Section Three — Theoretical Molecular Biology: Introductory Comments

Michael J. Behe — Section Chairman

Biological information must be expressed to be consequential. In the past half century, science has discovered that expression often takes the form of sophisticated molecular machinery. Information resides in the very shape of the machinery itself, as well as in the instructions to build the machinery, to regulate it, to allow separate systems to communicate with it, and more. In all these cases the information must be physically instantiated to be effective. This section focuses on systems that are known, or speculated, to instantiate information, and how they may be affected by evolutionary forces.

The chapter by **Macosko and Smelser** reviews the evidence that the genetic code used by nearly all life forms on earth is far from a "frozen accident" — that is, far from an arbitrary assignment of codons to amino acids that got locked into place because changing it would have been beyond the reach of Darwinian processes, as was speculated by early investigators. Rather, close analysis of the code has shown it to be better than the vast majority of possible codes in resisting the occurrence of deleterious mutations, in resisting their impact if they occur, and more. The conjecture that the code was optimized by Darwinian selection runs headlong into the profound difficulty that a change in the code used by an organism would affect all proteins coded for by its genome. Almost certainly such a change would negatively impact the functioning of many proteins, and be resisted by the very selection that is posited to shepherd the code to greater efficiency. Macosko and Smelser argue that the hypothesis of purposeful intelligent design better fits the data, and can lead to new insights into this basic feature of life.

The chapter by **Dent** seeks to discern how widely-separated molecules obtain the information with which to find their targets. Deeming the standard explanation of a random Brownian search to be inadequate in many cases, Dent hypothesizes that there exist coherent oscillator structures within chromosomes and proteins with a narrow range of resonant frequencies. Such oscillations are thought to attract biomolecules to one another with great specificity. In experiments using ultra-high-frequency Doppler vibrometry, live onion cells and fish eggs were scanned for the presence of vibrations in the gigahertz range, predicted of DNA. Although such signals were not detected in the present study, they may not in fact reach the cell surface, but be confined to the nucleus. Further work is planned to investigate this possibility.

The chapter by **Behe** investigates the tempo and mode of evolution with respect to information-bearing genetic elements such as coding regions, control elements, modification signals, and so on. It has been known since Darwin that evolution can proceed as readily by losing a pre-existing function as by gaining one. For example, in order to adapt to its environment the lineage leading to birds developed the power of flight. Yet, also in order to adapt to their environment, the lineages leading to ostriches and penguins lost the power of flight. A difficulty in judging the underlying basis of the modification is that a phenotypic loss of function may be caused by a genetic gain of function and vice-versa. In the past few decades, however, the informational elements comprising the genome have substantially been elucidated. It has been discovered that functional elements often consist of long stretches of contiguous nucleotides, many of which would lead to loss of function if they were mutated. A simple model demonstrates that in many situations loss-of-function genetic mutations will appear much more rapidly than gain-of-function mutations, and thus have the opportunity to spread in the population before alternative beneficial mutations appear. The model is shown to fit well with evolutionary results from the laboratory and from the wild in which the molecular bases of adaptation have been ascertained.

The chapter by **Wells** argues that important heritable biological information exists apart from the genome. While acknowledging that, for example, proteins involved in genetic regulatory networks (GRN) which are necessary for embryological development are coded in DNA, he points out that the spatial information necessary for development is not. Fertilized eggs already possess spatial information outlining major body axes before GRNs are activated, the result of determinants in the cell cortex, the point of entry of the sperm, and more. Endogenous electric fields exist within embryos, the result of the topological arrangement of ion pumps, which is not coded in DNA. External electric fields applied to probe their effect on the developing embryo show that such fields can induce cell migration in vitro, and disrupt normal development in vivo. The position in the cell membrane of nanoclusters of membrane proteins involved in intracellular signaling is often essential to their proper functioning. Glycolipids and glycoproteins on cell surfaces direct cell-cell interactions. Patterns of membrane proteins can be inherited apart from DNA, as shown most vividly by ciliates with inverted rows obtained from a surgically-rotated cortex, whose pattern has been stably maintained for thousands of generations. Wells concludes that the existence and inheritance of DNA-independent biological information fits poorly with standard evolutionary theory, and that to more closely describe nature evolutionary theory must take into account the higher dimensions of biological information.

The chapter by **Axe and Gauger** begins by pointing out that life consists of multiple layers of information, from the molecular to the cellular, to the organismal, to the ecosystem. A basic level, however, is that of bacterial metabolism. If Darwinian theory is to give a thorough account of life, then it at least has to give an account of such a basic level. Yet, the authors argue, it has failed to do so, and there are strong reasons to judge that it cannot do so. The authors review the systematic difficulties that a bottom-up development of a metabolic pathway faces, from the cost of gene expression to the need to combine rare events in a single gene to causal circularity (the need for the product of the pathway as a participant in the pathway itself). Not content to leave their discussion as a compilation of the difficulties a Darwinian process faces at a very basic level of life, Axe and Gauger go on to propose tentative principles that envision a top-down paradigm to replace it.

Can we draw an overarching theme from the chapters in this section? One such theme, I think, is that it is a basic task of biology, especially as motivated by a theory of intelligent design, to seek out new sources of information in life and new ways in which that information may be instantiated. While other general theories of biology do not physically prevent investigators from such investigations, neither do they encourage it and they may actively discourage it. At a number of points in the history of modern biology, Darwinism (since it is said to predict much waste in nature), has mistakenly discounted significant aspects of life as the unintended debris of inefficient natural selection. "Junk DNA" is perhaps the latest and most spectacular example of this. Minimally, the intelligent design hypothesis should help guard against a dismissive attitude regarding biological information and its origin.