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The limits of reductionism in biology: what alternatives?

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Abstract

Modern science has been grounded on reductionism at different levels from the very beginning. The reductionist approach still holds a significant influence on science, biology included, especially after the rise of molecular biology in the 1950s when biology went molecular, and life began to be interpreted as a molecular process regulated by genetic information. Reductionism resulted in becoming a very powerful analytical approach by which scientists were able to investigate many basic molecular and cellular processes. However as time passed, the limits of the reductionist project in biology have become increasingly evident. Under question was not the value of investigations at the molecular and genetic level, but rather the belief by which complex processes are reduced to certain molecules or genes and genome–phenotype relationships explained in terms of linear schemes. Life cannot be explained only on a molecular and genetic level. Biological systems should instead be understood as complex systems, which result from dynamic interactions of different components at different levels that operate as organized wholes. A different theoretical framework is required to study these systems that can lead towards a post-reductionist approach in science and biology. This paper discusses how the complexity theory can contribute to the development of this framework by providing a number of key notions, such as emergence, self-organization and complex causality.

Introduction¹

From the beginning, modern (or classical) science took on reductionism, introduced to Western thinking by Descartes, believing that God created the world as a clockwork mechanism. This conception was expanded by Newton with his idea of a 'clockwork universe', and ultimately culminated in Laplace's mechanistic view of nature. The world was thus described with the metaphor of the machine, being conceived as one big mechanical device operating according to natural laws in absolute time, space and motion. Organisms too were considered complex functioning machines. Mechanistic explanations were the only possible way to account for these systems. Reductionism fitted well into the conception of a clockwork universe, created by an external designer who combined and organized the parts in compliance with a project not inherent in the system itself.

Reductionist physicalism still holds a significant influence on science, including biology, especially after the rise of molecular biology. Molecular biology has fundamentally adopted a reductionist approach, on which basis biological systems are explained by the physical and chemical properties of their individual components. However, biologists and biomedical scientists are nearing the limits of this approach and this has become evident at different levels. For example, the human brain is a highly complex, nonlinear system, which resists reductionist and deterministic attempts to explain it (Singer 2007). The difficulties in coping with cancer are due for the most part to the complex nature of the disease, as well as the human organism (Soto and Sonnenschein, 2004).

Complex systems exist at different levels of organization ranging from the subatomic realm to individual organisms to whole populations and beyond. Molecules, cells, organisms, ecosystems and human societies are all examples of complex systems.

A new approach is required to study these systems. The complexity theory can provide new conceptual tools to move beyond the reductionist approach of modern science. It is then important to explore in what manner the study of biological systems can also be affected.

This paper is structured as follows: First, I introduce briefly the way in which mechanical reductionism has largely influenced the development of science and biology. I then describe how, with the discovery of new findings in biology, it has become increasingly more difficult to wholly explain life in molecular terms. Finally, a number of ideas associated with the complexity theory are illustrated, as they can contribute to the development of a new approach in science that moves beyond reductionism without assuming its opposite, i.e. holism, and be particularly

¹ This article is based partially on ideas discussed in Mazzocchi 2008 and 2010.

applicable in the biological domain, in which many paradigmatic examples of what complexity means are found.

Reductionism in modern science and biology

Reductionism, on which modern science is fundamentally grounded, can be described in term of a number of basic ontological, methodological, and epistemological assumptions.

Ontological reductionism corresponds to the idea that all things that exist in nature are formed by a restricted set of primitive and indivisible material elements. An understanding at this basic level is sufficient to explain any phenomena, including those occurring at higher levels that are regarded as epiphenomena. The (apparent) variety and complexity of the natural world is, thus, resolved by reducing phenomena to simpler structures of matter. An account of the formation of higher-level systems, as well as and their behaviour and evolution, can be obtained in terms of the fundamental laws governing the assembly of these primitive elements. In classical Newtonian physics, these elements are atoms; in contemporary physics, they are elementary particles. The only property that distinguishes them is their position in space. Therefore any change or development consists in a geometrical rearrangement owing to the movement of these elements, which is governed by the deterministic law of cause and effect (Heylighen *et al.*, 2007).

Methodological reductionism is the belief that the best way of scientifically investigate any system is at the lowest possible level. To understand any complex whole it is necessary to break it down to its individual components, investigate these components, find out the structures and functions in which they are involved, and then reassemble them together to see how they function together in the complex whole (Peacocke, 1985). Reductionism at this level is frequently instigated by the presupposition of ontological reduction, and very often sustainers of methodological reductionism are also sustainers of ontological reductionism. On the other hand, these two positions can be held separately.

Epistemological reductionism assumes that epistemic units (e.g., concepts, laws and theories) of a certain level of organization can be derived by implementing the rules of reduction from epistemic units that pertain to lower and more basic levels (Nagel, 1961). This implies a hierarchical arrangement of scientific disciplines, which is due to their different level of axiomatization, predictive power and scientific rigour, and that assigns the highest rank to physics.

Modern science adopted also a linear representation of causality, which emphasizes the role of one or a few key factors, and is associated with a deterministic view of the world. Determinism is the idea whereby any phenomenon in nature is entirely determined by pre-existing causes to which it is bound by a relationship of necessity, and that there is only one possible future. As a consequence, deterministic

causality, at least in the framework of modern physics, is associated with the idea of predictability: the evolution of a system can be completely determined by knowing the initial conditions and the mechanical laws governing its behavior.

Despite the fact that things have changed quite a lot since Descartes and Newton, reductionism (and determinism) still hold a significant influence on science, also on biology. Historically, the holistic view has played a significant role in certain area of biology. And yet, in the 1950s the general impression was that biology was about to be transformed by the rise of molecular biology and that it would finally go molecular.

Many leading scientists who contributed to creating the field of molecular biology actually came from physics, and as such they tended to extend the classical reductionist approach to the study of biological systems. In its early days, ideas of simplicity and linearity affected molecular biology. DNA structure is an essentially linear representation of genomic information. The genetic code is linear even though redundant. The central dogma of molecular biology holds that genes—ordered sequences of nucleotides along the DNA molecule that store genetic information—are transcribed into messenger RNAs, which are then translated into polypeptide chains (Crick, 1958). It is only from DNA to RNA to proteins that causal determination flows, and this cannot be reversed. The unidirectional information flow is simple and linear. Despite the fact that it introduces control genes and feedback loops, even the operon model of gene expression still advanced the belief that complex biological systems could be explicated entirely by interactions at the molecular level (Schaffner, 2002).

These conceptions and the fact that molecular genetics became a predominant focus of biological research, caused a major shift in biology. Life began to be interpreted as a molecular process regulated by genetic information. The molecular-reductionist approach resulted from a molecule-centred view of biology coupled with the idea of reduction as developed since Descartes's time and reframed in logical empiricist terms. It is made up of the belief that all explanations in the end involve the identification of relevant molecules and their rules of interaction. Generalizations attained at the level of cell physiology, for instance, are useful to furnish descriptions of functional regularities, and yet would not be explanations in themselves (Rosenberg, 1997).

This approach integrates reductionism at multiple levels with unifactorialism. The latter is associated with the central dogma as the thesis that DNA is the only causal agent. In view of the mechanistic relations between DNA and proteins, all the organismal phenotypic features are then explained in terms of genetic causation. Although the causal primacy of DNA does not imply, in principle, the existence of

genes, in practice it explicates the action of genes. These are considered as essential determinants of forms and functions (Powell and Dupré, 2009).

The signs of a crisis

Reductionism became a very powerful analytical approach by which scientists were able to investigate many basic molecular and cellular processes. Biological research has, however, reached a point in which many of the assumptions associated with the molecular-reductionist approach no longer satisfy many scientists.

For example, Keller (2000: 72) affirmed that “The function of a structural gene depends not only on its sequence but, as well, on its genetic context, on the chromosomal structure in which it is embedded (...), and on its developmentally specific cytoplasmic and nuclear context”.

As a matter of fact, the discovery of alternative splicing ² demonstrated that genes are not simple and linear representations of information. Instead a given stretch of protein-encoding DNA can give rise to numerous protein molecules, which again depends on a complex network of regulatory factors including both proteins and DNA. RNA editing, small regulatory RNAs and post-translational protein modification adjoin layers of complexity not controlled by genes, but rather the processes in which other molecules are involved. The central dogma of molecular biology that information flows in only one direction is put under discussion by epigenetics.

Most molecular biologists, however, still tend to rely on simple models with explanations based on a few individual factors. For instance, knockout experiments, which are employed to establish the functional role of a gene, overstate the role of individual genes and are of limited utility for understanding complex genetic networks. In effect, many of these experiments have no or unexpected effects, owing to the fact that genes and their products do not exist and act as isolated and autonomous entities. They are instead parts of complex networks at different levels of organization, which in turn influence their activity and function. Every cell possesses various molecular components with complex relationships between them, which are different from one cell or tissue to another.

² Most genes in eukaryotic genomes include introns and exons. An intron is any nucleotide sequence within a gene that is removed by splicing from the pre-mRNA to generate the final mature RNA product of a gene. Exons are instead sequences that are joined together in the final mature RNA after RNA splicing. Alternative splicing is the process by which exons in transcripts are recombined in multiple ways to express multiple mRNA variants, which can in turn be translated into protein with different structures and functions. This process is largely widespread in eukaryotes. By enabling that an individual gene may code for structurally and functionally distinct proteins, it functions as an important mechanism by which the information stored in the genes of complex biological systems can be edited in multiple ways (Kashyap and Sharma, 2007).

Other principles of macromolecular organization can cause these unforeseen findings, such as pleiotropy and redundancy (Morange, 2002). According to the former, genes and their protein products carry out a variety of roles in the development and functioning of organisms at different places and different times. Pleiotropy reveals itself solely at higher levels and depends on the different molecular constituents – with which the gene products interact – present in the cell at a certain moment. Redundancy corresponds to the presence of a large number of gene duplications in the genome, which can at least partly compensate the loss of function due to the deletion or inactivation of a gene. It is also important to note that all these principles are interrelated closely. For example, pleiotropy results from the fact that the same networks participate in many distinct functional processes. Redundancy guarantees the stability of networks.

What is put into discussion by the discovery of this complex organization is not, of course, the value of investigations at the molecular and genetic level. Instead it is questioned the belief by which complex processes are reduced to certain molecules or genes and genome–phenotype relationships explained in terms of linear schemes. As stated by Laubichler and Wagner (2001, 61): “the fact that all biological objects are made of molecules does not imply that molecules are the most informative level of analysis. Emergent properties of supracellular entities can be more informative and thus have more explanatory force than molecules”.

In point of fact, higher-level patterns are not always reducible to underlying lower-level mechanisms. Several findings have underscored the importance of higher levels of resolution and functional generalizations: “Molecular biology showed that molecular details do count, and may be richly explanatory. This prosaic yet productive discovery becomes potentially distorting only when it is combined with a commitment towards the simple, since that commitment so easily slips into the simplistic [...]. What biology keeps reminding us is that things can be complex, and that coming to know about complex things can be difficult. Any one approach, or any exclusive focus on one ontological level (in so far, indeed, as there really are such things), will almost certainly be inadequate to all aspects of the task” (Powell and Dupré, 2009).

Reductionism encourages also an experimental approach based on the removal of an object of study from its natural context. Experimental results attained under given special conditions or from a particular model – such as a mouse, *in vitro* cell cultures or computer models – are often extrapolated to more complex settings or organisms such as humans. And yet this extrapolation can be misleading. For example, the failure of many promising drug candidates in clinical investigation demonstrates that it is not always possible to transfer results from mice (or even primates) to humans (Horrobin, 2003).

In any case, it is becoming increasingly evident that life cannot be explained (only) at the molecular and genetic level. Biological systems should be understood as the result of complex dynamic interactions of different components at different levels – (structural and functional) genes, mRNA and tRNA, proteins, and metabolites – which operate as organized wholes. There is no a centralized (genomic) control of the biological functions. What is needed is to look beyond the genome: “Gene management involves interactive cellular processes that display a complexity that may be described only as transcalsculational [...]. This interactive complexity is epigenetic in nature; it involves open networks of genes, proteins, and environmental signals that may turn out to be coextensive with the cell itself” (Strohman, 1997). These epigenetic networks exhibit nonlinear behaviours, include multiple pathways and feedback circuits and react to environmental cues.

In the light of this, a different theoretical framework is needed, which recognizes the existence of higher levels of regulation—even beyond epigenesis (Strohman, 1997) –and is able to cope with nonlinearity, i.e. no proportionality exists between cause and effect. The complexity theory is contributing to its development through a number of key notions, such as emergence and downward causation, coupled with multifactorialism and complex causality (Mazzocchi, 2008 and 2010).

Insights from the complexity theory

The complexity theory can be seen as a moment of synthesis around some fundamental principles that are recognized at a trans-disciplinary level. However, this synthesis is incomplete. Complexity is still an amalgam of principles, methods and concepts, rather than a unified research program (Heylighen *et al.*, 2007). The community of practitioners does not seem to share a coherent conceptual framework, and on some crucial issues, reductionism included, there are quite contrasting positions. The following description follows the idea that complexity does not fit in with the reductionist view that is still dominant in science.

A number of categories, previously seen as basically meaningless for the study of natural phenomena, have been readmitted, such as singularity and contingency. Concepts that were considered as irreducible opposites, such as order and disorder, have been reconceptualized as complementary in the light of notions like ‘order by fluctuation’ (Prigogine and Stengers, 1979) or ‘order from noise’ (Atlan, 1972 and 1979; von Foerster, 1981).

The mechanistic worldview of modern science, together with its main explanatory principles, i.e. reductionism and determinism are above all questioned here. To properly describe the universe, notions such as emergency, non-linearity and unpredictability should be included.

The natural world is seen as stratified into multiple levels of organization, from the simple to the more complex. Within this order, the most fundamental—the physical—level has no ultimate ontological primacy over the others. Each level is typified and governed by (emergent) laws that do not appear at the lower levels. This implies, for example, that while

the biological level rests on the physico-chemical level, from whose laws is constrained, it is at the same time qualitatively different from it: “Phenomena on one level cannot be reduced to the lower level, but on the other hand they can never change the laws of the lower level: a lower level is a necessary but not sufficient condition for the higher level; the higher level supervenes upon the lower. Biological phenomena cannot change physical laws—but neither can physical laws as we know them fully explain biological phenomena” (Emmeche *et al.*, 1997).

Emergent properties are neither predictable nor reductively explainable in terms of the properties and relationships of lower levels of organization (Kim 1999). This implies that in order to explain the features and the behavior of a system as a whole an explanation operating at the corresponding hierarchical is required. For instance, phenomena that take place at the organismal level cannot be fully explained in terms of theories operating at the level of cells or macromolecules.

Besides, these emergent properties are believed to have their own distinctive causal power, which is irreducible to the causal powers of their basal components (Kim, 1999). This hierarchical organization creates in fact downward causation (Campbell, 1974). While the behavior of the whole is constrained by the properties of its components (upward causation), the behavior of its parts is affected to some extent by the properties of the global system (downward causation). In other words, the whole has a causal influence on its constitutive parts. The behavior of a cell, for example, is controlled by both the properties of macromolecules and the properties of the organ to which it belongs. This is a crucial aspect. Leading theoreticians of the emergentist movement early last century like Samuel Alexander (1920) assume, in fact, that for a property to be real means to possess a distinct causal power. The non reducibility (and reality) of higher level properties is explicable in that the additional causal power granted by their existence cannot be extinguished by the causal power conferred by their physical bases (Hendry, 2010).³

³ As often occurs, the increasing diffusion of given concepts, namely emergence and downward causation in biology, is a response to unjustified claims about theses with which they contrast, namely the explanatory value of reductionism. Nonetheless, these concepts require a further conceptual elaboration and a clear association with empirical findings in order to become more useful for scientists. Critical is the discussion about downward causation. This notion is still considered a paradox by many, since it contravenes the fundamental assumption about the direction of material causation, which is assumed to proceed solely from the basic molecular level to more complex domains (Kim, 1999). For this reason, many scientists and philosophers tend to regard emergence and downward causation only as epistemic concepts, and to conceive the hierarchical levels as levels of concepts and descriptions, instead of levels of properties and phenomena in the real world. Other key concepts retain a certain degree of vagueness or ambiguity. For example epigenetics, as stressed by Morange (2006: 358): “Epigenetics is a polysemic word, the significance of which has constantly changed since its creation by Conrad Waddington in 1942 (...). It means “over genetics”, but is more often used to mean “besides genetics”: it has essentially been used to answer the questions that were considered as not properly explained by genetics. Today, the term epigenetics is used for mechanisms responsible for an inheritable change in gene activity that does not result from a modification in the DNA sequence: modification of gene expression by DNA methylation or by alteration of the chromatin state. The attention paid to these epigenetic mechanisms clearly illustrates the limits of the present reductionist explanation of gene control. The dominant model, according to which gene expression is controlled by a combination of proteins bound upstream of the gene, does not explain either the observed specificity of control or its stability and globality. The concept of epigenetics is a way of extending the scope of genetics without precisely discussing the origin of its limits: epigenetics is frequently used in a very vague sense, only to mask the present ignorance about the relationships between the genotype and the phenotype”.

Emergence and downward causation are also believed to be involved in self-organization. This is a process in which patterns at the global level of a system arise out spontaneously from non-specific local interactions among the lower level constituents of the system (Camazine *et al.*, 2001).

Complex systems evolve towards the edge of chaos (Kauffman, 1993), i.e. a zone placed between the extremes of a rigid order not capable of change without being destroyed (the state of the crystals), and a constantly changing processuality which is irregular and chaotic (the state of the gases). At the edge of chaos, they self-organize, arranging spontaneously and unexpectedly their constituents and interactions in adaptive network structures with emergent properties. These structures are able to create and modify existing strategies to adapt to changing environmental conditions. Through dynamic change in the degree of interaction between the individual components that form the network, complex adaptive systems can self-regulate and reorganize into a new equilibrium in response to external events (Heylighen *et al.*, 2007).

Life can then be seen as an emergent phenomenon to be explained in terms of self-organizing processes. And self-organization seems to occur at different levels of biological organization. For example, as a general principles in the organization of the cell (Misteli, 2001), or in the brain that reorganizes itself to learn from experience (Coffey, 1998).

At the edge of chaos, complex (biological) systems are stable, and yet adaptive and evolving. Highly complex behaviours manifest themselves. These systems can go through sudden considerable and stochastic changes in response to what appear as minor modifications. In complex systems individual components interact in manifold ways, including highly dynamic regulatory and feedback mechanisms. As a result, minor (local) actions or fluctuations can lead to unexpected and dramatic (global) consequences, whereas similar causes can produce multiple effects and similar effects may be the result of very different causes. One of the key principles of complexity is that complex effects can derive from simple causes, that is from simple rules that are applied recursively. This implies that these systems, whose evolution is inherently unpredictable, cannot be explained in a deterministic way through causal linear chains or mechanistic models, or in terms of unifactorialism. The notion of causality should therefore take into consideration non-linear and feedback processes, as well as multiple factors and levels of control.⁴

⁴ For same thinkers, complexity should be defined in relation to this conception of causality. One of the distinctive attribute of science is the search for empirical regularities, which calls for theories to explain why these regularities occur, and to be expressed by (deterministic or probabilistic) laws. Prediction arises from combining the law with a set of initial conditions to deduce an outcome (Hempel, 1966). The true novelty of complexity would reside in the fact that it has developed new methods for the study of empirical regularities in nature that differs from traditional science. Whereas modern science tends to focus on simple cause-effect

Retroactive causality has also led to the development of the concept of self-reference, i.e. a phenomenon that generates an operational closure of elements in different separate levels intercrossed to form a complex unity (Varela, 1984).

A tradition of pioneering thinkers has used autoreferentiality in association with self-organization to render more intelligible the idea that life is an emergent property.⁵ The common insight of different streams of this tradition is that the most distinctive feature of biological systems is autonomy, intended as the ability to self-determinate and to be (relatively) independent from the environment (Damiano, 2010). Autonomy cannot be found in the physico-chemical components taken separately. Only the whole can exhibit it, as it depends heavily on organization, that is on the network of functional relations through which the physico-chemical component parts are unified into one cohesive and dynamic whole. This view represents also a major shift in respect to heteronomist conceptions according to which biological systems were seen by molecular biologists. Organisms are not mere machines ruled by a deterministic program encoded in the DNA sequence.

The question was to ascertain what kind of organizational scheme is able to generate autonomy as a feature of the biological whole. In response to this, a common minimal understanding was established that attributes to biological systems a circular organizational scheme. Through recursive loops a mutual interaction between higher and lower levels is established: autonomy is obtained as a process of mutual specification between the whole and component parts of the systems.

One of the most important theoretical proposals to define this circular organization came from Maturana and Varela (1980, 1987). It is based on the notion of *autopoiesis* that conceives autonomy in terms of self-production (including self-determination and self-stabilization), and self-distinction from the environment as well. The presence of autopoietic organization within a system is assumed to be a necessary and sufficient condition to classify it as living.

relationships, complexity “posits *simple* causes for *complex* effects. At the core of complexity science is the assumption that complexity in the world arises from simple rules. However, these rules (which I term “generative rules”) are unlike the rules (or laws) of traditional science. Generative rules typically determine how a set of artificial agents will behave in their virtual environment over time, including their interaction with other agents. Unlike traditional science, generative rules do not predict an outcome for every state of the world. Instead, generative rules use feedback and learning algorithms to enable the agent to adapt to its environment over time” (Phelan, 2001).

⁵ The interest for self-reference arose with the development of cybernetics at the beginning of 1950s. Many insights, which created the basis also for the future development of the notion of self-organization in biological systems, were produced in the so-called Macy Conferences (held in the period from 1946 to 1953), to which participate a group of prominent scholars from various disciplines, such as Warren McCulloch, Norbert Wiener, Claude Shannon, John von Neumann, Gregory Bateson, Margaret Mead, and successively Heinz von Foerster. A scientific genealogical hypothesis of the concept of self-organization has also been advanced by Isabelle Stengers (1985).

A crucial role in the development of the autopoiesis theory was played by the distinction, already advanced by Piaget (1967), between the notions of organization and structure. The organization is the invariant relational asset of biological systems, which assigns them a distinctive identity. The structure is the concrete and transient materialization of a living unit, which is constantly in flux in reason of its self-producing dynamics. The preservation of the invariance of the former (organizational closure) is obtained through modifications of the latter. Perturbations are compensated by multiple patterns of self-production. Organization and structure are mutually dependent on each other, in the sense that if, on the one hand in absence of an actual materialization in space and time the organization cannot exist, on the other hand for any concrete materialization to be possible a relational frame that integrates these elements into a cohesive unit is required.⁶

Maturana and Varela elaborated these concepts further. Organization is conceived as the invariant of biological dynamics at the ontogenetic and phylogenetic levels: “This unity is what remains unchanged during ontogenetic transformations that can at time render a living being unrecognisable from one observation to the next. This relational unity is also transmitted through reproduction. It is the living feature that remains unchanged generation after generation, and furthermore the feature shared by all the living” (Damiano, 2010).

Besides, in the autopoiesis theory the idea of a mutual dependence or co-emergence (of parts and whole) does not apply only to the relation between structure and organization, but also to the relation between an autopoietic unit and its environment. The key notion in this respect is structural coupling, which takes place when structural changes are triggered, and yet not determined, in autopoietic systems and their environment. It holds “whenever there is a history of recurrent interactions leading to a structural congruence” (Maturana and Varela, 1987: 75) between them. When modifications produced by structural coupling exceed the limits of a unity’s organizational boundaries, the system is forced to change its organization and acquire a novel identity, or it disintegrates.

Another important theoretical proposal was from Atlan, who advanced the principle of order (or complexity) from noise, incorporating ideas from Shannon’s theory of information, Prigogine’s notion of order from fluctuations in dissipative structures, von Neumann’s work on cellular automata, and von Foerster’s research on self-organizing systems: “randomness is a kind of order, if it can be made

⁶ An autopoietic system is organized (defined as a unity) “as a network of processes of production (transformation and destruction) of components that produces the components which: i) through their interactions and transformations continuously regenerate and realize the network of processes (relations) that produced them; and (ii) constitute (...) a concrete unity in the space in which they (the components) exist by specifying the topological domain of its realization as such a network. (Maturana and Varela, 1980: 79).

meaningful; (...) the task of making meaning out of randomness is what self-organization is all about" (Atlan, 1984: 110).

Noise (or "aleatory aggression") in the environment can have two distinct consequences, depending on the level of observation at which it is analyzed: i) it reduces the quantity of system's information by the accumulation of errors in the structure of its component parts; ii) it increases the quantity of information of the total systems by increasing the autonomy among these parts. If not integrated, noise can lead to the destruction of the system. And yet, when assimilated it allows for a more complex order to emerge, at a higher level of organization. This process, which implies the decrease of redundancy and interchanges between different hierarchical levels of organization, produces an internal augmentation of differences that can increase the system's adaptive capacities.

In the Atlan's understanding of its nature and dynamics, (biological) complexity is portrayed as an emergent (and thus unpredictable) phenomenon, in which a great number of component parts are involved that are interconnected in multiple ways. Due to the negantropic processes operating in organisms, an evolutionary trend "apparently *oriented* toward more complexity" is generated (Atlan, 1972). For Atlan (1979) the domain of living systems is the state between rigid structure (crystal) and vanishing structure (smoke). This intermediate state is not rigidly fixed, but allows systems to react to random perturbations through changes in the organization, which include a disorganization (at one level) followed by a re-organization (at a more integrated level), on which basis novel and apriori unpredictable properties emerge. This interstitial condition, described by Atlan and Kauffman, is what "makes the moment of complexity" (Taylor, 2001: 137).

Concluding remarks

As biology went molecular in the 1950s, it basically adopted a reductionist view, according to which complex biological systems are explained in terms of the physical and chemical properties of their individual components. However, as time passed by, the limits of the reductionist project has become increasingly evident. The notion of emergence has gained credit also in the natural sciences, and there has been a general tendency towards looking at nature in a more integrative way.

This is also demonstrated by the rising of new fields of research, such as systems biology. However, this process of theoretical renewal is far from being univocally oriented, as shown by the development of systems biology itself. As asserted by O'Malley and Dupré (2009), systems biology can, in fact, be best understood as consisting of two distinct streams. One emphasizes large-scale molecular interactions ('pragmatic systems biology'), whereas the other emphasizes systems principles ('systems-theoretic biology'). Pragmatic systems biologists, which make up most of

the today's systems biologists, recognize the importance of studying the interactions of molecular phenomena by integrating multi-level data and models, and take advantage of the fact that technology is progressively enhancing scientists' ability to collect and collectively analyze massive amounts of data (Aderem, 2005). Nonetheless, they still tend to view systems as mere collections of parts, not as ontological (emergent) realities. Systems-theoretic biologists are instead committed to adopting a systemic view, that is to refer to systems' principles, as established in the tradition of systems theory by pioneers such as Wiener, Ashby, and von Bertalanffy. Definitions of what a system is tend to be rather abstract. Systems correspond anyhow to ontological realities.

As discussed in the paper, the complexity theory might contribute to the development of a new (post-reductionist) approach in biology, to be applied in systems biology also.⁷ It is, nonetheless, important to underscore that complexity is not simply holistic, as perhaps occurs in some versions of the systems theory.⁸ And yet it requires a commitment towards a substantial shift in the scientific way of looking at nature. Despite the fact that many scientists and biologists are aware of this, there is still the tendency to avoid the fundamental problems posed by complexity, attempting only to find new laws, the "laws of complexity". As stated by Morin (2007: 10), "To some extent, one recognizes complexity, but by decomplexifying it. In this way, the breach is opened, then one tries to clog it: the paradigm of classical science remains, only fissured." What is instead needed is a clear epistemological rethink, moving beyond reductionism, which has dominated classical science, towards a new way of doing science. This is what can be put forward by the paradigmatic (although abused) idea of complexity.

⁷ What could be worth to be explored in future research is the possibility, which seems to have been rather neglected up to now, to integrate notions derived from the tradition of self-reference and self-organization in systems biology, in order to deal with the issue of emergence from an organizational standpoint, that is to investigate what kind of organizational scheme is able to generate autonomy as an emergent property of the biological whole.

⁸ Bauchau (2006: 29) asserts that, "Reductionism and emergence do not contradict, they complement each other. The aim of Science is to explain, and explaining a given phenomenon consists as much as the reduction to the micro-level than the prediction of the macro-level. Stating that consciousness is based on brain activity, is that a reductionist or emergentist statement? On one hand, the reductionist approach has been fulfilled by the discovery of the neuron and its working. On the other hand, this only gives us the basic component, which, grouped together in a proper way, support the higher capacity of the brain. Emergence can only be studied properly when the laws of the lower levels are known, *i.e.* when some reduction has been done. On the other hand, the reductionist program has to include the notion of emergence of complexity and, doing so, has to acknowledge potential limitations, as those discussed here". If intended as overall approaches having conflicting fundamental assumptions (see also Mazzocchi, 2010), I would not sustain the idea that reductionism and emergentism (or holism) simply complement each other. Nonetheless, I would certainly agree with the thesis that what is needed is a scientific approach acknowledging the importance of investigating nature bottom-up from the micro-level and top-down from the macro-level, which is close to the idea of sustaining the need of an integration between methodological reductionism and methodological holism.

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