depended on these being carefully reared through their different life stages; first, as egg-strings attached to females, and then as nauplii and copepodites in incubators before being put to various uses. Lice samples were frequently taken from LiceLab to the dry labs on the third and fifth floors for further processing. On other occasions, representational media, and experimental materials like synthetic, double-stranded RNA for use in screening experiments, moved the other way. In the next chapters, I delve deeper into the cognitive life of this traffic.

Fig. 3.3 Scenes from LiceLab. **a** Scientists counting lice larvae at workstation. **b** Cleaning single-tank system. **c** Wet table with hatching wells and incubators for lice strains and copepodites. **d** Novel system for small fish. Image **c** reproduced with permission from Lars Hamre.

Dividing Epistemic Labor

At one point, my story highlighted Nilsen's role as a broker and innovator in the science of salmon lice. But as history makes clear, scientific entrepreneurs are not "Robinson Crusoes" with only their own wits as guidance, and they do not develop productive research programs in solitude (Muldoon, 2013). Instead, they partake in a complex social and material fabric where many historical trajectories and different interests converge and interact. Therefore, my account has also given weight to the emergence of the SLRC as an epistemic community dedicated to solving a set of specific challenges, and the epistemic and non-epistemic motives involved in shaping the experimental system as a tractable problem-space. But in addition to these movements through time and physical space, we must also make another sojourn, through the social spaces of SLRC, and its division of epistemic labor.

Labor division profusely transforms the physical and cognitive capacities of human groups. But although it ranks among anthropology's most central topics, it has not received the attention it deserves from cognitive anthropologists (D'Andrade, 1995: 208). Distributed cognition attempts to fill the significant gap between Durkheim's assertions about the primacy of labor divisions, and actual empirical demonstrations of the transformative powers of people acting together by doing different things in pursuit of some common goal (Hutchins, 1995: 175). It does so on basis of a non-trivial fact, namely that social spaces constrain what information goes where, when, and in what form. Furthermore, labor division in epistemic activities, like those taking place in laboratories, presupposes two kinds of cognition: the cognitive practices involved in any given specific task, and the cognitive labor involved in organizing and governing a collection of practices (ibid.: 176). When these two cognitive processes are brought together in practice, a community of scientists can acquire quite different properties than those of its individual members.

We can now ask how the SLRC's experimental system was organized to transcend the capacities and limitations of individual researchers. A look at the official chart used in many of the Centre's public reports gives a useful overview of the day-to-day organization. From the chart, it appears

that the consortium is not spontaneously self-organized, but deliberatively constructed, according to a culturally widespread management pattern used in countless research projects. This template is a "social-orientational cultural model" that functionally orient and differentiate individuals through a set of authority relations (Shore, 1995: 64). As a cultural artifact, the schema reveals how members of the community represent themselves, and how the Centre was envisioned to be productively organized. However, the representation does not say much about how knowledge propagates and grows in the wild. In accordance with the principle of cognitive ethnography, it should be considered as a piece of datum, rather than an analysis of how knowledge production is achieved at the SLRC.

Administratively, the Centre consisted of an executive board with appointed representatives from the partnering organizations, an administrative unit consisting of the PI and the administrative project manager, a leader group composed of work package leaders *and* the administrative unit, and six different work packages each with an appointed leader (in one case, two leaders). Work packages varied in size and scope. WP4, for instance, collected several graduate students and postdoctoral research fellows, senior scientists, and professors to oversee operations. WP5, on the other hand, consisted of a leader, a postdoctoral candidate, and a Ph.D. student. Additionally, a scientific advisory board with two internationally renowned scientists was appointed to give strategic advice. Although work packages were modularly organized, there was a continuous and productive exchange of materials and ideas between them, with each work package leader being responsible for coordinating scientific efforts with others, in collaboration with administrators. Interactions between Package 4, 5, and 6 (Molecular Parasitology, LiceBase, and LiceLab) were particularly intensive, comprising a central hub for knowledge production[14] (Fig. 3.4).

In her comparative investigation of epistemic cultures, Knorr-Cetina observes that work in molecular biology is primarily mediated through *techniques*, and not exclusively through the symbolic language of complex mathematics, which mediates fields like experimental, high-energy physics (1999). At CERN's Large Hadron Collider, for example, which serve thousands of researchers, the main coordination problem is

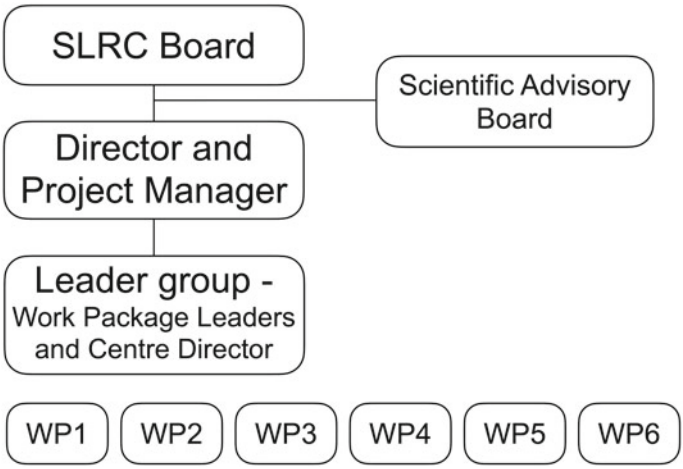

Fig. 3.4 Organizational chart for the Sea Lice Research Centre

that of integrating activities through a "central apparatus." This process, she notes, can potentially erase the individual as an epistemic subject (ibid.: 166–167). Similarly, the production logic of Big Biology has changed the division of labor in ways that occasionally displaces individuals as recognized makers of knowledge (Stevens, 2013). However, in contrast to fields like these, where the unparalleled scale of the experiment makes it difficult to delineate the agents of knowledge production, individual contributions to the growth of experimental knowledge were clearly visible at the SLRC. While research facilities certainly had limited capacity, in the sense that only a few experiments could be coordinated at the same time, individuals contributed to the accumulation of knowledge with their techniques. As such, they were meaningfully recognized as legitimate epistemic subjects, with personal ownership to their interventions in the lab. Interpretations of experimental data were usually made by the same individuals who carried out the trials, and their epistemic outcomes were not decided on a supra-individual level, although senior scientists would, occasionally, contribute to their analysis without engaging in hands-on laboratory work.

Also similar to Knorr-Cetina's observations, the division of labor at SLRC reflected a "dual organization" (ibid.: 237). On one level, the

Centre could be approached as the PI's arrangement of researchers and resources, with individual scientists and their projects functioning as elements within a much larger machinery for knowledge production. For example: since public debates about salmon farming were highly polarized, there was broad agreement that it was primarily up to the administrative leader to relay information to the outside about scientific results, and to officially represent the Centre in correspondences with media and industry. This illustrates that epistemic authority is not distributed evenly, even in the most egalitarian of scientific contexts, despite widespread acceptance of Mertonian norms like "communitarianism" and "disinterestedness" (Merton, 1973).

But at the same time, social organization of experimental life also enabled each researcher to pursue clearly defined individual projects, to advance their own careers and status, which resonated with the larger, programmatic goals of the Centre. Individuation of epistemic subjects was also reflected in the sociology of co-authorships. Most publications from the Centre were usually co-authored works, often between researchers internal to the Centre and collaborators in external research collectives. These partnerships included both other Norwegian research groups, as well as international experts on the molecular biology of salmon lice, notably Canadian laboratories run by Mark Fast at the Atlantic Veterinary College (UPEI), and Ben Koop at the University of Victoria. These scientific collaborations were not coincidental since Canada (like Norway) faces major challenges with ectoparasites in salmon aquaculture. In 2015, the average number of co-authors on publications from the Centre was 4.9, which tracks the general trend in the life sciences toward multi-authorships (see Vale, 2015). While negotiations about entitlements to co-authorships were not unheard of, there were clear demarcation criteria for accreditation on the author list, conforming to the sociological pattern in molecular biology described by Knorr-Cetina (1999: 167). First authorships were reserved for the individual who did the main bulk of the work, while names in the middle of the list were occupied by those who contributed technical procedures, reagents, and other kinds of analytical work. Finally came the lab director, who provisioned resources, guided the inquiry, and germinated big ideas. This ensured that individuals were sustained and recognized as

knowledge-making subjects, despite being faced with strong pragmatic and epistemic incentives for intense collaboration.

The Epistemological Features of *Lepeoptheirus salmonis*

Having historicized the physical and social spaces of the SLRC, I conclude this chapter with an account of the epistemic status of the organism at the center of this cognitive ecosystem. Experimental systems in biological research, the "things and techniques that together generate results" (Creager, 2002: 4), are often built around specific organisms, which are standardized to a particular domain of investigation. These resources are commonly referred to as "model organisms," by both scientists and those who study scientific practices (Leonelli & Ankeny, 2013).

Following Kohler's seminal work on the domestication of *Drosophila melanogaster* as a research technology for geneticists, we can approach the relation between salmon lice and its investigators as an "interactive and evolving symbiosis within the special ecological spaces of experimental laboratories" (1994: 19). This construction of experimental creatures for epistemic purposes involves a special type of domestication process, quite different from the one we saw in Chapter 2, where a suite of different social, material, and conceptual resources come together to form a dynamical and productive system of inquiry. The "friendly fruit fly" *Drosophila*, for example, displaced alternative organisms as a laboratory technology for genetic research. In part, this was due to its pedagogic utility as a teaching instrument (it was easy to cultivate and maintain). But it was also a result of Thomas Hunt Morgan's preference for an organism with "natural wildness and lack of Mendelizing characters, which could be used to study basic biological principles through experimental evolution" (Kohler, 1994: 43).[15] Another popular model, the nematode worm *Caenorhabditis elegans*, was chosen more deliberately by Sidney Brenner and colleagues because of characteristics like short generation times, increased likelihood of spontaneous mutations, a simple reproductive cycle, a small genome, and a tiny physical stature that made

it easy to cultivate, and which afforded good views in electron microscopes so that structural details could be mapped (Ankeny, 2001: 475). Similar stories from the history of science on Tobacco Mosaic Virus (Creager, 2002) and mice (Rader, 2004) show the delicate process by which other species become vehicles for materializing scientific questions.

As the "right tools for the job" (Clarke & Fujimura, 2014), model organisms are selected for intense study by biologists. Data and theoretical concepts derived from these investigations are then used to understand other, more complex, organisms. As with lice, the accommodation of specific organisms to laboratory conditions usually entails a long-winded process of domestication, including conceptualization and appropriate instrumentation. Sampled from a variety of different kingdoms and phyla, model organisms represent a suite of living processes, from fundamental molecular processes that are shared between species, to the ontogeny of whole organisms, and functional and evolutionary relations between phylogenetic groups.

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While all experimental organisms that scientists investigate can, to some extent, be used to model organisms and specific target phenomena beyond themselves, Ankeny and Leonelli have proposed that only a subgroup of experimental organisms should be identified as true "model organisms," due to their particular epistemological features (2011). While there is no firm boundary, these can be differentiated from the larger class of experimental organisms due to their function in biological research, where two dimensions are salient. First, model organisms have a broader "representational target" than other experimental organisms, in terms of the kind of mechanisms, theories, and questions that are investigated via the model, which usually aim to model "whole," intact species. Secondly, they have a wider "representational scope," as the number of other organisms the model is said to "stand in for" is much

greater, potentially extending to all living things. As Ankeny and Leonelli propose: "[…] while the representational target describes the conceptual reasons *why* researchers are studying a given organism, the representational scope defines the *extent* to which researchers see their findings as applicable across organisms" (2011: 320, my italics). In contrast to "true" model organisms, the representational scope for experimental animals is narrowly defined, with the representational targets being highly variable, and usually characterized along specific, disciplinary lines.

Since model organisms are both artificial tools *and* research objects, a means to knowledge *and* its embodiment, they have a distinctly hybrid quality. Often, though not always, their scientific attractiveness stems from biological and material affordances that work as "generators of surprises" when they are explored in detail (Rheinberger, 1997: 3). Baker's yeast (*Saccharomyces cerevisiae*) and fruit flies (*Drosophila melanogaster*) are convenient to manipulate, and they afford studies of detailed genetic maps because of short generation times, large breeding numbers, and the proliferation of a high number of mutants. Other species, like *Arabidopsis* ("thale-cress"), are more suited for certain molecular investigations due to having small genomes and, in the case of the mustard plant, relatively simple diploid chromosomes. Chickens and *Xenopus*-frogs, on the other hand, are less suitable for genetics since they are large, slow breeders that require complicated logistics and take up laboratory space, but they are nonetheless attractive for developmental biologists because of their embryonic properties.

As tokens of Big Science, the ambitious scope of model organism research has also propelled scientists to adopt political strategies that include long-term interdisciplinary collaborations to build unique infrastructures. These are sustained by a well-articulated communal ethos that emphasizes egalitarian sharing. Data, techniques, and materials are often circulated between peers as soon as they are available in any one part of the research community. Model organisms are thus institutionalized and embedded in a material environment involving specialized equipment, and standardized techniques that eventually become widely shared and adopted. Historically, information about models have been represented and propagated through media like newsletters, books, encyclopedias, and journals. But since research practices are now increasingly

virtualized, bioinformatic databases containing genome sequences and detailed information about regulatory elements, biochemical pathways, and protein structures, play a central role in these knowledge exchanges. At the SLRC, the work package centered around LiceBase exemplified this trajectory, as a database curated by many scientists, who contributed with standardized packets of information.

As we have seen, the story about how strains of *L. salmonis* was enculturated to an experimental system committed to understanding parasite–host interactions was quite different. As a "counter-insurgent of the blue revolution" (Blaylock & Bullard, 2014), the ectoparasite was domesticated as a direct response to pressing problems in fish farming. But despite being designed with a very narrow representational target and scope in mind (host–parasite interactions in fish farming), even laboratory strains of lice did not escape the persuasive logic of model organisms. A publication from 2011, for instance, proposed *L. salmonis* as a suitable "model" for studies on a range of parasitological phenomenon (Hamre & Nilsen, 2011). The argument for its aptness as a model was based on the animal's biological affordances, as well as the productivity of the experimental system designed to accommodate its exploratory potential. First, lice were flat, easy to manipulate, and had little pigmentation, meaning that the internal workings of live specimens could be conveniently inspected in a stereomicroscope. Secondly, the development and stabilization of effective RNAi-technology enabled careful studies on gene function in the species. Third, since the parasite had a short generation time, it would be easy to breed, and there was evidence that trait-specific strains could be maintained over many years. Fourth, lice strains could also be used for more general research to test the "nature of resistance mechanisms through experimental breeding," thereby offering scientists a productive genomic model for copepods and ectoparasites in molecular parasitology and evolutionary ecology.

Nonetheless, Hamre and Nilsen's paper was also aware of the system's inherent constraints, making the sobering observation that the facility's demands for tanks and fish hosts limited the parasite's broader appeal. Furthermore, the animal displayed high natural mortality, and showed little evidence of inbreeding depression in the lab. This could, as hypothesized in the paper, mean that harmful alleles were probably weeded out

from the lineages, making mutants difficult to find and maintain, since mutations most likely compromised survival and reproduction in the very hostile environment of the host immune system. This last point would likely lessen the appeal of *L. salmonis* as a genomic model for wider use, since a high number of mutants is one of the key attributes that makes certain organisms so appealing for modelling work.

Here, we see how model organisms not only function descriptively, but also have *prescriptive* force, since research funding and prestige in biology is increasingly allocated on basis of "philosophies of funding" that reward model systems and their associated infrastructures (O'Malley et al., 2009). As Leonelli and Ankeny note: "Many research groups are experiencing pressures as a result of the popularity of the term, for instance due to competitive granting systems that force researchers to focus on these organisms or to rationalize proposed research work on a particular organism by claiming that it is, in some sense, a 'model organism'" (2013: 209). So, while there was less in the way of epistemic justification for framing lice as a model, there were other good reasons for this reasoning.

In contrast to organisms like *Drosophila melanogaster*, which has been operational as a model system for well over a century, salmon lice join the ranks of the many odd species that are subject to experimental research without the social, epistemic, and biological commitments of "proper" model organisms. Like *L. salmonis*, these are studied simply because they demonstrate highly specific biological phenomena or have interesting properties in and of themselves. While the immediate relevance of any given trial at the Centre was negotiable in terms of applicability, scientists would only rarely pursue experiments aimed to address questions with a broad representational scope, or with only indirect relevance for lice management. Compared to "true" model organisms with a wide scope of application across biological domains, experimental animals like the humble lice has narrower target domains, and primarily work as tokens for specific classes of organisms, in this case, copepod ectoparasites.

As apt cultural models, these experimental organisms are therefore less likely to be widely propagated across scientific communities, and usually remain the providence of a few specialists. This stands in contrast to established models which are joint products of distributed

labor involving hundreds, if not thousands, of researchers. *Lepeoptheirus salmonis*, along with its close copepod relatives such as members of the genus *Caligus*, are therefore not widespread laboratory creatures of the "cosmopolitan" variety. Despite being one of our planet's most abundant types of biomass, they remain a curiosity for the vast majority of molecular biologists. Neither is the lice genome a standard reference for comparative genomics and phylogenetics. Rather, due to its limited representational scope, experimental research on this ectoparasite must be understood as a local specialty, that primarily address pressing questions with relevance to salmon farming, instead of supporting a wide and integrative research agenda. The logic of model creatures seems to incentivize researchers to adopt particular cultural and epistemic practices. But attending to how experimental animals like salmon lice are used to investigate specific questions within well-defined contexts in everyday science is certainly no less important from the perspective of a cognitive anthropology of knowledge.

Kohler suggested that we can adopt three complementary viewpoints when thinking about the material cultures necessary to sustain such creatures in the lab (1994). The first sees experimental organisms as technological artifacts sustained by the social and material ecosystems of scientific institutions. This is not just a clever analogy, since experimental organisms must often be "tricked" into doing things valued by their human interlocutors, but which are outside their behavioral repertoires in the wild. An example from LiceLab was the use of RNAi to down-regulate genes involved in host recognition, which makes the usually picky parasite attach to other fish species than salmon. While the extent of such interventions on an organism can vary, selective breeding and genetic interventions using more directly invasive biotechnological means, may also alter the physical make-up of the organism. As such, the organism can be re-engineered so it better conforms to the requirements of laboratory research. Physical alteration is not, however, the only kind of productive intervention. Sometimes this "construction-work" simply entails an accumulation of conceptual resources about how the organism behaves, along with opportunities for experimental manipulation. In turn, these insights can give rise to productive applications driving future research.

Secondly, Kohler points out that experimental organisms have biological histories that are independent of scientific interventions and their appropriation as artifacts that undergo cultural evolution. Just like the fruit fly (*Drosophila*) underwent evolutionary adaptations to the presence of human settlements, so did populations of salmon lice, with their short generation times and great fecundity, quickly adapt to intensive marine farming of salmonids. As such, the lice that my interlocutors worked on were already "second nature" (1994: 9). They were semi-domesticated to the engineered habitat of the farming pen, through the mutual causation process described in Chapter 2, long before they were transposed to the laboratory for targeted cultivation. Salmon pens and laboratories alike, thus present distinct ecosystems where creatures live and evolve in close relation to humans. From the parasite's perspective, life in both the farming pen and the lab entails a steady supply of salmonid hosts, which are themselves also fed and groomed by humans. The substantive difference, of course, is that while lice are unwelcome trespassers at the farm (and must be culled, even at great cost), they must be coaxed into becoming "commensals" in the lab. A prerequisite for this partnership is that the lice strains are continually nurtured and protected so that scientists may learn new things about them (although their hosts may beg to differ).

Kohler's observation that *Drosophila* was both a technical artifact, and a product of natural history, also extends to salmon lice. For example, lice strains cultivated in the lab originated in farming localities they were biologically adapted to. Some of these populations were subjected to strong selection pressures for drug resistance against therapeutics used locally in aquaculture. As a result of selective sampling from many unique locations, the Sea Lice Research Centre cultivated multiple unique strains of lice with different attributes, supplying around three dozen scientists and students with research materials. While three of these strains were sensitive to conventional drugs (in part because they had been sampled before resistance mechanisms accumulated in the population), one strain was inbred at the Centre, and the remaining five strains were resistant to either one or more drugs (commonly described as "multi-resistant"). The inbred strain, for example, was useful for research where discounting

of genetic variations was necessary to determine experimental outcomes, and for comparative assays between strains with very different properties.

As the mutual causation process described in the previous chapter makes clear, no clear-cut divide between "nature and artifice" can be said to apply in such cases (Kohler, 1994: 10). This brings us to the third viewpoint. As both technology and natural history, the organism is enrolled in the social and moral economies of authority relations, information and knowledge cascades, credit and prestige, characteristic of modern life science. In a case study on a controversy over the science of salmon lice in the Broughton Archipelago of British Columbia (Canada), the environmental historian Stephen Bocking observed that the analytical problems of field science, like marine ecology, are occasionally situated in places embroiled in political controversy (Bocking, 2012). This makes field sciences vulnerable to enlistment by political partisans. Local environmental features, when invoked through scientific practice and debate, can become "surrogates for local interests, values, and emotions, and local social dynamics of trust and coastal identity" (Bocking, 2012: 711). In such highly disputed cases, field scientists must grapple with how to bracket social complexities, without these creeping back into their choices of methods, theory, and interpretation in ways that can sharpen and prolong scientific controversies.

As a Centre for Research-based Innovation, dedicated to shortening time from basic science to application, laboratory work at the SRLC was highly connected to the outside world. But as a laboratory primarily dedicated to molecular research on lice, it circumvented the sort of political controversies that are attached to field studies on the parasite's impact on specific farming locations, fjords, and river systems. In the Norwegian public sphere, these tensions have played out as prolonged public disputes among different stakeholders about the role and legitimacy of science on biological interactions between wild and farmed salmon. Laboratories, in contrast to natural sites that are deeply invested with social, political, and economic values, are often further removed from these political ecologies of place. As Kohler notes, experimental work is credible precisely due to this "placelessness"; a value that goes back to the early history of Enlightenment experimentation, and helps to partially solve the "problem of trust" in science (2002: 7). Since we

may confidently assume that similar standards of evidence and procedure apply to all laboratories, biological knowledge derived from these sites have widespread epistemic currency.

Access to labs, for example, are restricted to qualified practitioners, with mechanisms like peer review promoting trust that research has been competently executed (even though the public has not directly observed them), under controlled conditions by experts. Kohler explains how this sentiment taps into the widely shared assumption that universality trumps locality: "When place affects laboratory experiments, we know that something went wrong. Field biologists, however, know that something is wrong if place does *not* affect the behavior of plant and animals; it indicates that human observers have been indiscreet and intrusive in the lives of their subjects and disturbed the natural relations of creatures and their habitats. In laboratories, experiments that turn out different on repetition are suspect. In nature, experiments that turn out the same every time and, in every place, may be suspect because life in nature is not so uniform" (2002: 9). While movement between lab and field was a source of creative innovation for the SLRC, laboratory work aimed at understanding the parasitology of salmon lice using cutting-edge molecular tools was not mired in the same level of controversy as colleagues working in other subfields of biology.

Laboratory creatures such as *L. salmonis* are enlisted in the epistemic and moral economies of science, as both technical artifacts and products of biological evolution. These dimensions are consequential for understanding the cognitive ecology of experiment at the Center. This chapter has taken seriously the observation that cognitive ethnography must approach its subject matter by journeying through social, material, and conceptual spaces (Hutchins, 1995: 7). In the next chapter, I focus on the conceptual terrain of RNA interference, to examine how the experimental community developed a set of distinct cultural, material, and cognitive practices for exploratory inquiry.

Notes

1. The concept of scientific "trading zones" was developed in seminal work on the history of admixture between subcultures of twentieth century microphysics (Galison, 1997), inspired by anthropological studies on pidgin-languages and creoles.
2. A micro-satellite is a stretch of DNA of 2–6 nucleotides, repeated in tandem. They may vary considerable between specimens (being "polymorph"), and can therefore be used as a comparative, genetic marker.
3. One hypothesis is that parasites evolve reduced virulence, as host death can also result in the parasite's demise. But if the parasite can transmit and reproduce, host death is not something that will be selected against. Another hypothesis predicts that fitness-increasing traits become more frequent over time, but this "short-sightedness" may cause a selection backlash against virulence, unless transmission to new hosts and reproduction is facilitated. A third hypothesis is that some parasites may not have coevolved with the host at all, and that virulence is not a target of selection, but a byproduct of selection for other traits (Poulin, 2011).
4. BM86 can only supply the host with a finite number of antigens in the blood stream, after which it must be resupplied at regular intervals to retain the antiparasitic effects. BM86 is also a "recombinant" antigen; the chain of amino acids from the tick gut cannot be directly obtained but is produced by a genetically engineered bacteria transfected with the genes coding for the BM86 protein.
5. In 2011 another team of researchers published promising data one a vaccine based on the my23 recombinant protein from *Caligus rogercresseyi*, a relative of *L. salmonis*. While the initial tests were promising, the follow up trials showed little effect.
6. The first 14 Centers were appointed in June 2007, and seven more in December 2010.
7. In theory, the National Research Council would contribute between 9 and 12 million NOKs annually, with total annual budgets for each CRI falling somewhere between 20 and 30 million NOKs.
8. Accountability by other peer-groups is exemplified by annual reports overseen by external advisory boards, and a mid-term evaluation, half-way through the funding period. Scholars disagree on whether Mode 2 captures fundamental properties of modern science. Etzkowitz and Leydesdorff claim Mode 2 is nothing new, but rather describes Kuhnian normal science

before its institutionalization in the nineteenth century, and constitutes the "material basis of science," while Mode 1 is just a widely accepted "construct" to justify scientific autonomy and carve an autonomous space for "pure' science after WWII (2000: 116). To describe and legitimize the making of knowledge across sectors, alternative models such as the "Triple Helix" have been proposed.

9. During my fieldwork, there were efforts to publish this genome in a prestigious journal. Publications describing genome architecture from novel phyla have become more commonplace as sequencing costs have dropped, which means that "genome-papers" must now tell particularly revealing stories to pass peer-review. Nilsen and colleagues were no strangers to publications in this genre, as several had collaborated on the *Nature*-paper outlining the cod-genome, revealing the genetic structure of a unique immune system not found in other sequenced vertebrates (B. Star et al., 2011). Ensembl's lice genome-assembly, dated January 2013 contained 695,449,161 nucleotide base-pairs, coding for 13,081 genes (https://metazoa.ensembl.org/Lepeophtheirus_salmonis/Info/Annotation/).
10. Elanco is the animal health subsidiary of Eli Lilly and Company. SLRC's original partner was the Swiss company Novartis, whose animal health division was acquired by Elanco in 2014.
11. The first two commercial patented applications emerging from the SLRC, for detecting resistance against the drug class of organophosphates and pyrethroids, were developed in close collaboration with PatoGen.
12. Centre management saw social relations as a success factor, and repeatedly stressed the importance of cultivating interactions between partner institutions through communal events like workshops and seminars.
13. In 2018, the two departments merged into a new Department of Biological Sciences.
14. WP1 Chemotherapeutants, WP2 Immune-modulation of the host, and WP3 Anti-attachment were decentralized across two campuses at the Norwegian University of Life Sciences (formerly the Norwegian School of Veterinary Science) in Oslo and Ås, and a research-facility for the feed-producer EWOS (now Cargill). Lacking space prevents me from describing crozz-fertilizations between all these work packages.
15. A reference to Mendel's discovery of discretely inherited traits, as opposed to continuously varied "quantitative" traits.

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4

RNAi: An Instrument for Exploratory Experimentation

In this chapter I take the reader deeper into the conceptual space of RNA interference (RNAi), the novel biotechnology briefly encountered in Chapter 3. Here, I examine its adoption as a research instrument at the Sea Lice Research Centre for screening genes by gene silencing in search of new therapeutic targets.

First, I sketch some developments in molecular biology from research on the diverse class of molecules known as RNA, focusing on the so-called "microRNA" (miRNA). Immediately, this historical context may seem out of place, given my preoccupation with the minutiae of experimental research at the SLRC as instances of distributed cognition. However, as my analysis makes clear, these episodes from the recent history of science cast light on novel modes of iterative knowledge production in biology. Through an anthropology of knowledge about RNAi, I address how this technology was co-opted and translated for research on salmon lice by Nilsen's group, as it dovetailed with the trajectory of their experimental system. My goal is not to paint the full picture of a technically complex field, but to sample historical and ethnographic cases that illustrate a continuously changing scientific landscape, and the material culture and modes of practical reasoning used to transect it.

M. Solberg, *A Cognitive Ethnography of Knowledge and Material Culture*, Culture, Mind, and Society, https://doi.org/10.1007/978-3-030-72511-2_4

I then turn to historical and philosophical work that have identified a poor fit between the kind of research practices that characterize microRNA and RNAi research, and conventional stories about how experiments contribute to the growth of knowledge. Particularly, I draw on the "New Experimentalists" and their descendants, and arguments for the centrality of practice and materiality, rather than theory, in experimental science. As part of a broader "practice turn" in science studies, these orientations illustrate how 'reverse vaccinology' through RNAi in the science of salmon lice did not just entail adoption of new methods, but introduced novel cultural practices of cognition, which had epistemic consequences on the level of the experimental system. Using ethnographic examples, I suggest these developments in salmon lice research can be productively analyzed under the rubric of "exploratory experimentation" (Burian, 1997, 2007; Franklin, 2005; O'Malley, 2007; Schickore, 2016; Steinle, 1997, 2016; Waters, 2007). This concept describes a set of open-ended research practices that does not easily map onto the conventional hypothesis-centered account of scientific experimentation. The interplay between domesticated lice strains, incubators, single-tank system, RNAi, and a suite of associated technologies from biochemistry to bioinformatics, was epistemologically productive because it enabled a range of epistemic pursuits, including "technology-oriented research," and "question-driven inquiry" (O'Malley et al., 2010). As I hope to make clear, not every act of experimentation is for testing hypotheses, making predictions, or settling the highly specific research questions associated with the "Hypothetic-Deductive Model." Hypothesis-driven research of this kind is usually reserved for situations with tightly delineated and regulated research contexts. It is therefore a poor descriptive model for the kind of open-ended, multidisciplinary approach to molecular parasitology that was carried out at the SLRC.

In examining these developments, I explore relations between scientific concepts and material culture through a distinct variation on the anthropology of knowledge that Roepstorff and Frith have described as "experimental anthropology" (2012). In this case, "going experimental" as they dub it, does not refer to a method or research aesthetic, but implies that I take as my object of study the cultural practice of scientific experimentation, and approach it as an activity of joint

meaning-making. This entails that one must take seriously the technical minutiae and "emic" accounts of central scientific concepts. I must, invoking Ludvig Fleck's words (1979), examine the experimental "thought style" (*Denkstil*) and "thought collectives" (*Denkkollektiv*) of contemporary biologists. This requires close analysis of criteria used by these collectives for assessing the validity of knowledge, their assumptions about why certain pursuits are valuable, necessary, and productive, as well as attention to how knowledge gets transformed through active engagements in the lab.

Screening Salmon Lice

On the third floor of the High-technology Centre, next to the water cooler and a small plaque informing visitors they are entering the SLRC, a Centre for Research-based Innovation funded by The Research Council of Norway, hangs a large poster. On the poster is a diagram that represents the Centre's complex workflow, or "pipeline." This will "facilitate development of new methods for lice control and shorten the time from basic research to new products and tools for parasite control in the aquaculture sector to achieve a true integrated pest management in the future." In the preceding, we have seen how key elements, such as lice strains, hatcheries, and single-tank arrays, were put to work in the search for therapeutic targets with the adoption of a relatively new biotechnology called RNA interference (RNAi). RNAi falls into the purview of "functional genomics." This approach to the complexity of life aims to understand relations between genotypes and phenotypes by investigating transcription, translation, and regulation of genes to answer where and when these are expressed in the organism. This includes how the expression of genes differs in cell types and cell states, their functional roles in cellular processes, the interaction between genes and gene products, and how gene expression changes according to environmental factors (Fig. 4.1).

The diagram depicts a multistage process where knowledge derived from the lice genome is used to identify candidate genes for RNAi screenings. It also marks a series of decision points dependent on the epistemic

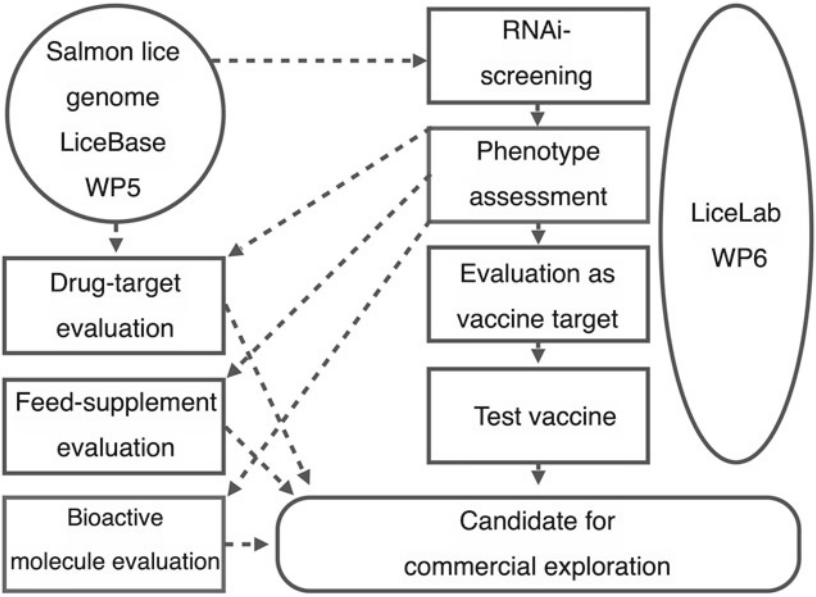

Fig. 4.1 Rendition of the Center's pipeline for discovery

outcomes of each preceding step, such as "phenotype assessment" and "drug-target evaluation." While this depiction suggests simplicity and linearity in the process of advancing from experiment via data to therapeutic application, the scientists working in this field are well aware of the intricacies obscured by such salient representations. They know that data production in contemporary biology is "out of sequence," messy, and contingent (Stevens, 2013: 108). The common sense intuitions described by David Hume as humankind's "original stock of ideas," which sustains our potential for knowledge production, evolved for active sensemaking in the medium-sized niche that humans are accustomed to (Atran, 1990). When we enter the world of molecular mechanisms like RNAi, these dispositions do not always serve us well. Our species cannot directly see biological macromolecules, like genes and proteins, with our bare eyes. Nor can we interact with them with

our bare hands, meaning that any relationships we have to such entities are necessarily mediated and enacted through material artifacts and representations.

SLRC's novelty lay in the application of RNAi to conduct "screens" for candidate gene targets. In this context, a screen is an experiment performed to assess the contribution of a particular gene to the organism's phenotype, which helps determine whether there is potential for pursuing further research on the candidate that could result in effective commercial vaccines, or other therapeutic biomolecules. RNAi screens are supported by high-throughput technologies, such as genome sequencing, microarray analysis, and RNA sequencing. It is a form of bioengineering practice known as "reverse genetics," where sequences of DNA or DNA products (such as mRNA molecules) are disrupted or altered so their systemic effect on particular molecular pathways can be observed, either at the cellular level or the level of the "whole" organism. Reverse genetics marks a distinction with the "forward genetics" of classical genetics. Reverse genetics looks at the phenotypes that result from changes to specific sequences of genes. In contrast, forward genetics, looks for genetic origins of traits by irradiation, chemical alteration, or insertional mutagenesis caused by jumping genes (or, transposons), sequences that may change position within a genome.

Biologists tell us that RNA interference is an ancient phenomenon, over 1.5 billion years. Eons before humans elucidated the biological processes that would later be unified as the "RNAi mechanism" in the late 1990s, eukaryotic organisms evolved a tiny molecular machinery. This protected their hereditary material against attacks from harmful genetic elements, such as viruses and transposons. As many other biotechnologies today, RNAi has a double nature. In one sense, it is an active cellular mechanism that has evolved in a vast number of living things. In another, it is domesticated and applied as a commercial technology, firmly entrenched as a staple ingredient in the material arrangement of numerous laboratories and experimental systems across the planet.

How did RNAi transform from a product of natural selection to one of cultural selection, or to use Rheinberger's concepts, morph from an epistemic thing in fundamental biology to a productive technical object

in the applied science of salmon lice? To appreciate this transformation, we must first examine the role of RNA molecules more broadly, including research into cellular processes that were first considered to be of minor interest, but turned out to be profoundly important.

RNA Basics

Ribonucleic acid (RNA) are remarkable polymeric molecules that serve many different biological functions inside the cells of all known organisms. Alongside DNA (deoxyribonucleic acid), its more famous relative, RNA is one of the essential macromolecules for life, as we know it. The molecule takes many forms but the most familiar, which is taught in high-school curriculums, is its role as *the* messenger molecule, a substance capable of storing information transcribed from double-stranded DNA by the RNA-polymerase machinery into an intermediate, single-stranded form known as "messenger RNA" (mRNA). This sequence of nucleic acids is then translated into a proteinaceous form with amino acids, by tiny molecular entities known as ribosomes and an adapter molecule, transfer RNA (tRNA). In eukaryotes, this process takes place in the cytoplasm of the cell. This cascade of molecular events, which results in the formation and modification of proteins, is known as gene expression and it is fundamental for living things. Francis Crick elevated this one-directional traffic of information from DNA via RNA to protein as the "Central Dogma of molecular biology."[1]

The molecule also come in other flavors, such as transfer-RNA (which transfers amino acids in protein-synthesis), ribosomal RNA (that combines with protein to form ribosomes), and small nuclear-RNA (processing mRNA into a mature form in eukaryotes). RNA molecules are synthesized in cells as single RNA strands but have the biochemical ability to base-pair with themselves and other RNAs, forming secondary and tertiary structures. RNA molecules are also classified by their size ("long" or "short") and on basis of their origins and mechanisms of operation. Molecular biologists have demonstrated how RNA molecules are central for *regulating* gene expression in cells. Proteins are usually not synthesized unless needed for a biological purpose, since this would be

highly inefficient. Cells are therefore equipped with tiny mechanisms ensuring that not every protein that is potentially in the genome gets synthesized all the time.

Biologists used to believe that gene regulation was achieved by proteins, complex polymers that twist and fold into a bewildering variety of shapes and can act as catalysts (enzymes) for a multitude of chemical reactions (see Myers, 2015 for an ethnography of protein research). Details about key mechanisms of action in genetic regulation of hereditary material were famously elucidated in work by the 1965 Nobel laureates François Jacob, André Michel Lwoff, and Jaques Monod. When Jacob and Monod proposed their famously elegant *lac*-operon model of gene expression four years earlier, using *E. coli* as their model system, it was not yet clear whether gene expression was regulated by proteins or RNA, although the two were convinced that RNA was the main regulatory molecule. But as narrated in a popular textbook, the notion that RNA governed gene expression was "largely forgotten as more and more protein regulators were found in both prokaryotes and eukaryotes" (Watson et al., 2014: 701). Still, considerable research on newly discovered regulatory molecules composed of RNA had accumulated by the mid-1990s. The idea that RNA could catalyze its own replication and synthesize other RNA molecules, even paved way for an influential hypothesis about life's origin, articulated by Nobel laureate Walter Gilbert (1986). In an ancient "RNA world," the molecule began acting as a self-replicating entity well before DNA evolved to become the central genetic material in organisms, with RNA only later assuming its familiar role as the messenger molecule, mediating between DNA and its protein products.

MicroRNA: Converging on Biology's Dark Matter

A massive research effort in molecular biology has since been directed at the complexities of a relatively newfound class of nucleic acids with noncoding functions, known as microRNA (miRNA). The first "glimpses into a tiny RNA world" came from the Boston region three

decades ago. Victor Ambros and Gary Ruvkun worked together in the 1980s as postdoctoral researchers in H. Robert Horvitz's molecular genetics lab at MIT (Ruvkun, 2001; Ruvkun et al., 2004). This worm became a favored model system for studying general principles of developmental regulation, after Sydney Brenner initiated the Worm Project in 1963 to map and describe the developmental lineages of all the thousand cells in this transparent, millimeter-long nematode which has a 3.5-day life cycle (Ankeny, 2001). Ambros and Ruvkun were descendants of this widely successful research program (O'Malley et al., 2010), which landed Horvitz, Brenner, and John Sulston a 2002 Nobel Prize for breakthroughs in "genetic regulation of organ development and programmed cell death."

Ambros and Ruvkun studied gene expression in mutant cell lineages to understand "heterochronicity," the timing of when cells transition between different life stages. They were focusing on features of a mutation (e912) in a gene known as *lin-4*, which caused developmental defects making the animals look deformed by reiterating extra larval stages, as well as the gene *lin-14*, which produced the Lin-14 protein, keeping cells in their larval state.[2] Further work on cell lineages suggested that *lin-4* and *lin-14* were part of a larger developmental switching system: "the same cell lineages that reiterated early programs at later larval stages in *lin-4(e912)* animals instead completely deleted their entire early larval programs in animals lacking *lin-14*" (Lee et al., 2004: 89). When Ambros and Ruvkun left the MIT to establish separate laboratories, at respectively the Massachusetts General Hospital and Harvard, they continued to investigate the complex details of this relationship. It was known that production of Lin-14 protein after the first larval stage led to the arrested development of adult cells and yielded sterile specimens that did not reach adulthood.

By 1987, it was clear that when *lin-4* was transcribed into a messenger RNA that decreased abundance of Lin-14 protein, *lin-14* mRNA lingered in the cell. This indicated a post-transcriptional mechanism at work, which at the time were assumed to be predominantly caused by proteins controlled by genes in conformity with the "protein orthodoxy" (O'Malley et al., 2010). In 1989, evidence from Ruvkun's group

showed that activation of *lin-4* somehow turned off production of Lin-14 by blocking translation of the mRNA, rather than preventing its formation as would be expected. Probing further into the regulatory relationship between these two genes over the next years, Ruvkun's lab found conserved sequences in a particular region of the mRNA responsible for downregulating LIN-14, and these sequences were suspected to contain the elements through which lin-4 acted (Lee et al., 2004: 90). The two labs then shared data hoping to learn more, with Ambros' group exchanging *lin-4* sequences for Ruvkun's data on *lin-14*. On June 11 in 1992, both investigators noticed a remarkable coincidence, and when Ambros called Ruvkun "each of them read the complementary sequences to the other over the phone, practically in unison" (Lee et al., 2004: 91), confirming a partial alignment between lin-4 RNA with noncoding sequences in the lin-14 mRNA.

With new information at hand, the groups unpacked these surprising relationships, building a strong case for a more direct interaction between lin-4 RNA and the lin-14 mRNA. Importantly, Ambros' lab showed that *lin-4* did not produce a regulatory protein as first suspected. Instead, it yielded a very short strand of RNA at the length of roughly 22 nucleotides, in addition to a longer RNA, around 70–80 nucleotides. The gene did not code for a protein at all, which was puzzling: what functions could such an oddball molecule serve? Working from a different angle, Ruvkun's group made the case that seven short stretches around 20–22 nucleotides long in the so-called "3-prime untranslated region" (3'-UTR) of lin-14's mRNA paired with *lin-4* RNA, albeit imperfectly. These surprising results were published in 1993, back-to-back in two papers in the prestigious journal *Cell*. But despite the new vistas opened up by this research, the findings did not "trigger a goldrush," as the insights were "novelty rather than a harbinger" (Ruvkun et al., 2004: 96). Furthermore, the representational scope of these observations appeared limited to *C. elegans* or was, at best, generalizable to other *Nematoda*, thereby pointing to a minor phenomenon.

But the perception that these findings were trivial, changed seven years later. In 2000, a second short RNA was detected in genetic analyzes of the same heterochronic pathway in *C. elegans*. *Let-7* also caused cell arrest at the larval stage, despite a diminutive stature of

only 21 nucleotides. But the bigger story about a tiny RNA world, that would radically change the science of gene regulation, came together when evidence from bioinformatic databases showed that *let-7* had clear phylogenetic relationships to genes coding for small RNAs in the genomes of *Drosophila* and even humans, eventually showing up with homologues in sequences from a range of other organisms. This was a major discovery. A radically new type of general and highly conserved and influential regulatory mechanism for gene expression, spanning across biological kingdoms, had been uncovered. The term "microRNA" (miRNA) was popularized by Gary Ruvkun in a 2001 commentary in *Science*, appearing alongside three groundbreaking papers on these mechanisms: "tiny RNA genes may be the biological equivalent of dark matter - all around us but almost escaping detection" (2001: 799). Today, thousands of miRNAs, which fold back onto themselves to form "hairpin" structures, are known to subtly influence gene expression. While some regulate cell development and homeostasis, others protect against viruses and transposons. It is to this latter category of regulatory elements we now turn.

RNA Interference

As the microRNA puzzle came together, different properties of RNA were also explored by other scientists. In the 1980s, research had uncovered the molecule's ability to regulate gene expression by binding with complementary target RNA, in a process known as "antisense RNA." But RNA held other secrets. Textbook accounts of the process later known as RNA interference, often start with some serendipitous results in molecular genetics from Richard Jorgensen and Carolyn Napoli. Working for a now-defunct transgene agribusiness company, the two were designing ornamental petunias. Eager to learn more about the enzymatic pathway that makes it intensely violet, the two introduced an exogenous gene into the plant, but their intervention did not deepen flower coloration as predicted. Instead, the exposed plants had scattered pigmentation, and some were entirely white. This suggested that some unknown effect was "cosuppressing" both the endo- and transgene (Napoli et al., 1990). But

while their observations were certainly interesting, they could not offer a sensible causal explanation. Nonetheless, publications of similar cases in plant systems soon began piling up. Since these cosuppression events also resulted in degradation of RNA after transcription, the phenomenon was rebranded "post-transcriptional gene silencing."

Soon, documentation of analogous processes emerged from other species. Studies on the model fungi *Neurospora crassa* described how exogenous gene sequences impaired expression of endogenous genes, an effect that was called "quelling." At Cornell University, Kenneth Kemphues and his graduate student Susan Guo made similar observations in animals, when they injected antisense RNA into *C. elegans* while studying a gene called *par-1*. "Antisense" RNA is complementary to the "sense" strand of the messenger RNA which is translated into a protein. In line with the reigning model of "antisense" interactions, Kemphues and Guo figured that injections would halt gene expression, since hybridization between RNA sequences (complementary binding) should effectively inhibit translation. Surprisingly, they got the same results in both experimental and control conditions, undermining their predictions. Since the RNA injections in the control were not complimentary, and thus could not bind to the mRNA transcript, some unknown process had to cause their strange results. "Identification of par-1 gene by injecting in vitro-transcribed anti-sense RNA" was first published in the *Worm Breeders Gazette* (13(3): 24 June 1, 1994), and disseminated in *Cell* only later. *Gazette* was an early precursor to bioinformatic databases, promoting an ethos of cooperation and open data. Its content was based on quick presentations of new results and methods in a digestible format, to be treated as personal communications and not citable without the author's permission.

Amidst these developments, the molecular biologists Andrew Fire and Craig C. Mello directed two different research groups working on DNA transformation in *C. elegans*, using "clever" new methods for microinjections as part of their experimental systems (Mello, 2008). Mello had trained on the worm under David Hirsch's supervision at University of Colorado in Boulder, in 1982. When Hirsch left to join the biotech industry, Mello moved to another alumni of Hirsch's lab, namely Dan Stinchcom's laboratory at Harvard. In Boston, Stinchom shared facilities

with Victor Ambros (of microRNA fame), and both supervised Mello in their Wormlab. Years later, Mello learned about antisense technology and RNA injections from Kemphues and Guo. He decided to apply the technique in his own research at the University of Massachusetts. Andrew Fire was also researching this phenomenon from his lab at the Carnegie Institution of Washington's Department of Embryology. Fire, on the other hand, became interested after data on the worm's response to RNA-triggered gene silencing from other labs "came together" in informal discussions in a heavily attended *C. elegans* meeting, organized by Mello in 1997 (Fire, 2007: 203–204).

Fire's group had long worked on *unc-22*, a favored gene he came to know during a fellowship in the mid-1980s, at the Medical Research Council Lab of Molecular Biology in Cambridge (England). At this time there were discussions in the worm community about whether a fraction of double-stranded RNA (dsRNA) was causing the observed gene silencing. Indications pointed to a relatively stable material whose effects persisted over days. And dsRNA, which is more stable than its single-strand variety, was a well-known contaminant in RNA synthesis, since the molecule can form double helices by folding and pairing with itself at complementary sites. Since *C. elegans* was a flexible and accommodating experimental system, "virtually any biochemical sludge could be concocted and injected into a worm, with a very rapid (and in most cases quite specific) assay at the end" (Fire, 2007: 204). It was therefore convenient for one of Fire's technicians, SiQun Xu, to perform double-stranded RNA synthesis of *unc-22*, a gene involved in muscle function, which produced a condition where the worm twitched strongly, even with minuscule amounts of RNA. Using a technique called *in situ hybridization*, Mary Montgomery from Fire's group also demonstrated remarkable efficiency of RNA-initiated downregulation of the gene *mex-3* in embryos. In Mello's lab, a graduate student named Sam Driver was rehearsing micro-injections of dsRNA into the nematode under Mello's tutelage, but he accidentally botched several injections. These ended up in the worm's body cavity instead of the targeted germ cells. To the team's surprise, even misplaced injections yielded significant downregulated phenotypes.

These systemic effects were deeply puzzling in light of the "antisense" model, and within a year, Fire, Mello, and their co-workers executed a series of experiments that probed these issues further, summarizing their results in a five-page letter in *Nature* (Fire et al., 1998). "Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*" drew six conclusions. First, double-stranded RNA was far more effective than single-stranded RNA for reducing gene function. Most likely, previous assays introduced double-stranded RNA unintentionally, an artifact that would unify disparate observations made by other research groups. Secondly, the silencing effects were specific for mRNA sequences homologous to the injected dsRNA, as other mRNAs were unaffected. Thirdly, the mechanism was likely *post-translational*, meaning that a mature mRNA sequence was required (neither introns nor promoter sequences triggered downregulation). Fourth, the target mRNA was somehow degraded in the cell. Fifth, only a few molecules of RNA were needed to manifest an effect. And finally, the results could systematically spread to other tissues and silence target genes in progenies.

Mello had already relabeled this phenomenon "RNA interference" (Fire, 2007: 203), since "antisense" was a misnomer. Similar effects were also caused by "sense" strands of RNA, and their work had a potential link to gene silencing reports from other organisms. This pointed to a significant evolutionary story, although the exact pathways were unclear: "Whatever their target, the mechanisms underlying RNA interference probably exist for a biological purpose. Genetic interference by dsRNA could be used by the organism for physiological gene silencing. Likewise, the ability of dsRNA to work at a distance from the site of injection, and particularly to move into both germline and muscle cells, suggests that there is an effective RNA-transport mechanism in *C. Elegans*" (Fire et al., 1998: 810).[3]

More investigations followed (Fire, 2007; Mello, 2007). Lisa Timmons from Mello's lab, modified *E. coli* to produce double-stranded RNA which she fed the nematodes. This unspecific treatment also caused interference. Another lab member, Hiroaki Tabara, simply soaked larvae in a double-stranded RNA solution to elicit the interference response.

Soon, more evidence that the mechanism was operating at the transcriptional level came from Fire's group, and a mechanistic model was proposed. Likely, a protein complex mediated between the injected RNA and target mRNA molecule. An evolutionary conjecture proposed that this response was part of a defense mechanism against viruses. Within a year, gene silencing by dsRNA was confirmed in a broad range of organisms, suggesting that the system evolved in a common ancestor over 1.5 billion years ago.

More biochemical features of RNAi were uncovered through work on in vitro cell cultures in *Drosophila melanogaster* (Hammond et al., 2000; Zamore et al., 2000). RNA between 21 and 23 nucleotides long were found to accompany the interference effect, with double-stranded molecules being processed into shorter, intermediary types that bonded to homologous mRNA targets and cleaving them. These shorter, processed molecules guiding the cleavage of mRNA transcripts were labelled "short-interfering RNAs" or siRNAs (Parrish et al., 2000). How these cellular events were directed was understood in 2001, when the small RNA pathways were shown to be governed by a "common processing machinery that generate guiding RNAs that mediate both RNAi and endogenous gene regulation" (Grishok et al., 2001: 23), offering decisive proof of a relationship between microRNAs and RNA interference.

Later models added a dsRNA endonuclease named DICER, a protein complex that cleaves double-stranded RNA molecules into smaller fragments, one of many actors in a longer molecular cascade involving the RNA-Induced Silencing Complex (RISC). Bioinformatic analyzes showed that this protein complex contained an evolutionary conserved class of endonucleases known as ARGONAUTE, which was identified across phylogenetically distant taxa. Endonucleases are enzymes that cleave the phosphodiester bonds that tie together nucleotides in DNA (deoxyribonucleasees) or RNA (ribonucleases). ARGONAUTE binds different small RNAs together into binding pockets in its three-dimensional structure, and the small RNA molecules appear to guide ARGONAUTE to target mRNA transcripts matching their sequence for either silencing or destruction. As evolutionary conserved proteins, these are involved in both the miRNA and RNAi pathways in many species,

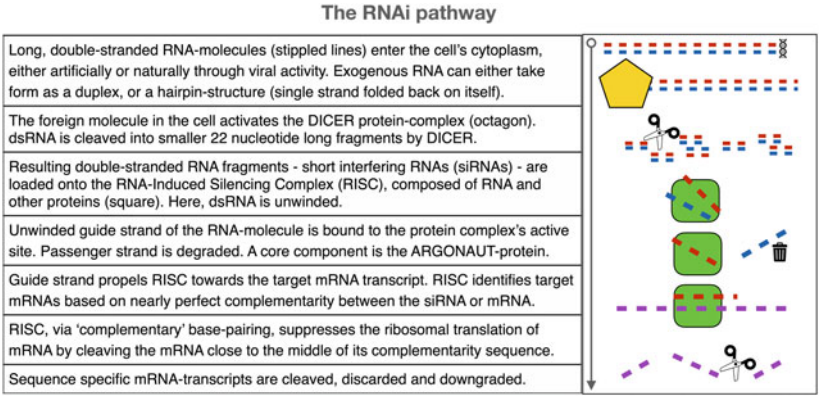

Fig. 4.2 A simplified diagram of the RNAi pathway

giving a unified account of a range of phenomena (Winter et al., 2009). A wealth of work has since characterized the biogenesis of these intricate, molecular machines (Fig. 4.2).

Reception

In their 2002 December issues, both *Nature* and *Science* declared RNAi among their Breakthroughs of the Year. The journalist writing for *Science* framed the story as follows: "Just when scientists thought they had deciphered the roles played by the cell's leading actors, a familiar performer has turned up in a stunning variety of guises. RNA, long upstaged by its more glamorous sibling, DNA, is turning out to have star qualities of its own" (Couzin, 2002). RNAi's ability to initiate gene silencing promised to shed light on the complexities of genomic regulation in specific model organisms as a tool for downregulating different candidate genes and assessing their functional consequences.[4] But it also promised more, as the silencing mechanism could potentially be harnessed for discovery and rapid validation of drug targets in human medicine. It also arrived with great timing, as massive amounts of genomic sequence data were being produced at an increasing rate, and RNAi offered a simple and reliable method for assessing specific genes. Even more enticing, RNAi

could possibly work as a therapeutic in its own right, by silencing a gene required for viral reproduction or a gene that a tumor needs to grow. Since many diseases are caused by problematic gene activity, RNAi could possibly block harmful genetic pathways. And before long, RNAi entered the public imagination as a potential panacea for many diseases.

RNAi was especially promising for diseases where known drug targets were difficult to reach by other molecular pathways. It could also potentially block cascades of gene expression in disease at the level of RNA, instead of the protein level, where most conventional therapeutics work. When the Nobel Prize in Medicine in 2006 was awarded to Fire and Mello, belief in RNAi's translational potential skyrocketed.[5] In the words of one analyst, RNAi therapeutics was like "stopping the flood by turning off the faucet instead of mopping up the floor" (Haussecker, 2008: 452). Technically speaking, it offered a chemically homogenous pathway with many applications, which gave a competitive advantage compared to pharmaceuticals based on chemically diverse target molecules that could be prohibitively expensive and difficult to commercialize. Since RNAi overlapped considerably with the miRNA pathway, there were also hopes of synergies between research on both systems. RNAi therapeutics had many attractive features for both small biotech companies and Big Pharma alike. Notably, Merck acquired Sirna Therapeutics in 2006 (then valued at 1.1 billion USD), and Roche entered a historically costly licensing deal with the RNAi pioneers at the company Alnylam, a de facto gatekeeper for RNAi therapeutics which possessed disputed patent rights. Despite its dependence on advanced scientific breakthroughs, application of RNAi as a technology offered low technical barriers, since dsRNA synthesis was both easy and affordable. RNAi was also a hot topic among academics, suggesting that high-risk projects could be outsourced to academic laboratories, instead of tying up in-company biomedical researchers (Haussecker, 2008: 452).

Despite these optimistic projections, more sober expectations for RNAi inevitably followed, as hype met the nitty-gritty reality of translational science (Haussecker, 2012; Krieg, 2011). Enthusiasm had been excessive, and after an initial period of sensationalism, the belief in a swift realization of its translational potential faded. As with other biotechnological frontiers like gene therapy, the technology saw great financial

volatility. In particular, the delivery challenge, getting RNA fragments into the right cells, manifested as a bigger obstacle than first assumed. Technology development also faced a backlash during the financial crisis of 2007–2008. In one high-profile case, biotech giant Roche decided to shut down their entire RNAi platform in late 2010, priced at 500 million USD. Other pharmaceutical giants like Pfizer, Merck, and Abbott also terminated their RNAi portfolios, despite the enticing technoscientific imaginaries that had fueled investment in these clinical pipelines during the gold rush.

Still, despite a long and bumpy journey, clinical development of RNAi therapeutics continued steadily, with less hype (Bobbin & Rossi, 2016; Haussecker & Kay, 2015). *The Scientist*, for example, predicted a "Second Coming" of RNAi within a decade, despite an "era of doubt and despair" having replaced the "era of irrational exuberance" (Bender, 2014). This prediction was correct, as better modalities for drug delivery in the liver, for example, paved new paths toward clinical development. Eventually, drug makers reentered the field of RNAi-based therapeutics through new investments (Haussecker, 2018). By 2020, several compounds had moved past Phase-III trials and were approaching the market. While its commercial potential remains untested, RNAi pharmaceuticals were among the best-performing stocks in 2019, leading one CEO to confidently assert that "RNAi has got its sexy back" (Dunn, 2020).

RNAi and the Science of Salmon Lice

I now turn to how this novel biotechnology was instrumentalized as a technical thing, in the science of salmon lice. Building on work on epistemic practices known as "exploratory experimentation," I argue that conventional models of experiment, which sees knowledge as mainly progressing through "hypothesis-driven" research, does not adequately capture the cognitive ecology of RNAi-based molecular parasitology at the SLRC.

According to a perceptive cognitive-historical analysis by Sung (2008), the elucidation of RNA interference began with an "anomaly" in

molecular genetics. The reigning model of gene expression, including antisense-RNA, implied that interventions with double-stranded RNA should have little effect, since these molecules were already hybridized. When these molecules caused gene silencing in *C. elegans* and other organisms, there was no alternative explanation for the resulting anomalies. Detection and resolution of these anomalous outcomes confronted experimental biologists with a unique problem-space, spawning several conceptual revolutions in the science of gene regulation. Sung's analysis builds on the assumption that science, like other creative pursuits, operates through embodied meaning construction known as "conceptual integration networks" or "conceptual blending" (Fauconnier & Turner, 1998). These cognitive dynamics elucidate the human capacity to integrate information from different domains and fashion new ideas from the resulting blends. In this view, language does not just *represent* meaning, but prompts for meaning construction in specific context, based on a repertoire of cognitive and material resources, cultural models, and conceptual structures originating from sensory-motor experience (a topic we shall revisit in more detail in the next chapters).

Meaningful resolution of the RNAi anomaly and its contradictions was the product of a cascade of conceptual linkages. First, Sung shows how biologists used distinct "reasoning strategies" that set up "interrelations" between bodies of knowledge produced by different techniques, so that aspects of a phenomenon in one field, namely, cosuppression in plants, could be transferred to the interference response in *C. elegans*, *Drosophila*, and other organisms. This move generated a plethora of novel ideas. Since existing interpretative frameworks, like antisense RNA, were unable to account for the observed experimental anomalies, this model was elaborated through a strategy of "complication," where new observations of gene silencing effects were accommodated through additions, deletions, and specialization of existing conceptual elements. This process entailed a series of "abductive" inferences across several experimental contexts to resolve the anomalous contradiction.[6] Relations were drawn between inserted double-stranded RNA and selected experimental observations about how exogenous strands of RNA were processed into shorter molecules. Furthermore, Sung notes that the laboratory context introduced embodied structure to anomaly resolution; experiments were

performed not simply to test theoretical propositions, but to observe surprising phenomenal regularities, create new concepts, and explore variables in more detail.

Fire and Mello's 1998 study on *C. elegans*, for example, linked RNAi to cosuppression and post-transcriptional gene silencing (PTGS) in plants and other organisms, paving way for interrelations with observations from other research groups, including in vitro systems built around *D. melanogaster* and plant experiments. These interrelations, in turn, helped formulate new experiments in molecular genetics that disentangled involved mechanisms, and compressed these into meaningful, coherent cause–effect relationships. Finally, a transition to the RNAi model was achieved by conceptual integrations between previously unlinked elements. New experiments facilitated compression of disparate relations into a coherent account sensible on "the human scale" through a cause-and-effect frame that was "easily apprehended by humans" (2008: 190). The resulting causal model of RNA-based gene silencing could then be transposed from the context of *C. elegans* into other experimental systems.

RNAi saw tremendous success as a tool for exploring individual gene function, and it was this aspect that made RNAi so appealing for salmon lice experimentation. By the early 2000s, the power to probe gene function could be unleashed with ready-to-use kits and protocols listed in the catalogues of commercial suppliers of reagents. As with other biotechnologies, RNAi was domesticated, cultivated, and commercialized to serve humans in their quest for controlling biology on the molecular scale. In Rheinberger's terms, RNAi was materially and conceptually transformed from an elusive epistemic thing, something unknown, into a technical thing; a standardized method for inquiring into other novels, epistemic things. In the laboratories of the Sea Lice Research Centre, my ethnographic field site, this long history of translational research was embodied by the MEGAscript^{TM} RNAi Kit from Thermo Fisher Scientific. Delivered in a small cardboard box, it contained all necessary reagents needed to synthesize double-stranded RNA molecules for knockdown experiments on salmon lice.

From an anthropological perspective, RNAi's life as a "technical thing" is lodged at the boundary between nature and culture. Since its effects in

the laboratory is partly an outcome of unintentional nature (biological evolution), and partly an intentional cultural product, RNAi transcends our commonsense intuitions about functions as the effects of artifacts and things. As noted by Sperber (2007), questions like "what is it for?" or "what is its function?" are properly asked for two kinds of entities: biological traits and processes (e.g., red blood cells, polymerase) and cultural artifacts (e.g., forks, calculators). While biological things have *selected* effects conferred via natural selection, artifacts are imbued with *intended* effects by their users.[7] A calculator's intended effect, for example, is to solve mathematical problems—although it may, as a byproduct, also be hurled as a projectile. The difference between intended and selected effects appears to nicely map onto the nature–culture distinction.

Some biological artifacts perform their role as cultural artifacts by doing the same thing as their selected functions, and in RNAi there is an overlap between its *selected* effects, conferred through evolution, and its *intended* effects, conferred through human meddling. RNAi performs its artifactual function (preventing translation of messenger RNA) through its biological function, which explains its adoption in countless laboratories. But using these molecular machines for experimental purposes also exploits biological properties which the entity has *not* been selected for, namely, the evolved ability of RNA to base-pair with complementary sequences of nucleotides. This property is not usually exploited in nucleic-acid metabolism, although it appears in nature as double-stranded RNA viruses, and possibly in other poorly understood cellular processes. But parasitologists at the SLRC exploit the organism's potential for sequence-specific gene silencing by *synthesizing* double-stranded RNA molecules with the MEGAscript™ Kit. Thus, the "cultural becoming" of RNAi as a research instrument co-opts multiple properties of RNA (see Sperber, 2007: 136).

As mentioned in the previous chapter, accommodating RNAi into the experimental system of Nilsen's research group, did not happen overnight, although RNAi had been successfully applied to other experimental organisms. While RNAi was available as a commercial kit, it still had to be coaxed into an interlocking fit with other components and practices in the experimental machine that had gradually developed around domesticated strains of *L. salmonis*. One main challenge faced

by those recruiting RNAi as a screening method, was to find a reliable delivery route for getting the synthetic double-stranded molecules into the parasite's interior. While *C. elegans* responded to a variety of delivery methods, a reliable transmission route had to be specifically adapted to lice at different life stages. The obvious choice for delivery into adult specimens, which are covered by a though exoskeleton, were microinjections. But making injections work was no trivial matter. It required fine-tuning a complex operation with many potentially confounds, within the cognitive ecology of the experimental system. This included:

- Perfecting the recipe of the double-stranded RNA solution, based on the MEGAscript^{TM} RNAi Kit.
- Identification of a non-lethal entry-point into the salmon louse in the dorsal region of the cephalothorax, where the plates on the lice exoskeleton are joined.
- Cultivating embodied skills and procedural schemas for handling the lice, down to the level of finding the correct angle for the microneedle, avoiding punctuation of vital organs, and applying sufficient pressure for fluid injection.
- Finding appropriate glass needles (as one technician explained, the best results were obtained when the group customized their own needles).
- Optimizing the amount of ds-RNA solution to be injected, and the amount of *bromophenol*-blue colorant that was used as a marker to identify successful delivery after injections.
- Calibrating post-injection incubation; the time between RNAi exposure and reinfection on hosts.
- Devising a new "production line" with intelligent ways of using laboratory space for coordinating research materials and staff during experimental events (we shall return to this matter in Chapter 5).

The first reported use of RNAi in salmon lice by Nilsen's group was published in 2009, two years before the official opening of SLRC (Dalvin et al., 2009). This study applied RNAi to functionally characterize a protein known as the "maternal yolk-associated protein" (LsYAP), which seemingly played a key role in the embryogenesis of salmon lice. Analyzes of microarray data taken during post-molt growth and maturation of

adult female lice had revealed a surge in mRNA transcripts just prior to the release of mature eggs. One of the most interesting transcripts identified during this search, was an mRNA encoding for an unknown protein. This protein had three Fascicilin 1 (FAS 1) protein domains, stretches of amino acids which were deeply conserved over evolutionary time. First identified in grasshopper embryos, these domains were later found in a range of organism and assumed to be functionally important for cell attachment and adhesion.[8]

Initial studies of lice at different life stages using methods like *quantitative PCR* and *in situ hybridization* then showed that LsYAP was a female-specific transcript, and that the protein was associated with the egg yolk. These proteins were most likely incorporated into the female oocyte after transportation from their sites of production in sub-cuticular tissue. In lice, oocytes are produced in the ovary and transported to the genital segment. This inference was based on observations that LsYAP was never observed outside of the genital segment and supported by the identification of LsYAP protein sources in sub-cuticular cells and the hemolymph, a fluid in invertebrates akin to blood. While there were few signs of any direct phenotypic effects on adult lice during silencing of the LsYAP protein, the interference response manifested as deformations in the offspring. In addition to morphological evidence, the potency of RNAi to produce highly specific knockdown effects was also confirmed independently by both quantitative PCR, microarray data, and western blotting methods. In sum, these formative experiments demonstrated a "proof of concept." RNAi could indeed work as a screening system for therapeutic targets in the lice genome.

In addition to these issues, a range of other relevant conditions for experimental success, such as the refinement of injections, and analytical techniques for procuring useful results from knockdown experiments, were also explored. For example, the group tested several methods for delivering double-stranded RNA into the animal, including a mechanized microinjector and a manual instrument that was operated by blowing into a long tube. Eventually, the latter was preferred since it afforded operators with better tactile control. The group also had to make a series of decisions with epistemic consequences for subsequent analyzes, such as the number of egg-strings to preserve for hatching and

the number of samples to be preserved, either frozen or stabilized for later processing with a substance known as RNAlater. Next, the RNAi-treated animals were screened using a method known as quantitative real-time polymerase chain reaction (qPCR), to verify the downregulation of targeted genes. This was necessary due to the potential for "off-target effects," where other genes than the target sequence get accidentally silenced. qPCR-measurements were also supported by antibody staining, an immunohistochemical technique where tissue samples are stained inspection in the microscope to visually confirm the phenotypical effects of gene expression. In the next three chapters I present multimodal analyzes of how these resources were orchestrated within the experimental system at the microlevel of specific events and interactions.

Following this feasibility study, the team also worked out additional techniques, including a method to silence genes in the early phase of the life cycle by soaking lice larvae in a solution of double-stranded RNA (a method already well-established in *C. elegans*). This research was published in 2014. A Scottish research group had reported gene knockdowns on the nauplius and copepodid stages using a similar technique in 2009, but these experiments showed high mortality and could not be replicated by the group in Bergen, who set out to develop more robust means for RNAi delivery. They hypothesized that the parasite at this life stage would be particularly receptive during hatching and molting, since the exoskeleton's structural integrity was weak, allowing RNA molecules to pass through the cuticular barrier.

Building on these developments, the group also performed a series of experiments to identify life stages where RNAi would be efficacious. These trials described the temporal onset of downregulation, when drops in gene expression could be detected, and its duration, comparing the interference response in eight different genes. While these experiments showed significant silencing when the nauplius I-stage was treated beyond its molting phase, they were unsuccessful in downregulating gene expression in the copepodid life stage. Furthermore, the silencing effects in lice lasted for over a month in adult females.

Together, these efforts to stabilize RNAi applications for lice, and make it cohere in a productive manner within the self-vindicating structure of thoughts, actions, materials, and marks of the experimental system, belongs to the class of epistemic practices that Hacking called "modelling of the apparatus" (1992).

Exploratory Experimentation: From Basic RNA Research to RNAi in Salmon Lice

Since the publication of *The Logic of Scientific Discovery* (Popper, 2005 [1935]), the two major "stock positions" on experimental logic and inference has been Baconian inductivism (after Francis Bacon), and Popperian falsificationism (Franklin, 2005: 891). Inductivism holds that data ought to be collected before theorizing, and that the search for patterns in data should take place afterward. The goal is to make inductive inferences from one instance to many and possibly confirm theories by showing how observations and theory agree. Popper's falsificationism was a critique of this view, pronouncing a set of normative principles for demarcating and justifying scientific beliefs. In this theory-centered view, which consist of an endlessly repeating two-step cycle, real knowledge can only be derived from hypotheses if they can be *refuted* by observation (Godfrey-Smith, 2009: 60). First, comes a theoretical activity whereby a hypothesis or prediction is launched in the form of risky conjectures that should be put to a test (there are no recipes for making conjectures in Popper's view). Secondly, there are attempted refutations through critical testing and observation. While Popper's model was not limited to experimental science, observations should ideally be performed under rigorous conditions, where scientists can deduce specific consequences from their theories and models, before succumbing their hypotheses to stringent testing. Predictions should be bold, risky, and so precisely formulated as to "forbid" certain observations. If the conjecture passes testing, i.e., are shown not to be false, the theory is said to be "corroborated." Popper's principle is thus *fallibilistic* as theories can never be confirmed. At best, scientists may hope to accumulate theories that have been shown not to be false, yet.

An offshoot of this idea circulates as the so-called Hypothetic-Deductive Method (HDM), a highly schematized account of science which is regularly conflated with the Popperian position (Schickore & Steinle, 2006: ix). Here, making observations that conform to predictions are said to *support* a given theory. However, as Godfrey-Smith points out, "this process has the basic pattern of what Popper describe, but the idea that theories can be supported by observations is *not* a Popperian idea" (2009: 69–70). Rather, textbook versions of HDM mix some of Popper's principles with an overtly optimistic view about the epistemic role of confirmation that Popper rejected. This model has public appeal, as a deeply internalized cultural model and normative ideal with moral force. Work in science studies, however, demonstrate how experimentation is not simply "handmaiden to theory," but is composed from a more complex tapestry of local tasks. A singular focus that limits the epistemic function of experiments to the appraisal and primacy of theory can thus obscure the generative potential of experimental practices in the research process. The empirical inadequacy of this account becomes especially clear when we compare this model to the canvas of experimentation I described above, ranging from early work on microRNA to the implementation of RNAi as an experimental method in the parasitology of salmon lice.

In a series of biographical mediations, Victor Ambros and colleagues write that the intellectual interests that led to the investigation of *lin-4* did not come from well-formed hypotheses about noncoding microRNAs or antisense regulation: "We were simply curious about an interesting worm mutant, and everything we found out about it was unexpected" (Lee et al., 2004: 89). Similarly, Gary Ruvkun's group points to serendipity as a prime mover behind their own findings, as their work involved "jackpot approaches" that were quite unsuccessful at first. As they conclude, elegance in molecular genetics is "aesthetically pleasing, but scientifically overrated" (Ruvkun et al., 2004: 94). Discovery of regulatory microRNAs was the product of a series of fortuitous experimental events, which generated new insight and resolved a series of anomalies in the absence of specific conjectures.

Links between the Ruvkun-group's research on regulatory RNA, and Fire and Mello's work on RNAi, for instance, were pursued on

rather unorthodox grounds. It was not motivated by well-formulated hypotheses derived from a theoretical edifice. The group's own words reveal unconventional justifications for their epistemic choices: "An even deeper connection to RNAi started with numerological considerations (it cannot be called reasoning). When siRNAs of 22 nt, the same size as lin-4 and let-7, were discovered by the Baulcombe and Tuschl groups in 1999 and 2001 […], Ruvkun noted that the number 22 (the number of letters in the Hebrew alphabet) is stressed in the Kabbalah, a Jewish mystical tradition celebrated in medieval Spain, alternative bookstores, and a number of helpful Web sites […]. We began to explore the action of the RNAi machinery in miRNA maturation and activity" (Ruvkun et al., 2004: 94).

Additionally, anomaly resolution demanded a variety of strategies, encompassing experimental tools from biochemistry and molecular genetics, along with new and powerful computational analyzes. These bioinformatic methods, which do not fit well with standard schemas of experimentation, helped identify patterns in larger datasets about networks of interactions and phylogenetic relationships between DNA, RNA, and proteins in the absence of specific hypotheses. As observed by the philosopher Maureen A. O'Malley and colleagues, these breakthroughs in RNA research were made possible by "a reinforcing epistemic transformation that is built on the marriage of wet bench biology to computational biology, as well as the high-throughput data gathering and analysis that such combined approaches enable" (2010: 412).

At the Sea Lice Research Centre, we saw examples of how the marriage between RNAi-based gene silencing and computational methods was critical for progress in studies on salmon lice. In contrast to the received view of experiments as tests of predictions and hypotheses explicitly derived from theory, the drivers of experimental actions at the SLRC were much broader. They included parameter variation, simplification and tweaking of the experimental arrangement, as well as the identification of appropriate concepts to express empirical rules governing the experimental project, mapping of patterns in data, description of regular phenomena, and not least: construction and tuning of new instrumentation.

From the perspective of an anthropology of knowledge, neither the falsificationist nor the Hypothetic-Deductive story offers a satisfactory empirical rendition of experimentation as a situated epistemic activity "in the wild." There is no uniform standard for what testing hypotheses entail in practice. Furthermore, what is considered an acceptable level of observational specificity for a given theoretical prediction varies across different epistemic situations and only obtains legitimacy through acceptance by a broader scientific community. Even though experimental demonstrations might appear to follow a deductive template in their *reported* form, they clearly do not have the closed-form of deductive formal logical arguments (Galison, 1987: 2). Instead, I propose that the cognitive ecology of experimentation at the SLRC was maintained through a set of epistemic strategies that is better articulated through the concept of "exploratory experimentation." Making this argument, I build on scholarship highlighting how experimentation is motivated by other epistemic concerns than merely hypothesis testing.

In the 1980s, science studies made a turn from theory-centered accounts toward greater pluralism in studies on experimentation, in reaction to "the impasse reached in the debate about scientific realism" (Schickore, 2016: 20). Known as the "New Experimentalism" (Mayo, 1994), this body of work encouraged a rethink of how stocks of robust knowledge accumulated from experimentation in relative independence from high-level theories. It is neatly summarized by Hacking's recognition that experiment "sometimes pursues a life of its own" (1983: 215; see also Galison, 1987). This rethinking increased awareness about important, but often disregarded, tasks of experimental science. These include accumulation of a material culture of finely tuned instruments, and the transmission of skills and propositional knowledge that help obtain accurate readings, and how to distinguish salient effects from artifacts and other background factors (Rheinberger, 1997). Scientists were not just theory builders, but also builders of tools that embody knowledge. Whatever the outcome in terms of "global" theory, researchers working on a given experimental set-up could at least be seen as gaining the know-how, skills, and abilities necessary to produce the observed experimental effects (see also Schickore, 2016: 23). The New Experimentalists renewed interest in observation as an enskilled practice,

by attending to how observation was mediated through instruments (Hacking, 1983: 168).[9] The turn also cast light on how diligent cross-checking of empirical results keep theorizing in check, and helps distinguish between substantial and speculative outcomes (Chalmers, 1999: 206).

Asking "how experiments end" in microphysics, Peter Galison found them to be "neither rule-governed nor arbitrary" (1987: 254). Dismissing "interest-theories" that reduced laboratory work to mere confirmations of preconceived theory, Galison instead examined the long-, medium-, and short-term constraints that shape experimental practices, and must be overcome through the course of research. Recognizing that experimental outcomes are subject to many theoretical and material constraints, Galison argued that these should not be seen as rigid and determinative, since repeated acts of bootstrapping enable experimentalists to solidify results in the face of shifting conditions. This solidity has two key dimensions: *directness* of measurement, and *stability* of experimental outcome (ibid.: 260). While directness refers to how insight enables novel causal understandings, stability refers to how experimentalists gain control over the experimental condition. Later, Galison presented an alternative model further displacing the role of theory, experimentation, and instrumentation (1997: 799). Here, these three elements of science were seen as periodically "intercalated", similar to how brick walls are stacked in a staggered pattern for resilience (see Fig. 4.3). The inertia and conservatism of different subcultures of research ensure that theoretical progress does not immediately translate into shifts in experimental work and instrumentation, and vice versa. For Galison, it is precisely this lack of synchronicity, or "disunity," that makes experimental science so robust.

Appearing independently in two case studies in the same year (Burian, 1997; Steinle, 1997), the concept of "exploratory experimentation" further elucidated the interplay between the material cultures of instrumentation, practice, and theoretical conceptualization, by problematizing ways in which experimentation assumed a life on its own, with quite other epistemic goals than hypothesis testing.

Drawing on historical sources from the scientific origins of electromagnetism, Steinle characterizes exploratory experimentation as a set of

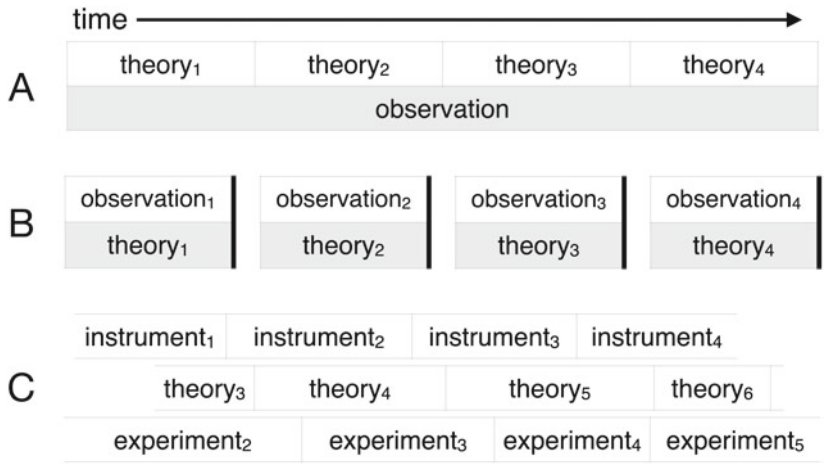

Fig. 4.3 The positivist model of scientific progress (**A**), which Galison dubs "reduction to experience" (1997: 785), aimed to build successive theories upon a solid foundation of observational primitives and logical operations on "protocol statements." Foundationalism was inverted by the anti-positivists (**B**), centered around the primacy of theory and the unreliability of observations due to contaminations by theory-ladenness (1997: 794). Kuhn postulated that revolutions in concept and theory caused incommensurability between paradigms. Despite epistemological differences, Galison sees Popper and Kuhn as espousing "reduction to theory." Here, theory and observation get coperiodized so that breaks in theory coincide with breaks in observation. Galison's model of intercalated periodization (**C**) gives contingent autonomy and parity to each, without coperiodization and abrupt changes (1997: 799). Centrally, the epistemic role of material culture, e.g., instrumentation is recognized. Figure redrawn on basis of Galison (1997: 785, 794, 799)

epistemic strategies used by Faraday to produce new and crucial insights about phenomenal regularities in the infancy of a new research field. He contrasts these strategies with the Popperian view, here construed as an empirical claim about how the experimental process unfolds in practice. Prototypically, "theory-driven" experiments are usually performed with a "well-formed theory in mind from the very first idea, via the specific design and the execution, to the evaluation" (Steinle, 1997: 69). Typically, these are based on detailed expectations concerning possible experimental outcomes. In this model, experiments are not for *generating*

theory, but highly constrained and fixed events, with respect to instrumental arrangements and expectations. Exploratory experiments, on the other hand, order complexity by producing novel concepts and classifications based on observation, rather than falsification of hypothesis derived from theories. Referring to Ludwig Fleck's work, Steinle suggests that the act of structuring a research field with respect to concepts and categories, profoundly shapes future research by propelling it in certain directions, at the cost of closing off alternative avenues of investigation. As such, these practices often form the undisclosed backstage of research.

Complementing Steinle's account, Burian invoked the notion of exploratory experimentation to highlight a particular triangulation strategy used by Jean Brachet, between 1938 and 1952, to quantify and localize amino acids biochemically. Lacking suitable methods, Brachet employed a wide arsenal of instruments and techniques from a variety of research fields to cast light on the nature of protein synthesis (1997: 41). By refining and cross-checking his techniques to avoid artifacts and independently confirm results, it was eventually possible for Brachet to localize distinct nucleic acids. Here, Burian extends on Rheinberger's argument about how the materiality of experimental systems is crucial for attaining novel insights in some contexts. By triangulation between different instruments, researchers can establish connections across experimental systems, opening new productive lines of research.

Additional studies have since applied the concept of exploration to understand a range of other case studies, which together paint a diverse and nuanced picture of experimental life (Burian, 2007; Elliott, 2007; O'Malley, 2007; O'Malley et al., 2010; Steinle, 2002, 2016; Waters, 2007). This record shows that scientists, when confronted with real-world complexity, often work on experimental arrangements with considerably more degrees of freedom and heterogeneity than what Popperian hypothesis testing entails. Sometimes, the objects of scrutiny are insufficiently described, or so anomalous and underspecified that it is impossible to conjure well-formed hypotheses and predictions about the target system's behavior. On other occasions, the performance of an apparatus must be described under a range of conditions, before it can be productively operationalized in the testing of conjecture. And occasionally, when robust theoretical accounts are lacking, experiments

are performed simply to probe unknown relationships to "see what happens." As such, the notion of exploratory experiment offers a fine-grained view of experimental activity that recognizes the fundamental importance of socially situated activities, including:

- Surveying various experimental parameters, or combinations of parameters.
- Separation of dispensable from indispensable conditions for achieving a given result.
- Identification of empirical rules, and creation of suitable representational modalities for these rules.
- Mapping empirical regularities within a system or phenomenon (such as "if-then" propositions), to afford new concepts and categories, or revise existing ones.
- Identification of necessary conditions for producing detectable effects, and to represent regularities in such a way that other effects can be reduced to epiphenomena of other empirical regularities.
- Movement between material experiments and computer simulations for descriptive purposes (a practice similar to thought experiments, a more "abstract" form of exploration).
- Development of new instruments, techniques, and protocols.
- Production of phenomena and effects that do not exist outside the laboratory.
- Checking whether an instrument or experimental configuration works as intended.
- Creating arrangements for exploring new phenomena through series of linked experiments.
- Replicating other results to verify them, or to explore new configurations of instruments.

While these exploratory modalities can entail expectations that are informed by background theory, they are not theory-derived tests of hypothesis in the strict sense, where instrumentation is designed to address one precisely formulated question from a body of theory to falsify a prediction. Neither does this entail "mindless playing around" in the laboratory, free of theory (Steinle, 2006: 186). As the above inventory

makes clear, exploratory experimentation involves definitive procedures and guidelines aimed to achieve specific epistemic outcomes. But where the standard model tests specific expectations about what is supposed to happen throughout the experiment, exploratory experimentation orders and categorizes regularities and patterns *after* the experimental activity ends.

Three Modes of Inquiry in the Molecular Parasitology of Salmon Lice

One reason why exploratory experimentation helps make sense of developments in the post-genomic life sciences is that practice in this field mainly pursues descriptions of mechanisms, rather than high-level theory (Tabery et al., 2016). A biological mechanism is a structure that performs a function in virtue of its component parts, operations, and their organization, so that the orchestrated function of the mechanism is responsible for creating one or more phenomena (Bechtel, 2006: 26). The reliance among biologists on diagrammatic accounts of mechanisms and cascades of molecular events, rather than propositional theories based on deduction from laws, reflects this approach to scientific explanations.[10]

In the pursuit of salmon lice therapeutics at the SLRC, this strategy manifested as actions to first localize critical target mechanisms within relevant biological subsystems. Subsequently, researchers would manipulate a range of variables, in attempts to decompose the constituent parts of these mechanisms. To determine how different parameters were situated toward the biological phenomenon and interacted to produce it, scientists had to simultaneously work across multiple levels of analysis and methods. As such, exploratory experimentation helps articulate a range of knowledge-making activities based around RNAi at the Sea Lice Research Centre, falling outside the purview of a theory-driven account of the experiment. These varieties of exploration were not only crucial for the historical emergence of the experimental system but could be observed ethnographically from everyday laboratory work on salmon lice.

Despite its productivity, however, the concept of exploratory experimentation is coarse, and cannot capture the entire spectrum of epistemic dynamics that occur in experimental activity. In a case study on the recent history of miRNAs and the turn from genetic to genomic regulation, O'Malley, Elliott, and Burian therefore augment the exploratory modality with two open-ended categories, which they respectively dub "technology-oriented" and "question-driven" research (O'Malley et al., 2010). Together, these modes of inquiry help us better understand the temporal evolution of SLRC's experimental system, and by extension, the nuance of RNAi screenings of salmon lice biology as an iterative research style.

Following O'Malley and colleagues, the exploratory modality is best reserved for cases of "highly systematic and rigorous variation of relevant parameters in an effort to characterize poorly understood phenomena" (O'Malley et al., 2010: 413). This includes identification of regularities, characterization of the underlying entities responsible for creating them, and the making of conceptual frameworks that can organize observed complexity. In contemporary bioscience, this modality is exemplified by a widespread use of high-throughput technologies in genomics and bioinformatic resources for problem-solving. In these fields, computational and partly automated data-mining approaches have become critical for analyzing the massive amounts of genomic data that is being produced at a rapid pace. These "neo-Baconian" instruments can be used as "induction machines" to discover patterns in data in the absence of specific hypotheses (Stevens, 2013). Easily accessed via the web browser, online bioinformatic resources like NCBI or Ensemble are central in this research process, as devices are more "oriented to the future than the past" (ibid.: 138). Since these tools are designed around known molecular interactions in different biological systems, they are not simply repositories for information, but rather objects of material culture that *embodies* biological concepts, thereby facilitating the making of new biological knowledge. Over time, scientific concepts have co-evolved in parallel with these bioinformatic systems; beginning with outdated assumptions about "one gene, one protein" interactions, to a current vision of an interactional gene web that works in concert within a complex network of regulatory elements. Models of these interactions

in turn, feedback and materialize in the ongoing redesign of bioinformatic databases and their associated analytical tools, as more is learned by applying them in specific research projects.

Computers and black-boxed algorithms have become indispensable for a research strategy that relies on bioinformatic systems to map interactions in gene expression at the genomic level (Allen, 2001; Kell & Oliver, 2004). But the legitimacy of such neo-Baconian practice in an increasingly "data-centric" field (Leonelli, 2016), has spawned considerable debate among biologists, and those who study their practices. The community at the SLRC, along with their peers in countless biology labs around the world have voted in favor of these facilitating technologies with their feet, as they have gradually embraced new methods without much concern for quarrels between epistemologists.

In this context, it is fruitful to distinguish between "wide" and "narrow" instruments (Franklin, 2005). Wide instruments, like micro-arrays and high-throughput sequencing make heavy use of computational algorithms to assemble genomes (in DNA sequencing), or populations of messenger transcripts (for RNA sequencing). Some wide instruments can make millions of measurements simultaneously, or in a very short time, through rapid serial processing. Narrow instruments, on the other hand, yield only a few data points, such as tools used to carefully examine stained tissue sections through the light microscope (a topic which gets extensive treatment in Chapter 7). According to Franklin, wide instruments are best understood as heuristic devices providing practical, efficient methods for solving problems. Neither optimal nor perfect, wide instruments are deemed *sufficient* for the tasks at hand. They accomplish immediate goals and speed up the research process, particularly in conditions with knowledge gaps about the specifics of a phenomenon or system. By measuring a large part of a domain, wide instruments maximize the likelihood of identifying "difference-makers"; decisive causal factors that change the state of measured outcomes in a biological system (Franklin, 2005: 896).

Still, wide instruments also have limitations. In many cases, they cannot be used in isolation from more narrow approaches. As the biosciences have progressed in their understanding of gene expression,

one remaining challenge has been to precisely map structures of macromolecules (DNA, RNA) to their functional expression as protein products under different conditions. There is, however, currently no system or body of biochemical theory capable of generating broad hypotheses that can predict detailed genotype-phenotype, or structure–function relationships for a large assortment of biomolecules (Burian, 2007: 286). One way this challenge manifested in everyday research at the SLRC was the difficulty of inferring functions based on wide instruments alone, such as high-throughput microarrays or RNA sequencing, given that a particular protein could be involved in many cellular processes. Completing the picture about what a particular enzyme did in salmon lice, for example, would therefore require alternative forms of exploration, using a combination of narrow instruments, such as RNAi and other methods.

The Nilsen group's study of the LsYAP gene, which I described above, exemplifies this experimental logic where wide and narrow instruments interplayed constructively. In that case, the report of high expression levels of the LsYAP gene which drew interest to the gene, came from microarray analysis.[11] Bioinformatic processing then identified the sequence and helped design primers for synthesizing double-stranded RNA, so that the gene could be silenced by RNA interference. By knocking down the gene it could then be functionally examined in detail, using a range of narrow instruments. As the authors of the study wrote in their conclusion: "The transcription profile of LsYAP on different life stages combined with *in situ hybridisation* shows that the LsYAP mRNA is purely transcribed in subcuticular cells lining the adult female louse" (Dalvin et al., 2009: 1414). The use of a wide instrument (microarray technology) interacted with a narrow one (visualization of gene expression through immunohistochemistry), to probe the candidate gene's potential as a therapeutic target. From here, more sophisticated interventions and models of the molecular cascade could be developed. Among other things, the description involved a bootstrapping procedure where microarray, a wide tool, was redeployed to verify the knockdown effect in samples subjected to RNA interference: "Microarray data also demonstrated that the RNAi against LsYAP was specific and the transcription level of remaining genes on the array was unaltered" (ibid.). There was

little need for specific predictions in the conventional sense, to reach new insights about the pathway.

An exchange between narrow and wide technologies also fueled RNAi-based explorations of other genes at the SLRC. One postdoctoral project examined the functional characteristics of an iron regulatory protein (IRP). Blood-feeders like *L. salmonis* must evolve systems for handling excess iron, a micronutrient that is lethal in high doses. From other organisms, it was known that the Iron Regulatory Protein 1 and 2 were involved in this process, and a database search along with comprehensive bioinformatic analyzes revealed two IRP homologues in *L. salmonis. In situ hybridization* was then used to localize where in the body these genes were highly expressed.[12] Later, an RNAi experiment on pre-adult female lice to check the functional role of these genes surprisingly demonstrated up-regulations of another gene, known as Ferritin.

A third example of exploratory applications of RNAi came from characterizations of three chitinase genes and a more detailed functional analysis of the gene known as LsChi2 (Eichner et al., 2015). Chitin is a polysaccharide and a structurally important component of the louse exoskeleton. It is also the target for chitinases, enzymes that break down the rigid exoskeleton of the arthropod body, during molting between life stages. This is the reason why pesticides like di- and teflubenzuron target the chitin-pathway, raising concerns about adverse effects on other crustaceans around farming sites. Candidates belonging to a particular family of chitinases were first identified in the lice genome through a database search for homologies to known chitinases in crustaceans and insects. The group then found that these relevant genes contained several sequences coding for a signaling peptide, suggesting that the proteins were excreted out from the cell. Identification of this extracellular role confirmed that chitinases either acted on the molting process or had a possible role in digestive functions. Three relevant sequences were then identified, and an expression profile was run using qPCR to detect their presence, coupled with an *in situ hybridization* trial to visualize gene expression in the sampled tissue. Although the intervention did not prevent molting in the parasite, RNAi-induced silencing of LsChi2 in nauplii larvae produced animals with "changes in body dimensions, locomotive behavior, and inability to infect fish" (ibid.: 47). Together,

the outcomes of this genetic knockdown provided biological data for exploring the chitin pathway and would be "a valuable tool in future efforts to combat this parasite using chemotherapy or vaccine strategies."

"Technology-oriented research," the second mode of inquiry proposed by O'Malley and co-authors, is based around the design and modification of instruments (2010: 413). An experimental system used in one field of inquiry may be operationalized as a tool for research in another. The transformation of RNAi from an epistemic thing in molecular genetics, to a technical object capable of modifying gene expression in salmon lice research, is an obvious example. We also saw the technology-oriented pattern exemplified in SLRC's historical trajectory, where a novel material culture for experimentation, composed of enculturated lice strains, incubators, and a new single-tank system, went through multiple iterations. Progress in the molecular parasitology of salmon lice depended on a continuous supply of new instruments, and modification of old ones. New knowledge about phenomena was enabled not just by changes in ideas, but also from novel orchestrations of material components. As such, the experimental system's potential to deliver new insights changed profoundly over time, as identification of new patterns and performances radically transformed the questions that could be asked. Historical knowledge of how instruments and other artifacts performed in the past, and how these fitted together in larger systems thus became crucial to produce a "machine for making the future" (Rheinberger, 1997: 28). Again, while these practices were undoubtedly epistemically productive, they get obscured when viewed through the Popperian lens on experimentation as merely hypothesis testing.

The last addition, "question-driven investigations," is present in interdisciplinary contexts where it is hard to generate highly specific hypotheses at certain points, due to a lack of existing knowledge. Here, open-ended questions can be productive, driving later breakthroughs in understanding. The basic research that led to anomaly resolution in the science of microRNA and RNAi was, as we have seen, profoundly question-driven. This was also the case with technical applications of RNAi in experimentation on salmon lice, and the infrastructure developed around domesticated lice strains. Question-driven experimentation often explore general questions, such as "how many X there are," or

"what kind of Y's there are," which may, or may not be refined into specific hypotheses later. In Chapter 6, I present an ethnographic description of a case where several genes coding for a protein known as fibronectin first had to be identified, before it was possible to select candidates for RNA interference experiments and characterize these genes at the molecular level.

At various points in time, the foundational experimental system of the SLRC exhibited shifts in the primacy and relative weighting of these three modes of inquiry. Meaningful variations in parameters of the system were introduced over time, as more central and indispensable conditions could be assorted from the more modifying and dispensable ones. The incremental process of acquiring new meaningful insights about lice biology also included efforts like determining stable empirical rules about the system's behavior. These efforts included the study of sex rations and hatching rates among lice strains, as well as research that eventually resulted in a critical revision of the salmon louse life cycle. In this new model, the number of molting stages in the cycle was reduced from ten to eight. The previous model, which reigned for five decades, was long considered to represent a unique copepod life cycle with eight "post-nauplius instars" and four "chalimus" life stages. However, systematic observations of molting in the incubator system, accompanied by morphometric analysis of the larvae and their shed exuviae (exoskeletal remains left in the incubators), demonstrated that *L. salmonis* only had two chalimus stages, and thus only six post-nauplius instars totally. These insights were tremendously important for future experimental applications, and for devising effective pest management regimes. It implied that the effects of various therapeutic interventions in the salmon pen were based on an erroneous model of the parasite's life cycle.

It was also necessary to work out new representational conventions for capturing invariances articulated by these empirical rules, like the formula for determining the "daily instantaneous loss rate" (see Chapter 3). This entailed efforts to engineer new representational tools, such as spreadsheet templates for keeping track of variables within the experimental system. As the system matured, it was then crucial to understand other aspects of its operational parameters. One example is the problematic interactional effects that were observed in communal

fish tanks, where statistical analysis revealed a high degree of unspecific lice loss. Other question-driven investigations in this cognitive ecology concerned subjects as different as fish welfare, water quality, feed-uptake, and the complexity of biological variations in lice strains.

Exploratory Experimentation as Distributed Cognition

In this chapter, I have shown how developments in RNA research converged with the science of salmon lice in unexpected ways. While the therapeutic promise of RNAi remains to be fulfilled, the method was embraced by Nilsen's research group as a highly adaptable and applicable instrument for molecular parasitology. Through diligent work over years, the research community was able to standardize RNAi technology as a means for their own epistemic ends, to probe the biology of salmon lice on a mass scale.

RNAi experiments gave researchers an opportunity to narrow the search space for potential vaccination targets in the louse genome. Using RNAi, candidates for antiparasitic interventions could be subject to preliminary testing without the costly and troublesome procedure of conducting live vaccine trials prematurely on many candidate genes. By simulating the effects of actual vaccines through silencing specific mRNA transcripts via injections or bath treatments of lice, RNAi provided an opportunity to observe and chart the downstream effects of certain genes through the parasite's life span. Potential antigens with negligible effects could thus be ruled out efficiently, and the Centre could focus their efforts on a few clinical vaccine trials for the most potent therapeutic candidates. Genes involved in critical processes like molting and female reproduction were of particular interest, as they had been effective targets in other cases of pest management.

Here, we see how the experimental system operated as a cognitive ecology, a "cultural ratchet" that accumulated adaptive solutions in an encompassing infrastructure for studying salmon lice biology across molecular, morphological, and behavioral levels of analysis. Just like

exploratory experimentation played a key role in basic research on regulatory RNA, so did applications of RNAi, as a technology for salmon lice studies, sustain exploratory efforts and discovery in new directions. This style of practical reasoning was a consequence of inheriting *technical things* from fundamental research on issues that, once upon a time, were *epistemic things*.

As critics of the logical-empiricist program demonstrated long ago, any experimental test of hypotheses is also simultaneously testing a web of interconnected beliefs (Godfrey-Smith, 2009: 33). RNAi trials at the SLRC were occasionally *informed* by theory in the sense that evolutionary theory informed the phylogenetic reasoning behind the selection of a particular gene target, or that theories concerning the molecular biology of the cell informed the selections of genetic target pathways. But the goal of RNAi experiments was not the refinement of high-level theories. Rather, their goal was to demonstrate the value of specific genetic cascades and mechanisms as therapeutic targets, through fine-grained analysis of the phenotypic details surrounding the functional action of specific genes and their involvement in mechanisms that mediated host-parasite interactions, reproduction, and so forth.

For the cognitive anthropology of knowledge, insights from the New Experimentalists, supported by conceptual work on exploratory experimentation, technology-oriented and question-driven inquiry, expose the cultural richness of experimental practice. Following these, I espouse a pluralistic approach to experimental culture, that goes beyond the hypothesis-centered view. While the value of the exploratory framework is subject to an ongoing debate in science studies, I find the concept ethnographically productive because it highlights a range of epistemic activities in the laboratory that would otherwise go unnoticed. An emphasis on exploratory modalities takes seriously the contribution of material culture to scientific knowledge production, that both conventional studies of epistemology and ethnographic studies of science, tend to disregard. By studying ethnographically, the exploratory conduct of scientists, in naturalistic settings, it is possible to push these backstage activities onto the frontstage.

Still, while the notion of exploratory experimentation is appealing, and gets us on the right track toward a cognitive anthropology of

experimentation, it is still too elusive to capture the variety of cultural productions occurring in the laboratory at the microlevel of interaction. To ameliorate this, I want to upgrade these analytical tools in the next chapters by adding resources from the toolkit of distributed cognition, slightly shifting the analysis in a more ethnographically satisfying direction that helps refocus how these cultural practices of cognition are configured.

In Chapter 1, I mentioned that cognitive approaches to science have been the target of unwarranted skepticism within science studies. One reason is that the notion of "cognitive" has erroneously been equated with "rationalism." Earlier cognitive accounts of science could be seen as "merely transferring the positivists' foundational logic and its purported virtue to lead to the truth within the heads of the scientists" (Heintz, 2004: 394). Cognitive anthropology, and the lens of distributed cognition, allows recasting questions about the iterative nature of knowledge, the transmission and propagation of scientific representations inside and outside the experimental laboratory, as well as the making of scientific intersubjectivity (Ellen, 2004: 433). The method of cognitive ethnography supports this project by offering portraits of how scientific action is productively constrained in the wild. Not by seeing experimental science as acts of reasoning that inevitably result in true beliefs, or by ascribing "Popperian" minds to scientists a priori, but by approaching these phenomena as vivid cultural productions that contribute to the growth of knowledge.

Distributed cognition is highly compatible with a view on experimentation as iterative and exploratory, given that both perspectives argue against a view of human knowledge and reasoning as primarily a theoretical activity, bounded by skin and skull. Together, this helps shift the analysis toward the process of experimental knowledge production, and not just its end products. This provides a toolkit for teasing apart scientific meaning-making by casting light on the interplay between material and conceptual resources that scientists have at their disposal. In what follows, I hope to show how mundane acts of experimental practice, like observations of instrument readings, are not just simple acts of perception, but forms of enactive sensemaking. Positivist, Popperian, and post-Kuhnian accounts of science have all overlooked central aspects of

these meaning-making processes, that are situated in the gaps between acts of perception, and the establishment of scientific fact (Galison, 1987: 8). An interactive and ethnographically informed view of scientific cognition and experimental action allows us to see, on the microlevel, how a rich cognitive ecology bridges this gap. Extending this view of science to specific ethnographic events sampled from the molecular parasitology of salmon lice is the task ahead in the next chapters.

Notes

1. The Dogma was revised after the discovery of enzymes known as "reverse transcriptase," but remains salient.
2. Following convention, I italicize letters for genes (lin-4) and capitalize its associated protein (LIN-14).
3. Mello recalls agonizing over this lack of a clear hypothesis in a lecture: "…We were really nervous that paper would not be accepted, that paper that was in Nature with Andy Fire. We were really nervous, because it was purely phenomenological. All we knew in that story was that if you give worms double-stranded RNA they responded to it in this amazing sequence-specific way […]. As cool as that was, we thought they were gonna ask us for the mechanism. You know, reviewer number three always says: "yes, it's an interesting story but there's no mechanistic insight, therefore" (author's transcription, Mello, 2013).
4. Around 2012, CRISPR-Cas 9, an evolved defense system in bacteria and prokaryote microorganisms, replaced RNAi as the great disruptor of biotechnology. While RNAi regulates genes post-translationally (at the level of mRNA), CRISPR works at the transcriptional level. Some predict CRISPR will replace RNAi in loss-of-function studies, due to its specificity, low cost, and ease, despite the inertia of experimental systems based on RNAi. CRISPR is already applied in research on salmon and lice.
5. Commentators agreed that Fire and Mello deserved the 2006 Nobel, but some lamented that others deserved recognition. In 2008, Ruvkun, Ambros, or David Baulcombe received the Lasker award. Ruvkun and Ambros received the Breakthrough Prize in 2015. All are predicted contenders for a second Nobel on RNAi, if the technology fulfills its promises.

6. A classic case of abductive reasoning is the following syllogistic construction from C. S. Peirce: "if a white ball and a bag full of white balls, then the white ball is from the bag" (Sung, 2008: 128).
7. Sperber uses the term *teleofunction*: "Let us say that an effect of type F is a teleofunction of items of type A, just in case the fact that A items have produced F effects helps explain the fact that A items propagate, i.e. keep being re-produced" (Sperber, 2007: 128). Teleofunctions of various entities have different mechanisms for propagation. Items with biological teleofunctions, like RNAi, are phenotypical features of organisms. Cultural teleofunctions are either mental, within-agent representations, or exist as public productions (practices, inscriptions etc.). While an artifact's function is the effect that explains why it was produced, its teleofunction is the effect that explains why it was "re-produced" (the prefix stresses this crucial distinction).
8. Parasitologists at the University of Aberdeen were introduced to RNAi by the Nilsen group, and used RNAi in their own studies on *L. salmonis.* While the Nilsen-group submitted their manuscript to the *International Journal of Parasitology* on March 4, 2009 (accepted April 16), the other group submitted to Parasitology a month later on April 13 (accepted May 18). Due to unforeseen circumstances, the Nilsen-paper was not published before November, while the Aberdeen-group published in *Parasitology*'s July issue. As a result, both papers claimed to be the first to use RNAi in lice. The Aberdeen-group's paper stated they were "[…] the first report to perform dsRNAi in any copepod" (Campbell et al., 2009: 873). Nilsen's group wrote: "Finally, we have demonstrated systemic RNAi for the first time, to our knowledge, in a copepod species […]" (Dalvin et al., 2009: 1414). Neither paper referred to work by the other group.
9. It is exemplified by Hacking's famous anecdote about how invisible entities are grounded in experimental applications. He recalls a dialogue with a physicist-friend about detecting electric charges ('quarks') using a superconducting ball of niobium: "How does one alter the charge on the niobium ball? [asks Hacking]. 'Well, at that stage', said my friend, 'we spray it with positrons to increase the charge or with electrons to decrease the charge'. From that day forth I've been a scientific realist. So far as I'm concerned, if you can spray them then they are real'" (Hacking, 1983: 23). Known as "entity realism," this position accepts the realism of manipulable entities but maintains skepticism towards higher-level theories about these entities.

10. In the context of molecular parasitology, evolutionary theory mainly figured as "systematic theory" (Hacking, 1992) for addressing functional questions, such as "what is X for" or "what does Y do"? In experimental work at the SLRC, evolutionary theory was a resource, and not a framework that should (or could) be challenged through laboratory tests on salmon lice.
11. Microarrays (or "gene-chips") were introduced in the mid 1990's to identify active from inactive genes. Chemically, microarrays exploit base-pairing rules between mRNA molecules and its DNA template.
12. In situ hybridisation (ISH) is a technique for visualizing gene expression in tissues by locating the expression of distinct DNA or RNA sequences in samples by fluorescent probes.

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5

Thinking Through Experiment: Enacting RNAi

In the preceding, I told a story about the emergence and organization of a novel experimental system for investigating questions in lice biology, and how the social and technical conditions for production of such knowledge coalesced in the Sea Lice Research Centre. Taking a cognitive-historical approach to this problem-solving complex, I situated a range of epistemic activities in their context. This analysis was couched in concepts drawn from science studies on the cultural diversity of experimental knowledge, occasionally invoking the language of distributed cognition and related "environmental perspectives" on the scientific process (Nersessian, 2009).

A focus has been on how scientific instruments and concepts become meaningful when inserted into a historical context of experimentation, capable of differential reproduction through repetition, variation, and iteration (Rheinberger, 1997, 2010). But a detailed account of how novel scientific meanings arise and propagate through instances of explorative inquiry, from which new bits of knowledge emerge, requires a different level of analysis than the one employed so far. In the next three chapters, I therefore shift focus and present a series of interactional analyzes based around cognitive ethnography that animate concrete episodes

M. Solberg, *A Cognitive Ethnography of Knowledge and Material Culture*, Culture, Mind, and Society, https://doi.org/10.1007/978-3-030-72511-2_5

observed in the lab. The goal is to give an ethnographic account of what information goes where, when, and in what form, during instances of bench work at the Centre. I do so, by underscoring how scientists together construct, develop, and maintain ecological assemblies within the cultural-cognitive ecosystem of the SLRC, spanning from the performance of RNAi experiments (this chapter) to measurements of gene expression (Chapter 6), and collaborative microanatomy of lice tissues (Chapter 7).

Springing from the framework of distributed cognition, cognitive ethnography's guiding heuristic is to ask about a given activity such as a lab experiment, "what information goes where, when, and in what form"? The basic procedure consists of first identifying a relevant cognitive task, and then using ethnographic insights to find out which elements play a causal role in completing the task by subjecting these components to a functional, interactional analysis. As a practice-based method, it samples the unit of analysis from naturalistic events. A primary concern is how agents use and coordinate conceptual resources with the material resources of their external surroundings to think, act, and construe meanings. These phenomena of interest span from social interactions manifested through language, via the use of gesture, to the manipulation of material artifacts, and so on. A central premise is that the meanings of actions are grounded in specific contexts of activity, which cannot be surmised from studies on cognitive processes in "captivity" (Hollan et al., 2000: 179).

This approach draws on the ethnographer's toolkit for attending to everyday interactions in peoples' lifeworld to better understand the nature of cognition. It examines how events unfold in communities of practice by extending the unit of analysis from individual minds to the interaction and propagation of representational states through various representational media in larger social systems, environments, and across time. By conceptualizing the laboratory as a cognitive ecology, the ethnographer of scientific knowledge can literally step inside and behold how experimental systems become "elaborate filters set up in the space of phenomena," to invoke a salient metaphor (Galison, 1987: 13).

Rooted in traditional ethnography, cognitive ethnography expands its reach and scope by taking seriously the interactive nature of meaning

and knowledge construction. Using digital video, it becomes possible to capture minutiae of real-time activities and to analyze dynamic interactions, thus complimenting classical participant observation with more elusive data points. These may, in turn, be augmented by historical materials, studies of artifacts, written media, interviews, and other items from the ethnographic toolkit. Together, these resources can redress human shortcomings in intuition and memory that inevitably follow when people self-report on the dynamics and structure of their own multimodal, semiotic activities. Often, these go unnoticed and they are too fleeting to be captured by ethnographic observation without technical augmentation (Alač, 2011).

This workflow, which Hutchins calls a "cognito-scope" for observing cognition in the wild (2014), starts out with regular participant observation of conduct in a community to identify patterns of important activity and gain insights of relevance for later analysis. After samples of naturally occurring events have been observed and recorded on video, the structure of events is then indexed, and scanned for salient segments of interaction that cast light on a given situation. On this basis, a selection of specific micro events is transcribed using multimodal transcription schemes, depending on the phenomenon of interest. It is also possible to align renderings of still-images from relevant interactions with transcripts to support further analysis (see Alač, 2011), as I occasionally do in the following. As such, cognitive ethnography attaches "descriptive comments" to ethnographic representations; "directions for use" that invites the reader to evaluate both interpretations and theoretical inferences (Sperber, 1985).

Disciplined attention to fine-grained accounts of talk, uses of artifacts and other forms of bodily interaction at the microlevel of social contexts, originates from conversation analysis of natural discourse, studies of speech-in-interaction, and ethnomethodological approaches (Goodwin, 2000; Streeck et al., 2011). Using video analysis in science studies offers an alternative route for grasping how mundane resources participate in local experimental accomplishments, and avoids the risk of "theoricism" (Sormani et al., 2016: 128). That said, the question of who is "doing what, why and how" in the performance of laboratory action only becomes meaningful when contextualized through immersive participant

observation over time (Chang, 2011). Like other methods in the human sciences, it is also selective in scope. It is not possible, as Goodwin underscores, "to work in some abstract world where the constitution of knowledge through a politics of representation has been magically overcome" (1994: 607).

Ordinary ways of thinking about knowledge as a property of individuals tend to break down when we examine aspects of contemporary science, a technology-driven and distributed enterprise involving many minds (Giere, 2002: 644). In their laboratories, scientists collectively mediate interactions with physical nature through a wide range of semiotic modalities and external representations that order access to the world (Coopmans et al., 2014). According to distributed cognition, our cognitive faculties fundamentally depend on the ability to engineer such external props to scaffold thinking. Echoing Hutchins, we can say that scientists build their cognitive powers in part by creating problem-solving environments where they exercise these powers (Nersessian, 2012: 223). Or in this case of molecular parasitology: by engaging an experimental system comprising domesticated organisms, instruments, other researchers, and a suite of epistemic activities. In these environments, arrangements of instrumentation and concepts are "laminated" through layers of semiotic action that eventually make epistemic things meaningful (Goodwin, 2013).

A primary function of this cognitive ecology is transformation of representational structures. Experimental science does not just encompass mental representations found solely inside the head as disembodied theory bounded by the epidermis, but fundamentally involves rearranging things in the laboratory to reveal informative patterns, by building external models through a suite of discursive practices that make unknown phenomena intelligible. When studying this cognitive niche, where scientists inherit resources from their predecessors that help enact new material transformations on the world to better understand and explain it, we must attend to representation and re-representation as both product (noun) and practice (verb).

In this chapter, I examine how RNA interference experiments are arranged in situ to produce and transform representations that mediate

the phenomenal objects of gene expression in salmon lice. By phenomenal objects, I mean the features and outcomes of experiments, that are the professional concerns of these biologists. In this, I build on Goodwin's insight: "central to the social and cognitive organization of a profession is its ability to shape events in the domain of its scrutiny into the phenomenal objects around which the discourse of the profession is organized" (1994: 626). I trace this shaping of events through critical steps in what my interlocutors colloquially referred to as their "pipeline"; the assembly line of material, conceptual, and virtual interventions on lice that transform RNAi experiments into useful data and insight. Despite the ubiquity of external representations in experimental systems, their status is often taken for granted by insiders in a scientific community. Inscriptions like numbers, letters, notational systems, diagrams, drawings, images, and other visualizations, appear to litter the work environment, simply as historically accumulated products of human activity. But getting them to work in a coherent, mutually supportive fashion, requires practical engagement across multiple semiotic fields. As such, they are far from trivial, but core elements in the architecture of scientific perception.

But what turns material representations, like squiggles on a piece of paper, a label, or a digital spreadsheet into productive, meaningful representations within a given experimental system? The answer to this question is "enactment," as material patterns achieve representational functions through engagement in a culturally shaped perceptual process. The phenomenological worlds of skilled scientists are not made up of isolated objects, but orchestrated in systems of "enacted understanding" (Hutchins, 2010: 429–430). Competent professionals, experimental scientists included, apply three key discursive practices to enact meanings (Goodwin, 1994). First, they use coding schemes to transform salient phenomenon into knowledge objects that animate professional discourse. Secondly, they mark out specific things for attention, often under complex perceptual circumstances, by highlighting them. And third, professionals articulate material representations in the domain of scrutiny to co-produce phenomenal objects of interest. Through such multimodal enactments, experimental systems jointly engage perception, action, and imagination (Hutchins, 2010).

A view of scientific representations as enacted, resonates with Hacking's taxonomy of elements contributing to the "self-vindication" of the laboratory sciences (1992). His materialist thesis state that the laboratory sciences create mutually supportive structures consisting of ideas (intellectual content), things (including targets, sources of modification, detectors, tools, and data-generators), and the manipulation of marks (data assessments, reductions, analysis, and interpretation). But although Hacking's inventory draws attention to what makes experimental practices cohere, I mentioned in Chapter 1 that this vocabulary lacks the grammar to go with it (Chang, 2011: 206). What is further needed in studies of experimentation in the wild, is a thesis taking seriously the relationships between "thoughts, acts and manufactures" (Hacking, 1992: 30). Distributed cognition is precisely a thesis about such relationships, and cognitive ethnography offers tools to investigate how they are socially arranged in practice.

Here, I flesh out this relationship empirically, through an ethnographic study of how representations are enacted in an activity system that encompasses the initiation and termination of RNA interference trials. Examinations of events, sampled from the preparation and execution of these experimental events, explore how RNAi trials establishes meaningful relationships between bioinformatic resources for digital handling of genetic sequences, lice samples, instrumentation, engineered nucleotides, sorting systems, written representations, and other scientific visuals like annotations, Excel spreadsheets, and digital photographs. By asking, what information goes where, when and in what form within these paradigmatic interactions at the Center, I show how novel scientific meaning emerges from laboratory organization. To do so, I must attend to the experimental system's representational states, and how the configuration of information-bearing structure changes over time. Ethnographic description of events ties together relations between disparate elements that only come together during certain moments of practice, and which are hard to articulate by members of the community when prompted outside the situated context of action.

In the labscape, representational structures in one medium are systematically transformed and re-represented into structures in a different medium. RNAi trials align the mental models of scientists with biological

samples, analog and digital inscriptions, verbal utterances, gene expression measurements, information from histological tissue sections and biochemical visualization methods. These alignments create interlocking models that support insights about relevant target structures. Theories of distributed, situated, and extended cognition suggest that such interlocking models indiscriminately combine internal and external resources, artifacts, and practical action. Applying the "cognito-scope," we see how the laboratory organization of the SLRC effectively sets up an ecology for exploring epistemic things in an interdependent space, satisfying the constraints of different resources in the system. Invoking the ecological metaphor here, allows us to think about interworking elements, and how they relate to epistemic outcomes. These scientific practices are fundamentally social, as they are coordinated and constrained by the practices of other humans, animals, and artifacts within a wider cognitive ecology. In this context, to "coordinate" simply means to "set oneself up in such a way that constraints on one's behavior are given by some other system" (Hutchins, 1995: 200). Rather than seeing the propagation of representations in the experimental environment exclusively in the narrow terms of "information transfer" between individual cognizers, I find it productive to view these accomplishments as alignments of resources in the experimental system. Attending to RNAi trials here, I use the next two chapters to examine how other resources for representing and intervening on lice biology get coordinated downstream in the experimental pipeline.

Orchestrating Molecular Manipulations: The Checklist

Although the lice genome was already sequenced, scientists only had indirect information about the biological role of individual genetic sequences in the living animal. As explained in Chapter 4, the Centre therefore conducted two types of RNAi experiments aimed to silence specific genes, so that more could be learned about their function. Between 2012 and 2018, the Centre executed 396 such experiments on lice at the nauplius stage (aimed at 234 different gene targets), and 380

experiments on the pre-adult stage (aimed at 330 different gene targets), not counting controls and replicated experiments (SLRC, 2018).

To probe gene expression in early planktonic stages of the life cycle, the group used a soaking method. Larvae at the molting stage were immersed in a sea water bath, to which synthesized double-stranded RNA fragments had been added. These fragments were then absorbed across the larvae body and set in motion the RNAi machinery to silence the targeted genes. As these experiments were relatively simple in terms of the necessary resources, they could be executed by individual scientists without much planning and coordination with other lab members. The more conspicuous screening events were those based on direct injections of pre-adult louse specimens. In these experiments, double-stranded RNA molecules were injected into large batches of salmon lice harvested from live fish, that were then reinfected to the salmon hosts, and placed in the single-tank system to maintain tight control over experimental outcomes. These events were laborious and required coordination between several researchers since the accompanying tasks were time sensitive. Here, practical constraints inherent to the experimental context necessitated a division of labor spread across two complementary task domains: while one group of researchers primarily handled nucleic acids and salmon lice, another group cared for the host fish.

When taking the distributed perspective on experimental science there is a need to distinguish between two categories of cognitive labor involved in the execution of tasks that are spread across a community of practice. First, there is the cognition that is the task itself. Secondly, there is the cognition that governs the coordination of participants, elements, and actions involved in executing the task. In the everyday flow of situated research activity, these interact as to create emergent phenomena whereby "the group performing the cognitive task may have cognitive properties that differ from the cognitive properties of any one individual" (Hutchins, 1995: 176). Note that while my focus in the following is on coordination of elements involved in large-scale RNAi trials on pre-adult specimens, this does not imply that there is no distributed cognition occurring in the smaller RNAi experiments where individual scientists apply the bath method at the nauplii stage. However, given my

ethnographic interest in epistemic activities on the level of the experimental machinery, I find conduct in these joint trials to be a particularly relevant unit of analysis for teasing apart how complex RNAi experiments make knowledge. I return to the cultural practices of cognition, and the ecological assemblies that enable situated individuals to accomplish computational spread to solve complex bench work, when we move further down the experimental pipeline.

How does an experiment produce a set of tractable representations that can lead to novel insight about biological phenomena? Getting research done within the constraints of SLRC's experimental system required copious amounts of work. Since the pipeline for large-scale RNAi had limited capacity, a senior scientist at the Centre was responsible for scheduling and keeping track of all past, ongoing, and future RNAi-screening experiments, and their main outcomes. This job involved gathering information from all the other researchers and students about the lice genes that people worked on, individually and jointly. To ensure uniform and coherent execution of these experiments, a public account spelled out how people, nucleic acids, artifacts, salmon lice, and salmon should be coordinated before, during, and after RNA trials. This document, which took the form of a normative and prescriptive checklist (hereafter referred to simply as "The Checklist"), was a "regulatory representation" that established RNAi trials as a particular cultural institution (Heintz, 2007). Building on Dan Sperber's epidemiology of representations, Heintz proposes that communal institutions of this kind get their identity from causal chains that distribute representations so that they cause and structure reoccurring events. In this perspective, an institution like The Checklist is defined as "the distribution of a set of representations which is governed by representations belonging to the set itself" (Sperber, 1996: 76). Institutions play an important role in distributed cognitive systems, as these both provide mechanisms that ensure the social reproduction of the system over time by regulating its function, and a distribution of representations that fulfil this function.

The Checklist circulated within the Centre as a public document embodying a cultural script that regulated how other representations ought to be processed within the socially legitimate performance of

an RNAi trial. The script spelled out by the document had normative force, providing authoritative instructions for the sequential nature of events and actions, how information should be codified in inscriptions (what information should be written down, which things should be labelled, and how), how artifacts, animals, people, and inscriptions should be coordinated and propagated, and not least: procedural descriptions for a range of different pragmatic and epistemic actions. As a regulatory representation, The Checklist also functioned as a "coordination device," controlling how representations within the activity system should propagate, by exerting constraints on possible moves in the sequence of action (Hazlehurst et al., 2007: 543). It achieved these regulatory effects by laying out an arrangement of resources for RNAi, specifying courses of action in five temporal orders: "preparations," "day of injection/initiation," "monitoring of experiment," "termination," and "hatching."

Choosing a Fragment

Let us start with the early preparations of nucleotide fragments. Before an RNAi trial, all participants must figure out which gene they want to silence. As The Checklist instructs: "find out what gene you want to knock down." How did my interlocutors accomplish this?

Several routes were available for homing in on relevant lice genes for experimentation. And like with other scientific accomplishments these were constrained by the Centre's division of labor. In science, division of cognitive labor is institutionalized on multiple levels, with macro-level divisions between disciplines (biology, physics, chemistry, and so on), within sub-disciplines (molecular biology, ecology, zoology), laboratories, and research groups, and within specific projects (Muldoon, 2013). At the SLRC, fine-grained labor divisions were necessary due to the biological complexity of lice, and the great diversity of candidate genes that could potentially be subjected to screening experiments using RNAi. Work Package 4 crystallized around three main topics of interest: host–parasite interactions, basic copepod biology, reproduction, as well as the endo and exocrine systems of salmon lice. These biological

domains were considered the most epistemically rewarding, with a high chance of resulting in therapeutic breakthroughs. Work in each topic was also coordinated on a more fine-grained level, including:

- *Genes related to molting, and general parasite growth*. One doctoral student worked on a class of genes related to a protein known as fibronectin (which we encounter in the next chapter). Another examined the function of genes predicted to be involved in chitin degradation. Chitin is a necessary component of exoskeletons, and enzymes called chitinases are required to degrade chitin when the parasite molts, making them popular targets for pesticides in both terrestrial and marine environments.
- *Endocrine regulation of ontogenesis*. One Ph.D. candidate extensively characterized the ecdysone receptor (EcR), using RNAi and other methods. This receptor was believed to be involved in biological mechanisms such as ligands, a type of hormone substance that binds to other molecules, forming larger complexes. If these receptors could be shown to act on key developmental transitions like molting, they would be interesting therapeutic targets. Part of this work involved an attempt to quantify steroid hormone levels through a novel assay developed in collaboration with staff from Work Package 1, based in Oslo. Another postdoctoral project worked on genes involved in the ferritin pathway, an intracellular iron transporter protein that was assumed to be central in iron regulatory processes. In this work, the postdoc screened fourteen different candidates involved with heme, a prosthetic group that binds to proteins like hemoglobin, using RNAi, as well as genes related to iron metabolism.
- *Germ-cell differentiation and maturation*. One Ph.D. candidate worked on the Nanos gene family, which are crucial for germ-cell development as they bind to mRNA molecules and block translation of key proteins necessary for growth and differentiation. While this project was eventually relinquished, another candidate examined genes involved in oocyte-formation, yolk deposition (vitellogenesis) and lipophorin regulation, transport, and uptake. These processes were central for bringing proteins and lipids for the growing embryo into the developing eggs (oocytes).

- *Chemosensory genes involved in host recognition*. Genome sequences revealed that the parasite lacked typical chemosensory receptors found in other species. A postdoctoral project examined the function of receptors suspected to process chemical communications with the environment, such as detecting host fish, and genes involved in chemoreception, reproduction, and lice behavior.
- *The molecular biology of exocrine gland structure*. A fourth postdoctoral candidate spent considerable time mapping these anatomical structures, as well as characterizing viruses shown to be present specifically in lice glands. We return to this work in Chapter 7.
- *Immune modulation*. A team of junior and senior researchers at the Centre characterized Prostaglandin E2 synthase (PGE2), an immune modulator suspected of inhibiting inflammatory responses in many parasite hosts. Despite much effort, the group failed to elicit any changes in phenotypical or reproductive output from lice after conducting RNAi trials on this gene.

The cognitive and practical divisions of labor exemplified by these efforts can be viewed as an epistemic and economizing strategy of "risk-hedging" through diversity in the context of scientific discovery (Muldoon, 2013: 123). As the Centre promoted a diverse portfolio of projects on a variety of critical genes and biological processes, priorities were set by individual researchers, who were specialists on their topics of interest in close dialogue with senior leaders, thereby combining a centralized, well-organized search based on the Centre's strategy with more local judgments concerning best practices and methods. Generating and maintaining this diverse portfolio was epistemically rational, despite the burdens associated with successfully coordinating it, since it was impossible to predict accurately which of the experimental targets would materialize as tangible breakthroughs.

Thinking Through Trees: Phylogenetics as Epistemic Enhancers

Two additional examples illustrate in detail the general schema for the selection and exploration of RNAi targets. My first example concerns a study that began with an evolutionary insight. It turned out that a type of receptor, here dubbed "R," is crucial for a cellular process related to gene regulation in all metazoan animals. While many studies had investigated this biological mechanism in other species, there was little knowledge about its role in salmon lice biology. With knowledge about genetic sequences involved in the R pathway from other genomes, a search for matching sequences was then performed in the louse. This yielded several hits for similar genes, including variants involved in general growth processes, as well as reproduction. Complete transcripts of these genes were then identified using a method known as RACE ("Rapid Amplification of cDNA Ends"). Further sequencing found differences in the domain's genetic structure, and quantitative PCR identified locations where these genes were highly expressed in the lice body. It turned out that the level of transcription and its location varied significantly through the life cycle. While some transcripts were identified in the gut, others were found in the reproductive system. The genes also appeared to express differently in males and females. An RNAi experiment probed the effects of silencing the expression of R, which yielded new insights about its biological function. Of interest, was the fact that RNA interference appeared to eliminate viable offspring in adult females. Further studies showed that many other reproductive genes were also disrupted by silencing R. Indeed, the use of "wide instruments" like the microarray, later showed a large effect on many diverse genes. Besides offering valuable insights about the function and evolution of this biological mechanism, the investigation concluded that R and downstream genes could be potential targets for therapeutic interventions, making them attractive for further study.

A second example concerns P, a protein previously described as an active modulator of the host immune response in ticks. It was suspected that P could also be active in the louse. In fact, a study of P had been conducted earlier by a competing research group abroad, but results were

inconclusive. Scientists from the SLRC had some novel ideas about how to improve on this research. First, P in lice was characterized at the molecular level, using a similar approach as the one used for R. Complete transcripts of a central gene involved in producing P were obtained via RACE, and computationally compared to a similar protein that was identified in 39 other species. An evolutionary (phylogenetic) model of these relationships was also compiled, along with an expression profile of genes believed central for producing P. When the patterns of gene expression in developing lice tissues were visualized, it turned out that the gene was expressed both in muscle cells and in the reproductive system of adult female lice. The group then decided to silence the production of P in specimens at the nauplii stage using the bath treatment, and adult lice using the injection method. These experiments showed no significant effects on nauplii nor adults, and the group concluded that observed expression patterns did not conform with the observations of previous studies. The disruption of P appeared to not affect any essential functions under these circumstances.

These two examples condense important features about how candidate genes were identified and subjected to experimental investigation through the pipeline. As an invertebrate with an exoskeleton, a segmented body, and jointed appendages, *Lepeoptheirus salmonis* is grouped among other crustaceans, arachnids, insects, and myriapods in the phylum of arthropods. From a parasitological perspective, genes in salmon lice are particularly salient objects of inquiry when they are involved in biological processes, whose associated mechanisms could be targeted by either vaccines or other therapeutics used against parasitic arthropods. Research on insect pests in other domains, where the sheer amounts of invested workhours dwarfed those of marine aquaculture, thus offered a scaffold of knowledge for parasitological work on the louse. It was not uncommon that therapeutics originally developed for terrestrial agriculture and husbandry could be successfully transferred to marine fish farming. The most appealing targets for vaccines and other pharmaceuticals would be those working on a narrow class of organisms, since indiscriminate side-effects could potentially affect the marine ecosystem negatively. This had long been problematic for some drug classes, such as chitin-synthesis inhibitors, which were suspected

to adversely affect a broad spectrum of crustaceans around salmon farms, including commercially important species like shrimp, crabs, and lobsters. This challenge made a vaccine against the louse especially salient, since vaccines work by stimulating the immune system to protect individual fish and would thus reduce environmental impacts compared to other therapeutics, like drugs added to fish feed or pesticides used in bath treatments in farms.

By searching the genome for genetic sequences involved in critical adaptations for the parasitic lifestyle, like those playing key roles in reproduction or regulating host interaction, it was possible to narrow the search space considerably from the roughly 13,000 genes that were identified in the louse. One way that scientists at the Centre could narrow this space of possibility and make qualified decisions about suitable targets for RNAi screening experiments, was to engage in evolutionary reasoning about the descent of sequence, as exemplified in the two examples above.

Biologists and laypeople alike, classify and order salient discontinuities between animals and plants hierarchically in taxonomies, in groups within groups (Ellen, 2004). Together with causal cognition and inference (the ability to go beyond available information), classifications are fundamental for learning about the world. Anthropologists of knowledge have long concerned themselves with the universality and structure of taxonomic reasoning and its degree of cultural infusion (Ellen, 2006). Atran, for instance, proposed that folk taxonomies are based on stable cognitive schemas, a "universal domain of cognition that produce special forms of worldly knowledge" (1990: 253, but see Ellen, 2004: 422–425 for a critical discussion). This continuum hypothesis of knowledge suggests that both laypeople and professional biologists draw on commonsense intuitions, like the folk notion of "species," when thinking about living kinds. Within the subfield of systematics, biologists have argued vigorously about how to order biological diversity in taxonomies and nomenclature (the appropriate rules and criteria for naming entities at different taxa), and how they should be ranked and ordered in classifications. While several traditions in systematics competed throughout the twentieth century, the approach known as "cladistics," or "phylogenetic systematics" became dominant as the majority of biologists agreed that the most effective classification was one reflecting the history of

Darwinian evolution (see Hull, 2010). In this scheme, organisms are assorted monophyletically into groups nested within groups descending from a single ancestor, a perspective that modern bioinformatics extends to the molecular level. Before DNA sequencing became widespread, the topic of phylogeny was mainly the providence of systematists. Today, however, it is widely used across all subfields dealing with sequence data. Phylogenies do not only describe evolutionary relations at the species level, but also helps understand the relationship between genes and their products.

Since Darwin, genealogical relations between organisms have commonly been represented as a branching tree, a motif with a long social history in various cosmologies, as revealed by a rich collection of cultural productions about living kinds. For instance, in his ethnography of marine microbiologists, Stefan Helmreich describes how the science of gene transfer in extremophile organisms dissolves assumptions about the evolutionary roots on the tree of life (2009, Chapter 2). Tree-like representations based on models of molecular evolution can diverge quite radically from folk intuitions about species relations. When reasoning reflectively about biological ancestry, professional biologists do not consider the species-level to be a container of essences (as laypeople tend to), but rather view this taxon as a construct for pragmatically grouping certain things together. For those working with phylogenies the main preoccupations are "clades," monophyletic groups of organisms and sequences encompassing a common ancestor and its lineal descendants, branching out over evolutionary time. In this view, individual organisms are not *instances* of a species, but rather comprise "one physical part of a large scattered object," situated in an evolutionary process (Godfrey-Smith, 2013: 108).

Molecular parasitologists at the SLRC estimate the deep histories of heritable materials, like nucleotides and their associated proteins, by building evolutionary models of relationships between sequences on their computers. The extrapolative task of comparing the complex structure of novel genes or proteins with known sequences from other organisms, presents a statistical and mathematical problem that can only be solved digitally.[1] Similarities between two conserved sequences may

indicate shared ancestry ("homology") and can reveal clues about potential entanglements in crucial biological mechanisms. It thereby helps to narrow the search space for suitable RNAi targets.[2] While manual examination of short strings of sequence is theoretically possible, and was common before the dawn of bioinformatics, the gene and protein sequences relevant for contemporary bioscience are now too multitudinous to be meaningfully compared this way. Today, they are primarily stored and analyzed in an automated fashion, as their one-dimensionality and symbolic structure make them tractable for computational and statistical procedures (Stevens, 2013: 41). On basis of shared characteristics, genes, and proteins can be organized into structural and functional groups by evolutionary descent, like "families," "multi-gene families," and "superfamilies" (which may contain hundreds of genes or proteins).[3]

Phylogenetic thinking is mediated through software based on mathematical algorithms for handling strings of nucleic or amino acids. These facilitate comparative analyzes of sequences stored in online databases, freely available to anyone with an internet connection. Such tools both represent evolutionary relationships of sequence, and function as critical infrastructures for data management. A sequence alignment, for instance, usually contains a list of species (from which relevant sequences are sampled using a database), and a long string of letters signifying the respective nucleotides in the case of a gene (or amino acids in the case of a protein). A computer program is then used to identify the best alignments between sequences and highlight salient positions, differentiating them by colors and other representational modalities. From these computer-aided comparisons, biologists gain a better understanding of the evolutionary history, functional expression, and developmental timing of lice genes. Like the sequences they contain, these digital tools have been continuously evolving since Margaret Dayhoff pioneered the collection and sorting of protein sequences in the 1960s. Consequentially, the computer infrastructures that render genomes visible are now something more than saturated repositories of data. Instead of mere catalogues, the way information gets linked in genomic databases embody biological theories and classificatory systems that describe historical interactions between the building blocks of life (Stevens, 2013: 168–169).

Phylogenies are tree-shaped representations consisting of nodes connected by branches. A tree diagram that represents sequences sampled from different organisms should be read as a hypothesis about the ancestral relationship between them, based on a specific model of molecular evolution. Estimating phylogenetic relatedness used to be a hard problem, due to the great many possible relationships that must be searched to fit the data, even for quite small trees. Phenomena like convergent and parallel evolution, as well as evolutionary reversals, homoplasy, massively complicate the estimation of evolutionary relations between sequences. Organisms may, for example, share traits that common ancestors lack. Crafting phylogenies, then, is about determining the best overall fit to the data, given that some data will inevitably fit poorly.

A thorough exposition of how statistical tools are applied in the practice of phylogenetic inference would quickly take us too far afield, but some basic principles are needed for making sense of how computers facilitate "tree thinking" that inform RNAi trials. Phylogenetic relations are best estimates of historical relations, reconstructed through either distance-based methods that compute pairwise distances from sequence, or sequence-based methods that use the sequence alignment to determine the structure of the phylogenetic tree based on an optimality criterion. In my observations of phylogenetic work at the SLRC, my associates preferred a class of sequence-based methods known as "Bayesian inference." "Bayes' theorem" provides a formal framework for incorporating prior evidence (priors) to estimate the probability that an event occurs,[4] and Bayesian inference is part of a family of "character-based methods" that compare all sequences in an alignment by calculating one site in the alignment against others.

To create these approximations, sequences were first sampled from lice and a diverse range of other organisms stored in curated databases, through a BLAST search.[5] BLAST is a collection of programs that can identify and compare regions of similarity among sequences and calculate the statistical significance of matches between them. The most important outputs of BLAST are defined through a "score" and an "E-value," which gives a quantitative estimate of similarity between the input sequence used for the search, and those pulled from the database.

A high score means there are many similarities between the sequences, which may be an indication of their biological relevance. The "E-value" on the other hand is a statistic that reveals the number of alignments that may be expected by chance, such that a lower E-value indicates a "better" hit. Salmon lice gene sequences (or amino-acid alignments) were usually obtained locally through LiceBase before it went public via the online genome browser Ensembl in 2015, or through targeted sequencing of specific genes of interest (when entries stored in LiceBase were inadequate).

Regions of interest were then aligned with genes from other organisms on the computer, using a Multiple Sequence Alignment (MSA) program, such as BioEDIT, and managed with software like Mesquite or MacVector to create a file in the format known as NEXUS. My interlocutors would then import this file into software packages that could run a "model test" to automatically detect the best fit between parameters and models of evolution for the given sequences of interest (such as ProtTest, for comparing amino acid sequences in protein evolution). Next, the challenge was running an evolutionary simulation, with software tools like "Mr. Bayes," or "BEAST.[6]" Here, researchers would choose the preferred parameters of the model for molecular evolution to be applied. While it is possible to get radically different trees as output based on identical sequence data, simply by changing these software parameters, my interlocutors frequently exchanged recipes and templates that specified relevant assumptions for their phylogenies, as these details ranged from the familiar to the arcane. After controlling all relevant parameters, including the number of generations to run (e.g., "two runs for a million generations"), researchers would then execute the phylogenetic inference on their dataset.

This Bayesian process, which evaluates the probability and degree to which a chosen evolutionary model fits with observed data, could sometimes take a day or more, depending on the number of sequences being compared and the available computing power. First, the procedure created a value known as the "posterior probability" by modelling the evolutionary process. This probability depends on what the user is willing to accept as true before initiating the analysis. But due to the number of possible trees, branching lengths, and other parameters, the application

of Bayesian methods alone to phylogenetics quickly leads to insurmountable analytical problems. Phylogenetics must therefore incorporate sophisticated algorithms known as Markov Chain Monte Carlo-models (MCMC) to compute Bayesian probabilities. Crudely put, the Markov Chain is a mathematical system that can model phenomena that jump between different states, while a Monte Carlo simulation is a way to sample random numbers (as in roulette) to simulate stochastic processes that are "too complex to calculate in full analytic glory" (Galison, 1997: 689–90).

A popular textbook for biologists by Wiley and Liebermann, explains the principle of MCMC in the following terms (2011: 223–224): "In general, MCMC involves using computer-generated random numbers and a set of rules to simulate a walk through the space of trees and parameters. One begins by either randomly picking a model (random tree topology and other associated parameters) or by picking a particular model (one considered a priori probable, usually a particular tree topology and associated parameters). One then randomly picks a second model and compares it to the first. If the proposed model has a higher posterior probability density, then adopt it and pick another random likelihood model to test. But if the proposed model has a lower posterior, then it can still be picked with some probability (the probability is simply the ratio of the posterior for the proposed state to that of the current state)."

Commonly, the pedagogic metaphor of hill-climbing is invoked to explain how a distribution is sampled from the evolutionary landscape. Here, one imagines a random process of "walking." Future events only depend on the current state of the process, and not what has occurred before. Each sampled point in the probability distribution depends on the most recently sampled point. First, the "walk" starts at a random point, and then makes a random move. Next, a "height-ratio" between the new and old state is calculated. If the ratio is higher than the value 1, the new state is accepted. If the ratio is lower than 1, a new state is sometimes accepted with the probability of the ratio. If a new state is not accepted, the process stays in the old state. When my interlocutors ran this computerized process for a sufficiently long period, usually for thousands of generations, the simulation would "travel" over this landscape

and approximate the posterior probability of all possible phylogenetic trees.

In practice, these "runs" were a two-stage process. First, there was a "burn-in" period where the program did a heuristic search to find a starting point for the analysis by throwing away some iterations of the MCMC procedure, for instance, the first 10%. Second, there was a "stationary" period where the program explored the parameter space. After finishing the MCMC-runs, the output would then be imported into software, such as TreeView or Figtree, for further analysis and phylogenetic visualization. Representations of phylogenetic trees, so-called cladograms, have a unique branching structure (a topology), containing information about the proximity of evolutionary relations between the represented entities. These are based on a Principle of Parsimony, where the simpler account is usually preferred. It is also possible to draw the same cladogram using different topologies. While some find it easier to assess the relative branching lengths of phylogenies with rectangular tree formats, the use of radial or curved formats is not uncommon, and the choice of cladogram format greatly depends on the representation's communicative and epistemic function.

A tree branch is conceptualized as a lineage evolving through time, and the nodes (the intersections between lines) represent the birth of a new lineage. In molecular phylogenetics, nodes represent gene or protein families and refer to duplication events or may constitute speciation events in cases where tree diagrams are used to represent species relations. By convention, the roots of trees represent the most recent common ancestor of all the taxa in that tree, the most ancient point in evolutionary time. It is also possible to embed information in phylogenetic trees by other means. A longer branch, for example, implies more genetic change, as measured in terms of nucleotide or amino acid substitutions per site. Usually, my interlocutors would annotate their trees with a legend containing a scale bar and a caption that identified this number. Depending on their use, tree diagrams could also be annotated with color-coding schemes that distinguished sequences in *L. salmonis* from other relevant organisms in the sub-phylum Crustacea (like *Caligus rogercresseyi*), or salient creatures like blood-feeders and model organisms.

Because the information used to guide the analysis deep into evolutionary time comes from genetic sequences in contemporary taxa, there was also considerable uncertainty attached to phylogenies. It is therefore necessary to estimate the confidence that a given cladogram reflects "real" evolutionary relationships, using mathematical tools. This meant that for a given tree, confidence in the respective branches could be represented with percentage values for cases where certainty in the branches was less than a 100%.

Researchers at the Centre also had other resources at their disposal to chart and predict genetic pathways of interesting genes before RNAi experiments, such as KEGG (the Kyoto Encyclopedia of Genes and Genomes, see https://www.genome.jp/kegg/). This tool makes it possible to model gene expression profiles and learn about potential gene targets by creating an interactive graphical wiring diagram, composed of hyperlinked representations, that visualize cascades of gene and protein interactions based on information stored in the KEGG PATHWAY Database. In sum, these representations could be used both as a basis for decision-making about further experimentation, and as supportive materials when disseminating experimental results to the larger scientific community.

Use of sophisticated mathematical tools from molecular phylogenetics instantiate what Humphreys calls "epistemic enhancers" (2004). Just like scientists have expanded their sensory apparatus with microscopes, binoculars, and telescopes, so have they expanded *computability* through the discovery and use of new mathematical relationships for learning about evolutionary linkages between genes across taxa. As bioinformatics faces a "quantity of data issue," or a "data deluge" (Strasser, 2012: 85), sequence comparisons have become a far too complex task to eyeball without sensory augmentation. Such analyzes therefore require "property detectors" that can determine the character of specific sequences and their relationships with each other (Humphreys, 2004: 28). Through computer simulations of evolutionary process using statistical models to handle data that are intractable for individuals with their "bare" minds, bioinformatic tools help biologists to extend the reach of their cognitive powers far back into the deep evolutionary past. This constitutes a form of perceptual enhancement through technology that supplements

mathematical skills with computation in ways that boost their cognitive powers.

Bioinformatic tools also increased the speed by which mathematics could be performed and expanded the complexity of problem-solving at the SLRC. In Humphreys terminology, this was achieved both through an "extrapolation" of senses, similar to how telescopes and microscopes aid perception of what cannot be seen with a naked eye, and through "conversion" between sensory modalities, akin to how a visual display can be attached to a sonar to convert soundwaves into a visual representation. Simple structures of short sequences of nucleotides and amino acids are, in principle, available for manual inspection, but the complex sequences of interest to my interlocutors could only be meaningfully compared with computational support. The results of such numerical comparisons can then be accessed in different representational modalities, and converted into a variety of graphical forms that enhanced legibility and support meaning construction (Humphreys, 2004: 4). Additionally, these bioinformatic systems afford what Humphreys calls "augmentation," since no chemical properties of nucleic or amino acids detected through sequencing methods naturally affect human sense organs without some transformation by technological means.

Like many other kinds of computer simulations, Bayesian analysis and Markov Chain Monte Carlo, were black-boxed and not open to direct inspection and verification by most users at the SLRC. This entailed a degree of "epistemic opacity" (Humphreys, 2004: 148). Such opacity was partly an outcome of the underlying mathematical processes, which required special expertise to be meaningful, and partly a result of the software not presenting its users with transparent information about all the stages of the computational process it performed. Rather, the use of phylogenetic instruments was based on practitioners trusting that there were members in the scientific community at large who possessed the necessary conceptual resources to verify what the apparatus accomplished and were familiar with the underlying mathematical principles and biological theory. Expert computational biologists within the practice community thus afforded non-experts with a set of dispositional beliefs that could be consulted when necessary to solve problems and give meaningful accounts of how these scientific instruments operated.

This "dispositional" function was also filled by a wide range of bioinformatic forums, journal articles, discussion groups, and user manuals on the web.

From the perspective of distributed cognition, the representational outputs of phylogenetic inference, like cladograms, summarized complex information about a dynamical process and afforded users with an inductive framework for drawing inferences beyond available information. Furthermore, phylogenies helped to attenuate reductionist thinking about the contribution of specific genes in biological processes. With respect to basic mechanisms involved in gene expression, Jaques Monod famously quipped that what is true for *E. coli* is also true for the elephant. Phylogenetic analysis helped corroborate where such reductionist logics were judicious or spurious.

Beyond their uses in identifying and selecting relevant target genes in the preparatory phases of RNAi experimentation, phylogenies were also useful to contextualize the functional characteristics of select genes in evolutionary terms, as indicated by the previous examples of Receptor R and Protein P. Phylogenetic accounts were therefore commonly included in journal publications, independently of whether these methods had been decisive for selecting the particular candidate genes characterized through RNAi experiments. But although bioinformatic tools were valuable for identifying relevant genes and key biological processes, it was not possible to simulate their empirical outcomes in salmon lice development in silico. Acquisition of robust knowledge of gene expression patterns, and its impact on the phenotypical development of lice, necessitated benchtop experimentation using RNAi in the wet lab.

Final Preparations

Let us now return to The Checklist. After deciding on a target sequence of interest, either through phylogenetic or other means, lab members are instructed by The Checklist to notify the coordinator for RNAi trials via email to schedule participation in an upcoming experimental event. Having notified the coordinator and provided essential information about the fragment of interest, like sequence data and primer positions,

participants would receive a confirmed slot in the queue. Essential information about the gene target was entered into a shared file containing a schedule for when different fragments were due for testing, which was hosted on a server accessible for all members at the Centre. Such queue systems for coordinating RNAi trials were necessary to fully utilize the finite capacity of the experimental facilities. The capacity of the Centre's single-tank system, for example, was often strained due to ongoing RNAi experiments, testing of feed compounds and vaccine candidates, limited because of wanting experimental animals from the proper life stage, or undergoing maintenance. Since sequence data travels easily in the age of computational biology, information that could point toward potential therapeutic breakthroughs were handled confidentially at this stage, due to the proprietary claims of the Centre's industrial partners.

The Checklist refers to RNAi trials using the injection method as "group experiments" for two reasons. First, they were collective endeavors since data from the experimental control group were usually shared between participants to facilitate statistically sound analyzes and reduce the number of fish and tanks spent on each trial.[7] A consequence of this joint arrangement was that experiments could not be terminated earlier or later than 40 days post-infection, unless there was no need for control animals. The rationale was that gene expression measurements from lice in both the control group and experimental condition had to be developmentally synchronized for the data to be comparable. While pre-adult II females were the default life stage according to protocol, experimentalists could also introduce changes, such as experimenting on male specimens or other life stages, if they had reasons to believe this would yield interesting outputs. Such modifications to procedure, however, required additional planning.

The second sense in which RNAi experiments were group-level performances, was that everyone who had candidate genes at stake in the trial was expected to contribute to its practical execution. Before the day of injection, the Coordinator would plan this in detail, such as the hands-on division of labor among participants who had signed on. According to The Checklist, this workforce should be composed of at least four persons, two to facilitate work in the wet lab, and usually a few post-docs, doctoral candidates, or master students, in addition to a

supervising research scientist. Senior scientists, on the other hand, usually took a more active role in the planning and selection of experimental targets, occasionally submitting interesting gene fragments for testing, and regularly contributing to data analysis after termination of the trial.

At this point in the chain of events, the Coordinator would also place an order to the technicians in LiceLab to ensure that an adequate number of lice at the correct developmental stage was ready for experimentation. Participants with a stake in the trial, also had to order primers from online suppliers and perform double-stranded RNA synthesis on the relevant fragments. These fragments were then diluted with a bromophenol blue solution. This solution, as we shall see in a moment, functioned as a colorant that provided a visual indicator that the RNA had been correctly injected into the parasite body. Furthermore, The Checklist also specified that filter papers had to be prepared in advance, to keep lice properly moist during handling. A seemingly mundane reminder, this matter was epistemically significant, since the parasite could be damaged from dehydration if left unattended on the lab bench for too long. A critical loss of lice caused by undetected dehydration at the stage of injection could wreak havoc on the interpretation of gene expression analysis downstream in the pipeline. Ideally, participants also had to prepare a list of prioritized targets, in case there were insufficient amounts of available lice on injection day. Finally, glass needles for the micro injector had to be pulled and sharpened.[8] The latter task was usually performed by the senior laboratory engineer, who also carried out manual injections at the Centre.

In cognitive terms, all this preparative activity of arranging resources in advance of the experiment are instances of "pre-computations" (Hutchins, 1995: 165). In the context of experimentation, pre-computations transform the nature of epistemic tasks and activities, as the performance of actions in the past redistribute workload across future events. In this case, pre-computations fundamentally change the informational environment of experimentalists by setting up novel structure in their task environments ahead, that help them perform time-sensitive tasks. By carrying out essential calculations and projections in advance, and embodying the outputs of these in representational artifacts, experimentalists can solve certain epistemic tasks using only simple perceptual

inferences and manipulations of material structure during the actual time-limited execution of the RNAi trial. Pre-computations thereby transform the experimental environment by capturing invariant properties pertaining to its design and activity-structure in physical artifacts, including representations of procedures, and arrangement of resources in physical space. The basic set-up in different experiments, for example, ought to vary as little as possible between different trials to produce reliable results, and experimentalists secured comparability of outcomes by managing instruments and ingredients in advance. With Hutchins, we can see these pre-computations as a window onto experimental practice as an extensive cultural process (1995: 168). In this case, a cumulative, material culture that has collected a plethora of representational modalities to help practitioners solve frequently encountered problems in a functional environment for knowledge-making (Fig. 5.1).

Injection day

The most conspicuous event spelled out in The Checklist is the "day of injection." Here, participants in the RNAi experiment are instructed to arrive in the lab early in the morning, since the procedure requires an entire workday to complete. Let us now look closely at an ethnographic vignette from an RNAi event at the Sea Lice Research Centre to understand how interactions between material, social, and cognitive resources for executing the experiment were managed.

Standing with our backs toward the entrance in a wet lab at the Institute of Marine Research, we are facing a narrow, brightly lit room that is tailored for the task at hand. There is a workstation to the left filled with various technical equipment: forceps, petri dishes, plastic bottles and containers in odd shapes and sizes, stacked boxes with disposable gloves, a wash station, and an under-the-counter dishwasher. A heavy, red plastic curtain bundled together with a piece of rope, divides the room in two. It marks off a separate "clean-space" for microscopy, computer work, and other delicate benchtop operations, like the micro-injections that will soon take place. On the right side, midway along the wall, is a door leading into a larger room, filled with rows of single-fish tanks

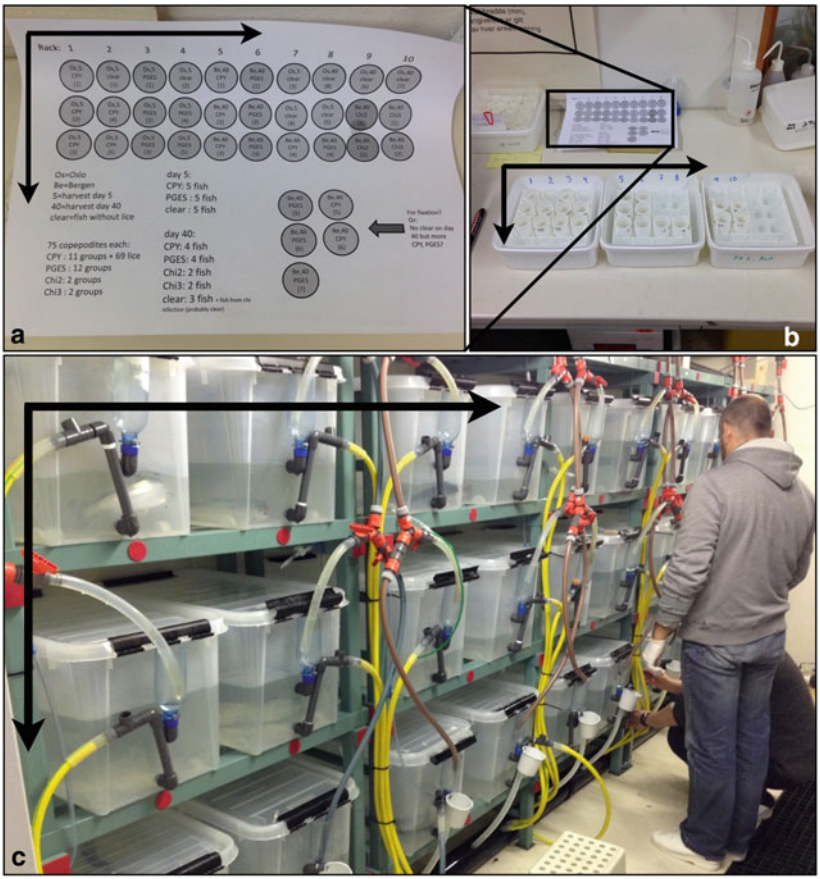

Fig. 5.1 Pre-computations in an RNAi trial. **a** Spreadsheets highlight the stabilizing role of pre-computations. Template and physical array of hatching wells **b** and single tanks **c** are set up in advance, providing mutually supporting structure to maintain order in biological materials and stabilizes enacted representations. "Trajector-based" cultural practices, and ecological assemblies, figure prominently (see Chapter 6). This experiment was executed in LiceLab in November 2013, in collaboration with an Oslo-based Work Package to study gene expression in interactions between salmon hosts and the parasite. One group analyzed gene expression data from lice, the other focused on the salmonid immune response. Genes relevant for the former are labelled BE, while those of interest for the latter are labelled OS. Each column represents an experimental condition. Top row, corresponding to tanks in rack 2, 4, 7, 8, 9, and 10 are labelled "clear" (fish without lice). CPY refers to the control fragment (see Chapter 6 for details)

stacked in columns containing juvenile salmon. The single-tank array inside this room is almost identical to the one we encountered earlier, in the basement wet lab at the High-technology Centre. The similarities between the two configurations are not coincidental. After all, this wet lab was designed and assembled by the same people now responsible for managing the wet lab at the University, during their previous tenure at the Institute. Now, the wet lab was tended by another group of technicians, who had inherited this habitat, adding their own modifications and routines to it. On this morning, the team responsible for injecting lice with double-stranded RNA and reinfecting fish included:

- Ada, a chief technician with extensive experience with RNAi trials. In the words of one PhD candidate she "knows everything" about the lab.
- Veronica, a doctoral student working on fibronectin type II-domains.
- Lena, a postdoctoral candidate working on aspects of the chemosensory system of salmon lice.
- Sara, Veronica's supervisor and one of the scientists who were instrumental in adapting RNAi technology for salmon lice. Sara coordinates the large-scale RNAi trials at the SLRC.
- Robert, the engineer responsible for the wet lab, and two other technicians who will tend the fish.
- The ethnographer.

The first task on the agenda was to tranquillize the salmon and carefully collect the pre-adult salmon lice using forceps. Afterward, the lice would be injected with synthetic, double-stranded RNA using a manual microinjector, upon which the modified specimens would be left to incubate, and then reinfected to new salmon hosts. On this day, Sara had a busy schedule, and had to supervise the experimental processes from her office on a different floor in the building, intermittently dropping by the wet lab to see how things were progressing. Accomplishing all the necessary tasks for a successful trial demanded a complex coordination of both people and things, so Sara had assigned specific duties to everyone upon convening in the lab. Additionally, participants were expected to assist with any time-limited tasks that arose from the activity stream.

At first, some of the participants were unsure about their designated role within the experimental choreography. But it did not take more than a few minutes before the group had distributed responsibilities underspecified by the Coordinator's instructions and settled into a pace that moved the work forward. As the researchers were busy preparing the wet lab for injections, Robert and two other technicians worked outside the main building in the December cold. Here, they harvested lice from the large salmons that were housed in the communal fish tanks occupying the Institute's courtyard. Geared up with headlights, gloves, and insulated boiler suits, the outdoor team used forceps to delicately remove salmon lice from sedated fish and aligned them in a 5 by 2 grid, on a moist wet paper in plastic petri-dishes. Each dish contained 10 females and 10 male pre-adult lice, which were then carried by a runner (and occasionally the ethnographer) to the team inside the building, who were responsible for organizing the actual injections.

Picking lice is a delicate, and by no means trivial, step in the execution of RNAi injections. As The Checklist underscores, mismanaging this step could have epistemic consequences: "Be careful when you handle the animals, avoid pulling or poking the genital segment and the abdomen. Make sure that the forceps you are using is in good shape. This can be time consuming if you are inexperienced, but remember that the lice prefer the environment to be cold and wet." Both fish and lice are fragile, and injuries on the experimental organisms at this stage could potentially introduce noise to data procured from the system, thereby threatening the veracity of subsequent analyzes. Although such knowledge was seldomly made explicit in external communications about experimental results, Kohler reminds us that craft skills of this kind have been essential to progress in the history of experimental biology (1994).

Microinjections

When the lice pickers in the courtyard outside had sampled ten pre-adult lice and arranged them on a wet paper placed in a Petri dish, this batch was swiftly brought inside to the benchtop where Ada sat in front of the stereomicroscope, ready to inject the specimens. To accomplish this task, the chief technician applied a micro-injector, driven pneumatically by manually controlling a mouthpiece. This exemplify what Hacking calls a "source of modification" (1992: 46), the part of the apparatus that actually interferes with the epistemic target. As such, the research group had made considerable efforts to fine-tune the injection technique, which had been a bottleneck for delivering double-stranded RNA to silence genes in lice.

Normally, an average of thirty lice were injected per gene fragment. The mouthpiece itself was connected to a plastic tube, approximately one meter long, which was casually slung across the technician's upper back to keep it out of the way from her dexterous hands as they worked swiftly in concert to expedite the parasite, one by one. To use the injector, the mouthpiece was first inserted between the lips, while the glass needle was held in the main hand. Then, a small amount of synthetic, double-stranded RNA, tailored to the genetic sequence of interest, was drawn into the needle from a test tube with the help of capillary action. At this point, the other hand introduced the forceps and positioned the louse specimen on the Petri dish below the stereomicroscope's objective, while gently keeping the animal steady. Looking through the eyepiece, the glass needle was then carefully guided toward the cuticle of the dorsal region, and once positioned there, aligned with a distinct location on the parasite's back, where the exoskeleton forms a natural segment which conveniently afforded insertion of the glass needle. Squinting through the ocular lens, the injector had to carefully guide the glass needle into the segmented area and insert it below the cuticle plate, while holding the lice steady. With the needle "in place," a verdict based on proprioceptive feedback from the tissue and visible confirmation from the stereomicroscope, the experimenter would then gently blow into the mouthpiece, pushing the solution of dsRNA and colorant into the organism.

As explained by Ada, this was the tricky part, since the fluid's viscosity was not homogenous and could therefore clot the thin needle. Blowing too hard could result in too much fluid being injected into the parasite, which not only made a mess, but could potentially kill it. On the other hand, if air was pushed through the tube too cautiously, the technician might fail to introduce sufficient double-stranded RNA into the parasite, and thus fail to get the desired interference response. Meanwhile, there was also a constant risk of crushing the specimen with the forceps, skewering it on the glass needle, or otherwise damaging it through careless handling. Participants therefore ensured that they did not disturb Ada's delicate work. After being dispatched in the animal, the bromophenol blue staining would yield instant visual feedback that the RNA was properly injected. If the colorant started bleeding excessively this could indicate that the procedure had missed its target and damaged the specimen.

To the extent that it was practically feasible, Ada conducted all injections for RNAi trials at the Centre. When I asked why this was so, her colleagues emphasized her dexterousness and experience, recognizing that she had simply acquired more tacit knowledge about the procedure than the others in the group. Additionally, there was an epistemic motivation for why she performed the job. I was told that, methodologically speaking, it was preferable that the same individual who injected the control fragments was also the one responsible for injecting fragments across experimental conditions. Since every member of the laboratory was assumed to hold idiosyncratic mannerisms that could influence the execution of injections and impact the experimental outcomes. It was better if one, reliable colleague conducted the injections, thereby minimizing variations within and across experiments to the largest extent possible.[9] This set up a positive feedback cycle, as Ada acquired more experience and proficiency with the task than others at the Centre. The drawback was that expertise in a crucial skill for the experimental system was concentrated in one highly entrained individual, as other lab members would require much training to accomplish the procedure as reliably and proficiently as Ada.

At this stage, it was crucial that researchers duly kept track of their samples, along with any inscriptions that were to accompany these

further down the experimental pipeline. For example, on the bench next to where Ada performed her injections, several square plastic containers were organized in a grid on the counter, next to a stack of additional wet papers. After each batch of lice were injected, the wet papers were then picked up by another participant and transferred to a plastic container filled with seawater, which carried a small note inscribed with the specific fragment number that had been injected into the lice, before it was left to incubate for several hours. In all caps, The Checklist reminded participants about the gravity of keeping track of representations as they propagated throughout the experimental system: "IT IS ESSENTIAL TO KEEP TRACK OF WHICH LICE GOES IN WHICH INCUBATOR, LABEL CLEARLY WITH FRAGMENT NAME." This simple act of marking significant content with inscriptions stabilized the relation between thoughts, acts, and manufactures. Following this pattern, injections would usually continue until all fragments were expedited, so that when the group started working around 8:30 in the morning, they could have their lunch around noon. The lice would then be left to recover for three hours. Specimens had to be well-rested so that the parasite could again latch onto a host fish during reinfections (Fig. 5.2).

Reinfection

After lunch, the group reconvened in the wet lab to place the RNA-treated lice back onto new salmon specimens. These fish first had to be anesthetized by the technician, which presented yet another bottleneck. As with lice, the fish had to be carefully handled to ensure adequate experimental results. Over time, the Centre had acquired routines for optimizing the drug combination and dosage time used for anaesthetization.[10] If the fish spent too little time in the sedative solution it would flap around violently, and its handlers could injure the fish, or themselves, on forceps and other sharp equipment. Too much anesthetic, on the other hand, could kill the prized experimental fish.

While fish were prepared in the adjacent single-tank storage facility, the scientists got busy collecting individual lice from the plastic hatching

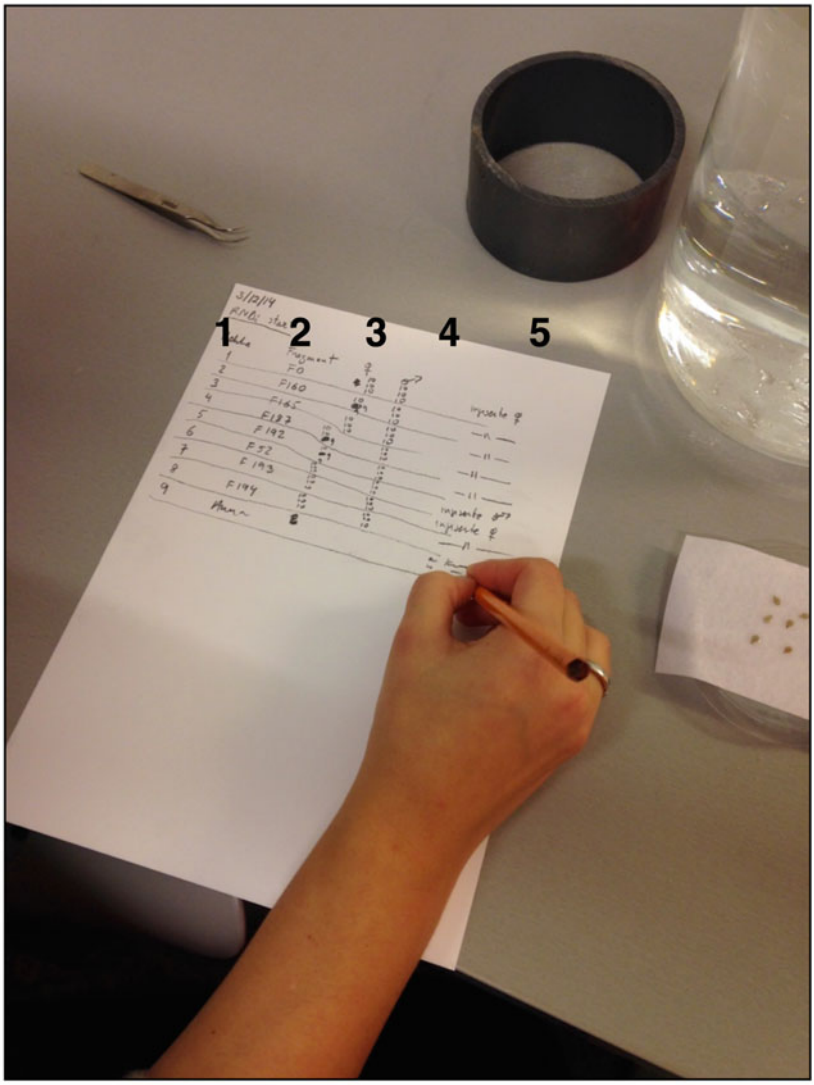

Fig. 5.2 Tracking experimentally modified salmon lice and RNA fragments. **1** Leftmost column contains the single-tank racks from 1 to 9. **2** The next column holds the fragment names. A running number (Fxxx) refers to a list of screened candidates. Column **3** and **4** lists the number of male and female lice for each fish. **5** Lists the sex of salmon lice injected with RNAi

wells they had been placed inside before lunch. Carefully, each louse was positioned on its back on a square piece of paper, using forceps or a gloved finger. The fish was then placed on the paper, which was labelled with a fragment number. Alternatively, the paper was aligned across the fish skin, and then gently pressed against it. The theory behind this maneuver was that the parasite would engage its chemo- and mechanosensory apparatus when coming into proximity with the salmon and then latch on to the skin. Lice are attached to salmon via a frontal filament during the chalimus stage, but at the mobile stages the parasite uses its smaller extremities and gains help from a body plan evolved to keep it tightly attached onto the surface of a swimming host. The wet paper was then removed, and the fish carefully reinserted in one of the single tanks. Single-tank arrays were designed so that three fish tanks in each experimental condition formed a stacked column, with each column sharing the same water supply and outlet, thereby marking of a separate experimental group. Information about the exact fragment that had been injected into the lice on a given salmon, as well as the coordinates of its tank (a letter/number combination) were then logged on a piece of paper which was subsequently plotted into an Excel spreadsheet. These routines, and the symbolic conventions that governed the experimental ingredients, were in continuous development to improve the system's determinacy and stability.[11] When all the fish had been infected and returned to their tanks, it was time to tidy up the lab, and clean the workbenches. It would take more than forty days before the outcome of this material remaking of the world could be revealed.

Running the Experiment

Clearly, RNAi screenings were concerned with more than the mere transformation of biological structures, as these epistemic events also created, propagated, and transformed representations through a variety of media, thereby setting up vital relations that supported the cognitive life of things in the laboratory.

As The Checklist instructs: "for each experiment there will be an Excel-sheet that need to be filled out for every sample taken during and at

termination of experiment." Every RNAi screen conducted at the Centre was linked to a running number, and individual samples were given a unique code in the order which the samples were taken. This information was then integrated in a digital spreadsheet that converted every sample into a trackable representation of salient events within the experimental system. These encodings provided a collective, external memory of how the phenomenal objects of interest moved through the pipeline of the experimental system. They also afforded a simple way to transform the representational states of each experimental event, as it moved through various *in vivo, in vitro*, and even in silico systems for handling biological data. For the latter purpose, "The RNAi Experiment Annotation Checklist" specified in detail the correct procedure for curating experiments in LiceBase, outlining two sub-checklists. The first was to be completed when an RNAi experiment was initiated, and included a free text summary, a general entry on metadata such as the Batch ID, date and contact information, as well as a description of the sample, the gene target, and the RNAi fragment. The second sub-list was to be followed when the experiment was terminated and included information about the efficacy of gene silencing, detailed accounts of the resulting phenotype, and relevant image files.

Scientists tracked the progression of their RNAi experiments during the prescribed forty-day period by visually inspecting lice in the tanks, as they were attached to the fish. During this phase, they would look for signs suggestive of whether there was a silencing response working on the targeted genes in the organism. But there was no general rule that articulated what they ought to look for. As The Checklist underscored: "The level of monitoring that you will perform from now on until termination of the experiments depend on YOUR experiment." The kind of observations that were relevant was contingent on the genetic pathway and the biological phenomenon under study. Delayed maturation, for example, could indicate a strong interference response in cases when RNAi aimed to silence genes related to developmental processes or reproductive functions. A critical lice loss in the post-infection period was another indication of an effective RNAi knockdown, but whether this was signal, or noise, was circumstantial. The Checklist specified: "We normally see an unspecific loss of lice, the first couple of days. These

are probably lice dying from handling damages. After that we have to consider mortality as a possible effect of the knock down." Instances of "unspecific lice loss," had an ambiguous epistemic status, and it was difficult to attribute the direct causes of such observations. RNAi-treated lice, for instance, could sometimes vanish into the water drain without trace. This latter problem could partly be mitigated by placing small nets on the outlet, but since biological debris like fish feed and mucus accumulated on the filters, they needed frequent inspection. On other occasions, free-floating parasites were eaten by their host. Poor infection rates by lice on the fish could also be a consequence of rough handling during the injection phase, and intermittently there were disconcerting interactions between the salmon and their tank environment, such as rubbing against the plastic walls. All these events could produce unspecific losses, so despite concerns over experimental control being a key motivating factor behind the move from collective fish tanks to the novel single-tank system, it was next to impossible to eliminate every potential confound when studying host–parasite interactions.

Termination

According to The Checklist, RNAi experiments are usually terminated after 40 days, which ensure that a second generation of egg-strings have developed on the female specimens. The main agenda for termination-events was the removal of lice and egg-strings from the fish hosts (both experimentally treated parasites, as well as the control group), and preparations of lice tissue for the physical, biochemical, and representational transformations that followed. In the end, these transformations would result in measurements of gene expression. By integrating such informational structures, scientists created meaningful accounts of the molecular characteristics of gene function, revealing new clues about potential therapeutic applications.

Like in the injection phase, the termination and handling of biological materials from RNAi-treated salmon lice, required participants to carry out a variety of new pre-computations. The Checklist instructed experimentalists to prepare stereomicroscopes and cameras, and to add

chemicals to small plastic test tubes that preserved lice for both tissue-sectioning and gene expression analysis. Preserving samples that would undergo anatomical study using the microscope or other imaging techniques, was achieved with "Karnovsky's Fix." A fixative substance is made up of molecules that easily form cross-linkages with biological targets, enabling the preservation of whole tissues.[12] Other tubes were filled with a substance known as "RNAlater." While Karnovsky's preserve whole pieces of tissue for visual inspection, RNAlater is a storage agent that conserves fragile RNA for molecular analysis.[13] Without RNAlater, the scientists would have to immediately process their samples, or freeze them in liquid nitrogen, which would entail a cumbersome process of grounding and homogenization, with constant risk of thawing the precious tissues and thereby compromising the valuable information carried by its molecular configuration. By placing samples in RNAlater, these could instead be stored for a month or longer, in the refrigerator or long-term at below minus 20°C, until there was time to transform and analyze the material, beginning with a biochemical procedure known as "RNA-extraction." In the next chapter, we learn how such materials are handled by scientists downstream, in order to learn more about gene expression profiles of experimental candidates.

Among the final preparations before the day of termination was a mundane, but critical, task that involved printing out a series of sticker tags. These labels carried the date of the experiment, its name, and sample IDs. Stickers were then placed on the tubes containing Karnovsky's and RNAlater. They could also be attached to paper sheets with inscriptions about what was to be observed. By attaching these on the hatching incubators used to rear the new egg-strings, it was possible to track the contents through further processing. A hatching sheet for logging lice numbers was also printed out beforehand, to afford easy inscriptions of relevant details about biological phenomena that materialized during the termination event.

Let us now approach an instance of RNAi termination and look closer at how representations are enacted through the experimental pipeline. By zooming in on minutiae in a video-recorded sample from one such event, we can better grasp the iterative material engagement and socially distributed cognition that sustain "contexts of discovery," and how these

become epistemically important for the generation and justification of experimental knowledge (Schickore & Steinle, 2006).

We are back in the same wet lab from our earlier visit. In this new scene, there are five individuals at work, busily preparing various technical equipment, documents, and biological samples. This time the participants include:

- Sara, the Center's RNAi coordinator.
- Hanna, who is a postdoctoral candidate at the SLRC.
- Greta, an exchange student from a German technical school with a laboratory internship.
- Robert, the wet lab engineer responsible for handling the fish.
- The ethnographer, who again observes and awkwardly participates by helping with simple tasks.

As with the initiation event described before, participation in the termination phase usually occurred on a rotational basis. A limited number of fragments were tested in each trial, and although not everyone who had a candidate fragment at stake in the experiment had to be present, it was expected that some of the graduate students and postdoctoral candidates volunteered to participate.

The main tasks during the termination were delicately removing the experimentally modified salmon lice from the fish (along with any control specimens), registering salient information, photographing each phenotype, tissue preservation for RNA analysis, and sampling lice on fixative for morphological analysis. As a regulatory representation, The Checklist specified a "cultural script" for how this activity should done within the experimental system (Shore, 1995; D'Andrade, 1995). This asserts a set of shared epistemic norms and values circulating in the community. But in addition to any conventions laid down by The Checklist, Sara also provided multiple instructions on the fly, further specifying who should do what, where, when, and in what form. So, while the written script offered a general plan for how the group could organize their experiment well, it was also necessary with additional micromanagement. These instructions pertained to a range of different ecological conditions to ensure the production of high-quality data, such

as the level of experience among the participants, the size of the experiment, and any unforeseen circumstances that might occur. Furthermore, several parts of the activity system remained underdetermined by both The Checklist and Sara's instructions. This meant that certain aspects of the situated action that were not covered by the plans for the termination event had to be determined on the spot, depending on unpredictable contingencies specific to the epistemic situation (Suchman, 2007). These episodes demanded that the experimental actors aligned their resources in novel ways to address the fleeting problems at hand. As the activity unfolded, the global script of the event even faded into the background, as every member of the team came to act only when certain environmental conditions were fulfilled.

Compared with the experiment's initiation phase, termination events required more coordinated work to be performed, and these activities were also more diverse. The nature of cognitive work during such interactions can usefully be understood as "sequentially constrained," to adopt Hutchins' vocabulary (1995: 198). We can say that a task within an activity system is sequentially constrained "if the execution of any enabled operation will disable any other enabled but as yet unexecuted operation." Whether actions are sequentially constrained or unconstrained, depends on both the formal properties of the action structure, it's execution, and how it is represented. Sequentially constrained actions often require hierarchical coordination between different subtasks, although they may, on occasion, also be improvised. In contrast, sequentially unconstrained actions require only loose connections and communications between the involved actors. Let us now see how this occurred in practice to support data production.

At the onset, Sara is seated by the stereomicroscope. Hanna is busy labelling test tubes together with Greta, using preprinted stickers that Ada prepared in advance with a special printer. Hanna and Greta are tagging two different kinds of tubes: Karnovsky's tubes are for tissues that require sectioning, and RNAlater tubes are for RNA extraction. Each tube is given a running number and labeled as either "FIX" or "RNAlater.[14]" A Styrofoam box with crushed ice keeps the tubes temporarily refrigerated on the workbench. Again, we see epistemic pre-configurations of the environment.

Just before the main action is about to start Sara, as the senior authority, explains in English the logic of what is going to happen next. She switches to English due to the presence of Greta, a German lab intern. Here is a simplified transcript:

Sara: Ok, so the idea is that Robert [the wetlab technician in the adjacent room] takes the fish out of the tank and he picks off the lice. And he will put them on a Petri dish and line them up. And one person then brings them in to the people sitting at the microscope. So, there would be one who can take it [points to the microscope], and one person pretty much sits and takes pictures. And the egg-strings have to go into the hatching [wells], and it has one person sit and note everything in Excel-sheets; how many females, and which females are going on RNAlater, and which females are going on to fix.

Ms: How do you decide which goes to fix and which goes to RNAlater?

Sara: As a default there is one animal per tank that goes to fix, but you have to look a bit at them. Like, if there is, if all look the same and there's one that's normal you don't put that on fix, and if there are very few animals, you have to have at least five animals on RNAlater. Cause you cannot do qPCR if there is less than five. So, in that case, we take less on fix. So, it's quite, yeah. There's sort of full-time, one person going to take the pictures and egg-strings off, and one full-time person doing the Excel. And then, maybe Hanna, you do the Excel, and I'll take the pictures. And Greta and you [points to the ethnographer] go back and forth [carrying lice]. And, yeah [goes on to talk to the technician picking lice of the salmon in the adjacent room].

Having communicated her expectations for appropriate future states of the experimental system, Sara went over to the bench and configured the microscope-mounted camera. In the following activity, she would be concerned with three epistemic tasks. The first was to visually inspect the salmon lice and carefully remove the egg-strings with forceps. There is a significant skill component involved in this task. Mature egg-strings,

brownish in appearance, are relatively easy to separate from the genital segment of gravid lice with a gentle pull. But the opaque and fresh egg-strings require more force to separate and can easily be crushed with the forceps. After separation, the egg-strings were to be placed in a hatching well, while the salmon louse is scrutinized for abnormal phenotypical traits resulting from gene silencing. Additionally, Sara must decide for each group whether a sampled tissue should go on FIX or RNAlater for processing.

As Sara made her final preparations, Hanna and Greta marked up the remaining tubes with running numbers. Hanna explains that her task is to log the number of lice, their sex, and the fragment number. She recalls that the last time she participated in this phase of an RNAi experiment, she sat by the microscope while another researcher performed the Excel logging. Then, before the cataloguing begins, Hanna, Greta, and Sara take another moment to coordinate a few last-minute details surrounding the order of work and tasks to be performed. Since this is the first time Hanna registers information in the spreadsheet, she worries about committing errors that may negatively affect the outcome of this collective work. Among the things she is hesitant about is whether each male and female louse is supposed to have a dedicated row in the spreadsheet, or whether they all go in the same one. When Sara starts to pick lice, Hanna should ideally have set up her spreadsheet with an adequate system of inscriptions so that she can quickly enter the relevant information into the cells. But she is unsure about the best way to organize and label the columns and rows. Sara calms Hanna's reservations by assuring her that they will start slowly (Fig. 5.3).

Robert intervenes to inform that one fish has unfortunately died during the experimental run. Since the lice specimens attached to this fish have perished, they can only harvest lice from 23 fish. One of the main challenges for Robert in the coming hours, will be to monitor the anaesthetization of each individual. He must carefully monitor the life signs of each fish by taking observations of its respiratory function. Ideally, it should be sedated for 90 s, which is roughly the time it takes to harvest lice from the proceeding fish. Since the parasite has now matured to the adult life stage, and is perceptually salient, picking them is relatively easy. Originally, the fish was infected with ten pre-adult females

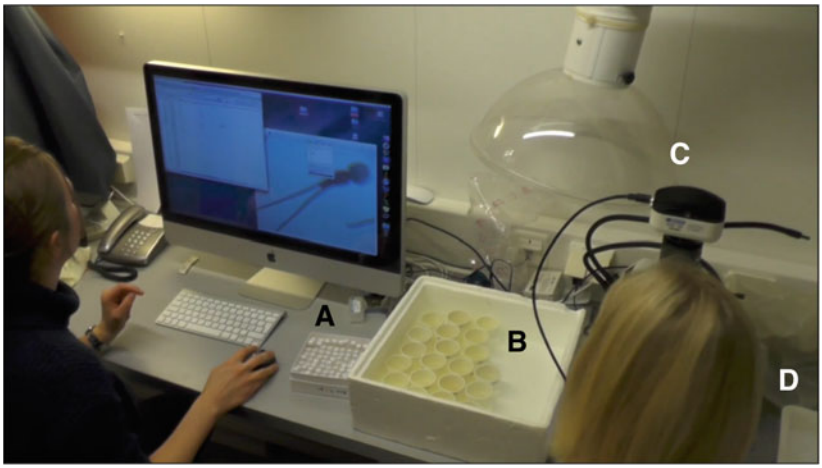

Fig. 5.3 Hanna is seated on the left; Sara sits on the right. The intern who delivers specimens from the technician in the adjacent room enters with fresh specimens from the left (not visible in image). Items on the workspace from left to right are: **A** Box with labelled test tubes with running numbers for fixative which is added under a fume hood later **B** Hatching wells immersed in seawater for the egg-strings. **C** Microscope mount with camera and Petri dish containing lice array. **D** Styrofoam box with ice for tubes containing RNAlater (partly visible white container in lower right corner)

and males. He explains that there are normally five to six lice remaining per fish based on experience, and roughly an even number of males and females. Each single tank has been fitted with a filter in the water outlet, so they can keep track of any lice that have fallen off.

As the harvesting begins, Hanna again expresses concerns about the organization of her task space, and how her activities should fit into the overall flow of action. Adding to the challenge, she also experiences problems with pre-formatting the cells in the Excel document. The lab computer is an Apple iMac, and she usually works on a Windows PC. "I hate Excel!" she frustratingly exclaims at one point, as she uses an unfamiliar keyboard shortcut to prepare the spreadsheet, entering identical dates into a set of columns.

Standing next to the workbench, Sara then gives an instruction to Hanna that they will first receive batches of lice from Rack 1, which contains the control fragment. She explains that each subsequent rack

containing three fish, will have lice injected with the same fragment. This introduces expected regularities, an ebb, and flow of activity. She will later notify Hanna about which fragment is being handled each time Hanna is supposed to enter information into the spreadsheet. The characteristics of each female lice are supposed to be inscribed on a separate row, while information about males is added separately. Generally, male specimens are not converted into critical data, and are regularly discarded at the end. Sara explains that the main function of the male count in this experiment, is to confirm that there were male lice around to impregnate the females. If there are no males present, they must make a small note, in case the female does not develop any egg-strings. Absence of egg-strings may either be explained by lack of mating partners, or by the efficacy of RNA interference. Occasionally, there are situations when males are examined more closely to get comparative data on gene expression and function. One example is research on regulatory differences in gene expression between males and females at various life stages, which offer insights about genes involved in reproduction.

After finalizing the preparations, Hanna and Sara receive their first batch of lice from the intern, who hands them over from the technician. Robert is now busily at work in the adjacent wet lab, anesthetizing fish, picking lice, and arranging them on the Petri dishes, carefully marking each dish with the rack number (for instance 2B), and the number of specimens from each sex next to a small Mars and Venus pictogram. By the bench, Sara reads out the relevant variables for each dish to Hanna, who inputs this information into the computer. When she receives a batch of lice from Greta, Sara calls out the rack/tank number (for instance, "three C"), as well as the numbers of males and females on the dish ("three females, one male"). She also adds additional information, such as: "the first goes onto fix!"

Intermittently, Hanna repeats the values called up by Sara. This serves two purposes. It provides Sara with a chance to correct Hanna if she has misinterpreted Sara's commands. Also, it helps Hanna form a more stable representation of the information that she is entering in the spreadsheet. This way, shadow talk works as a guide to epistemic action. Note also that this verbal interaction is not specified in any instruction and emerges on the spot, generated from the dynamics of the activity. Finally, Sara calls

out the number on the hatching well, where she will put the egg-strings for later studies of fecundity, so that Hanna can inscribe this information into the spreadsheet as well.

During this process, a picture is taken of each louse specimen from the dorsal perspective, looking top-down onto its backside.[15] Since the camera is operated via the computer, this task sequentially constrains Sara and Hanna's actions even further. Before the photo can be taken, Sara must first signal to Hanna that the louse is in focus, exclaiming "der!" ("there"). Upon hearing Sara's signal, Hanna then shoots a picture using the microscope-mounted camera, which is operated by the computer through the keyboard and a mouse. She then saves the picture in a folder dedicated to this unique experiment. The file is inscribed with the running number, and each louse specimen is then placed in tubes that also have been labelled with this same running number. Note here that Sara has access to their joint domain of scrutiny both via the computer screen and the ocular, while Hanna can only access the information on the screen and observe Sara's behavior. She cannot interact directly with the specimens. Sara's commands therefore provide directions for action that both captures salient features of the world, as Hanna makes a written representation in the spreadsheet, and transitions the experimental system into a new state. These utterances are "status reports" (Hazlehurst et al., 2007: 547), that intermittently create shared understandings of the current state of the distributed cognitive system of RNAi termination. Each report also sets up expectations for specific epistemic actions to follow.

Specimens were subsequently placed either on fix, or on RNAlater, and numbered in the order they were collected. This number corresponded to the number on the fish tank from which the lice was harvested. Egg-strings were placed in hatching wells numbered with a letter (designating a set) and a number (an exemplar within the set). This way the maternal identity of the egg-strings became linked to the incubator identity in the spreadsheet (for instance: "egg strings from specimen RN17, goes into hatching well A19").

As specified by The Checklist, the first louse from each tank would be placed on fix, while the remaining lice went into RNAlater (if the experiment produced more than five animals for RNAlater, it was okay to

put one more on fixative). Sara observed that while this was convenient, this pattern was not without epistemic risks, since it could introduce a slight chance of systematic bias into the data. The rule of putting the first specimen on fix would be fine, had it not been for the fact that pickers tended to be slightly biased, and therefore pick out the largest and most visible females from the Petri dish first. They could therefore, in the worst-case scenario, introduce a systematic sampling bias into the experiment that skewed later analyzes of the lice placed on fix. Vigilance about such factors was a consequence of deep familiarity with the experimental system and its biography.

Each movement of specimens and samples between containers was followed by an inscription entered on the spreadsheet. The spreadsheet would subsequently act as another coordination device within the experimental system. It connected a series of inscriptions with specimens on fixative and RNAlater, egg-strings in hatching wells, photographs of experimentally modified lice, and metadata associated with these photos. Deploying Hacking's terminology, we can say that these inscribed "marks" form a critical linkage between the constituent, biological epistemic things that make up the experiment, and the subsequent processing of "data" (1992). With reference to this taxonomy of self-vindicating elements in the lab, the human agent makes decisions and acts as a kind of "data generator", by productively transforming representations of one kind into a different kind. Downstream in the experiment, the various materials being handled, such as lice on FIX and RNAlater, and the egg-strings, will again encounter many other types of data-generators, of both the human and nonhuman variety.

From the perspective of distributed cognition, it is also interesting to observe that the flow of collaborative work on several occasions went out of sync during the operation, but it was also repaired without a plan. Intersubjectivity between the participants required the mutual fulfilment of expectations, but it was sometimes challenging for Hanna to predict what would happen next. Hanna had only partial access to Sara's task domain. Sara could freely inspect both the monitor, the microscope, and had a wealth of available information from her tacit interactions with the specimens at hand. But Hanna was only privy to information about pending actions from the computer monitor and the emergent structure

afforded by Sara's actions, without disrupting her workflow. This asymmetry necessitated intermittent creation of shared understandings and alignments about the current state of the system, particularly by using talk as a coordination device for joint action. On one occasion, Sara asked Hanna whether she had recorded whether they had harvested one or two egg-strings per female lice. When Hanna confirmed that she had not kept track of this information, Sara reassured her that it nonetheless mattered little. The number of egg-strings could instead be read directly off from the digital pictures stored on the computer. There was, fortunately, unplanned redundancies in the system that ensured that a slip-up only negligibly disrupted the downstream informational environment.

Photographing the specimens presented another coordination problem. Pictures of gross salmon lice morphology serves as the first traces of interesting phenotypical changes arising from RNAi exposure. But on several occasions in the sequence above, the egg-strings were simply too long to capture within the camera frame. It was therefore necessary to take two pictures, with an intermittent realignment of the specimens in-between, to satisfactorily document the whole animal. On other occasions, undesired processing anomalies known as artifacts, appeared on the pictures, potentially complicating interpretative work. At one point in the sequence, Sara notified her colleagues that something was wrong with one of the specimens they were working on. She signaled for the group to examine the monitor, then scrutinized the scene for a moment and reported that there were in fact two individuals in the image. It was soon evident for all that a male louse and female louse were mating under the microscope. On yet another occasion, the intern noticed that there was more than one pair of egg-strings in some of the hatching wells. It turned out that remains of old, dried-out egg-strings could be found in several wells. This called for additional problem-solving. Robert was duly notified to double-check the remaining hatching wells and make sure there were no old egg-strings mixed up with the fresh ones, as this could complicate analysis later in the pipeline.

From the distributed perspective, complex multi-agent activities like RNAi experiments are bound to face minor deviations that swiftly demand identification of problems and corrections of action (Hazlehurst

et al., 2007: 547). We can see "alert notifications," like those presented by the agents to each other, as stemming from events that caused a "perceived deviation" from the desired system state. But despite minor setbacks, the team was able to create updated and joint understandings of their shared problem-space, and quickly realign their practices. The meaning of these epistemic events emerged both from the affordances given by pre-configurations of the task scape, and emergent structures of interaction between the agents, such as the bootstrapping process by which Hanna corrected and caught up with Sara's instructions for what to do with the inputs to the spreadsheet. Interactions between these elements of the experimental system thereby offered new constellations of cognitive resources, that helped to order, propagate and transform the representational and biological outputs of the RNAi experiment.

Wrapping up

Just before the session ended, after approximately one hour and forty-five minutes, Sara instructed Hanna to shoot a blank picture with the camera and save the final picture in the folder with the other images, labelling the file as a "scale bar." This image file would contain information about the shutter speed, magnification, and importantly, information about the camera's pixel size (in μm), three variables which remained identical in all the photos taken during the session.

For photomicrographs of biological phenomena to be legible and meaningful for scientists, in article manuscripts, for example, the community needs to know how large the structures on the photos are. This is achieved by placing a small scale bar in the corner of the image, with a caption describing what length the scale bar represents (for instance "30 μm," "30 microns"). Getting the scale bar right, however, requires awareness of a concept known as "binning." This is a computational procedure that facilitates compression of data by combining a cluster of pixels into a single unit. Electronic sensor systems, such as digital cameras, have a signal-to-noise ratio, which says something about its performance. In unbinned images, each pixel has a certain amount of "read noise," with each pixel being read separately in an individual

"read-noise event." Sensor sensitivity in such imaging systems is partly a function of pixel size; larger pixels allows capturing more light. The drawback to unbinned images is that they take up a lot of hard drive space. However, by setting the image at 2 × 2 binning there is a compression of data, so that an array of 4 pixels get merged into one super pixel. When data such as digital photos are abundant, smaller pictures are beneficial because they are faster to process and take up less storage space. Sara explained that she preferred 2 × 2 binning, as a good trade-off between size and image quality. This time, however, she chose "bin 1" for reasons that were undisclosed.

While the scale bar and knowledge about binning may seem trivial, these settings are of epistemic importance, and play a role in propagation of representational states from the experimental system to the larger scientific community. Since image processing software depend on known pixel sizes and binning to calculate correct sizes of photographed objects, the degree of binning must be known to set parameters correctly and make the readings meaningful. The simple scale bar shows that even epistemic enhancers like photomicrographs, which extend human senses through augmenting sense modalities, require coding schemes, however minor, to be legible (Goodwin, 1994).

The final task for the day was to extract seawater from the tubes with salmon lice, and then add Karnovsky's fixative to samples, preserving them for later. This procedure was always performed under the fume hood due to the toxic formaldehyde in Karnovsky's. In this case, the intern extracted the saltwater from each tube with a micropipette and handed the tube over to Hanna, who added the fixative. Samples were then stored on ice in a Styrofoam box and brought back to the High-technology Centre for further analysis.

In the following days, all hatching incubators for the egg-strings were inspected daily down in the wet lab, and the hatching date for the eggs along with other important developments was noted in meticulous detail. Individual eggs hatch at different rates, and since early hatchers could perish before the late hatchers were fully developed into copepodites, the animals were usually collected in two batches for analysis on twelve and seventeen days after the RNAi termination. Hatched eggs were then counted around the copepodite stage, in order to learn

whether they developed through the molting phase as normal. When terminating this phase, the eggs were bathed in a mixture of 70% ethanol and saltwater. As per The Checklist's instructions, animals could at this point either be counted directly, or placed in tubes for later counting. Counting was by no means a trivial task. It was accomplished by pouring the sampled larvae into a small square container called a "counting tray," which was divided into columns. One end of this counting tray was then placed below the lens of a stereomicroscope. As the tray was gently pushed horizontally across the field of vision of the person performing the counting, juvenile parasites appearing in each column could then be enumerated by pressing a button on a mechanical laboratory counter. The number of copepodites, remaining nauplius stages, as well as unhatched egg-strings, were then inscribed into spreadsheets. These numbers made it possible to run fecundity statistics to figure out if the RNA interference had impacted biological functions, such as reproduction, by comparing the hatching rates from treated animals with those from the control group.

Concluding Remarks

Initiation and termination of RNAi experiments involve many kinds of discursive practices, such as coding, highlighting, and production of graphical representations. Together these make up a professional vision for studying gene expression in lice. The accomplishment of seeing the effects of RNAi on the louse is, following Goodwin, "lodged not in the individual mind, but instead within a community of competent practitioners" (1994: 626). To this, we can add that it is spread across situations, and artifacts. While previous chapters described the manifold branching points that led to the assembly of the experimental system, I here focused my situational analysis on representative time slices of key activities sampled from events within it. These illustrate the orchestration of material, social, cultural, and other cognitive resources that sustain the production of knowledge among molecular parasitologists.

Computer-supported phylogenetic thinking helps researchers to compare patterns of genetic sequences identified in the louse genome

with those of other organisms. This constrains the search space for salient pathways to target with RNA interference. Faced with the problem of sifting through massive quantities of data, biologists now depend on epistemic enhancers like bioinformatic software. These extend their cognitive powers and help them grasp the significance of deep evolutionary relationships between sequences, so that only the most promising candidate genes are investigated further. Computational analysis enables both an extrapolation of human senses, a conversion of information between sensory modalities, and augmentation to detect properties that human sense organs cannot access by regular means.

When exposing target sequences to RNA interference, experimentalists made use of coding schemes that systematically transformed the material world into categories and events of professional relevance. In the activities described above, we saw how a series of relatively low-level discursive practices such as browsing databases, synthesizing double-stranded RNA, picking and counting lice, injecting and repositioning them on salmon, preparing and attaching labels, punching numbers into Excel spreadsheets, taking microphotographs, making observations in the stereomicroscope, conserving samples, incubating egg-strings, monitoring fecundity and so on, facilitate higher level cognition about the function of genes. These events, by themselves mundane in appearance, show how cascades of representations are enacted, and how epistemic and pragmatic activities come together to enable the sequential propagation of representational states through the experimental system.

Action complexes for each assignment were abstractly described in The Checklist. But while this document functioned as a regulatory representation that governed several functions of the experimental system, and distributions of representations within it, The Checklist did not sufficiently specify a script with all the necessary details for accomplishing tasks critical for epistemic success. The collective had to organize themselves in a concrete situation for which there was no high-resolution plan. Hutchins points out that when we view the organization of such social events from the distributed perspective, we see that systems involving team performance sometimes remove the work of coordinating an activity away from the performing members themselves, and hands it over to structural properties of the larger activity system (Hutchins,

1995: 200). Here, we dealt with a specific type of complex coordination, the initiation and termination of RNAi, that was critical for determining the role of genes in ontogeny. While agents like Sara provided some additional coordination for certain phases of the termination procedure, much of the action was structured so that each member only needed to know what to do when certain enabling conditions occurred within the emergent ecology of the experimental system.

We also saw how pre-computations set up dependencies between elements within the cognitive ecosystem and afforded epistemic resources for RNAi trials. Information about the experiment was processed not just in the internal, biological memories of lab members, but also frequently delegated to the external environment. This illustrates two central reasons why an account of experimentation as a cultural practice must include the cognitive life of things. The cognitive properties of RNAi experiments are both removed from the properties of individual lab members through the transforming effects of tools and material environment, and through the production of emergent effects at the group level, which do not reduce to the cognitive powers of individuals.

In both the initiation and termination event, the coordinated elements included a heterogeneous collection of scientific apparatus, representational media, biological materials, human agents, and so forth. A myriad of written inscriptions provided a mutually supportive relationship between these resources in the situated arrangement of the experiment, thereby contributing to what Hacking called the "self-vindicating" structure of the laboratory sciences. As laboratory science and experimental systems mature, so are bodies of conceptual models, theories, and apparatus "mutually adjusted to each other" (Hacking, 1992: 30). All tests of theoretical and conceptual problems unfold against a material apparatus that has co-evolved along with theories, models, and different forms of data analysis, to form an interlocking, robust fit. It is the coordination between all these resources, that facilitate the kind of constraint satisfaction that made RNAi such a powerful tool for my interlocutors.

Different kinds of experimental data were coupled to each other through a myriad of written inscriptions. Coordination devices like spreadsheets, made it possible to keep track of genetically engineered lice, their offspring, and their genetic composition as they were propagated

and subjected to gene expression measurements further downstream in the system. Together, these cultural-cognitive experimental practices enacted a cascade of representations contributing to the "sifting of gold from pyrite" (Galison, 1987: 19). Sometimes, the first glimmers of the genetic pathways caused by the silencing of genes, could be glimpsed in the form of salient changes in the gross morphology and phenotypes of lice specimens that were observable by the naked eye, such as missing egg-strings and irregular body shapes. But the representational cascade did not end with observations of morphological change, of the sort visible through the eye, microscope, or from digital micrographs. These were certainly useful first approximations to answer questions about gene function, but they did not carry much epistemic weight on their own, as evidence in contexts of justification.[16] Other "filters in the space of representation" were required, to again invoke Galison's attractive metaphor. For any observation acquired via RNA interference to count as evidence for the larger scientific community, more data about the underlying molecular mechanisms involved in gene silencing was necessary. In the next chapter, we turn to how these transformations were enacted on biological tissues, further tracking how samples and their representations propagate through the pipeline. We will look at what happens to the samples placed on RNAlater, as they undergo an analytical procedure known as "quantitative PCR."

Notes

1. Efforts by the NIH to make a unified database in the 1980s exemplifies how computing was entwined with fundamental shifts in understanding gene expression over time (Stevens, 2013: 153).
2. Paralogs are genes related through a duplication event, while orthologs refer to similar sequences that are found in different species, evolving from a common ancestor. Orphan genes describe instances where a gene sequence cannot be assigned to an existing gene family due to insufficient knowledge.
3. Other relevant groupings are supergenes, neighboring genes that are inherited together due to genetic linkage and share functionality, and gene

complexes, linked genes that participate in the same biological processes, with similar but diverging functions.

4. Bayes theorem stems from a paper published posthumously in 1763 by Reverend Thomas Bayes. The foundation of Bayesian statistics, which incorporates prior beliefs into probability estimates, predates frequentist statistics by around 150 years.
5. BLAST is an abbreviation for Basic Local Alignment Search Tool (https://blast.ncbi.nlm.nih.gov/Blast.cgi).
6. See, for example, www.mrbayes.net.
7. Experimental activity involving live fish was guided by the three R's of animal testing, which encourages "replacement" or "reductions" of experimental animals where possible, and "refinement" of methods.
8. Glass needles could be purchased off-the-shelf, but the chief engineer explained that they had more success with "pulling" their own, custom-fitted to the morphological dimensions of lice targets.
9. My account is based on conversations with researchers, and reflections on my own failed effort under Ada's guidance. My cue for being in the "correct" position was that the needle no longer faced resistance from the exoskeleton when applying pressure, thus entering a softer tissue. But the tissue offers vague proprioceptive feedback, so the louse is easily skewered. Conveying this experience declaratively, beyond this, eludes my efforts. The difficulties of communicating this work propositionally, partly explains why the chief engineer, who routinely injected hundreds of salmon lice per assay, usually performed the task.
10. Fish were habituated to the tank before RNAi trials were initiated to reduce stress, indicated by their food intake and position in the water current. A precious commodity, salmonids were preferably reused for several trials, but sometimes euthanized after one single trial. Fish could also be euthanized when growing too large. Tranquillization was induced by immersing fish in a bucked for three minutes, in a combination of benzocaine and metomidate hydrochloride. Clover-oil was used to calm fish for less invasive procedures. Use of anesthetics required constant vigilance about locomotory functions and life signs. Use of salmon as laboratory animals is highly regulated, and experimenters were certified through a mandatory Laboratory Animal Science Course for Fish, introducing legal aspects of animal science, cognition, pain and nociception in fish, experimental design, and ethics. While salmon and Decapoda, like lobsters and crabs, are considered sentient under Norwegian animal welfare law, salmon lice are not.

11. Technicians eventually built an elaborate mobile installation of hoses and plastic pipes providing individual water supplies to each tank during RNAi, so that the water level could be lowered on demand to facilitate controlled infections with lice nauplii.
12. Karnovsky's has a high osmolality, a measure of the concentration of osmotically active particles in a solution and preserves cell structure with minimal alterations compared to its living state.
13. The chemical properties of RNA make it highly unstable compared to DNA.
14. Occasionally, tissues were processed directly after RNAi to biochemically capture molecules before degeneration, such as metabolites detected with enzyme-linked immunosorbent assay (ELISA), which uses antibody-markers and color to visualize substances.
15. When testing genes suspected to cause phenotypical differences in anatomical features that was not captured by the dorsal perspective, the termination team would photograph lice from other angles.
16. According to my observations, the distinction between data and evidence was not explicitly demarcated among my interlocutors. Evidence can usefully be considered a special form of contextualized data.

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6

Making Meaning and Measurement in Gene Expression Analysis

How are samples of lice-tissues, collected from RNAi experiments, endowed with biological meanings through work downstream in the experimental pipeline? This chapter tracks the representational and material cascades initiated in the previous chapter. It examines the making of meaningful measurements of gene expression in lice tissues, focusing on a widely used technology known as real-time quantitative polymerase chain reaction. By ethnographically tracing the work and situatedness of one researcher within the cultural-cognitive ecosystem of the laboratory, I show how everyday operations on the benchtop depend on "ecological assemblies"; small-scale cultural practices that orchestrate arrays of resources in the agent's immediate environment to house and extend cognitive processes that span beyond the boundaries of the individual. An important property of these functional systems is their role as material anchors for conceptual blends. I show how the cultural artifacts, which litter the lab, afford scientists a suite of external resources with remarkable computational properties. Together, these representational cascades shift the experimental system's epistemic states, as part of an extended cognitive process of thinking through things.

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Experimental activities in the laboratory rearrange accumulated resources and technical things to reveal and display the character of epistemic things, those elusive features of gene expression in salmon lice. We have seen how molecular parasitologists, as cognitive agents creating new knowledge, do not only think, but touch, move and otherwise engage with material objects and their colleagues, through a broad range of material engagements and semiotic activities. The analysis in Chapter 5 ended with the termination of an RNAi trial, where specimens were arranged in small plastic tubes, and placed either on fixative for histological examination in the microscope or immersed in a substance known as RNAlater, thereby setting the agenda for future work. When kept on RNAlater, lice were preserved for weeks in the fridge, or for months or longer in the deep freezer. Experimentalists could then, at their later convenience, study the effects of their RNAi interventions using molecular methods to probe the animal's gene expression, and align these readings with phenotypic data, like observations of gross morphology.

In this chapter, I examine how archived salmon lice tissues are further transformed within the experimental pipeline by sampling epistemic activities from the "DNA lab." Specifically, I look at how biological macromolecules are handled to reveal hidden features of genes that are immensely interesting for molecular parasitologists. I focus on measurements of gene-expression using a method known as "quantitative polymerase chain reaction," or simply "qPCR." The structural and functional dimensions of DNA, RNA, and proteins cannot be usefully studied with the naked eye, or even a microscope.[1] As scientists cannot see biological macromolecules directly, their properties are mediated through various representational artifacts (Myers, 2015). Here, I describe the material culture of the biology lab as a "historically sedimented structure" (Goodwin, 1995: 268). This structure enables working with invisible substances such as DNA and RNA in epistemically rewarding ways.

To an outsider who only catches a short glimpse of the action, the ebb and flow of activities in the socially organized setting of the lab may look rather mundane, verging on the prosaic (Hine, 2001). The bulk of laboratory life consists of highly repetitive tasks performed by the lab countertop, or on the office computer. Endless pipetting by the bench and in fume hoods; shuffling of boxes filled with plastic test tubes,

reagents, as well as bits and pieces of salmon lice; fetching of boxed samples from the fridge; assembling of devices; carefully putting slabs of fragile electrophoresis gels into UV-cabinets; monotonous interactions with paper printouts or digital interfaces; and seemingly interminable rounds of waiting for various devices and biochemical processes to finish, so that new results may, slowly, emerge. Despite such apparent mundanity, the cognitive ecosystem of SLRC presents an evolving and adaptive problem-space (Nersessian, 2006, 2012), for exploring the lice genome. This dynamic space was constrained by the Centre's research program, which was continuously reconfigured as the biology of salmon lice progressed into new directions. So, what may appear as pedestrian at first glance, are creative, multimodal semiotic encounters with artifacts and devices that couple with various forms of language-use, including literal inscriptions, numerical representations, and manipulations of scientific visuals. These constitute powerful epistemic action loops for generating new insight. Situated within a rich ecology, littered with meaningful representational structure, experimentalists enact critical resources for making knowledge about lice. When we zoom in closely on specific practices within this experimental system and make them our unit of analysis, apparently disparate domains of activity come together, and the boundary between pragmatic and epistemic actions, seems to dissolve.

With this in mind, one could ask where we should look to identify scientific cognition. The classical view, which Andy Clark dubs BRAINBOUND (2008: xxvii), suggests that the loci of cognitive activity are circumscribed by the skin and skull of individual scientists. In this view, the non-neural body of a researcher is just a "sensory and effector system" of thinking brains, and the environment surrounding this brain organ nothing more than the arena where adaptive problems arise and are sensed by brain and body. As a replacement to BRAINBOUND, Clark argues for EXTENDED, an alternative, composite picture where: "the actual local operations that realize certain forms of human cognizing include inextricable tangles of feedback, feed-forward and feed-around loops: loops that promiscuously crisscross the boundaries of the brain, body and the world. The local mechanisms of the mind, if this is correct,

are not all in the head. Cognition leaks out into body and the world" (ibid.: xxviii).

As part of this lineage of ideas to rethink the boundaries and unit of analysis for cognitive systems, the distributed approach picked out three ways that cognition is trafficked beyond the individual. First, cognitive processes can be distributed across members of a community, to create a division of labor required to complete different tasks and reach epistemic goals. Secondly, experimental science, as an embodied cognitive process, involves coordination between internal and external structures. To invoke Clark's evocative phrasing, the mind is "leaky," "shamelessly" mingling with the body and world as it seeps out from its assumed confines (1998: 53). Thirdly, this promiscuous organ participates in mutual feedback processes with material environments that can distribute cognitive practices through time so that the products of earlier events transform the character of later events.

Applying this vocabulary, we can understand experimental research as a cumulative cultural process that ratchet up solutions for solving frequently encountered epistemic problems that again feed back into the dissection of novel phenomena over time. Earlier, we saw how Rheinberger drew attention to this transition with his twin concepts of epistemic and technical things (1997). In a sense, their cumulative nature is summarized in that old maxim, famously expressed in a letter by Isaac Newton: "if I have seen further, it is by standing on the shoulder of giants."

As we zoom in on instances of laboratory benchwork, it is helpful to consider two additional principles from EXTENDED that minds the role of material culture and increases the resolution of my analysis of the DNA laboratory's role in this cultural-cognitive ecosystem. The first, is the "Principle of Ecological Assembly" (PEA), which states that agents promiscuously co-opt environmental and bodily resources to scaffold cognitive accomplishments: "according to the PEA, the canny cognizer tends to recruit, on the spot, whatever mix of problem-solving resources will yield an acceptable result with minimum effort" (Clark, 2008: 13). We saw instantiations of this process in the joint semiotic activities described in Chapter 5. The second is a methodological principle known as the "Parity Principle" (PP). It states that if a cognitive

process works in such a way that we could call it cognitive if it occurred inside the head, then we are justified in calling it "cognitive," even if its actual location is on the workbench.

In the context of an anthropology of scientific knowledge, these principles encourage us to "ignore old metabolic boundaries" and "attend to the computational and functional organization of the problem-solving whole" (Clark, 2008: 79). Accordingly, distributed cognition extends the computational language previously reserved for what takes place within the old boundary to account for coupled systems between human agents and material culture that can be observed in the wild. As such, the cognitive ethnographer's task when encountering such hybrid systems, is to ask what information goes, where, when, and in what form, during specific moments of interaction. In their natural habitats, scientists recruit a wide variety of resources and emergent structures arising from the interplay between morphology and control. This includes active sensing to retrieve information, deictic gestures like pointing, perceptual efforts that stabilize organism–environment relations, bodily and tool-based extensions, as well as material symbols like inscriptions and other "exograms" (Donald, 2010). In these "ecological assemblies" or "functional systems" (see Hutchins, 2011), interactions with external objects may instantiate genuine cognition and reasoning.

As we have seen, cognitive artifacts are critically important for supporting both short-term ecological assemblies, created on the fly for specific tasks, and larger cultural-cognitive ecosystems that outlive individuals. Here, it is worth noting that a cognitive artifact does not delineate a sharply bounded category of objects. Rather, it should be considered "a category of processes that produce cognitive effects by bringing functional skills into coordination with various kinds of structure" (Hutchins, 1999: 127). Without access to the affordances embodied by such epistemic enhancers, ranging from opportunistic use of natural structures to intentionally designed objects, scientists are significantly stripped of their powers.[2]

In the following, I track the work of Veronica, a Ph.D. student at the Centre, as she engages with an everyday experimental task known as "quantitative polymerase chain reaction" ("qPCR") to learn more about a class of genes that is the focus of her Ph.D. project. I first

situate Veronica's domain of interest within the overarching research program at the SLRC. Then, through a detailed description of a series of cultural practices that are taken-for-granted and rarely articulated by those involved, I present an analysis informed by distributed cognition, that illuminates the complexity of meaning-making in Veronica's performance of gene expression analysis using qPCR. In my ethnographic account of this multimodal activity system, I examine a series of seemingly simple cultural strategies for connecting conceptual and material structure which support Veronica's scientific activities. I address how these benchtop strategies, which are embedded within the SLRC's experimental system, help propagate representations of salmon lice biology, and contribute to meaningful conversions of nucleic acids in test tubes into novel information about gene expression. Following Goodwin, I emphasize how organization of space through various material engagements create the necessary structures for accomplishing experimental work (Goodwin, 1995). In the final section, I briefly examine relations between material culture and meaning-making in the pedagogical transfer of laboratory skills, and the advent of commercial "kits" in molecular biology.

While the previous chapter examined the execution of RNA interference as a team effort, my concern in this chapter is tracing how the DNA lab, as part of a larger cultural-cognitive ecosystem, was orchestrated by a single agent to accomplish scientific work. Some of these traces become invisible during front-stage performances of scientific knowledge, such as journal publications, due to discursive practices and epistemic norms in the experimental life sciences that regulate what counts as relevant information.

Again, a disclaimer. I have tried to keep technical details to the minimum necessary for readers to make sense of what I am conveying, which means that my descriptive account will be far from exhaustive of this rich domain of bioscience. The challenge of reducing the complexity of practice to what is sufficient for an adequate analysis is a familiar theme, both from cognitive ethnography (Hutchins, 1995b: 266), and from debates in science studies more generally about the relative weighing of internal and external factors when situating scientific knowledge production historically (Kitcher, 1998; Shapin, 1992).

Practical reasoning must operate on stable representations of relevant constraints in the specific domains being engaged by the cognitive agent (Hutchins, 2005: 1557). We often think that the complexity of a given practice owes to the richness of the internal, mental representations held by those who perform it. Surprisingly, however, the human trick where an agent structures the external environment informationally can itself provide a critical resource for successful cognitive accomplishments (Kirsh, 1995, 2010). Through operations with rather mundane artifacts on the laboratory bench, scientists can scaffold highly complex chains of reasoning about biological phenomena. Here, I propose that the cultural artifacts involved in qPCR acquire powerful epistemic functions, not due to any intrinsic qualities they possess, but because they can be used as "material anchors for conceptual blends" (Hutchins, 2005). Through cultural practices that mingle together concepts with material anchors, it is possible for scientists to increase the stability of conceptual structures, which enable more complex forms of reasoning than would otherwise be possible. In many domains of experimental science, the conceptual structures under scrutiny are so complex, that they cannot be managed and represented in a stable manner by researchers relying on mental resources alone. According to Hutchins, the production and maintenance of stable representation of conceptual elements in cases of real-world computation requires that involved elements are held or anchored in place. This "holding in place" can be accomplished "by mapping the conceptual elements onto a relatively stable material structure," thereby turning a material medium into a physical anchor for a conceptual blend (Hutchins, 2005: 1562).

The process by which cognitive artifacts merge into larger ecological assemblies in experimental biology are cultural elaborations of this general phenomenon. As I show, many epistemic events within the spaces where qPCR is accomplished, critically depend on blends created through associations between the conceptual and material. In this process, relationships between material structures, like arrays of nucleic acids in carefully arranged test tubes, can serve as a proxy for relations between conceptual elements, like different experimental treatments. Only when they get orchestrated correctly will such assemblies yield new insights about gene function in salmon lice. The case of executing qPCR,

I argue, makes visible some important relations between environmental structure, social organization, and the conceptual fabric of scientific knowledge production. Again, we step into the lab, "Cognito-scope" in hand.

Fibronectin Type II

Veronica is a Ph.D. student on a three-year fellowship at the Sea Lice Research Centre, where she is primarily affiliated with Work Package 4, which tackles the broad subject of "molecular parasitology." Her research is jointly supervised by the Centre director, and Sara, the senior molecular biologist responsible for coordinating all RNA interference trials. For her dissertation research, Veronica's supervisors have assembled a list of interesting genes, and it is expected that she will screen these candidates using RNAi, observe their biological function, and describe molecular characteristics.

Laboratories of contemporary experimental biology continually negotiate the pragmatic and epistemic tradeoffs between individual utility and the communitarian order (see Knorr-Cetina, 1999: Chapter 9). As on other frontiers of research, work at the SLRC can be construed as a race against time and other research groups; funding is finite, mistaken directions can be costly, and Ph.D. deadlines must be met. The scope of doctoral projects like Veronica's must strike a balance between what a student can reasonably achieve within a limited timeframe, usually three or four years depending on whether the scholarship includes teaching or administrative obligations, and the needs of the larger research program being pursued.

Veronica's list of genes had been identified via sequencing and annotation of the salmon louse genome, and they were predicted to be involved in an extracellular-matrix protein known as fibronectin. As we saw, a gene prediction is the outcome of a partly automated analysis of the genome (a "genome annotation"), combined with judgments made by human experts like Veronica and her supervisors about which genes are most likely to be worthwhile targets to research further. These judgments can be informed by findings reported in journals by other scientists who

pursue work on biological mechanisms in model systems that may be quite different from salmon lice.

A genome prediction attaches biological information to sequence data from all the chromosomes in an organism. Today, much of this process is automated through computational annotation tools that identify patterns in sequence data from the organism in question, and then compare these sequences directly to the sequence stored in other online databases, which contain the published genomes of other organisms. Genomic databases are organized to present information both about structural elements (chromosomal locations, genetic structure, coding and non-coding regions), and functional properties (regulatory cascades, interactions with other genes and known expression profiles). In Chapter 5, we saw how biologists employed the toolbox of phylogenetic inference to map the evolutionary contingent relationships between genes. Browsing through genomic libraries helps molecular biologists to identify genetic sequences that create distinct proteins involved in various cellular processes.

Veronica explained the logic behind the selection of her own candidate genes as follows. Previous research suggested that fibronectin (FN) interacts with the "extracellular matrix," a form of connective tissue that serves structural and biochemical functions in cells. Potentially, this plays a role in other cellular processes related to host-parasite interactions. Proteins are molecular structures made up of amino acids, and a "protein domain" is a sequence of functionally distinct amino acids that links up a larger polypeptide chain. Knowledge about the 64 possible codons of the "genetic code," the sequential rules governing how triplets of nucleotides such as A, T, C, and Gs get transcribed into RNA, and strung together as proteins in cells through transcription, can be combined with powerful computational tools for reasoning about biological matter. The genetic code describes which nucleotide sequences code for any of the twenty amino acids, as well as how these units configure into larger protein sequences. This makes the translation between genetic (nucleic acid) and polypeptide (amino acid) sequences a trivial task for professionals. Today, even lay individuals can perform such translations, compare sequences from different organisms, and predict a "protein sequence back-translation" through a portfolio of user-friendly web-based tools.[3]

Computer analysis showed Veronica and her peers that FN is part of the much larger Kringle-domain, a conserved protein structure named after the Scandinavian pastry due to its characteristic shape. Veronica focused on so-called "Type II" domains of fibronectin ("FNII"). The FNII class of structures bind to important molecules, such as collagen and gelatin (denatured collagen). She was particularly interested in how these genes influenced the collagen pathway, a main structural protein for connective tissues. To gain a sufficiently rich understanding of the domain, she estimated the need to sequence up to twenty of these genes and carefully observe their expression at different developmental stages using RNAi to silence their effects on the louse. In this case, the transcripts (messenger RNAs) coding for FNII-domains were found in exocrine glands. Exocrine glands are cellular structures that excrete biological substances to the parasite's outside surface. Transcripts of mRNA were identified by Veronica's colleague Hanna, in the area around the mouth tubule of the louse. Veronica's project will therefore help colleagues understand the functional relationships between FNII-genes and exocrine glands in lice, by characterizing a relatively unknown system.

Researchers used to believe that FNII was specific to vertebrates, but annotations of other genomes found the domain to also be present in invertebrates like the louse. A search in LiceBase, the in-house database for the lice genome, revealed the presence of roughly two hundred FNII-domains. In comparison, there are only twenty-five in *Homo sapiens*. Was the number of FNII-domains in lice suggestive of these genes' importance for louse biology and adaptations to a unique parasitic lifestyle? Furthermore, could disrupting the collagen-binding pathway have a cascading effect on louse development, and potentially offer clues toward a vaccine target, or other kinds of therapeutic biomolecules of some practical value for salmon farming? These were some of the questions motivating Veronica's research.

We saw that attractive candidate genes for any future lice vaccine should target critical biological pathways, such as those regulating the reproductive system, or food uptake and digestion through the gut and intestines. The gut, for example, is exposed to salmon blood extracted by the parasite and may contain potential antigens. A challenge for Veronica

and her peers, however, was that thousands of genes are likely involved in any of these biological pathways, with many of these being phenotypically redundant. This meant that secondary "backup" pathways involving alternative genes participating in similar biological processes were probable. Teasing these apart was a formidable challenge.

Using RNA interference, Veronica would systematically silence sequences of interest to functionally characterize a narrow selection of the most promising FNII-domains. She could then observe the effects of her intervention, with a keen eye toward critical processes such as molting and reproduction. Like the other scientists at the Centre, Veronica hoped that her explorative experiments in the end would yield interesting phenotypes; experimentally treated lice that developed differently from the control specimens. In these RNAi experiments, observations of changes in gene expression at the level of gross morphology were corroborated by taking measurements of downregulated genes, and comparing these with a non-functioning fragment, and with readings from a control group from the same experiment. The combination of an unviable phenotype, such as one without offspring, and a statistically significant downregulation, was an indicator that the gene in question was vitally involved in the targeted process. This fragment could then be further scrutinized through other methods, setting off a chain of activities extending far beyond a single RNAi trial.

Figure 6.1 depicts a "heatmap' of fibronectin type II-domains that Veronica used to guide her initial investigations. The "map," which belongs to a class of artifacts peculiar to computational biology, was handed down to Veronica by her supervisors. The diagram's X-axis specifies the life stage and sex of the sampled materials, as well as the body part these tissues have been sampled from. The Y-axis, on the right, enumerates a list of fragments that have been automatically generated in the genome database. EMLSAT, the initial abbreviation on each entry, describes which version of the genome annotation that specific fragment number is found. The histogram in the upper left corner displays a legend with color codes for the relative expression levels of genes as compared to an internal control fragment. Here, dark colors indicate low relative expression levels, while bright colors mean that the gene is highly expressed.

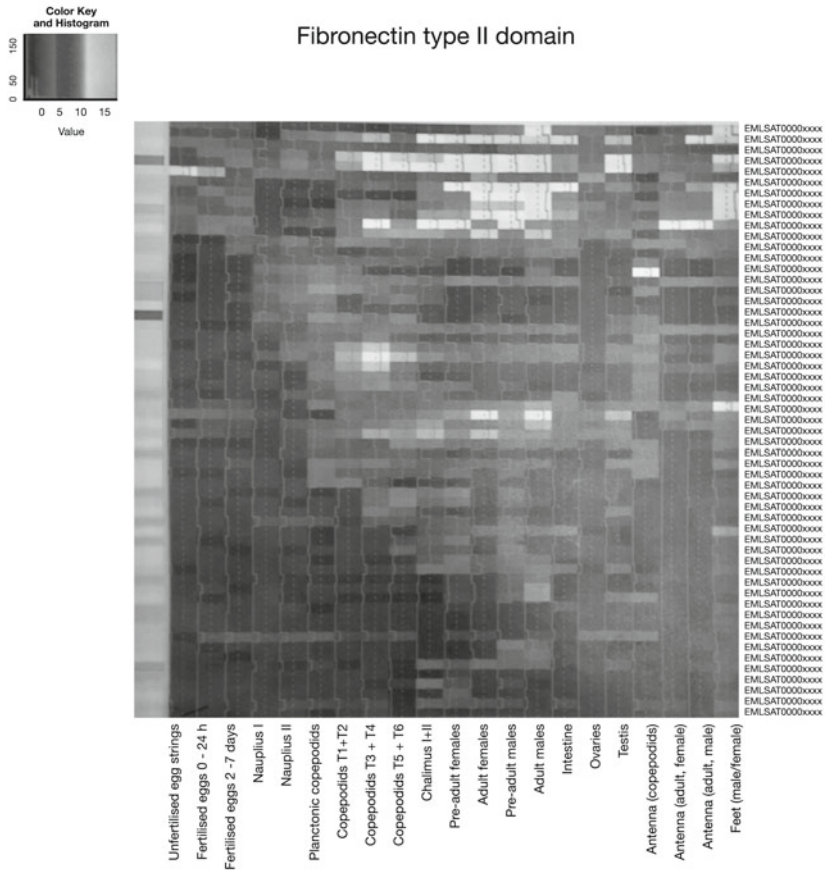

Fig. 6.1 Author's rendering of an annotated heatmap used by Veronica. The original diagram was based on RNA-sequencing, showing expression profiles of genes containing the domain

Heatmaps are artifacts that can summarize large amounts of information, thereby facilitating "many-against-many comparisons" (Stevens, 2013: 192–194). This heatmap does not directly represent the phenomenon but is created on basis of numerical representations from the output of RNA-sequencing experiments (RNA-seq). As a method characteristic of "exploratory experimentation," RNA-sequencing of salmon lice tissues offered an inductive, "broad" instrument capable of

producing thousands of datapoints instantaneously, which in turn facilitated the search for "difference-makers" in the biological data (Franklin, 2005). Without a heat map, the analyst would, in this case, need to visually scan a matrix with numerical data from over thousand different measurements to make sensible comparisons. In terms of distributed cognition, the ingenuity of heatmaps as a representational practice, lies in substituting a very hard computational problem of comparing a high number of possible combinatorial values to find patterns in multidimensional data, with a much simpler perceptual task in a visual search. Those familiar with data cultures of contemporary bioscience, can simply scan the matrix to identify meaningful patterns with little effort.

Veronica had recently terminated an RNAi experiment on a fragment from the list, which I here refer to simply as G1000. Targeting G1000 yielded some eye-catching phenotypes with obvious developmental irregularities. Veronica's RNAi treatment produced a condition where the resulting egg strings were largely deformed on most of her specimens, in contrast to the straight, regular form of wild-type egg strings. This offered a visual indicator that the gene may be involved in important pathways. Such visual representations did not however, provide direct causal evidence that G1000 was a suitable target for therapeutic interventions. She now had to verify that the genes in the relevant salmon lice tissues were actually silenced or "downregulated" vis-a-vis her control samples, thereby ruling out any spurious effects from unknown technical or biological mishaps. Only with an answer to this question at hand, could the research community evaluate whether they should throw more resources at studying the fragment in detail.

In the DNA Laboratory

December 14, 2014. I am seated next to Veronica, in front of an Applied Biosystems 7500 unit; a quantitative polymerase chain reaction-machine, colloquially known simply as 'the qPCR'.[4] The device looks like a large, bulky, off-white computer cabinet (see Fig. 6.2), and produces a faint humming, which joins the chorus of other fanned equipment running in the background. At the SLRC, the qPCR is regularly used by staff to

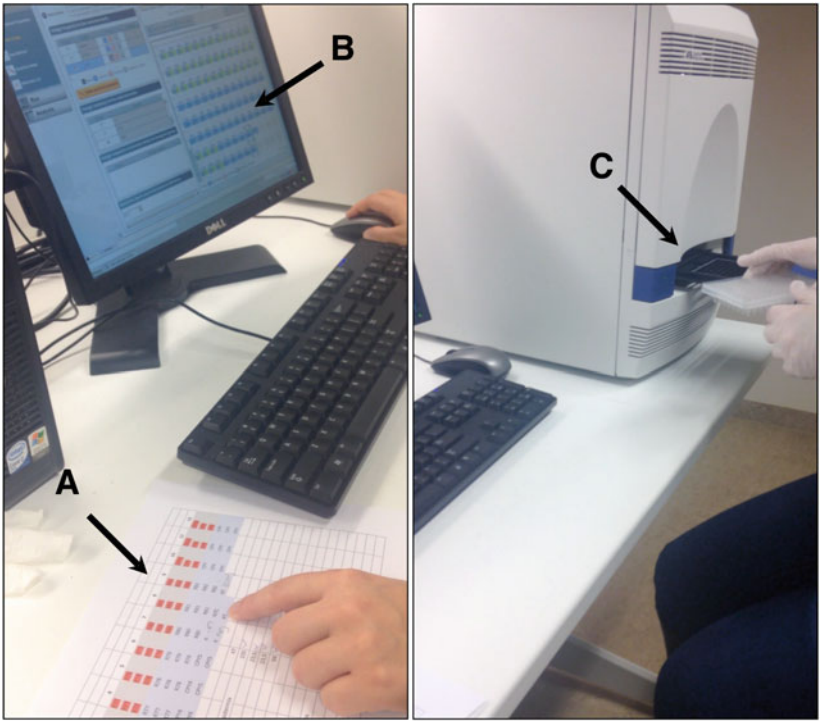

Fig. 6.2 Feeding the qPCR machine and setting up the reaction. Veronica creates an alignment between the array of items laid out on the paper spreadsheet **A**, with those on the computer monitor-interface **B**, and the coordination of reagents on the 96-well microplate inserted into the machine **C**

profile the mRNA content of salmon lice sampled from various experiments. Users primarily interact with this essential piece of technology via a software package running on a Windows PC platform. Veronica's goal for the day is to examine the expression levels of G1000, which she targeted with RNA interference in an earlier joint experiment. To determine whether G1000 has been significantly downregulated in her samples, relative to experimental controls, Veronica prepares and loads a specially engineered 96-well microplate with nucleotide samples into the qPCR machine's opening slot. Setting up the machine for this "run" only takes around ten minutes, with the device completing its analysis in

roughly two hours. However, a long chain of cumulative action on these genetic substrates, predates her efforts to initiate meaningful "structure-preserving" operations on her samples with the machine (Goodwin, 2013: 17).

After terminating a previous RNAi experiment jointly with her colleagues, Veronica first used a series of standardized procedures to isolate RNA from tissues that were preserved on tubes with RNAlater. To isolate RNA, she made homogenates of lice tissue and then, using centrifugation along with chemicals like TRIzol and chloroform, she separated this biological material into three phases: a protein phase, a DNA interphase, and an aqueous phase containing the RNA. She then transferred the RNA phase to a new tube along with isopropanol and incubated the samples. After this step, a new round of centrifugation followed, producing an "RNA pellet" that was washed with ethanol. This new sample was then mixed in a lab vortex and centrifuged again. Discharging the eluate, Veronica then dried the resulting RNA pellet and eluted it in RNAse free water, before storing the samples at -80 degrees Celsius. Using a Nanodrop spectrophotometer she also tested the sample's concentration and quality, ensuring their adequacy for further processing.

Veronica also treated her samples with DNAse, an enzyme which degrades DNA so that it does not contaminate the RNA sample further downstream, and reverse-transcribed lice-RNA into cDNA using the Affinity Script cDNA kit. Following this, Veronica carefully prepared her material substrates for the qPCR experiment by following the Centre's in-house qPCR protocol. This protocol instructs that any new qPCR-assay must be validated with a standard dilution curve (this process falls beyond the scope of my description here). Standardized protocols, which are offered for most technical procedures, are crucial infrastructures for any such transformations in the Centre's state of knowledge.

Other preparations included Veronica ordering reagents known as "primers," and some assistance from the chief engineer to prepare 10 micro-liter aliquots that were stored in a box in the clean-room freezer. While she could have done this herself, it was highly recommended that all primers were prepared in the same standardized manner to ensure reliable results. Furthermore, Veronica had to prepare a master mix for

the assay, making sure to include a bit of extra reagent to compensate for what would be lost during pipetting. She then moved from the clean room, where the risk of contamination is low, into the less strictly regulated template room. Here, a cDNA template was added to the microplate. For molecular biologists, this action signals that Veronica conducted a "two-step qPCR," and not the faster, but less flexible and slightly less sensitive "one-step" procedure, where everything is conducted in a single-tube reaction. After Veronica loaded her reactions onto the plate, she then placed an optical adhesive film on top, and centrifuged the object, spinning the liquid down to the bottom of each well. She also made sure that the plate's edge was not contaminated, which could potentially interfere with the machine analysis. Let us now take a detailed look at the sequence of action where Veronica sets up the machine to profile gene expression. Figure 6.2. depicts the scene, and the excerpt gives an overview of this process.

EXCERPT

00:00 Positioned in front of the qPCR-machine, Veronica creates a file for a new experiment on the computer. A "setup wizard" in the software guides her through the steps that must be taken before the analysis can begin. It asks for information about the trial: what kind of experimental design is being conducted, specifies the instrumental options, reagents, and temperature for the PCR-cycle. Having entered these parameters, Veronica names her fragments, and chooses the number of biological parallels to be used.

00:10 Carefully inserting the 96-well plate correctly into the machine, Veronica closes the tray. No longer risking contaminating the samples, she removes her nitrile gloves.

00:25 Veronica double-checks and confirms selection of reagent, in this case: SYBR Green.

00:45 She labels the different fragments that are being tested, according to the lay-out of a printed spreadsheet and defines the targets and names for each of her samples, including her controls so that each fragment is correctly labelled in the output file that she will later transfer to her office computer.

04:35 Veronica assigns samples to the selected wells on the graphical interface by a "click-and-drag" motion, highlighting in different colors where each sample is located on the microplate.

07:05 She double-checks that she has chosen the SYBR Green, standard curve-method.

07:30 Veronica changes reaction volumes for each well on the software interface so they correspond with the physical samples on her microplate.

07:45 The "run" is initiated through the interface and it takes roughly two hours before the analysis is complete. Checking the time, Veronica finds out she is delayed and edits an entry in the logbook's timetable that accompanies the machine, so that others in the lab will know the workstation is occupied for a while. The clock indicates that it is lunchtime.

The Polymerase Chain Reaction

On its own, this rather naïve description hardly renders Veronica's practices with the qPCR-machine meaningful as a scientific event capable of generating new insight. Why must she use this machine to study her samples? How does it work? What dense webs of meaning construction support the device, and what new knowledge is mutually supported by its use? Answering how qPCR contributes to the transformation of representational states within the experimental system, thereby supporting progressive co-adaptation of elements in the self-vindicating structure of experimental practices, first requires an appreciation of the problem that this instrument was designed to solve.

A challenge when working with genetic material at the start of the biotech revolution was that little DNA was easily available to researchers for manipulation. While the biochemical problem of DNA isolation, was crudely solved by Friedrich Miescher's work on "nuclein" already in 1869, one of the technical challenges faced by molecular biologists in the 1970s was developing assays that were sensitive enough to detect signals of small variations in the target DNA structures for medical applications. Molecular cloning technology had partly solved the problem of lacking abundance of nucleic acids when it entered the scene in 1972. It was

now possible to copy a gene and insert it into bacteria to produce the protein coded for by the gene. Still, these cloning-techniques relied on living organisms as the reproductive medium.

Polymerase chain reaction made humans less dependent on these cumbersome bacterial systems, and made laboratory life easier and more flexible, as plenty of nucleic acids became available for analysis. PCR solved the sensitivity-of-detection problem by amplifying the source, DNA, rather than the means of detecting its signal (Rabinow, 1996: 84). Like so many other biotechnologies, PCR did so by harnessing a natural mechanism in the cell; in this case a cellular machinery for duplicating and repairing DNA in chromosomes. So, while PCR did not solve a specific scientific problem, its availability as a convenient off-the-shelf technology created many new situations for use, across all of biology's subfields. Suddenly, it was possible to detect whether a gene of interest was present in a sample, and to compare this sample with others. PCR has since been transformed from a conceptual idea into a technique for copying DNA, embodied by many kinds of analytic devices, with multiple applications in a wide range of experimental systems.[5]

In technical terms, PCR is an in vitro method to copy genetic material exponentially by amplifying DNA segments extracted from organisms, or from cDNA, a DNA molecule "back-translated" from RNA. These substrates are known as the template. As the method's name implies, the process relies on polymerase (a macromolecule that catalyzes formation and repair of DNA), and a chain reaction (a series of events driven by positive feedback). Two short, synthetic nucleotide-sequences (primers) are designed to biochemically correspond to flanks on the segment targeted for amplification and added to a test tube as starting points (or "anchors") for the reaction. Small molecules called deoxynucleotide triphosphates (dNTPs) must also be mixed in, as building blocks for the new genetic material, along with various buffer reagents that help the chemical reaction run smoothly.[6] Additionally, an enzyme that can polymerize nucleotides is required to extend primers in each direction, forward and reverse along the segment to be copied.

Enzymes are molecules that can catalyze chemical reactions, and the DNA polymerase used for this process is a protein complex used by cells during DNA replication and repair, like in regular cell-division.

This enzyme was isolated from *Thermus aquaticus*, a bacterium discovered in the hot lakes of Yellowstone, whose heat-resistant polymerase was described in 1976. The advantage of adopting a heat-stable polymerase, was that lab workers no longer had to manually add new polymerase after each heating cycle. In the early days of PCR, the polymerase would degrade when exposed to the high temperatures of the process, with new polymerases having to be tediously added for each amplification run. In contemporary laboratories, Taq-polymerase is co-opted into a biochemical reaction that can be automatically repeated through multiple cycles in a special PCR machine. In this machine, the amount of DNA in the test tube doubles exponentially for each cycle. In a hypothetical case where a scientist starts with a single DNA molecule, cycle number one produces two copies. Cycle three makes eight, and cycle 29 makes 536870912. 30 cycles later one molecule of DNA has multiplied to 1073741824 copies.

The principles of PCR are common knowledge for biologists working on molecular topics. To duplicate a segment of DNA, the double-helix first needs to be separated in cells. In nature, this process happens with the help of helicase, another class of enzyme. In the laboratory, heating does the trick. When reagents are heated in the PCR machine, the double-stranded DNA molecules are separated by breaking the hydrogen bonds between the annealed nucleotide bases. Primers then bind to the separate strands, and polymerase replicates a new double strand. The two strands are anti-parallel and can only bind in one direction; the polymerase therefore moves directionally along the strand and links up the three-prime end (3') of one strand with the five-prime (5') end of the other. An original double helix is thus split into two single strands and used as a template to create a new double-stranded molecule in accordance with a complementarity principle: the adenine base (A) bond with thymine (T), while guanine (G) binds with cytosine (C) in the sequence-specific order of the original template. These cycles in the machine are based on three phases: denaturation of the double strand during heating, annealing of the primers by hybridization with the strand at a lower temperature, and finally the strand's extension by polymerase at a slightly higher temperature. After a couple of hours, the DNA molecules inside the thermo-cycler, the amplicons, are made abundant.

Quantitative Polymerase Chain Reaction

Since Rabinow's seminal anthropological account of the emergence and controversy over PCR technology (1996), a wide range of novel applications of this facilitating technology have emerged. One is quantitative PCR, which builds on conventional PCR, but expands its powers by combining three biochemical procedures. In the two-step procedure described here, there is first a reverse transcription of messenger RNA (mRNA) into copy DNA (cDNA) using the enzyme reverse transcriptase, which some RNA-based viruses use to insert themselves into the DNA of host cells. Secondly, cDNA is amplified using the polymerase chain reaction principle. The final step is "real-time" detection and quantification of the amplified materials.

In contrast to conventional PCR, which relies only on thermal cycling and biochemical reagents to amplify a stretch of DNA, quantitative PCR uses non-specific fluorescent dyes or dyed probes, that can intercalate with the strands of nucleic acid as they get amplified in the test tube. Additionally, while conventional PCR provides a result that is analyzed at the endpoint of repeated cycles of heating and cooling, qPCR takes "real-time" continuous measurements ("real-time qPCR"). When the dye or dyed probe binds with the DNA or RNA sequence as the number of molecules gets amplified over consecutive cycling runs, the chemical reaction emits fluorescence that is registered by a special detector in the machine. The intensity of the fluorescence in qPCR is then proportional to the increased concentration of the new amplicons. During each cycle, the device collects data for each sample, and outputs measurements of test tube activity at the end of each one, rather than giving a single endpoint reading after completing all the cycles. Due to its simplicity and power, qPCR has become the method of choice for quantifying nucleotides in a sample.

Molecular biologists use different chemical technologies to detect the amplified product in qPCR. The two most popular ones used in the DNA lab at the SLRC were TaqMan (a type of probe), and SYBR Green (a dye intercalate). TaqMan-quantification uses a short complementary DNA probe to detect the amplifying target, using a reporter dye in

one end and a quencher, a chemical structure that quenches fluorescence, on the other.[7] When polymerase produces new copies of DNA, the dye is cleaved from the probe, emitting fluorescence proportional to the number of molecules at the end of the previous cycle, or the beginning of the current one. A high cost per reaction is a major drawback of the method. We saw in the above vignette that Veronica instead selected SYBR green-based detection for her own experiment. When this dye is added to the reagent, it bonds to all the double-stranded DNA in the sample. During the denaturation phase, it is then released again, and fluorescence decreases. When the strand is extended once more during polymerization, SYBR Green binds to double-stranded DNA anew, and the machine can detect net increases in fluorescence as a measurement of relative gene expression. Lab associates explained that SYBR has lower specificity than TaqMan, which makes it liable to produce false positives by binding to nonspecific DNA, especially in the absence of well-designed primers. But since the method is less costly than TaqMan, which requires specially prepared assays for each gene, it can be used to run more reactions when resources are finite, making it highly suitable for the kind of screenings that Veronica and her colleagues regularly performed.

In Veronica's relative standard curve experiment, the relative concentration of the target gene in the sample was normalized vis-a-vis a reference, usually a gene that is expressed constantly in both the calibrator and experimental condition. These are then compared to a baseline, untreated control sample.[8] This way, experimentalists can also control for problems during RNA isolation, such as pipetting mistakes, and undesired chemical reactions that sometimes occur in the test tube. The machine gives a continuous measurement of the population of mRNA molecules in the sample, which reveals which genes are expressed in a cell at a given moment in time. Only when there is a statistically significant downregulation, can observed phenotypes be attributed to the causal effects of RNA interference experiments. Measurements of gene expression thus offer decisive moments in the lab. Depending on its outcomes, a qPCR-run may provide justification for pursuing new directions of research, and thus feed back into new arrangements of practices and

tasks in the experimental system. If the result is negative, the experimenter can move on to other, more promising candidate genes. Again invoking Goodwin's metaphor (2013: 18), qPCR is key to the "the laminated organization of action" that produces knowledge through webs of interlocking experimental resources in the SLRC community.

To better understand how new scientific meanings are construed through qPCR, let us examine the in-house protocol for the procedure. Written by a former postdoctoral candidate at the Centre, the protocol offers a survey of what should be included in the experimental design of a qPCR reaction. As with the RNAi checklist seen in the previous chapter, the qPCR protocol presents a regulatory representation for distributing cognition, and acts as a coordination device for orchestrating joint actions within the experimental system. From the perspective of cognitive anthropology, this recipe exemplifies a "task model" that helps improve the reliability of outcomes (Shore, 1995: 65–66). So even though the in-house qPCR-protocol is not a precise guide to how individuals perform qPCR, it has the virtue of making explicit shared expectations and epistemic norms that regulates its use, and provide information about the implementational-level details of the practice (Hutchins, 1995a: 28). As Lynch points out, laboratory scientists are deeply attuned to the necessity of interpreting protocols in the relation to performative contexts; there can be no discrete boundary between protocol and practice (2002: 205).

First, the qPCR protocol explains that users need at least three biological replicates of the samples. In these, which represent different RNAi targets and can be sampled from select life-stages or body parts, the target quantity of mRNA is unknown. In this case, Veronica is dealing with tissue from salmon lice where the G1000-fragment has been targeted. In Fig. 6.7, these samples are represented by the beige and red cells on her spreadsheet. Such replicates are necessary for statistical analysis since the numerical output of the procedure is based on averaging values from all the replicates. Each of these biological replicates was also paired with a control fragment. At the time Veronica executed her experiment, RNAi trials at the Centre used a fragment from a codfish gene known as CPY, which did not have any biological effect when injected into lice. In Fig. 6.7B, these fragments are found in cells 10–12/D-F and 4–6/G-H.

Also, at least two technical replicates are used to discount variations in the technical execution of the experiment (not visible).

A reference gene is used as an endogenous control by containing a target that is expressed at the same level in all samples. It is used to normalize the fluorescence levels that are detected by the machine. These are paired with the biological replicates and control fragments. Genes that are stably expressed throughout the organism's lifecycle, so-called "housekeeping genes," are used for this purpose. Eight years prior to the opening of the Centre, its Director and a collaborator had experimentally verified that the elongation-factor 1 alpha (El1α) was a suitable reference gene for transcription profiling due to low variation in transcription. This gene serves as a basis for quantitating the relative expression levels of the target fragment. Reference fragments were shaded blue on the spreadsheet in 6.7B.

qPCR must also include a no amplification control (NAC). The protocol explains that this is a real-time reaction without the enzyme known as DNA polymerase, also called -RT control. This control, which shows contamination of DNA in the sample, is highlighted in 7G (see 6.7B).[9] Additionally, the array contains a no template control, a PCR reaction without a DNA, RNA, or cDNA template, which monitors biochemical contaminations and byproducts that can produce false positives (so-called primer-dimers). These are highlighted in Cell 8G on the spreadsheet in 6.7B. Finally, the protocol contains instructions for programming the essential temperatures for the reaction, ranging between 50 and 95 degrees Celsius, and the timing of different cycles in the assay, which last from 15 seconds and up to 10 minutes, depending on the reagents. The SYBR Green program for qPCR chosen by Veronica completes 40 runs in around two hours.

Making Data

Laboratory novices acquire their theoretical familiarity with qPCR from textbooks and coursework but accumulate practical know-how about the method by interacting with the machine on specific research projects in

the lab. While many of the technical properties of the device is effectively black boxed in practice, detailed questions about the apparatus can be answered by consulting technicians, or the methods and application guide published by the manufacturer. Page two from the 260-page manual for Relative Standard Curve and Comparative C_T-experiments that accompanies the Applied Biosystems 7500-device explains the fundamental principles. Regardless of run or read type, the instrument collects data in three phases. First, there is excitation. The instrument illuminates all wells in the reaction plate and excites the fluorophores in each test tube. Then there is emission. Instrumental optics collect the residual fluorescence emitted from each well on the reaction plate, generating an image of light that corresponds to emission wavelengths. Next, the instrument takes this light image and digitally assembles a new representation of fluorescence, collected over fixed time intervals. A raw image is then automatically stored for analysis by the machine. When the run is complete, the machine uses "region of interest (ROI), optical, dye, and background calibrations to determine the location and intensity of the fluorescence in each read, the dye associated with each fluorescent signal, and the significance of the signals."

Before Veronica's session is over, she must intermittently monitor her run and deal with notification alerts given by the machine. When the run is finished, she unloads the plate from the instrument, and checks her amplification plots to screen for abnormal amplification patterns, making sure that the relevant values (such as the slope/amplification efficiency, the R^2-values/correlation coefficient, and the C_T-values) check out correctly. The output from a conventional PCR experiment is an abundance of amplified DNA molecules in the test tube. These can be visualized as a band on a gel using electrophoresis, or compared with a known concentration of a marker and measured using a spectrophotometer, like an instrument known as a "NanoDrop." Outputs from qPCR, on the other hand, is information about patterns of gene expression in the different samples in terms of relative levels of messenger-RNA. In practice, the most important output value for determining this relationship is the "C_T-value" (the "threshold cycle," or "quantification cycle"—C_q).[10] This value refers to the intersection between the curve of amplification and a set threshold. The manual describes it as: "the PCR

cycle number at which the fluorescence level equals the threshold," which is a central measurement for further calculations downstream.

The qPCR machine automatically represents its output in plots where the level of fluorescence can be read from one axis on a diagram, and the cycle number from the other. A comparison of fluorescence plots to cycle numbers for all the samples is then set against a background of fluorescence at the same starting point, known as a "baseline correction." A threshold level of fluorescence is also set, above the background level, but within the plot's linear amplification phase. This is done to provide a threshold for the cycle numbers. A central feature of qPCR is that the threshold cycle ("C_T") is inversely proportional to the amount of nuclei acid in the starting sample, so that a lower value indicates a higher concentration of nucleic acid (and vice versa). It is only when the nucleotide concentration has reached this threshold that it is possible to infer anything above the concentration from the intensity of fluorescent light. This also means that the more initial DNA or RNA template is present in the sample at the starting point, the earlier the C_T-value is reached for that sample. Being directly proportional to the number of amplicons that gets generated throughout the cycling process, the fluorescent signal provides the means to assess expression levels.

At this stage, the qPCR machine's software can display different plots for inspection, each with its own characteristics. These plots are usually inspected on the computer in the DNA lab before moving on to further analysis elsewhere. Here, the experimenter looks for the presence of reaction curves that might reveal whether something has gone amiss during the run.[11] If the curves are acceptable, there are several further epistemic actions that are necessary to secure a useful outcome. Although the machine automatically analyzes the wells, users can either choose to view the results by working directly in the machine's software package, or by exporting the data to an Excel spreadsheet. Veronica and her colleagues would often bring these spreadsheets to the undisturbed setting of their personal offices, rather than the communal lab space, to perform further calculations and compare expression profiles with data from other experiments.

In the specific procedure used by Veronica, known as "relative quantification," users of qPCR normalize the target sample ("gene of

interest," or GOI) to the reference gene, a so-called "housekeeping" gene whose expression level remains constant under most conditions. As we saw, housekeeping genes are usually involved in very basic cellular processes and have been experimentally vetted to be constantly expressed throughout the cell's lifecycle, thereby providing a baseline for making comparisons across samples. The relative value of this normalization is then compared to a "calibrator" or "control sample." There resulting differences in C_T-values can then be referred to as "fold-differences" that are either "up-regulated" or "down-regulated," depending on the context.

Although there are several ways to normalize and quantitate qPCR results, depending on what they are used for, Veronica and her peers relied on the "Livak-method," which was colloquially referred to as "the Delta-Delta C_T" ($\Delta\Delta$CT).[12] This method is founded on the assumption that amplification efficiencies of both the gene of interest and control fragment are equally at 100%, and within 5% of each, so that every PCR cycle doubles the amount of nucleic acid in the test tube.[13] Handily, template spreadsheets with ready-made algorithms for calculating the "Delta-Delta C_T" were handed over to newcomers from senior peers in the community. These historically accumulated resources could then be adapted to different experimental designs. Here, we see how the mutability and "unfolding variations" of inscriptions allow a scientific community to adapt inscriptions to their own particular uses (Kaiser, 2009: 7). Adaptability, not immutability, makes these representations efficacious within the cognitive ecology of the experimental system.

The calculation procedure used by Veronica and her peers had four steps. Here, a simplified example of the computation and its parameters must serve as an illustration:

- First, the difference between the C_T-value of the TARGET GENE in the *untreated* sample and the C_T-value of the REFERENCE GENE in the *untreated* sample is identified.
- Next, the researcher must find the difference between the C_T value of the TARGET GENE in the *treated* sample, and the C_T value of the REFERENCE GENE in the treated sample.
- She then calculates the difference between these two values.

- This difference is then squared over two, yielding the $2^{\Delta\Delta CT}$, which provides a measurement of down-regulation of genes in terms of relative, or "fold'-differences (in the work of Veronica and her colleagues, multiple genes were often tested at the same time, yielding a significantly more complex matrix than the simplified example displayed in Fig. 6.3.

At this point, researchers commonly ran statistical tests on C_T-values to determine whether the treated samples displayed significant down-regulation compared to a reference sample. As data from qPCR are seldomly normally distributed, meaning that data points do not form a bell-shaped curve when plotted in a diagram, I was told that

$\Delta\Delta C_T$	Treated	Untreated
Reference	15.5	14.3
Target	22.2	18.5

$\Delta\Delta C_T$ =
(CT (target, untreated) - CT (reference, untreated)) -
(CT(target, treated) - CT(reference, treated) =
treated - untreated

$\Delta\Delta C_T = (18.5\text{-}14.3) - (22.2\text{-}15.5) = 4.2 - 6.7 = -2.5$

$2^{\Delta\Delta CT} = 2^{-2.5} = \underline{5.66}$

The relative ratio of expression in the treated target sample is 5.66 fold lower, compared to the untreated sample.

Fig. 6.3 An algorithmic-level description of how "Delta-Delta CT" is calculated. This idealized table provides hypothetical values for a treated and untreated condition for a target gene. It highlights the arithmetic operations used to complete the computation. In practice, values are calculated based on averages from several biological replicates, which requires more complex spreadsheets. In Veronica's experiment we saw that the qPCR protocol advised using at least three replicates

null-hypothesis tests were usually of the non-parametric variety. (Occasionally, values were log-transformed, and parametric significance tests applied). Finally, the representational output from this procedure was a bar graph or boxplot. Here, expression levels, error bars displaying data variability (confidence intervals), and results of statistical significance tests (with a significance level, Alpha, usually set at 0.05), could be read from the same graphical representation[14] (Fig. 6.4).

These representational outputs from qPCR were an important source of evidence when considering claims about the effects of RNAi-induced gene silencing, and for making causal inferences about gene function. Together with morphological, and other sorts of molecular evidence, scientists at the Centre could use these to evaluate which genes were reliably silenced by RNAi, and the potential for investing more research in specific candidate targets. In the case of Veronica's qPCR experiment, the data turned out to be ambiguous. While she initially thought she had come across an interesting phenotype, later analysis showed that several experimental confounds were in play, such as the presence of a viral pathogen in the samples that caused doubts about previous interpretations of lice morphology. After laboriously cross-checking her results, Veronica concluded that these candidate genes were not worth pursuing further and that resulting phenotypes from the RNAi experiment could not conclusively be attributed to an interference response. In the time ahead, she would continue her research on fibronectin domains by performing new rounds of RNAi experiments and qPCR measurements on other genes from her list.

Making Meaning: Image Schemas, Conceptual Blends and Material Anchors

In the ethnographic descriptions above, we saw how Veronica's accomplishment of qPCR was afforded by chains of interaction with a number of "substrates" in the laboratory. Through reuse, decomposition, and transformation, these helped her to see patterns of gene expression. By substrate, I follow Goodwin and refer to the use of material and conceptual resources in the laboratory as a point of departure for building

Time	Sample Name	2^-ΔΔCt	SD upper	SD lower
3 dpi	Ctr	1,00	0,81	0,45
	RNAi	0,37	0,03	0,02
14 dpi	Ctr	1,00	0,16	0,14
	RNAi	0,18	0,02	0,01
17 dpi	Ctr	1,00	0,31	0,23
	RNAi	0,05	0,21	0,04

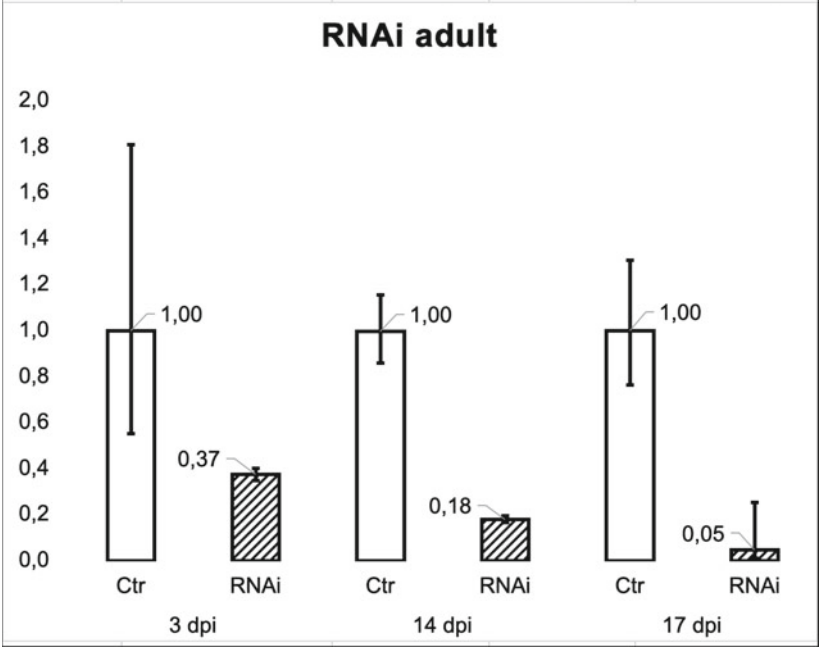

Fig. 6.4 Bar graph rendered by the author, based on a working spreadsheet exemplifying relative expression levels as a "fold-difference" in RNAi-treated adult lice. In this time series, measurements were made 3-, 14-, and 17-days post-injection ("dpi"). The first bar (3 dpi) shows under a 0.37-fold expression, compared to experimental control (normalized to a "1-fold" expression). The second (14 dpi), shows a 0.18-fold expression, while the third bar (17 dpi) shows a 0.05-fold expression, compared to the control. Results from tests of significance were occasionally placed on the bar chart to add information. This graph is based on a different experiment than the one performed by Veronica, but the general principle applies

subsequent epistemic actions (2013: 11). These substrates were not just a context for Veronica's actions but constitute a "semiotic landscape" for meaningful experimental work. In this section, I draw on theoretical resources from the distributed framework to scrutinize some ways in which qPCR emerges as a significant cultural achievement made possible by the material and social organization of the laboratory space as a cognitive ecology. What are the cultural practices that enable budding scientists like Veronica to wield artifacts in an epistemically productive way? To answer this, we must first review key developments in the study of meaning construction.

A key component of our capacity for meaning-making and reasoning about complex matters is a collection of basic "image schemas" based on how our bodies are constituted, which Turner describes as "skeletal patterns that recur in our sensory and motor activity under experience" (2003: 147). Evolutionarily speaking, image schemas derive from the fact that our primate bodies are positioned and act in three-dimensional space. They are "condensed re-descriptions of perceptual experience for the purpose of mapping spatial structure onto conceptual structure" (Oakley et al., 2010: 215). Image schemas are not fixed and static "pictures in the head," but flexible and dynamic activity structures representing different types of content. They are composed from spatial primitives through a process of schematic integration with non-spatial elements. Complex image schemas can be constructed on basis of simpler ones by combining, superimposing, specifying, and elaborating them. Through these prelinguistic, embodied image schemas, our species can draw on structures in sensory and motor modalities to make sense of abstract domains and infer the properties of very different entities, extending to higher-level mappings such as conceptual metaphors.

As products of embodied interaction, image schemas are exemplified by my own perceptions as they appear while I write this paragraph, sitting by my desk. Looking down on my feet I experience vertical orientation through a plane of reference running through my body's middle. Turning my head to each side provides a distinct sensation of a front and back, as well as two mirrored, opposing, lateral sides that I conventionally describe as right and left. Fingertips, arms extended, seem more distant from my body than my shoulders. I grasp the pen knowing that my

right hand is more dexterous than my left and enact movement through space by rising from the chair, stepping forward. Moving through the room, I experience my body as a trajector in an enclosed container. All of this is enabled by asymmetries in my body plan and the world, together creating spatial contrasts. These contrasts are powerful drivers of human reasoning.

Image schemas based around such embodied interactions inform both concrete and more abstract concepts. Not least, they underpin a variety of creative practices, such as science and mathematics (Lakoff & Núñez, 2000).[15] Higher-order concepts become meaningful via metaphoric expansions of familiar image-schemas derived from mundane somatic examples, like bodies positioned in space, manipulations of objects, and perceptual engagement with things (Oakley, 2010: 215). Conceptual metaphor theory argues that metaphoric thoughts arise by structuring one domain, a target, with elements from a different domain, the source. A familiar example from the history of biology is the conceptual metaphor A HEART IS A PUMP.[16] When William Harvey published his treatise on heart action and how blood moved through the body in 1628, he invoked the mechanical pump as his guiding metaphor. Properties of the source domain (PUMP), in this case a mechanical device with the ability to transport liquids to or from inaccessible places, could be transferred to the HEART muscle as the target domain. This, in turn, offered a heuristic scaffold that highlighted similarities and differences between hearts and pumps, making it possible to explore questions about pressure, circulation speeds of fluids, and so on. Understanding these aspects of pumps, however, depended on much simpler image schemas of patterned movement through space, force, displacement, containers, trajectories of motion, and kinesthetics. Here, basic image schemas become templates for the superimposition of perceptions, that mediate between experiences and our experiential representations. Interventions against salmon lice, for example, are often been framed through a conceptual metaphor of WAR: farmers talk about "winning the fight against salmon lice," and scientists talk about drug resistance as an "evolutionary arms-race."

Conceptual metaphors can be seen as special cases of a more powerful and ubiquitous process of human imagination that Fauconnier and

Turner call "conceptual integration networks," or simply "conceptual blending" (1998). This idea is based on the insight that background resources required for meaning construction are underspecified by grammar. Here, the proposed cognitive mechanism is a projection of selected elements from two different source domains in mental space that form a cross-space mapping that compose a generic, shared mental space which enables a dynamic "blend" of features. In this view, mental spaces are conceptual packets constructed by various frames and cognitive models through thinking and talking in ways that afford local understanding and action, where novel structure and features can arise according to the logic of the input spaces.

While conceptual metaphor theory is well equipped to account for entrenched structures of meaning held stably in long-term memory, blending theory better explains the structure of short-lived, local mappings for information integration generated in working memory, on the fly in various creative practices. As a basic mental operation that constructs partial matches between two inputs, and selective projections into a novel and emergent structure, blending produces new insight that can be co-opted by memory, aiding both construction and manipulation of meanings across domains of the human experience (Fauconnier, 2001: 2495). This process of conceptual integration produces a continuum of mechanisms for meaning-construction that unifies apparently disparate cognitive phenomena like categorization, analogy, metaphor, logical frames, and grammatical constructions, under one account.[17]

In its simplest form, as represented in Fig. 6.5, a conceptual blend or integration network is composed of two mental spaces that are cross-space mapped to a counterpart based on similarity judgments, providing partial input to a generic space. This generic space can later become a resource for building new integration networks. The blend itself constitutes a fourth mental space where the two inputs are being selectively projected to preserve certain features and compose new, emergent structures.

Figure 6.5 (left) illustrates ways that conceptual integration networks come together through mental simulation to create novel meaning. Composition sets up new relations among elements that are absent from the individual input spaces. Completion allows novel structure to be

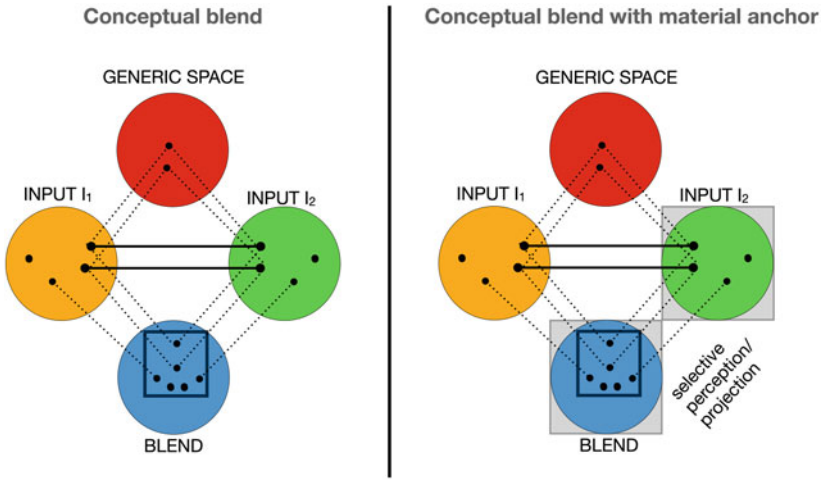

Fig. 6.5 Left: adapted from original notation by Fauconnier and Turner (1998: 143). Circles represent mental spaces. Generic space is made of a structure belonging to both input spaces. Solid lines define cross-space mappings of counterpart connections between two inputs. Dotted lines indicate connections between input space and the other space. In the blend, structures from the input spaces are run together. This creates novel structure from the selective projection from inputs (not all inputs are projected into the blend). Novel structures are represented with a square with additional dots in $BLEND_N$. Right: Hutchins (2005) introduces a new notation for conceptual blends with a material anchor as one of the input/source domains, marked by a square around the mental spaces of INPUT2 and the BLEND. Physical elements in the external world can enter conceptual practices via selective perception and projection

interpreted against a background of cognitive and cultural models, filling in certain missing aspects, patterns, and relations. In elaboration, or "running the blend," a new structure that is not present in the inputs develops according to the blend's internal logic. Patterns of activity in one domain can be coupled to another domain through partial cross-space mappings of counterparts in the input spaces, as well as selective projection and creation of emergent structure in the new blended space.[18] Resulting from these processes is a compression of entities like time, space, cause-effect, identity, and change into a distinctly species-specific human scale. These make reasoning about complex affairs possible for

enculturated and embodied minds. As a cognitive phenomenon, conceptual integration reveals that higher-level conceptual structures, like those accumulated through scientific practices, are composed from intermediate forms, which are in turn supported by more basic lower-level image schemas rooted in embodied experience.

Extending beyond language, conceptual blending also supports the "general and ancient" phenomenon whereby mental and material structure jointly enable and constrain a wide range of cognitive processes (Hutchins, 2005: 1555). By introducing external, material elements into the blended space as an input condition, as seen in Fig. 6.5 (right), new resources can be made available. This affords human cognition with stable computational properties and enable new forms of reasoning that are unavailable in more ephemeral, conceptual forms. Hutchins calls these phenomena "material anchors for conceptual blends". By taking seriously the effects of material culture on meaning-making, it is possible to account for many diverse cultural productions, including scientific practices. The notion of a queue, for example, can be produced by combining the image schema for a simple conceptual trajector moving through space, and superimposing it on a row of material elements. As such, the abstract cultural models studied by cognitive anthropologists are not just lodged in individual heads but embodied by the physical structure of material artifacts. In this view, scientific activities form a constellation of cognitive activities on a continuum of practices for meaning construction and knowledge-making (Ellen, 2004; Nersessian, 2010).

Maintaining Conceptual Structure in QPCR with Material Anchors

How do these cultural-cognitive abilities manifest in laboratory benchwork during qPCR? Much of the analytic work in Veronica's activity system is accomplished with support from machine computation. Some of this advanced instrumentation appears as epistemically opaque black boxes for her peer community. With respect to the Applied Biosystems 7500-machine, the constraints that must be satisfied to execute qPCR

and identify expression levels in targeted genes, are clearly given by the biochemical properties of reagents in the test tubes, the device's optical detectors, and assumptions built into the computational transformations that are carried out on digital signals that produce a graphical representation on the monitor. Here, some of the action has been separated from human agency, as "working knowledge" built into the reliable behavior of the artifact (Baird, 2004: 45). However, for the machine to do its designated job, producing useful outputs for the ensuing representational cascade involved meaningful measurements of gene expression, Veronica also had to solve a series of spatial problems drawing on a variety of plastic resources. These related to the ordering of test tubes and their content, as well as manipulating representations of the tubes in accordance with the internal logic of her experiment. This work was performed in ways that made inputs accessible for the machine, as well as making the outputs meaningful for her own subsequent interpretations of relative gene expression levels in the samples, considering accepted background knowledge.

Keeping track of representational states and their constraints, is a major challenge for any cognitive activity, qPCR included. To reason meaningfully about an object or process, its associated conceptual structures must remain cognitively stable while the object of scrutiny is manipulated and transformed. Many cultural practices solve this problem by using material anchors for conceptual blends (Hutchins, 2005). In the molecular biology lab, the challenge of stabilizing representations by anchoring them in a sea of conceptual and material complexity, becomes especially pertinent in the context of handling nucleic acids. The contents of test tubes are invisible to the naked eye and cannot be differentiated visually, without using additional resources. Given that the amount of liquid being manipulated on the bench is usually limited to a few microliters, nucleic acids and other biochemical reagents only appear as homogenous specks of fluid on the test tube's bottom. No matter one's level of expertise, the content of these containers looks the same, as there are few clues to tell tubes or well plates apart, except for occasions when dyes are used. Since mixing up samples has disastrous consequences for experimental outcomes, experimentalists like Veronica and her peers are deeply concerned about keeping track

of them as they propagate through the pipeline, by taking actions that exploit multiple layers of accumulated semiotic and material resources within their cognitive ecology.

To interact with these contents and maintain stable representations about relevant constraints, biologists incorporate meanings and sedimented structures built by coworkers into the organization of their own epistemic activities. One way of tracking items in the world is through the deceptively simple act of labeling something. In Fig. 6.6, we see how Veronica has marked the tube caps with unique inscriptions using waterproof markers. This act of labeling, as a cognitive practice, makes it easier for the agent to later assess and evaluate the state of the world and pick out relevant objects, thereby avoiding contamination or mixing up samples, in ways that would bring the experimental process to a halt. Time, experimental facilities, and reagents are all precious resources in molecular biology.

The photograph in Fig. 6.6 depicts an assembly on the bench from a brief procedure known as DNAse treatment, that I briefly described Veronica engaging in, before she synthesized cDNA from her sample of RNA molecules and initiated the qPCR. Here, we see how Veronica labels the caps on her test tubes with a sample number, having inserted them in a vial rack chronologically. When looking carefully, however, we see that labeling is not all there is to this process. Additionally, Veronica (like her peers) employed a range of other vehicles to create material and conceptual order in the work. In the picture, a red vial rack contains the original samples, while the other holds samples treated with DNAse. The black box contains special tubes that will be used for the PCR reaction. Here, we see that the experimenter has not merely labeled, but also individuated the tube containing the DNAse mix and a tube with H_2O, to avoid confusing them during pipetting.

When I asked Veronica about why she organized her workspace this way, she explained: "it makes pipetting very easy because I can now pipette the same sample many times over." Reliable qPCR results needed meticulous execution, and Veronica interpreted her actions as aligning with epistemic norms about proper benchwork in the lab, solving a set of practical pipetting problems in the process. Furthermore, this

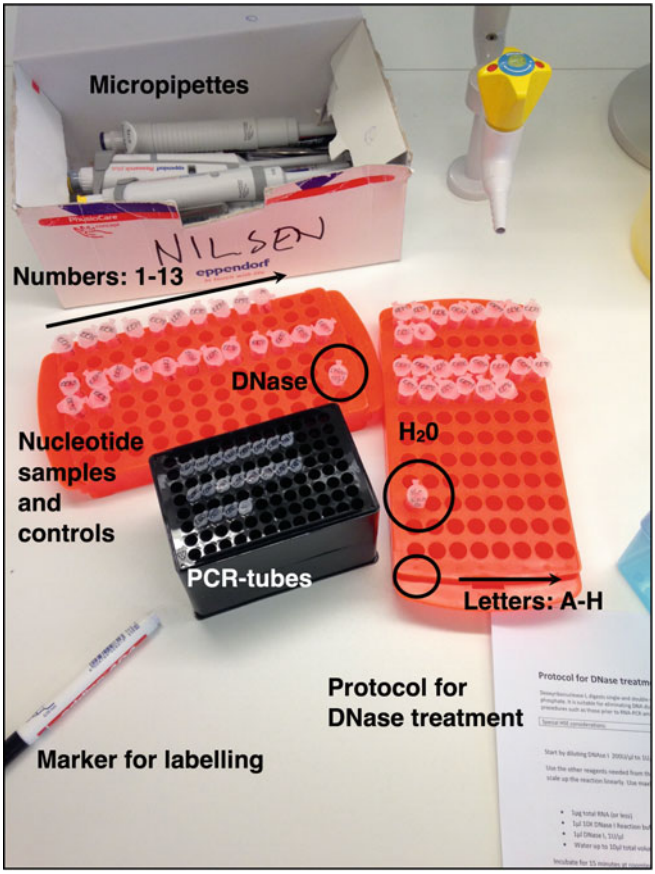

Fig. 6.6 Creating stable representations of phenomena and keeping track of test-tubes in DNAse treatment. Vial racks contain wells for organizing test tubes: rows are marked with numbers, columns with letters. A drawn arrow highlights the superimposed, imagined trajector in space that moves horizontally and vertically across the plate during work. Tubes are organized along the number line with labels. Notice the compartmentalization of reagents into clusters of similar kinds that can be noticed and exploited to accomplish the task. These spatial arrangements simplify perception. Out of view, there is ongoing "cultivated opportunism" on the bench (Kirsh, 1995: 49). Clutter and items are left around to strategically display their affordances in the lab, thereby multiplying chances of "getting something for nothing."

was not just an idiosyncrasy of Veronica's. Identical strategies for organizing benchwork could be observed among her peers, who accounted for their practices in similar terms. Complementing this insider perspective about how it makes pipetting "easy," I conjecture that we are not simply dealing with a pragmatic action on the bench, in the sense that it brought Veronica closer to her physical goal. On the contrary, these operations were profoundly epistemic in nature since they really concern the transformation of an informational environment with potentially far-reaching consequences for experimental outcomes. Of particular interest, is how Veronica engages in a set of sense-making routines that Kirsch calls the "intelligent use of space" (1995). This was achieved by using the physical space of the bench and her plastic vial racks as material resources to maintain conceptual order for later analytical processes. From a strictly representational perspective, one could misleadingly think that labels would suffice for this task. But not so for researchers who are enculturated to the laboratory. Here, they become capable of projecting conceptual structure onto the world and materialize cognitive processes through physical rearrangements of different media (Kirsh, 2010: 445).

Kirsh observes that we should not see management of spatial arrangements in our immediate environments as an afterthought, but as an "integral part of the way we think, plan, and behave, a central element in the way we shape the very world that constrains and guides our behavior" (1995: 32). To execute qPCR, Veronica outsourced some of the necessary computational work to her spatial environment, in such a way that the bench, and what it contains, becomes carefully maintained resources providing a continuous supply of affordances for thinking and action. Here, the Gibsonian notion of affordance is understood as an opportunity: "a dispositional property of a situation defined by a set of objects organized in a set arrangement, relativized to the action repertoire of a given agent" (Kirsh, 1995: 43). Mental representations of test tubes and their contents do not suffice to productively manage qPCR measurements.

In addition to inscribed labels on the tube caps, the edges on the red vial rack in the picture are also seeded with representational structure in the form of precomputed numbers and letters that encode spatial relations (together forming a coordinate system). During pipetting

and downstream processing, these precomputed inscriptions accomplish several things. First of all, they change the task structure and redistribute the workload of pipetting so that the users may read the letters and numbers from the well's edges, instead of counting each one and keeping the count lodged in working memory. Interestingly, Veronica made this artifact somewhat redundant, due to her exploitation of other available ecological structures that she assembled on the spot. Instead of using these fixed values while pipetting her reagents into the tubes, she rather superimposed a basic image schema, an imagined trajectory moving from the left to the right, on the physical array of tubes. By imposing this trajector, she effectively projected a queue on her materials for her pipetting actions that served as a guide for future activity. Thereby, she explicitly encoded information about which tube to operate next in physical space. When things form a linear pattern, they are predictable, and the agent knows where to look for the next item to complete her material engagements.

Insignificant as they may seem, these accomplishments are crucial for successful experimental results, and made possible by exploiting a broader class of "trajector-based" cultural practices (Hutchins, 2014: 38), a subset of material anchors for conceptual blends. In Veronica's case, the first input space in the blend contains the imagined trajector, while the second input contains the physical array of tubes. Here, the conceptual order of benchwork necessary to complete qPCR emerges from a composition that effectively creates an action sequence. The blend's actionable effect is that Veronica can now see a queue of tubes to be serviced in an order that aligns with the experimental design, and not just a line of random objects in space. By completing the blend, Veronica can also reason functionally about which element to service next. This creates more opportunities to reflect and elaborate on her task, such as which tube was used first, which sample goes last, how many she has left before she can take a break, the number of controls, and so on. As Hutchins points out, these simple building blocks have powerful cognitive effects since these questions cannot be answered when lines of objects are simply experienced as lines, and not as trajector-based queues (2005: 1559). Note that the reagents are also clustered in space and bundled together

on the array so that they form "equivalence classes" reflecting key properties. This creates an additional memory encoded in local space that helps track the array of samples as they move through the laboratory and get transformed into meaningful measurements of gene expression.

I contend that Veronica's encoding of samples and their properties in physical space presents us with a fundamental epistemic activity essential for obtaining productive experimental results from the system. While this constellation of resources was locally adapted to the needs of Veronica's problem-space, material engagements of this kind were ubiquitous in laboratory benchwork at the Center. These practices are not universal modalities for organizing cognitive work but situated cultural performances with a history.

Meaning and Measurement on the Benchtop

I mentioned that Veronica, in advance of entering the DNA lab, had created a template design for all her experimental replicates in the RNAi trial on a digital spreadsheet, which is visible in Fig. 6.7B. This template offered an additional solution to the problem of maintaining conceptual and material order in her samples. Its basic structure was inherited from senior predecessors in her community, who had successfully performed qPCR many times before. Veronica then adopted this shared spreadsheet template to her own experimental configuration and printed the modified sheet on a piece of paper, which she brought with her into the workspace of the DNA lab.

Initially, this spreadsheet functioned as a regulatory representation that governed the distribution of other representations within Veronica's ecological assembly, providing long-term structuring of her environment. But as can be seen in Fig. 6.7, the grid that emerged from the spreadsheet also provided a material anchor for subsequent bench interactions with the microplate. Later, this relationship was reproduced on the computer interface. This act preserved and stabilized structural correspondences between the various elements of her experimental design while she was busy labelling the correct input and proper relationships between the samples on the computer. Here, she ensured that

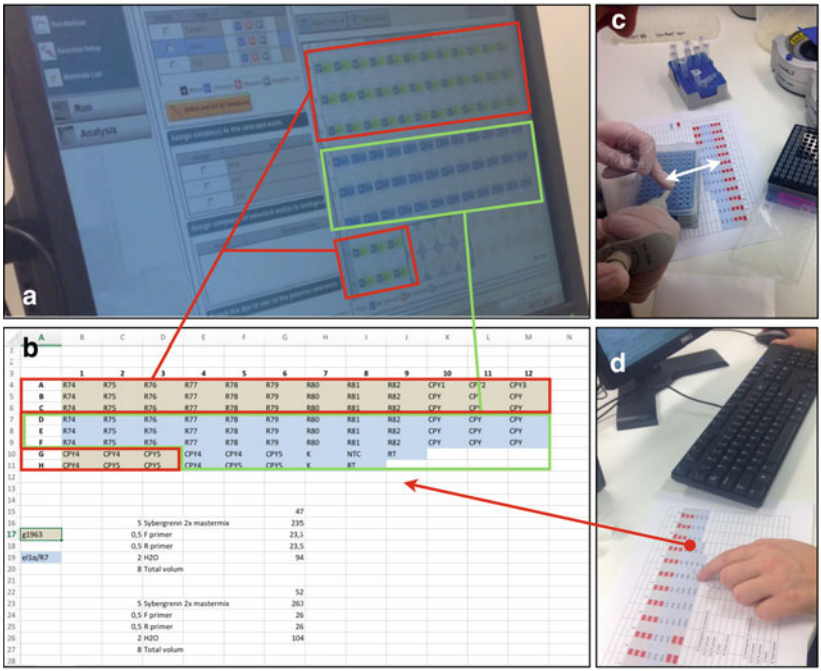

Fig. 6.7 A spreadsheet acquires epistemic function through ecological assemblies for the intelligent use of space. The artifact functions both as a regulatory representation for distributing experimental conditions and their accompanying inscriptions, as well as a "jig" in specific assemblies. **a** and **b** show alignment between the digital interface of the qPCR-machine and the spreadsheet prepared by Veronica before entering the lab. **c** displays how the spreadsheet is used by Veronica to organize an array of reagents as she pipettes her samples into a 96-well microplate before qPCR, according to her experimental design.[19] This action was accompanied by "shadow-counting" each step aloud, ensuing further representational stability for the operation. The bottom right picture (**d**) shows how the representation is physically enacted when setting up the qPCR-machine's interface. Veronica traces each column with her fingers to stabilize the layout, while entering the correct values and labels on the interface. In this diagram, cells with sample tubes are highlighted in red, while cells with various experimental controls are green

the machine's outputs, like the C_T values, would correspond to the correct physical structures and biological material on the microplate. Only then would they become meaningful in relation to the overarching experimental design. This assembly set up a multi-directional informational flow between Veronica and multiple artifacts, whereby each small incremental step in the configuration of elements not only determined the next stage of the task, but also changed the task structure itself (Heersmink, 2015: 585).

By executing these benchtop operations as part of her qPCR-experiment, Veronica created an interconnected ecological assembly using artifacts that simplified choices, reduced the complexity of perceptual processes and removed the strain of internal computation. Together, this helped to maintain conceptual order on multiple levels. Among the simplest constituents of her practice was the individuation of objects, the smallest informational structures possible in this physical space. Next, she used the cultural practice of counting, which can be technically defined as "the coordination of an internally generated sequence of number tags with a partitioning of perceived unitary objects" (Hutchins, 1995a: 138). Maintaining order in the samples as they were handled, required Veronica to track a partition as it moved in a trajectory across physical space. Here, it should be noted that the workbench itself limited the array of things that could potentially be noticed and attended to, setting up a physical "frame" for Veronica's actions.

Again, Veronica mobilized the cognitive strategy of trajector-based conceptual blends in her assembly. By imposing an imagined trajectory on the top of the microplate, as well as the grid constituted by columns and rows on the spreadsheet, new structure emerged on the bench. This compositional technique set up a queue that laid out the order by which fragments should be serviced, handled, and labeled on the computer. Although the 96-well microplates and vial racks were seeded with imprinted numbers and letters along the edges, these inscriptions were again made redundant by Veronica physically encoding the spatial order, as she consecutively partitioned the well plate's surface by servicing the tubes from left to right, top to bottom. Each tube being serviced thereby marked the position of the next sample in line.

Starting at the top, as seen in Fig. 6.7B, Veronica allocated her first fragment, named R74, in the working order of column 1A to 1F, and then proceeded to fragment R75, A to F, and so forth. During pipetting, the serviced tubes in the partitioned space were filled with a visible residue of fluids, effectively tagging them as "completed." But visual inspection did not tell Veronica which fragment was contained in each tube. By aligning the excel sheet with the microplate and test tubes, she used a graphical representation to place additional constraints on her action space, ensuring that the right substance went in the correct well.

Figure 6.7 shows how the spreadsheet, when orchestrated alongside dexterous hands, micro-pipettes, computers, and other lab equipments, assumes a different representational function than a regulatory one. Veronica effectively uses the spreadsheet as a "jig" (Kirsh, 1995: 37). Jigs are cognitive artifacts that stabilize processes, and they are critically important for expert performance in many domains. In her hands, the sheet stabilizes allocations of reagents and reduces degrees of freedom in the target objects, both during pipetting, and when she interacts with the computer setup-wizard for qPCR. Drawing on the vocabulary of Kirsh, we see that her action combines both physical and informational jigging. She plants information in the environment to reduce perceived degrees of freedom, but also litter her surroundings with material impediments that reduce physical degrees of freedom. Her coordination thereby generates representational stability through a series of intermediate, short-term structures so that, finally, each gene fragment can be correctly labelled in the computer interface in advance of running the qPCR analysis.

Successful accomplishment of this will result in the device naming the expression level values for each well in the output file correctly and in accordance with her experimental design, thereby preserving meaningful relations within the experimental constraints for later analysis. Here, we see that spatial structures in the laboratory were not only central for the discovery and commercialization of PCR as a novel biotechnology (Rabinow, 1996: 142), but remain epistemically vital for PCR as an everyday accomplishment, long after it has sedimented into a technical thing in countless laboratories.

Remembering the exact layout of all her eighty-nine fragments on the microplate would be extremely demanding in terms of the necessary

internal mnemonic resources. Instead, Veronica opportunistically made that information locally available by continuously consulting the representations on her paper sheet throughout her activity. Orienting this array to her own actions on the spot, she thereby updated the status of her activity system in accordance with the experimental design. At one point, visible in Fig. 6.7C, Veronica even aligned the paper sheet directly with her well plate during pipetting to further reduce the cost of her visual searches, supporting the correct transfer of materials from one location to another. Later, she used her finger to highlight the cell of interest on this grid, facilitating a comparison between sheet, tray, and screen when engaging the software interface on the qPCR machine. Besides using the sheet as a model representation, she also traced its layout with her fingers and verbally counted the units in the array while simultaneously engaging with the computer interface via the mouse to input the correct values and set her experimental settings right. In effect, she did not need to form a complex mental model of the objects of interest (e.g., the experimental design) and store this in memory. Nor did she need to mentally rotate the microplate or perform other demanding computations as she proceeded. Veronica used objects on the benchtop to make the world into its own best model for what she wanted to accomplish, a world that she could easily consult through embodied interactions before engaging in her next course of action.

As representational media, computers have become essential instruments to support reasoning about gene expression. The cultural accomplishment of scientific work like qPCR requires an intercalation of what Michael Lynch identifies as two orders of laboratory activities; the interface between the "opticism" of scrutinizing eyes at work with various epistemically enhancing instruments, and the "digitality" of fingers (digits) manipulating computer interfaces (1991: 61). As Veronica's actions during qPCR reveal, making sense of nucleic acids, their properties, and complex pathways requires both skilled manipulation of the computer, but also a precise orchestration of paper representations, and other materials, often in parallel. These interactions with material artifacts does not only translate between the world of sight and world of touch, as Morana Alač reminds us; they afford a permeability between

digital realms and the physical task space of concrete actions on the bench (2011).

The case of qPCR also highlights how cognitive artifacts simultaneously take on "representational" and "non-representational" functions in scientific practice (Heersmink, 2013).[20] Representational artifacts contain informational structures about the world. They accomplish cognitive effects through C. S. Peirce's familiar triad of iconicity, indexicality, and symbols. While icons create isomorphisms between the representation and what is being represented, indexicality relies on causal connections between an index as a representation and the represented object. Many artifacts also take on symbolic functions, based on representations whose meanings derive from conventional arrangements and shared use. Epistemic enhancers like qPCR, whose purpose is to give measurements of gene expression, achieve their cognitive effects by combining these three semiotic properties. The relation between machine-made curves that display relative gene expression levels and the nucleotide content of test tubes for Veronica and her peers is not only isomorphic, but also an indexical relation, since the detectors pick out causal properties of increased fluorescence. Additionally, a wealth of symbolic conventions annotates these displays, and meaningfully brings together isomorphic and indexical information. Non-representational or "ecological" artifacts, on the other hand, do not contain information about the world, but "as" the world. The trajector-based conceptual blends based on a choreography of test tubes, microplates, and other paraphernalia, exemplify how the world becomes its own best model by manipulating physical space.

The Pedagogy of Ecological Assemblies and Cookbook Biology

Scientific concepts like qPCR manifest through embodied, interlocking practices (Hutchins, 2012), situated in the social and material settings of the laboratory where these concepts are enacted through experimental efforts. Ecological assemblies, like those manufactured by Veronica as she meaningfully enacted qPCR, come together on the spot depending

on circumstances peculiar to the task at hand. Knowledge about proper workspace organization, and correct ways of handling specific artifacts within the experimental system, is part of a corpus of habitual practices instilled by senior community members in newcomers via a complex chain of cultural transmission. Many of these benchtop practices become institutionalized through the Centre's "hidden curriculum" (Mody & Kaiser, 2008: 382). Beside techniques, these include epistemic norms and values that motivate and guide research on the parasitology of lice. Reproducing this institutionalized knowledge, within the Center's cognitive ecology, counteracts disorder in practice by preserving functional continuities in the experimental system over long timespans. This is achieved by entraining novices to acquire necessary expertise before more experienced predecessors eventually leave the system (Hutchins, 2012).

At the department where the SLRC was hosted, students of biology underwent rudimentary laboratory training on the undergraduate level and were expected to master a range of practical tasks by the end of their graduate studies. When novices like Veronica joined the Centre, usually during their master's projects or early in their Ph.D. program, they would train with a laboratory technician to educate their attention and acquire the necessary skills to efficiently maneuver in their research. Experimental expertise was partly defined through the intelligent mastery of the material and spatial surroundings of the lab. One of the first tricks-of-the-trade that novices acquired was the skill of informational restructuring their work environment, like Veronica did, to constrain the scope of future activity in a focused environment for action. It was not uncommon that members of the community justified their practices with reference to something they learned from their predecessors, senior lab members who had epistemic success with a given practice in the past. Some of these resources were communicated explicitly, some unavoidably emerged from the spatial and temporal organization of the lab, and some were copied and adapted implicitly through participation in the craft. By institutionalizing certain cognitive practices within the experimental system, it could be robustly organized in the face of individual variability.

Many of the critical skills necessary for bench work cannot be transferred propositionally but were acquired through repeated performance.

A most critical competence for molecular biologists in the DNA lab was mastery of the micro-pipette, the device Veronica used to transport small amounts of reagent and biological matter while working the bench. Manual control of the micropipette was rehearsed during early training sessions, often under the supervision of a senior, and we saw that pipetting is always performed in orchestration with other artifacts within the lab's cognitive ecology. At the microlevel of material engagements, the ability to pipette correctly is cultivated through incremental and gradual coordination between hands, pipette, and eyes, and an assortment of supportive tools, through repeated motor routines which over time produces the skilled laboratory worker. While ostensive instruction plays a role to instill first principles about how pipetting should be executed, the acquisition of expertise depends on a significant portion of reinvention and entrainment that instills practitioners with the capacity to create the kind of ecological assemblies I have described above. With reference to Clifford Geertz's notion of "local knowledge," science historian Hanz Otto Sibum has introduced the term "gestural knowledge" to account for such complexes of skills and mastery, that are inevitably developed in real-time performances of experimental benchwork (1995: 76). Micro-pipetting, for instance, required intricate *fingerspitzengefühl*, fine-tuned gestural knowledges that concern performances such as:

- Choosing the right pipette for the job (generally, one should always use the smallest pipette possible to handle the volume, since accuracy decreases when smaller volumes are handled with larger pipettes).
- The ability to correctly hold the pipette in hand and set its adjustable volume.
- Maintaining the smoothness of "plunger" action, which requires tacit familiarity with the level of resistance exhibited by the "plunger" under different conditions.
- Correct immersion of disposable sterile plastic tips when drawing in liquids from samples or reagents.
- Properly coordinating the pipette with the receiving tube.
- Having a "feeling" for the relative viscosity of different solutions.
- Making routines for changing pipette tips between new liquids.

Adaptive use of the plunger, the lever sitting atop the pipette, exemplifies the dexterous complexity of the task. Plungers stop at two different positions when pressed. A first point of resistance presents the loading volume, as the user inserts the tip gently into the liquid to be extracted, just sufficient to cover the instrument's tip. The plunger is then released, and the content is drawn into the tip from the container. Following this, the pipette is then transferred to a receiving vessel, where the user presses the plunger all the way to the second point of resistance. This discharges the last drop of liquid. Subsequently, the tip is withdrawn, but without releasing the plunger, and the plastic tip is discharged using a special button over an appropriate waste bin before a new tip is pressed onto the pipette from a neatly arranged box.[21] At first, the pipette is opaque, and requires strenuous concentration to wield properly. But over a period of habituation, the device may become "transparent equipment," seemingly natural extensions of the body that effortlessly dovetails with the sensory-motor system of the unskilled user (Clark, 1998: 38).

Skilled practitioners must also learn to create downstream corrigible control systems to monitor proper execution of their own pipetting tasks. The sources of variation for a given qPCR experiment are not limited to biological samples alone, since actions like pipetting can potentially introduce major technical sources of variation. Depending on the performer's technique, tubes may end up with slightly different amounts of reagents, or nucleotide template, which has cumulative effects downstream in the pipeline when the qPCR reaction takes place. As Veronica herself reported, neat organization of the bench through the intelligent use of space presented one way of counteracting such disorder. But we also saw how Veronica set up technical replicates to help with error checking, as the protocol suggested use of three such replicates.

Before concluding this chapter, we must attend to a final, conspicuous piece of enabling material culture in Veronica's workflow, known as a "kit" among biologists. Kits, which are figured in the periphery of the ecological assemblies described above, refer to a collection of epistemic and cognitive artifacts, peculiar for the craft practices of benchwork in the molecular biosciences. Kits are functional systems, based around three constituent parts (Weiner & Slatko, 2008: 701). First, the kit contains one or several reagents with various input materials. Second,

it contains instructions that guide researchers in performing biochemical reactions on said materials. Third, the kit transforms the input materials in a way that creates similar outputs, as long as the input materials are identical. Everyday experimental biology, of the kind performed by Veronica and her peers in the DNA lab, is premised on the mastery of a wide range of what Walter Gilbert has laconically described as "cookbook techniques" (1991), which are based around the cultural availability of commercial kits as a pedagogical resource. Gilbert observed that graduate students in the early 1970s had to labor hard to make their own restriction enzymes, proteins that cut DNA at specific sites in the nucleotide sequence. By 1976, these enzymes could be purchased in standardized form from the sales catalogues of biotech companies. Today, very few molecular biologists know how to make restriction enzymes, and knowledge about these reagents, along with many other molecular techniques, are managed by a small number of specialized enterprises providing services to the global research community.

Nowadays, kits range from very simple assortments of reagents bundled together, to highly complex setups, with the most advanced kits enabling whole-genome sequencing. But the use of kits, or "systems" as they were originally called, was hotly contested at first. One reason for the controversy over these epistemic artifacts was that their "cookbook" nature effectively black boxed many scientific practices. In the past, newcomers to molecular biology would have to master these to be recognized as competent practitioners. One concern was that students would no longer be able to make sense of their own experiments, since kits make learning about foundational biochemical principles in laboratory work obsolete. Today, it appears that the epistemic benefits of speed, convenience, and experimental control have outweighed the arguments of critics, as progress in all fields of molecular life science has come to depend on kits (Fig. 6.8).

In practice, kits and the recipes that accompany them, are put to use in a variety of functional systems in the laboratory, such as RNAi and qPCR. But as Lynch and Jordan have remarked, laboratory protocols seldom provide their users with complete and exhaustive specifications of what is sufficient and necessary for successful performance (1995). Novice experimentalists must therefore rely on non-codified, situated

Fig. 6.8 Rapid Amplification of cDNA ends is a method to obtain full length-sequences of cDNA. An enzyme, reverse transcriptase, is used to reverse-engineer mRNA into cDNA before segments are amplified and sequenced. The figure shows the unboxing of a commercial kit from Sigma-Aldrich (Merck) for the 5′ RACE-reaction. The kit contains twelve standardized components that suffice for ten reactions

knowledge, derived from other members of the community to accomplish many central benchtop activities. Since not all these artifacts are informationally and procedurally transparent, there must also be widespread epistemic trust in the justification of "dispositional" beliefs concerning these complex technologies in the extended peer community. If necessary, these can be mobilized to give a precise scientific account of the how and why of a given technology. And while kits are shortcuts that outsource parts of cognitive and physical labor through time and space, they do not substitute for technical competency altogether. At the SLRC, for example, it was primarily senior laboratory engineers who had recognized expertise on the selection of kits, and who advised lab members about augmenting them in appropriate ways. Some reactions, for instance, could yield adequate results by using less amounts of expensive reagents in a reaction than suggested by protocol, thereby extending a costly kit's longevity.

A key epistemic feature of kits is their standardized nature, which ensures a level of quality without the need for labor-intensive control routines. Kits also embody a principle of modularity that underlies many practices in contemporary molecular biology. Modularity, according to Bradd Shore, "virtually defines the cognitive landscape of modernity" (1995: 117). While the adaptive benefits of modularity can account for the durability of natural forms of modularity, modularization is a pervasive design strategy that breaks complex cultural wholes into elementary constitutive parts that in turn can be recombined in a range of patterns. As a foundational schema for modern manufacturing, the modular strategy embodies values like flexibility, efficiency, and control. These values are highly regarded in the "Fordist" data-production regimes of contemporary biology (Stevens, 2013).

Traces of modular design are abundant in the laboratory practices of biologists. Like in many other universities today, the Centre relies on gene sequencing services offered by a "core facility" at the host university, which is operated by specialized, dedicated personnel. Veronica and her colleagues regularly handed over test tubes with nucleic acids to the shared Sequencing Centre on the 5th floor of the high-technology Centre. A few days later, they would receive an email with a file they could open on their computers to visualize the nucleotide sequence

belonging to their gene of interest. These practices are effectively kits "writ large," that outsource cognitive labor and puts additional distance between scientists as epistemic agents and the methods they depend on (Weiner & Slatko, 2008: 702). Here, the modular nature of social and technical practice makes it possible to distribute cognitive tasks beyond any one particular workbench and experimenter to originate new ideas and meanings in the laboratory.

Conclusion

This chapter has closely examined the tool-saturated environment of the DNA laboratory at the SLRC. Focusing on Veronica's execution of qPCR, a quintessential method for learning about gene expression patterns in salmon lice, it has explored how this space is constituted materially and semiotically. I showed how meanings are construed by attending to activities at the microlevel of material engagement that, at first glance, appear epistemically trivial. Closer scrutiny reveals these as central for epistemic success.

Once more we have encountered how epistemic enhancers in the lab extend cognitive abilities, far beyond the normally sensory range of human beings. Theories about gene expression and the biological properties of nucleotides are built into objects like qPCR machines and kits. But these devices do not work purely through an "instrumental objectivity" where human judgment has been removed and where the scientific object speaks alone, with human agents only as passive witnesses (Baird, 2004: 191). Rather, such enhancers are softly assembled into new ecological assemblies by canny users to become critical infrastructures for exploratory efforts. For the qPCR machine Veronica used here, there are nine different instructional booklets available. Additionally, there are dozens of available tutorials for specialized experiments on the device, such as genotyping, presence/absence experiments, standard curve experiments, and various reagents and their protocols, each with their own product number. A tech-support hotline, and software help-package addresses any issues that may appear while engaging with

the instrument. Using each of these materials to solve scientific problems requires new constellations of resources to be assembled on the spot.

Intuitively, cognitive artifacts may appear as pre-given, isolated objects in the problem-solving environment. This ethnography, however, shows how material practices throughout the experimental system's pipeline integrate resources with different properties in powerful ways to scaffold scientific thinking, and creates new representational structures in the process. My interactional analysis of how Veronica executed qPCR demonstrates a powerful role for materiality in the "descent of meaning" (Turner, 2003: 139). In the humdrum of mundane laboratory activity, we see how construction of material anchors for conceptual blends through the use of image schemas and the intelligent use of space, contribute to the production of novel biological insights about what genes do. "Superpositioning" of material structures on the bench to create order (Hutchins, 2012: 318–319), plays a central role in facilitating "conceptual sex" (2003: 140), the process whereby parent meanings come together, recombine, and begets offspring in the form of new structures of meaning.

Performance of qPCR is an interplay between physical, social, and conceptual elements, but the source of the observed organization in the activity was not simply lodged in Veronica's head. It emerged from the larger cultural-cognitive ecosystem. Knowing everything there is to know about the brains of young scientists like Veronica would still not be sufficient to explain her epistemic accomplishments. Ethnographic studies on these dimensions of laboratory practice offer clues about the representational structure of her activity, which again provide insight into the informational properties of the larger system and its emergent cognitive functions. Parts of this problem-solving environment were premade, like the structure of Veronica's pipette and reagents, test tubes and microplates, the machine and its computer software. These were put to creative use by the canny cognizer on the fly to create tailor-made affordances for actions that exceeded the properties of a handed-down material culture. In the end, the many representational and physical transformations undertaken by Veronica in the above, would eventually be integrated to produce an output in the form of a few single values that enabled further meaning-construction about biological entities. This

was a baseline for decision-making about functional questions like "what does this gene do?," "was the RNAi successful?," or higher-level questions such as "is this a good vaccine candidate?" Since Veronica reported that the particular gene described in the above events *did not* merit further pursuit, other explorative screening experiments would come to fruition in the future.

The availability of modular equipment and modular practices enables progress in contemporary molecular life science. Here, purely generic systems are few and far between; universally standardized artifacts become accommodated and assembled to specific organisms and experimental designs. qPCR offers a telling example, as the method has now expanded into medical diagnostics, and become a staple of fish health science and veterinary services. Fish health biologists and veterinarians in aquaculture now routinely use qPCR to detect and diagnose disease in fish. The technology has become so widespread, that even fish farmers with little training in molecular biology and biotechnology, have been envisioned as potential users of the method. In 2014, for example, the company Europharma advertised a new device known as the Genesig Q16 to salmon producers. Manufactured by Primerdesign Ltd., this small and cheap qPCR-machine was heralded as a potentially revolutionary instrument. Originally designed for testing consumables, infectious disease, biohazards, and for veterinary applications, the device, which comes with standardized kits for more than 500 applications, has been projected to play a role in the future of fish health diagnostics. With this device, the laboratory could be brought directly to the tissue samples, rather than the other way around.

As Arthur Kornberg, who received a Nobel-prize for his studies of DNA polymerase once said: "when sophisticated instruments and fine biochemicals become commercially available and affordable, research is extended a thousand fold" (quoted in Rabinow, 1996: 30). This statement can be read as a testament to the power of ecological assemblies for human cognitive flourishing. When transporting qPCR from the lab and into the wild, users will surely find new ways of creating representational and conceptual stability to reason about target domains. How this happens without the infrastructure of the laboratory raises interesting

questions from the view of distributed cognition but is far beyond the scope of this study.

The material practices examined in this chapter are powerful cultural ratchets. Cognitive ethnography helps us noticing phenomena that would be partly invisible for the analytical toolkit of a cognitive anthropology that sees mind and knowledge as contained by skin and skull. While communally shared cultural models provide one source of representational stability, I have used the distributed framework to highlight other sources for creating new knowledge and insight. When this view is adopted, it is clear that we cannot do without the notion of representation in the study of meaning-making and knowledge-production, in contrast to some anthropological proposals (Ingold, 2000; Toren, 2012).[22] But in recognizing the centrality of representations in the social production of knowledge, it should be clear that I do not suggest that a sole focus should be on disembodied, symbolic, mental representations lodged "in the head." Instead, we must refine and re-specify our conception of representation, in a way that recognizes the centrality of material engagements and allows us to recast the boundary of minds to consider what happens outside the individual agent. On this matter, I concur with Malafouris' diagnosis that "the science of mind and science of material culture are two sides of the same coin" (2013: 13).

In the final chapter, I direct the "Cognito-scope" toward the practice of collaborative microscopy. While some specimens from RNAi trials end up on RNAlater, others were placed on "fix" for further processing through visual inspection. Here, we will pursue the question of how scientists see meaningful biological complexity in lice tissues with the help of a microscope, among other things.

Notes

1. A long-standing debate concern levels of analysis in the study of "difference-makers" like genes (Godfrey-Smith, 2013: 89). "Classical genetics" and the "modern synthesis" of evolutionary biology, see genes as an abstract hereditary unit (a "factor"), using tools like linkage maps to study their position on chromosomes and calculate recombination

frequencies of inherited traits. This idealization was not based on biochemistry or the information-bearing role of molecular structure. In contrast, molecular biology "de-particlize" genes, as macromolecular sequences of nucleotides whose transcription and translation are regulated by factors organized on the scale of genomes. In biological practice, these conceptualizations productively co-exist.

2. Nersessian offers a useful ontology of laboratory artefacts (Nersessian, 2006: 131). "Devices" are engineered facsimiles used as in vitro models and sites of simulation; "instruments" generate measured output in quantitative or graphical form; and "equipment" assists with manual or mental labor. In my examples, artefacts functionally cut across this classification.
3. For a general introduction to bioinformatic tools for sequence translation, see http://www.ebi.ac.uk/Tools/st/.
4. Terms like "qPCR" and "real-time PCR" are used inconsistently. Here, I describe the latter, which uses RNA that is reverse transcribed into cDNA as a starting template. The Minimum Information for Publication of Quantitative Real-Time PCR Experiments suggest the abbreviation RT-qPCR for this kind of experiment. To ensure ethnographic fidelity, I refer to this procedure as "qPCR."
5. Therefore, answering the question of "who invented PCR" is hard, despite Kary Mullis winning the Nobel Prize in 1993 for his contribution. The story of PCR is too complex to elucidate here; as Rabinow's informant quipped about the messy affair: "Conception, development and application are all scientific issues - invention is a question for patent lawyers" (Rabinow, 1996: 6).
6. dNTPs are molecules made of ribose or deoxyribose sugar, covalently bound to a nitrogen base, which contains a nucleoside bound to three phosphates (it is sometimes called a nucleotide when it has phosphates connected to its 5-prime end). Technically, nucleotides are classified as nucleosides, and have a suffix describing the number of attached phosphates (e.g., mono- or triphosphate).
7. The method relies on a principle called "fluorescence resonance energy transfer" (FRET). The Molecular Probes Handbook from ThermoFisher Scientific, a supplier of scientific instruments, describes FRET as: "a distance-dependent interaction between the electronic excited states of two dye molecules in which excitation is transferred from a donor molecule to an acceptor molecule without emission of a photon" (Thermo Fisher Scientific: the molecular probes handbook, 2017).

8. An alternative type of qPCR is an "endpoint semi-quantitative PCR," where data is collected at the end of the amplification reaction, and where the template content is measured by back-calculation.
9. Commenting on a draft of this section, one researcher remarked: "The DNA polymerase translates RNA to DNA, but we don't know if there was DNA in the sample before (in case DNAse treatment didn't work sufficient). In that case we would get a wrong fluorescence signal, […] a mixture of the real signal from RNA and wrong signal from DNA. To avoid a wrong signal, we usually, if possible, also design primers in a way that they span over the exon-intron border."
10. Absolute and relative quantification are two main analytical methods supporting RT-qPCR. Absolute, or "standard curve"-quantification calculates the sample's amount of template (e.g., for estimating viral load). This description concerns relative quantification compared to a control sample, as my informants were comparing the results of an experimental condition with a baseline control.
11. Problems are determined by evaluating plots of variables in the experiment for outliers, atypical amplification, irregular amplification, threshold values and faulty baselines. The plots and their meanings are specified by the qPCR-machine's user manual.
12. Δ is the symbol for delta, meaning "difference," The "Livak-method" is named after the first author of "Analysis of Relative Gene Expression Data Using Real-Time Quantitative PCR and the 2-Δ ΔCT Method" in the journal Methods (Livak & Schmittgen, 2001), a highly cited paper in the history of science.
13. Lab workers occasionally ran a "standard curve" experiment alongside the variety described here, to account for deviations in the reaction's efficacy. This is done by diluting the template and checking how an idealized 100% efficacy compares to actual efficacy.
14. A significance level of 0.05 means there is a 5% probability of getting the observed result, or more extreme ones, given that the null hypothesis is true (usually that there is no difference between treatments).
15. This view contrasts with "the romance of mathematics"; a belief in mathematical Platonism, where the structure of mathematics is conceived as existing independently of minds (Lakoff & Núñez, 2000: xv).
16. Following conventional notation, I write analytical concepts like image schemas, conceptual metaphors, and blends in small caps.
17. Four prototype integration networks have been proposed (Fauconnier, 2001). Simplexes takes one input as a frame (schematic knowledge like

"buying groceries") and uses specific elements in the other to fill roles in the frame. In mirrors, network spaces share a common organizing frame. Single scopes take inputs from different organizing frames, but the blend inherits only one frame. Double scopes use identity properties and essential frames from both inputs to resolve clashes between fundamentally different inputs.

18. Conceptual blends follow optimality principles. A blend must be integrated as an event that can be operated on as a uniform unit, where input spaces and elements match its respective counterparts. Manipulation blends must also maintain a web of connections and facilitate unpacking, so that users can meaningfully understand the connections to other elements in the blend.
19. This formatting differs from the paper sheet used at the bench, due to the use of different software for reading the original file provided by Veronica. Structural relations between elements are identical.
20. Heersmink distinguishes between "technology," as intentionally made physical objects, and "technique" which comprise skills, methods and procedures for doing (2013: 468). While both are "artificially" developed by humans, only the former class constitutes physical objects. Techniques are internalized through enskillment (although people may rely on external instruction for complex actions). Heersmink suggests that natural objects adopted for cognitive goals constitute a separate class of "naturefacts."
21. Pipettes are calibrated at regular intervals to maintain their accuracy.
22. Toren, for example, mistakenly writes off distributed cognition as "dualist" and "ahistorical" (2012: 36).

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7

An Anatomy of a Microanatomy

It is Friday afternoon, and the Christmas of 2013 is drawing close. Activity at the Sea Lice Research Centre has noticeably wound down before the holidays. In one of the 3rd floor microscopy labs, adjacent to the rooms where nucleic acids are diligently being processed, we find two scientists leaning against their respective eyepieces, deeply engaged in an intense session of collaborative microscopy. Tom is a senior professor experienced in histological analyses of tissue sections, while Hanna is a postdoctoral candidate and a newcomer to the field. Trained as a molecular biologist, working with "whole" animals as her object of analysis is a rather fresh experience. It contrasts with the methods Hanna normally employs to understand the behavior of lice genes in the laboratory, where she usually interacts with the parasite at the level of gross anatomy and the molecular scale. Fascinated by microanatomy, Hanna has eagerly pursued this new gland-mapping project under Tom's guidance. They are motivated by the hope that better understanding the glandular system's organization and developmental timing in lice can offer useful insights for ongoing efforts to characterize molecular pathways involved in modulating and suppressing the host immune system.

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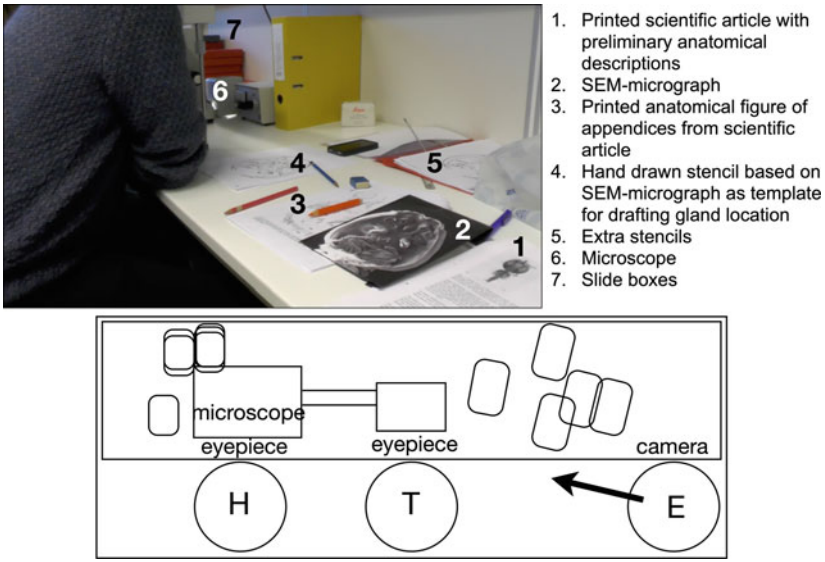

Fig. 7.1 Orchestrating representational artifacts on the bench during microscopy. Simplified birds-eye view of relevant parts in the scene, including placement of camera and ethnographer (E)

Laid out in front of the collaborators, on the professor's side, is an array of colored crayons, pens, pencils, a print-out from a photo taken with a scanning electron microscope (a SEM-*micrograph*), a scientific paper with an incomplete description of some other salmon lice glands using a whole mount staining technique, and a hand drawn stencil, based on the micrograph as its template. To the left, on Hanna's side, hidden in Fig. 7.1, are stacks of boxes containing hundreds of microscope slides of *L. salmonis* specimens.

In the moments leading up to the events in Table 7.1, Hanna has just inserted a new slide on the microscope stand and adjusted the instrument's focus to better see the specimen. The two then start scanning the slide's scene, looking for meaningful structures as their gaze shifts between landmarks on the histological landscape that is projected onto the eyepiece. By turning the microscope's knobs, Hanna can move the specimen around. Her interactions with the delicate instrument are careful; it is easy to lose one's bearings in the vast anatomical vista of a

Table 7.1 Excerpt from conversation

1	**Tom**	But what about those next to there? Is that the saliva-complex, no?	*Adjusts magnification with right hand*
2	**Hanna**	No, it is not	
3	**Tom**	But	
4	**Hanna**	They are pretty far down, now I started where we left off on the other side, or the other sections	*Moves her left hand and taps the slide box with a flat palm, three strokes*
5	**Tom**		*Taps fingers, twelve strokes*
6	**Hanna**	Because usually	
7	**Tom**	But there come three glands, or two plus a muscle, are the other big one hemolymphs?	*Waits, taps hands gently on the bench, thirteen strokes*
8	**Tom**	But is that, that one in the middle there, what?	
9	**Hanna**	Did you think of this?	*Moves specimen into focus with her right hand by adjusting knob on the stereo microscope*
10	**Tom**	Mmm, the one in the middle, what?	
11	**Hanna**	This one? I think we've seen it before, we thought it was a kind of muscle	*Moves to turn knob controlling arrow visible in the microscope's visual field*
12	**Tom**	Mhm, I just thought it did not look like much of a muscle, but I might be wrong	
13	**Hanna**	Yeah, we've tried to look at those before, but don't know if we concluded with certainty	
14	**Tom**	Yeah, but I think the one we saw, we concluded with certainty	
15	**Hanna**	Moving a bit backwards	*Removes the current slide and places a new one on the microscope's plate*

tissue slide, especially if the specimen is moved around suddenly. Also, eyes tend to tire after peering into the ocular for hours. As Tom admitted after a particularly long session, this sort of work requires a bit of "monomania" and the epistemic payoffs were far from guaranteed. In his words:

Fig. 7.2 In line 1–2 (left image), Hanna moves specimen into the center of the visual field by adjusting the knob with hand. In line 9 (right image), Hanna moves her hand from the lower knob to upper knob, to control an arrow pointer in the visual field that allows highlighting of microscopical objects

"the more you look the more nuances appear; the question is whether the nuances you see really matters."

The slow, steady pace of work also makes ethnographic observations challenging. As an experienced technician admitted, during a prolonged session in front of the electron microscope: "watching other people using the microscope is the best sleeping medicine." Unless, that is, one can maintain a disciplined and vigilant focus on the minute details of interaction between microscopists and their material environments, where meaning-making activities of deep interest to the cognitive ethnographer become visible (Fig. 7.2).

Above is a sample of what the two scientists say to each other and do to create meaning from a microscopic piece of salmon lice tissue within a time span of roughly 2 min and 40 s. Speech acts are written in plain font, while concurrent interactions in other modalities are written in cursive on the right.[1]

Overview

How do biologists, like in the interaction[2] above, arrive at shared understandings of microscopic phenomena, and jointly see them as meaningful entities? Previous chapters have looked at how representations are propagated through various representational media within the experimental system at the Centre, in ways that support new insights about the biology of salmon lice. Such knowledge does not spring from abstract sequences in a clean and tidy lab facility. They began accumulating on basis of observations of the gross behavioral repertoires of lice as they latched onto their prey. Strains of salmon lice, and their hosts, were then domesticated into new laboratory facilities. In wet labs, lice were subjected to bioassays that further probed behavior and physiology, all the way down to the molecular level with the help of RNAi and other biotechnologies. Salmon lice were physically transformed from living matter into tissue samples, and homogenates from which nucleic acids could be extracted. Later, these were converted into gene expression measurements, subjected to histochemical methods, and a variety of other representational modalities. In previous chapters, I looked closely at select examples from this experimental pipeline and described how these entities were represented, and what tools were needed to do the representing.

Here, I examine a series of events sampled from the activities of a small group of researchers at the SLRC who set out to describe the anatomical structure, distribution, and developmental trajectories of exocrine glands in *Lepeoptheirus salmonis*. In this work, insights about the secrets of salmon lice exocrine glands were acquired through the practice of "histology," anatomical studies of biological tissues with microscopes. After introducing the ethnographic context of microscopy at the SLRC, the chapter turns to some general epistemic issues concerning the acquisition of new knowledge about microscopic things. These epistemological mediations, which take Ian Hacking's work on representation and intervention as a point of departure, problematizes what it means to see and represent things using an apparently prosaic instrument.

This sets the stage for zooming in on a series of collaborative work sessions in microanatomy that stretched over a two-year period, and

mainly involved Tom and Hanna, with occasional help from other colleagues. Their mission was to map the biological landscape of exocrine glands in lice and provide a descriptive model of these structures, knowledge which was believed to be central for better understanding parasite–host dynamics. Tracking the work of Hanna and Tom as they interact with imaging technologies, I show how biological meaning is created by carefully examining and manipulating scientific visuals. As in previous parts, the methodological dictum for the cognitive ethnography is still asking the question of what information goes where, when, and in what form.

My analysis is based on participant observation in thirteen sessions of microscopy. Depending on the ethnographic circumstances like suitability, timing, respect for my interlocutors' need to focus, some of these events were audio-recorded while other segments were captured on digital video. Ethnographic observations were sampled from compound light microscopy, with additional forays into sessions involving scanning electron microscopy. Observations also covered laboratory preparations of tissue samples and the production of scientific visuals, such as *in situ hybridization*. I was also given access to drafts, notebooks, sketches, article manuscripts, and correspondences with scientific journals about the peer-review process.

In the excerpt above, we saw an example of how collaborative microanatomy, or "histology," requires participants to mutually orient their attention to the same phenomena of interest by creating spatial reference to aspects of the biological tissues at hand. Here, I demonstrate how spatial language, along with a range of other semiotic resources, enables practitioners of microscopy to mutually attend and create reference to microscopic phenomena to constructively reason about them. Through the cognitive ethnography of interactions in front of the microscope, analysis of inscriptions in laboratory notebooks, and anatomical descriptions from scientific research papers, I demonstrate how novel insights emerge through engagements with research materials and laboratory techniques. These discursive practices integrate and transform representations in ways contributing to the perception of novel biological structures and are thus a source of epistemic progress in the field of microanatomy.

Interactions between scientists and the microscope are neatly captured by Hacking's maxim "don't just peer; interfere" (1983: 189). To render their "domain of scrutiny" meaningful (Goodwin, 1994: 606), my interlocutors had to compare and crosscheck their microscopic observations with other scientific representations. These included digital media from other imaging techniques and scientific visuals produced through histochemical methods like *in situ hybridization*. Eventually, new biological meanings were created by fashioning multiple models of lice exocrine glands, bringing microscopic visuals into coordination with ephemeral language and more durable inscriptions and artifacts of various kinds. Here, my analysis builds on Alač, whose ethnographic study about fMRI-practice demonstrates how scientific visuals meaningfully orchestrate propositional language and multimodal representations to create hybrid semantic structures (2011: 144–145). When situated in the cognitive ecology of the lab, tissue sections become malleable substances and joint fields for multimodal interaction. This hybridity between language and other semiotic resources, becomes a precondition for how scientists perform, manipulate, and make sense of microscopic objects of interest.

Microscopes and Histology at the Centre

Like few other apparatuses, the microscope epitomizes the scientific instrument. Although I regularly observed staff practicing microscopy in the lab in a variety of contexts, its central role for knowledge production first dawned on me during one of the Centre's weekly lunchtime laboratory meetings. These events, which lasted up to an hour, offered an occasion for management to disseminate information about urgent matters. And although these meetings sometimes collided with time-sensitive experiments, they offered a forum for exchanging ideas and opinions about ongoing work at the Centre, presentations of novel research findings, and discussing matters of general relevance to the research community.

Outlining a program for an anthropology of knowledge, Fredrik Barth proposed that all knowledge traditions consist of "a substantive corpus of assertions, a range of media of representation, and a social

organization" (2002: 1). As social architectures that can serve many epistemic functions for the research group, lab meetings offer a microcosm for interrogating how different faces of knowledge interrelate to produce "tradition-specific criteria" for the validity, transmission, and reproduction of knowledge within a community. As Dunbar suggests, such meetings offer a most representative cross-section of the ways scientists think and reason in vivo (1999: 86). In these encounters, we can observe how scientists discuss competing models and diagrams, design and dissect experiments, examine errors, tell alternative stories and explore the feasibility of ideas. Dunbar also found that lab meetings are events where scientists freely move between analogy and metaphor, make deductions and inductions, expose unexpected knowledge gaps, determine next courses of actions, and distribute reasoning among colleagues. Laboratory meetings also highlight the germination of novel projects, and how the representations underpinning scientific breakthroughs can often have fuzzy origins. As ideas propagate, they get subjected to transformative exchanges between a cast of characters, rather than emerging fully fleshed out from the mind of individuals.

At the SLRC, laboratory meetings also served important pedagogic functions. They familiarized newcomers with the problem-space being explored, and the available means to explore this landscape. The knowledge being performed during meetings also displays the community's epistemic standards, and benchmarks for what is expected of newcomers. Such expectations were communicated through informal talk, presentations, and discussions about salmon lice biology, methods, and technique. This "hidden curriculum" of epistemic virtues serve as a guide to the research community's "moral economy" (Kohler, 1994; Mody & Kaiser, 2008). It lays out the bounds of acceptable behavior, and legitimate forms of knowledge production. While aspects of this moral economy can be rendered explicit on occasion, many dimensions are tacit and habitual, surfacing only when expectations are broken.

One Monday in early September 2013, the group gathered for their weekly update. After a general briefing by the Director about funding deadlines for the EU Horizon 2020 research program and Open Access publishing, the topic eventually turned to pressing issues concerning the staff's use of microscopes. Word was given to Tom, who was responsible

for overseeing these instruments and helped train newcomers in their use. He said that "a couple of accidents" had occurred in the lab weeks before, deserving the group's attention.[3] Among his main concerns was the soiling of an objective for a high-end microscope. An unknown perpetrator had made a mess during oil immersion microscopy, a technique developed to increase the resolution of microscopes under certain conditions. Microscopes consist of many parts, and when light passes through different materials like biological tissue, air, and glass, it is broken and bent as it travels at different speeds. Optical concepts, like the refractive index, describe how light bends and the ratio of radiation speeds. Microscopic lenses work by reconstructing scattered light. However, on very large magnifications the resolution of conventional "dry" objectives is poor, as light refracts on its journey through different media toward the eye. Consequently, it becomes hard for the viewer to separate two objects in the visual field. By immersing the specimen and objective lens in a transparent oil with the same refractive index as glass, this effect can be countered, as the microscope's resolving power at large magnifications is increased. Someone had attempted to use this oil immersion technique but applied oil on the wrong objective and without cleaning up the costly tools. Sorting this mess was exasperating work, so the next time somebody wanted to try oil immersion microscopy they would have to ask permission and get proper training. Microscopy called for a specialized craft pedagogy and legitimate practical apprenticeship.

Next, the professor lamented that their technician was overburdened by requests for tissue sectioning of lice. While researchers in other labs commonly prepare tissue samples themselves, microtome sectioning, mounting of tissue on slides, and staining was usually performed by an expert technician affiliated with the Centre. Tom announced that the research group had recently become too indiscriminate about which specimens they submitted for sectioning. When the technician had too much on her plate, the craftsmanship would suffer, he warned. Besides, many samples were likely never subjected to proper histological analysis. Meaningful scrutiny of phenotypes resulting from RNAi and gene expression profiling was time-consuming, and more sectioning was not always better. Such aimlessness was also costly and ineffective, in his opinion. Resources were being spent on sectioning tissues for no purpose

beyond storage, as a precautionary measure. Samples needed to be prioritized, as resources were finite. Unless sectioning was carried out in light of particular research questions, the Centre risked wasting its limited means. It was, in Tom's opinion, unnecessary to section controls for every RNAi experiment, and he reminded his colleagues that shared reference sections were available for comparative purposes. It was adequate to just section those biological structures that were targeted by the RNAi trial, and not the whole louse.

Tom's pronouncements spawned a lively discussion. Was the system rationally designed? Perhaps capacity really was too low? Could students learn to section their own specimens? One objection was that this craft would take too much time to master properly, as the lice cuticle tended to blunt the edge of the microtome and required considerable finesse to properly cut. Others disagreed about micromanaging sectioning requests; there was a real possibility of making novel discoveries in the absence of well-defined research questions. One professor observed that students had become so pressed for time in their research that they often "hedged" by sectioning a lot of specimens just in case they would be of use later. Other suggestions were floated. Could the Centre obtain sectioning services from other institutions, for a fee?

Although this discussion did not come to a satisfactory conclusion, reappearing from time to time, it illustrates that microscopy practice occupied a prominent role in the Centre's experimental system. Microscopes are instruments for seeing, and as Maurice Bloch suggests, the notion that "seeing is believing" has a long history, in both western intellectual life and various folk epistemologies (2008). In fact, there appears to be a preference for sight over other sensory modalities in many, if not all, societies. One reason why scientists do substantiate claims about the nature of biological entities with evidence from micrographs is because these representational media can be used for "showing and telling." This minimizes human intentionality and agency, placing more constraints on the veracity of a proposition than language alone can bring. Bloch hypothesizes that the deceitful nature of language, and its potential for lies, is the source of this widespread association: "Sight seems to offer a peep at the world as it appears to the senses, in contrast to the treacherous [linguistic] representations peddled by others"

(2008: 29). This presents a persistent challenge for scientific communities, which cultivate epistemic vigilance through an institutionalized imperative for organized skepticism. The gravity accorded to sight as the primary sense for empirical datum, for example, incentivizes deceptive uses of manipulated imagery. This has led to the emergence of rigorous guidelines concerning image integrity and processing. While adjusting contrast, color, and brightness of whole images is considered legitimate, any form of beautification, enhancing, obscuring, splicing, or elimination of specific items in ways that affect substantively the interpretation of images is considered deceptive and in violation of good conduct. Many journals have also effectuated procedures for detecting fraudulent manipulation of imagery, although there are multiple article retractions every year in molecular biology due to disagreements about the veracity of scientific visuals.[4]

Visualizing Biological Structure

Compared to the largest and smallest things in the universe studied by scientists, like galaxy clusters and the quantum realm, *Lepeoptheirus salmonis* is a medium-sized object. The size of the adult louse affords observation of gross anatomical features by careful inspection, without much visual augmentation. Adding a stereomicroscope, a sophisticated magnifying glass, affords an even better view of the well-adapted parasite at later life stages. However, many salient features of interest to my interlocutors exist on a much smaller scale. Seeing and reasoning about these biological phenomena necessitates an extension of sensory modalities, and they can only be accessed after lice tissues have undergone biochemical transformations that render properties usually invisible to a naked eye legible under a compound optical microscope. The stereomicroscope and the light microscope may look alike, but they are quite different instruments. Harnessing their powers requires different skills and background knowledge. When using the stereomicroscope, a researcher simply puts a specimen of appropriate size under the objective and peers into the eyepiece. Competent use of light microscopes, on the

other hand, requires transformative work on a much broader range of media to harness the instrument's representational properties.

To understand the logistical and epistemic challenge that tissue-sectioning presented for the research pipeline, one must grasp some basic principles of "histology," the study of normal tissue structures and how tissues are related to basic biological functions ('histopathology' is the study of diseased tissue). In contrast to the stereomicroscope, biologists cannot simply stick chunks of biological matter under light microscopes and gain much useful information just by looking through the ocular. As Hacking underscores, microscopes "does not work in the way that most untutored people suppose" (1983: 186). For microscopic materials to be informative, they must be intervened on in several ways. First, samples of relevant tissue are sampled from the organism in question. Small animals, like the salmon louse, can be sampled whole. This tissue must then be fixated to preserve affordances and maintain its structural integrity as close as possible to its live state, usually by placing it into a fixative solution, such as formalin in 10% concentration for a day or two, depending on the protocol being used.

Following fixation, the tissue is transferred to a small plastic cassette for processing and embedding. Water and formalin are removed from the sample and replaced with a solid substance that can be cut very thin.[5] While manual processing is possible, my interlocutors used a computerized device known as a "tissue processor" which could be left to run overnight. This machine is preset with programs that automatically administer reagents for dehydrating (using ethanol), clearing (chemically removing ethanol with an organic solvent), and infusing the tissue with warm paraffin wax (which is cooled), or other liquid mediums like epoxy resins (which require heating). These materials have different properties that may be harnessed depending on the histologist's interests. While resins can be cut super thin, paraffin embedding can be used when it is necessary to recover nucleic acids from the tissues after they are processed.

When infused with the medium, tissues are shaped into small blocks in special molds. These are then left to cool, usually submerged in a small tray filled with water (with a short stop in the freezer if paraffin is used). When taken out, the blocks can be cut into extremely thin sections on an

instrument known as a *microtome*. Extreme thinness is necessary so that the section is translucent enough that light may pass through the sample, about 3–5 μm. Operating the microtome requires fine motor skills and plenty of patience. A complete set of sections from a whole louse specimen, aligned in the dorsal to ventral direction, may consist of up to 300 individual sections (anterior to posterior cuts may run to the thousands, but are rare). After being carefully removed from the microtome, these delicate slices, only a few microns thick, are then floated in a water bath and left to straighten out before they are carefully transferred onto a glass microscope slide.[6] Finally, slides are placed on a tray and dried.

Although the first microscopes appeared in the seventeenth century, the work of making microscopical observations was very cumbersome (Hacking, 1981). While elites used microscopes as entertainment devices, the first aimed at a popular audience was based on ready-mounted slides for users to see anything at all; only expert technicians could use the instruments without such mounts. Hacking suggests that microscope technologies made little progress over its two first centuries, and optics did not become a branch of science before Ernest Karl Abbe, co-owner of Carl Zeiss AG, found a way to eliminate distortions in the 1860s. Despite some progress in optical theory, there was little headway in practical applications until people started staining tissues. Counter-intuitively, fresh biological tissues are almost translucent when cut thin, so placing them directly under a microscope yields little information, in contrast to the stereomicroscope.

The next step is therefore to stain slides for color and contrast. During staining, the paraffin or plastic is removed with a solvent, and sections are rehydrated. A wide range of buffered stain solutions (dyes) have been developed for different tissue types. For instance, when processing RNAi samples at the SLRC, my interlocutors would use plastic sections stained with toluidine blue. On the other hand, the principal "H&E" stain was used with paraffin sections, which consists of two counterstains that give a visually salient contrast: hematoxylin (H) stains cell nuclei blue, while eosin (E) stains cytoplasmic proteins, collagen, and muscle fibers red. Depending on the pH value of the tissue, various proteins may also appear strikingly different. After staining, slides are then either dehydrated in alcohol and treated with a clearing agent to remove alcohol to

make the tissue translucent or mounted without dehydration (the latter is often used in molecular visualization methods, like *in situ hybridization*). A synthetic mounting medium is then finally added to a small cover slip and placed on top of the sectioned tissue. The stained tissue is now protected, ready to be organized in a slide box, and further explored with the help of a microscope.

While the interactional analyses below are primarily sampled from events involving conventional light microscopes, I also observed multiple sessions with a scanning electron microscope (SEM). In the beginning of their quest, Tom and Hanna only operated this instrument with the assistance of specialists from the University's shared facilities for electron microscopy (*Elektronmikroskopisk Felleslaboratorium*), until Hanna acquired skills to productively wield the instrument unsupervised. SEM has much higher resolving power than a light microscope, which makes it possible to see whether two adjacent items are distinct objects at very high magnifications. Put briefly, the key difference between these epistemic enhancers is that a light microscope utilizes light beams for illumination and absorption of different wavelengths of light in the specimen, which are then focused and observed through an ocular. The electron microscope, on the other hand, uses an electron beam that scatters on the specimen's surface. On modern instruments, the resulting image is then reconstructed on a computer screen with three-dimensional depth of view. Scanning electron microscopy also requires specially prepared lice specimens. While having the advantage that samples can be "whole-mounted," the preparation for SEM is quite different from the thinly cut tissue sections used for optical microscopes or transmission electron microscopy (the latter yields flat, two-dimensional images of the object's *ultrastructure*).[7] Furthermore, "live" tissues cannot be subjected to SEM due to the electron beam's power (which heats the target), and the vacuum chamber (which focuses the beam, but require dry specimens to avoid water vaporization).

All innovators of novel scientific representations must persuade their peers that they denote objective states in the natural world (Gooding, 2004: 559). While Tom and Hanna used light microscopes to map internal structures, SEM was mainly used to explore the morphological

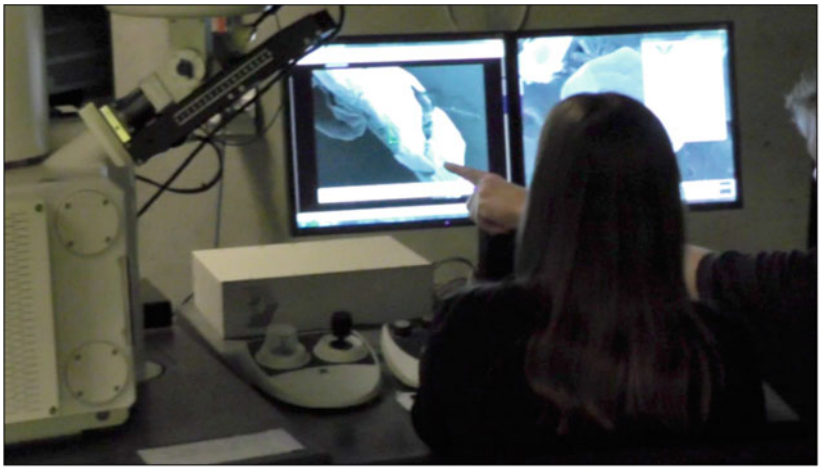

Fig. 7.3 Collaborative scanning electron microscopy of exocrine glands using whole-mount specimens. Tom annotates visuals on the screen for Hanna using deictic gestures

features of the parasite's outer surface, and to produce sharp three-dimensional images. As Tom explained in one session with the electron microscope, the main purpose of a future publication on this topic would, after all, be to showcase their observations of the lice exocrine system. Although no scientific representation is self-explicating and can speak for itself without a culturally elaborated coding scheme (Goodwin, 1994), a key ingredient in telling a scientifically interesting story about this system was annotated imagery that clearly and persuasively highlighted discovered structures to their peers. By observing the organism's exterior through the high-powered electron microscope, it was possible to get a holistic overview and collect data about novelties which could mutually corroborate their results from light microscopy (Fig. 7.3).

Exocrine Glands

Glands, the objects of scrutiny in Hanna and Tom's project, are biological organs composed of clusters of cells specialized for making substances

that the cells themselves have no need for, but are central for extracellular processes. Products of glandular organs are either released into the hemolymph, a fluid analogous to blood in vertebrates, and internal cavities. They may also be transported to the parasite body's outer surface through exit channels (although these may also be adapted for internal secretions). In the first case, the glands are classified as *endocrine glands*, and in the second case they are called *exocrine glands*. Their motivation for working on exocrine glands was twofold. More knowledge about the body plan and biological organization of salmon lice would be an asset for much experimental work, since functional macro-physiology provided an interpretative resource for molecular and computational analyses. Another motivation was the need for a detailed account of how exocrine glands in blood-feeding parasites produce substances that are secreted to the outer host environment. By investigating these glands and their anatomy there was also a slight chance of identifying potential therapeutic candidate genes that were highly expressed in these organs.

As Tom, Hanna, and colleagues argued in a draft manuscript on the subject, these glands "may secrete substances that modulate the immune response of the fish and limit clotting of blood from the host during feeding." Knowing where and when certain genes were expressed, could not only help resolve *structural* questions about the involved mechanisms, but also provide *functional* answers about how host interactions are regulated. This, in turn, could usefully inform therapeutic applications down the line. Work of this kind required fitting microscopic data to evidence from molecular biology, so that structures observed in the microscope could be individuated by their biochemical properties. Vice versa, these molecular data would ideally be interpreted in the light of macro-biological structures and processes, creating an interlocking fit between different levels of analysis (Fig. 7.4).

According to Tom, investigations at the molecular level were frequently launched in the absence of well-grounded models of higher level anatomical structures, where the purported molecular processes were assumed to unfold. As he expressed with some disbelief; some of their more molecularly oriented colleagues were not even aware that the structures they now dedicated time to meticulously describe were *glands*. They were simply referred to as "sub-cuticular tissue" in the literature.

Fig. 7.4 Slide boxes with stained lice tissues. Each slide is numbered and chronologically organized from the first to last section. This facilitates easy location and retrieval of relevant points of interest

Thus, researchers needed "a vocabulary" to describe what they saw, in his opinion. He considered the language of microanatomy to be "a language of its own." Detailed models of molecular pathways were not sufficient to make sense of the biological complexity of these organisms. Previous research on lice glands by others had only resulted in a rough draft of the topology and organization of structures like the frontal filament, its mucus-producing glands, and some pores and exocrine glands specifically located around the parasite's mouth tube. Additionally, there was some documentation of glands in the cephalothorax region and its genital segments. Previous attempts at whole-mount staining of the animal had only visualized the largest glands and revealed precious little functional information about the mechanistic nature of these structures and their classification. Arthropods have a complex segmented body plan with many joints and appendages, which become an immense and vast landscape under the microscope. Time and technical constraints therefore restricted the scope of Hanna and Tom's investigation to the head, the thorax region (*cephalothorax*), and thoracic limbs.

Contemporary life scientists primarily aspire to give mechanistic accounts of how biological systems operate (Bechtel, 2006; but see Myers, 2015 for a contrasting perspective). Tom and Hanna, for instance, wanted to craft an anatomical account of the structural relations between the different parts that constitute the louse exocrine glands, both in terms of the glands' spatial contiguity and the functional organization of different components within the larger system. As Bechtel points out, the preferred strategy of mechanistic explanation in biology requires both *structural* decompositions, by taking structures apart into their component parts, and *functional* decomposition, by looking at how the components operate in concert (2006: 31). While the microscopic journeys explored in this ethnography primarily concerned the structural decomposition of the exocrine system, this structural information could yield functional insight into the operation and orchestration of component parts, especially when coupled with molecular evidence.

The Scientist's Microscope and the Blind Man's Stick: Theory and Technique

What kind of cognitive artifact is a microscope, and what epistemic actions does the use of one entail? As popular icons of scientific practice, it is easy to imagine that you can just peek into the eyepiece and that a new, micro-sized landscape will open in front of your eyes. But while microscopes appear deceptively simple, as Hacking stressed, the scientific uses of this device are complex, multimodal activities, quite different from everyday notions of what it means "to see" something. This first became apparent to me, as I one day was sitting by the workbench next to Hanna, observing her microscopy work through an extra ocular on her instrument. As I was tracking her activities early in my study, she suddenly notified me that she was observing "interesting things". But although I was trying hard to see what she was saying, the tissue only appeared as homogenous mush to me. I realized my lack of crucial skills and concepts for making sense of what undoubtedly was there, somewhere in front of my very eyes.

Scientific visuals can sometimes be the starting point of an investigation, and at other times its endpoint. As such, they play an epistemically prominent role in both what philosopher Hans Reichenbach called "contexts of discovery" (i.e., the generation of novel ideas or hypotheses), and in "contexts of justification" which concern their defense, test, and verification (see Schickore & Steinle, 2006). To acquire epistemic status as evidence within any given research project, tissue sections must be subjected to considerable interventions. Acts of visually inspecting and reasoning about biological samples via the microscope also require human–instrument couplings that delegate some cognitive processes beyond the human investigator. As malleable materials, scientific visual must be transformed and manipulated to support reasoning. They are not just disembodied data resources for thinking about phenomena, but stuff that scientists think *with*.

One lesson from studies on the interplay between visual representation, instrumentation, and the perception of scientific objects we cannot ordinarily see, is that the couplings between scientists and their representational tools may take on surprising forms. To conceptualize such

couplings in terms of a cognitive ecology, Ed Hutchins invokes a thought experiment from Gregory Bateson, then inspired by the nascent field of cybernetic systems and regulatory feedback loops (2010: 706). Bateson asks us to imagine he is a blind man who taps around with his white cane: "Where do I start? Is my mental system bounded at the handle of the stick? Is it bounded by my skin? Does it start halfway of the tip of the stick? But these are nonsense questions. The stick is a pathway along which transforms of difference are being transmitted. The way to delineate the system is to draw the limiting line in such a way that you do not cut any of these pathways in ways which leave things inexplicable. If what you are trying to explain is a given piece of behavior, such as the locomotion of the blind man, then for this purpose, you will need the street, the stick, the man, the street, the stick, and so on, round and round" (1972: 459). His message is that prematurely demarcating the boundaries for our unit of analysis may hide central resources that emerge from mutual dependent relations among elements. By widening the notion of epistemic processes to include the exchange of representations between scientists and their situated environment, we can better account for the nature of such couplings. While the notion that "everything is connected" may be a truism, science still depend on exploiting nonuniformities among elements in different systems, and since Plato it has been a general principle of scientific inquiry to "carve nature at its joints" (Hutchins, 2010: 705). Articulating the world in a scientific manner, usually means looking closely at sites where there is low connectivity between things. This requires accurate representations of the world, including its unobservable parts. If we want to understand how microscopes and other instruments contribute to meaning-making, we must look closely at scientist–microscope assemblies as coupled systems. The microscope is to the scientist, as the stick is to the blind man.

Here, it is tempting to reach for analogies between a microscope's power to reveal the unseen, and visual aids like reading glasses. But like other imaging techniques, such as fMRI scans (Alač, 2011) and X-ray protein crystallography (Myers, 2015), microscopes do not afford views of the very small with the same ease as when we assess the weather by looking through a window, or put on a pair of glasses to read tiny print. Such analogies are deceptive and misleading.

It is, however, true that microscopes, like the blind man's stick, are interfaces that can become "transparent equipment" that works effortlessly for the user, with adequate training (Clark, 2008: 34). So, in what sense then is the act of seeing something with a microscope distinct from using a pair of glasses?

Well, let us again do some imagining. We train a chimpanzee with poor eyesight to wear glasses and examine a cluster of bananas at some distance, so the appropriate glasses help our chimp to better see the bananas, just like a human with poor vision can better see the fruit using the right spectacles. Now, we make the chimp and human layperson to peek into an eyepiece on a microscope that projects light through a stained louse section. Neither is familiar with microscopes or modern cellular theory. Would chimp and human see the same things? Well, since the projections to each species' receptor cells are fairly similar (both have trichromatic color vision), the difference between what they "see" in a restricted sense is likely not very different, and the scenery is unlikely to appear meaningful. However, switch out the layman with a properly trained biologist, and the human would see a different landscape manifest itself. Competent use of microscopes requires an arsenal of discursive practices, and the histologist would come equipped with conceptual coding schemes and practical resources for interacting with the device and construct meaning from what appears. Together, these resources constitute an actionable "professional vision" for probing the specimen (Goodwin, 1994), and the histologist can meaningfully articulate and engage what is being projected to her retinas. In what Michael Polanyi called the "tacit faculty" (2005: 105), sense perception, thought and articulation stands in an asymmetric relationship.

So, given that microscopes challenge everyday notions about what it means to see something, how does this seemingly mundane artifact help scientists achieve accurate representation of the world? Hacking clarifies this question, which he believes presents such a compelling argument for "medium-size scientific realism that philosophers blush to discuss it" (1983: 186–187). His first illustration comes from a former president of the Royal Microscopical Society: "There is and there can be *no* comparison between microscopic and macroscopic vision. The images of minute objects are not delineated microscopically by means of the ordinary laws

of refraction; they are not di-optical results but depend entirely on the laws of *diffraction*." Hence, the perceptual niche of microscopy is *sui generis*, as the view of a specimen is based on a synthesis of diffracted light rays, rather than "normal visual physics." In this context, talk of "seeing" in the ordinary sense is quite misplaced, bordering on a category mistake. This impreciseness is not due to a lack of correlations or fidelity between projections on the retina and what lays below the lens, but simply because the physical process of creating images with a modern microscope is not the same physical process that unfolds when we perceive something with a naked eye. What we usually see around us is a consequence of reflected light, but when peeking into the microscope we perceive a transmission or absorption of light traveling through very thin slices of tissue captured on glass slides. Dark or light areas correspond to the amount of light transmitted or absorbed. In a microscope, light is spread apart, so it appears to be emanating from a larger object than what is actually on the plate, and light scattered by the examined object is then reconstructed for the viewer who peeks through the ocular. Different microscopy technologies can exploit very different physical principles, far away from the domain of unaugmented human vision.

In contrast to a *sui generis* notion of microscopic vision, Hacking adds a different textbook conception where the microscopic image is said to instantiate a map of interactions between specimen and imaging radiation (Hacking, 1983: 190). This view appears to imply that microscopy is somehow a theory-loaded activity, where background theory is necessary to elucidate a map-like structure. To this Hacking objects. Microscopy is not "theory-loaded" in the sense that one needs theories of optics to successfully use the instrument. Theories are certainly necessary to *make* good microscopes but *using* them simply requires practice. So, while theory might explicate physical principles behind functional tools and help mitigate distortions, including *chromatic aberrations* (deviations caused by wavelength differences in light) or *spherical aberrations* (smearing of the object due to lacking focus of light rays near the lens' edges), competent practitioners can also learn to discount such issues through trial and error learning.

But although microscopic observation is not theory-loaded by necessity, neither is it entirely devoid of theory, as the practice has co-evolved

with conceptual systems like modern cellular theory. This body of supporting resources for sense-making offers detailed models of biological mechanisms and pathways, which help to articulate distinct entities with different shapes, properties, and variations. Since organismic materials are transparent and uniform regarding light absorption in microscopy, we saw that tissue sections had to be stained with dyes to enhance their legibility. This transformation is crucial for turning tissue slides into a meaningful structure, as the staining introduces salient bits of information through what Bateson called "differences which makes a difference" (1972: 315). Knowledge about how preparations of tissues affect their visual properties further illustrates how theory can be a meaning-making resource. As Hanna and Tom taught me during one of our sessions: since the use of solvents during the staining phase of tissue preparation changes the appearance of a section, the resulting patterns can support inferences about biological functions.

Importantly, some meaningful patterns could be used as discriminatory markers to distinguish between different types of glands. For instance, a working assumption was that if glands displayed differentiated patterns of extracted fat (characterized by tiny beads) or showed vesicles of radically different sizes, the glands did probably not produce the same content, and likely served different biological functions. In one type of gland being examined, salient patterns were found accumulating around its exit channels, in another, smaller and evenly dispersed patterns were located around the cytoplasm. In yet a different case, the glands under scrutiny were identified as potentially being multinucleated cells (*syncytia*), structures seemingly packed with secretory vessels. For a while, my teachers also hypothesized that there was a difference in the size of certain gland structures between starved specimens and lice that had been fed before sectioning. The assumption was that when lice fed on their hosts, they also produced and excreted substances that modified the salmon's immune response, which would alter the visual appearance of those glands.

Theoretical knowledge could also serve as a scaffold for deciding whether certain observations were "artifacts," anomalies due to processing errors like folding, tearing, and crushing, or biologically salient. During one stretch of electron microscopy, my interlocutors used

what they referred to as "the fat-test" to resolve whether an observation was an anomaly stemming from tissue preparations, or something of biological relevance. Solvents used for preparation of specimens would occasionally fail to extract all fat molecules from the sample. In cases of ambiguity, it was possible to focus the electron beam at the suspected artifact and increase its power to 15 kilovolts, thereby causing any remaining fat to be energized and crack the gold–palladium coating enclosing the specimen. Consequently, conduction in the specimen was reduced, which manifested on the screen as halos or smears. The cultural evolution of such techniques for discounting artifacts is central to the epistemic resolve of these instruments (Bechtel, 2006; Rasmussen, 1993). In microscopy, theory and practical technique have thus come to mutually support each other (Pitt, 2011: 191), to the extent that it is now possible to automatically censor noise and even reconstruct lost information in digitized micrographs using imaging software. It is the ability to mobilize this rich set of internal and external conceptual resources to construct meanings from what appears through the eyepiece, that sets a competent practitioner of microscopy apart from the chimp and untutored human.

Questions about observational realism with respect to what microscopes can reveal, thus largely hinges on the semantic issue of what we mean when invoking the verb "to see." While the antirealist would be skeptical about its utility in the context of microscopy, a pragmatist position suggests this word should be of little concern. After all, it is already put to good use to describe entirely intellectual pursuits with little reference to visual perception, as exemplified by statements like "I see what you are saying" (see Alač & Hutchins, 2004 for an intriguing ethnographic example). As Pitt observes in an essay "on the epistemology of the very small," the verb "to see" has changed meaning many times over, as new technology has become available to us (2011). Consequentially, ordinary language use has been modified in such a way as to disregard distinctions between augmented and unaugmented sight, so that it now works as an extended metaphor in the context of many different technologies for visual support. Furthermore, despite that the eye, rather than the embodied mind, is widely seen as the primary locus of perception (Hacking, 1983: 169), scientists do not accept the veracity of what they

see solely on basis of theoretical beliefs. Hacking, for instance, defends a realism of microscopical observation with reference to scientists' material engagements with their thinking tools. First, they can manipulate things under the microscope, to gain new perceptual skills in the process. Secondly, it is possible to craft microscopic entities with the same properties as things that can be observed without visual augmentation.[8] And third, different technologies for microscopic vision may display the same phenomena, dismissing the possibility that they are artifacts of any single instrument, or that observations are overdetermined by theoretical presuppositions.

As such, what counts as seeing and observing in the laboratory sciences today entails a liberal extension of what it means to see something. It is "a long way from the eye" since we do not see *through* a microscope, but *with* it (Hacking, 1981). Competent microscopy requires learning how to use it properly, like the seemingly trivial habit of not focusing with the eyes, but to instead manipulate the physical settings on the instrument to sharpen the image. This includes the acquisition of a highly specialized vocabulary for conceptualizing spatial relations between biological structures. To exercise this professional vision, biologists' apply schemes for coding, highlighting, producing, and articulating material representations in a domain of scrutiny (Goodwin, 1994). This includes familiarity with standard interpretations, the properties of dyes, and knowledge about cellular theory, as well as specialized insight in domains like salmon lice biology, embodied by scientific texts, diagrams, and other peers. While it is certainly possible for individual scientists to productively use the microscope, the achievement of "seeing" meaningful structure in microscopic tissues should be understood as a social accomplishment.

A key output from microscopy is malleable visual representations. As such, the act of "seeing" something as meaningful biology also includes manipulation and inspection with the hands and other sensory modalities. External representations in the form of scientific visuals, such as micrographs, afford the possibility of shared "thought-objects" which can assume multiple epistemic functions through embodied interactions (Kirsh, 2010). Not only do thought objects allow material media to be reorganized, they also create physical persistence through time, so that

perspectives and relations can be explored from different vantage points. Furthermore, thought-objects make it possible to reformulate ideas and render them explicit by recoding information in different formats. Encoding insights in other material media in turn enables use and reuse of representations for additional purposes, through actions like superimposition of media, transformation of structure, and novel opportunities for additional tool use. The digitization of photographs taken with the microscope, micrographs, offers a simple illustration. With micrographs it is possible for the same image to exist in analog, durable form on printed paper, as a digital representation manifested through projections on a computer screen, and as a fleeting representation animated through gesture and talk-in-interaction. These scientific materials invite different semiotic interactions when "lodged" in a community of practice (Goodwin, 1994: 67), and can be orchestrated on the benchtop alongside other media to propel inquiry forward and reveal new epistemic things.

Clearly, scientific visuals cannot be conceptualized as static representations if we want to understand how they work in epistemic activities (Alač, 2011; Myers, 2015). Instead, they must be approached as thought-objects in motion, co-produced through representational technologies that mediate between embodied social interaction, material culture, communication, sensory perception, and visual inference. Microscopy may, on the surface, seem like a trivial technology, but on closer scrutiny its enactment raises deep questions for the anthropology of knowledge, and is therefore "good to think" (Lévi-Strauss, 1964: 89).

Establishing Spatial Reference During Microscopy

As we saw in the introductory vignette, Hanna and Tom's microanatomical observations were motivated by a set of spatial questions about the location and extent of exocrine glands, biological structures believed important for regulating parasite–host interactions. "Space", whether we are talking about the microanatomical domain or entities at the

human scale, is not a restricted domain like color, kinship, and ethnoecological classifications (Levinson, 2003: 64). These are spheres of life where anthropologists have asked and found clearly delineated and systematically encoded linguistic distinctions. Molecular parasitologists conducting microanatomical investigations, must regularly direct the attention of their peers to establish mutual reference toward things located in multiplex histological landscapes. Establishment of common ground and shared intentionality through spatial reference in microanatomy is, in turn, a precondition for evaluating scientific claims, and for achieving consensus about biological questions. For two agents to even disagree about the nature of a particular scientific claim, they should ideally be mutually attending to the same things in the world.

Cultural variation in spatial representation has been a topic of great interest in recent psychological and cognitive anthropology. As Stephen C. Levinson puts it, our knack for spatial thinking is ubiquitous. Our ability to transform nonspatial problems into spatial issues appears as "one of the fundamental tricks of human cognition" (2003: 16–17). The disposition to transform certain problems into spatial form is exemplified by diverse diagrammatic traditions and spatial schemata found across cultural contexts. This pervasiveness raises the question whether there is a computational advantage to using spatial models for thinking, since people have an almost compulsive tendency to visualize relations and problems in spatial form. Citing Levinson, again: "If humans do in fact convert problems into spatial models for this reason, then we can readily see the efficacy of diagrams, graphs, tables and the like: a picture can be worth a thousand words because a spatially presented problem can be more readily translated into spatial thinking – it is already as it were in the right format […]" (ibid.).

In technology-saturated environments like the lab, participants in an epistemic activity have many cultural protheses at their disposal to establish spatial reference and draw attention to things in their vicinity through interlocking social actions (Hindmarsh & Heath, 2000; Koschmann et al., 2011; Streeck et al., 2011). Spatial reference in both scientific and everyday contexts makes use of "construal operations" (see Croft & Cruse, 2004: 46, for a useful typology). According to the continuity hypothesis, the cultural practices of science are partly based on

mundane linguistic operations of construal that structure experience, conceptualizations that manifest in public language as a reflection of more general processes for meaning construction. Laypersons and scientists alike use public language, and other communicative modalities, to highlight and bring attention to relevant parts of their spatial experiences. In contexts of scientific reasoning, these operations can be harnessed for epistemic uses in a myriad of ways. They are also associated with specific expectations and standards among professionals. As Hanna and Tom oriented themselves toward the morphology of lice, they organized thought and action to meet the requirements of each encounter by mobilizing a variety of linguistic alternatives to grammatically encode relevant objects and events. These "online" processes for conceptualizing events, readily encodable in language, exemplify what Slobin calls "thinking for speaking" (1996).

Making scientific observations with microscopes entails taking different perspectives toward interesting phenomena in a complex work environment. Successful cultural transmission of these scientific findings usually require that observational claims be supported by data, a heterogeneous category that lumps together many kinds of cultural representations. When aggregated and situated in the context of specific scientific questions, about microanatomy, for instance, these representations may acquire status as "evidence." Scientists use language, alongside a variety of representational media, including photographs, diagrams, tables, and graphs, to articulate, scaffold, and externalize such observations.

Public language figures prominently in these collaborative interactions by helping scientists to focus their scope of attention on specific selections of the world, making spatial conceptions accessible to each other. These external thought-objects also enable adjustments in scope, making them fit with coarser and finer scales as needed. Public language does not construe a static spatial world but can draw dynamic attention to selected aspects by imposing causative semantic categories like fictive motion and force dynamics. In turn, sequences of events may be framed as scripts for action. Language also provides resources for comparisons between figure and background, forming judgments, categorizing experiences, and supply metaphors to highlight contrasts between source and target domains. By framing observations through public language,

microscopists may also conceptualize part–whole relations, individuate phenomena, and articulate topological and geometrical associations in a scene.

As observations with the microscope are situated, practitioners rely on public language to create deictic pointers that support perspective-taking and focal adjustments to objects of interest. By assuming novel viewpoints, scientists can use these referential meanings to accommodate the views of their conspecifics and organize space in ways that help disambiguate meanings through mutual orientations toward the same objects. In turn, perspectives may be articulated as to accommodate the presence of other agents in the communicative event, thereby creating common ground between speakers and addressee. Deictic demonstratives make it possible to establish reference relative to who or what is acting in each epistemic event. Time-reference in public language also enables scientists to define things relative to situations, turning time and place into deictic centers for attention. This way, abstract entities can be rendered manifest, as things to be pointed out, in the literal sense of the term.

In the context of practicing microscopy, we can usefully see such linguistic constructs as "new layers of material structure in an already complex world" (Clark, 2006: 373), which are produced not simply due to their communicative effect, but as "parts of self-stimulating cycles that scaffold their own behavior". Keeping in mind these diverse features of how language and other semiotic modalities individuate aspects of the world, let us now look at situations where spatial reference is coordinated in the quest to anatomically map exocrine glands in salmon lice. Following the methodical mantra of "what information goes where, when and in what form," I ask how mutual reference is accomplished when the world one is orienting to is only accessible with a microscope. What kind of transformations of representational states and media are required to support microanatomical reasoning?

For histologists like Hanna and Tom, tissue slides are the key media delineating their "domain of scrutiny" (Goodwin, 1994), as it is here that glands first become manifest. Notably, the slides have a "dual" status in their work. In one respect they are specially prepared pieces of individual lice specimens, but they also serve a representational function with respect to the parasite's biological constitution more generally. As

we saw, accessing this domain is not straightforward, as tissue sections undergo many preparations that render visible its features in the form of a bewildering variety of odd forms, shapes, and colors. These scenes must be decomposed so that meaningful biological structures can emerge. To individuate relevant features of exocrine glands with the microscope, Hanna and Tom had to cultivate an ability to relate structure and form to function, and achieve a perceptual alignment between eyes, hands, and concepts.

Key to the success of widespread cultural-cognitive systems like the observer-microscope assembly are "normative patterned practices" (Menary & Gillett, 2016); patterns of activity spread across multiple agents and which operate at social, individual, and sub-individual levels to govern brain-body-niche dynamics. In the excerpt from the chapter's beginning, we saw how zooming in and out, adjusting the instrument's focus, as well as moving and repositioning the specimen at the right moments helped Hanna and Tom to see and attune to the same anatomical structures. But in addition to these skilled, sensory-motor operations, competent histologists must also partition observable space via concepts by engaging in verbally mediated interactions with their peers. Through the use of linguistic and conceptual resources available in the biological community, canny cognizers acquire the competency to relate what they see in the microscope to the world by building and manipulating information structures in public space, including shared linguistic content and material structures, which can be jointly elaborated through narrative dialogue (Menary & Gillett, 2016: 3).

In Hanna and Tom's case, these normatively patterned practices of microscopy were acquired by the novice "sitting-with-Nellie"-style, a type of co-participatory arrangement that has long been of interest to ethnographers of cognition and learning (Ellen & Fischer, 2013; Lave & Wenger, 1991), including apprenticeships in science (Alač, 2011; Mody & Kaiser, 2008).[9] Initially during my ethnographic inquiry, Hanna often sat by the bench next to the professor, who guided her practices and attuned her professional vision by highlighting objects of interests. This guidance introduced new coding schemes that Hanna could use to "circumscribe and delineate the world" (Goodwin, 1994: 608), essential

tools for domesticating her perception through shared schemes so that disparate events became "equivocal observations."

Within this category of action, apprenticeship training is characterized by active exploration, with less emphasis on direct, formal instruction. Hanna would practice her craft alongside the experienced old-timer Tom; observing, participating, and asking questions while also replicating procedures and techniques independently as the context of learning gradually transitioned to one of discovery.[10] One important part of their framework for participation was "corrective practices," a type of exploratory inference that proceeds through action looping via the environment to correct future actions (Menary & Gillett, 2016). In the vignette at the beginning of the chapter we saw how this iterative, actionable bootstrapping process unfolded. In the excerpt (7.1), Tom drew attention to a structure he was ambivalent about how to classify. Hanna, in turn, suggested that what they attended to was unimportant muscle tissue; they had previously investigated it, and she believed they should explore other anatomical entities instead. However, the apprentice was not completely confident in her own conclusion and entertained the possibility that she had failed to appreciate its importance, saying: "Yeah, we've tried to look at those before, but don't know if we concluded with certainty?". They did not proceed to investigate other locations on the slide until Tom concurred with Hanna's interpretation and verbally articulated an epistemic update of the situation, thereby transitioning the coupled system of humans and microscope into a new cognitive state.

In both gross anatomy and microanatomical work, the location of salient biological objects is disambiguated by dividing biological space into subregions, and then partitioning subregions into more fine-grained segments. By using positional terms from everyday language, and specialized terminology referring to the organism's "standard anatomical position," histologists can identify relevant phenomena and carve anatomical landscapes into fine-grained parts. Special purpose anatomical jargon avoids confusions that may arise due to imprecisions and helps to resolve between conflicting interpretations of phenomena. But as we shall see, practitioners of microanatomy use a variety of additional cognitive resources beside anatomical terms of location to fulfill epistemic actions.

Like other bilateral animals, the body plan of *Lepeoptheirus salmonis* is described as segmented. It has a distinct front and backside. The front is the direction faced by its key organs of perception, and the part that arrives first during normal locomotion. Its body also has a top and a bottom (the area that attaches to the fish). Like other objects with a front, back, top and bottom, the organism is ascribed with two lateral sides. Biologists capture such invariances with specialized shop talk that identify biological phenomena as they are located and extend through physical space. Conventionally, these descriptors are mainly oriented along three hypothetical and intersecting planes.[11] The frontal/coronal plane divides the organism into a dorsal–ventral axis (back-front orientation). A sagittal/longitudinal plane forms an axis that divides the body into left and right sides. Finally, the transverse/horizontal/axial plane defines a cross-section between the superior (upper) and inferior (lower) parts. These anatomical planes specify polar pairs of locative items; each term has a counterpart with an opposite meaning, such as *dorsal* (upper surface/back) versus *ventral* (toward bottom/belly), and so on, relative to the plane in question.[12] Biological objects can be described as positioned along these planes, and by drawing on this idealized model, biologists can fashion "neutral" spatial descriptions that are meaningful without access to the same situated semiotic resources that were available to the microscopists who crafted the description.

Despite the centrality of spatiality for thinking and action, it is generally believed that humans cannot represent spatial scenes any way they like, since different linguistic systems structure the available scenery (Levinson, 2003). Usually, a portion within a scene is marked out for a primary focus and is characterized with reference to a second, and occasionally a third object. Here are two examples of constructions in Hanna and Tom's work, from a draft report on the anatomy of exocrine glands in lice:

1. "Teg 2 glands are always located in close proximity to a teg 1 gland."
2. "The pores are found anterior on the exopod distal segments (Fig. 3F), while on the thoracic leg 2 endopod they are located at the margin between two of the distal segment pinnate seta."

Table 7.2 Relative properties of figure and ground constructions, based on Croft and Cruse (2004: 56)

Figure (referent)	Ground (relatum)
Spatial properties to be determined	Location known
Smaller	Larger
More moveable	More permanent
Simpler	More complex
More salient	More in the background
More recent in memory	Earlier on scene/in memory
More dependent	More independent

These spatial descriptions belong to one of two classes of structures known as figure or *referent* ("Teg 2 glands," "pores"), and ground or *relatum* ("exopod distal segments," "thoracic leg 2 endopod"). Table 7.2 shows relative differences between these.

In the example above, the structure labeled as "pores" are contrasted to the larger and established "exopod distal segments." Briefly, a Figure is the object to be located, for instance, a moveable object whose location, orientation, or direction (path) is in question. The Ground (or "relatum") on the other hand, is the object used to identify the Figure's location. Ground is often stationary and may also be used to define direction or orientation vis-à-vis the Figure. These spatial descriptions help focus attention on smaller parts of a larger field and to determine asymmetrical spatial relations between the Figure and Ground. In contrast to metaphor and analogy, which depend on similarities for their cognitive effect, the Figure–Ground relation emphasizes contrast and difference. Additionally, modifiers like proximity and distal contrasts (nearer/further away), as well as dimensionality contrasts (bigger/smaller), may be used to specify locative descriptions in spoken language. During salmon lice microscopy, the role of Figure (referents) and Ground (relatum) was ascribed to different biological entities such as glands, channels, exit ducts, and a variety of landmark tissue structures that appeared in a histological scene as seen with the microscope.

"Where"-questions about the location of things are primarily answered in two very different ways and it is now generally accepted that all known languages accomplish spatial reference by a combination of non-angular and angular specifications. In the non-angular case, the strategy

is to "choose a ground or landmark object in close contiguity with the object to be located" (Levinson, 2003: 67). Spatial descriptions of this variety can be based on three different operations. The first kind is the familiar use of *placenames*; a Figure is located at named place G (Ground). A second construction is known as *deixis* (Greek for "pointing").[13] Deictic reference, such as "it is here," belongs to a class of complex communicative acts where receivers of a message must know about key, extralinguistic circumstances for the communicatory act to be perceived as meaningful. In these constructs, a Figure is located relative to Ground (often the ego) using radial categories ("here"/"there"), or by pointing gestures that use hands, eye-gaze, or other embodied modalities. Such acts create a special ground or landmark. This semiotic resource, deixis, exemplifies deep entanglements between language processing and context, what Levinson describes as "a big black fly in the ointment" for disembodied theories of language (2008: 97).[14]

The third kind of non-angular operation is known as *contiguity* or *topology*. In this construction, the Figure is located contiguous with Ground. In English and Norwegian this is accomplished through prepositions that mark spatial coincidences like proximity and contiguity, containment, coincidence, and the like, for example, subdivisions such as *on*, *at*, *in*, *between,* and *such*.

In addition to these three non-angular constructions, spatial reference is also achieved using a second class of angular constructions. These locative constructions mark out a prominent ground object away from the Figure or object of interest, and then provide a "search domain from the ground by specifying an angle from that landmark" (Levinson, 2003: 67). Here, Figure–Ground relations can become components in more complex coordinate systems. These systems construct an orientation space that identify spatial relations between objects in a scene through a coordinate system of intersecting axes across the horizontal and vertical dimension. It uses one among three unique spatial "frames of reference" that operate across natural languages: the relative, intrinsic, and absolute. In Norwegian and English, the working languages of my interlocutors, it is possible to use all three frames, but some languages

manage without all three. Note that in Norwegian and English, the absolute frame of reference is mainly used for the topographic domain ("the fish farm is *north* of Bergen"). It will not be discussed further here.

Relative, intrinsic, and absolute reference frames are differentiated by how they construct the origin-center of the coordinate system and its orientation. Common to all, is a minimally required specification of an object to be located (a Figure), its Ground (which the Figure refers to), and the origin and orientation of the said coordinate system. While frames of reference can be conceptualized independently of language, they become apparent when triggered by utterances. As Levinson observes, the difference between angular and non-angular forms of spatial reference is complicated, as the relative frame of reference also provides a conceptual schema for interpretations of spatial deixis, the second item in the non-locative class. The use of deixis through demonstrative pronouns such as *here*, *there*, *this*, *that,* and so on, establishes a form of joint attention by marking a central spatial viewpoint within the speech situation known as the *deictic center* (or *origo*), from which the coordinate system should be understood. In language interactions between competent speakers, this deictic center may continuously shift between the participants, and the use of demonstratives is usually accompanied by pointing gestures.

Traveling Through Histological Landscapes

Microanatomical studies of salmon lice rely on spatial description to answer "where"-questions by utilizing a combination of angular and non-angular locative resources. Due to the nature of anatomical practice, which requires scientists to interact closely with two-dimensional material media like tissue sections, it is variations on the first locative class that will mostly concern us in the remaining analysis. First, we look at some thick ethnographic descriptions that flesh out how Hanna and Tom create biological meaning during microscopy by transforming spatial representations while they actively explore and reason about the internal lives of lice. Later, we revisit the object-centered, intrinsic frame of reference, to examine how this form is used as a resource in

a scientific manuscript for making spatial descriptions couched in the special purpose language of anatomy to pinpoint the spatial properties of exocrine glands.

Again, we encounter Tom and Hanna at work tracing exocrine glands and other biological structures that reveal their presence, like the channels transporting substances from glands to other anatomical locations. This time they are sitting in a new microscopy lab, working on a recently acquired microscope of considerable sophistication. Like in the first montage, the two are oriented toward the instrument, with the tissue sections held in place by clamps on the microscope stage. Preferably, tissue slides are always aligned with the "standard anatomical position," which makes mappings of landmarks along the axial planes convenient for the viewer and facilitates easy comparisons with external diagrams like anatomical sketches. In contrast to the first montage, where both observers had access to separate oculars, Hanna is the only one who intermittently peers into an eyepiece here. Eyes are mostly fixated on a screen projecting a cable-transmitted image from the microscope-mounted camera. This makes it possible for both investigators to orient and concert their bodies with respect to the specimen, as Hanna directs the plate with the slide on top (Table 7.3).

The Professor's first utterance (1) combines a topological/coincidental element ("That turquoise here") with a dynamic, deictic gesture by pointing to a location on the screen that identifies and demarcates an object he wants to further explore. This signals to the novice that she also should attend to this location. Deictic gestures, such as pointing, stand in contrast to iconic gestures like a thumbs up. The spatial location of "that turquoise," the Figure of interest, is topologically determined with reference to a general anatomical structure marked by "here," which functions as the Ground in this interaction. As the old-timer further reason about the nature of this object, he continues to highlight a specific area on the screen by adding three new deictic gestures in rapid succession. By superimposing this dynamic, handmade triangular structure on the screen, Tom materially anchors what first is a fleeting, conceptual object for a second time, thereby making it stable and available as a thing-like thought-object that Hanna can scrutinize on her own (Fig. 7.5).

Table 7.3 Excerpt from conversation

1	**Tom**	That turquoise here, that is the same as we have seen?	*Tom points to an area on the left of the screen ('here'). He then moves his left hand a few centimeters to the right and brings his thumb and index-finger together above a specific location. Tom widens the gap between his thumb and index-finger as he moves it across the screen toward the left, tracing a triangular shape in the area delineated by his index finger and thumb (1–4)*
2	**Tom**	Will the two meet, or?	*Tom's first gesture is followed by pointing gestures identifying three specific locations on the screen, whose lines intersect to constitute a triangle of the same size he drew above (5–7)*
3	**Hanna**	It is strange because they are attached in a way, the two balls, the two sacks, so one would think this was a bit further down, so maybe this is another channel coming?	*Hanna brings her two hands together in an iconic gesture and creates a three-dimensional model of the two 'balls' or 'sacks' she describes seeing on the screen (8)*

Immediately, microscopic visuals seem to constitute an inert and static space, but Hanna and Tom's actions show how this scenery is dynamically and functionally animated by competent practitioners. Static scientific visuals can be activated through grammatical constructions denoting speed, movement, transitivity, and persistence, as well as embodied gesture that superimpose fictive motion on immovable models. Together, these actions produce a kinetic space suffused with spatiodynamic features, which in turn may facilitate novel insight (Alač, 2011; Becvar et al., 2008; Myers, 2015; Ochs et al., 1994, 1996). In his first and second utterance, for instance, Tom's epistemic actions create a conceptual blend composed of an image schema based on a projection of two separate trajectors moving away from each other along paths

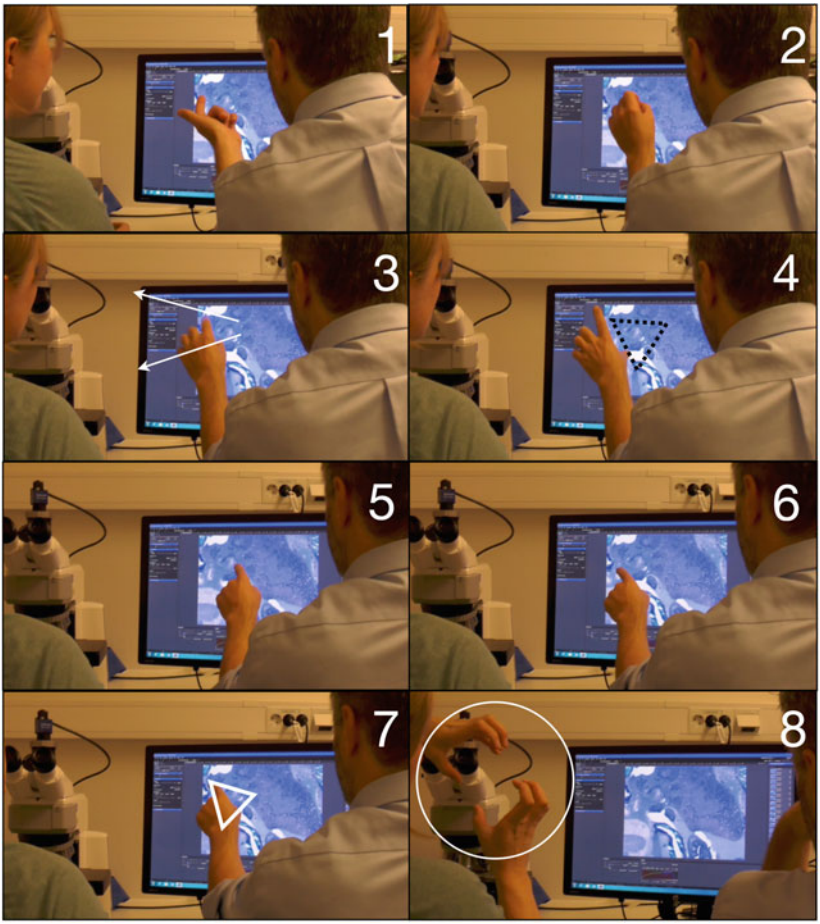

Fig. 7.5 Establishing spatial reference in collaborative microscopy. Tom refers to an observed gland-like complex by first pointing and then superimposing a triangle-like structure on the monitor (1–7). Hanna responds by making an iconic gesture, illustrating a related composite structure shaped like "two sacks" by bringing her hands into proximity and using them to form a model of a round object (8).

originating at the same point. This is an invitation to an imaginary "journey" through tissue, that also encourages Hanna to project the direction of this structure as it extends through other slides in the deck, and more generally throughout the parasite *in vivo*. When Tom makes this thought-object manifest, Hanna can then consider if the two observed structures are likely to "meet" at some future point, by simulating their extension through anatomical space.

Tom's utterances are also invitations for Hanna to participate in the reasoning event. Hanna fulfills Tom's expectation about her involvement by adding layers of meaning about the spatial organization of the anatomical region. He articulates a relevant question along with an iconic "environmentally coupled gesture" that links up things in the world to actions and classifications (Goodwin, 2017). These representational gestures are effective cognitive artifacts, created on the spot during microscopy to sustain situated reasoning about the phenomena in question. Hanna's final co-speech gesture in (3) presents an example of an "iconic mapping" between the gesture's properties, and the structure represented by it (Becvar et al., 2008: 122). Together, Hanna's hands and talk props up a concrete, three-dimensional model of epistemic significance for Tom, who can compare this structure with the two-dimensional visuals he sees on the screen, and then engage in collective reasoning about the features of the relevant anatomical space and surrounding exocrine channels.

Note also that the Professor's deictic highlighting of the triangular structure, and Hanna's iconic gesture of the "two sacks," create conceptual blends that use material structure to move a microscopical phenomenon up to the human scale for further inspection. The fleeting, physical model that Hanna creates by bringing her hands together allows for a comparison through pattern matching with the structure that is available on the monitor. Together, these joint acts of embodied reasoning eventually produce a new insight that there might be another exit channel for glandular products coming up to the same area. Hanna and Tom now had to consider this alternative scenario, as they further explored the properties of the histological scene in detail, adding a new constraint to subsequent interpretations of lice anatomy.

Scientific discourse in this action sequence also seamlessly conflates two different frames, like in descriptions by Ochs and colleagues from a series of illuminating analyses of physicists at work (1994, 1996). For example, Tom's utterance (in 1), grammatically encoded a frame that we can call the "anatomist as experiencer." By uttering "that is the same as we have seen?," Tom establishes the microscopists as two active, reflexive subjects that experience and react to the anatomical entities they have observed. The anatomist is construed as an "active participant," an experiencing agent making scientific discovery (Ochs et al., 1996: 335). However, in the next instance, the professor also verbally and deictically encoded a second, "anatomy-centered" frame. This frame specified certain aspects of the anatomical organization, including changes in its state and spatial distribution.[15] Practicing scientists appear to construe such blended identities to support meaning-making frequently and ubiquitously, in ways that pose no interpretative problem for their peers, despite blurring distinctions between the observing practitioners and their objects of enquiry. It is possible that such indeterminate constructions, whereby scientists retain a certain level of "referential ambiguity" in collaborative interactions, helps to scaffold mundane problem-solving through identification with entities they "struggle" with understanding (Ochs et al., 1996: 348).

Having established spatial consensus about the objects of interest in this anatomical landscape, the newcomer and the old-timer could then proceed to investigate other structures in the near vicinity. But they only did so after having attended to, and blended insights from, three very different referential planes. One plane is provided by the coinvestigators' physical presence and coordination with human-sized objects available in the immediate physical environment. A second, hybrid space of symbolic gestures with deictic and iconic properties, that are superimposed with graphic representations on the screen. And finally, a referential plane that involves imaginative journeys through physical states in the anatomical landscape of lice tissue, such as the alternative paths taken by channels that connect exocrine glands with their openings on the surface of the animal's body. Collaborative microanatomy thus requires establishing precise spatial references that retain sufficient

referential ambiguity and allow co-investigators to productively imagine and deliberate on alternative anatomical spaces.

Tracing Anatomical Reasoning in Notes

Let us turn to a different set of cultural-cognitive practices that contribute to the representational cascade of lice microanatomy, now by examining written notes and graphic displays made by Hanna on basis of repeated sessions in front of the microscope. One of the first external outputs of Hanna and Tom's work, beyond micrographs of exocrine glands and fragments of knowledge embodied by their internal, biological memories, was a trail of entries kept in a hardcover notebook. These handwritten and chronologically organized notes were maintained by Hanna in real-time, as she performed histology. While Hanna collaborated closely with Tom in many microscopy sessions when their project started, she also spent long hours by the instrument on her own.

Similar to the famous notebook kept by the Alzheimer patient Otto in Clark and Chalmer's pioneering essay on *The Extended Mind* (1998), we can usefully conceptualize Hanna's notebook as a type of representational media that supports cognition by extending her biological memory. Merlin Donald, who consider symbolic technologies that represent, store, and transmit knowledge to be revolutionary for the emergence of modern human cognition, coined the term "exograms" to describe such extraneous mnemonic tools, in contrast to the "engrams" of our internal memories bound by the nervous system (2010). Laboratory notebooks, and other forms of paper technology, have long been objects of interest for science studies, since their use provides a window on the weave between information, memory, meaning, and scientific insight (see Holmes et al., 2006: XII; Yeo, 2008). Rheinberger advised careful attention to this "economy of the scribble," as it serves important generative functions in the laboratory as a "trail of rough notes, scripts and scribblings and revised write-ups that offer insight into concrete processes of knowledge formation" (2010: 244).

Scribbles serve many epistemic functions. They are not just tools for information management. In one respect, notes and other kin technologies work as *interfaces* between experimental systems and their conceptual outputs. On its most basic level, writing up microscopy work in external media like notebooks facilitates a process that Rheinberger calls "redimensionalization" (2010: 245). Temporal and spatial dimensions of an investigation can be organized, rearranged, and inscribed on a two-dimensional surface to support a deeper understanding of the epistemic thing in question. Using various representational conventions widespread in the sciences, including discipline-specific tables or diagrams for ordering observations, it becomes possible to synchronically represent sequential events, and render temporal relations in the laboratory into spatial form. Redimensionalization also creates "condensation effects," like the compression and filtering of information over time, through iterations that bring new patterns into view.

Cognitive ethnography and historiographic studies of science share an obsession with minute details of material artifacts involved in the scientific process, such as research notebooks. For Holmes, Renn, and Rheinberger, these media offer a lens on scientific novelty as it emerges in daily interplays between thought, action, and the manufactures of the research lab, potentially challenging our ideas about scientific discovery (2006: xii). To this, the cognitive ethnographer would simply add that valuable insights about this relationship can also emerge from situated examinations of lab work, where notetaking as a generative practice can be studied in real time. By attending to notetaking and its associated representational resources, ethnographically, one can also situate these in a larger sociocultural context where epistemic processes unfold.

Erving Goffman famously made a distinction between the frontstage and backstage of social interaction (1978), which is echoed in the notions of "day science" and "night science", put forth by Nobel-laureate biologist François Jacob (1998: 126). Whereas the former "calls into play arguments that mesh like gears, results that have the force of certainty," the latter "wanders blind": "doubting everything, it is forever trying to find itself, question itself, pull itself back together." Night science stumbles, "a sort of workshop of the possible where what will become the building material of science is worked out," and where "phenomena

are still no more than solitary events with no link between them." We read about day science in reviewed articles and press releases. In these accounts, traces of the inevitable mucking around in the lab that occurs at "night," as new concepts and results take shape in a messy process, have seemingly been scrubbed away (Steinle, 2003). Notebooks like Hanna's, I suggest, offer an interface for attending to transitions between night and day science.[16]

Staff at the SLRC kept meticulous records of their laboratory work in hardback notebooks, and their use reflected widely shared epistemic norms which all newcomers to the lab were expected to abide by. One event illustrates the moral economy of laboratory notes. In a weekly lab-meeting in November 2014, the ethnographer presented some work on information management and the use of databases in biology from a historical and philosophical perspective. When the ensuing discussion turned to the issue of lab notes, the PI remarked that he did not wish to impose restrictions concerning how his research group should organize their logs, and he stressed that staff were free to find their own adequate solutions. He also emphasized the egalitarian ethos of the community, which he contrasted with more hierarchically organized research groups abroad, where notetaking practices were highly regimented. Bioscientific laboratories that are heavily invested in commercially attractive, high-stake research, where competition is fierce and patent disputes frequently arise, are especially prone to require maintenance of notebooks with permanently bound pages, written in pen using conventionalized formatting, and with each page signed and dated. In such contexts, the policing of notes become important because any traces of scientific knowledge production may assume a de facto legal status. While scientists at the Centre were expected to abide by basic epistemic virtues by keeping clearly written, transparent and dated notes, they could maintain these systems of inscription according to personal preference.[17] A notable exception was annotations of RNAi experiments in LiceBase, the Centre's bioinformatic database. As a tool for information management, all were responsible for curating a shared communal directory of data abiding by criteria specified in a checklist.

When viewed as a cognitive artifact, we can identify several epistemic functions in Hanna's notebook. A striking feature was the fact

that Hanna herself was the main recipient for the meanings encoded in the document. Notes were written from her own viewpoint; containing streams of semi-formed sentences and rough descriptions, based on impressions from microscopy events carried out on tissue sections, as these were experienced and recollected by her at the time of writing. While the third-person view was preferred in narrations of her observations, there were occasional interjections of the first-person perspective. In Jacob's words, the notes trace how "writing substitutes a well-ordered train of concepts and experiments for a jumble of untidy efforts, of attempts born of a passion to understand" (1998: 126).

Figure 7.6, a transcript of two typical pages in the notebook, contains the following information from top to bottom. The first sentence indicates what specimen was being examined. Histological specimens made with a variety of staining methods, were frequently exchanged between colleagues at the Centre to support comparative analyses. The second line in Fig. 7.6 introduces a preliminary categorization of exocrine glands ("Type 5"), based on salient traits identified from different staining patterns ("very bright"), and morphological characteristics ("sponge-like"). When supported by other indices, such differences yield the inference that these two structures might be involved in different biological functions. The numbers ("476, 484, 486," etc.) refer to different glass slides in a particular slide box.

In addition to these descriptive listings of salient content from each slide, the notebook is also scribbled with fun facts, jottings of sudden insights, unfinished thoughts, practical tips, reminders, and highlights of specific locations that should be photographed, rudimentary sketches of preliminary structures, groupings, typologies and classifications of glands. It also contains idiosyncratic nicknames for various structures based on salient characteristics. In this case, Hanna refers to "the blue one" (*blåingen*), "the weirdo" (raring), and "the butterfly" (*sommerfuglen*). Together, these scribbles outline a preliminary sketch of a composite model of the exocrine system of *L. salmonis*.

As visible from the figure, Hanna's notebook was organized as a list of observational events, chronologically ordered by section number. This narrative structure facilitated quick and robust information retrieval. A number, usually entered on the left side at the start of a descriptive

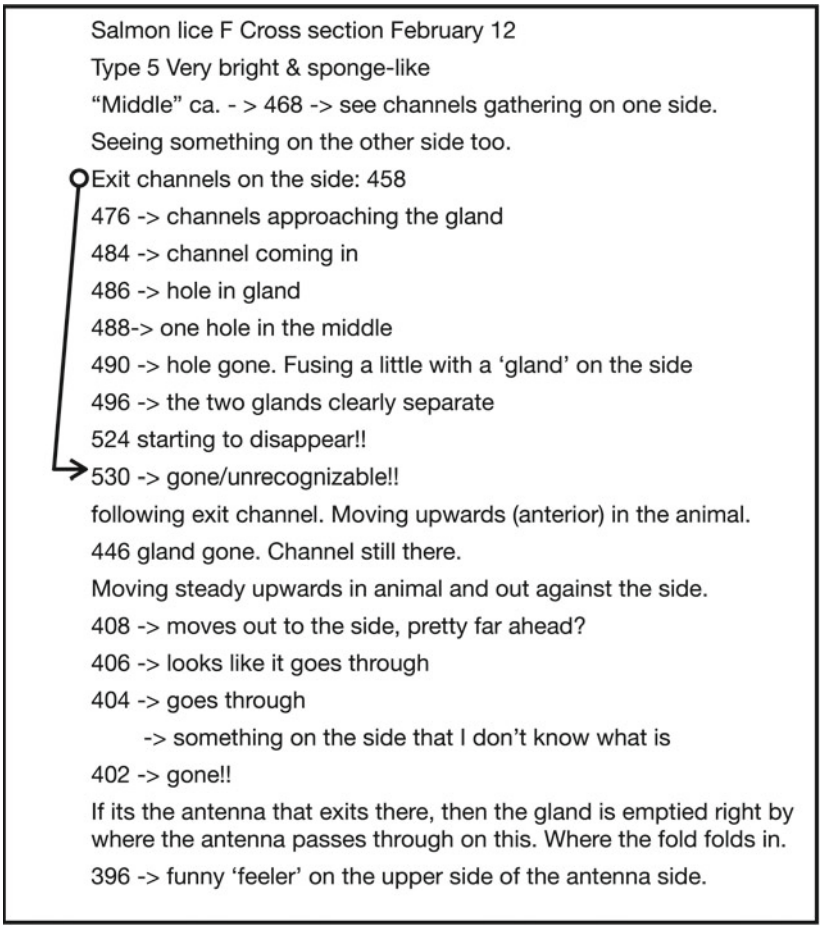

Fig. 7.6 Transcript from two pages in the notebook

sentence, would refer to a corresponding slide in a given slide box. This array efficiently cross-linked the temporal space of observational events with concrete physical locations in the specimen. Note that in the example above, the list of numbers suggest that Hanna has occasionally "jumped" a few slides to speed up her search. The parsimonious inference behind this move is that observed structures remain continuous across consecutive sections: if certain phenomena are visible on both slide

1 and slide 5, they are part of a continuous structure that also appears on slide numbers 2, 3, and 4. A broad search, where Hanna would inspect every slide in each sequence, would likely be too time-consuming to be practically feasible.

The epistemic effects of this bookkeeping effort, such as its mnemonic function, were determined both by its structural qualities and its situated use. First, the device functioned as a cumulative external long-term memory of Hanna and Tom's experiences in front of the microscope. She could, for example, use the entries as what I previously referred to as a "jig" (Kirsh, 1995: 37): a cognitive device that helps to structure and stabilize her informational environment, facilitating easy re-entry to the workflow when resuming work after breaks away from the microscope. Instead of having to inspect each slide in an entire series to relocate interesting landmarks on the individually numbered tissue sections based on internal memory alone, Hanna could instead consult her recent notebook entries. Doing so she could quickly identify critical landmarks and recover regions of interest in the microscope to pursue whatever questions she was addressing.

The notes also served another critical mnemonic function as Hanna was writing up the results in a manuscript for a scientific article. In this context, the rudimentary descriptions in her notes would become one source of data in addition to representations like micrographs, sketches, biochemical evidence from gene expression studies, micrographs from *in situ*-hybridization analyses, and anatomical descriptions found in other scientific publications. Situated in this cognitive ecology, the notebook both served as a record of past accomplishments, but also a springboard for new itineraries and a guide for future action (Fig. 7.7).

This twofold mnemonic character of Hanna's bookkeeping, as both a device for cuing long-term memory *recall* and a storehouse for more direct information *retrieval*, illustrates how epistemic resources are concerted within the larger cognitive ecosystem. According to Richard Yeo, we should see the sophisticated and systematic notetaking practices that developed among English Enlightenment philosophers as important precursors for how contemporary scientists handle their data (2008). English virtuosi like John Locke and Robert Hooke cultivated distinct compilations of knowledge with the help of so-called "commonplace

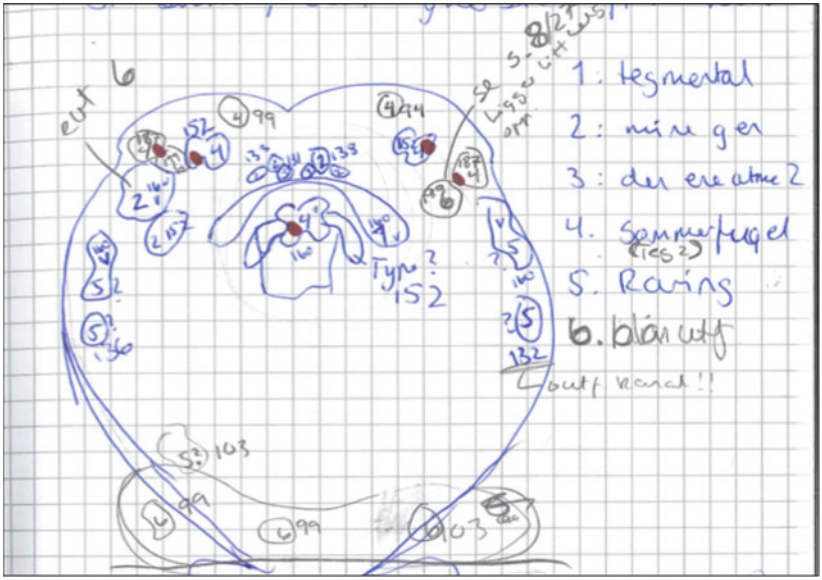

Fig. 7.7 Sketch of a preliminary anatomical map, marking assumed locations of the exocrine system. The numbered legend on the right lists rudimentary working classifications ("1. Tegumental," "2. my genes," "3. the one next to number 2," "4. the butterfly (teg 2?)," "5. Stranger," "6. blue ex[it].")

books." Before the advent of experimental science, natural philosophers conceptualized these individually kept notebooks mainly as memory *prompts* used in the context of memory training, and not as storehouses for knowledge. The purpose of maintaining this species of epistemic artifact was to evoke specific recall events for the individuals maintaining them. According to Yeo, it was not until later that commonplace books were viewed as an external resource for information retrieval. Hanna's notebook constituted a hybrid form of information management that reflected both these epistemic usages. In one way, it was an external record of Hanna's observations. But its fragmented character suggests that the notebook also functioned as a contextual prompt for Hanna's reconstructive and reflexive needs, rather than an external and transparent record where she could retrieve complete information about the anatomical structure of exocrine glands.

The number line, a trajector-based cultural artifact that maps numbers onto a unidirectional space, was frequently used as an organizing device in these exploratory efforts. As a cognitive resource, the number line made it possible to organize entries as *a list that simultaneously encoded both a spatial address* (an anatomical location from a particular tissue section), and *a temporal sequence of observational events* (the situated moment when Hanna made her observation). A "train-of-observation"-style of writing, described the order whereby specific observations were made and how they were interrelated. Each description also referred to numerically arranged tissue slides, neatly organized in plastic boxes. This number line tracked the tissue sections chronologically along the axis from the animal which they had been cut, either top to bottom, or front to back along the sagittal, coronal, or transverse plane.

By organizing her entries as a running list of observations, Hanna also made use of an ancient cognitive device that harkens back to the origin of writing systems. In *The Domestication of the Savage Mind*, a comparative anthropology of the impact of writing technologies on knowledge, Jack Goody asked the intriguing question of "what's in a list?" (1977). This question has deep cognitive implications, although Goody's examples are rather mundane and familiar. Tables with columns and rows are cultural tools whose transmission chain stretches back to inventive scribes in ancient Mesopotamia, working on ledgers in cuneiform script engraved on clay tablets for the public administration. Goody also suggests that lists, as a peculiar form of inscription, have cognitive properties that amplify the mind beyond its "mnemotechnic functions" by encouraging reflection and reclassification of information (ibid.: 109).

Laboratory notebooks are usually ordered as lists of procedural steps adopted from institutionalized biochemical protocols (containing information about temperatures and reagents, for example), as listed sequences of nucleotide or amino acids and lists of research equipment. Sometimes, systems of columns and rows or matrices, are used to order the content. As an example of what Goody dubs "technologies of the intellect" (ibid.: 16), the writing of lists performs quite different operations than what is achieved by ephemeral spoken language, like that uttered during collaborative microscopy. Writing lists of what has been observed and discussed do not only stabilize fleeting perceptual events,

but also domesticates attention, and fixes salient phenomena in a form so that they may later be ordered, classified, and reclassified, on basis of abstract relations. This is why examining the many uses of lists in experimental science, *Listwissenschaft* in Goody's terms, has the potential to open new research agendas and help us better understand how conceptual transitions in science occur (Müller-Wille & Charmantier, 2012). As such, even the humble notebook can be a transformative technology for propagating representational states in the cognitive ecosystem of the laboratory.

Creating Spatial References in the Notebook

When looking closely at how Hanna's notebook accomplishes spatial reference, we see clearly that the entries primarily were tailored to her idiosyncratic requirements for recall, retrieval, and reasoning. While she occasionally created references to anatomical locations using spatial descriptors, such as anatomical place names and constructions of coincidence/topology, her listed observations, as a whole, appears to perform a kind of imaginary, egocentric "gaze tour" in the histological landscape (Levinson, 2003: 33). Hanna's notes achieve this phenomenological effect through a combination of deictic references that point to scientific events of interests *outside* the text (extralinguistic, *exophoric* reference), and by using non-deictic (*anaphoric*) references to earlier descriptions of phenomenon in the preceding text.

Deictic constructions relativize reference to "properties of the speech event" (Levinson, 2003: 69). It locates a Figure *relative* to a Ground (often the "ego"). This is achieved with radial categories like "here" and "there," or with a pointing gesture using hands, eye gaze, or external artifacts. Sometimes called a "viewer-centric" frame, the deictic *origo* (the observer) creates a link between talk and the world. While locative deictic markers in everyday discourse normally evokes the circumstances of a speech-act situation, spatial deixis in Hanna's notebook instead points to an observational context, the moment when her notes were inscribed. As

a result, Hanna's notes appear "semantically deficient," since its "descriptive content" does not identify a clear referent in the absence of other contextual clues (Levinson, 2008: 97).

One reoccurring type of deictic construction used by Hanna to mark spatial reference in these data was exophoric, "gestural" deixis. Ostensive inscriptions of this kind require a form of physical monitoring of the context where the scribble took place to be meaningful (usually in the form of visual information). In the following excerpts, sampled from the image reproduced above, a semantically sufficient interpretation requires access to a range of contextual information, and even graphical representations outside the text:

> *Looking at brighter/larger vesicles in the midline. Laying in plane with the butterfly. Ex. channel exits 154.*
> *NB > not the one that is lying outside.*
> *Following it down in the animal.*
> *169 > see channel cut lengthwise. Moving up in the animal.*
> *168 > moving upwards again!!*
> *Waving its way to the top 166.*
> *Following this all the way out.* (170)

These contextually dependent spatial references were often framed in terms of directional contrasts, and relied extensively on demonstratives ("these," "those," "here," "there," etc.)[18]:

> *774 > channel goes out of the glandular tissue.*
> *Jump back to 780.*
> *764 > channel no 2 moves sideways.*
> *764 > it moves out!*
> *748 > none of the glands were there. It is seen near good* [sic] *748.*
> ….
> *722 > starts to show up in middle.*
> *706 > butterfly is here.*

Both excerpts from Hanna's dataset depend on supporting information of a contextual kind to be adequately meaningful for the user. To complete the meaning of these inscriptions, the reader must have

access to a range of media, such as other pencil sketches, particular micrographs, and knowledge about the material qualities of specific slides, as well as intimate familiarity with observational events from the course of microscopic work. Occasionally, these notes also illustrate how Hanna conducted "interpretative journeys" (Ochs et al., 1994), in the anatomical landscape on her own:

S06 > it moves alongside, outwards to the right (if I was the louse).

In this inscription Hanna, as the observer, creates a blend for spatial reference that takes directional aspects from the anatomically conceptualized body plan of *L. salmonis* as one input, while the other input is materially anchored through her own phenomenal experience of a *situated* body-as-louse. Given that Hanna had carefully examined each of the tissues described in the notes with her hands and eyes before, she could recall these observational events and simulations by using the scribble as a cue.

The notebook was also littered with deictic references. Fillmore described the contrast between deictic and non-deictic spatial reference as analogous to the difference between a three-dimensional sculpture of a human figure in the middle of a courtyard, and a photograph of this figure (1997: 28). While the former is not fixed and can be inspected from any vantage point, the photograph is always taken from a fixed place and perspective relative to the figure's position. For example, we can see from the transcript (Fig. 7.8, line 2 and 3, page 2), that Hanna made the following note:

404 > goes through.
> something on the side that I don't know what is.
402 > gone!!
If it's the antenna that exits there, then the gland is emptied right by where the antenna passes through on this. Where the fold folds in.

These examples of textual-discursive and gestural deixis ("exits there," "passes through on this"), require both the textual availability of preceding information, in addition to other sources of memory about the observational event to constitute meaningful spatial reference. In turn,

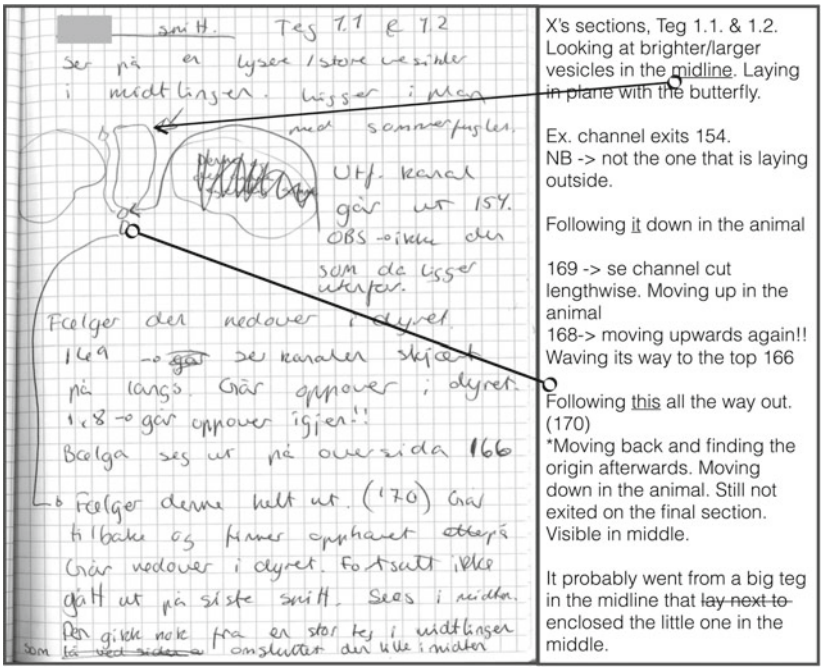

Fig. 7.8 Sample from a notebook entry with a transcript (on the right). Disambiguating a complex anatomical structure, the sketch contains examples of "gestural" deixis in the form of an annotated sketch that highlight relevant locations, and "discursive" deixis referring to observational events that precede the moment of writing. Hanna's use of gestural deixis requires a visual inspection of the hand-drawn arrows for meaning completion (here, annotations highlight the words that the original arrows in her transcript refers to)

this informational gap can only be bridged by Hanna who conducted the histological investigation, as she is capable of coupling internal, representations "in the head" with external representations inscribed on paper and other media in the material world. She can thereby exploit whatever Gibsonian "affordances" are available on the spot, through acts of embodied, pragmatic meaning-making (Levinson, 2008: 106).

To appreciate why Hanna's notes were structured in this particular manner, one must look at the context of their production. They were written down while she was orienting toward the microscope, sometimes during engagements with her mentor Tom, or other colleagues. Chains

of interactions with the microscope assembly were translated into trains of thoughts, recorded onto paper. Her representations in the notebook transformed anatomical phenomena mediated by the microscope into tangible symbolic inscriptions. Commenting on an early draft of this manuscript, Hanna added that she also operationalized a word document on her PC as an additional reflexive medium to engage with the material. After a session in front of the microscope, she would return to her office, notebook in hand, to trace out her observation directly in a draft scientific manuscript through repeated iterations.

Another function of lab notebooks, as data management tools, is to ensure a transparent and redundant record of information, in case a member leaves the research community, for example. One could imagine a hypothetical situation where Hanna's colleagues used the notebook entries to partially reconstruct her anatomical work on exocrine glands. For example, by combining the notes with graphic descriptions like micrographs and diagrams from other sources. But due to the notes' semantic deficiency this would be challenging. Hanna's entries required the author's contextual know-how to be composed into a meaningful whole. For this reason, the notebook cannot be considered as simply a data recording device. Her entries are not "immutable mobiles" that travel easily across time and place (Latour, 1990: 26). Instead, the notebook's epistemic status can best be understood as a "data generator" (Hacking, 1992: 48), whose cognitive role was to facilitate the transformation of one type of representation into a different format. Its full epistemic potential could only be attained when these generative scribbles were coupled with Hanna's embodied know-how, alongside other media such as graphical outputs from the microscope-mounted camera, to build accessible accounts of microscopic observations. It was in these productive couplings that the scribble's true power resided.

Spatial Reference in the Manuscript

I have described Hanna and Tom's eclectic use of cognitive resources, including angular and non-angular constructions, for establishing spatial reference and joint reasoning about microscopic exocrine glands. Their

shop talk in these interactions was littered with construal operations like topology, place names, and varieties of deixis ("point-out-ables"). We also saw how spatial reference was idiosyncratically encoded in Hanna's notebook. But strikingly, spatial representations, both in their natural discourse and the notebook, revealed surprisingly few traces of anatomical terminology. One might assume, *a priori*, that this specialist vocabulary would be essential for conducting microscopy. For example, a simple content analysis of the 81 pages in Hanna's notebook revealed only nine instances of explicitly anatomical terms of location to render spatial descriptions: four instances of *dorsal*, three of *ventral*, and two of *anterior*. Now, compare the spatial descriptions we have encountered in excerpts of natural discourse and Hanna's notebook with the following examples of spatial reference. These are sampled from a draft manuscript for a peer-reviewed scientific article that was the primary output from Hanna and Tom's investigation: "The most anterolateral pair of teg 2 glands have a duct extending anteriorly and out together with a teg 1 gland where the anterior margin of the cephalothorax contacts the antennules. The next cephalic pair secretes their content dorsally. The teg 2 glands in the thoracic leg 1 and 2 sympods have ducts leading adjacent to the joint between the sympod and exopod/endopod, while the teg 2 glands in the exopod/endopod have ducts protruding into the distal segment. The pores are found anterior on the exopod distal segments (Fig. 3F), while on the thoracic leg 2 endopod they are located at the marginal margin between two of the distal segment pinnate seta."

Here, each sentence in the paragraph provides a detailed description crafted through the use of anatomical terms of location. Each descriptor is also cross-referenced with annotated collages of micrographs assembled from both light microscopy and scanning electron microscopy. Together, these representations offer a dense model of the parasite's exocrine system, saturated with anatomical meaning for expert readers. This constitutes a remarkable transformation in the representational format used to describe the spatial characteristics of exocrine glands. Everyday language, as it appeared across many interactions in the wild, has been substituted with careful anatomical descriptions of the parasite, using terms of location derived from Latin and ancient Greek. The translation follows established standards in the biological community

for disambiguating meaning and communicating about the location of biological entities. Reducing referential ambiguity in anatomical descriptions is critically important when dealing with epistemically vigilant peers, whose job is to evaluate the reports of other research colleagues. A reader cannot usually access the same contextually embedded resources that were available to the authors who performed the inquiry. Instead, readers rely on technical descriptions and annotated, two-dimensional figures. According to Hanna, a key resource for developing the right vocabulary and accomplish this transformation, was a "fantastic" paper describing the major body parts of the salmon louse.

Another excerpt exemplifies this representational "upgrade" through an elaborate locative description of a specific type of gland. Hanna and colleagues eventually categorized this as "teg 3": "The teg 3 glands are found evenly distributed laterally along each side of the cephalothorax within the subcuticular tissue (Fig. 4B), with five glands on each side. Their ducts run posterolateral, extending through the cuticle ventrally on the marginal membrane in the vicinity of an innervated bifurcating sensilla seen at the margin (Fig. 4C, D). The sensilla nerve follows the course of the teg 3 duct, but synaptic contact between the nerve and the gland could not be confirmed with light microscopy. Teg 3 glands are also seen within the distal segment of the endopod/exopod of the thoracic leg 2, and posterior within the sympod of thoracic leg 3 near the interpodal bar and more laterally near the base of the thoracic leg 3 exopod with a cuticular pore at the margin (Fig. 4B). Pegs with pores (Fig. 4G) are seen nearby the teg 3 pores at the posterior margin of the thoracic leg 3 sympod (Fig. 4B, F)."

In addition to the non-angular terms of location encountered earlier, descriptions in these two excerpts rely on what Levinson describe as an "intrinsic frame of reference" (2003: 41). This is an object-centered coordinate system based on anatomical planes. In this system, coordinates are based on features, sidedness, or facets of objects that function as Ground (the relatum). Levinson points out that these features are not inherent in the objects, as is sometimes assumed, but get assigned by language-users on case-by-case basis. Anatomical terms of location can be conceptualized as a box-like, six-sided framework superimposed on objects in the standard anatomical position. As with other intrinsic

systems in English and Norwegian, it is oriented by gravity. The bottom becomes the undermost facet, and the animal's top is the uppermost facet. Front and back are decided by establishing the direction of the organism's perceptual apparatus, like its usual direction of motion. Bilateral, symmetrical animals like *L. salmonis* are also attributed with sides. This yields a total of six polar opposite facets. Three pairs of polar opposites yield three axes intersecting at right angles, together constituting a three-dimensional geometry (Fig. 7.9).

In Norwegian and English, language users normally employ functional criteria to assign the features, sides, or facets of objects in the

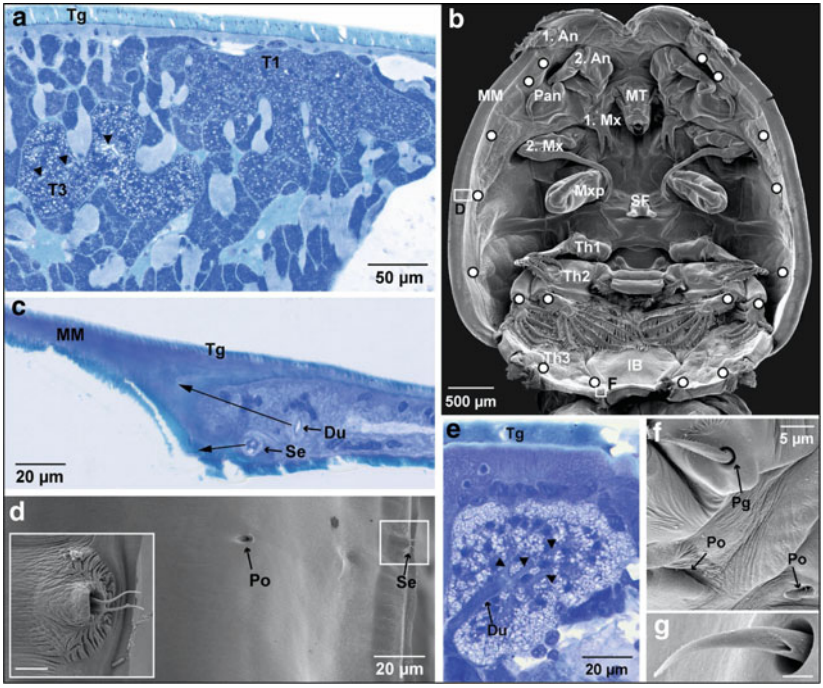

Fig. 7.9 An annotated montage of micrographs from SEM (b, d, f and g) and light microscopy (a, c, and e), supporting the locative description (Øvergård et al., 2016). Figure and accompanying text contain inscriptions that assist in the interpretation of data, such as a scalebar and information about lens magnifications (Reproduced with permission from Wiley & Sons)

intrinsic frame, while other languages can solve this problem differently. Conceptual properties of objects like shape, canonical orientation, characteristic motion, and use are all attributes that may be employed for this rendering. In the intrinsic system then, the Ground (relatum) and the Origin of the coordinate system constitutes the same object, creating a spatial binary between Figure and Ground (as opposed to the ternary relations used for the relative reference frame, see Levinson, 2003: 43). Having established the "front" (anterior) of a biological object, the cognizer can anchor "a ready-made system of oppositions" such as "back" (posterior) and "side" (lateral) along the organism's intrinsic axes (ibid.: 41). This is done by extracting an angle or line radiating out from the Ground object's centroid mass or facet. The main object of interest (the Figure) will then be located within or on this angle/line at a determined, specified distance. So, having identified the "anterolateral pair of teg 2 glands," the glands positioned in front and to the side in the above quotation, a proficient biologist can then identify a duct that extends frontally together with the teg 1-gland. The position of the teg 1-gland gets defined by an arc from the frontal facet of the cephalothorax, a body part which is adjacent to the antennules.

In contrast to the natural discourse and the notebook descriptions surveyed above, no circumstantial information about their context of production is necessary for these descriptions to be meaningful for specialists. With special purpose anatomical terms of description, named facets of objects provide anchors, instead of anchors being defined based on the direction of gaze or gesture by an observer, as in the relative frame of reference.[19] In the intrinsic frame, rotation of the viewer and the entire array will yield equivocal descriptions, while a rotation of the Ground object will not. In the relative frame the opposite would be the case: rotation of the viewer and the whole array would yield different descriptions, and rotation of the ground object will yield the same description. Being allocentric, the intrinsic system thus yields an "'ego-invariant' picture of the world out there" (Levinson, 2003: 54), highly suitable to convey precise renderings of a complex, microanatomical domain to others. Here, we see that spatial reference to the phenomenal objects of interest has transformed into a specific, external coordinate system. This intrinsic frame uses the facets of anatomical objects as a Ground to

establish the position of the salient Figure to be described by mapping each one along the object's intrinsic axis. Through such representational means, "any whiff of the personal, any human odor" is removed from a research process that is inherently situated and embodied (Jacob, 1998: 117).

To appreciate the absence of anatomical terms of location during microanatomy and in the notebook, it is necessary to keep in mind that Hanna started out as a novice in microscopy. As she progressed through her project, one of the major changes in her practice was a transition from using everyday folk language for marking spatial reference to become a competent practitioner. This included the ability to recast and articulate her observations of lice exocrine biology in specialized anatomical terminology. Throughout this process, the novice learned how 'to see' phenomena like exocrine glands, exit channels, and other structures with the microscope. This cognitive accomplishment required her to move between complex representations, integrating information from different domains in ways that represented and re-represented the problem-space many times over. Hanna articulated how the translation of her notebook description into the professional discourse of microanatomy, the precision tools of the trade, involved a major learning transition from her background as a molecular biologist, primarily working on gene expression. Commenting on this section, Hanna also believed that a trained histologist would have used more anatomical terminology in their scribbles, and she suspected that Tom did not want to overburden her with too many technicalities when they set out on their anatomical quest.

The manuscript's fate reveals another dimension to Hanna's challenges with becoming a professional, as she also had to navigate between the expectations and epistemic interests of morphologists and molecular biologists. Differences in scope and interest proved difficult to reconcile at first, as the researchers submitted their work to a specialist journal on arthropod anatomy. One reviewer was quite positive about the manuscript and the figures, with the exception of some minor disagreements about dyes and staining methods. Unfortunately, the other reviewer was harder to satisfy. Finding the paper's claim inadequately substantiated, the review argued that that the paper contained no detailed morphology of gland *structure*. According to the reviewer's

understanding, this necessitated a more extensive use of transmission electron microscopy. This critic also identified a mismatch between the scope laid out by the paper's title, and the types of data that was presented to fulfill the stated ambition. There was also disagreement about interpretations of empirical data concerning some of the proposed glands. While Hanna rectified the title, and addressed all of the peer comments, including what she considered to be serious misunderstandings by the most critical reviewer, the journal's editor ultimately rejected the paper. Here, the main point of contention was that the figures, in agreement with the latter reviewer's objection, contained "no high-quality morphology." In Hanna's opinion, the Centre's emphasis on a functional genomic approach to exocrine glands for understanding host–parasite interaction did not resonate well with the journal's *structural* emphasis. After this rejection, Hanna resubmitted the article to a journal with a broader appeal, that could perhaps better appreciate both its scientific and applied relevance. While the second round of peer-reviewers also commented on lacking data from transmission electron microscopy, and requested alterations to figures and more detailed annotations, the paper was eventually accepted and published.

In crustaceans, exocrine glands serve many roles depending on the organism's lifestyle requirements. By the end of their investigation of the exocrine system, the team converged on a classification of four types. The first three were labeled "Teg 1," "Teg 2," and "Teg 3," because they were functionally associated with the outer body ("tegument"), while the fourth group were named "Labial" because these glands were located in the *labium*, the lower part of the parasite's mouth tube. As categories, these functional groupings of glands can themselves be understood as conceptual blends, containing input spaces from a wide range of domains like morphological information about form, texture, and color, functional aspects, developmental timing, anatomical position, and sites of secretion, that together constitute new groupings of biological structure. Hanna and Tom conjectured that Teg 1, the most numerous glands in adult salmon lice, excreted substances that maintained the tegument, while Teg 2 most likely produced substances protecting high-friction areas around the organism's body. Teg 3 was predicted to have several functions, since its development coincided with the virulent, pre-adult

stage of the lifecycle, the time when lice attach and start inflicting serious damage on the host. Along with the Labial-gland, Teg 3 was suspected to secrete factors that modulate the salmon host immune system. While tegmental glands consisted of only one secretory cell, the labial glands were composed of two larger secretory cells with individual reservoirs emptying into a joint duct that released its content when the parasite fed off the host.

Multiple methods helped to meaningfully home in on these groupings. Morphological data was supported by identification of marker genes detected through fluorescently labeled RNA-probes that visualize locations of gene expression of target sequences in tissue. Applying *in situ hybridization* to the Teg 1 glands revealed two *astacin*-coding genes. These genes belong to a family of enzymes known as *metallopeptidases*, which are used by parasites to modulate their host. *In situ* also revealed a *fibronectin type II*-domain gene that possibly served antimicrobial functions. The Teg 2 glands expressed a *heme peroxidase* gene, which was of interest because of an earlier inconclusive study on lice glands that detected activity of this enzyme in the parasite's oral cone (a finding reproduced by Hanna and Tom). At one point during the investigation, these enzymes were hypothesized to protect against the salmonid immune cells by limiting the narrowing of blood vessels and reducing general inflammatory responses. Additionally, the *in situ* method yielded fine-grained structural information about Teg 1 glands, which were shown to have three subtypes based on differential expression patterns. Awareness of these be valuable in future experimental work.

Structuring Microscopic Experience

How does a small group of biologists move from stray observations of microscopic objects on a thin section of biological materials embedded on a glass slide, to plausible descriptive models of a biological system on the human scale? They do so by reasoning with different representational artifacts and scientific visuals through a variety of ecological assemblies. Tissue slides are tangible entities: tiny pieces of biological matter sampled from salmon lice that contain the phenomena of

interest. These phenomena also appear as second-order graphic representations projected on the computer screen, and as third-order graphic representations embodied by environmentally coupled gestures and embodied notebook scribbles which animate and tie language to specific phenomena situated in a cognitive ecology.

By fashioning many different forms of attainable structure through their heterogeneous interactions, the investigators could, over time, coordinate and navigate their way through the salmon louse. Traveling through different parts of the organism, section after section, Hanna and Tom used a range of different construal operations to jointly structure their visual experience and create spatial reference. Instantiating what Alač calls "malleable fields of interaction," the media I have surveyed here affords scientists with many different opportunities to explore their investigatory materials (2011). Although camera-generated images of microscopic phenomena, for example, may seem to be salient because they embody 'objective' properties of the world, their epistemic powers really derive from such malleability. Like many other kinds of scientific visuals, micrographs have a double identity. They are epistemically productive precisely because they are both indexical and iconic signs. Their indexicality stems from the causal relations between the tissue structure, and how it appears when seen with the microscope. But micrographs also have iconic properties; they not only share similarities in an image-like manner with the target object of the investigation (gland structures *in vivo*), but also require embodied enactments through skillful acts of perception that function as "infrastructures for seeing" (Alač, 2011: 24).

Hanna and Tom's observations of exocrine gland anatomy, across fields of interaction, were deeply structured by a collection of basic image schemas, the embodied and generative cognitive structures for meaning construction, described in the previous chapter. In particular, both an embodied logic of CONTAINMENT, as well as a SOURCE-PATH-GOAL-schema, were central for supporting reasoning about lice glands both in first-order, second-order, and third-order representations. The CONTAINMENT-schema, for example, has a physical basis in human phenomenology and consists of an inside, an outside, and a separation between these two domains by a boundary, with the inside seen as a

bounded region in space (Johnson, 2008: 138). Our bodies have boundaries, and so do the vessels we encounter in our environments, exocrine glands included. Containers, like glands, can be filled, or emptied. The CONTAINMENT-schema also has transitive properties. If an entity X is inside of Y, then placing Y inside of Z also transfers X. Exocrine glands are conceptualized as locations contained in three-dimensional space within the organism, which can be further partitioned into specific tissue regions. With respect to the substances produced in these locations, glands are conceptualized as containers for biochemical substances within the larger container of the louse body (Fig. 7.10).

A shared logic of CONTAINMENT allowed Hanna and Tom to perform a variety of conceptual transformations during their observations across representational substrates, such as reasoning about entries, enclosures, partial closure, and force-dynamic transformations. As seen with the microscope, individual tissue sections do not afford a direct view of the salmon louse as a three-dimensional structure. Instead, a fictive three-dimensional model had to be created by imaginary, and physical movements, through consecutive sections of tissue. As mentioned, Hanna would occasionally make observational jumps from one slide (number 346, for instance) to another section (say, 357) in a given specimen, depending on the necessary level of resolution that was required to identify the biological structure. On basis of these sampled observations from a larger biological segment, a composite model could then be scaffolded from a wide variety of mnemonic resources.

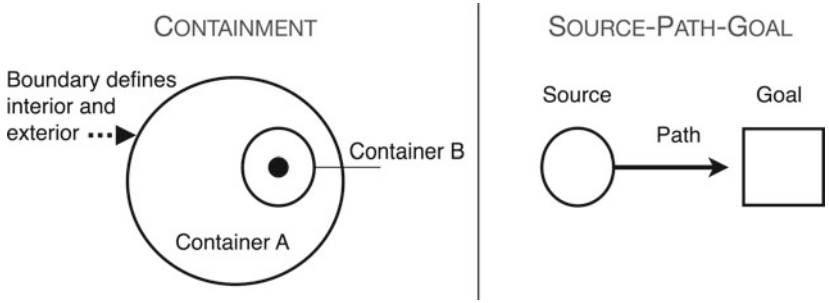

Fig. 7.10 Basic schematic structure of containment and source-path-goal

Exocrine gland anatomy was also supported by another key conceptual structure, namely the SOURCE-PATH-GOAL schema of directed motion (Johnson, 2008: 142). This schema guided Hanna and Tom's conceptual movement "through" the louse specimen, as they followed channels that ran from individual glands to surface exit points. The schema was also activated when substances were described as moving in and out of cells and the glands' exit channels. Such operations involved a superimposition of the SOURCE-PATH-GOAL schema onto the CONTAINMENT schema. Like CONTAINMENT, SOURCE-PATH-GOAL was invoked for event structures where an object moved from one location to another. It included a trajector (a moving object), a source from which movement originated, and a target goal. Reasoning about these properties also entailed questions of locality (i.e., a trajector's current location along a path), and directional forces moving away from the source toward the target. These movement schemas, which may include passage of time, stem from embodied experiences with movement of self, other agents, and objects.

SOURCE-PATH-GOAL was indispensable for Hanna and Tom's generations of rich meaning during gland anatomy. For example, what the two called *secretory tubules* originated in a *syncytium* that together constituted a *gland*. Glandular contents were collected in *ducts*, which moved via body parts like the *cephalothorax*, and exited on the parasite's *cuticle*. According to this logic, ducts could be traced in order to see whether they exited on the top or bottom of the parasite. The schema thereby scaffolded inferences about the structural–functional relations between the glands, such as whether the glandular content was for maintaining the tegument (top exit), or for modifying the host's immune system (bottom exit). But due to its salience, this schema could also support spurious inferences. In one case, illustrative for the power of schemas to structure experience, my informants painstakingly followed a sequence of objects leading out from a particular gland for hours, across many tissue slides. Initially, these objects were assumed to be an exit channel for glands. Only after intense checks and re-checks, did Hanna realize that the structure they had been tracking was not an exit channel at all. Probably, it was a neuron that ran alongside, and eventually branched off from, another structure they correctly figured was an exit channel.

Cognitive anthropologists assume that metaphoric expressions, as manifested through language and other communicative modalities, are tokens of more widely shared, instituted cultural models (Shore, 1995: 53). Such models are not just privately entertained by individuals, as internal mental representations, but may be publicly distributed in various forms, including those stemming from joint action and practice. The dynamic between publicly instituted and private mental models, what Shore aptly calls "the twice-born character of cultural forms," gives rise to a diverse dynamic of cultural transmission (ibid.: 68). The conceptual metaphor of GLANDS ARE CONTAINERS, for example, creates a shared cognitive artifact whose twice-born nature mediates the mapping of exocrine structures in salmon lice. It is both internalized by each practitioner, but also shared through public representations and intelligent actions within a scientific community.

Toward a Cognitive Ethnography of Microscopic Vision

In this chapter, I have stressed the importance of linguistic modalities for how cognition gets distributed during microscopy. But I do not suggest that knowledge is always encoded in language, or that language is a privileged channel for knowledge. Such a view would conflict with the cognitive framework chosen here. Instead, the emphasis on language has been empirically motivated since it emerged as an epistemically valuable resource for my interlocutors during microscopy. As science is "a world of ideas in motion" (Jacob, 1998: 117), language and writing are technologies to domesticate fleeting impressions in the laboratory.

I have shown how joint spatial attention to scientific phenomena during socially situated microscopy is achieved by a range of semiotic means. One way that vision was domesticated in these interactions was through verbal triangulations between several adjacent landmarks in anatomical space. In part, Hanna and Tom navigated their landscape by peering into the microscope's ocular and consecutively highlighting salient structures by verbalizing topology, deictic descriptions,

and anatomical placenames. Through these linguistic means, each participant encouraged the other to shift their attention among entities by alternating between Figure–Ground relationships. Andy Clark captures how language confers epistemic powers through such mundane referential operations: "To formulate a thought in words (or on paper) is to create an object available to ourselves and to others, and, as an object, it is the kind of thing we can have thoughts about. In creating the object, we need have no prior thoughts about thoughts – but once it is there, the opportunity immediately exists to attend to it as an object in its own right. The process of linguistic formulation thus creates the stable attendable structure to which subsequent thinkings can attach" (2006: 372).

With these vehicles for practical thinking, Hanna and Tom could engage in scientific explorations, like the "interpretative journeys" identified by Ochs and colleagues in ethnographic studies of physicists at work. These are "sojourns that may take place both in the world of physical events (through taking on the identities of physical objects, or by animating and anthropomorphizing them), and the world of constructed visual representations as a cognitive and spatial domain to inhabit and wander in" (Ochs et al., 1996: 350). Sometimes these journeys happened without alteration of the physical media that was being traversed. On other occasions, transformations of media were crucial for the making of novel conceptual blends that could spur new insights about exocrine biology in salmon lice.

The ecological assemblies facilitating such microanatomical journeys required opportunistic use of a range of semiotic modalities besides language. In the first ethnographic vignette (Fig. 7.1), the pair examined biological structure in a microscope equipped with two individual eyepieces. In this session, both collaborators could monitor the specimen while Hanna directly manipulated the tissue slide. Here, there was a limited range of communicative modalities available to the two collaborators; since the material affordances of the assembly required both to peek into the ocular to see the objects of interest, resources like pointing hands and directive eye gaze were not immediately available for inspection. The communicative act of pointing and creating spatial reference

to locate a shared referent had to be solved differently. We saw how physically moving the specimen and changing the object's focus to highlight phenomena of interest, gave Hanna alternative, nonlinguistic means to create shared spatial reference. The microscope was also equipped with a deictic pointer, a small arrow superimposed on the visual field, which a skillful user could use to support a visual search and construe shared reference and meaning. In other contexts, these epistemic actions were conveniently served by other semiotic modalities.

We saw an example of these modalities in action when the two histologists worked on a microscope equipped with digital camera mounts that projected images to a computer monitor. This setup afforded the use of alternative representational media for meaning construction, with the screen providing an additional field of interaction for joint attention. It made accessible resources for shared spatial reference through deictic marking, using the mouse pointer, various pointing gestures, and forms of touch. The screen also afforded the invocation of iconic signs. These could be used to annotate the existing anatomical landscape by providing a material anchor for conceptual blends that could be richly elaborated by both Hanna and the Professor through interaction. Iconic gesture also facilitated visual comparisons between gestural models and the structure available on the screen, adding concreteness to abstract models of exocrine biology. While not shown in the above transcripts, I observed multiple instances where the objects of interest in the microscope, as seen through the ocular and on the computer screen, were compared and juxtaposed with various other external representations and models on paper, such as printed anatomical diagrams from scientific articles and other sources. These ecological assemblies created additional stability between different visual representations and were central for "seeing" glands as a scientifically salient phenomenon.

My ethnographic observations of these microscopical journeys resonate with Gooding's proposal that visual inference in scientific practice basically consists of a series of generative transformations (2004). In his analysis of how paleo-biologists reconstruct extinct organisms, Gooding shows how "word-image-object hybrids" become epistemically powerful by integrating different forms of multimodal knowledge and experience. This, in turn, supports a continuous movement between the

personal domain of internal, mental representations to public tokens of meaning and the conventions that govern these (ibid.: 581). Transformations carried out on plastic representational media can either reduce or increase this informational complexity, with far-reaching epistemic consequences. The act of extracting features, relations, and patterns in the many figures and diagrams fashioned by Hanna and Tom, occasionally simplified complex representations like tissue slides by *reducing* their informational content. Such reductions could serve to highlight exocrine gland structure, along with meaningful, explanatory accounts of their organization. But the scientists also made enhancements to integrate information from different sources in ways that *increased* representational content, by juxtaposing and aligning representations that were inadequate alone, but together captured invariant features of a microscopic world. As we saw, any derived model of salmon lice exocrine morphology had to satisfy constraints from several domains, not just microanatomy. Such technologies of the mind worked through a complex interplay of internal (private) and external (public) representations.

This ethnographic investigation has described how complex low-level cognitive processes such as stereoscopic visual perception becomes culturally orchestrated through language, acting bodies, and a suite of material artifacts. Together, these provide tools for thinking about biological systems at the microscopic level. Here, I have used cognitive ethnography and the framework of distributed cognition to reconstruct some of these practices. The video camera, coupled with participant observation and scrutiny of artifacts, and inscriptions that are produced and consumed by the community in question, show the value of attending to night science. Night science is not epistemically dubious. However, scientists may sometimes express discomfort when talking about these aspects of their research. Not only does night science detract from idealized, normative models of scientific work, but there is also a perceived trade-off between making and publishing new discoveries and investing in deep reflexive engagement about its many facets.[20]

We have seen why microscopes do not facilitate perceptual augmentation for seeing the microscopic in the same way as eyeglasses help people with poor eyesight to see better. Microscopic vision is not passive, but an

interactive process of meaning-making that requires skillful integration of many types of supportive media. These cognitive practices, in turn, facilitates modeling of an otherwise invisible world.

Notes

1. These conversations were done in Norwegian. All translations by the author.
2. Commenting on a draft, Hanna explained that the structure in question probably was a muscle tendon attachment. When cut straight across, the structure could be mistaken for a gland.
3. Someone had also replaced expensive objectives from one of the labs with lower-quality microscope objectives. This event raised questions how access to the facilities should be regulated.
4. Retraction Watch monitors these events. See: www.retractionwatch.com.
5. Although similar in many respects, electron microscopy uses other reagents, and sections are cut thinner.
6. Different microscopes use different techniques, e.g., microtomes with diamond knives for transmission electron microscopy, and cryo-sectioning with cryostat-devices for oncological applications.
7. Scanning electron microscopy was first used in 1942, 11 years after transmission electron microscopy appeared. TEM relies on a transmitted electron beam passing through the sample to form an 'internal' image of the specimen beyond the surface. It is used for thin sections, to visualize an extremely small scale (around 0.5 Angstrom). Electron microscopists used six epistemic principles to decide what biological experiments show: validation of theory by instrument, calibration with precedented knowledge, calibration with independent methods, practicality, aesthetics, and the inference to function (Rasmussen, 1993).
8. This is the 'grid-argument' about the reality of unobservable entities. Make a machine that carve consecutively smaller grids on a surface, some being invisible to the naked eye. Look at the surface through a microscope and see the same grid-structure as those visible without augmentation. It would be unlikely that this is a coincidence. Hence, we can be confident that microscopic entities exist. A skeptical response is that we cannot assume what is in dispute; namely whether we actually made the grid to be that way.

9. The term 'Sitting-with-Nellie' is used to describe situations where a trainee learns a job poorly by observing an experienced person, often haphazardly without a plan. The trainee might learn much, but can also pick up bad habits, since the senior does not always have the skills necessary to train others well. My use here does not imply any value judgements.
10. Mody and Kaiser points to similarities between this pedagogic style, often based on legitimate peripheral participation where newcomers gain experience through low-risk tasks, and participant observation (2008).
11. In some clinical contexts, other planes of reference, such as the parasagittal plane, are used to carve an organism into unequal halves, as well as composite planes for distinct regions or body-parts.
12. Distal (away from) versus proximal (close to) are polar opposites, used independently of axial planes.
13. Deixis and 'indexicality' are overlapping terms used in different traditions of linguistics and philosophy. The latter describe contextual dependency in meaning, while the former is used in a narrow linguistic sense.
14. Person-deixis refer to speaker-identity, place-deixis refers to individual location, and time-deixis refers to (a) when a message is sent, and (b) decoding time. Interpersonal relations manifested in honorifics, politeness, and intimacy-talk may constitute social deixis, and audiences of deictic reference do not always participate in the speech act, as deictic elements can display two layers of conceptualization: one relative to participants' situatedness in the speech act, and a construal displacing the situation to a different time and place, i.e. 'deictic projections' that displace the deictic center to an imaginary agent (Croft & Cruse, 2004: 60).
15. Ochs et al. show how scientists frame and enact objects of inquiry as sentient agents (1996: 338).
16. This distinction mirrors that between the context of discovery and justification. Logical empiricists claimed that the purpose of philosophy was to describe the logical structure of scientific theories, and relations between theory and evidence. A consequence was the exclusion of scientific discovery and practice from the scope of philosophical investigations, and a lack of interactions between epistemology and the empirical enterprise of science studies, broadly construed. This separation has been challenged by "Friends of Discovery" in the philosophy of biology, for instance (Schickore & Steinle, 2006: vii–viii).
17. Under the slogan 'no insider information', the Open Notebook Science-movement works to set free 'dark' data (failed experiments included), by transparently sharing notebooks without limitations.

18. In Norwegian, Hanna's working language, demonstratives are determined by the gender, number and distance in relation to the deictic centre that determines its form (dette, den, det, disse, de, her, der). Some languages use demonstrative systems that indicate different distances from the speaker, listener or both, while others use more complex systems.
19. Levinson claims that for informational content in spatial descriptions there are only two semantically acceptable translations between Frames of Reference (2003: 59). One can move from an orientation-bound, relative frame to the orientation-free, intrinsic frame, or from the absolute to the intrinsic.
20. Peter Medawar provocatively asked if this means that scientific papers should be considered fraudulent (1996). On the perils of sanitizing research in science education, see Howitt and Wilson (2014).

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8

Concluding Remarks and Future Prospects

In 2015, the Sea Lice Research Centre received its long-awaited midway evaluation along with the six other projects, who all began operating in 2011 after making it through the Research Council's second funding call for new Centres for Research-based Innovation. On the evaluation committee sat four recognized experts: two specialists on the Centre's field of research, and two authorities on innovative collaborations between academia and industry. Their report, which contained a set of recommendations for the future organization of this funding scheme, would form a basis for the Council's decision about whether they ought to discontinue research after the first five years, or extend funding for three more.

In their report, which was partly based on a site visit to Bergen in late March the same year, the four evaluators were impressed by what they considered an "excellent and highly performing Centre," with a wide range of expertise crosscutting scientific disciplines (RCN, 2015: 30). At that point, the group had published dozens of peer-reviewed articles, presented widely in conferences, filed patents, and helped their industrial partners better understand how to deal with salmon lice. The Centre's administrative efforts were also praised, as its financial reporting had

M. Solberg, *A Cognitive Ethnography of Knowledge and Material Culture*, Culture, Mind, and Society, https://doi.org/10.1007/978-3-030-72511-2_8

established "best practices." The panel would, however, like to see "the remaining Centre funding period to be more focused on specific innovation goals including development of vaccines and drug candidates," as well as a strengthening of international collaborations, improvement of communications within the Centre's network, and with the appointed Scientific Advisory Board. Additionally, the committee stressed the need for increased international exposure of research, improvements in its translational potential, and further cultivation of relations with industry stakeholders. Specifically, the Centre was encouraged to plan for the long-term sustainability of its "unique" experimental system beyond the funding period, and secure the "LiceLab infrastructure, including the line-bred sea lice strains, as an international research facility" (ibid.: 31). Based on the Council's Key Performance Indicators, those vital constructs of contemporary audit culture, there was little doubt that the SLRC would get an extension, and its endpoint was soon pushed to the 31st of August 2019.

In early February 2017, the Norwegian Seafood Research Fund convened their annual Cleaner-fish Conference in Trondheim. During a session on drug-free lice control, director Frank Nilsen reported that the Centre had completed a clinical trial with a "common garden"-design on recombinant test vaccines with eleven targets based on synthetic antigens in collaboration with the veterinary pharmaceutical giant Elanco. While these tests were inconclusive in terms of the antigens' protective activity, he reported that the Centre planned preliminary tests on seven other therapeutic targets in 2018, ready for termination by spring 2019. These two vaccine trials would be organized using separate replicate tanks.

On the third slide of his talk, Nilsen presented a cartoon of two scientists dressed in white lab coats. One was peeking into a microscope, telling his colleague: "You're right - it's wearing red cape and blue tights!". The caption read: "Scientists discovering a new superbug." Intended as a humorous reference to the issue of multiresistant lice strains, the imagery subtly underscored the situation's gravity. Surely, the director could not guarantee the crowd of industrial representatives, public servants, and other scientists in the audience, that his group's experimental research would yield new efficacious therapeutics in the immediate future. But

Nilsen's progress report at least offered a reassuring token of the productivity of SLRC's research pipeline, no matter the impact new vaccine trials would have on future lice management. After all, the experimental system had pinpointed salient targets among the roughly 14,000 predicted genes from the louse genome. Through hundreds of explorative RNAi-experiments, this search had uncovered a trove of insight about lice biology, and propelled multiple vaccine candidates to the testing stage.

There was, however, no mistaking from Nilsen's message that a lot of work remained. Having described how interventions against salmon lice had to be understood as an evolutionary "race between two genomes," Nilsen then surveyed some ways his team was working toward improving lice-control. One line of investigation probed the feasibility of making Atlantic salmon respond to lice attacks with similar mechanisms as other salmonid species like Coho salmon (*Oncorhynchus kisutch*) and Pink "humpback" salmon (*Oncorhynchus gorbuscha*), whose immune systems appear to rapidly reject the parasite. On this topic, they had for some time collaborated with a research group led by Mark Fast at the Atlantic Veterinary College (Prince Edward Island) in Canada. If they elucidated key genes for this immune response in the Pink salmon, they could perhaps, transfer some insights into their ongoing search for vaccine-candidates on Atlantic salmon. This work combined research on other salmonid species and breeding families with different genetic profiles and benefited from a novel experimental system for probing other salmonid species than *Salmo salar*, developed by Fast and colleagues. In the autumn of 2016, a new laboratory facility modeled after the cultivation-system developed at SLRC had also opened in Chile. Then in 2018, tanks for the maintenance of host fish were constructed at CARGILL's facilities in Dirdal (formerly known as EWOS), thereby multiplying experimental capacities worldwide. While molecular parasitologists still faced what Nilsen framed as a "needle in the haystack"-kind of problem, the Centre had accumulated a good assortment of instrumentation and techniques for detecting small differences in infection levels when testing interventions. The Centre's capacity to identify efficacious therapeutics had become more advanced, and there were plans to invest more in computational and mathematical methods for simulations and in silico

modeling of biological complexity in lice. The Centre's wetlab also made forays into cultivating strains of *Caligus elongatus* (colloq. *skottelus*) for experimentation. A close relative of *L. salmonis*, *C. elongatus* had gradually become a problem for farmers, particularly in Northern Norway. Being a more generalist species than the salmon louse, *C. elongatus* infects both salmon, the cleaner fish used in salmon pens, along with other fish species. Such indiscriminate host preferences raised intriguing biological questions.

By 2018, Centre management and its appointed board had laid an exit-strategy for the period after their funding would expire. In response, the University of Bergen's board agreed to support a future incarnation of the Centre as a strategically important unit in the domain of marine science. Additionally, the Institute of Marine Research also committed resources to ensuring continued investigations of biological prophylactics, including vaccine work and host resistance mechanisms. Likewise, players in the farming industry, such as Lerøy Seafood Group, began a process to secure a research infrastructure for the next years.

In their annual report for 2018, the final full year of operations, the Centre reported that the initiative had achieved all but one of the main goals. Moreover, their only unfulfilled objective pertained to developing true integrated pest management techniques for the industry, an ambition that was terminated due to a shift in lice management practices in the fish farming community. With regard to the RNAi pipeline, the Centre had conducted over 700 RNAi-experiments targeting over 550 genes by the end of 2019. Combined, researchers from the Centre had produced over 80 scientific publications and given well over 200 presentations at meetings and seminars, in addition to hundreds of appearances in the news media.

Whatever effects these new directions of research would have for lice management in industrial salmon farming, the Center had successfully institutionalized a sophisticated and productive sandbox for experimentation, capable of spinning off in new, unforeseen directions, where knowledge about copepod ectoparasites is in demand.

Surmounting Crisis

Mounting challenges in the management of fish health, such as the disease-outbreaks that plagued farmers in the late 1980s before vaccines were available, or the multi-resistant lice-strains emerging around 2009–2010, could have brought Norwegian industrial farming to a grinding halt (Hersoug & Hovland, 2014; Hovland, 2014; Kolle, 2014). Instead, these crises, which were entangled with other bottlenecks like feed-supply management and biological control of the salmon lifecycle, spawned a plethora of entrepreneurial initiatives to devise new methods for managing the perennial problem of fish health (Lien, 2015). This dynamic ability to adapt to shifting circumstances was driven by breakthroughs in biological science (increasingly focusing on the molecular level), novel engineering-solutions, as well as social, administrative, and logistical technologies. What could have been critical breaking points during moments of past crisis instead led to a swarm of scientific research on specific technical problems, resulting in the emergence of integrated systems for pest management, employing a range of interventions to help farmers cope with lice and other pathogens.

As a result of this intensified knowledge production, Norway exported a record high 1.1 million metric tons of salmon in 2019, valued at 72.5 billion NOKs (Seafood Norway, 2020). But despite record-shattering numbers, the direct costs of lice-management have risen to unprecedented levels and were estimated to surpass 5 billion NOKs annually the same year, excluding indirect costs. Several delousing regimes introduced in recent years, such as mechanical removal and applications of cleaner fish like lumpfish and wrasse, have also spurred concerns over fish-welfare on a mass scale (Overton et al., 2019). In the absence of anti-parasitic drugs and efficient prophylactics, which include new, lice-resistant salmon breeds and delousing technologies, *L. salmonis* will continue to trouble open-net salmon farmers in Norway, and the authorities will not allow significant increases in biomass before this challenge is overcome.

There is also a chance that competing technologies may become viable solutions before any real breakthroughs in vaccine prophylactics are on the table. In the worst case, such developments could make high-risk

solutions like vaccines less attractive as an investment choice. Closed-pen technology, land-based farming, and offshore-farming offer three major alternatives to existing production-regimes. While each foregrounds old and new challenges, the industry's critics have longed pushed for a transition toward new modes of production, which some consider to be more long-term, sustainable solutions to current farming practices.

While research on closed-pen farming, on land and in the sea, is backed by significant capital, the technology is still on the trial stage. Marine Harvest, the world's biggest salmon producer, has invested millions in a new technology known as *The Egg*, a closed pen-structure for the sea. And although some early phases of the production-cycle of farmed salmon already take place on land, other producers are considering moving their entire operation on-shore. Biological, technological, and cost-related hurdles must be overcome to scale up a viable and fully integrated land-based production cycle. But this is an intriguing development from a historical perspective. Especially since problems with fish health were one of the key motivations for why salmon entrepreneurs transitioned from land-based pond-culture to marine farming, half a century ago. The gambit of the technological optimists is that such problems will be overcome in due time, spurred by intense scientific research.

Offshore-farming with deep water installations, partly based on technical know-how from oil drilling, another main Norwegian export commodity, offers the newest addition to this diversified portfolio of production methods. It has long been suspected that the light-seeking (phototactic) salmon louse is less adapted to deep offshore habitats than current farming locations in fjords and inlets. Several companies are now investing in these offshore megaprojects. One example is the *Havfarm* initiative from Nordlaks, a 385-meter-long, 60-meter-wide semisubmersible offshore rig with farming pens weighing 33,000 tons. The first exemplar arrived in Norwegian waters from a shipyard in Yantai (China) in June 2020. It is, however, far from certain that these ambitious and risky initiatives will succeed and emerge as cost-effective solutions to the salmon lice challenge.

The appeal of such installations, which may host up to 10,000 metric tons of fish, stems from a special concession system for incentivizing

experimentation and innovation, managed by Norwegian authorities. However, the current schema which includes conventional R&D concessions, and the apportioning of "green concessions" for developing new technologies with a lower environmental footprint than conventional farming, has proven fickle and generated plenty of controversy within the industry. With the current cap on maximally allowed biomass and production quotas, these highly attractive research concessions have become one of the few ways that production volumes can be increased. Their allotments are therefore highly sought-after by farming companies.

Considering these prospects for radical transformations in the production chain, it is hard to predict how the seascape of marine salmon domestication will change over the next decades. Despite an increasing global demand for marine protein, it is not possible to accurately forecast the role of vaccines against salmon lice in the long term. Neither is it clear how the Sea Lice Research Centre's experimental system will be appropriated to tackle new questions arising from shifts in modes of salmon production. My interlocutors often stressed that a viable vaccine, although helpful, would not present a silver bullet capable of vanquishing lice once and for all. But as fish farmers face soaring management costs, a highly effective vaccine against the ectoparasite could secure the position of open-net farming as an attractive production form, compared to alternatives like closed-containment, land-based farming, or offshore installations.

The environmental history of salmon domestication (as surveyed in Chapter 2) teaches us that salmon farming, whatever form it assumes in the future, will have to cope with parasitological challenges. This pathogenic arms race never ceases. It is a fundamental biosocial relationship in the evolution of life, and inevitably entangled with social and political aspects of any modern domestication project. Clearly, new experimental systems for making sense of these dynamics will accompany and help push the industry along whatever trajectory it assumes. How the social, material, and cognitive dimensions of experimental science jointly contribute to the mutual causation process unfolding between humans, salmonids, and parasites entangled in "the blue revolution," should be a fertile arena for future anthropological analyses of knowledge.

Toward a Cognitive Anthropology of Experimental Knowledge and Material Culture

At the outset of this book, I reviewed some key developments in cognitive anthropology and described how cognition should be re-specified as a socially and materially distributed process. My goal has been to show how anthropological studies of knowledge can benefit from ethnographically informed models of cognitive practices and embodied interaction. These extend the unit of analysis beyond the thinking individual, to a wider context that seriously considers the role of material culture. By sampling epistemic actions through cognitive ethnography of lab work at the Centre, I integrated the conceptual framework of distributed cognition with work on historical, philosophical, and social dimensions of scientific experimentation.

At the core of this observed scientific activity was an "experimental system," which Rheinberger identified as the working units of the molecular life sciences: "systems of manipulation designed to give unknown answers to questions that the experimenters themselves are not yet able clearly to ask" (Rheinberger, 1997: 28). These systems are not primarily for generating answers, but "vehicles for materializing questions." I argued that the domestication of salmon lice strains, the incubator system, the single-tank setup, as well as RNAi-screenings, and a multitude of practices associated with this activity, together constituted a distributed cognitive ecosystem that afforded molecular parasitologists with opportunities for exploratory, technology-oriented, and question-driven experimentation. These material engagements facilitated the making of new biological meaning through a range of other epistemic modalities than experimental tests of hypotheses in the strict sense of the term, where an experiment is deployed to make observations that can falsify a precisely formulated conjecture derived from a body of theory.

To account for these processes in cognitive terms, I invoked a generalized notion of computation as the "propagation of representational states across representational media" (Hutchins, 1995a: 118). Pairing this distributed framework with the method of cognitive ethnography yields

a compound lens for situating scientific cognition in an interactional perspective. Examples included the cognitive historiography of social and material dimensions of the experimental infrastructure; epistemic activities in SLRC's wetlab during RNAi-initiation and termination; engagements with computer interfaces and other epistemic enhancers for sequence analysis; ecological assemblies procured on the benchtop in the DNA-lab for executing gene-expression measurements through "qPCR"; and in exocrine gland microanatomy where the microscope played a key role in the epistemic process. This compound lens made it possible to follow how representations propagated through historical time within the Centre, and how they moved through physical, social, and conceptual space, productively constrained by cognitive divisions of labor.

Key to knowledge-production in this "evolving problem-space" for interdisciplinary exploration, was "cognitive partnerships" with various artifacts, through representational couplings between the internal and external resources of participating agents (Nersessian, 2009). These integrations between scientists and artifacts in a cognitive ecology were characterized by different degrees of malleability, accessibility, transparency, durability, and intensity (Heersmink, 2015). My analysis showed both how such partnerships matured over time, and how they were orchestrated in moment-to-moment flows of everyday practice. Osbeck and Nersessian have suggested that we should think about knowledge in such cases, not as something *acquired* by atomistic agents, but in terms of activity and situated processes (2014). This entails a perspectival shift that sees cognition as a system-level property that does not originate with any specific agent, but "stretches" out between actors in an ongoing traffic of representations.

This perspective also helps us see how the material culture of the Sea Lice Research Center instantiated what David Baird has described as "thing knowledge" (2004), a concept that draws attention to how material devices can be vehicles for cumulative scientific knowledge. Overwhelmingly, science has been conceptualized and exalted as primarily a theoretical enterprise. But as we learned from the New Experimentalists, apparatus and varieties of epistemic artifacts do not belong in "the intellectual basement," but deserve a seat among great theoretical achievements (Baird, 2004: 12). For Baird, one of the ways that things

and instruments can embody knowledge is by acting as models of the world, what he calls "model knowledge." Artifacts can also fulfill its knowledge functions by performing certain activities; specific actions can be partly separated from the agency of humans and built into the behavior of devices. This is "working knowledge" in Baird's terms. Some artifacts, like measuring instruments such as thermometers, are hybrid entities that perform their knowledge by producing representations. When both forms of material knowledge are integrated, instruments may also appear to "extract information from nature" (Baird, 2004: 73). This way of thinking about the epistemic role of artifacts in scientific activity resonates with that of distributed cognition; cognitive artifacts are more than just people's beliefs about them, since instruments may become cognitively autonomous in the sense that they provide a cognitive channel with quite different properties than theories and propositions (ibid.: 30). Furthermore, the knowledge embodied by cognitive artifacts can, under some conditions, be operationalized independently of the mental states of their users, as they acquire emergent features through practical engagements in functional systems that transcend the individual cognizer. In Chapters 6 and 7, we saw ways in which parasitologists established relationships between themselves and the molecular realm through artifacts and instruments that became cognitively efficacious by enaction of integration networks and craft skills that anchored a range of conceptual blends in different ecological assemblies on the benchtop.

These dynamics raise intriguing questions about epistemic trust and where agency should be located in distributed cognitive systems (Giere, 2004). While artifacts and instruments can be productive participants in epistemic processes, I would argue they still stand in an asymmetric relationship with humans when it comes to the question of agency. One reason for maintaining a distinction between humans and artifacts is that it is the human agent who engages in trusting relations with cognitive artifacts. As Heintz points out, trust is the "cement" of distributed-cognitive systems (2007: 319). Secondly, it is overwhelmingly humans who exercise epistemic vigilance and agency as a higher-level representational capacity for meaning construction, by evaluating and engineering the informational environment. On this basis, I found Malafouris' advice to ask when an agent is, rather than what an agent is (2013: 51),

to provide a useful heuristic for navigating the problem of agency in distributed cognitive systems of science.

Bounding the System

In a reflexive spirit, one could argue that ethnographic studies of laboratory action provide anthropologists with a kind of experimental system in its own right; a window on knowledge production as a cultural process. This idea is not entirely novel (Fischer, 2007), but usefully draws attention to how the laboratory circumscribes a microcosm, where the propagation of representations can be traced across relatively bounded units of time and space. But, as Osbeck and Nersessian remind, the boundaries of distributed cognitive systems are never self-evident (2014: 92). Throughout the book, we have seen traces of how activities at the Centre were embedded in a larger epistemic community of fish health science, situated in a knowledge society governed by politically defined managerial systems, participated in new relations with industry and transnational innovation networks, and contributed to expanding the tradition of molecular parasitology. While some representational practices were indubitably local, others were constrained by the affordances of globally distributed artifacts and widespread cultural practices in the sciences of life. As soon as the representational activities that sustain laboratory knowledge travel to locations outside the lab, spanning large distances in time and space through what Sperber calls "social cognitive causal chains" (2001), it becomes methodically challenging to track these rich cultural productions and their transformations.

The problem of bounding scientific cognition in the lab is also a segue into more general debates about the merits of "internalist" versus "externalist" perspectives in science studies. What weight should be accorded to respectively endogenous, technical accounts by insiders and the role of exogenous sociocultural factors in shaping the research process? A main objection against internalist accounts is that they sanitize science by not sufficiently incorporating external factors in shaping what occurs within the confines of the lab (see Shapin, 1992). In this work, I have rather unapologetically adopted an internalist position, because I find

it most useful for making sense of empirical questions regarding the nature of epistemic practice (cf. Hacking, 1992: 51–52). An interactional framework like distributed cognition shows how technoscience and their associated material engagements are already unavoidably cultural. Further additives like politics and stakeholder interests may, depending on the level of analysis, be useful and relevant, but these ingredients are not necessary nor sufficient for understanding science as a cultural process. This becomes apparent when we are zooming in on minutiae of knowledge production as the object of study (Kohler, 1994: 3–5).

One way to delineate the boundaries of cognitive ecologies like the experimental laboratory, is to simply specify the task function which the system executes. In this view, an activity should count as an instance of distributed cognition "only if the process is not enclosed by the epidermis of the people involved in carrying out the task" (Magnus, 2007: 299). By closely following the traffic of representations and its patterns of organization, the boundary problem at smaller scales becomes more tractable (Giere, 2004). But, in the end, we never come face-to-face with self-evident fault lines, joints by which distributed cognitive systems on different scales can be easily carved. All such delineations are perspectival and products of the analyst's own "discursive practices" (Goodwin, 1994). These rely on the identification of sites where traffic among elements within the distributed system is low (Hutchins, 2010a: 705–706). So, while analytical boundaries may pick out substantial patterns of cognitive organization they are seldomly naturally given and they are, ultimately, artificially determined (Osbeck & Nersessian, 2014: 92). Deciding how to set these parameters, however, has not just been a problem for distributed accounts of cognition, but is a recurring challenge for social analysis that is attuned to network or system level descriptions of how local phenomena interconnect with dynamics unfolding across multiple spatial and temporal scales. The anthropology and ethnography of knowledge traditions is no exception (Barth, 2002).

An implication of the boundary problem is that ethnographic inquiries into the nature of distributed cognitive systems must begin with an artificially determined perimeter, which must be updated as more insights about the system's functional characteristics and empirical

regularities are acquired. Throughout the preceding chapters, I continuously shifted the boundary locations of my unit of analysis depending on what information went where, when and in what form, in specific epistemic practices associated with the experimental system. Imposition of any boundary beyond the smallest units of human interaction will, to some extent, be perspectival, reflecting the analyst's interests and epistemic values. Use of video-supported multimodal interactional analysis helps restrain interpretations and keep them in systematic check. It thereby avoids the fallacies associated with "free indirect speech" as a key ethnographic modality to represent the native's point of view (Sperber, 1985: 19). But all representations, whether in ethnography or science generally, must balance between fidelity to real-world phenomena and pragmatic effectiveness in human communication. I hope that my own representations of scientific practices in this account, have been sufficiently transparent so that the reader can evaluate the cogency of the claims being made.

Still, any account of cognition that puts descriptions of meaningful practice front and center, can be subjected to a critique that may be directed against any study that relies on a high degree of interpretation (Osbeck & Nersessian, 2014: 90–91). Since meanings are always created, negotiated, and maintained through local practice, thick, contextual accounts may produce transferrable insights, but seldom lead to generalization in the conventional sense that is afforded by inference from controlled experimentation. The complex representations used in scientific practice, always carry multiple meanings, and require active interpretation by their users, cognitive anthropologists included.

Dark Matters

In an illuminating comparison of distributed cognition and pragmatist philosophy, in particular its cognate tradition of "functional psychology," which stressed the adaptivity of agents in interactive contexts, Osbeck and Nersessian argue that the role of values in distributed cognitive systems warrants attention (2014: 93). Scientific problem-solving, for instance, is directed by epistemic values and preferences like parsimony,

coherence, simplicity, transparency, efficiency, adequacy, aesthetics, etc., all which challenges the fact-value distinction. Pragmatist philosophers saw values as deeply intertwined with functions, since any function for a human agent implies that some value is involved. The opportunities that our artifacts afford, for example, are determined by the value that object holds for the agent in a context. For Osbeck and Nersessian, this suggests that representational states are not value neutral. One challenge for future research on the material dimensions of scientific cognition then, is to understand how epistemic and other values enter distributed systems and the communities of practice creating them. In anthropological terms, the question of value, what people find good and important and connect to wider webs of meaning that motivate social action, is closely related to questions of identity, political and economic interests, as well as the personal biographies of individuals and their communities. A thorough analysis of these interconnections falls outside the scope of this book, but merits scrutiny in future work.

When taking value into account, one must also come to grips with the role of affect. As Hutchins have underscored, enacted representations in embodied and distributed cognitive systems are "saturated with affect" (2010b: 434). A topic ripe for future investigation is the relationship between affect and trust, which as the cement or glue of distributed cognitive systems "binds researchers' testimonies about products of their distributed epistemic labor into collective knowledge" (Miller & Freiman, 2020: 26.1). Still, it has been notoriously difficult to move beyond paying lip-service to the issue of affect, which continues to pose a deep challenge for cognitive anthropology, broadly speaking (see Anderson, 2011 for a review). Taking a somewhat different, and explicitly interpretative approach, Natasha Myers has produced a laboratory study sensitive to affect's role in the work of protein crystallographers (2015). Myers ethnography unpacks the affective entanglements of "kinesthetic imagination" and "visceral sensibilities" that sustains embodied reasoning about the structure and function of complex biomolecules. She addresses questions about how intuition and affect about molecular mechanics is cultivated and performed, how the truth-status of protein models are imagined, and how analogy and

anthropomorphism help render their structure across different materials. Other promising directions in this regard include efforts to study the role of affect in enactments of "epistemic identities" among laboratory scientists, which help sustain certain kinds of cognitive practices and collaborative, adaptive problem-solving at the intersection between disciplines (Osbeck & Nersessian, 2017).

While I have exemplified some of the guiding values and identities that were enacted within the SLRC's experimental system in preceding chapters, future studies of epistemic action should aspire to integrate "affective" analyses with microlevel descriptions of interaction in specific cases of knowledge-production. While my own work adds to a small collection of studies on systems of practice by which representations propagate in the laboratory, the enactment of epistemic identity, value and affect, remains uncharted territory as dark matter in the cognitive ecologies of science.

Cumulative Culture, Materiality, and Scientific Progress

What does my cognitive ethnography of practice and material culture in the laboratory have to say about the cumulative nature of science? While scientific progress is often conceptualized as positive theoretical progress, I think that a view on scientific activities that takes practice and material culture seriously let us better see the ways in which scientific knowledge grows. I assert that a distributed analysis of experimental science, as fleshed out empirically in this book, is in broad alignment with an account of scientific progress articulated by Hasok Chang (2007). Attempting to move beyond stock positions like foundationalism and coherentism, Chang shows how it is possible to have successive stages of improvement in knowledge building on past achievements, without an "indubitable" foundation.

Foundationalists dreamt about justifying scientific knowledge on a firm foundation of first principles. An appealing vision for positivist philosophy, surely, but it was soon apparent that this approach simply failed to capture many critical historical developments in the empirical

sciences. Foundationalists assumed self-justifying propositions could be identified, and that new knowledge could be based upon these. But it is now well-known that even seemingly self-justified propositions also need some justification, which quickly leads to the problem of infinite regress. Another, more empiricist, variety of the foundationalist project was therefore conceived. Here, science was conceptualized as progressing by accumulation of secure facts derived through observation, and by the generalization from such facts to theories. This version of foundationalism had a longer lifespan. However, we have seen how a "theory-centered" blueprint of science, which characterized both logical positivist and post-positivist models, offers a poor scheme for understanding the growth and distribution of many scientific practices in empirical terms.

A major blow to the veracity of the foundationalist template was the problem of the theory-ladenness of observation; history shows that even the simplest observation requires scientists to make theoretical assumptions on some level. Chang offers a musing example, namely the logical positivist's fundamental protocol sentences: "If we were to seek observations that do not embody theoretical interpretations, we are reduced to the level of "sense-data"; not anything like "The photon emitted by a distant star has the wavelength of 8000 angstroms," not even "I see a red star," but "Red here now," whose desperate incorrigibility is entirely useless for building scientific knowledge" (2007: 3). From the viewpoint of distributed cognition, even the simple act of seeing a red star, which entails picking out an individual item from an array of stars clustered in constellations on the celestial sphere, is reliant on cultural transmission. Specifically, it presupposes a cultural-cognitive ecosystem in support of a family of epistemic actions for exploiting and activating "the practice of imagining particular trajectors on particular visible arrays of points of light" (Hutchins, 2014: 39).

Coherentism was launched as a replacement to foundationalist doctrines by advocating that epistemic justification was possible when the beliefs of a community were coherent with other beliefs entertained by the group. The metaphor of Neurath's boat famously summarizes this alternative to foundationalism. For Otto Neurath, scientists are analogous to mariners who must continuously rebuild their faulty ship at sea

with the best means available, making odd materials fit with each other without ever getting into dry-dock to do a thorough rebuild of the hull (1973: 199). But despite its appeal, the coherentist notion that any two belief systems will be equally justified, if each is internally consistent, inevitably raises the specter of relativism. If internal consistency is the sole criteria by which knowledge claims are evaluated, there would be no way to justify and privilege one knowledge system over another, nor assess if progress has been made.

Chang offers "progressive coherentism" as an alternative view on scientific development, that helps move beyond the "false dichotomy" of these two positions (2007: 5). Progressive coherentism rejects the search for firm foundations for knowledge (e.g., there is little need for Truth, capitalized), but accepts that progress can still be achieved in the absence of ultimate justifications. Instead, progress is the outcome of repeated bootstrapping exercises that refines and correct initial assumptions in the knowledge system. Material culture plays a key role in sustaining this process. In previous chapters we have seen how sensation through instrumentation is widespread in scientific practice. And with the ability to detect, measure, and quantify things under controlled circumstances follows opportunities for increasing precision. This process of calibration, which Chang spells out using examples from the history of thermometry, requires epistemic trust both in other instruments as well as other actors within the community of practice (see also Bird, 2014; Wagenknecht, 2015). Prior standards for measurement provide an initial justification for later standards, which can subsequently be used to refine and correct the priors. Conceptually, the relevant metaphor for Chang is not one of building knowledge *upwards on firm ground*, but *outwards on a round earth*; a dense, large body in perpetual motion that attracts other objects, but is never firmly fixed (2007: 7).

In Chapters 3 and 4, I described how an experimental system for probing salmon lice, emerged as a "self-vindicating" structure over a decade long process (Hacking, 1992), through coordination, alignment, and fine-tuning of various laboratory resources, encompassing ideas, things, and the manipulation of marks. The domestication and cultivation of lice strains, the introduction of a single-tank system, and the application of RNAi, were all critical steps towards building a reliable

system of detection that was sensitive and precise enough to discover "sources of error" within the system (Chang, 2007: 11). In the end, this system could transform signals about patterns of gene expressions and lice loss into data and controlled information for identifying, developing, and evaluating vaccine candidates through clinical trials. Having domesticated the louse, opportunities arose for identifying and describing new phenomena. During this bootstrapping process, even the phenomenal body of investigators became instrumental resources for animating static representations and making sense of fine-grained, microscopical biological structures.

These activities afforded a myriad of opportunities for "epistemic iteration" (Chang, 2007: 18), an answer to how there can be progress if we accept that: (a) we can only learn on the basis of what is already known, and (b) we know very little initially. Epistemic iteration addresses this problem by pointing to the process of cultural selection whereby scientific knowledge gets continuously refined through iterations, without postulating eternal, absolute foundations. Successive stages of knowledge build on what is imperfectly known, to satisfy epistemic goals and values such as consistency, explanatory power, scope, simplicity, precision, transparency, testability, unity, and opportunities for exploration, without indubitable facts. There are no fixed algorithms for these processes of self-correction and bootstrapping.

To illustrate, Chang invokes another metaphor, that of an extremely near-sighted man who examines his own defective reading glasses (Chang, 2007: 19). Taking them off he cannot see the fine scratches on the lenses. So, what can be done to learn more about their defects? Well, by putting them on and looking at the glasses in a mirror, it is possible to see some of the respective deficiencies. But there is a problem; how can he trust the image that becomes available through the deficient glasses? Well, he can gain epistemic confidence from the consistency and clarity of the image, no matter how it was obtained, by provisionally accepting that defects in the glasses do not influence this or that aspect of his field of vision, or the image of the defect itself. Observing a smudge, he can infer that its boundaries may be sharper than they appear. By gradually correcting the resulting image based on observations with the mirror, it is possible for the epistemic agent to not only use the

glasses to reveal defects, but to support more precise understandings of their characteristics, and to even correct for potential distortions. Likewise, instrumentally augmented practices in science can progress without the need for a foundation of ultimate truth. By assembling resources of various kinds, scientists can build on imperfections by launching new inquiries, and through the investigative process, return to examine their initial assumptions. These coherent iterations set up successive stages of knowledge that can "ratchet" up new solutions, based on what was known during earlier stages, but which cannot be directly deduced from what was known at the onset.

Due to the emphasis placed on materiality and practice for understanding science in action, Chang's progressive coherentism through epistemic iteration bears similarities to Ronald Giere's "perspectival realism" (2010). According to Giere, whose position is explicitly informed by distributed cognition, science is not just a point of view among many other equally valid viewpoints, as a casual and relativistic use of the term "perspective" would imply. Instead, perspectival realism suggests that scientists build models of the world and explore the coherence of these models through the perspective of their instruments, which are sensitive to certain types of input when making observations. A salient feature of this view on science for the anthropology of knowledge is that the position recognizes that knowledge as cultural, fallible products are mediated by artifacts and other elements of distributed cognitive systems, and that knowledge is not inherently propositional. This also carves a space for reflexivity. As scientists succeed in creating more detailed or general perspectives on phenomena, via an instrumentally augmented bootstrapping process, so can those of us who study scientific activities historically, ethnographically or in other ways, do the same. As Giere puts it: "it is the best that any of us can do" (2010: 15).

While the question about whether and which parts of science are cumulative and why, has been the subject of fierce disputes, Chang's notion of progressive coherentism offers a naturalistic account of how cultural ratcheting of adaptive solutions within the sciences over time become possible. As my ethnography of molecular parasitologists has shown, productive experimental systems offer scientists a kind of playground or sandbox for epistemic iteration, supported by a garden variety

of epistemic values. This view also challenges simplistic conceptions of the scientific process, that see scientific theories and innovations as sprouting from prodigious, individual minds; the prototype of reasoning exalted by Rodin's iconic sculpture The Thinker. Despite that the history of science tells us differently, time and time again, this model of the lone genius form the basis for many reward systems in contemporary science. But the social character of scientific knowledge and innovation is not secondary, as the evolutionary anthropologist Joseph Henrich exhorts (2015: 6). It is the result of a distributed process and a product of our "collective brain": a "flow and recombination of ideas, practices, lucky errors, and chance insights among interconnected minds and across generations." To this swirl, we should add a vast repertoire of material culture that makes us smart.

Prospects for Future Studies

Comparative studies on the relation between mind, culture, and society used to be the providence of psychological and cognitive anthropology. Now, it has become a vibrant area of research, attracting funding and interdisciplinary collaborations that dwarfs earlier initiatives to synthesize new insights about culture in mind. As mentioned in Chapter 1, the growing field of studies on cultural transmission, aims to describe mechanisms and dynamics relating to the "emergence, acquisition, storage and communication of ideas and practices" (Cohen, 2010: 194). Although I cannot survey this burgeoning literature here, this broad church of scholarship represents an attempt to productively rethink the contested topic of cultural evolution in ways that avoid the fallacies of evolutionism, after the subject was mostly abandoned in mainstream anthropological theory, for good reasons (see Bloch, 2012).

A shared goal of these initiatives is to integrate different levels of analysis, by unifying an anthropological focus on localized events and contexts with explanations of evolutionary trajectories on larger temporal and spatial scales (Ellen & Fischer, 2013). These analytical models address the tendency of cultural forms to exhibit both conservatism and undergo radical change under different circumstances (see Henrich,

2015; Lewens, 2015; Morin, 2016 for representative positions). As proposed by Lewens (2015: 2), we may call "historical" those approaches that specify how cognitive capacities change over time, while "selectionist" accounts focus on how cultural representations and practices are subject to Darwinian competition and selection. A third, "kinetic" perspective, encompass those analyses of the social that combine adaptationist mechanisms and population thinking to explain cultural products and their evolvability as aggregate outcomes of interacting individuals engaged in a constructive process. It is worth noting that these ideas long have had a fellow traveler in science studies, namely "evolutionary epistemology," a naturalistic theory of knowledge that sees the growth of science as a special case of biocultural evolution (see Heintz, 2018 for a review from a "kinetic" perspective).

Yet, most studies on the emergence, selectivity, and partiality of cultural transmission, have largely drawn on other frameworks than the distributed approach to cognition. Cognitive ethnographies, sensitive to the role of material culture in the constructive process that enables communities of practice to build upon the efforts of earlier generations, can and should play a critical role in this joint interdisciplinary effort. I hope that this ethnography has highlighted how microprocesses of cultural transmission in science relate to a broader set of issues beyond the question of how information arises in an individual and gets transferred from one agent to another. By interacting with a broad range of material artifacts in an ecology of practice, scientists can significantly upgrade their cognitive capacities.

In a commentary on the future of anthropology's relationship to cognitive science, Bender et al. remark how the empirical and comparative study of cognitive diversity, knowledge, and its enculturation requires both disciplinary diversity and epistemic humility (2015). If one recognizes the embodied, distributed, and situated grounding of cognition, as revealed by the current sciences of mind, then the kind of "cultural apprenticeships" undertaken by ethnographers to access everyday life is essential for arriving at reasonable hypotheses. It is also key to understand how participants in experiments interpret their tasks, for safeguarding against studies with poor ecological validity, and for identifying new phenomena and research questions (ibid.: 684). While

naturalistic observations of practices in the wild are essential for such a project (see Rozin, 2009), this enterprise places onerous requirements on anthropologists to fashion ethnographic representations that can be epistemically productive for a wider community of researchers interested in theorizing the cultural dimensions of cognition. But while parts of anthropology are now reorienting toward a renewed effort at addressing "big questions" about the nature of culture and its proximate and ultimate levels of analysis (Ellen & Fischer, 2013), not all ethnographic representations are equally suitable for supporting this ambition (Sperber, 1985). Thick descriptions attuned to the fine-grained minutiae of multimodal semiotic interaction spanning talk, body, and world, offer one promising direction for taking up the "cognitive challenge" through ethnography (Bloch, 2012).

When taking a pluralist view on the material engagements characteristic of experimental science, instead of seeing experiments as practices solely aimed at falsification of theory through relentless testing of hypothesis, it also becomes easier to see how the "continuity-hypothesis" of science connects with work on different folk knowledges. This has conventionally been the domain of anthropologists outside the sphere of science studies. The hypothesis that scientific thinking and practice is continuous with everyday thought has precursors in both the ethnoscientific work of Bronislaw Malinowski, who proposed that "primitive" knowledge was the basis from which other developments in human knowledge sprouted, as well as Ludvig Fleck's studies of biomedical practice in the early twentieth century (Gonzalez et al., 1995). As Ellen has remarked, our use of science and indigenous knowledge as two "epistemological meta-categories," tends to obscure evidence that there are many different ways that humans can gain predictive knowledge about their material environments, each "characterized by a distinctive configuration of cognitive and technical features, and which in several dimensions cut across the usual dualism between science and indigenous knowledge" (2004: 411). One implication is that the activities of contemporary science cannot be properly understood unless one considers both the building blocks of everyday knowledge, and the more specialized practices for reasoning in action taking place in scientific institutions.

Following Morgan, scientific facts present us with a useful but ill-defined category of historically formed thing-like entities; all communities appear to have things they assume to be facts or fact-like, possessing qualities like being public, autonomous, short, specific, and reliable; something held in good belief according to standards of evidence at a particular time and place (2011: 8). The salmon farming industry has a long tradition of operationalizing scientific facts from experimental science to intervene in the salmon pen, in concert with other kinds of technical and tacit knowledge. Appearing in many guises and sizes, a steady stream of facts continuously traveled to and from the laboratories described in this ethnography, to new sites for use, including fish farmers, policy and decision-makers, other scientific communities, and the public. Examples of facts in transit from the SLRC included models of biological mechanisms (some embodied in patents for detecting drug-resistance in lice populations), domesticated louse specimens, equipment designs transplanted to other research labs, and a range of propositions about the relationship between lice and salmon. Both scientific papers and LiceBase, the Centre's bioinformatic database, exemplify such traveling media, replete with facts on the move. The database, for instance, contained data, packed and labeled according to shared standards, to ensure frictionless migration from the production line in the lab to reuse outside of it. Taking a broad view, this family of facts may come to include new tools that enable control and management of salmon lice in the future which, in turn, connect to and embody countless other facts about lice biology.

One pertinent question concerns the process by which these grains of knowledge about salmon lice travel from the experimental laboratories to the farming pen. We should not always assume that facts remain stable over time and space. Do scientific facts about salmon lice "travel well" in the sense that their integrity is preserved, or are they transformed (Morgan, 2011: 12)? If the answer is yes; what productive transforms are such facts subjected to, and by which agency? How do experimental facts about salmon lice acquire new users, and how do they function when deployed in novel contexts? Do these facts, big and small, acquire a life of their own when they enter new configurations of materiality, cognition, and action?

Addressing these questions will require other levels and units of analysis than those presented in this book. But I want to briefly propose one interface where it is possible to discern, empirically, how scientific facts about lice are lodged between different epistemic practices pertaining to salmon aquaculture; namely, the process by which farmers intervene to control the parasite. As we have seen, multi-resistant lice strains are, in part, a product of aggregate human decision-making, a collective action problem resembling other complex, decentralized pest-management systems in human history (see Lansing, 2006 for a case-study). This is recognized in §4 of *Regulation No. 1140 on control of salmon lice in aquaculture*, which require that Norwegian farming facilities within a geographic area coordinate their treatments (MTIF, 2013). However, one potential driver of resistant lice populations is idiosyncratic variations in therapeutic interventions. Despite being under the auspices of authorized fish health biologists and veterinarians who prescribe treatments, these can exhibit variation in dosage, timing, and drug selection. During fieldwork, I was made aware of this intriguing issue in a conversation with a biologist working for a pharmaceutical company. He was frustrated by many of his clients, who failed to follow the manufacturer's guidelines for drug use, which was derived from experimental tests that set optimal parameters for the compound's efficacy. In his experience many farmers instead preferred their own treatment-schemes, which produced suboptimal results at best. He worried that failures to comply with best practice were not only economically and environmentally costly but could accelerate evolutionary adaptations making current therapeutics even less efficient.

Could the toolkit of distributed cognition be used to examine interfaces between scientific facts and the "ethnoecological" knowledge of fish farmers and other stakeholders on the technical frontier of modern food production? A cognitive ethnography of these encounters must inevitably face up to both the boundary problem of distributed systems, and the interface between science and non-science, embodied by the intermingling of salmon farming and fish health science. As lice management is governed by a variety of regulatory instruments, this would also bring

into view anthropological questions about intersections between politics, power, and knowledge, topics ripe for cognitively informed analyses (Vike, 2011).

Articulating Scientific Practices

How a community conceptualizes knowledge, and its transmission, affects how knowledge develops in that community. Many schemas for science funding are based on an inadequate appreciation for the importance of investigatory modes in experimental science that fall outside a linear model of hypothesis-testing, and unreasonably restricts opportunities for epistemically productive work of an exploratory kind (O'Malley et al., 2009: 613). As one of The Research Council of Norway's designated Centres for Research-based Innovation, the Sea Lice Research Centre was created with the goal of shortening time from basic science to valuable industrial applications. Consequentially, it was supported by a "philosophy of funding" which recognizes the inherent multidimensionality of experimental science (ibid.). Here, the interplay between explorative, technology-oriented, and question-driven modes of inquiry, was seen as legitime expressions of the iterative process whereby knowledge is created, despite that these dimensions of experimentation do not correspond well to linear models and schematic blueprints of how these systems of practice produce insight.

As we have seen, exploratory experimentation on salmon lice often required practitioners to expand their domain by systematically varying the system's parameters, identify regularities, and find novel ways to describe, measure, and represent observed biological phenomena, every so often in the absence of theory. Routinely, this process was oriented around exploring the potentials of technology; progress demanded that old apparatus or techniques were modified, or that new ones were conceived. Without the research community's capacity to transform biological phenomena into new technologies, and to fashion technical objects from unknown, epistemic things, advances in the science of salmon lice would not have been possible. Domesticated lice strains,

the single-tank system, and novel applications of RNAi for screening experiments exemplified the trajectory of this process.

As an anthropologist of knowledge, it is not my role to adjure about the epistemological robustness of my interlocutors' work, or the demarcation principles they should use to justify their science. My project has mainly been descriptive, trying to answer how molecular parasitologists are able to accomplish what they do. The resulting ethnography of laboratory science is based on the fact that it is carried out by "natural-born cyborgs" (Clark, 2003); a species whose cognitive niche ubiquitously rely on a suite of external props and tools to transform its problem spaces, in a myriad of ways that recurrently escapes our attention.

The inhabitants of experimental systems designed to explore epistemic things face an open-ended problem-space, probing the unknown by tackling unprecedented problems. In contrast, the ecological assemblies of highly standardized domains like aviation and ship navigation are deeply routinized, as the desired target states of the systems under manipulation are known in advance, with solutions remaining stable over long timespans (Hutchins, 1995a, 1995b). For the past decades, our dependence on such elusive looping interactions with environmental scaffolds through cultural practices has become even more visible as digital computational devices now augment much of our modern constitution. But applying the distributed framework on experimental science does not predict, that more widely distributed processes inevitably produce better cognitive or epistemic outcomes. Answers to such questions must be determined empirically, case by case. Two heads may, as the saying goes, be better than one, depending on the circumstances, but two heads may also perform spectacularly worse.

A naturalistic view on knowledge implies that science and its associated epistemic activities cannot transcend the human perspective. Here, I have laid out some of the cultural practices of scientific cognition that biologists use to create new perspectives on a troublesome parasite in their laboratories. The many means by which science represents the world should concern us all: anthropologists, biologists, and laypersons alike. But understanding how experimental knowledge comes to

life, requires something more than a model of mind that conceptualizes thinking as wedged between perception and action; it requires that we take the cognitive life of things and their engagement seriously.

Cognitive ethnography helps determine what things mean to participants in an activity, how meanings are made, and document systems of meaningful practice (Hollan et al., 2000: 182). As this book has primarily been a contribution to the anthropology of knowledge, I do not believe that my account holds straightforward implications for normative epistemology. But I do hope that the ethnographic materials laid out above can offer biologists some new perspectives on what makes their investigations productive. It offers a meta-scientific vocabulary for articulating the multidimensionality of their epistemic niche, as an alternative to elegant, but simplified models of experimental science. These accounts have a strong grip on our collective imagination about what experimentation is and why it works, but these models do not always resonate with the activities I have described and analyzed here.

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Index

M. Solberg, *A Cognitive Ethnography of Knowledge and Material Culture*, Culture, Mind, and Society, https://doi.org/10.1007/978-3-030-72511-2