Complementarity in biology

A reassessment in relation to molecular-reductionist and systemic approaches

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At the beginning of the twentieth century, a range of seemingly unexplainable observations challenged the Newtonian view of the physical world and plunged physics into a major crisis. This crisis and the resulting intellectual advances led to the birth of quantum mechanics in the 1920s, a theoretical field that provided a new framework for the explanation of phenomena that were defying classical laws of mechanics. One of the main insights that emerged from quantum physics was the principle of complementarity, which Niels Bohr (1885–1962) formulated to explain the fact that, in quantum physics, two theories regarded as mutually exclusive are required to explain a single phenomenon (Bohr, 1958).

In particular, Bohr was dealing with wave–particle duality: light exhibits different properties depending on the means of observation. Some phenomena, such as diffraction patterns, are best explained if light is considered as electromagnetic waves, whereas others, such as the photoelectric effect, require that light behaves like particles. Bohr's principle of complementarity established that, for investigations at the subatomic level, light could be considered as either, depending on the methods of measurement; that these two descriptions should not be regarded as contradictory, but as complementary; and that it is not possible to formulate a synthesis of the two.

Interestingly, Bohr also believed that complementarity could be applied to contexts other than quantum mechanics and the realm of subatomic particles. In a lecture titled *Light and Life* that he gave to a congress on light therapy in Copenhagen in 1932 (Bohr, 1933), he proposed that a notion of complementarity might be needed for understanding biological phenomena. Bohr suggested that experiments to analyse

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the molecular properties of organisms and biological functions were basically incompatible—the complex organization of living systems cannot, in fact, be preserved under the experimental conditions of a complete quantum mechanical analysis (McKaughan, 2005). Instead, both types of experiment are needed.

Within the theoretical framework of complementarity, Bohr reformulated the idea, previously advanced by the German philosopher Immanuel Kant (1724–1804), of the impossibility of reducing all aspects of life to mechanical causes. To obtain a full understanding of living systems, two mutually exclusive modes of description are equally necessary: the mechanistic and the finalistic descriptions, which are complementary to one another.

Bohr envisioned that biology would need two distinct fields of investigation in order to progress: one to describe the physical mechanisms on which phenomena at the subcellular level depend and another concerned with the organismal level and how organisms interact in larger systems, for which the concept of purpose is relevant. With the discovery of DNA structure by James D. Watson and Francis Crick (1916–2004), is this notion of complementarity in biology still meaningful?

In spite of advances since the 1930s, the situation in biology remains characterized by tensions between two approaches that take different stands on the possibility of

reducing biology to physics: a reductionist approach focused on individual molecules and a more systemic approach—historically associated with types of holism—to study higher levels of organization. Both approaches represent different traditions of thought and refer to distinct metaphysics, methodologies and guiding principles. In practice, the dominant view in biology is rooted firmly in reductionism, while the systemic approach often defines itself as a critique of the former. Thus, in order to re-evaluate Bohr's original idea of applying the principle of complementarity to biology, we need a more thorough analysis of each.

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Since the time of Descartes and Newton, classical science has adopted a reductionist approach in which both ontological and epistemological assumptions are merged. Ontological reductionism is based on the idea that all things are constituted by a limited set of primitive and indivisible material elements. Moreover, an understanding at this fundamental level is sufficient to explain any phenomena, including those occurring at higher levels that are regarded as epiphenomena—that is, consequences of primary phenomena that do not have a real causal power themselves. Thus, the variety and complexity of the world—and the human experience of it—can be resolved by reducing phenomena to simpler structures of matter. To explain the formation of higher-level systems, their behaviour

and evolution, we need to discover the fundamental laws governing the assembly of these primitive elements.

In classical Newtonian physics, these elements are atoms; in contemporary physics they are called elementary particles. The only property that distinguishes them is their position in space. Any change or development is thus viewed as 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). The Newtonian world is an ordered machine operating according to natural laws in absolute time, space and motion; it is basically made of closed systems in equilibrium and isolated from their environments. Even living beings are considered mere machines of a particular type. Mechanistic explanations are therefore the only possible approach to understanding these systems. Reductionism fits well into this idea of a clockwork universe, created by an external designer that combined and organized the parts in accordance with a project not inherent in the system itself.

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Epistemological reductionism concerns the relationships between different domains of knowledge. It assumes that epistemic units—such as concepts, laws and theories—of a given level of organization can be derived by implementing the rules of reduction from epistemic units that apply to lower and more fundamental levels. As formulated by the Czech–American philosopher of science Ernest Nagel (1901–1985), these rules include ‘logical derivability’—the possibility to derive logically the laws of the reduced theory from the laws of the reducing theory—and ‘connectability’—the possibility to link the concepts of the two theories by means of bridging principles (Nagel, 1961). This conception implies a hierarchical arrangement of scientific disciplines according to their level of axiomatization, predictive power and scientific rigour, which attributes a dominant position to physics.

Other assumptions are also incorporated in the conceptual framework of classical science, including unifactorialism (Powell & Dupré, 2009)—explanatory practices that focus on the role of one or a few essential factors—and a linear model

of causality that leads to determinism. In addition, the epistemology of classical science strives to seek univocal explanations and simplifications at different levels.

Things have changed quite a bit since Descartes and Newton, with the advent, for example, of quantum mechanics and general relativity in physics, and chaos theory in mathematics. Nevertheless, the reductionist paradigm still holds a significant influence on molecular biology. Many of the influential scientists who created the field of molecular biology in the 1950s actually came from physics, so it is not surprising that they extended the classical reductionist approach to the study of living entities. Theoretical physics had a key role in the development of new directions in biology, particularly in the fertile period between 1940 and 1960, during which the double-helical structure of DNA was resolved, the genetic code deciphered and new analytical techniques originating from biophysics and biochemistry were introduced (Rheinberger, 2009).

One of the founding fathers of molecular biology was Bohr’s student Max Delbrück (1906–1981), who aspired to finding an empirical justification for Bohr’s idea of complementarity in biology. However, in pursuing this task, he did not regard biology as an autonomous science. He was more interested in proving the need for new physical laws to explain living systems, rather than recognizing that some biological phenomena were not reducible to physicochemical terms (McKaughan, 2005; Roll-Hansen, 2000).

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The molecular-reductionist approach results from a molecule-centred view of biology coupled with the notion of reduction as developed in the philosophical framework of logical empiricism. It is based on the belief that “[a]ll biological properties are realized by combinations—sometimes vastly complex combinations—of molecular properties” (Rosenberg, 1997). According to this view, all explanations ultimately involve the identification of relevant molecules and their rules of interaction; generalizations obtained at the level of cell physiology, for example, might provide descriptions

of functional regularities but would not be explanations in themselves.

Nagel’s general model of reduction can be applied in terms of successional theory reduction, whereby one theory is reduced to a new one, which is usually considered an empirically more adequate and complete theory than the former. One example in biology is the attempt to reduce classical Mendelian genetics to molecular genetics with its physicochemical description of genes and their functions.

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Genes are ordered sequences of nucleotides along the DNA molecule that store genetic information. The central dogma of molecular biology holds that genes are transcribed into messenger RNAs, which are then translated into polypeptide chains (Crick, 1958). The information flow is unidirectional. It is only from DNA to RNA to proteins that causal determination flows, and this cannot be reversed. This dogma, and the fact that molecular genetics became a predominant focus of biological research, provoked a major shift in biology. Most biologists began to interpret life as a molecular process regulated by genetic information.

This approach incorporates a number of claims pertaining to classical science, namely ontological level reductionism—the belief that an understanding of the fundamental molecular level is sufficient to explain any cellular or organismal processes—and unifactorialism, which can be referred to the central dogma according to which DNA is the only causal agent. In light of the mechanistic relationship between DNA and proteins, all phenotypic features of an organism could therefore be explained in terms of genetic causation. Even if the causal primacy of DNA does not imply, in principle, the existence of genes, in practice it explicates the action of genes, which are regarded as key determinants of forms and functions (Powell & Dupré, 2009).

In its early days, notions of simplicity and linearity influenced molecular biology: DNA structure is an essentially linear representation of genomic information; the genetic code is linear although redundant; and the central dogma of unidirectional

information flow is also simple and linear. Even the operon model of gene expression—although it introduced control genes and feedback loops—still prospected the idea that the complexity of biological systems could be explained by interactions at the molecular level (Schaffner, 2002).

With the advent of molecular biology, it seems that Bohr's idea of life as not entirely explainable in physicochemical terms—as it comes from the pre-DNA era—retains only an historical interest. However, biological research has moved on since then. It has reached a point in which many of the assumptions associated with the molecular-reductionist approach no longer satisfy many practitioners.

The discovery of alternative splicing showed 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 add layers of complexity that are not controlled by genes, but rather the action and activity of other molecules. Finally, epigenetics shatters the central dogma of molecular biology that information flows in only one direction.

In general, genes and their products do not exist and act as isolated and autonomous

entities; they are parts of complex networks at different levels of organization that in turn influence their activity and function. Every cell has many molecular components with complex relationships between them, which are different from one cell or tissue to another.

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There are other principles of macro-molecular organization (Morange, 2002). One is pleiotropy, according to which genes and their protein products fulfil several roles in the development and functioning of an organism at different locations and different times. Pleiotropy reveals itself only at higher levels and depends on the different molecular constituents—with which the gene products interact—present in the cell at a given moment. Another principle is genetic redundancy: the presence of a large number of gene duplications in the genome that can at least partly compensate the loss of function incurred by the deletion or inactivation of a gene. All these principles are interlinked closely. Pleiotropy results from the fact that the same networks take part in distinct and multiple functional processes. Redundancy ensures the stability of networks.

The discovery of this complex organization does not challenge the importance of investigations at the molecular and genetic level, or the possible value of explanations in terms of the properties of the constituent parts. It does, however, question the reductionist conception that reduces complex processes to certain molecules or genes and explains genome–phenotype relationships in terms of linear schemes. “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 & Dupré, 2009).

Higher-level patterns are not always reducible to underlying lower-level mechanisms. Rather than being grounded in the internal structures of analytically distinguishable entities, biologically relevant causal powers can reside in the relations between them (Powell & Dupré, 2009). Indeed, several findings have pointed out the importance of higher levels of resolution and functional generalizations.

As life cannot be explained only at the molecular and genetic level, we need to look beyond the genome. "Gene management involves interactive cellular processes that display a complexity that may be described only as transcascational [...]. 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" (Strohmman, 1997). These epigenetic networks exhibit a nonlinear behaviour, include multiple pathways and feedback circuits and react to environmental cues. Thus, the behaviour of biological systems cannot be explained by theories that are based on notions of linear causality and simplicity.

A different theoretical framework is required that can embrace non-linearity and complexity and that is open to admit the existence of higher levels of regulation—even beyond epigenesis (Strohmman, 1997). In this regard, systems theory and complexity science are now contributing various key ideas, notably emergence and downward causation, coupled with multifactorialism and complex causality (Mazzocchi, 2008). Some of Bohr's intuitions on life and the irreducibility of biology to physics could be reinterpreted in the light of this new conceptual framework.

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Contemporary versions of emergence can be better understood by focusing on a number of claims (Kim, 1999). The first is the idea of the emergence of higher-level entities and higher-level properties. Entities with a higher degree of organizational complexity arise from the assembly of lower-level entities in novel structural arrangements. Moreover, the properties of higher-level entities arise from the properties and relations typifying their parts. Here, it is important to distinguish between 'resultant' higher-level properties and 'emergent' higher-level properties. In contrast to resultant properties, emergent properties are neither predictable from basal conditions, nor explainable or mechanistically reducible in terms of these conditions.

In addition, these emergent properties are believed to have their own distinctive causal power, which is irreducible to the causal powers of their basal components. Here is where downward causation enters the scene (Campbell, 1974). While the behaviour of the whole is to some degree constrained by the properties of its components (upward causation), the behaviour of its components is also constrained to a certain extent by the properties of the whole. In other words, the whole has a causal influence on its constitutive parts. The behaviour of a cell is controlled both by the properties of its macromolecules and by the properties of the organ of which it is a part.

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

The idea of emergence and this conception of causation, which involves a vertical directionality in two opposite directions (upward and downward), are also associated with the idea of a layered model of the world: the natural world consists of and is stratified into hierarchical levels of organization, from the simple to the more complex, from subatomic particles to molecules to ecosystems and beyond (Kim, 1999). Within this order, the most fundamental—the physical—level has no ontological primacy over the others, and each level is characterized and governed by emergent laws that do not appear at the lower levels of organization. As a consequence, the organizing principles of the higher levels cannot be deduced from laws at lower levels. "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). In his lecture on light and life, Bohr expressed a similar idea: "life is consistent with, but underivable from physics and chemistry" (Bohr, 1933).

The increasing diffusion of concepts such as emergence and downward causation in biology is also a response to exaggerated claims about

the explanatory value of reductionism. However, these concepts need to be further refined to be more useful for scientists. For example, emergence is still a vague concept and the popular motto, "the whole is more than the sum of the parts", is too simplistic.

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Moreover, the idea of downward causation is still regarded as a paradox by many. It contravenes fundamental assumptions about the direction of material causation, which is supposed to proceed exclusively from the fundamental molecular level to more complex realms. As Kim (1999) has argued, "higher-level properties arise out of lower-level conditions, and without the presence of the latter in suitable configurations, the former could not even be there. So how could these higher-level properties causally influence and alter the conditions from which they arise?" Many other authors are inclined to interpret emergence and downward causation as epistemic concepts in the sense that hierarchical levels are regarded as levels of concepts and descriptions, instead of levels of phenomena and properties in the real world.

During the history of biology, the opposition between reductionist and more systemic approaches has taken different forms. A classical distinction is between functional biology and evolutionary biology (Mayr, 1961). It is clearly relevant to our discussion as molecular biology is ascribed to the former, whereas various systemic assumptions are embraced by the latter. The notion of complementarity has been used to highlight the relationship between their distinct modes of explanation (Dobzhansky, 1964; Simpson, 1964). Functional biology is, in fact, concerned with describing 'how things are' and the physicochemical causation of biological phenomena. Evolutionary biology, instead, deals with 'how things got to be the way they are' and their purpose at an organismal level.

In principle, by arguing for distinct but complementary levels of organization and

explanation, this relationship could be understood in light of Bohr's notion. In practice, what seems to prevent this is the lack of a single and coherent conceptual framework in which it can be implemented. In physics, complementarity concerns the logical relationship between mutually exclusive concepts: despite the fact that both concepts are needed to provide a complete description of the phenomenon, they cannot be considered simultaneously as this would create logical errors. However, both concepts still exist in the language of the same theoretical framework. The situation is different in biology. The two modes of explanation originate in two distinct and autonomous theoretical systems that are characterized by several conflicting assumptions and by a different notion of causation (Fantini, 1976). Thus, it is necessary to analyse whether these contrasting views could be integrated in one cohesive theoretical framework.

Other interpretations of complementarity could also be relevant. Complementarity might be considered as analysis and synthesis, which are favoured cognitive means of reductionism and holism, respectively. Analysis decomposes a whole into its constituent parts to produce detailed knowledge. It does not, however, claim that all explanatory power resides at the most basic level or that all could be reduced to the study of the parts, as does reductionism. Synthesis, conversely, is about reconstituting a whole from its parts and investigating how the constituents assemble to form compounds. However, it does not claim that the holistic aspect is sufficient to understand a given phenomenon. Analysis and synthesis are both essential to investigate a given phenomenon and complement each other on many levels.

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To cope with this analysis–synthesis implication, Morin (2007) has advocated the need for a circular model of explanation, according to which the viewpoint is shifted from the parts to the whole and back again: “The knowledge of the parts is not enough, the knowledge of the whole as a whole

is not enough, if one ignores its parts; one is thus brought to make a come and go in loop to gather the knowledge of the whole and its parts.”

Another related meaning of complementarity could be implied in the relationship between system and environment, as far as these are conceived as the viewpoints internal and external to the system. The French scientist Henri Atlan, who investigated biological organization in the light of information theory, has suggested that in a hierarchical biological system, it is the higher organizational level that can be regarded as the external observer. He explains that, owing to the existence of these distinct viewpoints, different ‘meanings’ can be assigned to the same phenomenon. For example, the meaning of ‘noise’ depends on the observational perspective: a decrease or an increase in information content, respectively, according to “whether one is interested in the information transmitted in the channel or in the information transmitted to the observer from a whole system in which the channel is part of a redundant communication network” (Atlan, 1974). Thus a cell, in order to avoid unforeseen and possibly deleterious consequences, attempts to suppress noise in its communication pathways, whereas the organ to which the cell belongs is able to assign a different and positive meaning to noise as a factor increasing variability and therefore overall fitness, provided that the cell is not destroyed.

Finally, the idea of complementarity could function as a general epistemological principle. For Prigogine & Stengers (1979), it reminds us of the perceptual, cognitive and linguistic limits of any human observer. The astonishing richness of reality exceeds any possible language or logics; the ‘assumed’ reality is therefore the result of a cognitive selection process by the observer. In order to ‘view’ something, something else has to be disregarded: “each philosophical idea and each scientific principle and theory not only opens up new vistas into the depths of reality unknown to us until now, but it also closes other avenues of theoretical thinking and discovering” (Meyer-Abich, 1955).

In other words, an epistemology that incorporates the notion of complementarity should be able to overcome the idea of an all-inclusive representation and acknowledge

that several viewpoints and distinct levels of explanation might be required for the understanding of a given phenomenon. If elaborated further, complementarity could have the potential to resolve many existing theoretical opposing views and to contrast the (Western) tendency towards disjunction—the opposition between reductionism and holism is an historical example of this tendency. It is perhaps interesting to note that other cultural or philosophical systems, such as those of ancient China, conceived the world as made by complementary couples of opposites and incorporated the idea of complementarity in their associated knowledge systems.

CONFLICT OF INTEREST

The author declares that he has no conflict of interest.

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