Self-Organization, Natural Selection, and Evolution: Cellular Hardware and Genetic Software

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Self-organization is sometimes presented as an alternative to natural selection as the primary mechanism underlying the evolution of function in biological systems. Here we argue that although self-organization is one of selection's fundamental tools, selection itself is the creative force in evolution. The basic relationship between self-organization and natural selection is that the same self-organizing processes we observe in physical systems also do much of the work in biological systems. Consequently, selection does not always construct complex mechanisms from scratch. However, selection does capture, manipulate, and control self-organizing mechanisms, which is challenging because these processes are sensitive to environmental conditions. Nevertheless, the often-inflexible principles of self-organization do strongly constrain the scope of evolutionary change. Thus, incorporating the physics of pattern-formation processes into existing evolutionary theory is a problem significant enough to perhaps warrant a new synthesis, even if it will not overturn the traditional view of natural selection.

Keywords: natural selection, self-organization, complexity theory, adaptation, evolution

A diverse group of researchers in mathematics, physics, and several branches of biology have argued that self-organization should be placed alongside natural selection as a complementary mechanism of evolution (Nicolis and Prigogine 1977, Kauffman 1993, Camazine et al. 2001, Denton et al. 2003, Kurakin 2005, 2007, Newman et al. 2006, Karsenti 2008, Wills 2009). Ignoring these calls, most evolutionary research has continued along traditional lines. This article is an attempt to put the rich experimental and theoretical work on self-organization in biological systems into intuitive terms that demonstrate the role of self-organization in the evolutionary process.

First, we briefly review evolutionary theory with an emphasis on those aspects critical to our discussion of self-organization. We then introduce self-organization with a general definition and several examples from biological systems. Following this introductory material, we explore the intersection between natural selection and self-organization. Here, we have two goals: (1) to clear up the misunderstanding that self-organization competes with natural selection as the organizing force in evolution, and (2) to explore the myriad ways that self-organization affects the evolutionary process. In the course of these discussions, we argue that evolutionary biology historically has dealt with the gradual evolution of structures and plans, whereas the evolution of controlled but largely spontaneous processes is the chief unanswered question of today. Further, as several authors have suggested (Kauffman 1993, Kurakin 2005, 2007, Wills 2009), evolution at the macroscopic level and evolution dependent on self-organization at the molecular level are so different that the resulting expansion of evolutionary theory ultimately may be considered a new synthesis. As the first modern synthesis incorporated genetics into natural selection, this new synthesis seeks to incorporate the physics of complex systems (Nicolis and Prigogine 1977, Kauffman 1993, Camazine et al. 2001, Newman et al. 2006, Karsenti 2008).

A brief historical preface

Although evolution by natural selection is one of biology's most well-supported theories, it is important to keep in mind that the theory's common derivation was fully formed before the rise of molecular biology. We cannot overemphasize this fact because it sets the stage for our basic problem, which is that evolution by natural selection was conceived using data at the macroscopic level. This does not imply that principles derived from macroscopic studies will not be applicable to the molecular world (they often are); it simply means that we could sometimes face an apples-and-oranges problem when we apply traditional evolutionary principles to the evolution of molecular mechanisms. When molecular biologists suggest that traditional approaches to natural selection do not seem fully appropriate to their systems, an evolutionary biologist should not be skeptical. In fact, given the history, it would be surprising if a major new approach to evolution were not necessitated by data on life at the molecular level.

Evolutionary biology

Evolution requires a broad definition that encompasses the diversity of processes and patterns involved. We prefer to define it as the historical process that leads to the formation and change of biological systems. On the subject of evolution much effort has gone into the study of two topics: genetic drift and selection (Lewontin 1974, Roughgarden 1979, Maynard Smith 1986, 1989, Li 1997, Hartl and Clark 2007). We focus on selection, as our interest in this study is the evolution of function, and selection is the only mechanism by which functional relationships evolve. The core functional properties of enzymes and sensory receptors, for example, are not the products of random drift.

Natural selection is usually defined as the consequence of three properties of organisms: (1) variation among members of a population, (2) differential reproduction, and (3) heritability of traits important for survival or reproduction (Lewontin 1974, Roughgarden 1979). In short, if individuals vary in a trait that is heritable, and if such variation is the cause of differential reproductive success, then a change in the average phenotype of the population will occur as a result of the greater contribution to each generation from the most fit individuals. Much of contemporary evolutionary biology focuses on this basic mechanism by developing mathematical models of competing alleles that contribute to differential fitness among members of populations with particular spatial or demographic characteristics (Slatkin 1987, reviewed in Maynard Smith 1989). We focus, however, on some of the key corollaries of the basic mechanism of selection that have always fascinated biologists.

Although the mechanism of selection is simple, the nature of the historical process it engenders is complicated and requires the inclusion of additional concepts. These concepts either clarify the three basic components of selection described above or explore predictable consequences of the action of selection. The first concept is adaptation. Adaptation refers to form and function in traits (Dawkins 1986, Maynard Smith 1986, reviewed in Reeve and Sherman 1993). The human hand, for example, is well suited for the use of tools, whereas the hand of the gibbon is well suited to swinging through trees. The form of the hand in these cases is an adaptation to a particular lifestyle. Given that selection "chooses" the most fit individuals with respect to a given trait, it often (though not always) leads to adaptation (Maynard Smith 1986). In general, adaptations are functional relationships shaped by natural selection.

Our second concept is that of functional constraint (Maynard Smith 1999, Müller 2007). Constraints focus on the nature of variation among members of a population. In short, are all variations of a trait possible, or do traits vary in a finite number of ways? If traits are enormously labile, then selection can result in whichever of countless possible adaptive outcomes best enhances fitness. If, however, variation in traits is limited as a result of chemical, physical, or genetic constraints, then many seemingly adaptive outcomes may be unlikely to evolve (Gould 1977, Maynard Smith 1990, 1999).

The third concept follows from the second, and concerns the nature of evolutionary trajectories. Does selection quickly form new adaptations by favoring radically different variations of phenotype, or does selection lead to gradual changes in phenotypes that vary only quantitatively (Maynard-Smith 1986)? The last concept has to do with the relationship between genotype and phenotype and is involved in the basic principle of heritability (Maynard Smith 1986, Müller 2007). Here the question is, How expansive and complex are the genetic bases of traits? Are traits controlled by a few genes that work independently, or are genes organized into large networks that contribute to one or more modules of biological organization (Müller 2007, Monteiro and Podlaha 2009)? If genes work independently, then the effect of differential reproductive success, on average, will be to shape traits independently of one another. If genes often affect multiple traits, however, then selection acting on one trait can affect many others as well. This last concept is partly encompassed by the notion of the evolutionary constraint, as it explores proximate explanations for the constraint of variation.

Self-organization

In contrast to conservative systems, in which energy is conserved, self-organization occurs in dissipative systems through which energy is flowing (Nicolis and Prigogine 1977, Kauffmann 1993, Camazine et al. 2001). Such systems produce what are called dissipative structures. A dissipative structure is one that breaks down without the continual input of energy (Nicolis and Prigogine 1977, Maynard Smith 1986). A dissipative structure is thus not a structure at all, but a metastable pattern. For instance, many weather patterns, such as clouds and hurricanes, are dissipative structures (Whitesides and Grzybowski 2002, Arsenyev et al. 2004); in fact, we are surrounded by complex, purely physical self-organization patterns. In this section, we introduce the nature of self-organization in biological systems. For reasons outlined in the next section, we focus on cell biology, but self-organization is equally important in developmental biology and several other branches of biology (Camazine et al. 2001, Salazar-Ciudad and Jernvall 2002, Newman et al. 2006, Johnson 2009).

The cell: The functional unit of biology

Our biological self-organization examples come from the field of cell biology for two reasons: (1) self-organization is the fundamental mechanism within the cell (Misteli 2001, 2007, Kurakin 2005, 2007, Maini et al. 2006, Tabony 2006, Karsenti 2008), and (2) the importance of the cell to the evolutionary process is usually downplayed in basic texts on evolution (Cavalier-Smith 2004). To put the importance of the cell into perspective, we begin with two facts certainly known to all biologists: First, genes do not code for the construction of cells; a cell must be inherited, as are the genes, from a parent. Second, the cell's mechanisms, independent altogether of the influence of DNA, are enormously complex. Let's consider the consequences of these simple facts from an evolutionary perspective.

Because the cell must be inherited, and because its processes cannot always be constructed de novo from genetic instructions (Cavalier-Smith 2004), genes often manipulate ongoing cellular behavior. DNA is the cell's information-storage device, but only some information is stored. The basic mechanisms of life must be inherited as ongoing processes. Thus, if life evolved as a coupled set of interconnected processes, then it has remained so ever since (Nicolis and Prigogine 1977, Kauffman 1993, Newman et al. 2006). Therefore, the perspective on evolution that focuses solely on shuffling genes propagating through time is limited because the cell propagates as a whole and its processes are the engines of life.

Biological examples of self-organization

The simplest cases of self-organization are essentially dynamic examples of self-assembly. Self-assembly is the term for the processes exemplified by, for example, the construction of the tobacco mosaic virus coat (reviewed in Nicolis and Prigogine 1977, Camazine et al. 2001): Essentially, the pieces of the structure act like a puzzle that puts itself together. Further, in self-assembly, once a structure forms it is stable and requires no further energy (Nicolis and Prigogine 1977, Camazine et al. 2001, Karsenti 2008). The formation of microtubules (the filaments that form the cytoskeleton and do mechanical work within the cell) is similar, with the exception that the units of the spindle come and go in a dynamic process (Nedelec et al. 1997, 2003, Maly and Borisy 2002, Cortes et al. 2006). Thus, energy must be continually supplied to get the dissipative structure to form and maintain itself. Organizationally, this requires the addition of the right amount of energy to the right ingredients. Where and when the metastable structures form must also be guided (reviewed in Karsenti 2008).

For a more complex self-organizing mechanism, we turn to DNA transcription and repair. Although these processes were initially thought to be controlled by huge molecular structures (or machines), it is now known that they are self-organizing processes. In short, when damage occurs, or when translation of a particular region of DNA is required, the subunits of the necessary RNA polymerase, which are dissolved in the cytosol, self-organize to do the work (Houtsmuller 1999, Hoogstraten et al. 2002, Vermuelen and Houtsmuller 2002, reviewed in Kurakin 2005). The mechanism of energy input and the need for the work are coupled such that as soon as the work runs out, so does the energy, and the metastable structure (or process) dissipates back into the cytosol. What is important to consider is that although the structure forms spontaneously, the concentration of each subunit in the nucleus must be optimized. Further, molecular crowding, which facilitates large numbers of random interactions, must also be maintained (Ellis 2001). The cell thus has a considerable problem to overcome to create just the right conditions for these spontaneous processes to occur.

Although there are not rigorous experimental examples, it is nonetheless useful to discuss some ways the cell could harness self-organizing processes evident in well-studied geophysical systems. Rain forms when condensation seeds combine and fall to Earth (Bruintjes 1999); this occurs only in clouds in which the air is saturated above a threshold. Recently, scientists have been able to induce rain by supplying large numbers of artificial nuclei to clouds (Bruintjes 1999). Such a seeding mechanism could be of use to the cell. Consider a substance dissolved in the cytosol. The cell has the problem of gathering together the substance for use. Rather than evolving a mechanism that actively gathers the substance at low concentration from the medium, if the cell waits until the cytosol is saturated, then sends out seeds specifically to interact with the substance, concentrated packets of the substance would quickly form at very low energetic expense (Clark and Zhang 2008, Loose et al. 2008). Further, the seeds could be produced by the endoplasmic reticulum at a rate commensurate with the demands of the cell for the substance (Barlowe et al. 1994, Liu and Fletcher 2009).

Another possibility that might change the way one thinks about the cell and how gene products work therein is that instead of using transport mechanisms with great specificity (such as vacuoles), the cell could simply mark its many export products with an identifier, and then send them into streams flowing through the cytosol (Shimmen and Yokota 2004, Esseling-Ozdoba et al. 2008). As long as the identifier on the product matches complementary markers on the destinations, substances could be fished from the stream. Of course, such streams could be maintained only by the careful manipulation of the environment of the cytosol.

Self-organizing mechanisms are the focus of intense study in cell biology. The interested reader can consult the literature for more in-depth treatments of self-organizing processes, such as the regulation of the cell cycle (Murray and Kirschner 1989, Novak and Tyson 2003), construction of the Golgi body (Glick 2002), and maintenance of cell morphology (Carazo-Salas and Nurse 2006). General reviews of self-organization in cell biology are also available (Misteli 2001, 2007, Kurakin 2005, 2007, Karsenti 2008).

Is self-organization an alternative to natural selection?

It has been suggested that because self-organization is the basis of much biological pattern formation, it challenges the idea that natural selection is the mechanism underlying the origin of life and its subsequent radiation into a multitude of forms (Kauffman 1993, Denton et al. 2003, Wills 2009). Here we explain why self-organization plays a subservient role to selection in the evolution of biological complexity. The basic question we address is whether self-organizing mechanisms evolve by natural selection or are simply intrinsic properties of physics and chemistry. If self-organizing mechanisms are intrinsic properties, then the importance of natural selection to the evolutionary process would be drastically decreased. However, as we will argue, self-organizing mechanisms within biological systems are adaptations that evolve by natural selection.

Although not all biological self-organizing processes are like physical ones, they all have common properties

illustrated by the physical processes. Take the following classic demonstration of self-organization: Benard convection cells are polygons that form on the surface of a thin layer of heated oil (reviewed in Camazine et al. 2001). They are caused by the interaction between upwelling and downwelling currents, in conjunction with the effects of surface tension, within a temperature gradient. These cells form rapidly and spontaneously under the right conditions. The key, however, is that they do not form robustly. If too much heat is applied, or if the layer of oil is too thick, for example, the cells will not form (Nicolis and Prigogine 1977). This is not unique to Benard convection; it seems to be generally true of self-organization processes. We are reminded of the fickle nature of the weather. Weather is difficult to predict because there are many variables, and changes to any of them can amplify and change the overall pattern (Pasini 2006).

Considering the sensitivity of self-organizing processes, let us discuss whether a biological instance of self-organization can be considered an intrinsic property. First, an organism has to go to great lengths to create the conditions for a self-organizing process to commence (Karsenti 2008). In the case of many cellular self-organizing mechanisms, this means ensuring that the necessary interactants are present at high concentrations within a confined compartment. Further, finding elements, gene products or otherwise, that can interact with one another in a self-organizing process capable of doing work is not trivial. It is analogous to finding a string of amino acids that can fold into just the right conformation in a given medium. There are infinite possibilities, and some process must be in place for selecting combinations of elements that work. Further, in the case of self-organization, because the ongoing dynamics of self-organizing processes are sensitive to environmental perturbations, mechanisms must be in place to maintain the conditions necessary for the process. Organisms are full of such regulatory procedures for maintaining homeostasis in the face of environmental perturbations, whereas self-organizing processes in isolation have no such ability. As in the example of weather systems, unregulated self-organizing processes fluctuate in incredibly complex ways that would not be conducive to accomplishing the concrete tasks they perform when controlled in biological systems.

In conclusion, a self-organizing mechanism in isolation is an intrinsic property, or a purely spontaneous process, that is the product of given circumstances. When a system is actively regulated such that it adaptively creates conditions that invoke self-organizing processes, and then maintains those conditions even in the face of environmental perturbations, then the process can no longer be considered spontaneous. Essentially, selection has to fine-tune and control many parameters to get work out of a self-organization process. Thus, although selection does not need to construct an elaborate plan to generate complexity when self-organization is involved, it does have to drive the evolution of elaborate mechanisms for invoking self-organizing processes and controlling their dynamics. Therefore, selection should play the dominant organizing role even when much of the complexity one observes appears to be spontaneous. Previous authors have referred to this as "buffered self-organization" or "evolution of parameter control," but have not stressed how difficult and involved the buffering is likely to be (Kauffman 1993, Camazine 2001).

Self-organization, adaptations, and evolutionary trajectories

We introduced four corollaries of the basic mechanism of natural selection that are central to an understanding of evolution. In this section, we briefly explore how consideration of the self-organizing nature of many biological processes influences these corollaries. We start with adaptations and evolutionary trajectories. The success of classical evolutionary theory with respect to these issues is exemplified by our understanding of the evolution of the vertebrate eye. Here, we have discovered a clear progression through time from simple to complex that supports a gradual process of selection, leading to increasingly elaborate structures. Thus, in classic examples, selection crafts adaptive complexity over time by favoring individuals that vary in relatively minor quantitative ways.

We contrast the formation of an eye with the formation of vesicles within the cytosol or the coat of the tobacco mosaic virus. Under appropriate conditions, these structures, or dynamic patterns, form spontaneously (reviewed in Segota and Tezak 2006). Such pattern-formation processes are so robust that some organelles can even be formed *in vitro* on glass surfaces (Baumann and Walz 2001, Borgese et al. 2006). Therefore, adaptation at the macroscopic morphological and molecular levels can have fundamental distinctions. At the macroscopic level, the core functional basis of the adaptation is the product of a long evolutionary history. The shape of the hand, for example, did not come about all at once, but rather was "crafted" over many generations of gradual selection. The self-organizing pattern-formation processes we observe, in contrast, are sensitive to environmental conditions, and in many cases happen either in their entirety or not at all. Thus, selection does not always build complexity step by step at the molecular level (Kauffman 1991, Denton et al. 2003, Karsenti 2008); rather, natural selection discovers complexity. To conjecture about how this might happen (since we do not understand the process), one might imagine that a mutation triggers an incipient self-organizing process that has some fitness effect on the organism. At this point, the adaptation (the core functional relationship) is essentially present, but is not well controlled; there is selective pressure to evolve the capacity to trigger the self-organization process at the right time and place, and to focus its effects to the desired end. In general, instead of building up from scratch, selection starts with an ill-formed, but functional, adaptation, and then adds increasingly complex organizational controls.

Further, instead of choosing between individuals that vary in quantitative ways, the evolution of the self-organizing process is dependent on an initial qualitative jump in phenotype. Further still, exploring the vast universe of qualitatively different molecular conformations for those that work and then selectively favoring them is probably widespread in molecular evolution and differs from the traditional notion of the gradual construction of adaptations through incremental evolutionary change.

Evolutionary constraints and self-organization

Much research has been conducted on how the characteristics of self-organization define the boundaries of what is likely to evolve (Kauffman 1993, Newman et al. 2006). The dynamics of a seeding or reaction diffusion process, for example, can be manipulated, but only within boundaries imposed by the physics of the process. If a seeding process is used for solute collection, for example, then the cell could collect substances from the cytosol only after their concentration exceeds a certain threshold. Little could be done to change this. Likewise, many cellular processes depend on molecular crowding, which ensures rapid interactions between the elements of self-organizing processes. If a cell is going to evolve a larger size, compartmentalization might be necessary to maintain this crowding. Thus, a eukaryotic cell might need prokaryote-sized organelles able to maintain the requirements of the self-organizing processes that evolved in the prokaryotic ancestor.

Evolutionary developmental biology (evo-devo) is a rapidly expanding field concerned with the consequences of developmental biology for evolutionary theory (Müller 2007). An interesting evo-devo model addresses the formation of cusps on mammalian teeth (Salazar-Ciudad and Jernvall 2002). In this example, conserved genes interact with one another during development through a reaction diffusion mechanism that leads to variable numbers of cusps, depending on factors such as the rate of secretion of activator and inhibitor signals and the receptivity of cells to them (Salazar-Ciudad and Jernvall 2002). Changes in the expression patterns of these signaling peptides therefore have the potential to affect many tooth properties, possibly constraining the scope of adaptive outcomes of selection (Kangas et at 2004). Self-organization models of cell morphology and evolution have also been proposed that are of broad significance to the early evolution of living systems (Newman et al. 2006). In short, an understanding of self-organization is necessary for an appreciation of the relationship between genotype and phenotype that is central to evolutionary developmental biology.

Cellular hardware and genetic software

At the heart of this article is the idea that the cell is the basic functional unit of biological organization and that an understanding of its role in the evolutionary process is necessary to understand topics such as evolutionary constraints and the nature of adaptations. To make the relationship

between the cell and the evolutionary process clearer, it is useful to develop an analogy between the organization of biological systems and a computer's hardware and software (figure 1). Essentially, although software is the source of information underlying how a computer solves problems, it is not more important than the hardware. Hardware—the computer's random access memory, hard disk, and processor—set fundamental limits on what the computer can do, independent of the sophistication of the software. For these reasons, when people discuss "good" or "bad" computers, it is typically the hardware that they discuss. The key is that it is pointless to discuss a computer's capabilities without placing equal emphasis on both its hardware and software.

The nature of hardware and software in biology is more complex than in computers because the "software" in biological systems partly defines the hardware, and the hardware itself can store information. Nevertheless, the analogy is useful if one keeps to broad strokes. In short, all the chemical compounds within a cell, and the stable organizational relationships between them, form the hardware of the biological system. This includes the cell membranes, organelles, and even the DNA molecules. These structures and processes encompass information stored in genes, as
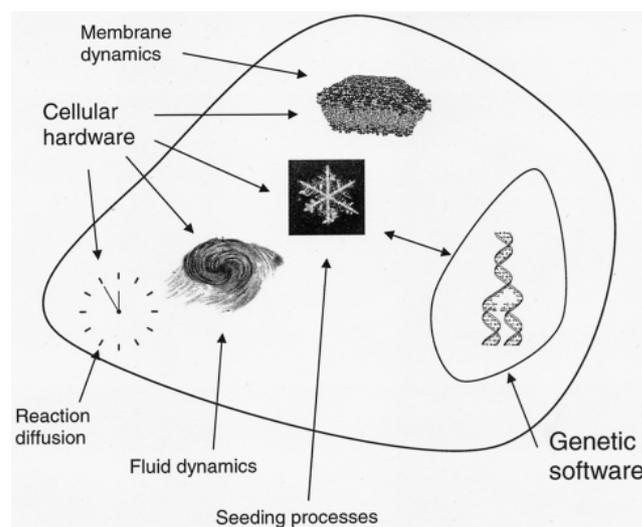

Figure 1. The computer science concepts of hardware and software provide a useful metaphor for understanding the nature of biological systems. All the chemical compounds within a cell, and the stable organizational relationships among them, form the hardware of the biological system; this includes the cell membranes, organelles, and the DNA molecules. These structures and processes encompass information stored in genes, as well as information inherent in their organization. The software of the cell corresponds to programs implemented on the hardware for adaptive responses to the environment and for information storage and transmission. Such programs are contained not only in DNA but also in stable self-organization patterns, which are inherited across generations as ongoing processes.

well as information inherent in their organization. The software of the cell corresponds to programs implemented on the hardware for adaptive responses to the environment and for information storage and transmission.

Such programs are contained not only in DNA but also in stable self-organizing patterns, which are inherited across generations as ongoing processes. Using this hardware and software approach, the notion that DNA contains all the information of life is clearly misleading. The cell membrane, for example, may well precede DNA, as many models of the origin of life posit that a barrier to the outside world may have been central to creating the conditions for life (Luisi et al. 1999, Svetina 2009). In any event, genes fundamentally affect membranes by changing their shapes (Farge and Devaux 1992). By creating depressions or hills, for example, materials on the surface of the membrane can direct molecules toward or away from particular regions. The mechanism for how a cell does work in this case is inherent to the properties of membranes and is not contained in the DNA. The cell's DNA, in contrast, contains instructions for how to take advantage of the membrane's properties at the appropriate time and in the correct manner. Further, such genetic information would be useless without a fully functional membrane, inherited from a parent, on which to act. Thus, a membrane that evolved in the distant past has subsequently passed from one generation to the next ever since, with instructions that modulate its properties accumulating over the years.

In a nutshell, the current view of genes and the evolutionary process is a Platonic ideal in which genes are seen as permanent forms that propagate through time within a relatively unimportant cellular background. One can summarize the evolutionary process this way (it is particularly convenient mathematically), but this is not an explanation of how evolution constructs the mechanisms of life. In other words, we currently focus on the evolution of changes to the software, and neglect the evolution of both the hardware and the ways that the hardware and software interact. To describe the problem in traditional terms, with the evolution of an eye, for example, we can trace a trajectory from simple to complex. At each step we can explain how selection made a change to the system that improved function. We are not merely concerned with changes in gene frequency, but changes in function and how they are caused by selection's alteration of structures. To do this sort of evolutionary biology at the molecular level, we need to recognize how genes exert their effects on cellular processes with elaborate self-organizing rules.

Conclusions

The nature of pattern-formation processes within the cell challenges the traditional view of genetic circuit boards (Kurakin 2005, 2007). According to that view, gene products—structural or enzymatic—do the work within the cell. When thinking about what sorts of genes should evolve and why, one naturally considers genes as acting either independently or in concert with one another. If, however, gene products guide processes already in motion, then the emphasis changes to selection for genes that manipulate and control pattern-formation mechanisms that have their own complex properties. This constrains (at the molecular level) what sort of evolutionary change is possible and also leads to a vision of evolution in which saltatory changes are more important than traditionally thought, as self-organizing mechanisms do not seem to be the products of slow, incremental change.

When Wöhler produced urea using a purely chemical process, it changed the way we perceived biology, as it showed that the substances of physical and living systems are identical. Beginning with Turing (1952), and continuing with Nicolis and Prigogine (1977), Kauffman (1993), and many others, a similar change in perspective is currently under way. We now know that life is not only made up of the same substances as the inorganic world but also that life's processes are often the same as those we see in the natural world. It is therefore possible for both biologists and geophysicists to study different examples of the same process, and a change in perspective, and perhaps educational curriculum, is necessary for contemporary biology. The teaching of the physical sciences to evolutionary biologists is well established. All students learn that cells do not get beyond a certain size because of the familiar surface-to-volume problem of gas exchange. Further, young biologists are taught the importance of the electrostatic force, as one could not understand how enzymes work without grasping that concept. It is the hope of self-organization researchers that an appreciation of the fundamental roles played by physical pattern-formation mechanisms will soon be treated in the same manner.

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