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REGULAR ARTICLE

# Properties of Life: Toward a Coherent Understanding of the Organism

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**Abstract** The question of specific properties of life compared to nonliving things accompanied biology throughout its history. At times this question generated major controversies with largely diverging opinions. Basically, mechanistic thinkers, who tried to understand organismic functions in terms of nonliving machines, were opposed by those who tried to describe specific properties or even special forces being active within living entities. As this question included the human body, these controversies always have been of special relevance to our self-image and also touched practical issues of medicine. During the second half of the twentieth century, it seemed to be resolved that organisms are explainable basically as physicochemical machines. Especially from the perspective of molecular biology, it seemed to be clear that organisms need to be explained solely by the chemical functions of their component parts, although some resistance to this view never ceased. This research program has been working quite successfully, so that science today knows a lot about the physiological and chemical processes within organisms. However, again new doubts arise questioning whether the mere continuation of this analytical approach will finally generate a fundamental understanding of living entities. At the beginning of the twenty-first century the quest for a new synthesis actually comes from analytical empiricists themselves. The hypothesis of the present paper is that empirical research has been developed far enough today, that it reveals by itself the materials and the prerequisites to understand more of the specific properties of life. Without recourse to mysterious forces, it is possible to generate answers to this age-old question, just using recent, empirically generated

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knowledge. This view does not contradict the results of reductionistic research, but rather grants them meaning within the context of organismic systems and also may increase their practical usefulness. Although several of these properties have been discussed before, different authors usually concentrated on a single one or some of them. The paper describes ten specific properties of living entities as they can be deduced from contemporary science. The aim is to demonstrate that the results of empirical research show both the necessity as well as the possibility of the development of a new conception of life to build a coherent understanding of organismic functions.

**Keywords** Agency · Autonomy · Information · Notion of life · Organismic biology · Systems biology

## 1 Historical Perspective

When we see an animal or a plant, we usually perceive immediately that it is a living being and we experience something different than seeing nonliving things. In scientific terms, however, specifying this difference turned out to be particularly problematic. Despite all modern knowledge about living organisms, it is still difficult to answer the question of what life really is. In a certain sense, life is still an enigma.

Throughout history several possibilities have been proposed to deal with this question. For Aristotle, life was an expression of the soul that he saw as a fundamental and irreducible property of nature, which he described in a hierarchical structure. His concepts dominated for a long time, until in the seventeenth century Descartes formulated his dualism of mind and matter. This was quite influential for understanding life, as the living body was assigned to matter, which then had to be explained mechanistically. All physical processes, nonliving and living alike, had to be explained by physical principles. Only the human mind was distinguishable from this, experiencing its existence exclusively within its own thinking.

Especially during the nineteenth century, the tendency to reduce life to physical and chemical principles grew stronger. Classical physics, especially mechanics, became very successful and advanced to the leading science. It increasingly demonstrated how to control and gain advantage of the physical world and developed as the basis for nascent technologies. As a consequence, organisms were increasingly described as machines, whereby the explanation in linear chains of cause and effect, like in classical physics, was regarded as the epitome of science in general. Even human beings were expected to be—at least in principle—describable as machines.

This physicalism fueled the attempts to reduce all biological and also psychological phenomena to the smallest material components in which the driving causal processes were expected. This is the reductionistic method, which has been characterized by Emil Du Bois-Reymond in his famous lecture "Über die Grenzen des Naturerkennens" ("On the Constraints of Understanding Nature"):

> Understanding nature […] is to attribute changes in the material world to movements of atoms, which are caused by central forces independent of time, or the dissolution of natural processes into the mechanics of atoms (Du Bois-Reymond 1872, p. 2).

This attitude, however, also generated resistance from scientists questioning the world-view of physicalism. They were referred to as vitalists, which was mainly a label offered by their opponents trying to distinguish and enforce the mechanistic doctrine. In different approaches, the vitalists assumed that life has its own principles. Many of those who looked for alternatives posed important questions and made major contributions to biology (Normandin and Wolfe 2013).

A common problem of many alternative theories was that they assumed forces that turned out to be untestable and thus unprovable: a "vital force," an "entelechy," an "élan vital," a "vis essentialis," etc. The mystery of life was therefore to be explained by an even more mysterious term. By the mid-twentieth century, the vitalists became overshadowed by experimental research, which dominated science with its systematic search for causal factors.

Especially from the perspective of molecular biology during the second half of the twentieth century, it was apparent that organisms could be explained solely by the properties of their component parts. The concept of the machine seemed to have finally won recognition and science saw the world, the living as well as the nonliving, as a large and complicated apparatus of gears and levers (Lewontin 1991). The confidence grew that life could be explainable ultimately as a complex form of chemistry.

Until today this research program has been working quite successfully, so that we know a lot about the physiological processes in organisms. However, new doubts continue to arise regarding whether the mere continuation of this analytical approach will finally generate a fundamental understanding of living entities. At the beginning of the twenty-first century the quest for a new synthesis comes even from analytical empiricists themselves. Carl Woese, for example, asked for "A New Biology for a New Century." He first refers to the attitude of many of his colleagues who think that we will soon know how organisms work by just completing the molecular analytical program.

> Look back a hundred years. Didn't a similar sense of a science coming to completion pervade physics at the 19th century's end — the big problems were all solved; from here on out it was just a matter of working out the details? Deja vu! Biology today is no more fully understood in principle than physics was a century or so ago. In both cases the guiding vision has (or had) reached its end, and in both, a new, deeper, more invigorating representation of reality is (or was) called for.

> A society that permits biology to become an engineering discipline, that allows that science to slip into the role of changing the living world without trying to understand it, is a danger to itself. Modern society knows that it desperately needs to learn how to live in harmony with the biosphere. Today more than ever we are in need of a science of biology that helps us to do this,

> shows the way. An engineering biology might still show us how to get there; it just doesn't know where 'there' is. (Woese 2004, p. 173)

Some pages later he demands: "Let's stop looking at the organism purely as a molecular machine." (p. 176)

In "Nature," Paul Nurse (2008, p. 424) formulated:

> Biology stands at an interesting juncture. The past decades have seen remarkable advances in our understanding of how living organisms work. […] But comprehensive understanding of many higher-level biological phenomena remains elusive. Even at the level of the cell, phenomena such as general cellular homeostasis and the maintenance of cell integrity, the generation of spatial and temporal order, inter- and intracellular signaling, cell 'memory' and reproduction are not fully understood. This is also true for the levels of organization seen in tissues, organs and organisms, which feature more complex phenomena such as embryonic development and operation of the immune and nervous systems. These gaps in our knowledge are accompanied by a sense of unease in the biomedical community that understanding of human disease and improvements in disease management are progressing too slowly.

And Turner (2013, p. 272) formulates:

> We are, arguably, presently at such a point, where the limits of the materialist approach to life are beginning to rise dimly into view.

Thus, the beginning of a new search for a more general understanding of life is clearly put on the agenda. Many recent publications point in this direction (Bock and Goode 1998; Denton et al. 2013; Dupré 2012; Fuchs 2009; Gilbert and Sarkar 2000; Grunwald et al. 2002; Henning and Scarfe 2013; Kather 2003; Kirschner et al. 2000; Nagel 2012; Noble 2006, 2008a, b, 2011; Normandin and Wolfe 2013; Nurse 2008; Penzlin 2014; Rehmann-Sutter 2000; Rose 1997; Rose and Rose 2013; Turner 2007; Woese 2004). Looking further back in time, the list could be enlarged substantially.

## 2 Thesis

The mechanistic approach to biology has been legitimate and fruitful. Will it, however, be able to describe the complete reality of the living world and the nature of organisms? I propose that this approach is valuable from the epistemological, but insufficient from the ontological perspective.

However, empirical research is developed far enough today that it reveals by itself the material and prerequisites to understand more of the specific properties of the living. My hypothesis will be that without recourse to mysterious forces it is possible to generate answers to the old question of the specific properties of life, just using recent, empirically generated knowledge. It does not contradict the results of reductionistic research, but rather grants them meaning within the context of the whole organism and also may increase their practical usefulness.

The following text will describe ten specific properties of living entities. The aim is to demonstrate that the results of empirical research show both the necessity as well as the possibility of the development of a new conception of life to build a coherent understanding of living entities.

This approach will neither try to define life nor will it try to find criteria to differentiate "living" from "non-living." There have been many attempts for both in the literature, but they have not enjoyed a consensus among scientists, although these attempts include valuable concepts. An overview of this discussion is provided by several contributions to a special issue, which is introduced by Gayon (2010); further examples of this discussion are Cleland (2013), Emmeche (1997), op Akkerhuis (2010), Kolb (2007), Oliver and Perry (2006), Popa (2010), Ruiz-Mirazo et al. (2004), Tsokolov (2009). Hengeveld (2011) even objects to giving definitions of life, since they may bias the work that follows. Cleland and Chyba (2002) state that many proposed definitions of life suffer problems, often in the form of counter examples, or in the form of criteria being also valid for systems that are not alive, such as fire. Van der Steen (1997) indicates that even if an overly general definition existed, it would probably be difficult to apply it to specific situations.

Also the specific properties that will be discussed below are not intended to provide another list of necessary and sufficient conditions in order to characterize life, as it is often done in textbooks and courses (Emmeche 1997). Origin of life questions, which are often the occasion for definitions, are not addressed either.

Here, I do not argue against such approaches, and the intention is quite different: independently from questions of definition or from discriminating criteria, recurring and specific properties of living beings are described as they are typically found during empirical work. Thus the approach is predominantly phenomenological: what characteristics do living organisms typically exhibit when they are studied by physiology, embryology, molecular biology and so on?

Specifically, here I mean that living beings exhibit properties and characteristics that are especially shown by life processes and that are not reducible to mere physical processes and chemical reactions. They are typically not present in non-living systems, although in some cases superficially comparable phenomena may be found. Consequently, it cannot be the goal of scientific inquiry to describe organisms in terms of non-living machines.

Of course, chemical reactions as well as physical processes are involved in organic functions, but they are integrated within an organized and autonomous living entity. Therefore chemical and physical inquiries are a legitimate part of biological studies, but are not sufficient to come to a full-fledged understanding of living beings. It is not possible to reduce life to mechanistic interactions of matter. Consequently, these specific properties require special empirical methods as well as a different reasoning in order to understand life and to represent these properties.

The representation of 10 such properties is preliminary. There may be more or less to be discussed, or they could be organized and summarized differently. It is of secondary importance how many properties are found. An explicit advantage of the representation given here should be that the concept is flexible: whatever needs to be described as a specific property can be included in order to develop a coherent and approximately complete picture. For this the concept can be expanded or corrected in further work. Important, however, is that the specific phenomena can be taken as guidelines for the study of living beings, thus overcoming the reductionism prevalent in recent biology. An empirical science that regards these specific properties as starting points and framework will look different than a science that seeks explanations from mechanistic premises. Therefore the reader is invited to expand and modify the properties discussed here by further perspectives.

The envisaged synthesis refers to the representation of these properties within one overview. Most of them have been discussed among philosophers of biology before, but usually apart from each other, focusing on just one or a few of them and their associated concepts. It is a drawback that there are only occasional points of contact between such different concepts, leading to a heterogeneous picture regarding what the topics and tasks of an organismic biology may be. This is one reason why the theoretical consequences have only little impact on empirical disciplines in biology, although the empirical work itself constantly produces examples of the properties discussed. The philosophical work around some of these properties is usually unknown among empirical scientists, and attempts to discuss them even produces mistrust.

However, just to represent these properties within an overview may be no more than a first step. But it may provide at least three advantages: (1) To get a general idea about which properties need to be taken into consideration, even if they are not yet complete, (2) to get an impression about how extensive the knowledge about organismic principles already is, clearly pointing beyond mechanistic thinking, (3) to find some relationships among these properties.

However, point 3 can only be rudimentary. A full synthesis in the sense of a unified notion of life seems to be unavailable thus far and a multi-perspective approach might be a preliminary solution.

Gayon (2010) describes that historical development of biology led by its empirical results and driven by phenomena towards unifying concepts of the living. The cellular theory was the first step. Then came evolutionary theory, and then biochemistry and molecular biology, which showed that all known living beings are made of the same stuff (nucleic acids, proteins, etc.), and exhibit a remarkable metabolic unity (universal existence of core functions and metabolic pathways). Gayon remarks that these sub-disciplines usually did not try to define life, but all of them have definitely shown that there are very strong reasons to believe that living beings share a number of properties that distinguish them from any other natural things, and that justify the existence of a methodologically autonomous science. The present paper attempts to place these properties into focus.

## 3 Properties of Life

As a preliminary framework, 10 properties of living beings are discussed in the following sections: (1) the principle of reciprocal interdependencies in organic functions, (2) the principle of autonomy, (3) the principle of integrative system functions, (4) the significance of information content and processing within organisms, (5) the description of the unity of process and shape in the sense of embodied physiology, (6) the autonomy of time processes, (7) the ability of adaptation to environments, (8) the ability to evolve, (9) the principles of growth and development, and finally (10) reproduction and death.

### 3.1 Interdependencies

Most biologists still regard the analysis of causal chains as the fundamental method of explanation for organic processes. It is expected that a cause A will of necessity be followed by effect B, as is the case in classical mechanics.

However, in the analysis of an organic process, this form of explanation is usually limited. Bechtel (2007) describes an example for such a case: when the pioneers of biochemistry at the beginning of the twentieth century began to analyze biochemical processes, they generally assumed that metabolic reactions occurred serially and hence the pathways of reactions would be linear. Often, however, they could only arrange some intermediates in a linear sequence leading to a product with unclear further outcome. The discovery of the most famous biochemical cycle, the citric acid cycle, resulted from such a circumstance. A number of organic acids could be arranged in a chain of reactions. But then scientists faced a problem in specifying what happened next. After they dealt for a substantial time with this question, it was proposed that the last product was the new starting point for the whole process. This was at first a speculative proposal and it took significant time to describe further intermediates. Finally it became clear that the process was a cycle. Bechtel emphasizes that this result was not construed as theoretically significant but was just the result from trying to articulate plausible pathways of chemical reactions.

This is exactly what emerges in large parts of biochemistry and molecular biology: many processes are cycles. One component is dependent on the next one; there is neither a first cause nor a final effect. Rather one process is the prerequisite for the next one, which is the prerequisite for the next one and so on. Such processes are dependent on each other (interdependent) within cycles or regulatory networks, what often is called "circular causality."

One advantage of cyclically organized processes is that they provide means of effective regulatory feedback. In recent years this has also become obvious in genetics. It was previously thought that information always flows in one direction, from DNA to protein and finally to the phenotypic character, whereas today it is acknowledged that there are many feedback systems and regulatory cycles, so that it is not possible to identify DNA as a sort of primary cause (Fig. 1). Some geneticists saw this quite early (Lewontin 1991, 2000; Lewontin et al. 1984; Strohman 1993, 1997, 2002, 2003), but only recently its conceptual and practical consequences are becoming clearer (Dupré 2012; Krimsky and Gruber 2013; Noble 2006, 2008a, b). Today information is described that is not coded within DNA, but is found within regulatory systems of the cell. This perspective derives from the new and much debated field of epigenetics (Jablonka and Lamb 2005; Jablonka and Raz 2009).

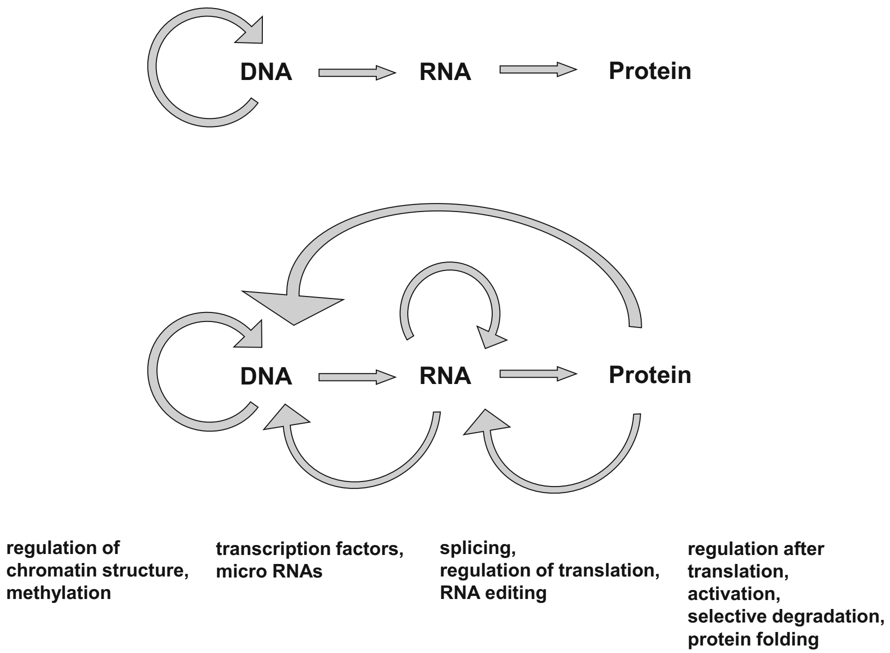


**Fig. 1** *Top* Older view of DNA transcription and translation. *Bottom* modern view (*draft* Johannes Wirz)

In general the resolution of causal chains is successful on the molecular level. However, the analysis runs into difficulties when the context of further systemic levels is regarded. Even the simplest living system, a bacterial cell, is a highly complex network involving literally thousands of interdependent chemical reactions. This is increasingly recognized within present-day molecular biology, so that new ways of description of such systemic functions are being investigated (Boogerd et al. 2007; Kaneko 2006; Noble 2006).

Different proposals have been brought forth to describe organic functions more adequately in form of reciprocal interdependencies (Fuchs 2009; Haken 1983; Rosen 1991; Schad 1982; Thompson 2007). Fuchs (2009) describes the principle as "circular causality" and differentiates a horizontal from a vertical form. Horizontal circular causality is found for example within cellular metabolism or between cells or tissues. Vertical circular causalities are relations between different system levels such as cells, organs, and organisms. Fuchs describes them both together as integral causality.

Other attempts focus more on the network principle itself, seeing living systems predominantly as self-organizing networks, the components of which are all interconnected within "nonlinear dynamics" (Capra and Luisi 2014; Stewart 2002).

The limits of causal reasoning in biology have often been discussed (Wuketits 1981; Mahner and Bunge 1997). The development of more far-reaching concepts, however, is still a challenge.

### 3.2 Autonomy

What do organisms generate and maintain with such interdependent functions? The answer is diverse, of course, but one common ground is that a certain autonomy is established. Living systems are autonomous in the sense that they maintain themselves in form and function within time and achieve a self-determined flexibility. These living systems generate, maintain, and regulate an inner network of interdependent, energy-consuming processes, which in turn generate and maintain the system. They establish a boundary and actively regulate their interaction and exchange with the environment. They specify their own rules of behavior and react to external stimuli in a self-determined way, according to their internal disposition and condition, and they maintain phenotypic stability (robustness) in the face of diverse perturbations arising from environmental changes, internal variability, and genetic variations (for details and forerunners of this definition see Rosslenbroich 2014, chapter 3. See also Fuchs 2009; Kitano 2007; Maturana and Varela 1987; Moreno et al. 2008; Ruiz-Mirazo and Moreno 2012; Varela et al. 1974).

This matches with the systems approach, which will be discussed below. Hofmeyr (2007) suggests that, "for systems biology, the defining difference between a living organism and any nonliving object should be that an organism is a system of material components that are organised in such a way that the system can autonomously and continuously fabricate itself, i.e. it can live longer than the lifetimes of all its individual components. Systems biology, therefore, goes beyond the properties of individual biomolecules, taking seriously their organisation into a living whole." (p. 217).

Essentially, a single celled organism distinguishes itself from the surrounding fluid medium by actively creating its boundaries. Simultaneously it regulates its interactions with the environment. The existence of a boundary is a central element of a living system (Luisi 2003; Maturana and Varela 1987; Varela et al. 1974). Inside the boundary of a cell, many reactions and chemical transformations occur; the cellular membrane encloses a defined reaction room, thus contributing to the maintenance of the cell's identity.

Metabolic processes within the cell construct the boundaries, but the metabolic processes themselves are made possible by those boundaries. In this way, the cell emerges as a figure out of a chemical background. Metabolism establishes dynamic disequilibrium, a dynamic stage of order within a network that characterizes life. A cell that drifts toward equilibrium is dying.

Autonomy is also achieved by the use of energy-rich molecules. In face of the hydrolyzing and oxidizing influences from the environment, energy-rich bonds are maintained in a relatively stable state. Organic molecules are always reduced compounds and thus they are rich in energy. Energy from the environment is accumulated within these complex molecules so that an energetic gradient can be maintained.

In addition, each organism establishes a genetic system for building an order to escape from the tendency of its material components toward entropy. Genetic and epigenetic instructions make it possible to build temporary islands of self-determined order again and again. These principles enable the identity of the individual as well as that of the species, i.e. its characteristic identity with respect to other individuals as well as that of other species, and its relative stability over many generations. Information is the source for building up a higher degree of order than exists within the environment. This informational self-determination is part of autonomy and has also been called organizational closure (Moreno and Mossio 2015).

Taken together these are some features of autonomy: boundaries, metabolic processes, self-regulation, dynamic disequilibrium, energetic gradient and informational self-determination. In an extensive study, it was demonstrated that this ability for autonomy changed during evolution (Rosslenbroich 2014). The ability for regulation and stabilization of endogenous functions, as well as the flexibility within the environment, have been enhanced throughout evolution. In this sense, organisms not only adapted to the environment, but also expanded their own individual autonomy.

The principle of autonomy is tightly linked to agency. While agency has usually been understood and discussed by cognitive science in connection with high-level human cognitive abilities, it is now increasingly considered that the concept of agency can be applied to phenomena throughout all of biology, at least in the sense of minimal agency (Arnellos et al. 2010; Barandiaran and Egbert 2013; Barandiaran et al. 2009; Hoffmeyer 2013; Moreno and Mossio 2015; Shani 2013; Thompson 2007). Minimal agency can be understood in the sense of a capacity of a unit system to generate directed behavior. Together with a minimal form of autonomy, agency appears within single cells like bacteria. A cell is an autopoietic system based on a self-organizing network of biochemical reactions that produces the described features of autonomy (Maturana and Varela 1987; Varela et al. 1974). Such a cell actively relates to its environment to maintain its viability. Its sensory responses serve to trigger motor and other behavior subject to the maintenance of its autonomy and regulated by internal needs, thus existing within an interactive relationship to its environment. In this sense, individual entities exhibit agency. This mode of coupling with the environment is recapitulated in a more complex form by more elaborate organisms, including their nervous systems. The nervous system establishes and maintains a sensorimotor cycle, whereby what one senses depends directly on how one moves and behaves, and how one behaves depends directly on what one senses.

Hoffmeyer (2009, 2013) explains that the field of biosemiotics is based on an understanding of agency as a real property of organismic life, a property that is rooted in the capacity of cells and organisms to interpret events or states as referring to something other than themselves or, in other words, the capacity to interpret signs. These signs need not necessarily be emitted with a purpose of communication; in fact, by far most signs are not part of a sender-receiver interaction at all but simply important cues (internal or external) that organisms use to guide their activities. This semiotic perspective introduces a further aspect of the properties of life, exhibiting a strong relation to information processing in organisms, which will be discussed below.

### 3.3 Integrative Biological Systems

Currently there are efforts to understand the abundance of detailed knowledge about organisms, which is available todayin the systems concept (Boogerd et al. 2007; Kaneko 2006; Noble 2006). Recent systems biology consists of two schools of thought. O'Malley and Dupré (2005) call them "pragmatic systems biology" and "systems-theoretic biology." The majority of today's systems biologists belong to the pragmatic school, which integrates and studies large sets of molecular data in order to reconstruct system properties. Here the term "system" covers a range of molecular interactions, which generate the whole function in question. For systems-theoretical biologists, however, it is crucial to analyze systems as proper systems, not as mere collections of parts, in order to understand the emergent properties of compound interactions. Systems are taken to constitute a fundamental ontological category.

This second position is the older concept and was introduced in the 1920s by Ludwig von Bertalanffy and Paul Weiss, who are regarded as the founders of biological systems theory. Especially Paul Weiss presented a concept with a consequent integrative character, and many results of modern research are in accordance with his concept (Drack et al. 2007; Drack and Apftaler 2007; Drack and Wolkenhauer 2011; Rosslenbroich 2011a, b; Sonnenschein and Soto 1999).

Weiss defines a system as a relatively independent and stable entity (Weiss 1963, 1968, 1969, 1971, 1973, 1977). Accordingly, a system generates restricting and regulative functions and imposes them upon its component parts, so that the functionality of the whole system is maintained. Thus the system itself contains constituting properties and also information, which do not necessarily derive from the components. At the same time each system depends on its components. The central illustration of Weiss is shown in Fig. 2 (left).

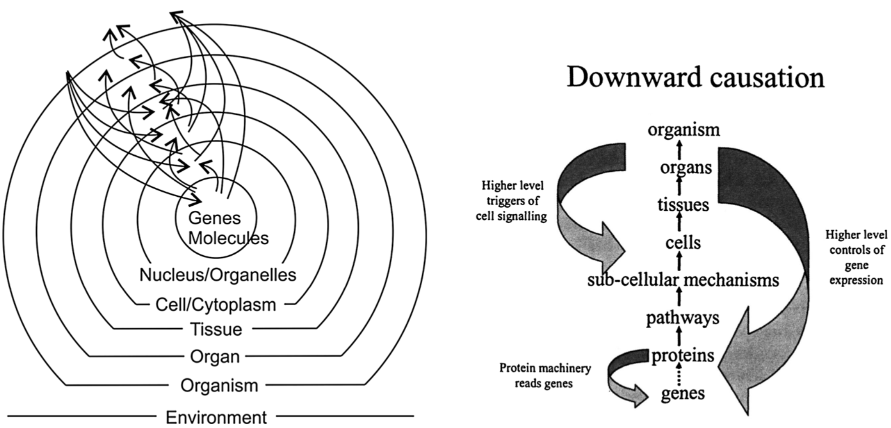


**Fig. 2** Schematic representations of the systems concept of Paul Weiss (1969; *left*, slightly modified concerning the levels indicated) and Denis Noble (2006; *right*)

The cell is an example of such a system. It contains many components, but the system integrates them into a functional whole. The cell depends on the components but is only viable by regulating them within the system.

> …the basic characteristic of a system is its essential invariance beyond the much more variant flux and fluctuations of its elements or constituents. (Weiss 1969, p. 12)

This means that the component processes are not bound within determined processes, but rather can be variable, as is well known from cell biology today. Whether and when information is transcribed from DNA, whether certain proteins are generated and how long they stay in function, or which components are integrated into the membranes in order to keep them within an optimal state of fluidity, is permanently regulated by the cell, according to its respective situation.

> This is exactly the opposite of a machine, in which the structure of the product depends crucially on strictly predefined operations of the parts. In the system, the structure of the whole determines the operation of the parts; in the machine, the operation of the parts determines the outcome. (Weiss 1969, p. 12)

Weiss further describes that a cell does not always work directly with its molecules, but rather has subsystems, the organelles, which perform partial functions. Also the whole organism can be regarded as a system with several subsystems, the organs. Hierarchic stepwise delegation of tasks to sub-systems is nature's efficient instrument to let an organism keep order without having to deal with all its molecules directly.

The model also contains the principle of vertical interdependence, which has been discussed earlier, since the system builds upon the functions of sub-systems and at the same time integrates them into the larger context.

This concept of Weiss is compatible with the more recent writings of Denis Noble, who draws new consequences from the knowledge available today. Noble (2006) describes how within recent decades much progress has been made in dissecting systems into their smallest components. Now the challenge is to extend that knowledge up the scale. At each level of the organism, its various components are embedded in an integrated network of systems. Each such system has its own logic, so that it is not possible to understand that logic merely by investigating the properties of the system's components. The challenge is to learn more about the properties and conditions of each of these systems.

In this sense the genome is not privileged, but is rather just one level within this hierarchy, and there is no reason to assume that the whole complex of integrated networks is determined by that level. Noble argues that we must look beyond the reductionist gene's eye view to answer the question of life. To understand what life is, we must make a radical switch of perception and view life at a variety of different levels, with interaction and feedback between gene, cell, organ, system, body, and environment.

Noble uses the representation of Fig. 2 (right), which also points out the interdependencies between the different system levels. This concept has clear parallels to the ideas of Weiss. The object, life itself, seems to imply such concepts, which obviously have been developed independently.

### 3.4 Processing of Information

Whether matter immanently contains information is controversial in physics. Organisms, however, deviate fundamentally from non-living things by continuously gathering, concentrating, and processing information. This is not only the case in DNA, but also in higher levels of the cell.

The information content of DNA is well studied today, including many molecular details of its transcription and regulation. Open questions are whether this information provides something like a body plan or a blueprint for the whole organism (Oyama 2000; Oyama et al. 2001; Sterelny and Griffiths 1999) and whether this information has a determining character for features of the organism (Lewontin et al. 1984; Moss 2003; Shapiro 2011; Strohman 1997, 2002). In recent years, however, further levels of information have been identified by the field of epigenetics, describing principles such as chromosome condensation, DNA methylation or histone modifications for example. In addition, some form of informational processing must be involved in alternative splicing of mRNAs, which transfer the information from DNA to the cytoplasm. By way of RNA processing different types of mRNAs and thus different resulting proteins can be generated. Additionally, other components, like micro-RNAs, are generated, which have feedback functions for the regulation of gene expression. There are also extensive feedback functions to the DNA by proteins like transcription factors and so on, and within all these steps a transfer of information takes place. Within a very informative and up-to-date review of recent knowledge in genetics, Parrington (2015) calls this principle "multi-layered information" (see also Farnsworth et al. 2013; Morris and Mattick 2014; Shapiro 2011).

Proteins contain information from the translated RNA in the form of the primary structure, and further information may be involved in building the final form of the protein. All this can be called embodied information. Farnsworth et al. (2013) maintain "Information is therefore not just stored in nucleotides: it is the whole biological system that embodies effective information…." It can be assumed that such embodied information is present in structures of the cell. The precise composition of the cellular membrane, chemically describable by phospholipids, proteins, glycolipids, and glycopeptides, contains a robust order. Nonetheless, order is only possible by means of an embodied information. Therefore, Nurse (2008) states that among the most pressing needs in biological analysis is the development of appropriate approaches to analyze the management of information flow within whole organisms. "Living systems do not merely passively accumulate and store information, they also actively process it" (Walker 2014).

Cavalier-Smith (2004) has described some inherited features of animal and plant cells as the "membranome," as lipids are not formed from DNA templates. Thus, an organism needs to inherit the membranome, and it comes complete with the fertilized egg cell.

The principle can also be applied to the supracellular order. Basically all structures of the organism must contain embodied information, whether it comes from the genotype or not. At present it is unusual to talk about such a form of embodied information. But already the necessity to search for information on further levels than DNA, as it is done in epigenetics, shows that conceptual expansions are necessary. It can be predicted that, on all levels of the organism, information content is involved, forming its order and its functions. Organisms permanently process and concentrate information, and knowledge about this on different levels will be essential in the future (Nurse 2008; Walker 2014). In the same sense, Farnsworth et al. (2013, p. 205) formulate:

> Every aspect of life may be regarded as a product and elaboration of the physical world, clearly made of the same matter and energy, ordered in space and time as is every physical system. What makes life special is not the material brought together to take part in living, it is the functional information that orders matter into physical structures and directs intricate processes into self-maintaining and reproducing complexes.

Farnsworth et al. propose the description of a "functional information content" concerning patterns of molecules, cells, tissues, and other components.

Longo et al. (2012) argue against the concept of information in biology because it encouraged genetic determinism. The problem, however, is the assumed determinism, not the notion of information itself. Recent data from genetics show that cells as well as whole organisms can operate quite flexibly with a given information content (Parrington 2015). This may even be the case during evolution (Jablonka and Lamb 2005; Jablonka and Raz 2009; West-Eberhard 2003).

Also organisms permanently process information from their environment. This includes all perceptions, from their simplest form found in prokaryotes to signaling processes that rely on cognition and language. Biosemiotics studies sign processes between the organism and its environment as well as within the organism. This may also be a perspective on information processing, with the attempt to understand the very content and meaning of the information in these processes (Hoffmeyer 2009, 2013).

Until now, organisms have been described only rudimentarily in respect to these aspects. It is, however, remarkable that molecular biology, which is expected to provide a firm chemical and physical basis for understanding life, early on introduced the notion of information and thus already relinquished a purely materialistic explanation. It became increasingly clear that information processes are essential in all life functions. With information, a new quality emerged, which does not exist in the physico-chemical terminology, which focuses on material interactions, atoms, molecules, and crystals, and about forms of energy and their transformation (Eigen 1987; Fox Keller 2011; Penzlin 2014; Shapiro 2011).

Shapiro (2011, p. 4) sees in recent developments even a general change in biology toward an informational understanding of life:

> The contemporary concept of life forms as self-modifying beings coincides with the shift in biology from a mechanistic to informatic view of living organisms.

### 3.5 Processes of Shape

Another specific property of organisms is their overall shape and form, their design ("Gestalt"). First and foremost, shape describes the exterior appearance and the systematic relationship of the organism's distinguishing features. Secondarily, the phenomenon also concerns all lower levels and substructures. Vertebrae exhibit a certain shape in close relation to their specific function, as well as a heart, a brain, an epithelial cell or a protein. Morphology is the biological discipline that studies this phenomenon. The seemingly endless variability of forms and shapes in nature belongs to the specific properties of life as well.

However, not everything that possibly appears is called a shape in this sense. Pathology shows many structures that do not exhibit a shape, which is integrated into the overall building principles of the organism. Such structures apparently lack the necessary information for subordination into the context and functionality of the system. If the tumor of a sarcoma is compared with the image of a healthy connective tissue, it has the appearance of a loss of integration and regular shape. This makes pathology possible and shows how our understanding of the living shape depends on the presence of not just any order but of a specific order.

Form and matter are not identical. If the form of an organism is destroyed, only matter is left, which demonstrates that form contains a non-material property. The term form is included within the word in-form-ation. In biology form and shape are often used to acquire information about an organism. Taxonomy, for example, relies on this type of information.

In addition there is a close relationship between form and function. The work of Scott Turner indicates this in a fairly instructive way (Turner 2007). Turner studied the physiology of termite chimneys, which are known for a very effective ventilation system, providing homeostasis concerning parameters like $O_2$ and $CO_2$, constantly being adapted to requirements of the growing colony. The question was how do the termites manage to control this homeostasis? As it turned out, termites continuously transport material from points with a higher concentration of $CO_2$ to points with a lower concentration, which at once modifies the air current within the chimney. This amounts to a continuously adapted form fulfilling the regulatory functions in an optimal way. The termites are equipped only with the necessary sensitivity and the behavioral repertoire needed at each point. For the chimney as a whole, this summarizes to an "embodied physiology" or an "embodied homeostasis," simultaneously resulting in the form of the chimney.

Referring to the physiologist Claude Bernard, Turner calls this principle "Bernard machines." I would prefer "Bernard processes," as organisms are not machines. Turner describes how he revised his thinking about biological structures in a fundamental sense:

> I had been thinking about biological structures in entirely the wrong way. I had been subscribing to the conventional notion that a living structure is an object in which function takes place. That's all wrong, I came to see. A living structure is not an object, but is itself a process, just as much so as the function that takes place in it. Even the convenient dodge that structure and function are inextricably linked is wrong, I decided. That implies that structure and function are somehow distinct, […]. But living structures are not distinct from the function they support; they are themselves the function, no different in principle from the physiology that goes on there. In this sense, the mound is not a physical structure for the function of ventilation, it is itself the function of ventilation: it is embodied physiology. (Turner 2007, p. 20)

Turner describes further examples of embodied physiology, such as the architecture of smaller blood vessels in complex organisms. It cannot be genetically determined in all details, but rather branches according to the necessities of tissue supply. Basically the same principle is known from neuronal wiring within the brain. During child development neuronal structures are generated only in a rough manner, while the fine wiring is configured by usage and function. Gerhart and Kirschner (1997) call this "exploratory systems." These are systems that develop their form according to their function.

Very likely such interdependencies between form and function have been significant during evolutionary changes as well. Turner (2007, p. 1) states:

> My thesis is quite simple: organisms are designed not so much because natural selection of particular genes has made them that way, but because agents of homeostasis build them that way. These agents' modus operandi is to construct environments upon which the precarious and dynamic stability that is homeostasis can be imposed, and design is the result.

It may be more appropriate to talk about "processes of shape," as the shape at any single moment is just a window into the overall process. Life is always process (Dupré 2012), and shape is no more than a moment within the continuous flow of functions. As all this contains embodied information, the complex of matter, form, function, and information generates the process of shape (Fig. 3).

### 3.6 Time-Autonomy

A process is performed within time, and in organisms it has a certain time structure. When physiological processes are measured in their course, they exhibit a certain time order and they typically oscillate. Today these biological rhythms are being extensively studied by chronobiology (Dunlap et al. 2004; Koukkari and Sothern 2006). When the discipline was young during the 1970s, the phenomenon of biological rhythms did not at all match with ordinary mechanistic thinking. But today chronobiology belongs to the established disciplines of biology and human physiology and has considerable relevance in medicine.

It is interesting that many of these rhythms are endogenous. They are generated by the organism itself and maintain certain frequencies and amplitudes. Another

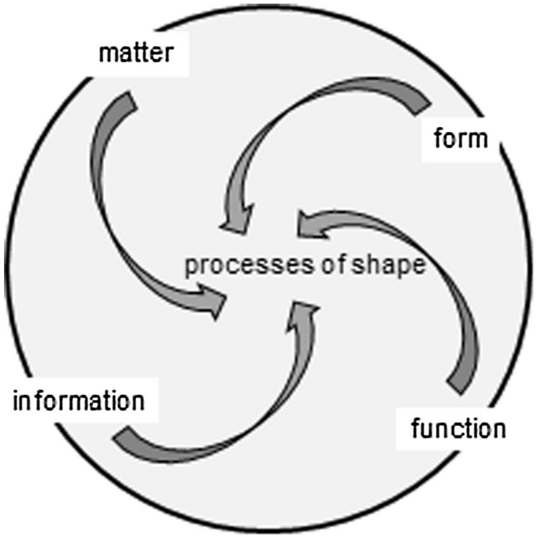


**Fig. 3** Schematic representation of the process of shape

critical feature of circadian phenomena is that they are relatively unaffected by temperature; that is, they are temperature compensated. This presents a significant explanatory challenge since biochemical reactions proceed more rapidly at higher temperature. Thus, rhythmicity is an autonomous function of the organism.

Autonomous also means that organisms are not always fully synchronized with external periodicities. The endogenous daily rhythm in humans typically tends toward a length of 25 h, with some individual differences. The actual frequency then has to be synchronized with the external day. This is why chronobiology describes "circadian rhythms." Today it is clear that most physiological functions exhibit a circadian rhythm (Dunlap et al. 2004; Koukkari and Sothern 2006).

While the circadian rhythm is the most well-known oscillation in organisms, there are also oscillations of different frequencies, below and above the daily rhythms. They superimpose each other, resulting in a complicated time pattern within the organism (Hildebrandt 1979; Hildebrandt et al. 1987).

When the knowledge of circadian rhythms in animals and humans grew, a search began for a central organ that would generate these processes. A structure in the anterior hypothalamus has been identified as the locus of the circadian clock in mammals including humans, the suprachiasmatic nucleus (SCN). Genes and proteins have also been identified in the cells of the SCN, which were related to this clock, and there was hope that it might be possible to find the molecular components that are responsible for the phenomenon. Bechtel (2010) describes the history of this research and the associated concepts and explanations. In these early explorations, a linear causal model was initially assumed (Fig. 4).

Further research showed how intertwined the different components of the system are within the organism. First, there are peripheral oscillators, which are able to generate a circadian rhythm themselves, and which provide feedback to the SCN. And it was discovered that genes and proteins, described in the SCN cells, were

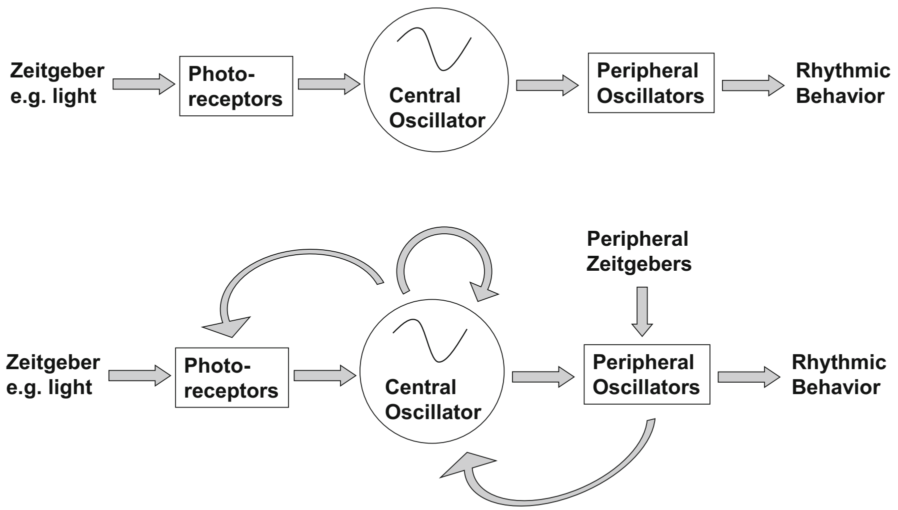


**Fig. 4** *Top* Classical linear-causal model of the circadian system. *Bottom* integrated circadian system (modified from Bechtel 2010, p. 323)

present in peripheral oscillators as well. The SCN gets stimuli also from sensory organs and in turn it influences them as well. Thus, within the oscillatory system there are clear interdependencies and feed-back processes, and the SCN has a coordinating function, rather than being the causal origin of the oscillation.

Bechtel presents an alternative representation of this system in Fig. 4, which shows some of the existing interdependencies. The example shows how such a research area grows over and above its own paradigmatic prerequisites, guided by the phenomena themselves. It also shows how necessary the analysis of the components is, being the prerequisite for developing an integrative concept.

The SCN itself comprises approximately 10,000 cells on each side of the brain. Each cell has the genes and proteins to generate the rhythm. However, when single cells from the SCN were cultivated, substantial variability between the rhythms of individual cells was detected. Only groups of some hundred cells generated the exact rhythm (Mohawk et al. 2012). Thus, only their synchronization delivered the exact rhythm in order to coordinate the circadian system of the whole body.

The same principle can be traced observing the genes involved. When genes are transcribed, the transcript leaves the nucleus and enters the cytoplasm, where it is the template for proteins, which are involved in generating the rhythm. Some of these proteins return to the nucleus and inhibit further transcription of these genes. Thus, here too a feedback system exists.

Noble (2008a) describes the consequence of this relation and asks, where is the genetic program? He concludes that the assumption of a genetic program is misleading. The genetic information on how a protein is assembled is not a program for the entire system. To maintain the sequence of processes that generate a rhythm within a cell, not only the genes and the proteins are necessary, but also the whole cell, the nuclear membrane, certain forms of mRNA and microRNAs and so on. It is more a gene-protein-lipid-cell network that is responsible for the effect, not simply a gene.

Networks of interactions generate the circadian rhythms on the cellular level as well as in the central oscillator and in the whole system. Scientifically it is valuable to learn about the components of the system. However the expectation to find a first cause is misleading. In the future it will be important to learn more about the integration of the whole system (Bechtel 2010).

This autonomous creation of time processes is of central importance not only within the adult organism, but especially during embryogenesis. This has been highlighted in a special issue in *Science*, beginning with an editorial under the heading: "Time for Chronomics?"(Duboule 2003, p. 277):

> Animal development is, in fact, nothing but time. From the cell cycle to the beating of the heart, our own lives are composed of a multitude of microscopic and molecular oscillations…The goal of the developmental clock is not simply to mark off time, but to integrate and unify the myriad temporal signals received from throughout the organism […]. The spatial construction can be understood only in the light of time.

### 3.7 Adaptability

In biology the term "adaptation" has been used with numerous different meanings. Mahner and Bunge (1997) found eight meanings for the term. For the present topic, it is enough to regard adaptation as the ability of organisms to adapt to changes within their environment. In the first place, this has nothing to say about the evolutionary process, which might have produced this ability. This understanding of adaptation is often called adaptedness.

The ability of organisms to adapt is again a specific property, which is not found in the non-living realm.

Adaptedness is a relational property of an organism or rather a property of the organism-environment coupled system. Then, autonomy and adaptation become a central pair of this system. Both are dependent on each other: on the one hand there is the organism, and on the other hand there is the environment. The organism—even in its simplest form—always establishes its life functions together with the generation of a boundary and thus produces its "being different" from the surrounding environment. To maintain this state, the organism not only needs regulatory and stabilizing functions but also needs to react appropriately to cope successfully with the environmental influences. Self-assertion (autonomy) needs adaptations (Di Paolo 2005; Rosslenbroich 2014).

The polar bear possesses great autonomy with endothermy, flexible movement capacities, and flexible behavior, but to survive in the extreme climate it needs adaptations such as the thick white fur and many others. The dolphin has the extensive regulation capacities and behavioral flexibility of mammals. These functions of autonomy are not prerequisites for life in water, as they are not present in fish, and most of them can be traced back to the dolphin's phylogenetic history. At the same time, the dolphin exhibits many adaptations to the aquatic environment, such as blubber for insulation, secondary homodont dentition, fins and fluke, streamlined shape, nasal openings that have migrated to the top of the head, and many more. This means that two elements are involved: (1) the individual biological integrity and (2) maintaining its autonomy while contending with the factors of the environment. Autonomy theory describes that Element 1 changes during evolution, as does Element 2 (Rosslenbroich 2014).

In evolutionary biology it has become increasingly clear that the phrase "adaptation to a given environment" is one-sided also in another sense, as organisms do not just adapt to a given environment but also may themselves strongly influence the environment. This has been discussed by means of the notion of "niche construction" (Laland and Sterelny 2006; Lewontin 2000; Odling-Smee 2010; Odling-Smee et al. 2003). The concept describes the dynamic interaction between organism and environment and regards environment or niche not just as a given factor with which the organism has to deal. Niche construction describes the feedback processes between organism and environment.

The picture now becomes complicated: organisms that maintain their autonomy are intertwined with given and with constructed factors of the environment. The organism can adapt to some factors as well as change others in order to maintain its autonomy. The organism as well as the environment can change during this process. There are mutual dynamic interactions between organismic autonomy and environments, thus again exhibiting features of a system. In ecology this system character has been recognized already for a long time (Looijen 2000), but with regard to evolutionary changes it has only recently received more attention.

### 3.8 Ability to Evolve

With these considerations the next property of living things has already been introduced: the ability to evolve. The energetic-metabolic-informational state of disequilibrium, which organisms generate again and again during ontogeny and adulthood, can be modified in the long run.

If the principle of individual biological integrity, as it has been described in previous sections, is taken into consideration, it must be noted that organisms are subjects that evolve, not objects which are forced to change by external factors (Kather 2003; Weingarten 1993). This is not only the case when organisms are actively involved in evolutionary changes, which has been considered anew in some recent theories (Kirschner and Gerhart 2005). It is also the case when evolution takes its starting point from random variants. When such variants are able to deal better with the given environmental conditions by making some changes, it is still the living subject that produces them. Also, in this case, the organism is not just an object that is induced to evolve. Basically, it is the subject in its continuous endeavor to maintain its life and to preserve the species.

Thus, the process of biological evolution also differs fundamentally from mere physical and chemical processes. There are extensive conversions within the non-living world, as they are described in geology and cosmology, but not the generation of new systems, which lead to new self-determined abilities and possibilities of subjects, including the long-term continuation of this very process.

Reductionist science attempted to ignore the qualitative differences between organisms generated by evolution, describing only various forms of adaptation. However, the phenomena show something different (Rosslenbroich 2006): beyond various forms of adaptation, there also have been qualitative modifications and innovations with fundamental changes in structure and functionality. Besides the broad radiations of vertebrates, for example, there also appeared major changes in body plans. Beginning with the first chordates, these alterations led to cartilaginous and bony fishes and further to amphibians, reptiles, mammals, and birds. As has been described before, a central pattern within these transitions were transformations in the ability of regulation, the stability of functions, and the evolution of new possibilities within the environment (Rosslenbroich 2014).

### 3.9 Growth and Development

The process of growth and differentiation is an essential constituent of all multicellular organisms. Plants, fungi, and animals do not only become larger, but undergo a complex developmental process of rearrangements in order to generate their characteristic form. How a single fertilized egg cell transforms itself into a complex organism is still a miracle and a mystery (Purnell 2012).

Morphological and histological studies had already been collecting a wealth of knowledge, when in the last decades molecular biologists promised to uncover the causes of the observed processes. Although this research delivered a major step forward in understanding details, doubts are increasing now that the cascades of genes and proteins alone are able to describe the generation of macroscopic forms, and that they can be identified as the primary cause and origin of the whole process (Fuente and Helms 2005; Gilbert 2014; Purnell 2012; Radlanski and Renz 2006).

Often not only single genes are involved but rather complex networks of genes, transcription factors, gradients, and so on. Certain regulatory genes operate in diverse situations, so that the same gene can have different functions at quite different times and places. Therefore genes cannot simply contain information for the respective organ. Some contemporary authors propose that genes are predominantly *mediators* in the generation of tissues and organs, rather than the main cause for the generation of structures (Fuente and Helms 2005; Radlanski and Renz 2006).

Thus, genes are not determinants of development; they are part of the system and they depend on being integrated into the system (Dupré 2012; Noble 2006). One tool the organism uses for this integration is generating a protein gradient along a certain region, so that cells differentiate along such a field according to the concentration at each single point. The system generates a signal, which induces the differential expression of genes. For the generation of the protein gradient, of course, a gene was necessary as well, but when it is available it is used as a signal by the system. The continuous interactions between genome and gradients within the system, or between genome and nearby tissues, enable the respective steps. Thus, genes work only within a certain context and are only one factor within a cascade of interactions and interdependencies (Dupré 2012; Gilbert 2014; Willmer 2003).

Today, additional factors are known to contribute to these networks. These include, for example, physical organizational effects. Data indicate that different forces like tension, pressure, and differential adhesion influence the expression of developmental genes and the differentiation into cell types. More generally, cells in embryos have the ability, via contractile and protrusive activities, to exert forces on one another and on the extracellular matrices (ECM) they produce. Tissue structure often is involved and is mediated by signals between cells and the ECM. These elements contribute to the regulation of cellular proliferation, migration, differentiation, and apoptosis. Apparently, geometrical and mechanical signals contain information about tissue and organ properties as a whole (Forgacs and Newman 2005; Fuente and Helms 2005; Newman 2012; Piccolo 2013; Purnell 2012; Radlanski and Renz 2006; Wozniak and Chen 2009).

Once again, time processes are involved. It is not only important for regular development *where* a certain gene is expressed and *where* certain tissues are generated, but also *when* this takes place (Duboule 2003). Some genes are activated early, others later, which has been called differential gene activation. Probably there is a certain time in which a gradient works as a gradient so that cells react to it ("competence period") (Kicheva et al. 2012). In some cases also rhythmical pulses play a role in the activation of genes, as during the generation of somites in the chick embryo ("*hairy*-Oscillator," Gilbert 2014).

This all leads some authors to assume that during morphogenesis the cells do not follow an intrinsic genetic program but rather react to different situations, into which they maneuver themselves by growth (Radlanski and Renz 2006). The context of space and time is just as important as the genetic information itself. The first differentiation, which occurs in the early egg cell, is one of the evident examples of the function of an integrative system, as the local distribution of certain cytoplasmic factors induces the first genes to be expressed.

Already in the 1980s Susan Oyama developed the theory that DNA does not contain the entire information necessary for building an organism in the sense of a body plan. In her "developmental systems" approach, DNA is only one type of factor, even if certainly a very significant one. Neither DNA sequences nor any other type of factor can be privileged as the bearer of ultimate causal control in the developing organic system. Rather, the whole complex of factors—be they related to cellular morphology, to the dynamics of biochemical transitions, to external circumstances, to previous developmental history of the system or to the DNA sequences available—is considered as equally important for explaining the occurrence and the regularity of developmental steps. DNA only transmits information about some possibilities of how to build a protein. The organismic form then is constructed during the developmental process and is a result of interactive processes taking place between the parts and processes of the organism and between elements and processes in the environmental context. Thus, as the organismic form is constructed during ontogeny, as opposed to being preformed in the genome, Oyama calls her approach "developmental constructivism" and expands her approach also beyond the time of embryonic development so that every organism can be seen as "self-constructing" during the whole lifetime (Downes 2001; Dupré 2012; Oyama 2000; Oyama et al. 2001; Rehmann-Sutter 2002).

Also Lewontin (1991, p. 63) states:

> […] the organism does not compute itself from its DNA. A living organism at any moment in its life is the unique consequence of a developmental history that results from the interaction of and determination by internal and external forces.

Recent results of modern genetics increasingly vindicate at least the basic assumptions of these considerations and also show that there are again processes involved as they have been described in previous sections of the present paper: there are interdependencies rather than single causes, the systems concept is important for the patterns of differentiation, processes of shape are involved and generate a feedback on further cellular differentiations, and patterns of time generate the sequential frame of the process. In addition, changes within developmental patterns and processes are a source of evolutionary innovations, which is being studied in the modern field of evolutionary developmental biology ("evo-devo") (Carroll 2005; Müller and Newman 2003; Pigliucci and Müller 2010).

### 3.10 Reproduction and Death

It is undisputed that reproduction exists only in living organisms. However, the process is as fascinating as mysterious, although it seems to be so natural. Again and again a complex organism is constructed from simpler intermediate stages. The adult form itself only has a limited lifetime, but the species is preserved only by means of the sequence of generations. Speculatively, a long-term continuation of life might be possible. The normal case, however, is that multicellular organisms go through a continuous process of reproduction, self-renewal, and death.

Self-renewal also takes place within the adult organism itself. Each cell sends its macromolecules and its organelles through a permanent process of degradation and reconstruction. The same is the case for many cells of a whole organism. In humans there are tissues with higher and with lower rates of regeneration, using permanent processes of mitosis and apoptosis, being part of the normal healthy physiology (Hug 2000). Apoptosis also contributes essentially to embryonic development.

Single cells are regarded as potentially immortal. Two new organisms are created by division and they can continue this process without limitations. Death comes from the environment, when unfavorable conditions decimate or destroy the population. Thus, here too death processes belong essentially to life, as populations of single cells would destroy their ecosystem and themselves if they would live and reproduce without limits. With the formation of multicellular organisms, however, death processes are also internalized. Due to the development of somatic cells, the final death of organisms and the sequence of the succeeding generations with the consecutive renewal by means of individual developments becomes the normal case.

Reproduction, growth, development, and death are intimately intertwined. The same holds true for ecosystems, in which continuous assimilation must be in balance with degradation. How essential death processes are becomes quite obvious when they are lacking, so that a constantly growing tumor threatens the life of the whole organism. Nevertheless, aging and death are among the least understood processes in biology.

In addition to these phenomena one can also count that lifetimes are species specific and vary only within certain limits. The potential lifetime of an annual plant differs from that of an oak tree, and that of a mouse differs from that of an elephant. A horse is born, has a childhood, becomes adult and then old, and finally it dies. This sequence can‘t be reversed or stopped. There seems to be a characteristic order of time, possibly intertwined with the physiological time structure, which has been described above.

Many animal species also have a strong interrelation between reproduction, aging, and death, such as with salmon and eels. Most insects die when they have completed their reproductive cycle.

Reproduction, aging, and death expand the possibilities of evolution, as the process increases the opportunity to produce variants. The phenotype is not just passed on from one generation to the next, but must be constructed anew each and every time (Oyama 2000). It must run through its process of shape each time and in each generation the growing organism must integrate itself into the interdependence of individual autonomy and the conditions of the environment.

Thus, life is only understandable within the continuous polarity between synthesis and death. Production and reduction are interdependent.

## 4 Conclusion

In summary, it can be asserted that research has been generating knowledge of specific properties of living entities that do not belong to the realm of the inert, but which are derived from empirical studies and the observation of life, without postulating any mysterious forces. They do not contradict chemical or physical principles, which organisms depend on in order to operate their functions of metabolism, reproduction, and change. Chemical and physical processes are integrated into the self-organizing principles of organisms. By studying these processes we can identify and describe them in a meaningful way, but in order to gain a much more adequate picture, we need to consider their integration with specific properties.

The attempts to reduce life exclusively to inert principles cannot be successful. Dupré (2012, p. 85) formulates: "Mechanistic models have given us extensive knowledge of many of the elements of which living systems are composed, but they are inadequate to provide a full picture of life as a dynamic system."

Figure 5 shows an overview of the properties discussed. Perhaps this overview is not complete, and further properties may be identified. Some of them might be controversial. However, it can serve as a starting point for further considerations. Nonetheless, they are still isolated properties out of a basically uniform process. Presently, their theoretical linkage works only rudimentarily, so that their representation still contains a certain reduction.

Of course, there are hints of a synthesis, as these properties are not without interconnections. *Interdependencies* can be found in all the properties identified.

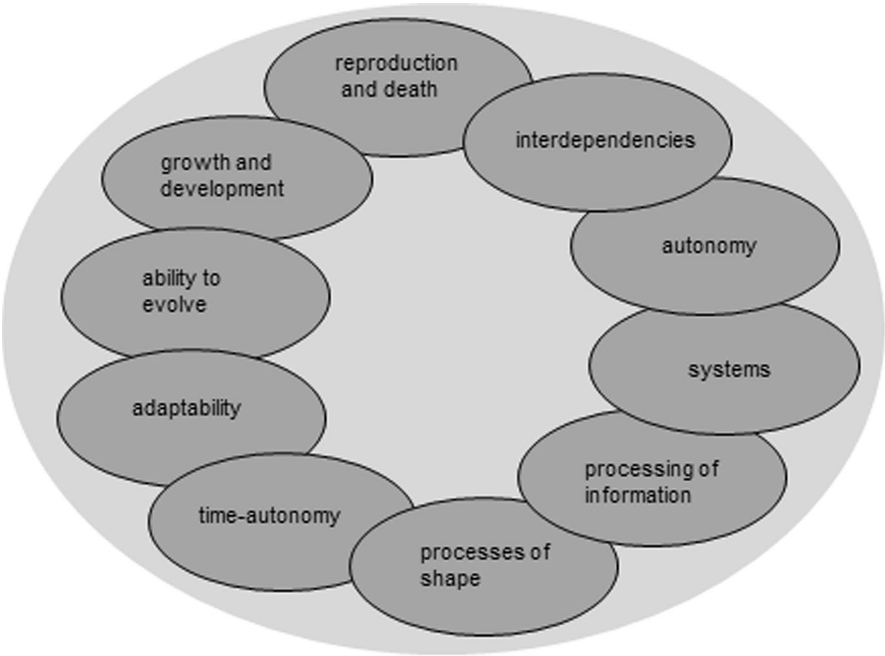


**Fig. 5** Overview of propeties of life

Different system levels, for example, are interdependent and are generated during growth and development. Also within the circadian oscillatory system there are clear interdependencies and feedback processes of different components involved, so that networks of interactions generate the resulting rhythmicity. *Autonomy* depends on the robustness of systems involved, which generate metabolic and informational self-determination, and changes in the capacity for autonomy are features of the ability to evolve. *Integrative biological systems* generate the processes of shape during growth and development, which may undergo evolutionary changes as well. *Processing of information* takes place on different systems levels and is involved in growth and development. *Processes of shape* establish organismal autonomy and integrate the parts into the overall building principles of the organism, thus generating systems integrity. *Time-autonomy* is part of the overall autonomy of the organism anyway. All processes are integrated into a well-regulated order of time, which can be adapted to time structures in the environment. *Adaptability* is based on the flexibility of autonomous systems, so that autonomy and adaptability become an interdependent pair of properties. Organisms that maintain their autonomy are intertwined with both given and constructed factors of the environment, and changes in this dynamic interaction between organism and environment can result in evolution. The *ability to evolve* is based on the capacity of organisms to modify in the long term their energetic-metabolic-informational state of disequilibrium, which organisms generate again and again during a *process of shape* as a consequence of development. *Growth and* *development* take place by means of interdependent factors within systems, rather than by single causes, and patterns of time generate the sequential frame of the process. *Reproduction* and development, growth and *death*, are prerequisites for evolution, as these processes provide opportunities to produce variants and and in each generation the growing organism needs to build up its *relative autonomy*.

The anticipated synthesis of these properties points far beyond a strictly physical model of the organism, thus raising questions that underscore the need for an "organismic biology" (Bock and Goode 1998; Fuchs 2009; Gilbert and Sarkar 2000; Henning and Scarfe 2013; Kirschner et al. 2000; Mayr 1988, 1996; Noble 2006; Nurse 2008; Rehmann-Sutter 2000; Ruiz-Mirazo and Moreno 2012; Woese 2004; Wuketits 1981). The point is that the existence of these properties has consequences for how we think about organisms and how they are studied in science, and thus what is offered here is more than the usual list of features of living entities. Accordingly, these properties need to be taken seriously concerning their qualitative content. In the long term, the synthesis of these and possibly additional specific properties may lead to the development of a more complete idea of what life really is.

Such a concept will certainly also influence the further development of biology, as these specific properties might get more explicitly into the focus of empirical research. Such an organismic view of living beings also will influence applied fields, such as medicine and agriculture, and move them further away from mechanistic explanations (Buchman 2002; Deppert et al. 1992; Joyner and Pedersen 2011; Rosslenbroich 2011a, 2016; Saetzler et al. 2011; Sonnenschein and Soto 1999; Soto and Sonnenschein 2005, 2012; Strohman 2003). Finally, it will influence our understanding of nature in general and of our own human nature specifically.

Thus "to attribute changes in the material world to movements of atoms, which are caused by central forces independent of time…", as Du Bois-Reymond formulated in the sentence cited above, cannot be appropriate in the case of living organisms. Biology must abandon this atomistic view if it wants to advance its understanding of the genuine properties of the organic. The essential process is not the movement of atoms or molecules. It is the regulation of networks and a hierarchy of complicated time patterns, which coordinate the multiple functions on different system levels within the organism.

**Compliance with Ethical Standards**

**Conflict of interest** The author declares that he has no conflict of interest.

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