Developmental Biology Meets Ecology

Ecological Developmental Biology: Integrating Epigenetics, Medicine, and Evolution
Scott F. Gilbert and David Epel
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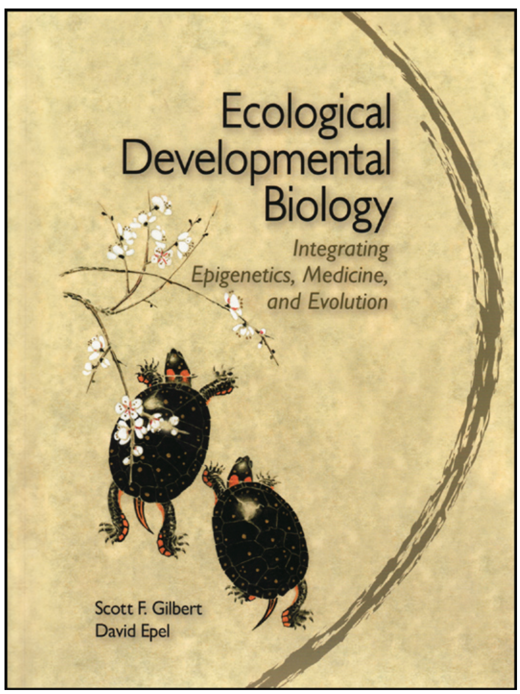

Outside a controlled lab environment, organisms confront a multitude of challenges in the natural world, such as temperature fluctuations, food shortages, pesticides, and predators. A new textbook, *Ecological Developmental Biology*, by the developmental biologists Scott Gilbert of Swarthmore College and David Epel of Stanford University focuses on how these ecological factors impact and guide normal organismal development. This new view of developmental biology highlights the relationship of organisms to one another and to their physical surroundings.

The book covers vast territory, describing how the environment can influence everything from cancer in humans, to wing patterns in butterflies, to sex determination in turtles. Yet, despite the broad scope, the writing is synthetic, and the authors use clear, simple, and accessible language with beautiful, colorful, and informative illustrations throughout. The book uses case studies, all cleverly strung together, to provide empirical support for three main topics: the influence of the environment on normal development; the impact of environmental degradation on the incidence of diseases in natural populations; and the contribution of development and ecology to a new evolutionary synthesis.

The first third of the book showcases examples of developmental plasticity in a variety of species and discusses the mechanisms behind them. Factors ranging from temperature to the presence of predators trigger changes in development. In turn, altered development results in different organismal form, sex, or behavior. Hormones, whose production is triggered by the nervous system in response to the perceived environment, are the effectors for most of these changes, but the environment also directly affects patterns of gene regulation through gene methylation. For instance, a pregnant mouse fed a “methyl-donor rich diet” can give birth to offspring with different morphologies and behaviors as a result of epigenetic changes to the offspring. Most importantly, data are rapidly accumulating that show how these environmentally induced patterns of gene silencing can be inherited over multiple generations. Finally, the role of symbiosis in development is highlighted. Apparently most, if not all, organisms have “outsourced” some of the cues important to their own development to other organisms living within them. For instance, although differentiation of the gut can be initiated in germ-free mice, signals from bacterial symbionts are required for the completion of differentiation. The same applies to the development of the immune system. The message is clear—an organism’s normal development depends not only on environmental factors to cue developmental decisions but also on interactions with other organisms.

The middle third of the book details the precise modes of action of several natural and man-made chemicals in the environment that disrupt normal development. Teratogens, such as thalidomide, and endocrine disruptors, such as the pesticide DDT, are all dealt with in turn. The molecular interactions of these substances with developmental processes are presented, along with their resulting effects that range from extra limbs in frogs to declining fertility in humans. In addition, we learn, alarmingly, that many endocrine disruptors also produce transgenerational effects through inheritance of epigenetic modifications. These chapters should be required reading for regulators at the U.S. Environmental Protection Agency, chemical company CEOs, and anyone considering spraying their front lawn to keep out dandelions.

The environmental causes of human diseases, such as diabetes, hypertension, and cancer, are also discussed. It is argued that early environmental influences on the fetus and disparities between the in utero and postpartum environments are factors that predispose an individual to disease. Early environmental influences can set certain genes to be expressed in particular ways—changes that are difficult to reverse later in life. Epimutations (changes in histone or DNA modifications that are heritable across development and that affect gene expression) appear to be responsible for these irreversible changes. These are presented as examples of adaptive plasticity because they prepare the fetus in anticipation of being born into a similar environment. For example, mothers that are deprived of nutrients during critical gestation periods produce infants that tend to be good at storing fat and metabolizing and extracting calories from food. But are these results really an evolved, adaptive response? The data presented fall short of showing fitness differences. Are these stories of exquisite adaptation, or are they just complex regulatory mechanisms gone awry?

Environmentally induced epimutations surface again in the context of cancer. The authors point to studies showing that tumor suppressor genes gradually become silenced by methylation as the organism ages. These are, indeed, exciting results, but in the end I found the purely descriptive mechanistic narrative of this section disappointing, especially given the larger goal of the book: to marry ecological development to evolutionary theory. For instance, none of the fascinating explanations for the origin of cancer and disease, as often discussed in terms of life history evolution, are brought forth. Why are tumor suppressor genes being methylated and oncogenes demethylated as we age? Do these data support the notion that aging is an evolved adaptation? A discussion of how these new discoveries might impact evolutionary theories of aging should perhaps be incorporated into the second edition.

In the last part of the book, the authors turn to the discipline of evo-devo. After reviewing some of its major themes (such as modularity, robustness, and deep homology) and presenting some classic case studies that show how evolution of body form depends on changes in both *cis*-regulatory and protein-coding regions in developmental genes, the authors return to the main topic discussed earlier, the system of epigenetic inheritance, and add two others, genetic assimilation and genetic accommodation. These three themes are the "new" themes that the authors advocate incorporating in the new eco-evo-devo synthesis. I agree. They are also central themes in books by Jablonka and Lamb (*Evolution in four Dimensions*, 2005) and West-Eberhard (*Developmental Plasticity and Evolution*, 2003), although in these books they are discussed in less molecular detail.

These themes underscore how changes in the environment may lead the process of genetic change, where genes are followers, rather than leaders, in adaptive evolution (West-Eberhard, 2005, Proc. Natl. Acad. Sci USA *102*, 6543–6549). Genetic assimilation refers to the genetic stabilization and fixation of a trait that is originally only induced by the environment, whereas the broader term genetic accommodation refers to the process of selecting genetic variants to create an adaptive new trait after either a mutation or an environmentally induced developmental rearrangement takes place. Although both genetic accommodation and assimilation fit nicely within standard evolutionary theory (see Braendle and Flatt, 2006, Bioessays *28*, 868–873), epigenetic inheritance does not. Epigenetic inheritance involves the inheritance of environmentally modified genes, a somewhat Lamarckian proposition. In addition, recent experiments on genetic assimilation have shown that epimutations, rather than DNA sequence variation, could be responsible for the process of genetic assimilation (Sollars et al., 2003, Nat. Genet. *30*, 70–74). How these results impact evolutionary theory is still unclear as few of the examples available so far demonstrate how environmentally induced phenotypes result in better-adapted phenotypes (for two excellent updated reviews, see Youngson and Whitelaw, 2008, Annu. Rev. Genom. Hum. Genet. *9*, 233–258 and Jablonka and Raz, 2009, Quart. Rev. Biol. *84*, 131–176). The data presented come primarily from lab experiments with domesticated organisms such as the fruit fly *Drosophila*, the model plant *Arabidopsis*, and mice. The one example on artificial selection for genetic accommodation in the moth *Manduca sexta* is perhaps the closest to showing some adaptive significance of the selected trait—in this case a change in larval coloration due to environmental temperature (Suzuki and Nijhout, 2006, Science *311*, 650–652). Perhaps we should view these early studies as proof of mechanism, and with increased attention to the role of the environment in leading genetic change in natural populations, examples with adaptive significance may gradually emerge.

Ultimately, I feel that despite the laudable efforts in the last chapters to tie together ecology and developmental evolutionary biology, many aspects of the complexity of developmental systems are still left unquestioned from an evolutionary perspective. For example, how did modularity in gene regulation evolve? Why have genes that are expressed in serially homologous structures, such as fly segments or wing veins, evolved separate *cis*-regulatory elements? What was the ancestral state of these genes? Did they have a single enhancer element that drove the gene's expression in all the repeated structures and later got fragmented into individual elements? Or did these elements, and the corresponding serial homologous traits, evolve one at a time? Answering these questions requires a comparative approach, exploring gene regulation in a variety of nonmodel systems in a phylogenetic framework. Another unsolved mystery in evo-devo is to figure out how real innovations, such as insect wings, actually originate. Evo-devo really has to embrace the origin of novel complex traits, rather than just their gradual modification or elimination, which is what most of us in the field have been doing (Monteiro and Podlaha, 2009, PLoS Biol. *7*, e27). Gilbert's and Epel's book provides a framework for integrating the environment in the evolutionary developmental process, but I remain skeptical that environmental input is a major factor in the origin of novel complex traits. Nevertheless, this is a must-read for graduate students interested in integrating ecology, developmental biology, and evolutionary biology. And, with added conceptual structure to the mid-section of the book, it should also be suitable for an upper-level undergraduate course aimed at pre-medical students.

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