Self-Organization and Irreducibly Complex Systems: A Reply to Shanks and Joplin*

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Some biochemical systems require multiple, well-matched parts in order to function, and the removal of any of the parts eliminates the function. I have previously labeled such systems "irreducibly complex," and argued that they are stumbling blocks for Darwinian theory. Instead I proposed that they are best explained as the result of deliberate intelligent design. In a recent article Shanks and Joplin analyze and find wanting the use of irreducible complexity as a marker for intelligent design. Their primary counterexample is the Belousov-Zhabotinsky reaction, a self-organizing system in which competing reaction pathways result in a chemical oscillator. In place of irreducible complexity they offer the idea of "redundant complexity," meaning that biochemical pathways overlap so that a loss of one or even several components can be accommodated without complete loss of function. Here I note that complexity is a quantitative property, so that conclusions we draw will be affected by how well-matched the components of a system are. I also show that not all biochemical systems are redundant. The origin of non-redundant systems requires a different explanation than redundant ones.

1. Introduction. In the past half-century biology has made astonishing progress in understanding the molecular and cellular basis of life. In light of this progress it is fair to ask whether Darwin's mechanism of natural selection acting on random variation appears to be a good explanation for the origin of all, or just some, of the molecular systems science has discovered. In *Darwin's Black Box: The Biochemical Challenge to Evolution* (Behe 1996) I argued that some biochemical systems, such as the blood clotting cascade or bacterial flagellum, are resistant to Darwinian expla-

nation because they are irreducibly complex. I defined irreducible complexity as

> a single system which is composed of several well-matched, interacting parts that contribute to the basic function, and where the removal of any one of the parts causes the system to effectively cease functioning. (1996, 39)

The difficulty for Darwinian theory is that

> An irreducibly complex system cannot be produced directly (that is, by continuously improving the initial function, which continues to work by the same mechanism) by slight, successive modifications of a precursor system, because any precursor to an irreducibly complex system that is missing a part is by definition nonfunctional. (1996, 39)

To illustrate the concept with a familiar example for a general readership, I pointed to a simple mechanical mousetrap, composed of several parts such as the base, hammer, spring, and so on, and noted that the absence of any of the parts destroys the mouse-catching ability of the trap. Darwin's vision of natural selection gradually improving function in "numerous, successive, slight modifications" (Darwin 1859) appears not to fit well with such systems. I went on to argue that, since intelligent agents are the only entities known to be able to construct irreducibly complex systems, the biochemical systems are better explained as the result of deliberate intelligent design.

But are gradual Darwinian natural selection and intelligent design the only potential explanations? Shanks and Joplin (1999) direct our attention to complexity theory, which concerns the ability of systems to self-organize abruptly, sometimes in surprising ways. They suggest that irreducibly complex biochemical systems might in principle be explained by self-organization, eliminating the need to invoke intelligence. They then go on to argue that biochemical systems are "redundantly complex"—that is, contain components that can be removed without entirely eliminating function.

After briefly describing the Belousov-Zhabotinsky reaction—Shanks and Joplin's main counterexample—I will first argue that the reaction does not meet the definition of irreducibly complex, because the interacting components are not "well-matched." I will then agree that redundant complexity exists, but show that not all of biochemistry is redundant.

2. A Closer Look At Chemical Self-Organization. The dissipation of energy in nature can organize matter and produce reaction pathways. A simple example is the clumping of matter into stars under the influence of gravity. More complex examples are tornados and the stellar nuclear pathways

that lead to the production of the heavy elements. These examples, however, have no direct relevance to the origin of biochemical systems. Shanks and Joplin (1999) offer what they think is a more pertinent example—the Belousov-Zhabotinsky reaction, a self-organizing chemical system discovered in the 1950s by B. P. Belousov in an attempt to model the Krebs cycle. The term "BZ reaction" is applied to a group of chemical reactions in which an organic substrate is oxidized by bromate ions in the presence of a transition metal ion and acid. Instead of proceeding monotonically to equilibrium, the reaction oscillates between two pathways because of a competition between bromide ion and bromous acid for reaction with bromate ion. Bromate oxidizes the metal ions, which in turn are re-reduced by reaction with organic substrate. When the reaction is well-stirred, the visible result is a solution that switches from one color to another at constant time intervals until the reaction materials are consumed. When the same reaction is set up as a thin, unstirred layer, waves of color change propagate through the layer. For details of the reaction pathways, see Gray and Scott 1994 and references therein.

Shanks and Joplin write that the BZ reaction "satisfies Behe's criteria for irreducible chemical complexity" because if any of the chemical components is removed "the characteristic behavior of the system is disrupted." Thus "Irreducible complexity in a self-organizing system" can be generated "without the aid of a designing deus ex machina" (1999, 272–273).

I disagree that the BZ reaction "satisfies Behe's criteria" for an irreducibly complex system. Although it does have interacting parts that are required for the reaction, the system lacks a crucial feature—the components are not "well-matched." The appearance of the modifier "well-matched" in the definition I constructed (above) reflects the fact that complexity is a quantitative property. A system can be more or less complex, so the likelihood of coming up with any particular interactive system by chance can be more or less probable. As an illustration, contrast the greater complexity of a mechanical mousetrap (mentioned above) with the much lesser complexity of a lever and fulcrum. Together a lever and fulcrum form an interactive system which can be used to move weights. Nonetheless, the parts of the system can have a wide variety of shapes and sizes and still function. Because the system is not well-matched, it could easily be formed by chance.

Systems requiring several parts to function that need not be well-matched, we can call "simple interactive" systems (designated 'SI'). Ones that require well-matched components are irreducibly complex ('IC'). The line dividing SI and IC systems is not sharp, because assignment to one or the other category is based on probabilistic factors which often are hard to calculate and generally have to be intuitively estimated based on always-incomplete background knowledge. Moreover, no law of physics auto-

matically rules out the chance origin of even the most intricate IC system. As complexity increases, however, the odds become so abysmally low that we reject chance as an explanation (Dembski 1998).

Just as I think that a gradual origin by natural selection is a good explanation for some things, I agree that a discontinuous origin by self-organization explains some things too. Nonetheless, I do not think either explains irreducible complexity. I argue that Shanks and Joplin's counterexample—the BZ reaction—is not IC; it is SI, because the components are not well-matched. To justify my position, let me first illustrate a well-matched system using the blood clotting cascade (Stubbs and Bode 1994). The active form of one protein of the cascade is called thrombin, which cleaves the soluble protein fibrinogen to produce fibrin, the insoluble meshwork of a blood clot. The chemistry catalyzed by thrombin is simply the hydrolysis of a certain fibrinogen peptide bond. However, all proteins are made of amino acid residues joined by peptide bonds. A typical protein contains several hundred peptide bonds. There is nothing remarkable about the bond in fibrinogen that is cleaved by thrombin. Yet thrombin selects that particular bond for cleavage out of literally hundreds of thousands of peptide bonds in its environment and ignores almost all others. It can do this because the shape of thrombin is well-matched to the shape of fibrinogen around the bond it cleaves. It "recognizes" not only the bond it cuts, but also a number of other features of its target. The other proteins of the clotting cascade (Stuart factor, proaccelerin, tissue factor, and so on) have similar powers of discrimination. So do virtually all of the components of the molecular machines I discussed in *Darwin's Black Box*.

Let us contrast this biochemical specificity with a comparable chemical reaction lacking such specificity. The peptide bonds of proteins can also be cleaved by simple chemicals. A typical procedure calls for incubating the protein in $6N$ hydrochloric acid at 110°C for twenty four hours. If fibrinogen were incubated under those conditions, the peptide bond that thrombin cleaves would be broken, but so would every other peptide bond in the protein. It would be completely reduced to amino acids. If thrombin were in the mix, it too would be completely destroyed. If the other proteins of the clotting cascade were there, no clotting would take place, even though the peptide bonds that are cleaved in the cascade would be cleaved, because all other peptide bonds would be hydrolyzed too. There is virtually no specificity to the chemical hydrolysis beyond the type of bond that is cleaved.

Similarly, the reactants of the BZ reaction are small organic or inorganic chemicals that show little specificity for each other. One ingredient, sodium bromate, is a general purpose oxidizing reagent and is capable of degrading a very large spectrum of chemicals besides the ones used in BZ reactions (thus its transport aboard airlines is forbidden). Another re-

quirement of the reaction is simply for a transition metal that can change its oxidation state, and a number of such metals are known, including iron, cerium, and manganese ions (Field 1972). A third requirement is for an organic molecule that can be oxidized. Many candidates could fulfill this role (ones that have been used include malonic, citric, maleic, and malic acids), and organic molecules can be oxidized by many reagents other than bromate. The last ingredient is simply a high concentration of sulfuric acid. As Field (1972, 308) noted, setting up BZ reactions "is an exceedingly easy task as they will occur over a wide range of concentrations and conditions."

The BZ class of self-organizing reactions—chemical oscillations—is surprising and interesting. Nonetheless, its complexity can be likened to other self-organizing systems found outside of biology, such as, say, tornados, which, although they command our attention, do not approach the specificity of well-matched, irreducibly complex biochemical systems.

3. Biochemical Self-Organization: Behavior vs. Origin. The dynamical behavior of the BZ reaction has been modeled by a set of two ordinary differential equations (Tyson 1994, 577). Because some biological systems can be modeled by similar mathematics, Shanks and Joplin (1999) conclude that self-organization can explain the behavior of the biological systems. There are several reasons to question the relevance of their point. First, they also note that "the substrates and products in these systems are very different from those in the BZ reaction" (1999, 273). In other words, we have traveled far from cerium, sodium bromate, and the other constituents of the chemical system. Second, and more importantly, the behavior of a system must be distinguished from its origin. As an illustration, consider highway traffic flow. A number of mathematical models have been used to describe traffic flow, some drawing on theories of self-organization (Schreckenberg and Wolf 1998). The mathematics, however, have not called the automobiles into being. The mathematics simply try to describe the typical behavior of traffic when a certain density is reached under conditions of restricted movement on a highway.

Examples of biological processes that show BZ dynamical behavior include glycolysis and aggregation of dispersed cells of the slime mold *Dictyostelium discoideum* into a slug. But consider the sophisticated components of the aggregation-signaling system of *D. discoideum*, which include: a cyclic AMP membrane receptor protein that can exist in an active and inactive form; an adenylate cyclase that binds to the active form of the receptor and itself becomes activated; a protein to export cyclic AMP into the extracellular medium; and more (Goldbeter 1996, Part I). All of that complicated machinery is ignored in BZ models—treated as a black box. Oscillations in the cellular concentration of glycolytic intermediates

are due in large part to the multi-talented phosphofructokinase (PFK), a tetrameric enzyme that can exist in two conformational states (an active form and a less-active one) and which has binding sites for a dozen different activators and inhibitors (Goldbeter 1996, Part III). Mathematical models of BZ behavior do not explain the origin of the impressive abilities of PFK any more than models of traffic flow explain the origin of brakes or gas pedals. Thus, even if a biological system displays self-organizing behavior, the question of its origin remains.

4. Not All Biochemical Systems Are Redundant. In contrast to claims about irreducible complexity, Shanks and Joplin write that "Real biochemical systems, we argue, manifest *redundant complexity*—a characteristic result of evolutionary processes" (1999, 268). By this they mean that biochemical pathways overlap and are interconnected, so that removal of one or even several components does not completely destroy the function. In support of their position they cite a diverse array of biochemical examples: the synthesis of an alternate pine tree lignin with increased content of dihydroconiferyl alcohol; viable mice in which the gene for the tumor suppressor *p53* was knocked out; and more. Their initial illustration is the metabolic pathways for the synthesis of glucose-6-phosphate. They point out that the molecule can be made by "several different isoforms or variants of hexokinase, and all are present, as a result of gene duplication, in varying proportions in different tissues." What's more, "Knock out one enzyme isoform and the other isoforms in the tissue can take over its function" (277).

True enough. The observation that some biochemical systems are redundant, however, does not entail that all are. And, in fact, some are not redundant. Consider the following examples of nonredundant metabolic pathways. Primates, including humans, cannot synthesize ascorbic acid (vitamin C) because they lack a functional gene for L-gulono-gamma-lactone oxidase, although a pseudogene is present (Nishikimi and Yagi 1991). Vitamin C is made by no other pathway. Hexosaminidase A is required to catabolize ganglioside G_{M2}; its loss results in Tay-Sachs disease (Kolter and Sandhoff 1998). These enzymes are parts of "real biochemical systems," but they do not "manifest redundant complexity." (For many, many additional examples, see Scriver 1995 or other texts on inborn errors of metabolism.) Therefore, arguments developed about the origin of redundant systems do not necessarily apply to all biochemical systems.

Shanks and Joplin's argument for redundant complexity has the same strengths and weaknesses when the subject moves from metabolic pathways to other biochemical systems. That is, they are right to notice that some systems or components are redundant, but wrong to extrapolate the conclusion to all systems. For example, they point to mice in which the

gene for the protein *p53* has been knocked out. *p53* is "involved in a number of fundamental cell processes, such as affecting gene transcription, acting as control points in the cell cycle, initiating programmed cell death," and more. Shanks and Joplin write that "Looking at this case from the standpoint of a 'genetic mousetrap model', one would naturally predict that the removal of this gene . . . would lead to catastrophic collapse of the developmental process. . . . . Such is not the case" (1999, 279). Yet contrast this case with that of mice in which the gene for either fibrinogen (Bugge et al. 1996a), tissue factor (Bugge et al. 1996b), or prothrombin (Sun et al. 1998) has been knocked out. Those proteins are all components of the blood clotting cascade, which I discussed prominently in *Darwin's Black Box* (1996, Ch. 4), claiming it is irreducibly complex. The loss of any one of those proteins prevents clot formation—the clotting cascade is broken. Thus Shanks and Joplin's concept of redundant complexity does not apply to all biochemical systems.

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