Chapter 3
The Concept of Biological Autonomy

3.1 Systems Biology

The principle of autonomy as a trait of living organisms has been discussed within some approaches that can be subsumed under the field of systems biology. Although the field is heterogeneous and covers ideas that are not fully unified, it has a common agenda in the search for approaches to understand the coherence of functions within a living system. In general, it attempts to understand whole systems through an integrative view of all known regulatory and molecular processes.

Systems biology was founded in the 1930s by Paul Weiss and Ludwig von Bertalanffy and received further stimuli from cyberneticists such as Norbert Wiener and W. Ross Ashby, mathematical biophysicists Nicolas Rashevsky and Robert Rosen, systems engineer Mihajlo Mesarović, and systems theorist James Miller (O'Malley and Dupré 2005). For several decades, systems biology has been making its progress in the shadow of genetics, molecular biology, and other analytical disciplines. However, since the beginning of the 21st century, systems biology has become one of the most widely discussed fields of modern biology (Noble 2006, 2008; Soto et al. 2011; Kitano 2002a, b).

There is emerging some consensus that the analytical approaches of many fields of modern science require a move from the dissection of things to the dynamics of processes and to the question of how all these mechanisms, which are being studied in increasing detail, are integrated into a coherent whole, an organism. However, there is still need for the development of a clear account of what biological systems are and how the respective definition affects research agendas (O'Malley and Dupré 2005; Rosslenbroich 2011). The emerging consensus revolves around understanding biology as a science of systems with dynamic stability (Kather 2003). Within such an understanding, autonomy is at least implicitly present within the term *stability*. However, there are several schools of thought that can be included in the field of systems biology in a wider sense and that explicitly discuss autonomy as a fundamental characteristic of living systems in general.

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3.2 Autopoietic Systems

Some of these schools are inspired by the formulations of Humberto Maturana and Francisco Varela, who introduced the term *autopoiesis* as a description of living systems (Maturana and Varela 1987; Varela 1979, 1981; Luisi 2003; Barandiaran and Ruiz-Mirazo 2008; Kauffman 2003; Margulis and Sagan 2002; Di Paolo 2004, 2005).

A living system is generally described as an autopoietic unit capable of sustaining itself because of an inner network of reactions that generate and regenerate all the system's components. All the pertinent processes needed to maintain the network within a living system have their efficient cause within the system itself. The structures, based on a flow of molecules and energy, produce the components that, in turn, continue to maintain the organized bounded structure that gives rise to these components. Self-reference and automaintenance are central notions for this approach (Luisi 2003; Roth 1981; an der Heiden et al. 1985; Ruiz-Mirazo and Moreno 2012; Kather 2003). Coherent and ordered global behavior of the system constrains or governs the behavior of the individual components so that they no longer have the same behavioral alternatives as outside the system. At the same time, the behavior of the components generates and sustains the global order (Thompson 2007). This two-sided or double determination is known as circular causality (Haken 1983).

Varela founds his considerations on the idea that a living system maintains its specific organization through the active compensation of deformations (sometimes called perturbations). Here, Varela invokes Cannon's notion of homeostasis, which he expands by making every reference to homeostasis internal to the system itself through mutual interconnections of processes and by positing this interdependence as the source of the system's identity as a unit. Thus, all homeostatic operations in organisms are efficiently caused from within the system, and it is the continued existence of the set of causally dependent processes that constitutes the continued existence of the system (Bechtel 2007).

Because autopoietic systems actively distinguish themselves from their surroundings, they are autonomous: "In fact, the notion of autopoiesis can be described as a characterization of the mechanisms which endow living systems with the property of being autonomous; autopoiesis is an explication of the autonomy of the living" (Varela 1981, p. 14). An autonomous system acquires the property of specifying its own rules of behavior (Luisi 2003). Such systems need to be seen as sources of their own activity, specifying their own domains of interaction, not as transducers or functions for converting input instructions into output products (Thompson 2007).

Thompson (2007) describes this autonomy for a single cell: The cell stands out of a molecular soup by actively creating the boundaries that set it apart from what it is not and simultaneously regulate its interactions with the environment. Metabolic processes within the cell construct these 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. Should this process of self-production be interrupted, the cellular components no longer form a unit, gradually diffusing back into a molecular soup.

The existence of a boundary is a central element of a living system (Luisi 2003; an der Heiden et al. 1985). 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. At the same time, the membrane establishes and regulates contact to and exchange with the environment.

Thompson (2007) qualifies the necessity of a strict physical boundary for an autonomous system. He states that a system can be autonomous without having this sort of material boundary; the members of an insect colony, for example, form an autonomous social network, but the boundary is social and territorial, not material. Autonomous systems are organizationally closed in the sense that their organization is characterized by their internal network processes, which recursively depend on each other and thus constitute the system as a unit. These processes generate a far-from-equilibrium situation as long as the system is living. Equilibrium with the processes in the environment arises when the system is dead. At the same time, living systems are materially and energetically open to their environment. They receive energy and nutrients from the environment and excrete products and waste. Luisi (2003) emphasizes that there is an interesting contradiction between biological autonomy and dependence on the external medium and that all living organisms must operate within this contradiction.

In a series of papers, Moreno and coworkers work toward an understanding of a most basic form of autonomy of living organisms (Ruiz-Mirazo and Moreno 2004, 2012; Moreno et al. 2008). They see autonomy as a fundamental characteristic of life and stress explicitly the significance of the principle for understanding the origin of early life on Earth. A motivation for their search for a basic autonomy is to provide a link between this fundamental principle of life and physics and chemistry, so that the idea of autonomy itself is naturalized and can serve as a bridge from the nonliving to the living domain. Because they are crucial for the generation of simple self-maintaining and self-constructing systems, they understand that these systems must engage in an interactive loop with their respective environment across some boundary condition (gradients, influx/outflux of different compounds, energy transduction mechanisms, etc.) to sustain the processes of generation of internal "order" in accordance with the generalized second law of thermodynamics.

Moreno et al. describe that, unlike physical or chemical dissipative structures, in which patterns of dynamic order form spontaneously but whose stability relies almost completely on externally imposed boundary conditions, autonomous systems build and actively maintain most of their own boundary conditions, making possible a robust far-from-equilibrium dynamic behavior. Thus, a central question is how a system develops the capacity to channel the flow of matter and energy through itself to achieve robust self-construction (i.e., self-construction that includes regulation loops with its immediate environment).

Thompson (2007) introduces the distinction between heteronymous and autonomous systems. Whereas heteronomy literally means other-governed, autonomy means self-governed. A heteronymous system is one whose organization is defined by input-output information flow and external mechanisms of control.

Traditional computational systems and many network views, for example, are heteronymous: They have an input layer and an output layer; the inputs are initially assigned by the observer outside the system, and output performance is evaluated in relation to an externally imposed task. An autonomous living system, however, is defined by its endogenous, self-organizing, and self-controlling dynamics and determines the domain in which it operates. It has input and output; however, these do not alone determine the system. It is the internal self-production process that controls and regulates the system's interaction with the outside environment. For Thompson, the principle of autonomy is essential for understanding principles such as intentionality and subjectivity of living entities, which in complex forms generate a continuity of life and mind. He attempts to understand the relation between these entities by his "enactive approach," focusing on the conditions of this continuity.

3.3 Philosophical Description of Organismic Autonomy

Fuchs (2009a) gives a description of the concept of organismic autonomy to prepare a view of the human neurophysiologic functions that is more integrative. He draws on results from ecological and philosophical biology with its main exponents J. von Uexküll (1973), Plessner (1975), and Jonas (1966) and those of system theories such as those of Bertalanffy (1973) and Maturana and Varela (1987).

Fuchs also describes living beings as complex entities or systems that maintain themselves in form and structure within time, although there is a continuing exchange of substances with the environment. This maintenance is an active self-organization as the organism subordinates the substances under its own principles and transforms and integrates them. They gain new properties, which they only have within the systemic context of the organism. Fuchs points to an example: The ferrous ion in hemoglobin behaves differently from iron in the outside world – it does not oxidize irreversibly but is able to bind oxygen reversibly, which is a crucial prerequisite for the turnover of energy in animals.

Beyond this, metabolism leads to a transformation of substances during decomposing digestion and resynthesis. The nutritional components are transformed into substances with the characteristics of the organism and integrated into its processes. By means of these dynamic processes, the living being encloses itself from the environment and gains – in different degrees – self-determination or autonomy. This means that its processes and its behavior are not primarily determined from the outside but rather depend on its internal disposition and condition. External influences predominantly are stimuli, which are answered by reactions of the whole organism, rather than causal effects as in mechanical cause-and-effect relations, as long as they are not destructive.

The basis for autonomy is the special interdependence between the whole and its parts within the organism, which include a differentiation in subsystems and organs. Although the organism consists of the sum of its macromolecules, cells, organs, and circulatory and nervous systems, it has a different relation to these component parts than a crystal to its components. The organism is itself the condition of its parts because it enables their existence. It produces and reproduces them while consisting of them. Self-maintenance is continuing self-generation. At the same time, the parts fulfill their respective functions within the organism and contribute to its overall functioning.

Of course, Fuchs also describes that the autonomy of living beings is not possible in autarky. The organism only gains its sovereignty for the price of certain requirements. The changing substances need to be available and incorporated to maintain homeostasis. Thus, organisms are always in need of factors from their environment (Jonas 1966).

According to Plessner (1975), Fuchs further describes that plants exhibit a predominantly open relation to their environment, whereas animals have a more closed form of organization. In animals, the exchange surfaces for metabolism are turned to the inside. Special internal organs and internal cavities appear, while exchange surfaces on the outside are reduced. Thus, animal life steps to a certain extent out from the direct environmental relation. The enclosure from the environment requires – on the other hand – a sensorimotor interzone, which restores the contact with the environment, however, on a new level. This condition shows separate organs for sensory and motor activity and their central nervous connections. The principle of a closed-body organization enables the independent movement of the animal.

According to Fuchs, the loss of a direct environmental relation corresponds to a gain in degrees of freedom. Whereas the mimosa reacts directly to touch, the stimulus-response relationships in animals tend to be less tightly connected. Animals tend to modulate a reaction so that the probability of a certain behavior can be modified. Signals can internally be enforced, compared to other signals, and memorized. Thus, not a rigid, but rather a flexible relation between organism and environment emerges.

3.4 Robustness

In recent years, a somewhat-new term developed in some areas of molecular biology. It was increasingly comprehended that many structures and functions as well as proteins and genes have certain stability in the face of environmental variations and genetic changes. Many physiological and developmental systems are resistant or "robust" to such perturbations. That is, despite these natural perturbations, the systems produce relatively invariant outputs (Masel and Siegal 2009; Masel and Trotter 2010; Stelling et al. 2004; Wagner 2012; Kitano 2004, 2007; Gerhart and Kirschner 1997; Larhlimi et al. 2011). Robustness is understood as a property that allows a system to maintain its functions against internal and external perturbations and uncertainties. It encompasses a broad range of traits, from macroscopic, visible traits to molecular traits, such as the expression level of a gene or the three-dimensional conformation of a protein.

"Biological systems maintain phenotypic stability in the face of diverse perturbations arising from environmental changes, stochastic events (or intracellular noise), and genetic variation. It has long been recognized that this robustness is an inherent property of all biological systems and is strongly favored by evolution" (Stelling et al. 2004, p. 675). Masel and Siegal (2009) see it as impossible to understand whole biological systems without understanding their robustness. Stelling et al. (2004) note that robustness encompasses a relative, not an absolute, property because no system can maintain stability for all its functions when encountering any kind of perturbation.

Robustness is concerned with maintaining the possibility of a system to function rather than maintaining an actual state of a system. Thus, Kitano (2007) differentiates it from stability and homeostasis, which predominantly describe a function that keeps a condition relatively constant. A system is robust as long as it maintains functionality, even if it transits to a new steady state or if instability actually helps the system cope with perturbations. Such transitions between states are often observed in organisms when facing stress conditions. One such condition can be extreme dehydration, to which some organisms can react with a dormant state, becoming active again on rehydration. These examples of extreme robustness under harsh stress conditions show that organisms can attain an impressive degree of robustness by switching from one steady state to another rather than trying to maintain a given state.

Wagner (2012) divides the perturbations that can affect a phenotype into two broad categories. The first consists of environmental perturbations. These include changes in an organism's exterior environment, such as changes in temperature, in available nutrients, or in the abundance of other organisms, such as potential prey. They also include changes in an organism's internal environment, such as temporal fluctuations in gene expression levels, which are caused by ubiquitous intracellular noise. The second kind of perturbations is mutations, changes in an organism's genotype. Mutations affect an organism more permanently than environmental change because the changes they cause are readily inherited from generation to generation. For this reason, Wagner states that they are especially an important object of study for students of evolution.

Because the term *autonomy* describes living systems as actively distinguishing themselves from their surroundings (see Definition 1 further in the chapter), it overlaps to some extent with the term *robustness*. However, it is not congruent with it. Robustness can be seen as a prerequisite for autonomy. Self-determination and self-maintenance need robust functions to defy perturbations from the nonbiological and biological surroundings as well as from the internal variability.

However, it is also justifiable to regard robustness as a part of autonomy itself. Robustness, also in different actual states of a system, maintains basically that the system is kept in a far-from-equilibrium state. Even dormant forms are different from their immediate surroundings in a self-organized manner, including when the metabolism is completely reduced. If the system becomes like the surroundings, this results in an equilibrium state and death.

Stelling et al. (2004) mention the important point that the primary function of a system may usually be robust to a wide range of perturbations, whereas the system can show extreme fragility toward other, even seemingly smaller, perturbations. They think that the coexistence of extremes in robustness and fragility ("robust yet fragile") perhaps constitutes the most salient feature of highly evolved complexity. Making one feature robust to a class of perturbations can make the same or other features fragile to that or other perturbations. In this sense, they expect a necessary connection between complexity and robustness.

In this discussion, several principles are seen as relevant for maintaining and establishing robustness (Stelling et al. 2004; Kitano 2004, 2007). One strategy to protect against failure of a specific component is to provide for alternative ways to carry out the function the component performs. This can be called "redundancy of components." At the genetic level, this backup strategy or "genetic buffering" (Hartman et al. 2001) might be brought about by duplicate genes with identical roles or by different genes that constitute alternative but functionally overlapping pathways. In contrast to redundant systems in engineering, however, identical genes that do not diverge in functionality or regulation would not survive in evolution. Instead, structurally different entities perform overlapping functions, which seems to be a common principle in organisms, on other levels in addition to the genetic.

A further principle discussed in this regard is that of "feedback circuits" (Stelling et al. 2004; Bechtel 2007). Control circuits play a decisive role in maintaining cellular functions in the face of internal or external uncertainties. By using the output of a function to be controlled to determine appropriate input signals, feedback enables a system to regulate the output by monitoring it. Negative feedback can reduce the difference between actual output and a given set point, thereby dampening noise and rejecting perturbations. Positive feedback can enhance sensitivity. This is primarily required for robust cellular decisions that need to be derived from noisy and graded input signals and to be maintained. Well-balanced positive and negative feedback can lead to a blend of sensitivity and stability. Another possibility for achieving higher robustness consists of combining multiple levels of regulation, for instance, controlled transcription, translation, posttranslational modification, and degradation. Often, when highly precise and reliable behavior is indispensable for overall cellular functionality, multiple intertwined feedback loops operate. The different levels of control for circadian clocks (Bechtel 2010a; Hogenesch and Herzog 2011; Mohawk et al. 2012) and developmental control circuits (Carroll 2005a, b) provide good examples of these aspects.

The principle of modularity might also contribute to the robustness of organisms. The composition of cells and of organisms from "functional units" or "modules" is under increasing discussion in the literature (Stelling et al. 2004). Modules constitute semi-independent entities that show dense internal functional connections but looser connections with their environment. Modularity, as the encapsulation of functions, can contribute to both robustness of the entire system (by confining damage to separable parts) and evolvability (by rewiring of modules or by modifications in modules that are not noticeable from the outside).

Finally, the integration of cellular functionality across hierarchies seems to be important. Stelling et al. (2004) describe that cells, which under normal operation provide a certain robustness of their behavior, can collectively reduce the impact of environmental perturbations when they are components of an organism network. Thus, the “collective of cells” inherits some of the cells’ robustness, augmenting it by synergistic network-level interactions. An efficient means for coordination in such networks and in complex systems is to organize the system hierarchically, namely, to establish different layers of integration. This not only might reduce the costs of information transmission but also might further enhance robustness by different level regulations, multiplying each other.

3.5 Homeostasis

Homeostasis is the ability of a system to regulate its internal conditions to keep some or several functions stable. Examples are properties such as temperature or blood composition in animals.

The principle was developed by Claude Bernard and later by Walter B. Cannon. Bernard focuses on the internal organization of a living system to find causal principles that would allow a description of organisms as mechanically determined entities (Bechtel 2007). He argues that the internal parts of a living mechanism reside in an internal environment that is distinct from the external environment in which the organism as a whole dwells and that a relatively strict determinism could be found in their response to fluctuating conditions. The internal environment provides a buffer between conditions in the external environment and the reactive components of the mechanism, thus insulating component parts of the mechanism from conditions in the external environment. Bernard proposes that this buffering is achieved by individual components of the organism, each performing specific operations that serve to maintain the constancy of the internal environment. The constancy would render the organism independent from vagaries of the environment and would free the organism from environmental restrictions (Bernard 1859, 1878). Most famous is his formulation of the “milieu intérieur,” a phrase he coined to refer to the extracellular fluid and its physiological capacity to ensure protective stability for the tissues and organs of multicellular organisms.

> The living body, though it has need of the surrounding environment, is nevertheless relatively independent of it. This independence which the organism has of its external environment, derives from the fact that in the living being, the tissues are in fact withdrawn from direct external influences and are protected by a veritable internal environment which is constituted, in particular, by the fluids circulating in the body. … The fixity of the milieu supposes a perfection of the organism such that the external variations are at each instant compensated for and equilibrated. … All of the vital mechanisms, however varied they may be, have always one goal, to maintain the uniformity of the conditions of life in the internal environment. … The stability of the internal environment is the condition for the free and independent life. (Bernard 1974, p. 188)

Walter Cannon (1932) introduced the term *homeostasis* for the capacity of living systems to maintain a relatively constant internal environment. He also sketched a taxonomy of strategies by which animals are capable of maintaining homeostasis (Bechtel 2007). The simplest involves storing surplus supplies in time of plenty, either by simple accumulation in selected tissues (e.g., water in muscle or skin) or by conversion to a different form (e.g., glucose into glycogen) from which reconversion in time of need is possible. A second type of homeostasis involves altering the rate of continuous processes (e.g., changing the rate of blood flow by modifying the size of capillaries to maintain uniform temperature). In this sense, it somewhat overlaps with the large field of cybernetics.

The concept of homeostasis was extremely successful in different biological and medical disciplines, such as physiology, and is elaborated and described in many details today. Homeostasis is an important means to maintain an autonomy of properties of organisms that is relatively stable against environmental fluctuations as well as internal functional variations. The organism itself sets the range at which a variable is maintained and uses several functions (e.g., positive or negative feedback) to achieve this autonomy.

Both the general formation of a difference toward factors of the environment and the buffering of fluctuations establish the autonomy of the respective function. Typically, several functions at a time can be regulated, which contributes essentially to overall autonomy of the organism and some independence from external conditions. However, organisms use this principle in different degrees and sophistication.

3.6 Time Autonomy

A continuous characteristic of any living entity is that it establishes its own sequences in time. Development, reproduction, metabolism, rest-activity cycles, and many other functions have their respective time order. This concerns not only the well-known circadian rhythmicity, which is an endogenous rhythm, synchronized with the daily cycle of the environment, but also all biochemical, cellular, and organic processes, with different arrangements of their duration and order of sequences (Hildebrandt 1979; Hildebrandt et al. 1987; Koukkari and Sothern 2006).

Basically, all chemical reactions need a certain time, the reaction rate. However, the cell regulates these reaction rates with the help of enzymes to integrate them into its own order of sequences. It performs extremely refined sequences by subordinating the reaction rates under its own time management. The emerging time order is typically characterized by oscillations, as chronobiology describes them. The crucial point is that the sequences in time are not adopted from the environment but directed by the rules of the organism itself. The oscillations of different frequencies are endogenous, and they are compensated for temperature. Only secondarily are they synchronized with cycles of the environment. In this sense, there is also an autonomy of time in living entities, as it is both robust and tunable (Gore and Oudenaarden 2009; Duboule 2003).

Circadian rhythmicity is an excellent example of an integrated system with interdependent functions and processes (Bechtel 2010a). After research tried for a long time to find the components of the oscillations along a linear feed-forward view, it is now becoming clear that there are multiple feedback loops between a central oscillator in the brain, several peripheral oscillators, and several sensory inputs. Thus, there are indications to the effect that it is an integrated circadian system, and that a step up to a systems level that considers interactions throughout the organism is needed to understand how circadian oscillators are entrained and influence other biological processes.

3.7 Organisms as Hierarchically Ordered Systems

Several of the concepts mentioned are grounded on a systems view of the organism, so it might be useful to take a closer look at the notion of a biological system. There have been several attempts to define or describe organic systems. However, in my view Paul A. Weiss, who was among the first to introduce the notion into biology, developed the most coherent and consequent definition (Rosslenbroich 2011; Drack and Wolkenhauer 2011; Drack and Apftaler 2007; Overton 1997; Köchy 1997).

Weiss (1963, 1968, 1969, 1971, 1973, 1977) sees a living system as an entity that imposes restricting (i.e., regulating) functions on its component parts so the functionality of the whole system is ensured. The system itself contains constituting properties and thus possesses information that does not stem from the parts themselves. The system must be regarded as a spatiofunctional entity that integrates the functions of its parts. It has an ontological weight of its own.

Weiss expresses this in his working definition of a system: "Pragmatically defined, a system is a rather circumscribed complex of relatively bounded phenomena, which, within those bounds, retains a relatively stationary pattern of structure in space or of sequential configuration in time in spite of a high degree of variability in the details of distribution and interrelations among its constituent units of lower order" (Weiss 1969, p. 11). Not only does the system maintain its configuration and integral operation in an essentially constant environment, but also it responds to alterations in the environment by an adaptive redirection of its componential processes in such a manner that the external changes are countered in the direction of an optimal preservation of its systemic integrity.

One such system is the cell: The cell hosts a number of components, such as organelles and molecules. However, the cellular system integrates all these components into a functional unit. It needs these components and depends heavily on them, but the cell is only able to live because of the regulation imposed on the components by 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). Therefore, the elementary functions of a system may be variable. This corresponds exactly with modern knowledge of the cell (Shapiro 2011): Whether and when information is transcribed from the DNA, whether certain proteins are built or which components are included in the cell membrane to keep it within an optimal stage of fluidity, constantly change according to the functional state of the cell and its environmental conditions.

> 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)

A cell has subsystems (i.e., the organelles) that perform partial processes. So, a mitochondrion can be seen as a subsystem that integrates the molecular devices for processing energy. Looking at the next-higher level beyond the cell, there is the tissue in which the cells are organized. Such a tissue is also a system in which functions of single cells are integrated and regulated. One example would be epithelium, in which a boundary is established by systemic cooperation of many cells. In this case, the system can have certain characteristics, such as a barrier, that are not characteristics of the single cells. They are a property of the association of the cells. A further possible level is constituted by the organs of an organism, such as a heart, a lung, or a liver. Finally, the organism integrates all these subsystems into a coherent whole.

Thus, the integral systems operation, whether of the body as a whole or of an organ such as the brain within it, "deals with the molecules not directly, but only through the agency of intermediate subordinate sub-systems, regarded in a hierarchical scale of orders of magnitude. … Each sub-system dominates its own subordinate smaller parts within its own orbit or domain, as it were, restraining their degrees of freedom according to its own integral portion of the overall pattern, much as its own degrees of freedom have been restrained by the pattern of activities of the higher system of which it is a part and participant" (Weiss 1969, p. 14).

Weiss describes organic systems as simultaneously relatively closed and relatively open to environmental influences. They have a certain stability and thus an organizational closure; at the same time, they are open for influences from their surroundings. For example, a cell is a well-characterized entity and can be regarded as a system. However, in a multicellular organism, it needs to be regulated, requiring it to have a certain openness to regulative influences. To guarantee this, the cells of multicellular animals have a multitude of membrane receptors that mediate signals from the surroundings. They also need to have a regulated exchange of substances with the environment to maintain their basic functions.

Coincidences of this type, with two opposing principles present simultaneously, are a typical feature of organic life and can be found in many other examples. Typically, organisms balance such contradictory demands. Organismic thinking has to take such properties into account. This is the reason why Weiss presents such a long-winded definition of a system as provided previously, using formulations such as "relatively bounded," "relatively stationary," and so on.

Now, we have the components to understand Fig. 3.1, which represents the hierarchical order of the systems of an organism. Each system has relative invariance and autonomy as well as relative openness to regulative influences from

Fig. 3.1 Schematic representation of the hierarchical concept of Paul Weiss (Redrawn from Weiss 1969 with slight changes in the levels indicated)

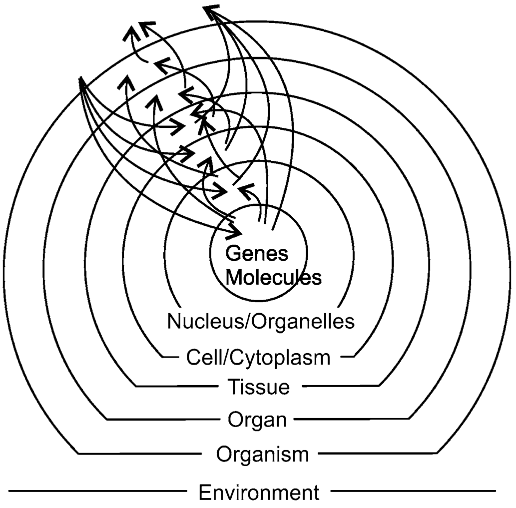
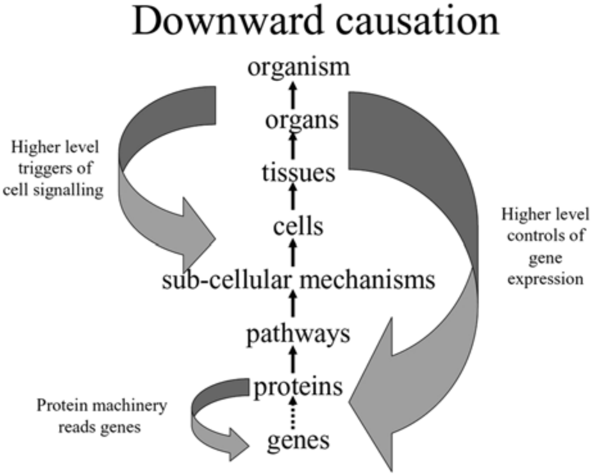


Fig. 3.2 Schematic representation of causal relations within an organism according to Noble 2006, by permission of Oxford University Press



superimposed higher-level systems. The arrows indicate pathways of possible interactions that must be taken into account in studying such an organism. Also, the whole organism cannot be regarded as a closed system. Rather, it is integrated into its environment with many forms of exchange.

Basically, this systems view is congruent with some of the more recent views, which however show important differences among each other (O’Malley and Dupré 2005; Rosslenbroich 2011). In particular, the presently widely discussed approach of Denis Noble (Noble 2006, 2008, 2011) shows clear parallels, although it was obviously developed independently from the earlier definition of Weiss (Fig. 3.2). One could have the impression that both definitions were developed closely along the actual organic phenomena by two experienced researchers, who thus derived similar results. (Comparable approaches are to be found in Soto et al. 2011; Soto and Sonnenschein 2012; Saetzler et al. 2011; Sonnenschein and Soto 1999; Cornish-Bowden and Cardenas 2005; Cornish-Bowden 2006; Mesarovic et al. 2004; Mesarovic and Sreenath 2006; Joyner and Pedersen 2011; Bechtel 2010b; Köchy 1997.)

Even the ovum is such a system. It is not only a nutrient solution for the genome but also a real organism itself, comparable to single-cell organisms. Today, it is well known that the cytoplasm of the ovum transports many components needed for normal development. Development then takes place through continuous interactions between factors of the cytoplasm and DNA, with DNA methylation patterns introducing additional levels of information. Within these processes, the genetic information and the cytoplasmic factors are equally important. When the embryo develops into a multicellular organism, extracellular factors such as the position within the organism also become relevant. In each cell, the pertinent genetic information must be expressed at the right moment and at the appropriate place, which are dependent on a spatial order as well as a temporal order, which in turn are important in themselves and cannot simply be reduced to the genetic information.

To explain this principle, Susan Oyama developed a theory she calls the "developmental systems theory" (Oyama 2000a, b; Oyama et al. 2001; Downes 2001; Rehmann-Sutter 2002; Sterelny and Griffiths 1999). She argues that the information for the assembly of the organism can be found in neither the genome nor the environment, but it is put into effect by the process of development within the developmental system. In this context, DNA is only one of several factors for the process of development, albeit an important and necessary one. Nonetheless, sequences of DNA and any other factors cannot be privileged as bearers of ultimate causal control of the developing organism. Instead, the whole complex of factors is equally important to explain the appearance and the regularity of the steps: cellular morphology, the dynamic of biochemical processes, environmental influences, the previous history of the system, and the DNA sequences involved.

Because the embryo is "constructed" during development, Oyama calls her approach "developmental constructivism." She also expands this principle beyond the time of the development of the embryo, so that each organism can be considered as continuously "self-constructing" during its lifetime. This is a consequent systemic view applied to the ontogeny of organisms, however, basically using an organismic approach comparable to that of Paul Weiss. According to the concepts of Oyama and Weiss, it is not surprising that heredity can be found on different levels of the cell or the organism, as recent epigenetic research describes (Jablonka and Raz 2009; Jablonka and Lamb 2005).

The notion of organic systems is also applied to evolution (Riedl 2000; Wagner and Altenberg 1996; Shapiro 2011). Shapiro sees the systems view as essential for the further development of our understanding of evolution. He states that it will be possible to articulate a more interactive and information-based set of evolutionary principles without departing from the realm of established empirical observations.

I propose that the systems approach in the formulation of Paul Weiss is the most consistent one for the understanding of living entities (Rosslenbroich 2011). According to Weiss, insofar as a system can be seen as an entity that maintains its configuration within the environment and responds to alterations of the environment by an adaptive redirection of its componential processes to counter external changes, the system can be seen as the medium of the autonomy of the organism.

As a compilation of the concepts discussed so far, I propose Definition 1 for general autonomy:

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

I. Generate, maintain, and regulate an inner network of interdependent, energy-consuming processes, which in turn generate and maintain the system;
II. Establish a boundary and actively regulate their interaction and exchange with the environment;
III. Specify their own rules of behavior and react to external stimuli in a self-determined way, according to their internal disposition and condition;
IV. Establish an interdependence between the system and its parts within the organism, which includes a differentiation in subsystems;
V. Establish a time autonomy; and
VI. Maintain a phenotypic stability (robustness) in the face of diverse perturbations arising from environmental changes, internal variability, and genetic variations.

3.8 Autonomy and Evolution

To this point, I have focused on a definition of autonomy as a general trait of living organisms. In the next step, I include the evolutionary view and examine changes of autonomous capacities of organisms. I try to answer the question of Ruiz-Mirazo and Moreno (2012): Is the idea of autonomy in any sense also helpful for understanding evolutionary transitions, that is, the appearance of new, more complex forms of biological organization in time?

Bechtel (2007) indicates that Moreno's notion of basic autonomy suggests additional levels of autonomy. Moreno describes that some of these may involve internal functions that enhance the system's ability to maintain itself. Others may involve ways of interacting with the environment. Basic autonomous systems, Bechtel describes further, remain highly dependent on the moment-to-moment conditions of their environment as they must continually extract energy and raw materials from it and excrete waste into it. If energy and material resources are not provided in high-enough concentration so that the osmotic or pumping functions in the membrane are able to bring them into the system or if waste accumulates, the viability of the system is undermined. By developing additional functions to ensure the needed conditions, the system can increase its ability to maintain itself.

Table 3.1 Authors who mentioned increasing autonomy of organisms during evolution

Herbert Spencer 1864
Hermann Jordan 1908, 1913
Heinrich Quiring 1931
Karl Beurlen 1937, 1949
Ivan Schmalhausen 1949
Julian Huxley 1953, 1974
Friedrich Kipp 1948, 1949
Ludwig v. Bertalanffy 1949
Klaus Günther 1950
Homer Smith 1953
Maria-Josef Heuts 1953
Emil Kuhn-Schnyder 1954, 1967
Edwin Hennig 1955
Paul Overhage 1957, 1963
Bernhard Rensch 1959
Conrad H. Waddington 1961
Erich Lange 1976
Wolfgang Schad 1977, 1992
Verne Grant 1985
Ludwig Kämpfe 1985
David B. Wake 1986
Jeffrey S. Wicken 1987
Hubert Hendrichs 1988
Wolfgang H. Arnold 1989
Josef Reichholf 1992a, b
Jürgen Bereiter-Hahn 1996
Kristian Köchy 1997
John Gerhart and Marc Kirschner 1997
Yoav Yigael 2000
Andreas Suchantke 2002
Walter Streffer 2003, 2009
Bernd Rosslenbroich 2007, 2009
William Bechtel 2007
Gerhard Neuweiler 2008
Kepa Ruiz-Mirazo and Alvaro Moreno 2012

Bechtel states that it makes sense to construe these additional functions as enhancing the system's autonomy.

Bechtel maintains that evolution is a process that, over time, can develop systems with greater autonomy. Although not denying the traditional accounts of evolution, he holds that the focus on autonomous systems provides a different perspective. First, it places the organism in the central role and emphasizes that an organism needs to be able to maintain itself as an autonomous system; otherwise, there is nothing to evolve. This does not mean that individual organisms must be totally self-sufficient. Organisms can evolve to rely on features of the environment that are regularly present in relation to them. However, they need to create and maintain all the mechanisms on which they rely so they can use these resources. Second, each addition to the basic system involves a cost, such that the system must generate and repair these mechanisms itself. Recognizing the organism in this sense as a subject of evolution rather than its object matches several recent approaches within the changing view of evolution (Weingarten 1993; Shapiro 2011; West-Eberhard 2003).

The idea is that during evolution the internal processes, prerequisites, and functions can change in such a way that the organisms gain increased abilities to compensate given perturbations and thus become more independent from environmental factors. Through these changes, they become more flexible and self-determined in many of their life processes, including behavior.

The principle has been noticed occasionally by scientists of relatively different provenance (Table 3.1). Deliberations on the pattern began in Darwin's time. Spencer (1864) defines life as the continuous adjustment of internal relations to external relations and formulated a "rule of increasing independence from the environment."

In the first half of the twentieth century, the pattern was occasionally included in evolutionary considerations with rather different theoretical backgrounds

(Beurlen 1937, 1949; Jordan 1908, 1913; Quiring 1931). Later, Rensch (1959) included it in a list of various factors of anagenesis, arguing that it leads to increasing plasticity of structures and functions, which allow a greater variety of reactions to the surroundings.

> "In many cases, such increased autonomy is the result of improved sensory and nervous systems. In man this autonomy finally led to control of the factors of environment. Another essential means of increasing the autonomy was the establishment of homoiothermy, by which the higher groups of vertebrates became more or less independent of the environment. … General characters of increased autonomy, then, are a growing independence from environmental factors, and an increase of plasticity, of internal, or internally caused, physiological processes" (p. 298).

The pattern was either seen as centrally important (Bertalanffy 1949; Kipp 1948; Kuhn-Schnyder 1954, 1967; Lange 1976; Schad 1977, 1992; Schmalhausen 1949; Smith 1953) or discussed in combination with other patterns (Grant 1985; Kämpfe 1985; Overhage 1957, 1963; Waddington 1961; Köchy 1997).

The considerations of Julian Huxley (1953, 1974) are the most well known. He sees an "increased control over and independence of the environment" as a "raising of the upper level of biological efficiency" as the best definition of evolutionary progress, which was mainly achieved in the evolutionary line of the vertebrates leading to birds, mammals, and humans (Huxley 1974, p. 564). However, there are several problematic points in his discussion. One problem is the fact that relatively primitive organisms are also biologically efficient; otherwise, they would not have survived for a long time. Also, he focuses heavily on the line toward humans. I show in the forthcoming chapters that this is not necessarily the case if one assumes my definition of increasing autonomy. Beyond this, other groups with no phylogenetic relation to vertebrates – at least since the Cambrian – developed their own types of independence from the environment.

Huxley also does not define what he means by "control over the environment," especially as he does not restrict it to human beings, as Rensch does in the text cited previously. Thus, the relation of "independence" and "control" remains unclear, as McShea and Simpson (2011) indicate: They argue that it may be easy to see an exoskeleton, a shelled egg, or life cycle with a resting-cyst stage as ways to achieve some degree of independence from the external environment, but that it is difficult to see them as controls over the external environment in the same sense as a beaver or a human, building a dam, is. It seems that both criteria need their own respective definition. A somewhat clearer definition is provided by Huxley (1953), who defines biological progress as a "trend towards increased efficiency in dealing with the challenge of the environment, and an increased independence of the changes going on in it" (p. 114).

Huxley (1953, 1974) fleetingly mentions some important examples of independence from the environment. This demonstrates that he clearly saw the principle and recognized how pervasive it is. The following are some of his examples: the step to multicellularity as essential for the attainment of more-than-microscopic size and more than an elementary degree of division of labor among tissues and organs; the generation of bilateral symmetry, which allows exploration of the environment by forward movement; the capacity of higher fish to keep their internal environment chemically almost constant, while lower marine organisms have blood or body fluids identical in saline concentrations with that of the seawater in which they live, and if the composition of their fluid environment is changed, that of their blood changes correspondingly; the method of swimming in vertebrates with the aid of a tail, which gave them greater speed and power than any of their competitors and the potential to grow to a larger size; the emancipation of early land vertebrates from changes in moisture content of the air; and the ability of birds and mammals to maintain a constant temperature for their internal environment and thus be independent of a wide range of external temperature changes. These considerations belong to the most interesting ones, especially because they stand in line with the other chapters of Huxley's book with fairly pluralistic considerations about evolution in general, in fact being more pluralistic than the considerations of some other contributors to the "Evolutionary Synthesis" of Huxley's time (Witteveen 2011).

In a Dahlem workshop as presented in *Patterns and Processes in the History of Life* (Wake 1986, p. 53), "increasing autonomization" as the "degree of homeostasis or autonomous buffering of environmental variables" was included in a list of general patterns of evolution. There, it was claimed: "Across the spectrum of metazoans and metaphytes, from invertebrates through vertebrates, and algae to seed plants, autonomization and complexity obviously increase." However, the authors also stated that patterns such as this were inadequately defined and studied.

Sometimes the concept of autonomy reemerges in recent literature without sparking a broader resonance (Reichholf 1992a, b; Schad 1992, 1997; Yigael 2000; Neuweiler 2008; Bereiter-Hahn 1996). Occasionally, it appears in textbooks, especially on physiology and comparative animal morphology, again without conceptual consequences. The notion has also been discussed in the context of constructional morphology (Gutmann 1981; Weingarten 1993), and philosophical considerations of it have also been published (Jonas 1966; Spencer 1864; Steiner 1964; Fuchs 2009a).

Gerhart and Kischner (1997) argue in their inspiring book that the essential step in the transition to multicellularity of organisms was the new capacity to effectively shield themselves from the vagaries of the environment by producing their own internal conditions. "Whereas single-celled eukaryotes had little control over their environment and evolved mostly in response to it, the cells of multicellular eukaryotes could largely produce their own intercellular conditions and respond to these, as they could to the external environment" (p. 238). They call the capacity of the cell to create its own conditions "conditionality" and discuss the prerequisites for this. They regret that this has not been discussed by theoreticians, although in their view it has considerable bearing on the ability to evolve and seems to be a major evolutionary innovation.

Regularly, this idea of conditionality emerges in formulations that describe the gist of this principle without seeing the necessity for conceptualizing it further. To present just one example, the following is a passage from Vermeij (1987, p. 421):

> "It is possible, however, that species have improved in their capacity to survive in the physical environment. Many of the characteristics associated with competitive and defensive superiority – large body size, high body temperature, parental care of the young, and a tightly sealing exoskeleton, for example – also buffer individuals against short-term fluctuations in temperature and other physical factors. Consequently, individuals are able to carry on normal activity, or at least to survive, when physical conditions are temporarily unfavorable. Without such characteristics, individuals would be able to persist in a much smaller range of physical conditions."

Also within the topic of robustness cited are arguments for increases in robustness during evolution. Thus, Wagner (2012) points to the question of changes in robustness. He states that the robustness of macromolecules can change on evolutionary timescales. If robustness benefits both individuals and populations, then natural selection may favor robust phenotypes. If so, he concludes, the robustness of phenotypes might increase over time.

Even clearer about increasing robustness through evolution are some considerations of Kitano and Oda (2006). They argue that biological robustness fosters evolvability and that selection tends to favor individuals with robust traits; thus, evolvable robust systems progressively adapt to become more robust against the environment in which they are embedded. They suggest that over evolutionary time robustness against external perturbations is enhanced by adding diverse new functions to the input and output components of the organism.

However, it is conspicuous that these remarks rarely make reference to each other. This results in fairly different understandings of the topic. Usually, some examples are given, but there has been no attempt to date to define the pattern more precisely or to describe the respective phenomena systematically. This produces a rather strange situation: In some sense, one has heard of the idea. Occasionally, some people even take it for granted, so it seems unnecessary to elaborate on it in greater detail. In any case – whether it is completely overseen or is just taken for granted – evolutionists refused to integrate the principle into evolutionary theory building.

Many details of the pattern are still unclear because of the lack of further scientific endeavor on this topic. This holds true for questions on the systematic level, at which changes in autonomy can be described and whether there are autonomy-neutral and autonomy-destructive processes and events. We also know little about the relation of autonomy to adaptation. Many of the underlying details are hidden in the physiological, morphological, and paleontological literature and need to be compiled from this source under this aspect, and other questions may need to be addressed empirically.

In many considerations of large-scale evolutionary patterns, increasing autonomy is not mentioned. So, McShea (1998) did not feel compelled to include it in the overview of possible largest-scale trends in organismal evolution that are under discussion. Even in a specific chapter on this topic in the work of Rosenberg and McShea (2008), they do not take it into consideration. However, more recently McShea and Simpson (2011) saw it as a promising conceptual work to follow these lines of considerations.

3.9 Definition of Increasing Autonomy

A definition of increasing autonomy is attempted here in three steps. First, I present a list of features that are able to contribute to changes in autonomy of an individual organism. Second, a formal definition is developed. This definition most likely will still be a preliminary one, which could become more precise in the future. However, it is a suitable starting point to bring the phenomenon into focus. Nonetheless, it is open to further consideration. Third, more clarity is achieved by the presentation of facts and observations in the following chapters, especially for the major transitions in evolution, to which the definition and the list of features are applied.

The hypothesis is that organisms not only show autonomy as a general trait, but also that there are *differences in the degree of autonomy* within taxa. The evolutionary process generated organisms with distinguishable degrees of autonomy. Thus, there are organisms that are more subject to the direct physical, chemical, and biological conditions of their surroundings and others that can act more on their own behalf because they are more active, flexible, and selective in their interaction with the environment. Increasing autonomy can also be summarized as opening new possibilities for the organism.

I do not attempt to describe organisms as entities, which are isolated units within their environment. The inference is rather that each organism is deeply embedded in the systems of its environment. However, this inclusion can be effected either by direct physical and chemical influences that are more direct or by processes in the organism that are more emancipated, establishing organs for interactions with the environment that are more active and selected.

The term *autonomy* cannot be taken in an absolute manner but always describes *relative* autonomy. This important aspect distinguishes the concept used here from previous ones in evolutionary biology. As Ayala (1974) correctly argues: No organism can be wholly independent from the environment. In the present definition, the emphasis is, instead, on the balance of the organism-environment relationships and their changes.

A typical example is boundaries: As described previously here, the internal compartment is established within a boundary, which the system generates as a spatial separation from the environment. In its simplest form, this is realized in a single-cell organism by means of a cell membrane. However, even the simple example of the cell membrane shows that in a biological system complete separation is never obtained. Instead, we see the double function of a boundary and an exchange with the environment through and across the boundary. Each cell membrane and each integument of an animal has to perform this double function. Organisms have to balance these two requirements, and each solution looks different.

Generally, an extrinsic relation and an intrinsic relation of autonomy can be distinguished. The extrinsic relation describes the system-environment relation. The intrinsic relation describes the self-referential, internal organization within the system (e.g., homeostatic stabilization of processes, intraorganismal signaling, connectivity within neuronal systems). This is basically identical with what has been called *interactive autonomy* (how autonomously a system behaves in interaction with its environment) and *constitutive autonomy* (within the context of the biological system itself) (Bertschinger et al. 2008; Moreno et al. 2008).

This differentiation is important if we want to look for changes in autonomy because both aspects can underlie variations. Thus, changes in interactive autonomy take place when, for example, boundaries such as skins and shells are elaborated or when movement devices such as legs or wings are developed. When the capacity of

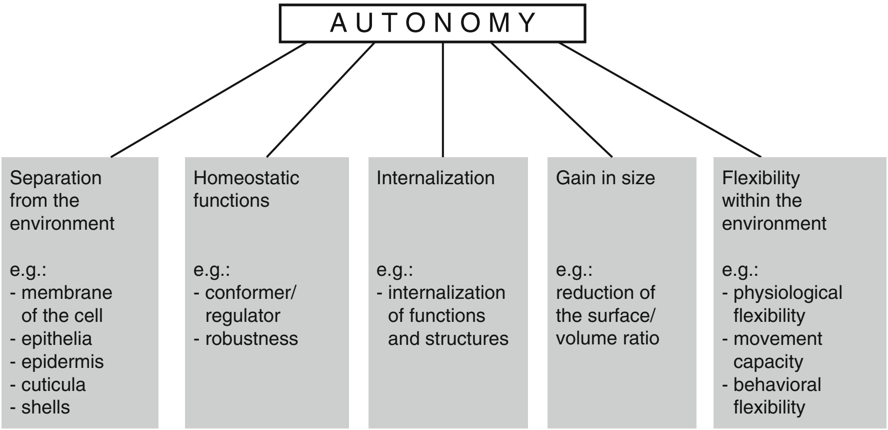


Fig. 3.3 Set of resources to change autonomy

homeostasis in body fluids or of central nervous processing is elaborated, this is more a change in constitutive autonomy, although both also have relevance for interactive autonomy.

Several biological elements can contribute in different degrees to changes of autonomy (Fig. 3.3). They are not general rules or some sort of continuous trends. They rather function as a set of resources that can – singly or in combination with each other – increase autonomy.

These elements are probably not complete. The various relations of the somewhat-heterogeneous elements to each other will also need further examination in the future. However, they can at least be identified within the major evolutionary transitions, and changes in them can also be described. Thus, they are relevant.

One such element is *spatial separation from the environment*, such as with cell membranes, cell walls, integuments of metazoans with cuticles, shells, hairs, or feathers. To different degrees, they all serve to keep the environment outside the organism and to regulate and direct the exchange with it. Changes in their organization can contribute to an essential degree to changes in the organism-environment relation.

Homeostatic functions are means to establish and enhance internal functional stability. This overlaps to a large extent with changes in robustness. Another element is the displacement of morphological structures or functions from an external position into an internal position within the organism, here summarized as *internalization*. Multiple processes of internalization are involved in building up the inner anatomy of organisms, ontogenetically as well as phylogenetically. During ontogeny, gastrulation and neurulation are typical internalizations. During phylogeny, for example, the transition from prokaryotes to eukaryotes included the internalization of some organisms within others (endosymbiosis).

A *gain in size* during many transitions leads to a reduction of the surface-to-volume ratio. This means that in larger animals there is less direct contact to the immediate environment relative to the existing body mass. The smallest cells we know, bacteria, have a large surface for environmental exchange. In larger bodies, this direct exchange capacity is reduced relative to the body mass. The rates of change of state internally are much slower, giving them an “inertia” effect, which smoothes the fluctuations and gives time for regulatory functions to operate. Larger organisms may have better opportunities for storage of energy and substances, and they may have room for internal regulatory structures that are more complex. It is well known in physiology that larger animals are more likely to be regulators that stabilize their internal conditions also under fluctuating environmental circumstances (Willmer et al. 2000). Although there are no linear increases in size, evolution deals with it so that size matters and is not random.

These elements are prerequisites for establishing a certain amount of physiological flexibility within a given environment, that is, a capability of organisms to generate *flexible functional answers* to conditions and changes in their environment. Finally, this principle can be widened to include all forms of *behavioral flexibility*, emancipating organisms from mere short-term reactions to environmental factors. Together, these elements are able to generate certain degrees of physiological and behavioral freedom.

These principles can be summarized as follows in Definition 2:

Increasing autonomy is defined as an evolutionary shift in the system-environment relationship, such that the direct influences of the environment on the respective individual systems are gradually reduced (interactive autonomy) and stability and flexibility of self-referential, intrinsic functions within the systems are generated and enhanced (constitutive autonomy). This is described as relative autonomy, while, at the same time, numerous interconnections with and dependencies on the environment are retained. Thus, organisms can undergo relative emancipation from environmental fluctuations, gaining self-determination and flexibility of behavior.

A set of resources can be involved to change autonomous capacities:

I. Changes in spatial separations from the environment;
II. Changes in homeostatic capacities and robustness;
III. Internalization of structures or functions;
IV. Increase in body size; and
V. Changes in the flexibility within the environment, including behavioral flexibility.

In the following chapters, some of the major evolutionary transitions are described, and it is demonstrated that these specific elements can be identified in many of them. Thereby, their significance is outlined further. In the sense of Fuchs (2009a, p. 9), the present study is based on a combination of phenomenological thinking and approaches of organismic biology and philosophy of the living.