

Autonomous Systems and the Place of Biology Among Sciences.

Perspectives for an Epistemology of Complex Systems

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Abstract This paper discusses the epistemic status of biology from the standpoint of the systemic approach to living systems based on the notion of biological autonomy. This approach aims to provide an understanding of the distinctive character of biological systems and this paper analyses its theoretical and epistemological dimensions. The paper argues that, considered from this perspective, biological systems are examples of emergent phenomena, that the biological domain exhibits special features with respect to other domains, and that biology as a discipline employs some core concepts, such as teleology, function, regulation among others, that are irreducible to those employed in physics and chemistry. It addresses the claim made by Jacques Monod that biology as a science is marginal. It argues that biology is general insofar as it constitutes a paradigmatic example of complexity science, both in terms of how it defines the theoretical object of study and of the epistemology and heuristics employed. As such, biology may provide lessons that can be applied more widely to develop an epistemology of complex systems.

1 Introduction

The question “what is life?”, the title of the seminal essay by Erwin Schrödinger (1944), keeps raising several theoretical and epistemological issues. Theoretical issues concern for example what types of systems living organisms are, the identification of their distinctive features and their differences with respect to other natural systems such as physical, chemical ones, or ecological and social ones, not to mention hard questions such as how life originated. An example of the complexity of this question is the wide and intense debate on the definitions of life, characterized by a lack of consensus and by the proliferation of definitions proposed (Popa, 2004; Bich & Green, 2018).

Moreover, the question about life has important epistemological implications. It raises the problem of how to characterize, describe and explain living systems and biological phenomena in general. The study of living systems has shown the inadequacies of the framework of deductive nomological explanation that had dominated discussions of scientific explanation in the middle decades of the 20th century. The deductive nomological framework had emphasized the importance of scientific laws, with physics as the science of reference. The study of biological systems, instead, has given rise to an interest in notions such as emergence, due to the difficulties or impossibilities of using one level such as that of physical systems and its laws, to account for a different one, the biological, or to understand a system on the basis of a description of its parts alone. In the last decades an increasing attention has been paid to the specific types of explanations used in biology. Recognizing that biologists seldom refer to laws when advancing explanations, Bechtel and Richardson (1993/2010) focused on the fact that biologists often explain a phenomenon by describing the responsible mechanism, identifying the parts involved, their operations, and their organization rather than identifying or referring to laws. This view has been at the origin of the neo mechanistic approach in philosophy of science (see also Machamer et al., 2000; Bechtel & Abrahamsen, 2005; Craver & Darden, 2013; Glennan, 2017).

The distinctiveness of biology and the complexity underlying the notion of life may lead one to inquire into the epistemic status of biology. Among others, Jacques Monod directly addressed this issue at the beginning of the preface to his book “Chance and Necessity” (Monod, 1970). He did so by somehow acknowledging the ‘special’ character of biological system, and by identifying ‘special’ with ‘rare’. Biological systems constitute only a minimal fraction of natural systems, and therefore, according to Monod, the study of biology might not lead to the discovery of general laws applicable outside the biosphere. In his view biology is marginal.

In this paper I address this issue and question Monod’s claim. I do so by starting from a characterization of living systems in terms of autonomy (section 2), to discuss the general theoretical and epistemological implications of understanding biology as (in a specific sense) special (section 3). As suggested by Robert Rosen “perhaps the first lesson to be learned from biology is that there are lessons to be learned from biology” (2000: 275). I argue (section 4) that biology is not marginal and provides important lessons that may be applied more widely to develop an epistemology of complex systems.

2 What is life? an organizational view

When Erwin Schrödinger, as a physicist, addressed the basic question of biology, “what is life?” (Schrödinger, 1944), he brought forth the idea that understanding biological systems might have required extending the framework of physics by providing new laws and concepts. This idea of developing a new physics and

introducing new laws was later pursued with a different approach by Stuart Kauffman (2000), among others. This attitude is different from Monod's. Acknowledging, as Schrödinger and Kauffman did, that life cannot be accounted for by current physics, leads to questioning the generality of physics and to expanding or renewing physics itself.

Schrödinger tried to identify what is the invariant element that might allow understanding the distinctive character of biological systems. He identified it with a specific type of order. In opposition with the statistic order of physical systems ("order from disorder"), that might give rise to macroscopic patterns, he identified the invariant element of living systems in what he called "order from order". The basic idea is that of a positional order, embedded in a specific rigid molecular structure, an order which is then propagated throughout the system. Positional order is realized in terms of rigid spatial organization, found at the molecular level in an aperiodic crystal and embedded in a specific sequence (see Bich & Damiano, 2008 for an analysis of different types of order and organizations). In Schrödinger's view, living processes are controlled by highly stable groups of atoms which transmit their structural order to other molecular structures: in contemporary language, from the sequence of bases in the DNA to the sequence of amino acids in proteins. The constancy of positions and sequences and the regularity of the relationships between parts (solid bodies whose form is maintained constant) is what allows organisms and machines such as mechanical clocks to function. Both are characterized as mechanisms and understood in terms of the relative positions of stable (ordered) components, a form of organization.

This is not the only way to look at living systems in terms of organization. Organization can be understood in terms of static spatial relationships such as in this case, but also in terms of dynamic relationships between components and processes that undergo continuous transformations. In fact, if one focuses on processes and on the activities of components that realize living organisms, regularity and constancy might be the exception rather than the rule, or even the sign of a pathology (Bich et al., 2020). Organisms are adaptive systems whose internal dynamics and the fate and behavior of parts depend on the state of the system and its environment (Bich et al., 2016). Living systems constantly modify their components, and their internal mechanisms are highly dynamic. They are continuously modulated, activated or inhibited by regulatory mechanisms. From this point of view, which considers living systems as dynamical, the invariant aspect cannot be found in some structural regularity of sequence or positions at the level of parts but in a relational property at the level of the organization of the system. It is a property of the whole living system. It cannot be referred to any specific component of it; rather, it rests on the peculiar and distinctive way the components—and the processes they are involved in—are related.

A theoretical approach focused on this type of organization has been developed at the crossroad between cybernetics and systems theory by the tradition of biological autonomy. It considers organization between parts and processes as the invariant that captures the distinctive character of biological systems. Pioneering

conceptual and methodological intuitions in this respect can be found in Rashevsky's work (1954), specifically in his emphasis on relations as what allows identifying a system as a living one, and on the thesis that there is a core set of relations that is common to all living systems.

The autonomy approach has been developed with the aim of identifying and understanding the nature and form of these relationships. This theoretical framework was built upon pioneering work carried out by Jean Piaget (1967), Robert Rosen (1972), Humberto Maturana & Francisco Varela (Varela et al., 1974), Howard Pattee (1972), Tibor Ganti (1975), among others. Recently it was further developed by Stuart Kauffman (2000) and by Alvaro Moreno and collaborators (Moreno and Mossio, 2015). This approach characterizes a biological organism as an autonomous system capable of producing its own components and maintaining itself far from equilibrium with its environment. To explain this capacity, this tradition appeals to the internal organization of the organism, which is maintained in spite of the continuous transformations that an organism undergoes at the level of components.

The core feature of this approach is the focus on the organization of the system. Organization refers to the way production and transformation processes are connected so that they are able to synthesize the very components that realize them, by using energy and matter from the environment. In this view, the fundamental feature of the organization of (biological) self-maintaining systems is its circular topology as a network of processes of production of components that in turn realize and maintain the network itself. This distinctive type of generative circularity that characterizes biological systems is known as 'organizational closure' (Piaget, 1967).

This tradition answers at a different level Schrödinger's question on life and on the invariant order that characterizes it: the abstract level of relationships between parts and processes instead of the level of the intrinsic properties of parts. As argued by Rosen, the idea of a circular invariant organization "looks very much like an aperiodic solid, and indeed it possesses many of the properties Schrödinger ascribed to that concept. The novel thing is that it is not a "real" solid. It is, rather, a pattern of causal organization" (Rosen, 2000: 23).

These ideas have important epistemological implications. The first concerns what level of description is considered as the more pertinent to understand a biological system: material parts, and therefore a bottom-up approach, or relationships, and therefore a top-down approach. While not excluding the first, the autonomy approach focuses mainly on the second, and characterizes the constituents of a biological system in terms of their dependence on and contribution to the system that harbors them: as functional components rather than material parts (Bich, 2012). I will come back to this point in the following sections.

Another more general epistemological implication concerns the descriptive approach developed in the autonomy framework, which is based on organization. The organization of a system is defined as the topology of relations which allows scientific observers to identify a system as a unity belonging to a certain class, that is, the class of living systems (Maturana, 1988). Such a definition entails the impossibility

of giving distinctions for granted and of considering scientific knowledge as independent from the activity of observation and categorization performed by an observer. The underlying idea, which is of particular interest when focusing on theoretical and formal modelling, is that an object studied by science is co-constructed: the observer gives it an objectual form through the categories she resorts to, while the world, limiting the range of their applicability, defines the area in which nature can be handled in terms of those objects categorized by the observer (Damiano, 2012).

It is important to emphasize a couple of points. In the first place, this epistemological thesis does not mean that categorizations are arbitrary. It is the opposite; they are constrained by interactions with the world and they need to be theoretically coherent. The second is that when focusing on living organisms as self-producing and self-maintaining systems, whose existence and activity coincide, one makes a special type of distinction. An observer identifies a living system as autonomous in the same domain where the system specifies it through its internal operations.

The theoretical and epistemological dimensions of biology are therefore distinctive, or “special”, if life is addressed from the point of view of autonomy. In the next sections I discuss the implications of these ideas.

3 Biological emergence and the autonomy of biology

Looking at living systems from the perspective provided by the autonomy framework has deep implications for an understanding of biology and its relationships with other domains of scientific investigation. The first derives from the identification of a causal regime that is distinctively biological: that of organizational closure, according to which biological systems are capable of producing their own components and maintain themselves, unlike other classes of natural and artificial systems (Moreno & Mossio, 2015). The focus of the autonomy framework is primary on the self-maintaining organization of the system and on the consequent idea that the existence and activities of parts depend on such organization. This approach centers on organization and activities of parts (i.e. interactions between parts, operations of parts on processes). The starting point is not components themselves. More specifically, organization refers to the way production and transformation processes are connected so that they are able to synthesize the components that realize them by using energy and matter from the environment. Components are characterized functionally in terms of their activities within a given organization. Studying the role of parts within the system, therefore, needs to take into account the type of organization that harbors them.

This approach raises the problem of how to describe such a highly integrated system and how to decompose it into its parts in order to understand its internal functioning. Surely, a living organism is not an ‘aggregative system’ or ‘component system’ (see Wimsatt, 1986; Bechtel & Richardson, 1993/2010). The parts that

contribute to biological phenomena of interest cannot be easily localized, and their activities cannot be considered as fully determined (once their triggering conditions are met) by their intrinsic properties.

Instead, living systems can be considered as a type of ‘integrative system’ or ‘semi-decomposable’ system (Bechtel & Richardson, 1993/2010): a class of systems in which the organization contributes to determine the activities of the parts, and the actual results of such activities depend on how their functioning is orchestrated. More precisely, living autonomous systems might be considered as *highly integrated systems*, because not only the activities are ordered in such a way as to achieve specific results, but: (1) the parts depend on one another and on the system for their existence and (2) their activities are not regular and depend on the operations of other regulatory components within the system, which modulate the activities of parts on the basis of the state of the system and the environment (Bich et al., 2016). Decomposing such systems and identifying the parts that are relevant to understand a specific phenomenon or mechanism is a complex endeavor, as showed for example by the history of the discovery of cell mechanisms, metabolic cycles, etc. (see Bechtel, 2006).

For these reasons, in principle an approach based on autonomy privileges decomposing strategies that proceed top-down from the system to the components that contribute to its activities (Rosen, 1991). One way to do so is functionally: to identify one or more activities that are necessary for the organisms to maintain itself and establish which type of operations are necessary to carry it out, and then to identify and characterize in terms of these operations the parts that realize them. It is what Rosen calls ‘analysis’ (Rosen, 1991). The alternative would be to identify the anatomic components of the system, to study them and to use them as a starting point to conceptually reassemble the system. It is what Rosen calls ‘synthesis’ (Rosen 1991).

The relationships between top-down and bottom-up descriptions – i.e. trying to establish a correspondence between functional parts (identified and characterized top down), and structural ones (anatomic or material parts characterized through a bottom-up approach) – is highly problematic (Bich, 2012). Privileging either approach may result in shortcomings. An exclusive focus on top-down approaches might result in a functionalism characterized by an excessive degree of abstraction and lack of relevant concrete details (Levy & Bechtel, 2013). The risk is to overlook the importance of materiality and of physical aspects to understand how a living system is actually realized. The other way around, a bottom-up approach might lose sight of the causal regime that characterizes the system, with problems of selecting which properties of components are pertinent or not, what components are relevant to describe how a phenomenon is realized, how they behave in different ways depending on the state of the system (Bich et al., 2016; 2020), and when they are not working properly (Saborido & Moreno, 2015; Bechtel, 2018). While irreducible, at least in practice, these two approaches need to proceed hand in hand.

Moreover, it is important to point out that some of the challenges faced in describing biological autonomous systems is that some of the elements needed to

define the dynamics of the system are determined, at least in part, from within. By interacting with the environment and establishing their own internal environment, living systems contribute to determine some of the *boundary conditions* that allow them (and their internal processes) to exist; they also determine and modulate some of the *parameters* of their internal dynamics, for example by activating or inhibiting the activity of enzymes and regulatory proteins, and finally, the *rules of interaction* between parts depend on what components are produced and how their operations are modulated by regulatory mechanisms (Kampis, 1991; Bich & Bocchi, 2012; Longo et al., 2012; Koutroufinis, 2017). One may also argue that the organization of the system has a role in determining or constraining the behavior of the parts (El-Hani & Queiroz, 2005; Mossio et al., 2013).

The idea of a distinctive causal regime of self-maintenance and the epistemic implications it brings to surface with regards to the study of biological systems, have often led to associating biological autonomy with emergence (Rosen, 1991; Varela, 1997; Kauffman, 2000; Bich, 2006; Mossio et al., 2013). The causal irreducibility of the regime of organizational closure is paired with an epistemological irreducibility: a number of limitations regarding the possibility of understanding, modelling and formalizing these types of systems. Different types of descriptions (such as in term of material and functional parts) coexist, and so do irreducible notions (such as sequence and function).

In general, there is no preferential or more pertinent heuristics in general. What types of heuristics one needs to adopt may depend on the specific phenomenon under investigation. For example, let us think about the strategies employed in the discovery of physiological processes such as fermentation and oxidative phosphorylation, which sought the opposition between reductionist and anti-reductionist approaches, with competing agendas and heuristics (Bechtel & Richardson, 1992). In the late nineteenth century, while reductionists associated fermentation with independent chemical reactions, anti-reductionists such as Schwann and Pasteur argued that fermentation required taking into consideration the circumstances found in living cells instead of looking *only* to parts. The discovery of the mechanisms of fermentation happened in several steps in a period spanning from the last decades of the nineteenth and to the first ones of the twentieth centuries. It did not result in the reduction of this phenomenon to a chain of reactions, although reactions had to be identified. Looking also at the types of connections between the reactions involved resulted in the discovery of an organized biochemical system characterized by several causal loops: “a highly integrated, interlocking *system* of reactions” (Bechtel & Richardson, 1992: 273).

Similarly, the discovery of oxidative phosphorylation also showed the difficulties of identifying the pertinent levels for explaining the phenomenon under investigation. It required considering not only individual reactions and their dynamical organization, but also including structural aspects at a different scale than that of chemical reactions, such as the macroscopic structure of the mitochondrion and in particular of its systems of endomembranes, which were studied through electronic microscopy. Moreover, as shown by Bechtel and Richardson (1992), techniques

that were relevant for one level of descriptions often concealed or even destroyed crucial aspects of the phenomena investigated, which were only available, instead, at other levels of description.

Many of these considerations, apart from those derived from the notion of organizational closure, are not exclusive of biological systems. Physics provides examples and formal models of natural phenomena that can be considered as emergent and that cannot be predicted or deduced from a description of their constituents or from an initial state. These phenomena, therefore, are described by employing models that are irreducible to one another (Pessa, 1998). From physics itself comes a questioning of the very idea of a fundamental level of description and of fundamental objects (Pessa, 2011; Bitbol, 2007).

However, I focus here, from a systemic perspective, on a few elements which, among others, are distinctively biological and ground some degree of autonomy for this discipline. They are useful in order to discuss then the epistemic status of biology. Among the differences between the domains of physics and biology, Longo and Montevil (2013), have discussed what are the features of the objects characteristic of either domain and how to describe their behaviors. Physical objects are generic because different objects of the same category have the same intrinsic features and behave in the same way. Their trajectories in phase space are instead specific and defined by the relative equations. For biological objects, the opposite is true: they are specific while their behavior is generic as they follow a possible evolutionary trajectory in the phase space.

What about some core biological concepts such as teleology, function, integration, regulation, control, neither of which has a counterpart in physics nor has been reduced to physical concepts? These concepts make biological explanation theoretically independent from the physical and chemical ones. They enable explanations that are directly grounded in the specificity of biological phenomenology rather than derived from lower-level explanations. These concepts may constitute heuristic tools that are useful to address biological phenomena in practice, but different attempts have also been made to naturalize them and make them well-grounded theoretical notions.

One interesting case is that of processes oriented towards a final state. In physics one can find, among others, the Geodesic Principle, Le Chatelier's principle and the Second Law of Thermodynamic, which describe how the trajectories of certain systems tend to proceed towards a final state such as for example, thermodynamic equilibrium. Biological systems exhibit a similar yet qualitatively distinct feature: they actively pursue certain states, which can be considered the goals of the system. What for physical systems are end states, for biological ones become goals, aims, purposes. All these notions, which belong to the category of teleology, are not just ways of speaking or heuristic tools, useful to describe the behavior of a system, but can be provided a naturalized grounding in the autonomous organization of living systems (Mossio & Bich, 2017, see also Schlosser, 1998; Delancey, 2006). A living system is characterized by the distinctive capability to produce, transform and repair its components which realize and maintain the system through its interactions with

the environment. Its own activity and those of its parts are, in a fundamental sense, oriented toward an end. The goal of the system is to maintain itself. It is true that there are other systems, among artifacts, which are considered as goal-oriented in their behavior. An example is a thermostat, which controls the temperature of a room to maintain it within a certain interval of temperature. Yet there is a fundamental difference between this type of goal-oriented behavior and the teleological one of biological systems. It amounts to the difference between *following* or *having a goal* (Jonas, 1953). Artifacts *follow a goal*. The goal of artifacts is determined *extrinsically*, by the designer or the user. Following this goal does not contribute to the existence of the artifact. Biological systems “act on their own behalf” (Kauffman, 2000). They *have an intrinsic goal*, which is their own existence.

Another fundamental concept for biology is that of function, which also has a teleological dimension. Functional explanations are widespread in biology, and parts and traits of living systems are often characterized in terms of what they do. There are general accounts of functions, such as the dispositional one, which are generic and can be applied to almost any class of system (Cummins, 1975). The dispositional approach identifies the function of a part with its causal role in a larger system. Yet the generality of this concept sacrifices other aspects which are important in developing a scientific explanation. Ascribing functions to a part in terms of causal role may be arbitrary and it may not provide a normative basis for distinguishing which among many causal effects to count as the function of a component.

Nevertheless, there are principled way to ascribe functions that are specifically biological (i.e. capture the distinctive and irreducible character of biological functions) and, unlike the dispositional account, justify claims such as that the function of the heart is to pump blood (and not, for example, to make noise). The most widespread account is based on evolutionary considerations, and characterizes a function as a selected effect of a trait of an organism which contributed to the survival of the ancestors of that organism (Millikan, 1989; Neander, 1991). The autonomy framework, instead, characterizes functions in terms of contributions to the maintenance of the organism. A function is understood as a contribution of a trait to the maintenance of an autonomous organization (e.g., a living cell) that, in turn, contributes to producing and maintaining the trait itself (Collier, 2000; McLaughlin, 2001; Christensen & Bickhard, 2002; Mossio et al., 2009). The way functional ascriptions are justified and employed in biology does not have counterparts in physics and chemistry.

4 Is Biology marginal? Insights for an epistemology of complex systems

The previous sections have discussed the theoretical account of living systems based on the notions of biological autonomy and organization. They showed how, if one adopts this perspective, biological phenomena can be considered emergent from the

causal and epistemological points of view. In this scenario, the biological domain can be considered as exhibiting distinctive phenomena and requiring concepts that have no counterpart in other scientific domains that focus on lower levels of organization.

However, biological phenomena are rarer than physical and chemical ones, and biology as a discipline concerns distinctive phenomena, exhibits a certain degree of autonomy (although not self-sufficiency) with respect to other sciences, and employs its own concepts. Does this mean that biology is marginal, as argued by Monod (1970)? And is there a wider lesson to be learned from biology? These questions can be addressed in multiple ways by either focusing on theoretical aspects or epistemic ones. I argue that, from both points of view, the answer is that biology is not marginal and there are lessons to be learned from it.

One way to approach these issues is theoretical. If the tools of sciences such as physics and chemistry, although useful and unavoidable, are unable to provide an understanding of what living systems are and how they function, one needs to expand science. This answer is in line with claims such as the one made within philosophy by Hans Jonas. When discussing life, he argued that “if life is not within the competence of an alleged cosmic principle, though it is in every sense within the cosmos, then that principle is inadequate for the cosmos as well” (Jonas, 1966: 65). The research projects carried out by Schrödinger (1944) and Kauffman (2000) – aimed respectively at developing a new physics, or new laws, to make sense of living systems as natural phenomena – constitute attempts to respond to these questions within science. These attempts aim to extend a cohesive set of theoretical tools. Another possibility, more in line with the autonomy framework, is to complement the tools provided by physics and chemistry with new tools, such as organizational closure, specifically developed for addressing living systems. In the first case, biology would not be marginal because it would be part of an extended, more general, physics; in the second case because it would be source of new theoretical tools and principles applied in combination with those of physics and chemistry: a more general science. In both cases, biology would be a source of new lessons for science.

Acknowledging the distinctive character of biological systems implies on the one hand the idea that the biological domain should not be considered as a particular case of other domains considered as more fundamental, such as physics and chemistry. Biological systems can be investigated in their specificity only by building new types of theoretical and descriptive models. On the other hand, it makes it necessary to consider the natural world as characterized by a range of phenomena much wider and richer than what can be addressed through the tools of one discipline or approach alone, be it biology or physics. This, according to Rosen, is one of the meanings of Schrödinger’s insight on a new physics, which becomes the foundation for a theoretical research program for biology and for complexity sciences in general. According to Rosen, Monod’s thesis on the marginality of biology rests on the idea that organisms are “just specializations of what is already on the shelf provided by old physics, and that to claim otherwise is mere vitalism” (Rosen, 2000: 26). Organisms are indeed rare if compared to other material systems. Yet Rosen argues

that Monod's argument builds upon an artifact of sampling: a confusion between 'rare' and 'special' (in the sense of marginal).

In sum, from the theoretical point of view, organisms are more general, insofar as they exhibit properties and phenomena that require the development of new conceptual categories, capable to capture also those aspects, such as closure, teleology, functionality, regulation, control, that escape other conceptual frameworks. There is something qualitatively different in biological systems, invisible to other sciences, and that requires a conceptual rethinking and new categorizations to be employed together with those derived from other sciences such as physics or chemistry. In this sense the study of living systems and of their distinctive character carries a lesson on nature and science in general.

The other way to address the questions is to focus on epistemic aspects, and to consider biological systems as paradigmatic cases of complex systems. This epistemological thesis is specifically connected to the problem of the relationships between scientific disciplines and descriptive strategies. It supports a non-reductionistic approach oriented towards establishing of communicative circuits between disciplines and between different heuristics within a discipline: biology as a model for an epistemology of complex systems characterized by different irreducible approaches and descriptive tools which coexist and interact; a domain characterized by multidirectional transfers of models, questions and theoretical structures.

Let us consider some issues deriving from the difficulty of establishing connections between different types of observations, models, observables, etc. As discussed in Section 2, the relationships between directions of observation is one of these cases. In the autonomy approach the observables that are built bottom-up from the observation of intrinsic properties of the parts and those built top-down in terms of functional properties (identified with regards to the contribution of components to the system) do not necessarily coincide (Rosen, 1991; Bich, 2012). Material and functional components may not be one and the same thing. An example is the case of enzymes. A bottom-up analysis in terms of sequence of amino acids may not convey the same information as a structural analysis of the configuration and functionality of the folded molecule. For the same sequence there might be several configurations, depending on the boundary conditions present during folding, the activity of chaperons, and of several regulatory interactions such as phosphorylation and allosteric control. A mixed approach is often fruitful to predict possible regulatory sites, and how interactions at these sites changes the probability of having a given configuration (and functional capability) of the molecule.

Moreover, differences in the types and scales of observation may provide different pictures of the biological phenomenon under investigation. Let us think again of the discovery of phenomena such as fermentation and oxidative phosphorylation (Bechtel & Richardson, 1992). Whereas a study of individual chemical reactions, or sequences of reactions, was an important aspect, it proved to be insufficient to provide an understanding of these two phenomena. Some gestalt switches were needed. In the case of fermentation, a different type of perspective was needed, focused on the topology of the relationships between the reactions, i.e. their

organization, which led to the discovery of chemical cycles. The case of oxidative phosphorylation showed the importance of taking into account different irreducible scales by complementing the investigation of chemical reactions with that of the role of macroscopic structures such as membranes, which constrain these reactions and enable different types of processes.

Similar considerations can be made with respect to general strategies employed to describe and model living autonomous systems. As argued by Moreno and Suarez (2020), two irreducible strategies provide information on different aspects of the system. One is network modelling: a holistic tool used to study and predict global dynamical properties of large sets of interacting entities. It has often been employed to investigate the dynamical properties (e.g. stability and robustness) of abstract theoretical models of the organization of biological autonomous systems (Piedrafita et al., 2010). The other strategy is the new mechanistic one, which aims to provide a causal explanation of how the individual parts of the systems, or the parts of one or several subsystems, functionally operate and interact within autonomous systems to realize specific phenomena. This strategy has been recently applied to model and analyze phenomena such as mammary organogenesis (Montevil et al., 2016) and glycaemia regulation (Bich et al., 2020) from an autonomy perspective. Network and mechanistic strategies provide different information on the system. Although irreducible to each other, they can be combined. Network modeling, for example can be used to support mechanistic descriptions. Identifying the most connected nodes of a network may provide insight into what may be the relevant functional components responsible for producing the phenomenon under investigation (Bechtel, 2015).

These examples show both the importance of considering how the system is organized in different layers—which instantiate distinct and complementary descriptive domains—and to take into account the role of the observer who needs to adopt different modalities of description in order to account for them. The common aspect to these examples is that sets of models derived from different observational operations or descriptive strategies provide different, though complementary, information about the system under study. They show the failure or the inadequacy of a single descriptive modality and the consequent necessity to include new ones. Some modalities might be more relevant or pertinent than others depending on the phenomenon to study and the aims of the scientist, but there seems to be no privileged one so that best results are obtained when more strategies are used in combination.

For these reasons it can be claimed that biological systems are emergent from an epistemological standpoint. Emergence in this sense depends on the relationship between different models that are needed in order to describe the system and depends on the experiences performed by an observer who interacts with it. In this framework it can be expressed as the lack of a direct relationship between different descriptions made in distinct domains or different types of descriptions of the same phenomenon (Bich, 2012).

These conclusions, drawn from the discussion of a systemic account of biological systems, have a more general relevance. They are in line with Rosen's

epistemological account of complexity, according to which “To say that a system is complex [...] is to say that we can describe the same system in a variety of distinct ways [...]. Complexity then ceases to be an intrinsic property of a system, but it is rather a function of the number of separate descriptions required [...]. Therefore, a system is simple to the extent that a single description suffices to account for our interaction with the system; it is complex to the extent that it fails to be true.” (Rosen 1978, p. 112). This notion is focused on the relationship between classes of observables that converge in different models. Complexity can be defined as the insufficiency of a single model, and of the set of observables related to it, to describe a system. Consequently, a model needs to be replaced or complemented by other ones, because the system exhibits to the observer new characteristics which were not present before or at a different level of description, and which are thus invisible to the chosen observables that constitute the starting description.

This perspective is also in line with a heuristic of complex systems such as the one proposed by Minati, Penna and Pessa (Minati et al., 1998; Minati & Pessa, 2006), based on the dynamical usage of models: the interaction between different, and often complementary, models which work in the traditional way just inside their limited domain of validity. This means not just that one needs to choose an individual model as the more appropriate in order to address a specific issue, but also that to investigate complex systems one may need to employ more than one descriptive modality at the same time and multiple interacting models.

On this basis, one may argue that biology is general insofar as it constitutes a paradigmatic example of complexity science, both in terms of how it defines the theoretical object of study and of the epistemology and heuristics employed. Addressing biological phenomena from an autonomy perspective brings to the attention in a wider context the limitations of approaches based on simple systems and the virtues of adopting ones based on complexity. Focusing on organization, function, teleology and other biological notions, for example, shows how scientific investigation needs to combine analytic and synthetic strategies. Understanding what makes a system a living organism, which exhibits distinctive features with respect to physical and chemical systems, has relevant consequences not just for those “rare” phenomena pertaining to biology but for scientific explanation in general, more so for the study of complex systems. It provides theoretical and epistemological grounds to advocate a pluralist perspective combining different points of view and descriptive and explanation strategies.

Therefore, addressing question “what is life?”, that is, the problem of defining and characterizing living systems, does not consist only in responding to the needs of one discipline. It has wider consequences, or lessons, and introduces more general questions that cut across scientific domains. Focusing on biological systems and their specificities shows how complex phenomena may escape individual strategies, how general fundamental issues related to complex systems such as the notion of system as an integrated organized entity, the relationship between wholes and parts need to be addressed in more than one way and direction. The challenge,

each time, is to understand how to combine these different tools and strategies rather than extend a given one or choosing one among many.

5 Conclusions. A practice of complex systems

The passage from a conceptual discussion of complex systems to their study and modelling in practice, from theory to art one might say, is not direct and it may be quite difficult. This is especially relevant for philosophers, whose goals are often generality and abstraction, but who constantly face the risk of the excess of idealization, of striving for clear-cut concepts and distinctions that as a result may be too detached from scientific work. In the study of complex systems, where the activity of scientists and its limitations play a crucial role, this might create a gap between epistemological thought and actual modelling, and even lead to naïve conclusions about the relation between theoretical science, modelling, and the natural world. In particular, the study of theories and models of complex systems requires tools and heuristics to identify and analyze their limitations and to discuss how such limitations can be faced by employing multiple strategies.

In this context, virtuous examples are fundamental to develop epistemological thinking. I consider myself honored and lucky for having had the opportunity to know Eliano Pessa as teacher, supervisor and then colleague. He guided me through my first steps into complex systems thinking from the point of view of science. Not only he introduced me to the notion of emergence and to the theoretical work of Rashevsky, Rosen and of Maturana and Varela, but with his generosity and honesty he gave a virtuous example of the art of studying and modelling complex systems, with all the difficulties and stimulating challenges that characterize this practice, and he transmitted his enthusiasm to students and colleagues. In particular, I remember his capability of making explicit the idealizations underlying models and discussing their implications, of explaining with incredible clarity the ingenious models he developed while at the same time always showing their limitations with irony, precision and detail. With his example, Eliano Pessa demonstrated that striving for honesty is a fundamental epistemic value in scientific research and showed the importance of giving substance to epistemological and theoretical thinking.

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References

Bechtel, W. (2006). *Discovering cell mechanisms: The creation of modern cell biology*. Cambridge: Cambridge University Press.

- Bechtel, W. (2015). Can mechanistic explanation be reconciled with scale-free constitution and dynamics? *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences*, 53: 84-93.
- Bechtel, W. (2018). The Importance of Constraints and Control in Biological Mechanisms: Insights from Cancer Research. *Philosophy of Science* 85:573-593.
- Bechtel, W., & Abrahamsen, A. (2005). Explanation: A Mechanist Alternative. *Studies in History and Philosophy of Biological and Biomedical Sciences*, 36:421-441.
- Bechtel W., Richardson R. C. (1992), Emergent Phenomena and Complex Systems. In A. Beckermann, H. Flohr, J. Kim (Eds.). *Emergence or Reduction? Essays on the Prospects of Nonreductive Physicalism* (pp. 257-288). Berlin: de Gruyter.
- Bechtel, W., & Richardson, R. C. (1993/2010). *Discovering Complexity: Decomposition and Localization as Strategies in Scientific Research*, Cambridge, MA: MIT Press (1993 edition published by Princeton University Press).
- Bich, L. (2006). Autopoiesis and Emergence. In G. Minati, E. Pessa & M. Abram (eds.), *Systemics of Emergence. Research and Development* (pp. 281-292). New York: Springer.
- Bich, L. (2012). Complex emergence and the living organization: an epistemological framework for biology. *Synthese*, 185(2), 215-232
- Bich, L. & Bocchi, G. (2012). Emergent Processes as Generation of Discontinuities. In G. Minati, E. Pessa, M. Abram (eds.) *Methods, Models, Simulations and Approaches Towards a General Theory of Change* (pp. 135-146). Singapore: World Scientific.
- Bich, L. & Damiano, L. (2008). Order in the nothing: Autopoiesis and the Organizational Characterization of the Living., *Electronic Journal of Theoretical Physics* 4 (16), 343-373.
- Bich, L. & Green, S. (2018). Is defining life pointless? Operational definitions at the frontiers of biology. *Synthese*, 195(9), 3919-3946
- Bich, L., Mossio, M., Ruiz-Mirazo, K. and Moreno, A. (2016). Biological regulation: controlling the system from within. *Biology & Philosophy*, 31(2), 237-265.
- Bich, L., Mossio, M. & Soto, A. (2020). Glycemia Regulation: From Feedback Loops to Organizational Closure. *Frontiers in Physiology*, 11:69.
- Bitbol, M. (2007). Ontology, matter and emergence. *Phenomenology and the Cognitive Science*, 6, 293-307
- Christensen, W. & Bickhard, M. (2002). The process dynamics of normative function. *The Monist*, 85(1), 3-28.
- Craver, C. F., & Darden, L. (2013). *In Search of Mechanisms: Discoveries across the Life Sciences*. Chicago: University of Chicago Press.
- Collier, J. (2000). Autonomy and process closure as the basis for functionality. *Annals of the New York Academy of Science*; 901:280-290.
- Cummins, R. (1975). Functional analysis. *Journal of Philosophy* 72: 741-765.
- Damiano, L. (2012). Co-emergences in life and science: a double proposal for biological emergentism. *Synthese*, 185: 273-294.
- Delancey, C. S. (2006). Ontology and Teleofunctions: A Defense and Revision of the Systematic Account of Teleological Explanation. *Synthese*, 150(1), 69-98.
- El-Hani, C. N. & Queiroz, J. (2005). Downward determination. *Abstracta*, 1(2), 162-192.
- Gánti, T. (1975). Organization of Chemical Reactions into Dividing and Metabolizing Units: The Chemotons. *BioSystems*, 7:15-21.
- Glennan, S. (2017). *The New Mechanical Philosophy*. Oxford: Oxford University Press.
- Jonas, H. (1953). A Critique of Cybernetics. *Social Research*, 20, 172-192.
- Jonas, H. (1966), *The Phenomenon of Life. Towards a Philosophical Biology*, New York: Harper and Row.

- Kampis, G. (1991). *Self-modifying Systems in Biology and Cognitive Science*. Oxford: Pergamon Press.
- Kauffman, S. A. (2000). *Investigations*. New York: Oxford University Press.
- Koutroufinis, S. A. (2017). Organism, Machine, Process. Towards a Process Ontology for Organismic Dynamics. *Organisms. Journal of Biological Sciences*, 1(1), 23–44.
- Levy, A. & Bechtel, W. (2013). Abstraction and the Organization of Mechanisms. *Philosophy of Science*, 80:241-261.
- Longo, G., & Montévil, M. (2013). Extended criticality, phase spaces and enablement in biology. *Chaos, Solitons & Fractals*, 55, 64–79.
- Longo, G., Montévil, M., & Kauffman, S. (2012). No entailing laws, but enablement in the evolution of the biosphere. *Proceedings of the Fourteenth International Conference on Genetic and Evolutionary Computation Conference Companion - GECCO Companion '12*, 1379. Doi: 10.1145/2330784.2330946.
- Machamer, P., Darden, L. & Craver, C. F. (2000). Thinking About Mechanisms. *Philosophy of Science*, 67:1-25.
- Maturana, H. (1988) Reality: the search for objectivity or the quest for a compelling argument. *Irish Journal of Psychology*, 9 (1), pp 25–85
- McLaughlin, P. (2001). *What Functions Explain. Functional Explanation and Self-Reproducing Systems*. Cambridge, UK: Cambridge University Press.
- Millikan, R. G. (1989). In Defense of Proper Functions. *Philosophy of Science*, 56, 288-302
- Minati, G., Penna, M. P., & Pessa, E. (1998). Thermodynamical and Logical Openness in General Systems. *Systems Research and Behavioral Science*, 15(2), 131-145.
- Minati, G. & Pessa, E. (2006) *Collective Beings*. New York: Springer.
- Monod J. (1970), *Les hasard et la nécessité*. Paris: Seuil.
- Montévil, M., Speroni, L., Sonnenschein, C., & Soto, A. M. (2016). Modeling mammary organogenesis from biological first principles: Cells and their physical constraints. *Progress in Biophysics and Molecular Biology*, 122, 1–12.
- Moreno, A., & Mossio, M. (2015). *Biological Autonomy: a philosophical and theoretical enquiry*. Dordrecht: Springer.
- Moreno, A., & Suárez, J. (2020) Plurality of Explanatory Strategies in Biology: Mechanisms and Networks. In W.J. Gonzalez (Ed.) *Methodological Prospects for Scientific Research*. (pp. 141-165). New York: Springer.
- Mossio, M., and Bich, L. (2017). What makes biological organisation teleological? *Synthese*, 194(4), 1089-1114.
- Mossio, M., Bich, L. & Moreno, A. (2013). Emergence, closure and inter-level causation in biological systems. *Erkenntnis*, 78(2), 153-178.
- Mossio M., Saborido C. & Moreno A. (2009). An Organizational Account of Biological Functions. *British Journal of Philosophy of Science*, 60(4), 813-841.
- Neander, K. (1991). Functions as Selected Effects: The Conceptual Analyst's Defence. *Philosophy of Science*, 58, 168-184
- Pattee H. H. (1972). The nature of hierarchical controls in living matter. In R. Rosen (Ed.), *Foundations of Mathematical Biology Volume I Subcellular Systems* (pp. 1–22). Academic Press: New York.
- Pessa, E. (1998), Emergence, Self-Organization, and Quantum Theory. In. G. Minati (Ed.) *First Italian conference on Systemics* (pp.59-80). Milano: Apogeo.
- Pessa, E. (2011). The concept of particle in quantum field theory. In I. Licata & A. Sakaji (Eds.), *Vision of oneness* (pp. 13–40). Rome, Italy: Aracne.
- Piaget J. (1967). *Biologie et Connaissance*. Gallimard, Paris.
- Piedrafita, G., Montero, F., Moran, F., Cardenas, M. L., & Cornish-Bowden, A. (2010). A Simple Self-Maintaining Metabolic System: Robustness, Autocatalysis, Bistability. *PLoS Computational Biology*, 6(8).

- Popa, R. (2004). *Between necessity and probability: searching for the definition and origin of life*. New York: Springer.
- Rashevsky, N. (1954). Topology and life: In search of general mathematical principles in biology and sociology. *Bulletin of Mathematical Biophysics*, 13, 317-348.
- Rosen R. (1972). Some relational cell models: The metabolism-repair systems. In R. Rosen (Ed.), *Foundations of Mathematical Biology. Volume II Cellular Systems*. Academic Press: New York (pp. 217–253).
- Rosen, R. (1978). *Fundamentals of measurement and representation of natural systems*. New York: North Holland.
- Rosen, R. (1991). *Life itself: A comprehensive inquiry into the nature, origin, and fabrication of life*. New York: Columbia University Press.
- Rosen, R. (2000). *Essays on Life Itself*. New York: Columbia University Press.
- Saborido, C., & Moreno, A. (2015). Biological Pathology from an Organizational Perspective. *Theoretical Medicine and Bioethics*, 36:83-95.
- Schlosser, G. (1998). Self-re-production and functionality: A systems theoretical approach to teleological explanation. *Synthese*, 116, 303–354.
- Schrödinger E. (1944). *What's Life? The Physical Aspect of the Living Cell*. Cambridge, UK: Cambridge University Press.
- Varela, F. J. (1997). Patterns of Life: Intertwining Identity and Cognition. *Brain and Cognition*, 34, 72-87.
- Varela F. G., Maturana H. R., and Uribe R. (1974). Autopoiesis: The organization of living systems, its characterization and a model. *BioSystems*, 5(4), 187–196.
- Wimsatt, W. C. (1986). Forms of Aggregativity. In A: Donagan, , A. N. Perovich, M. V. Wedin (Eds.), *Human Nature and Natural Knowledge* (pp. 259- 291). Dordrecht: Reidel.