

Life in the Interstices: Systems Biology and Process Thought

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Insights gained by contemporary biology should interest philosophers, whether or not they agree with E. O. Wilson's statement (2006, 106):

[Biology] has become foremost [among the sciences] in relevance to the central questions of philosophy, aiming to explain the nature of mind and reality and the meaning of life.

Clearly, philosophy of science finds significance in current biology. Vigorous discussions of levels of selection, mechanistic explanation, and other technical topics are now in progress. However, Wilson suggests (correctly, in my view) that philosophers other than philosophers of science (e.g., metaphysicians) also should take insights gained in recent biological research into account. In particular, investigation of how interactions between components of biological entities lead to the behaviors and properties of those entities — the currently active field of “systems biology” (Klipp 2005) — will repay philosophical attention. As eminent bioinorganic chemist R. J. P. Williams (2005) puts it:

Studies of biological sciences can be approached in two ways: reductively, as in molecular biology, or holistically, as in systems biology. ...The future lies with the second [way] as the first is nearing completion.

The research program that grew into contemporary systems biology developed in the decades just before the middle of the 20th century. The main features of the quantum interpretation of microphysics and Whitehead's “philosophy of organism” also matured in the same period. C. H. Waddington (1959), a pioneer of systems biology, recognized that

Whitehead’s philosophy was directly relevant to what he called “theoretical biology.” Many authors have called attention to connections between quantum-mechanics and Whitehead’s philosophy. The possible relevance of both quantum considerations and process thought to the philosophy of mind has often been discussed (e.g., Eastman 2004; Gunter, this volume). However, as Atmanspacher (2006) remarked:

It turns out that the implementation of events in Whitehead’s sense into quantum theory is everything else than straightforward. The even more difficult inclusion of mental time remains mostly unaddressed.

This paper reviews Whitehead’s doctrine that indeterminacy is essential for both life and mind, and suggests that necessary indeterminacy is more likely to arise from networks of relationships (such as those considered by systems biology) rather than from quantum-mechanical features of microphysics. I also sketch a neo-Whiteheadian metaphysical approach (Process Structural Realism, PSR) that can incorporate both the findings and the spirit of systems biology.

I

Whitehead rejected dualistic metaphysical approaches that have long history, widespread influence, and vigorous present defenders (e.g., van Inwagen 2002). But Whitehead’s own notions of life and consciousness seem to be subject to interpretations that tend to shade toward dualism. In this respect, an especially problematic feature of Whitehead’s system is his doctrine that:

...life is a characteristic of ‘empty space’ and not of space occupied by any corpuscular society.... Life lurks in the interstices of each living cell, and in the interstices of the brain. ([1929] 1978, 105-106)

To the unwary, this might seem to suggest that some microscopic entity (perhaps a *res vivens*) jumps from cavity to cavity inside each biological cell, and some kind of homunculus (*res cogitans*) cavorts inside the skull of each conscious human individual. To avoid these notions, so foreign to the spirit of Whitehead’s project, one must recall that Whitehead replaced the notion of ‘absolute’ space and time that Newton had laid out in his *Scholium* (and which still provides an unexamined basis for much thinking, even among philosophers) with the concept of “the extensive continuum” – a plenum of possibilities. For each actual entity in the course of its

concrecence, the infinite potentiality of the extensive continuum is reduced to a definite finite actuality by antecedent actual occasions that constrain the concrecent entity in its coming-to-be.

Continuity concerns what is potential; whereas actuality is incurably atomic. ([1929] 1978, 61)...An extensive continuum is a complex of entities united by the various allied relationships of whole to part, and of overlapping so as to possess common parts, and of contact, and of other relationships derived from these primary relationships. The notion of ‘continuum’ involves both the property of indefinite divisibility and the property of unbounded extension. ([1929] 1978, 66). Actual entities atomize the continuum. This continuum is in itself merely the potential for division: an actual entity effects this division. ([1929] 1978, 67)

For living entities, however, constraints arising from antecedent actualities are not totally effective.

The emergence of life is ... a bid for freedom on the part of organisms, a bid for a certain independence of individuality with self-interest and activities not to be construed purely in terms of environmental obligations. ([1927] 1985, 65.)

It is essential to Whitehead’s notion of life that some flexibility always remains to be resolved by the self-creative decision of each living organism. Isabelle Stengers (forthcoming) emphasizes the importance of “non-conformal propositions” (possibilities not fully specified by past history and a particular environment) in achieving the novelty in concrecence that life requires. I now suggest that what Whitehead calls “‘empty’ space” should be considered to be a metaphorical space of indeterminacy, rather than some gap in extension in Newtonian absolute space. In this view, what Whitehead refers to as “interstices in the brain” would be real possibilities for mental coherence that are not yet realized — and therefore are available for prehension in the course of self-creation of a conscious superject. Those interstices should not be regarded as otherwise-unoccupied spatial volumes within a human skull but rather as unrealized possibilities for coherent neural activity.

... It seems as if the last delicacies of feeling require some element of novelty to relieve their massive inheritance from bygone system. Order is not sufficient. What is required is something much more complex. It is order entering on novelty so that massiveness of order does not degenerate into mere repetition and so that the novelty is always reflected upon a background of system.... It is by reason of

the body with its miracle of order, that the treasures of the past environment are poured into the living occasion. The final percipient is perhaps some thread of happenings wandering in ‘empty’ space amid the interstices of the brain ([1929] 1978, 339).

Whitehead’s doctrine of “order entering on novelty” may be regarded as a direct anticipation of an important concept of systems biology — that evolutionary systems generally tend towards “the edge of chaos” (Kauffman 1993).² It has been found that evolutionary systems generally tend towards an organized state that differs from disorderly regimes only in relatively small variations. Each life-form that is not stuck in an evolutionary backwater³ has two characteristics. Every successful species has properties that reproduce successfully from generation to generation. Each type of organism also has some features that result in occasional large changes. Most such major alterations do not actually lead to higher fitness — and therefore have no long-term consequences. However, from time to time, such a jump will lead to significantly higher fitness — an evolutionary advance will have occurred. This coupling of characteristics (general conservatism and occasional adventurousness) corresponds to a situation where order prevails, but which is similar to a disordered (chaotic) regime. A variety of evidence shows that evolutionary systems generally tend to such “edge-of chaos” states. Whitehead’s notion of the essential connection between freedom and life (“order entering on novelty”) anticipates this recently-developed conclusion of systems biology.

II

Since biological systems are made up of components that follow physical and chemical regularities, how could the indeterminacy that Whitehead’s view requires arise? Many authors have suggested that such indeterminacy may arise from quantum-mechanical features of microphysics. Penrose (1999) and Hameroff (2002) have provided an unusually detailed model of one way that sub-microscopic quantum-mechanical phenomena might be relevant to human mental functioning. They propose that the network of micro-tubules that exist within each individual neuron may provide their contents sufficient isolation from their surroundings to permit “quantum superimposed mass movements which are well insulated from their environment. It may well be that within the tubes there is some kind of large scale quantum coherent activity, somewhat like a computer.” (Penrose 1999, 131-132). A small-scale example

of the type of coordinated mass motion that this model requires has been reported to account for rapid synchronization of remote active sites in a specific enzyme (Frank 2004). In this case, the surface of a catalytic protein molecule includes a region in which amino-acid residues are so organized that simultaneous shifts of protons occur between neighboring atomic centers along an extended line of such centers (a “proton wire”). This results in effective transfer of a hydrogen nucleus to a quite remote site in a remarkably short time. Identification of such coordinated movement of atomic nuclei indicates that the Penrose-Hameroff model is not totally impossible, but also shows the tremendous degree of self-organization that would be required within microscopic tubules for that mechanism for quantum neuroscience to be effective. The properties of non-locality, quantization, and computational power that are sought in quantum neuroscience are certainly available more readily by other means.

III

Generally, the state of any natural system depends on relevant boundary conditions. When we observe two of a given kind with different properties (say one object has a blue color, and another otherwise identical thing is red) we often suppose that some difference in conditions accounts for the difference in properties. Koutrofinis (this volume) points out that “bistable systems” are common in systems biology, and are philosophically interesting. In each such case, objects of a single type have quite different properties (such as being blue or being red) under conditions that are *identical* in all particulars. It turns out that what differs between the two states is the *history* of the systems. By *what means* identical conditions are arrived at determines the properties of each situation. Otherwise identical conditions may correspond to two quite different property-sets depending on past history. This remarkable situation is not some peculiarity of living organisms. Similar behavior (called ‘hysteresis’) is encountered in chemical and physical systems that are only moderately complicated — and certainly are much simpler than any biological system.

Geissler (1981) described a rather simple chemical system that illustrates main features of bistability. Two solutions are pumped into the lower parts of a reaction chamber that contains a stirring device (a ‘continuously stirred tank reactor,’ CSTR). The solution thus produced makes its way to the top of the CSTR chamber and then exits through an overflow tube. Suppose the experiment starts with the pump operating slowly (say at a rate of 0.1, in appropriate units).

Under those conditions, the solution in the chamber (and in the exit stream) is blue. If the pump is gradually speeded up, the solution in the cell remains blue until a rather high pump rate (say, of 9 units) is reached, then the solution rapidly becomes red. The transition pump-rate is quite precisely defined. In a typical experiment, the solution remains blue at a pump-rate of 8.999 units, but is definitely red at a pump-rate of 9.000 units. What is remarkable about this system is that when the experiment starts with a high pump-rate of 10 units (the solution is definitely red) and the pump-rate is gradually lowered, the solution in the reaction chamber *remains red* long after the pump-rate is lowered well below 9 units. The transit from red to blue occurs only at a quite low value of pump rate, say 1.0 units. (The solution will remain red indefinitely if the pump-rate is set at 1.001 units.) For the extensive region of pump-rate variation between 1.000 and 8.999 units the solution in the exit-stream and in the chamber may be *either blue or red*, depending on the past history of the system!

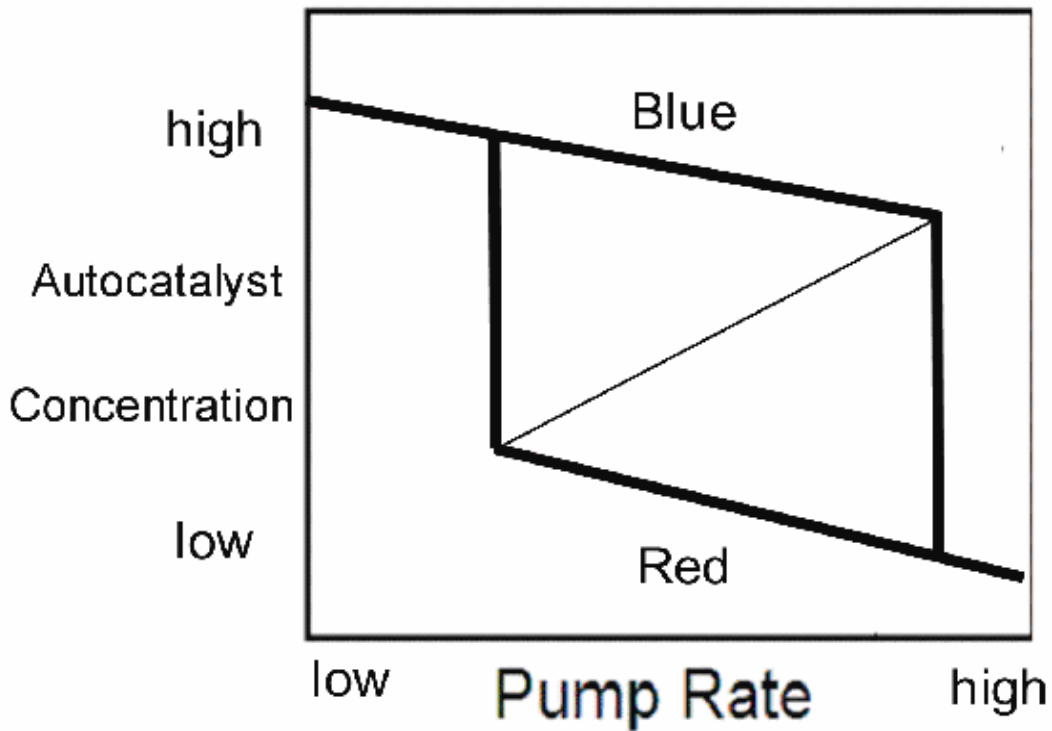


Figure 1 Schematic diagram of the behavior of a bistable chemical system in a continuously-stirred tank reactor. At high pump-rates, the system has low concentration of autocatalyst and a red color. At low pump-rates, the system has high autocatalyst concentration and a blue color. At intermediate pump-rates, the system may be either red or blue, depending on whether the intermediate pump-rate was reached by increase or decrease.

The chemistry involved in this behavior is well understood (e.g., Scott 1994, 53-58). When chemical reactions involve a process that gets progressively faster as it proceeds (autocatalysis) and some second process slowly destroys some necessary component of the first reaction, then there may be *two* stable non-equilibrium steady states (labeled blue and red in the figure) as well as an unrealizable unstable steady state (thin diagonal line in the figure). At a constant pump rate, a system that exists in either stable steady state will stay in that state unless some external factor takes the system beyond the unstable state.⁴ What accounts for this behavior is the concentration of one especially important chemical, called “the autocatalyst” (low in the red state, high in the blue). The rate of formation of this autocatalyst is slow, but once its concentration exceeds a critical value (the autocatalyst concentration characteristic of the unstable state) the color of the solution promptly changes. When the pump operates at a high rate, the residence time of the solution inside the reactor is not sufficient for enough autocatalyst to be generated to reach the critical concentration value. If the pump slows, reaction solutions remain in the reactor longer and more autocatalyst is produced. The transition of color occurs when autocatalyst concentration exceeds the critical value.. When the pump is operating slowly, ample autocatalyst is generated and the system stays in the blue steady state. If the pump is speeded up from a low value, the second process may destroy more autocatalyst than is produced, and the autocatalyst concentration declines. Eventually, a pump-rate is reached at which autocatalyst concentration falls below the critical value and the blue to red transition occurs. The pump-rate at which this blue to red change occurs with pump-rate increasing is significantly higher than the pump-rate that corresponded to the red to blue change in the experiment with pump-rate decreasing.

A question that arises in all bistable situations is: How is one state or the other to be reached?⁵ This question is related the medieval conundrum known as “Buridan’s Ass”. Does a hungry donkey starve when placed precisely midway between two identical bales of hay?⁶ On what basis do biological systems, and individual biological organisms, resolve ambiguities? By what means do natural systems settle on one of two alternative states (blue or red, say) in situations of bistability — when either of two states is compatible with the underlying conditions of the system? One approach to this question is to assume that if there is an “action,” there must be an “actor” — every incident of apparent agency may be considered to imply the existence of an agent. On this view, if a selection is made, someone or something must have decided. This

view is consistent with features of human mentality that have long evolutionary history. The harm an animal suffers in falsely identifying an agent that does not in fact exist is generally much less than the evil that would result if clues indicating a present predator were ignored. False positives are less risky than incorrect negatives.

An alternative approach to the question of how systems wind up on one of two possible results builds on Whitehead’s observation:

However we fix a determinate entity, there is always a narrower determination of something which is presupposed in our first choice. Also there is always a wider determination into which our first choice fades by transition beyond itself. ([1925] 1967 92)

Clearly, biological organisms are composed of subsystems (e.g., digestive systems, organs, tissues, cells, molecules...) that have greater or lesser degrees of integrity. Just as clearly, each biological organism is a component of larger units (breeding groups, broods, swarms, local ecologies, regional ecosystems...). Each of these persistent coherences, at both smaller and larger levels of size, is characterized by “homeostasis” – intricate balance of dynamic processes that maintains approximate constancy of overall properties under a range of environmental conditions. Further, each biological organism is the outcome of a long historical process of development; each species results from millennia of evolution. At each of the myriad stages of that evolutionary history, and at each of the many critical points of growth and development of each individual organism, units (of any and every level) that were not able to sustain homeostasis under whatever conditions actually prevailed failed to persist and/or to leave progeny.

Each biological network of processes involves features that are the functional equivalent of switches – variation in external conditions or of internal state gives rise to transitions of processes from one dynamic condition to another – from “off” to “on” or the reverse. Normally, such biological switching involves bistable systems. What may appear to be a basic ambiguity or indetermination of the state of an entity at one level may well be a feature that is intrinsic to a control network at another level. Bistable systems are relatively simple examples of coherent networks of dynamic processes. Those same bistable systems are also integral parts of more complex and larger dynamic networks. The characteristics and requirements of inclusive networks must be taken into account in understanding the factors that determine the state of a specific bistable system at a particular time. Chemists and other scientists can easily generate

models of bistable systems that are largely independent of their environments. In natural systems such as those studied in systems biology, bistable systems (themselves networks of dynamic process of less-inclusive coherences) are quite generally functional parts of more-inclusive entities. Those larger networks must be taken into account in any attempt to describe why a particular bistable network functions as it does.

When the function of a network is unchanged over a range of values of the parameters that characterize that network, the network is said to be “robust” (Wagner 2005). In the CSTR experiment described above, quite similar results are obtained with solutions that are only approximately the same in concentration.⁷ Another kind of robustness can be seen in “neural networks” — combinations of computing units have some similarities to how neurons may be connected in the human brain. (Cattell 2006, 55-70) In such cases, the configuration in which units are connected is more significant than the properties of the individual units. Robustness is more the rule than the exception in the many classes of networks described in systems biology

Persistence of an inclusive (‘upper-level’) network requires that included (‘lower-level’) networks continue to function within certain tolerances. Lower level networks may be robust enough to have large degrees of flexibility — considerable lower-level variation may be undetectable in upper-level functioning. There may well be room for considerable variation among the details characteristic of the lower-level system. The robustness of networks can provide the ‘empty’ space and interstices (indeterminacy) that Whitehead’s notions both of life and of consciousness require. Reasoning that involves network stability as a central concept is not as familiar as is discourse in terms of substantial things. Behavior of networks of processes displays strange and counterintuitive behavior, reminiscent of the problems and paradoxes that engaged early students of quantum mechanics. It seem much more likely that the properties of networks of dynamic relationship give rise to both mental and microphysical phenomena, rather than that mental phenomena result from some peculiarities of microphysics..

Understanding of complex networks has advanced rapidly in recent years, aided by progress in computer technology and also by advances in mathematics (e.g., Klipp 2005). This progress in nonlinear dynamics has contributed to major conceptual shifts in several scholarly fields. For instance, in economics, the myth of *homo economicus* — a fully rational agent who acts on the basis of complete information and pre-established values (utilities) — is being replaced by a view that envisions economic agents as *emerging* from dynamics of strategic

interactions conducted under uncertainty (Bowes 2004, Beinhocker 2006). Philosophical understanding of progress in systems biology will also require attention to what may seem to be arcane details of nonlinear dynamics.

IV

The long-running discussion of scientific realism seems to have entered a structuralist phase that seems quite congenial to process philosophy. Elsewhere (Earley 2006a, forthcoming A, forthcoming B) I have developed aspects of an ontological approach that seems capable of dealing with concepts, methods, and results of systems biology and which also shares the basic intellectual thrust of research in that discipline. The main point of this approach is that when a group of processes achieves such closure that a set of states of affairs recurs continually, then the effect of that coherence on the world differs from what would occur in the absence of that closure. Such altered effectiveness is an attribute of the system as a whole, and would have consequences. This indicates that the network of processes, as a unit, has ontological significance. Whenever a network of processes generates continual return to a limited set of states of affairs, the system may function as a “whole”— with respect to appropriate interaction partners. The balance achieved by the processes provides the form of definiteness of a unified agent. The causal powers of such coherent aggregates are indeed just the powers of the “constituents acting in concert” (Merricks 2001). However, the components act in concert in the specific way they do *only because of* their inclusion in the closed set of interactions that defines the coherence. This renders the causal powers of the coherence defined by that closure non-redundant, and hence the coherence, as a unit, is ontologically significant. The form of definiteness that provides internal coherence also grounds external efficacy of the societal aggregation. The closure is a *structural* feature of the coherence — possibly, but not necessarily, apparent in spatial structuring. One can show (Earley 2006b)⁸ that every such coherence is the representation of a mathematical “group” or “semi-group.” What is fundamental is achievement of effective coherence — the level of size on which that achievement occurs is irrelevant. Combinations of processes produce effects that are not simply attributable to the constituents. Whenever that efficacy is relevant,⁹ non-redundant causality warrants recognition of those coherences as ontologically significant. This ontology is a variety of structural realism — related to Ontological Structural Realism (OSR) (French 2003), but it is also a kind of process

philosophy. The designation “Process Structural Realism” (PSR) seems appropriate. This approach can provide a unified account that includes quantum microphysics, systems biology, and the philosophy of organism — without reducing any of these to another.

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Endnotes

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- 1 Mailing address: 502 W Broad St, Apartment 501, Falls Church, VA 22046-3247, USA. earleyj@georgetown.edu
 - 2 It is usual to represent the state of any evolutionary system as a point on a multidimensional ‘fitness landscape.’ (This is based on a map that has one dimension for each of the many factors that influence the reproductive success — the “fitness”— of that system. The fitness of a system is represented by a height above the plane of such a map.) Such a landscape is analogous to a relief model of a mountain range. Usually, such fitness landscapes are ‘alpine’ — with sharp peaks, deep ravines, and few relatively even plateaus. More-fit systems necessarily out-reproduce less-fit ones (reproductive success under the conditions that prevail is identical with fitness). Therefore, evolutionary development by gradual incremental alteration always leads to higher fitness. That is, evolutionary systems necessarily climb to higher altitudes on a fitness landscape; they always move up-hill.

Therefore, the eventual fitness of each system will be limited by the height of the ‘local peak’ on the side of which that system started, even if the same landscape contains peaks that correspond to much higher fitness. Those higher peaks will not be accessible to a system that has already moved to the top of the hill on which it started. Downhill migration on an unchanging fitness landscape is never possible for evolutionary systems, but there is no way to reach a alpine peak from a distant lowland by surface travel without sometimes going down a slope. In order to escape evolutionary dead-ends (becoming stranded on low fitness peaks), biological systems need mechanisms that lead to non-incremental (discontinuous) change. This sketch assumes that fitness landscapes are constant, i.e., not influenced by changes in the environment or variations in other species. Closely-related conclusions can be reached without this unrealistic simplifying assumption.

- 3 The lamprey seems to have reached such an evolutionary dead end. Fossils indicate that ancient forms were indistinguishable from present lampreys.
- 4 If a perturbation large enough to take the system beyond the unstable state were to occur, then the system would change to the alternate stable condition (from blue to red or the reverse).
- 5 As the ancients said: “Which road leads to Delphi?”
- 6 There is little comfort in the advice attributed to Yogi Berra: “When you come to a fork in the road, take it!”
- 7 This experiment is sufficiently robust that “bartender’s accuracy” suffices.
- 8 This involves Cayley’s theorem.
- 9 Whether or not coherence is ontologically significant depends on the detailed characteristics of entities with which that coherence interacts.