Biological Reductionisms

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The biological hierarchy

It has been widely noted that terrestrial life is organized in a hierarchical manner which may be sketched as follows.

Biosphere
Species
Organisms
Organs
Cells
Processes of replication
Genetic transcription
Biochemical cycles
Biomolecules
Molecules

In considering this diagram, several comments are in order. First, it is only the general nature of this hierarchy that is of interest, not the details. One might include fewer or more levels in the diagram or account for branchings into (say) flora and fauna or various phyla. Although such refinements may be useful in particular discussions, the present aim is to become acquainted with the general nature of a nonlinear dynamic hierarchy, so a relatively simple diagram is appropriate.

Second, the nonlinear dynamics at each level of description generate *emergent structures*, and nonlinear interactions among these structures provide a basis for the dynamics at the next higher level (18).

Third, the emergence of a new dynamic entity stems from the presence of a closed causal loop, which leads to positive feedback and exponential growth that is ultimately limited by nonlinear effects.

Finally, it should be noted that philosophers disagree about the ontological nature of emergent levels. Are they mere designations convenient for academic organization, or do they mark qualitatively different realms of reality? In attempting to answer this question, it is important to know whether the upper levels can be derived from lower levels, which brings us to a consideration of *reductionism.*

Bases for biological reductionism

Since the days of Galileo and Newton, the reductive program has been surprisingly successful in providing explanations for natural phenomena and is now widely accepted by the scientific community as the fundamental way to pose and answer questions. Basically, the reductive approach to understanding proceeds in three steps.

- *Analysis.* Assuming some higher-level phenomenon is to be explained, separate the dynamics of that phenomenon into *components*, the behaviors of which are to be individually investigated.
- *Theoretical formulation.* Through empirical studies and an exercise of imagination, develop a *theory* of how the components interact.
- *Synthesis.* In the context of this theory, *derive* the higher-level phenomenon.

Among the many aspects of nature that have fallen to this approach, one can mention planetary motion (based on the concepts of mass and gravity and on Newton's laws of motion), electromagnetic radiation (based on the concepts of electric charge, electric fields, and magnetic fields related through Maxwell's equations), atomic and molecular structures (based on the concepts of mass, electric charge, and Schrödinger's equation), hydrodynamics (based on the concepts of mass density, viscosity, compressibility, and the Navier–Stokes equations), and nerve impulse propagation (based on the concepts of voltage, membrane permeability, ionic current, and the Hodgkin–Huxley equations). Generalizing from such specific examples, the philosophical perspective of reductionism asserts that *all* natural phenomena can be understood in this manner (21).

Some, on the other hand, believe there exist natural phenomena that cannot be completely described in terms of lower-level entities—life being an outstanding example. In its more extreme form, this position is called *substance dualism*: the view that important aspects of the natural world do not have a physical basis. A less

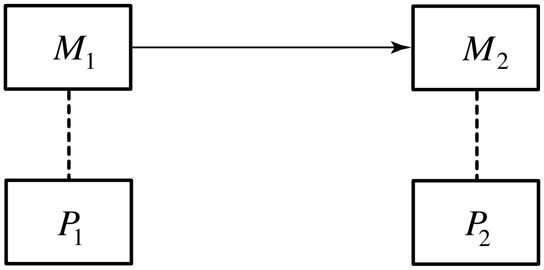

Figure 1: Higher-level phenomena and lower level properties. The causal interaction of higher-level phenomena (M_1 and M_2) that supervene on lower-level properties (P_1 and P_2))

salient position is *property dualism*, which asserts aspects of the physical world that cannot be explained in terms of atomic or molecular dynamics.

To a statement of belief there is no scientific response, but if we can agree on the physical basis of natural phenomena, the scope of the discussion narrows. Let us assume, therefore, that all natural phenomena *supervene* on the physical in the following sense. If the constituent matter is removed, the phenomenon in question disappears, or as philosopher Jaegwon Kim puts it ((15), p. 12): "Any two things that are exact physical duplicates are exact psychological duplicates as well." This position is called *physicalism.*

Among biologists, it is now widely accepted that the physicalist position holds for the phenomenon of life. If the atoms comprising a living organism are removed one by one, it will surely die. Thus two interesting questions are: *Does reductionism follow from physicalism?* and *Does physicalism allow property dualism?*

Since the 1980s, such questions have been carefully considered by Kim, who reluctantly concludes that physicalism does indeed imply reductionism and sits uneasily with property dualism (15). Let us briefly review his central argument with reference to Figure 1.

This figure represents a higher-level phenomenon (M_1) that supervenes on the lower-level physical properties (P_1), where supervenience is indicated by the vertical dashed line. In other words, if the properties P_1 are removed, then the phenomenon M_1 will disappear, with a similar relationship between P_2 and M_2.

Now suppose that there is observed to be a *causal relationship* between M_1 and M_2 (5), indicated by the horizontal arrow in Figure 1. Thus the initial upper-level observation of M_1 always leads to a corresponding upper-level observation of M_2. Because under the assumption of physicalism P_1 (P_2) must be present to provide a basis for M_1 (M_2), we could as well say that P_1 causes P_2, which is a formulation of the upper-level causality in terms of the lower-level properties. Furthermore, one could interpret the phenomenon M_1 (M_2) in terms of P_1 (P_2), thereby undercutting a position of property dualism.

In the view of physicist Steven Weinberg (21), the dashed lines in Figure 1 can be replaced by upward-directed arrows at every level of description that show the direction of reductive implication. These arrows ultimately emanate from the most fundamental element of physical reality (nowadays known as the "Higgs boson"). Such a perspective does not suppose it to be practical or currently possible to describe the dynamics of (say) a bacterium in terms of the fundamental fields and particles of physics but that it can be done "in principle."

Finally, it can be argued that even if reductionism turns out not to hold in all aspects of biological organization, it is still a prudent strategy for the majority of biologists to take as a working hypothesis. Why? Often the riddles of one generation become standard knowledge of the next, leaving the dualist (substance or property) ever in danger of giving up too soon on the search for reductive explanations.

Objections to reductionism

Clearly, biological reductionism based on physicalism is a serious philosophical position meriting careful response. Those who object to the reductionist position must offer more than mere intuition that it does not make sense. Concrete objections and alternative suggestions must be provided. What are some of these objections?

CONSTRUCTIONISM VERSUS REDUCTIONISM. Interestingly, the physics community is itself divided on the merits of reductionism. In general, theoretical physicists agree with Weinberg, whereas condensed-matter physicists—those who grapple with the details of understanding aggregates of matter—tend toward a somewhat different view. Thus Philip Anderson asserts that (2):

> the reductionist hypothesis does not by any means imply a "constructionist" one: The ability to reduce everything to simple fundamental laws does not imply the ability to start from those laws and reconstruct the universe. In fact the more the elementary-particle physicists tell us about the nature of the fundamental laws, the less relevance they seem to have to the very real problems of the rest of science, much less to those of society. The constructionist hypothesis breaks down when confronted with the twin difficulties of scale and complexity.

What is it about "scale and complexity" that creates problems for the constructionist hypothesis?

IMMENSE NUMBERS OF POSSIBILITIES. Computational difficulties arise from the fact that the number of possible emergent structures at each level of the biological hierarchy is too large to be counted. To sharpen ideas in theoretical biology, physicist Walter Elsasser introduced the term *immense* to characterize a number that is both finite and greater than a *googol* (10^{100}) and thus inconveniently large for numerical studies (6; 8).

To see this in detail, consider the proteins. These biochemical workhorses are valence-bonded strings of amino acids, each of which is designated by an underlying DNA code. Because there are 20 different amino acids and a typical protein comprises some 200 of them, the number of possible proteins is greater than 20^{200}, which in turn is greater than a googol. Thus the number of possible protein molecules is immense.

What does this mean? All the matter in the myriad galaxies of the universe falls far short of that required to construct but one example of each possible protein molecule (8). Throughout the eons of life on earth, in other words, most of the possible protein molecules have never been constructed and never will be. Those particular proteins we know were selected in the course of evolution through a succession of historical accidents that are consistent with but not governed by the laws of physics and chemistry.

So it goes at other levels of the biological hierarchy. The possible number of new entities that can emerge from each level—to form a basis for the dynamics of the next level—is immense, suggesting that happenstance, rather than basic laws of physics, guides important aspects of the evolutionary process (13).

It follows that biological science is fundamentally different from physics. The physical scientist deals with *homogeneous* sets, in which all of the elements are identical. Thus a physicist has the luxury of performing as many experiments as are needed to establish *laws* governing the interactions among electrons, protons, neutrons, and atoms. In the biological and social sciences, on the other hand, the number of possible members in any empirical category is immense, so experiments are necessarily performed on *heterogeneous subsets* of the classes of interest. Because the elements of heterogeneous sets are never exactly the same, causal laws cannot be determined with the same degree of certainty in the biological and social sciences as in the physical sciences.

In other words, psychologists establish *rules* rather than laws for interpersonal interactions, and your doctor can only give you the probability that a certain pill will make you feel better. At the levels of biology and social science, therefore, the horizontal arrow in Figure 1 should often be drawn fuzzy or labeled with a percentage of reliability.

THE NATURE OF CAUSALITY. Whether one is concerned with establishing dynamical laws in the physical sciences or seeking corresponding rules in the biological and social sciences, the notion of *causality* requires careful consideration (5). Some 24 centuries ago, Aristotle put it thus (3): "We have to consider in how many senses 'because' may answer the question 'why'." As a "rough classification of the causal determinants (*aitiai*) of things," he suggested four types of cause.

- *Material cause.* Material cause stems from the presence of some physical substance that is needed for a particular outcome. Aristotle suggested that bronze is an essential factor in the making of a statue, but the concept is more general. As an example, note that the epidemic of gunshot wounds in the United States is materially caused by the large number of loaded handguns in private homes, just as alcoholism in Russia is materially caused by the availability of vodka.

- *Formal cause.* The material necessary for some outcome must be given the appropriate form. Thus, "the interval between two notes is not an octave unless they stand in the ratio of 2 to 1." Other examples of formal cause are easily imagined: the blueprints of a house are necessary for its construction, the DNA sequence of a particular gene is required for synthesis of the corresponding protein, and a violinist needs the score to play a concerto.

- *Efficient cause.* For something to happen, according to Aristotle, there must be an "*agent* that produces the effect and starts the material on its way." Students of physical science deal primarily with efficient causes during their introductory courses in dynamics. Thus, a golf ball moves through the air in a certain trajectory because it was struck at a particular instant of time by the head of a club, and a radio wave is emitted in response to the current flowing through an antenna.

- *Final cause.* Often, things come about because they are desired by some intentional organism: a house is built—involving the assembly of materials, reading of plans, and pounding of nails—because someone wishes to have shelter from the elements. Such purposive answers to the question "why" are problematic in the biological sciences.

For those interested in viewing causality from a mathematical perspective, the following paraphrasing of Aristotle's definitions may be helpful.

(1) At a particular level of the biological hierarchy, *material causes* might be time or space averages over dynamic variables at lower levels of description that enter as slowly varying *parameters* at the level of interest.

(2) Again, at a particular level of the biological hierarchy, *formal causes* might arise from values of dynamic variables at higher levels of description that enter as *boundary conditions* at the level of interest.

(3) An *efficient cause* is represented by the *stimulation-response* formulation. Following Galileo, this is the primary sense in which physical scientists currently use the term causality (5).

(4) In mathematical terms, it is not clear (to me, at least) how one might formulate a *final cause*.

Although this classification seems tidy, reality is more intricate. Thus Aristotle noted that causes may be difficult to sort out in particular cases, with several often "coalescing as joint factors in the production of a single effect" (3).

Distinctions among these "joint factors" are not always easy to make. A subtle difference between formal and efficient causes arises from consideration of the metaphor for Norbert Wiener's *cybernetics*: the steering mechanism of a ship (22). If the wheel is connected directly to the rudder (via cables of some type), then the forces exerted by the helmsman's arms are the efficient cause of the ship executing a change of direction. For larger vessels, however, control is established through a servomechanism in which the position of the wheel merely sets a pointer that indicates the desired position of the rudder. The forces that move the rudder are generated by a feedback control system that minimizes the difference between the actual and desired positions. In this case, one might say that the position of the pointer is a formal cause of the ship's turning, with the servomotor of the control system acting as the efficient cause.

When a particular protein molecule is constructed within a living cell, sufficient densities and varieties of amino acids in the vicinity of the messenger RNA are material causes. The DNA code, controlling which amino acids are to be arranged in what order, is a formal cause. Lastly, the chemical (electrostatic and valence) forces acting among the constituent atoms are efficient causes. Because far more intricate situations are readily imagined, the reductionist should remain aware that the causal relations sketched in Figure 1 are not at all simple in the biological sciences.

For mathematicians, it is not surprising for several different types of causes to be involved in a single event. We expect that parameter values, boundary conditions, and forcing functions will all combine to influence the outcome of a given computation.

What other complications of causality are anticipated?

NONLINEAR CAUSALITY. In mathematics, the term "nonlinear" is defined in the context of relationships between causes and effects. Suppose that a series of experiments on a certain system have shown that cause C_1 gives rise to effect E_1; thus

$$C_1 \to E_1 \,,$$

and similarly

$$C_2 \to E_2$$

expresses the relationship between cause C_2 and effect E_2. This relation is *linear* if

$$C_1 + C_2 \to E_{12} = E_1 + E_2 \,. \qquad (1)$$

If, on the other hand, E_{12} is *not* equal to $E_1 + E_2$, the effect is said to be a *nonlinear* response to the cause.

Equation (1) indicates that for a linear system the cause can be arbitrarily divided into convenient components (C_1, $C_2, \ldots, C_n$), whereupon the effect will be correspondingly divided into (E_1, $E_2, \ldots, E_n$). Although convenient for analysis, this property is seldom found in the biological world.

Far more common is the nonlinear situation, where the effect from the sum of two causes is not equal to the sum of the individual effects. The whole is not equal to the sum of its parts. Nonlinearity is less convenient for the analyst because multiple causes interact among themselves, allowing possibilities for many more outcomes and confounding the constructionist. For this reason, however, nonlinearity plays a key role in the course of biological evolution.

THE NATURE OF TIME. Causality is intimately connected with the way we view time—thus, the statement "C causes E" implies that E does not precede C in time (5)—yet the properties of time may depend on the level of description (10; 11; 23). The dynamics underlying molecular vibrations are based on Newton's laws of motion, in which time is *bidirectional*. In other words, the direction of time in Newton's theoretical formulation can be changed without altering the qualitative behavior of the system. At the level of biological processes, on the other hand, time is unidirectional. In appealing to Figure 1, therefore, the reductionist must recognize that the nature of the time used in formulating the causal relationship between P_1 and P_2 may differ from that relating M_1 and M_2.

DOWNWARD CAUSATION. The doctrine of reductionism assumes that causality acts upward through the biological hierarchy, where the causality can be interpreted as both efficient and material. Formal causes, on the other hand, can act *downward* because variables at the upper levels of a hierarchy can place constraints on the dynamics at lower levels (1).

A dramatic example of downward causation occurred eons ago when certain bacteria began to harvest and store energy from the sun's light, creating atmospheric oxygen as a poisonous waste (17). The presence of oxygen in the atmosphere led to the emergence of the animal kingdom, in which we humans participate. Other examples of downward causation include modifications of DNA codes caused by interactions among species, germination of an ovum following sexual activity, the disintegration of an organism upon death, and so on.

Although such examples seem to provide convincing evidence of downward causation, the means through which it acts are not well understood. To this end, Claus Emmeche and his colleagues have defined three sorts of downward causation, as follows (9).

- *Strong downward causation* (SDC). Under SDC, it is supposed that upper-level phenomena can act as efficient causal agents in the dynamics of lower levels. In other words, upper-level organisms can modify the physical and chemical laws governing their molecular constituents. Presently, there is no empirical evidence for the downward action of efficient causation, so SDC is almost universally rejected by biologists.

- *Weak downward causation* (WDC). WDC assumes that the molecules comprising an organism are governed by some nonlinear dynamics in a phase space, having attractors—which include the living organism—each with a corresponding basin of attraction. Death, in this formulation, is but another of the attractors shared by the interacting molecules, and a physician's job is to keep the molecules of a patient within the basin of the living state. (Unfortunately, the basin shrinks as we age, making the task ever more difficult.)

  Because many examples of such nonlinear systems have been carefully studied both experimentally and theoretically (18), there is little doubt about the scientific credibility of this means for downward causation. Building on the seminal suggestions of Alan Turing (20), biologists Stuart Kauffman (14) and Brian Goodwin (12) have presented detailed discussions of ways that WDC influences the development and behavior of living organisms.

- *Medium downward causation* (MDC). Although accepting WDC, supporters of MDC go further in supposing that higher-level dynamics (e.g., the emergence of a higher-level structure) can modify the local features of an organism's phase space through the downward actions of formal causes. (An example of MDC is provided by the *automatic frequency control* of an FM radio receiver. Here, a time average amplitude of the demodulated signal is used to adjust the input tuning capacitor, leading to the familiar experience of locking onto a particular signal.)

  In biology, MDC opens the possibility of closed causal loops spanning several layers of the hierarchy. In this picture, an organism emerges from the underlying phase space, which it in turn modifies. Such closed causal loops can be represented as a positive feedback diagram:

$$\begin{tikzcd} \textbf{Emergent organism} \arrow[d, shift right] \\ \textbf{Underlying phase space} \arrow[u, shift right] \end{tikzcd}$$

  Over two decades ago, biochemists Manfred Eigen and Peter Schuster suggested that closed causal loops around at least three layers of dynamic description were necessary for the emergence of living organisms from the oily scum of the Hadean oceans (7).

Open Systems. Biological organisms are *open systems*, requiring a steady input of energy (sunlight or food) to maintain their metabolic activities. As a simple example of an open system, consider the flame of a candle. Computing the propagation velocity of the flame (v) from considerations of power balance (18), it is possible to establish a rule for where the flame will be located at a particular time. Corresponding to

$$M_1 \rightarrow M_2 \,,$$

in Figure 1, one such rule is the following. If the flame is at position x_1 at time t_1, then it will be at position

$$x_2 = x_1 + v(t_2 - t_1)$$

at time $t_2 > t_1$.

Because the flame is an open system, a corresponding relation

$$P_1 \rightarrow P_2$$

cannot be written—even "in principle"—for the physical substrate. This follows from the fact that the physical substrate is *continually changing* (4). The molecules of air and wax vapor comprising the flame at time t_2 are entirely different from those at time t_1. Thus, the detailed positions and speeds of the molecules present in the flame at time t_2 are unrelated to those present at time t_1. What remains constant is the flame itself: a *process*.

Closed Causal Loops. In his analysis of reductionism, Kim also fails to grasp the concept of a closed causal loop, asking: "How is it possible for the whole to causally affect its constituent parts on which its very existence and nature depend?" (16). Causal circularity, he claims, is unacceptable because it violates the following "causal-power actuality principle."

> For an object, x, to exercise, at time t, the causal/determinative powers it has in virtue of having property P, x must already possess P at t. When x is being caused to acquire P at t, it does not already possess P at t and is not capable of exercising the causal/determinative powers inherent in P.

There are two replies to this argument, one theoretical and the other empirical. From a theoretical perspective, Kim is led astray by supposing that a coherent structure somehow pops into existence at time t, which would indeed be surprising. In Kim's notation, both x and P are functions of time (t), which may be related as

$$\begin{aligned} \frac{dx}{dt} &= F(x, P)\,, \\ \frac{dP}{dt} &= G(x, P)\,, \end{aligned}$$

where F and G may be general nonlinear functions of both x and P. (For example, the time scales of F and G might be very different, allowing P to remain approximately constant during the dynamics of x.) The emergent structure is not represented by $x(t)$ and $P(t)$ (which are functions of time), but by x_0 and P_0, satisfying

$$\begin{aligned} 0 &= F(x_0, P_0)\,, \\ 0 &= G(x_0, P_0)\,. \end{aligned}$$

Assuming that x_0 and P_0 are an asymptotically stable solution of this system,

$$\begin{aligned} x(t) &\to x_0\,, \\ P(t) &\to P_0\,, \end{aligned}$$

as $t \to \infty$, exemplifying the establishment of a dynamic balance between downward and upward causations. Thus, Kim's causal-power actuality principle is recognized as an artifact of his static analysis of an essentially dynamic situation.

Applied science offers many examples of positive feedback and subsequent emergence of coherent structures (18). Engineers employ negative feedback to control the performance of amplifiers, routinely designing closed causal loops in which a signal from the output terminals is carried back to the input. Occasionally, this feedback signal becomes positive rather than negative and leads to unwanted oscillations (called "singing") that can be viewed as emergent structures.

In the physical sciences, corresponding emergent structures include tornadoes, tsunamis, and Jupiter's Great Red Spot, among many others (18). A biological example is provided by cellular reproduction, wherein a DNA code is necessary to produce protein molecules and proteins are needed for transcription of the code.

Conclusion

Although based on careful arguments, the belief that a reductive perspective is relevant for living organisms faces serious challenges that accept the doctrine of physicalism. Among such objections are: the immense intricacy of biological hierarchies, the uncontrolled nature of causality in nonlinear dynamics, the unidirectional nature of time in biological systems, the implications of downward causation, and the special properties of open systems. Similar challenges are faced by those who support reductive formulations in neuroscience (19).

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