Reframing Developmental Biology and Building Evolutionary Theory's New Synthesis

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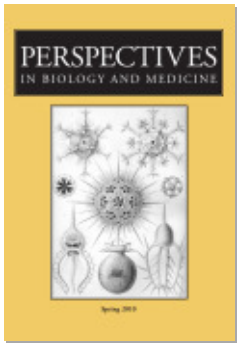

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Essay Review

Reframing Developmental Biology and Building Evolutionary Theory's New Synthesis*

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ABSTRACT Gilbert and Epel present a new approach to developmental biology: embryogenesis must be understood within the full context of the organism's environment. Instead of an insular embryo following a genetic blueprint, this revised program maintains that embryogenesis is subject to inputs from the environment that generate novel genetic variation with dynamic consequences for development. Beyond allelic variation of structural genes and of regulatory loci, plasticity-derived epigenetic variation completes the triad of the major types of variation required for evolution. Developmental biology and ecology, disciplines that have previously been regarded as distinct, are presented here as fully integrated under the rubric of "eco-devo," and from this perspective, which highlights how the environment not only selects variation, it helps construct it, another synthesis with evolutionary biology must also be made, "eco-evo-devo." This second integration has enormous implications for expanding evolution theory, inasmuch as the Modern Synthesis (Provine 1971), which combined classical genetics and Darwinism in the mid-20th century, did not account for the role of development in evolution. The eco-evo-devo synthesis thus portends a major theoretical inflection in evolutionary biology. Following a description of these scientific developments, comment is offered as to how this new integrated approach might be understood within the larger shifts in contemporary biology.

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IN THIS BRILLIANTLY conceived and executed book, presumably written to serve as a primary textbook for developmental biology courses, Scott Gilbert and David Epel provide much more than an introduction for college students. Indeed, why would Gilbert write another introductory text, when his *Developmental Biology* (Gilbert 2006), now in its eighth edition, has become the choice for the field? The reason is that the book under review is actually a stimulus for those who teach development to catch up to a new way of thinking about their discipline. Gilbert and Epel offer an alternative way to thinking about and teaching developmental biology. The new "developmental synthesis" they describe, arising from revised disciplinary boundaries (developmental biology and ecology melded with classical genetics and molecular biology), signifies a reframing of the basic theoretical questions underlying evolutionary theory and the very basis of understanding organismic biology. I think it no exaggeration to state simply that their elegant exposition (bringing together a historical perspective, primary scientific research, and critical interpretations of other theorists) captures a major conceptual change.

The authors' thesis maintains that development must be understood as an integrated response to evolutionary demands and places that discussion in its broadest ecological context. Thus they have reconfigured developmental biology, not so much by showing the successes of molecular studies (of which there are many), but by breaking the disciplinary boundaries that have previously confined development to two research traditions, embryology and genetics. By incorporating an ecological perspective they have placed development within a much wider arena that highlights epigenetics as an important mechanism for evolutionary change. To be sure, there have been many previous calls to formulate models of evolutionary pressures in various stages of development and thus present a theory of evolution that is more than a theory of adults (Buss 1987; Lewontin 1974), but this is the first sustained effort to make that synthesis based on current research.

We have waited about 25 years for the publication of a textbook that captures the important synthesis of hitherto distinct biological sciences, developmental biology and ecology, and also assesses current speculation on such an amalgamation. The genesis of developmental biology's realignment occurred during the mid-1970s, when a few theorists and developmental biologists recognized that the exclusion of embryology in the history of evolution theories was about to end (Laubichler 2007; Müller 2007). That intuition, and it was only an ill-formed idea at the time, was based on a rekindled interest in epigenetic effects in development.

Epigenetic effects refer to a variety of mechanisms whereby extra-genetic factors regulate the embryonic genome, transforming it from a prescribed sequence of instructions to a targeted substrate for variable modes of transcription and production of genetic variation. Together, these mechanisms generate novel adaptive structures and functions in the adult. The concept has a long history in biology and has been generally opposed to preformation theories, of which clas-

sical genetics serves as the modern paragon (Maienschein 2005). The dispute between the rightful place of epigenesis in the context of evolution begins with Darwin, extends to Thomas Huxley, and continued with the prescient views of Conrad Waddington 60 years ago. But the dominance of genetics in the 20th century swamped the fuzziness of epigenetic hypotheses with the hard facts of genetic determinism based on simple inheritance patterns. Newly discovered modes of genetic variation and the plasticity underlying them have, however, revised notions of a static genome to one characterized in dynamic terms, thus strengthening the claims of epigenesis against classical genetic preformation. The constellation of epigenetic findings, which serve as the focus of this text, range across phyla to reveal a basic precept: temporal and spatial contexts profoundly influence gene expression. With that insight a repositioning has occurred between these two competing theories of development.

The epigenetic "shift" demands full consideration of the context of development, namely, the environment of the developing embryo. This interactionist and contextual perspective has pervaded many of the life sciences (e.g., immunology; Tauber 2008a, 2008b) and is foregrounded in the Gilbert-Epel presentation of developmental biology. Exploring the dialectical relationship between the organism and its ecology (Levins and Lewontin 1987), even in the developing stages well before maturation, has radically widened the scope of understanding gene regulation, and thus the authors have presented a treatise on "ecological developmental biology," or "eco-devo" for short, to capture this ecological dimension of development. And with this synthesis a major revision in evolutionary biology's theory has followed, because of the implications of recent findings concerning the genome's plasticity. Developmental biologists have been invited to find their seats at the evolutionists' table, and the feast has been splendid. Indeed, this robust synthesis of evolution theory and developmental biology has also spawned another new field, "evo-devo" (Gilbert 2003; Gilbert, Opitz, and Raff 1996; Hall 1999). Finally, bringing these two hybrids together, Gilbert and Epel offer a more comprehensive synthesis, "eco-evo-devo," to encompass the reframing of developmental biology. To what extent this revision represents a "New Biology" will be considered after presenting a summary of the text.

Synopsis

The ambitious eco-evo-devo program is not easily summarized, but in brief, the presentation is made in three parts: (1) environmental signals and normal development; (2) ecological developmental biology and disease states; and (3) a developmental-evolutionary synthesis.

In part 1, the authors introduce the key concepts of plasticity and "eco-devo," which refers to the interactions between a developing organism and its environment. From this perspective, the ability to assume various phenotypes through a "choice" of developmental routes reflects the plasticity of development and thus

denies the rigid heredity of early genetics. In offering numerous examples of how developing organisms are influenced by their environment, Gilbert and Epel convincingly illustrate the dynamic character of growth and the dialectical interplay of the developing organism and its environs. The organism's response to the larger milieu, albeit limited by a genetic blueprint, must be fully accounted for in any theory of development.

They explain how embryonic responses occur at the molecular level with the regulation of gene transcription through differential gene expression (e.g., through DNA methylation). Microbial induction of gene expression is also an important environmental signaling mechanism in many species, and beyond responding to other organisms in the environment, some embryos "outsource" developmental cues to symbionts (organisms of different species living in close association with the host). Any theory of development must account for survival of unprotected embryos, and here we see the role of embryonic defenses that must counter potentially hostile challenges, including toxic substances, environmental stress (irregular temperature, radiation, oxidative stress, etc.), and predators. How well those defenses work determines the overall viability of the species.

After establishing the importance of environmental signals for normal development across phyla, Gilbert and Epel consider how pathology can be understood from an ecological-developmental perspective. "Ecological" refers to the environment writ large, so the effects of drugs, cigarette smoke, and alcohol, as well as natural compounds like retinoic acid, can affect normal development. Beyond these well-known teratogenic factors, so-called endocrine disrupters, which include certain plastics, cosmetics, and pesticides, dramatically remind us that we live in a sea of potentially toxic agents, whose ubiquitous use is difficult to control and whose long-term effects are not fully appreciated. Developmental biology research attending to this challenge will help guide regulatory policies in assessing the environmental impact of seemingly innocuous substances with unforeseen side-effects or of chemicals used for one purpose and resulting in calamitous effects in other systems (e.g., DDT, diethylstilbestrol, and bisphenol A). In other words, Gilbert and Epel rightly see an enormous public health impact resulting from a scientific program that more fully appreciates the ecological context of development.

In parallel, many challenges in adult health, ranging from diabetes and heart disease to cancer and aging, appear to have epigenetic origins and represent a second front in a public health program building on the eco-devo orientation. Whether originating from maternal effects, the environment, or lifestyle, genetic alleles and epigenetic changes in the genome suggest preventive measures and new drug therapies based on understanding that "development" does not stop at birth, but that its fundamental mechanisms remain operative throughout life (a view that dates at least to the end of the 19th century; Tauber 1991a). Simply put, lessons from the embryo have direct impact on adult medicine.

The third part of the text summarizes the most challenging aspects of developmental biology by explicitly bringing evolutionary biology onto the eco-devo stage. This broadened discussion of "evo-devo" to include "eco-devo" (Gilbert 2002; West-Eberhard 2003) serves as an excellent introduction to the current debate about newly discovered mechanisms of evolutionary change that operate in the developmental phase. I believe this is the heart of the book, because it clearly presents the most expansive implications of the discussions from the previous two sections.

After offering a concise and precise historical survey of evolutionary theory, Gilbert and Epel explain that evo-devo conceives evolutionary change as hereditable alterations in development through changes in gene regulation and developmental plasticity that account for selectable variation. In other words, following the Modern Synthesis of Darwinism and classical genetics (beginning in the 1920s and completed during the 1940s), the "Developmental Synthesis" presents evolution as inherited changes in the pattern of development and focuses on the mechanisms whereby such changes are effected. This evolutionary theory now addresses the embryonic origin of adult variations based on alterations at the level of gene regulation, and thereby supplements the accounts of survival of the fittest with illustrations of the "arrival of the fittest" (p. 324).

Evolutionary theory depends not only on understanding the generation of genetic variation, but also the basis of developmental plasticity (Amundson 2005)—the preconditions for what the authors call "mechanisms of tinkering" (p. 325). Three basic mechanisms at the level of gene regulation are molecular parsimony, molecular modularity, and robustness. *Parsimony* refers to the strong homologies of genes across phyla exhibiting powerful regulatory functions (e.g., transcription and paracrine factors, adhesion molecules, and signal transduction cascades). Numerous developmental regulatory genes (e.g., the Hox genes, responsible for posterior-anterior axis specification), exhibit high degrees of homology, and coupled to gene duplication and divergence, differing patterns of expression generate the variations observed across phyla. With structural or regulatory modification, these genes then assume different functions and generate new structures.

Modularity, the second basic precondition for developmental regulation, takes the same set of genes, for instance those responsible for forelimb development, and alters the timing of their activation and thus dissociates that aspect of embryonic growth from the rest of the body. Such a modular mechanism largely explains the difference between the wings of bats and the shortened arms of kiwis, for instance. Not only anatomical units, but gene enhancers are also modular, so that the differential activation of transcription factors gives rise to different anatomical structures. For example, enhancer elements allow particular sets of genes to be activated together and thus permit the same gene to become expressed in several discrete places (e.g., the Pax6 transcription factor regulates protein production in the eye that forms the lens and in the pancreas that acti-

vates the somatostatin gene). With this understanding, macro-evolutionary change is understood as a function of the genome's plasticity, where gene expression depends upon the local molecular context. Accordingly, the effect of gene products depends on the particular location and sequence of molecular events in which gene activation occurs. Indeed, given the striking similarities between humans and chimpanzees, some have postulated that the principle difference between ourselves and apes is the timing of regulatory gene activation.

Robustness comprises the third basic mechanism of developmental regulation and represents a conservative balance to plasticity by buffering against minor genetic perturbations. For instance, in "knock out" experiments, the function of a single gene may be compensated by the actions of others, so that no alteration in phenotype occurs. Robustness thus insures phenotype preservation as developmental interactions adjust to compensate for genetic or environmental differences. However, if robustness is too rigorous, variation cannot induce evolutionary change. To account for a balance between change and stability, robustness may be regarded as a gatekeeper: it provides a threshold for phenotypic change so that only large genetic or environmental perturbations produce phenotypic variants; alternatively, robustness allows for the accumulation of mutations that may be expressed as an ensemble under stressful conditions.

As Gilbert and Epel describe development, gene expression becomes a complex interplay of genes and their regulation in internal self-regulatory dynamics, as well as a dialectical "dialogue" with an environment that both provides the context for normal development and the challenges requiring adaptation and evolutionary change. So when they move their discussion to how the environment not only selects variation, it helps construct it, they arrive at the last stage of the new synthesis, "eco-evo-devo." This view of evolution incorporates three modes of inheritance. The first is *epigenetic inheritance* systems, whereby phenotypic expression of the information in the cell is transmitted to the next generation (Jablonka and Lamb 2005). This smacks of Lamarckianism, but that stigma is quickly dismissed as evidence has accumulated that inherited traits may be passed on to the next generation through changes in chromatin structure as well as changes in DNA sequences.

Second, *niche construction* describes how the developing organism can modify its own environment to maximize the attributes of its habitat (Lewontin 2000; Lewontin and Levins 2007). Increasingly, evidence has accumulated to demonstrate how organisms change their environment to accommodate themselves, and how that environment must be understood not only as the context in which organisms live, but also as an integrated aspect of their identity. Simply, "organisms do not experience or fit into an environment, they construct it" (Lewontin and Levins 2007, p. 33). In this view, the environment might be better regarded as external organs of physiology and even extensions of the animal's phenotype (Turner 2002). Indeed, organisms create their niches and this process is highly dynamic, inasmuch as they choose their habitats and resources and, through their

metabolism and behavior, they actively help create and destroy their own niches on scales ranging from the local to the global (Day, Laland, and Odling-Smee 2003). Couple this orientation to the thesis that environmental influences on development, not mutation, are the first order of design (West-Eberhard 2003), and rich new possibilities emerge in which to think of evolutionary processes.

Finally, *heterocyberny* is the concept that environmentally induced changes of a phenotype, when adaptive over a long period, can become the genetic norm of the species. Genetic assimilation (and the related "Baldwin effect") describes how novel phenotypes generated by developmental plasticity, if adaptive (and continuously induced by the environment), will spread under continued selection. So, allelic frequency follows repeated phenotypic induction and the selection of genotypes that are capable of generating the favored phenotype. Simply, if the phenotype is beneficial for fitness, the genes will stabilize it, or in other words, genes more often follow than lead evolutionary change.

In sum, the key underlying issue is plasticity, which can be enhanced or repressed. Genetic assimilation represses plasticity by narrowing the range of variation from a plastic state to a fixed one. This process, which Waddington called "canalization," produces a robust phenotype best suited for the animal's environment and its perturbations. Genetic accommodation is the other side of the coin, where plasticity, not canalization, is selected, and again this mechanism is regulated by the conditions of environmental pressures and the species' choice of adaptive mechanisms.

A New Frontier?

Gilbert and Epel have presented a picture of a dynamic genome in constant interchange with the environment. In this view, developmental biology has moved from a descriptive embryology to "systems biology," that is, a science concerned with accounting for the system-as-a-whole. The authors have joined those who maintain that to understand how components of complex systems function, better integration with causative factors must be understood. To organize and regulate those elements requires a new kind of analysis. Accordingly, explanatory models of the dynamic, emergent properties characteristic of biosystems demand a holistic approach coupled to the products of reductive analyses. On that train, they arrive at a station already crowded with those exploring other biological systems with similar scientific aspirations.

History pervades *Ecological Developmental Biology*. Indeed, a historical ether seems ever-present in this text, which reflects both Gilbert's broad approach and the general acknowledgment that understanding how embryology fits into contemporary biology requires a historical perspective (Laubichler and Maienschein 2007). Here, the narrative insistently demands redress of a misstep that occurred during the early decades of the 20th century, when theories of evolution, having abandoned comparative morphology as a central experimental program,

were written without embryology. Strikingly then, the current evo-devo New Synthesis places form back within the theoretical construct, and development becomes, again, a guiding aspect of evolutionary theory. Repeatedly, the reader is reminded that something new is afoot, and when a historical perspective is adopted, we are tempted to conclude that a significant theoretical inflection in the course of biology is underway, one that must account for "the causal and reciprocal interrelations between development and evolution at multiple scales and multiple levels of analysis" (Müller 2007, p. 504). The shift may well require a new "epistemic space" to account not only for the inner dynamics of the conceptual evolution of evo-devo (Laubichler 2007), but also better to comprehend the changing social and technological context in which this new field emerged (Gerson 2007).

There is good reason to believe that the life sciences, more broadly, are undergoing a major transition in their conceptual foundations. Adopting the 17th-century Cartesian method of reductive analysis, 19th-century biology followed the physical sciences with obvious success. Twentieth-century biophysics, biochemistry, and genetics each pursued a dissecting strategy to reveal the elements of complex processes in hopes of explaining their interactions and to offer explanations based on mechanistic models. Those biosciences that remained committed to a more holistic approach, most notably embryology and ecology, found investigators employing methods quite at odds with those wedded to the molecular approach of the reductive biological sciences (Tauber 1991b).

The 21st century has already witnessed a significant revision of this division, as the molecularists are now seeking integrative strategies. Furthermore, as holistic approaches are undergoing impressive expansion, older disciplinary boundaries are being redrawn as different kinds of skills (information theory, cybernetics, systems and operational theories, computer and mathematical modeling) are required to fashion "systems biology." The shared goal, stimulated by the inability to process the myriad, complex data derived from modern molecular techniques coupled to the frustration to adequately model the organization and regulation of complex systems, has tentatively placed all the players on the same playing field, which has been called, perhaps optimistically, a "new biology" (Woese 2004). This orientation builds on the general intuition that evolution, development, metabolism, immune responsiveness, and neurological functions each require explanations of the plasticity, emergent phenomena, self-organization, and nonlinear, dynamic causation pathways characteristic of organic phenomena. Of course how the new biology is practiced varies from one discipline to the next, but the general movement towards multi-variant analyses, nonlinear dynamics, and holistic description suggests a unified theme that incorporates eco-evo-devo in this general theoretical and methodological movement of an integrative biology.

In seeking to comprehend the complexity of biological phenomena as intact systems, the "new biology" is hardly new. Dissidents have waged attacks against

the triumphant march of reductionism throughout the 20th century in both evolutionary theory and developmental biology (Beurton, Falk, and Rheinberger 2000; Levins and Lewontin 1987). That history began in the 1840s, when German physiologists (led by Hermann von Helmholtz) declared that they sought to establish all biological phenomena on a common chemical-physical basis that would characterize the organic on the basis of forces, analogous to what was established in the physical sciences (Galaty 1974). These so-called reductionists did not argue against the unique character of life, only that all causes must have certain elements in common. They connected biology and physics by equating the ultimate basis of their respective explanations in physical laws, and proceeded to analyze organic processes within the framework of attractive and repulsive forces in order to link the physical sciences to the biological. Theirs was a metaphysical move against vitalism, and in that challenge, they pronounced a new biology, and justly so. By the 1860s, this novel scientific ethos had taken over the life sciences, and in the ascendancy of the reductionist strategy and its obvious advances, physiology assumed a new hegemony on claims of biological knowledge. On that stage, genetics joined biochemistry, and it is within this context that "soft" inheritance (epigenetics) encountered a massive and unyielding resistance.

The earlier tensions between old and new biologists were not so much over methodological reductionism, or even reductive epistemology, but rather over the underlying metaphysical issue of establishing cause. Traditionally (and typically), the biologist with reductionist commitments seeks causal linkages that are best described as linear and "mechanical." Only in the late 20th century has complexity theory coupled to systems-wide analyses suggested how multiple, nonlinear causation might serve as a better depiction of physiological and genetic processes (Alon 2007). Evolutionary theory has also reflected such shifts (Depew and Weber 1995; Jablonka and Lamb 2005), and now in developmental biology, Gilbert and Epel have clearly outlined a view of embryogenesis in which epigenetics has come of age, because the reductive pathway from gene to protein clearly fails the singular linear sequence predicted by the central dogma. Those who now envision how epigenetics might lead to a more comprehensive account of development and evolution share the basic insight—broadly acknowledged in the other life sciences—that regulation and organization cannot be explained by simple mechanical models and thus more complex modes of causation must be elucidated.

Developmental biologists have often employed "emergence" to capture the missing links of embryonic growth and differentiation. Traditionally, emergence has been used to capture those phenomena that are not directly related to the underlying characteristics of organisms and systems exhibited by reductive analysis. How to reconcile such phenomena in the context of epistemological reductivism remains a beguiling philosophical problem, because the character of causation is not established and appears as a kind of "top-down" control and even

"anti-naturalistic" (Bedau and Humphreys 2008; Corradini and O'Connor 2010). Recognizing that such explanations are wanting, developmental biologists still must account for how parts of the organism develop in relation to the whole, and within this larger context, causality must be better defined. It may well be that induction mediated through recognition proteins (Edelman 1988) and humoral regulation at a distance may ultimately suffice to explain what had earlier been called "field effects," but the jury continues to deliberate. Similar problems of explanation, resulting from reciprocal induction, resonate with basic precepts of the ecological sciences and readily expand into evolution theory. This general issue then applies in each domain and across the disciplines, or as the authors state, "entities need to be thought of in terms of several geometries at the same time. They are defined by braiding of down-top and top-down . . . networks built from patterns of reciprocal causation" (p. 410). These insights will have profound effects on the science of developmental biology (its methods and teaching) and beyond, for the lessons learned in this discipline portend a more complete integration of ecological considerations in constructing a biology with reconceived disciplinary boundaries. And from that restructuring, a new biology may well emerge.

Gilbert and Epel end their text with a philosophical "coda," which, in brief, suggests that placing developmental biology firmly within the mainstream of evolutionary and ecological perspectives raises intriguing questions about the ontological basis of the individual, where cooperative relationships vie with competitive identities in characterizing the relationship of the organism to its environment. Indeed, the borders separating one organism from another are often indistinct, and even when we refer to complex mammalian immune systems that sort out issues of identity—the relationships of "friend" and "foe," "attack" versus "tolerance," "self" distinguished from "other"—do not always follow categories that fulfill criteria that remain stable and may, in fact, vary with time and context (Tauber 2008a, 2008b).

The plasticity of individual development also suggests plasticity of interorganism relationships, and this in turn suggests that highly dynamical, dialectical processes are at play and only beginning to be appreciated:

> What does evolution look like when the proper unit of analysis is not the individual but the relationship (at each individual level)? What does evolution look like when selection may be on "teams" of organisms and on the relationships between these teams? What does natural selection mean when the environment is not only an agent that selects adaptive phenotypes but also contains agents that help instruct the formation of adaptive phenotypes (and may undergo changes itself because of it)? Moreover, how do we revise our views about the environment and evolution when germline DNA methylation can effect the transmission of environmentally induced characters from one generation to the next? (p. 414)

Indeed.

And beyond these questions, other philosophical issues loom. While stirrings of success have appeared, whether a different paradigm has emerged is not clear, because it is hardly apparent that the basic reductive strategy of the past century has been eclipsed, notwithstanding current efforts to revise the basic questions that organize research in genetics, developmental biology, metabolism, neurosciences, ecology, and immunology (Tauber 2009). As new investigative strategies in each of the biological sub-disciplines seem noteworthy and point to new vistas of research, the criteria for success of establishing new kinds of analysis have not been well established, nor have the outlines of research programs directed at these challenges been unambiguously explained. So, despite the excitement, a clearly articulated New Biology has not yet emerged, and we are left with promissory notes that must await collection. I detect a certain vagueness in these discussions, and I am reminded of the comment made by Justice Potter Stewart of the U.S. Supreme Court, who explained in an obscenity case that his own definition of hard-core pornography rested upon an enigmatic recognition, i.e., "I know it when I see it" (*Jacobellis v. Ohio* [1964]). I think new biology fits into that category—for, like pornography, the verdict is in the eyes of the beholder.

Conclusion

I remain agnostic about New Biology's promise. On the one hand, Gilbert and Epel show that new disciplinary boundaries are being formed and with that reorganization, the context of study is shifting. Thus it seems reasonable to suppose that the "Modern Synthesis" of R. A. Fisher, J. B. S. Haldane, Sewall Wright, Theodosius Dobzhansky, and Ernst Mayr (Provine 1971) will be dubbed the "Old Synthesis," as the new epigenetic thought collective becomes the "Refreshed Synthesis" (or something like it) to capture a theoretical shift in modeling biological processes—something less than a revolution but more than a modification. On the other hand, the *methods* used in these disciplines need not be affected by redrawn disciplinary borders and, consequently, reductive approaches remain in place. Note, while new modes of investigation have been introduced to organize and process data, the underlying epistemological reductivism is unchanged. Accordingly, epigenetics may already have been absorbed by the "old biology."

My cautious assessment of the New Biology rests on the judgment that reductive strategies seem fundamentally unaltered by new technologies designed to discover new regulative and organizational principles of complex systems. That is not to say that the questions being pursued and the scientific borders within which the problems are defined will not reveal new, possibly profound insights, but I am concerned here with the *philosophy* guiding these pursuits. From that perspective, contemporary biology, while acknowledging complex causation streams, has yet to reveal biological systems with different *metaphysical* characteristics than those envisioned by Helmholtz and his colleagues. Plainly

put, the elements defined by contemporary reductive techniques will likely be assembled to reveal more complex kinds of organization and regulation, and predictably, these too will be explainable by physical law and derivative understandings of causation originating in the 19th century. So while epigenetics (highlighting the plasticity of individual development as well as the plasticity of the organism in its environment) exhibits dynamical, dialectical processes, our understanding of the underlying character of biological causation has not fundamentally changed. Thus the reductionists' metaphysical agenda remains, albeit more complex than they might have envisioned given the state of the material sciences in their own era.

But enough! Let the philosopher contemplate while the scientist proceeds. The epistemological fruits of research will guide our metaphysics, and meanwhile we all watch with varying degrees of expectation. And returning to the subject of this review, at the very least, having presented an emerging shift in the research "thought collective" (Fleck 1979), for the uninitiated, *Ecological Developmental Biology* makes an important contribution to understanding a field breaking down old borders and establishing new alliances. I applaud Gilbert and Epel for so clearly showing the rapid methodological and theoretical changes in developmental biology and the corresponding impact on evolutionary theory. Their portrait of these contemporary sciences signifies an important movement of the conceptual parameters by which all biologists might reconsider their governing concepts, teach their science, and practice their craft.

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