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BIOLOGY, HISTORY, AND INDIVIDUALITY

For the last 100 years, biology has been dominated by reductionism—the belief that all of its complexity can be reduced to and ultimately explained by the laws of physics. A contrasting view has emerged recently that looks for explanations at a higher level of organization and that pays particular attention to the role of history and contingency in biology.

Scientific thinking has had a long history of influencing the Humanities. What began as the quiet spreading of new modes of thought became an invasion in recent times as academic disciplines from history to literature adopted quantitative measures and analytical methods from the natural sciences (Whitehead, 1925; Barzun, 1964). Opponents argued the inappropriateness of applying abstraction to matters that are necessarily particular, or of objectifying realms of human experience that are inherently subjective. Proponents asserted that it increased the power of analysis and the verifiability of research.

The converse phenomenon, an influx of Humanistic thinking into the natural sciences, has scarcely been permitted. From its beginnings, science defined itself as interested only in what is general and what is abstract, and has had little use for ways of thought that are mired in the diversity of the particular (Butterfield, 1951). In doing so, it assumed a protective armor that effectively excluded any modes of thought from the Humanities. Physics as practiced by Galileo and Newton was the first science to adopt this philosophy and it subsequently became the gold standard for the rest of the natural sciences. Several assumptions were implicit in this view: the universality of underlying principles, the embodiment of these principles in an isolated system independent of any particular context, and the predictability of a system’s behavior based on knowing its starting conditions. The life sciences were late in meeting this criterion, but it came with the elaboration of a new viewpoint at the start of the 20th century known as “reductionism,” in which complex biological phenomena were believed to be reducible to the laws of physics.
The major advances in biology in the past 50 years are due in large measure to the fruits of this approach.

Signs are appearing, however, that a deep explanation of biological phenomena defies the physicists' gold standard. After 100 years of treating biological questions as reducible to the laws of physics, a flaw has appeared. Difficulties in applying molecular reductionism to questions of genetics, embryology, and neurobiology have recently emerged, and are forcing a confrontation with the fact that biological phenomena are intrinsically historical and depend heavily on context. While not violating any laws of physics, biological explanations must be found at a higher level of organization than is adequately captured by existing physical laws. Most importantly, when events are scrutinized at this higher level of organization, there is an inherent limit to the predictability of the phenomena.

Biology raises the particular to a level of importance that is perhaps unique in the natural sciences. It is not accidental that we humans, as biological creatures, reflect this irreducibility of the particular in so many of our activities. Individuality is fundamental to biology.

History and Biology

For most of its own history, biology and its antecedents have been distinctly anti-historical in outlook. From the time of Aristotle until the 18th century, the living world was generally assumed to be stable and essentially unchanging. Linnaeus' \textit{Systema Naturae} (1735) epitomized this tradition, introducing the system of classifying living things still in use today. He viewed his own work as discovering and describing the natural, divinely created order in which each species represented a fixed unit of Creation.

Linnaeus' contemporary, Georges Buffon, departed from this tradition. From a belief that the earth had a geological history, he postulated the mutability of species and marked the beginning of a tradition of evolutionary thought that culminated with Charles Darwin. This view was inherently historical in its recognition of distinct and irretrievable stages through which first the earth and then its living inhabitants passed before reaching their current state.

Darwin’s \textit{Origin of Species} (1859) added an important new element to the historical nature of evolutionary thought: chance. Not only did species undergo transformations over time, and not only were some species lost forever, but randomness was a major factor in these events. This has several important implications for the historical aspect of biology. If evolution is not determinate \textit{a priori}, then the particular series of historical events that produces a species is unique. Biological organisms thus became firmly rooted in a world of particulars.

The Darwinian view of historical speciation has stood unchallenged for a century and a half and no biologist today seriously questions it. At the same time as Darwin's theory was gaining acceptance, a very different biological world view was developing in the experimental discipline of physiology. Under the leadership of Herman von Helmholtz in Germany, Michael Foster in England, and, later on, Jacques Loeb in America, the experimental mind-set of physics was being applied in the analysis of biological function. The debt to physics was not limited merely to the adoption of its experimental approach, it extended to the principles underlying the phenomena as well. They assumed that biology was nothing more than physics and chemistry. These physiologists were the founders of modern reductionism and started a powerful movement that spawned the development of biochemical, embryology, and genetics. The contemporary descendants of these disciplines now dominate the life sciences.

As believers in a view of biology that was essentially Newtonian, they accepted its basic assumptions: the whole is equal to the sum of its parts; the essential properties of the whole are preserved in any subset of it; and, if the starting conditions are known, the outcome can be reliably predicted from known laws. It was only a matter of discerning those laws.

Anti-History and Biology

The Newtonian view of biology was reinforced by several successful lines of research in the late 19th and early 20th centuries—each one characterized by the universality of its findings. First came the finding that fermentation could be carried out in a non-living extract made from yeast cells—the "zymase" of Buchner (Fruton, 1972). If this most biological of all chemical
processes could be preserved in a test tube in the absence of living cells, it fulfilled the criterion of the embodiment of a principle in an isolated system independent of any particular context. The subsequent progress in enzymology led to the elaboration of metabolic pathways whose universality was shown by their presence in all living things.

The next realm to come under the reductionist program was the transmission of hereditary traits in plants, resulting from the so-called "re-discovery of Mendel" (Brammigan, 1979). The designation of the principles as "Mendel's Laws," the statistical basis for their demonstration, and their subsequent extension to animals such as mice and fruit flies, all argued for a principle that cut across species to achieve true universality. More pointedly, the stability of the gene cut across generations and thus transcended historical contingency.

Finally, advances in electronics as a result of the First World War—the invention of the vacuum tube—made possible the finding that simple electrical impulses underlie the senses. These studies showed that even our subjective experience might be explicable as simple physical phenomena (Adrian, 1928). In all of these cases, properties that had seemed to be an exclusive property of living things—fermentation, heredity, sensory experience—were subsumed under the laws of chemistry, mathematics, and physics.

The success of the reductionist program permeated virtually all of the life sciences in the 20th century, spawning the modern fields of cell biology, molecular biology and neurobiology, and more recently, biotechnology and genomics. Reductionism became the standard for maturity and explanatory power. Research publications could no longer report anecdotal evidence; statistical rigor became the norm. Case histories, a traditional mainstay of medical journals, disappeared from the literature. Above all, the discoveries made it seem as though the life sciences could escape from the detail-ridden realm of natural history into the ethereal world of abstract laws.

Reconciling Diversity

The diversity found in living things has always presented the major obstacle to making generalizations and deriving universal principles. Darwin was one of the first to achieve universality in a biological principle and he did it by making the diversity of individuals in a species fundamental to his theory of evolution. But he was the exception. In contrast, the successful new disciplines of modern biology aimed at leveling the heterogeneity of their data; variation was considered to be "noise." This presented a challenge, however, as an increasing and bewildering variety of biological molecules (proteins) was discovered.

Initially, this variety was explained away by assuming that individual proteins (enzymes, receptors, or antibodies) could change their properties and mold themselves to whatever situation they encountered. Improved techniques for isolating these large protein molecules, however, revealed that they had stable properties and fixed affinities. Once the nature of DNA was worked out, this could be explained by establishing a link between the DNA's linear code and the specific structure of each protein. The obstacle that the diversity of proteins presented to the reductionist program was thus solved by invoking the concept of "molecular specificity" (Judson, 1979), in which each protein was thought to have a highly specific and dedicated role.

Much of the effort in contemporary biology has been devoted to tracing the specific roles of genes and proteins, and to defining the intricate relationships among them. Many descriptions of their coordinated activities have been generated, based on the premise that they act as an interlocking system, each fitting exactly into its rightful place. The picture thus painted has provided a first glimpse into a wide range of biological events ranging from embryonic development to the formation of long-term memories in adults. There seemed to be no limit to the explanatory power of the approach and, with the arrival of the human genome sequence, expectations are now running high that all remaining mysteries will be solved. Some have even postulated that human consciousness will be explicable in terms of molecules. The organism seemed to be revealing itself as a miniature Newtonian universe—a dynamic jigsaw puzzle, each microscopic piece performing its designated task in a beautifully choreographed ballet.
Trouble in the Ether

Not everyone, however, was content with this picture. Biologists studying evolution and ecology had not found the same kinds of abstract principles fitting neatly into a Newtonian view of life. Their material seemed inherently variable, unpredictable, and multi-factorial when it came to assigning causality. The same difficulties attended the study of behavior.

As applied to the workings of the brain, the Newtonian approach made the assumption that the brain encodes memories which exist as physical representations, as if "written" somewhere in the brain. The concept ran into serious difficulty in trying to account for the vast number of individual memories we are capable of retrieving and led to the reductio ad absurdum of the "grandmother cell"—a nerve cell whose only role is to store the memory of your grandmother faithfully over a whole lifetime. An analogous problem comes up in the attempt to account for the complex circuitry of nerve cells in the brain as being the product of a genetic "program" that specifies in detail which nerve cell connects to which. Finally, a composite of these two issues arises in how to account for the ability of the brain to perceive the world accurately and to coordinate so precisely between that perception and the individual's actions. The volume of detail required for a program to accomplish these tasks is daunting—excessive even for the most generous estimates of gene number prior to the Human Genome Project's soberingly small finding of 32,000. Beyond the problem of how to store so much information, a rigid program would be hard put to exhibit the kind of flexibility that permits evolution of a structure such as the human brain.

Among the sciences most imbued with the Newtonian spirit, recognition that there was a conceptual problem with that view came first to neuroscience (Edelman, 1978). The problem, however, is not confined solely to the workings of the brain. The growing awareness of the complexity of gene and protein networks in cells has also challenged the picture of a predictable system (Greenspan, 2001a). We find that most genes contribute to more than one characteristic. Moreover, the organism can often compensate for damaging mutations in individual genes through realignment of the activities and relationships among the rest. There must be more to it than just a simple system in which each effect has a clear and exclusive cause. The genetic counterpart of the "grandmother cell" is the "gene for ________" (fill in the appropriate trait: obesity, schizophrenia, novelty-seeking, etc.). The fact that genes do not account exclusively for any of these characteristics is a separate issue that has been discussed extensively in both the scientific and popular literature. Predictability is thus further compromised by the influence of extrinsic factors outside of the organism. In sum, the Newtonian approach fails to account for the complexity found in the living world.

Despite the conundrum of fitting biological beings into a Newtonian world, biologists are reluctant to let it go. Why has it been so tenacious? The sheer number and obviousness of the many accidents of evolution might have been enough to convince anyone that this could not be an accurate description. On the other hand, the impressiveness of the explanations from its offspring disciplines (physiology, genetics, and cell biology) has been overwhelming. The practical results coming from these fields made their reductionist explanations even more enticing.

Resolving the Conundrum

There are now inklings, however, that historical context is an essential part of any scientific explanation of biological events. This is true not only in the sense that embryonic development proceeds sequentially from egg to adult, or that species diverge over time. The playing out of biological events in time is fundamentally historical in the sense that there are alternative paths (mechanisms) to the same outcome, they are not exclusive of each other; and there is no predetermination as to which path will be taken. The actual path that is taken depends on which ones are available at the given time and place, the external conditions around the individual, its past history, and a certain amount of chance. This principle applies at all levels of biological function: communication between molecules in the cell and between cells, the activities of genes, the generation of signals in the brain, and the emergence of behavior from all of these processes. It helps account for the historical uniqueness of individuals, quite apart from any external differences in the environment they may experience. In fact, it accentuates the effect of environment.

Historical perspective on biological function is not much help
accomplish a step in embryonic development or to effect a behavioral action. More than one may actually be employed if the outcome is favored. These options give us a reservoir of alternatives for different occasions that allow us to tolerate some degree of insult to our systems (e.g., disease, injury, mutation, stroke, toxin) without having evolved a specific back-up mechanism for each unanticipated occurrence. We are flexible networks that are always responding to external conditions, internal state, and past history.

Homo Historicus

The upshot of this line of thought is that we are uniquely historical beings and thus unavoidably subject to context and contingency. An important part of context is our genetic make-up. Most creatures (all that reproduce sexually) are made up of a unique combination of their species’ gene set, inherited from their parents. All humans have the same set of genes, but not exactly the same versions of each. The only exceptions are identical twins and clones. These variations are parts of what make us all different from each other (Hirsch, 1965). The contextual aspect of genetic make-up has been shown in studies of behavioral mutants in fruit flies and in mice where the same mutation may have a strong effect in one strain but not in another (Greenspan, 2001a,b).

Beyond genetics, all creatures experience a non-identical sequence of life events. This is as true for genetically identical bacteria growing in a uniform environment as it is for a person living in New York City. Granted, the New Yorker encounters a greater degree of differential experience relative to other New Yorkers than any two bacteria in a test tube culture, but the principle holds nonetheless. Genetically identical bacteria represent an extreme case—we expect them to be uniform. If contingency holds for them, then it certainly holds for us.

The biochemical regulation in a cell is not so exact as to ensure an identical number of molecules in any two bacteria. Nor would this be demanded in a Darwinian mechanism. Given that any two cells may also be using different response strategies to their environments, the differences could be more than just a few molecules. Behavioral individuality can even be found in cultures of bacteria grown under identical conditions and subjected to
identical stimuli (Spudich and Koshland, 1976). Moreover, the order in which events occur produces a unique history, even for the same set of events. Identical bacteria subjected to the same set of growth conditions, but presented in different order, come out with distinctive characteristics (Remold, 2001). Thus, each biological individual is truly unique.

Word of our biological uniqueness and indeterminacy may come as a source of comfort for many who have been distressed by the relentless message in the popular science press that we are servants of our genes. While it is true that we could not live without genes, we are far from determined by them. Even more appealing is the realization that biological uniqueness is not just a by-product of the way things work, it is fundamental to the Darwinian mechanism.

Capturing Indeterminacy

If biological beings are fundamentally indeterminate, then how much can we ever hope to explain? Clearly, we cannot expect to make predictions comparable to the positions of the planets in our solar system. Nor is there any sense in which a person can ever be fully “explained.” We can, however, hope to identify some of the principles that govern biological systems in general. This may take the form of defining classes of phenomena as opposed to writing immutable laws. Examples include pinning down key selectional events, the repertoires on which they act, their mechanisms, and their criteria. While not being fully able to specify outcomes, we may be able to draw boundaries around possible ones. We cannot know all of the details, but perhaps we do not need to know them all. If we can exercise a modicum of Pascal’s esprit de finesse, we may find that the answer is neither in the details nor in a universal law but somewhere in between.


