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BOOK REVIEW

Life = epigenetics, ecology, and evolution (L = E^3): A review of *Developmental plasticity and evolution,* by Mary Jane West-Eberhard

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Developmental Plasticity and Evolution. West-Eberhard, M. J. 2003. Oxford University Press, New York. xx + 794 pp. Hardcover $100. ISBN 0195122348.

This extension and elaboration of West-Eberhard's earlier ideas regarding the paramount role of phenotypes and developmental plasticity in evolution yields a milestone classic of epic proportion. The book comprehensively explores the mechanisms and implications of developmental plasticity to numerous aspects of both micro- and macroevolution. The book has already received prominent accolades, and each chapter was scrutinized by numerous experts. This is a tour de force of scholarly achievement amounting to 637 pages of nicely illustrated text. The 31 chapters are grouped into four sections: (a) *Framework for a synthesis,* (b) *The origins of novelty*, (c) *Alternative phenotypes*, and (b) *Developmental plasticity and the major themes of evolutionary biology.* Chapters indeed can stand alone, and the chapter abstracts are very useful. West-Eberhard seamlessly shifts between a broad mastery of the classical literature and up-to-date modern science. The number, depth, and breadth of supporting examples are more than comprehensive, spanning numerous phylogenies of lower organisms, plants, and animals while considering levels of organization from the molecular to the social. Animal behavior is integrated throughout as a crucial aspect of phenotypic flexibility, and an entire chapter is devoted to learning. The book has a well-defined advocacy that deemphasizes genetic determinism and concepts of integration. This will undoubtedly evoke appropriate scientific controversy.

I place greatest emphasis on the first two sections where perspective and theory are developed. The book begins by attacking a host of concepts that are viewed as metaphors for development or barriers to an evolutionary theory based on developmental plasticity (e.g., epigenetic landscapes, genomes as blueprints, genotype–environment interactions, genetic programming [of development], canalization, stabilizing selection, homeostasis, developmental constraints, and coadapted gene pools). Consider the following:

- Page 3: "The conceptual gap that should be filled by development has been filled instead with metaphors, such as genetic programming, blueprints for organisms, and gene-environment interactions."
- Page 4: "If recurrent phenotypes are as much a product of recurrent circumstances as they are of replicated genes, how can we accept a theory of organic evolution that deals primarily with genes?"
- Page 7: "Cannon's (1932) idea of physiological homeostasis …Waddington's (1942) idea of canalization, plus the idea of stabilizing selection…put evolutionary theory on a track that that has made it difficult to reinstate development as an innovative factor in evolution."
- Page 15: "The genetic program metaphor does not suggest the possibility that environmental elements are partly or entirely responsible for the development (or nondevelopment) of a phenotypic trait.
- Page 15: "… genotype-environment interaction is misleading as a description of development because genes do not interact directly with the external environment during development. All interaction is indirect, via effects of both factors on a preexisting phenotype."
- Page 17: "Yet if we accept the dual nature of the phenotype—the undeniable fact that the phenotype is a product of both genotype and environment, and the equally undeniable fact that *phenotypes* evolve, there is

no escape from the conclusion that evolution of a commonly recognized sort can occur without genetic change."
- Page 20: "Genes are followers, not leaders, in evolution."

Major themes are deemphasis of genetic determinism and concepts of integration that imply phenotypic stasis or inflexibility as opposed to emphasis of environmental induction of phenotypic novelty that always precedes changes in genes. Arguments are cogent, although the perspective is actually quite radical (e.g., evolution without genetic change). Waddington's famous figure (p. 13) of the epigenetic landscape is described as "incomplete, and potentially misleading, because developmental potentialities change as development proceeds."

However, Waddington's figure clearly indicates bifurcation points arising in later development, which is about the best a static diagram could do. Furthermore, Waddington must be credited with recognition that environment can drastically shift development, and it is difficult to see how any of his ideas represent any barrier to considering development as an innovative factor in evolution. The crux of criticism amounts to whether potentialities are ultimately genetic versus West-Eberhard's emphasis on environmental induction (p. 13):

> Waddington's diagram is static. It shows only potentials defined genetically at birth. All that environment can do, in Waddington's scheme, is deflect development into a new genetically specified path.

To me, the genome can be considered as a compressed code that is developmentally unzipped. That many impacts of genes are indirect or environmentally malleable does not need to detract from the fact that there can be no initial phenotype without a genotype and no evolution without selection that alters the genome (including heritable changes in chromatin structure). For example, differential success among social insects may depend on the effectiveness of divergently canalized sterile castes to reduce risk, provide environmental homeostasis, and promote the reproductive success of queens. The specialized adaptive suites represented by various castes evolve entirely via indirect selection on queens, and if environmental features are co-opted as part of the regulatory Bauplan, this does not uncouple the genome from the colony phenotype. Kauffman (1993) and Goodwin (1994) emphasize that the genome may harness intrinsic properties of nature, such as extragenomic mechanisms yielding spots, stripes, or spirals. The resulting phenotype is still genetically directed and may have high stability as well as the potential for environmental modifications.

I was not convinced to surrender concepts I consider very useful because I have not found them any obstacle to evolutionary theory encompassing developmental plasticity. The selfish gene has been moribund for some time, and evo-devo fully embraces concepts of integration, flexibility, and plasticity without contradiction. Marginalization of genetics and integration seems unnecessary and runs the risk that more could be lost than gained. Although sentiments expressed in Chapter 1 resurface throughout the text, better balance actually prevails for most of the book. West-Eberhard's arguments are extensive and compelling, and each reader will need to form their own opinion.

Chapter 3 provides an overview of plasticity, with an interesting emphasis on "phenotypic accommodation": "the integration and exaggeration of both developmental and evolutionary change without genetic change" (p. 34). The idea is that plasticity in integrative adjustments can accommodate or exaggerate developmental variation to yield functional phenotypes. The example of a two-legged goat is used throughout the book. Highlights include discussion of animal behavior, learning, and numerous tissue responses. Somatic selection, particularly of overelaborated components, is discussed extensively with no reference to the complex regulatory systems determining both susceptibility and criteria for programmed apoptosis common to many such systems. I also continued to have problems with references to evolution without genetic change.

Chapter 4 (Modularity) is a masterpiece and complementary cornerstone to Chapter 3. Modularity is argued to provide escape from cohesiveness, facilitating the generation of phenotypic novelties and mosaic evolution. Moreover, this is argued to be the predominant organization of phenotypes. This in turn bears strongly on West-Eberhard's criticisms or deemphasis of mechanisms or concepts related to integration and cohesion in favor of pervasive flexibility. Although most of the book applies this vision to full purpose, it is notable that the last two chapters do somewhat of an about face. Chapter 30 (devoted to punctuated evolution) deemphasizes the importance of speciation to punctuated change while favorably recognizing evolutionary stasis (which is suggested to be maintained by plasticity). Chapter 31 is largely an argument that sexual reproduction is maintained by developmental constraints or traps.

Chapter 5 (Development) emphasizes switches and developmental flexibility. The importance of the genome is acknowledged initially (p. 90): "The genome affects development at nearly every turn, so genes obviously play an important role in any theory of development and evolution." The emphasis, however, is on condition-dependent gene expression and utilization of environmentally supplied materials, leading to the statement (p. 93) that "Contrary to the impression given by genetic–control metaphors for development, the bare genes in isolation are among the most impotent and useless materials imaginable." The question comes down to whether indirect actions of genes mean they have harnessed higher order, extragenomic organization or vice versa. The question itself may be circularly inappropriate. Whereas I have suggested that phenotypes are lineage products because initial genetic and developmental steps are maternally derived (Rollo 1994), West-Eberhard argues that such continuity (p. 93) "implies that the individual's genome does not control its development: the zygotic genome is constrained to play upon the responsive structure that is in place when particular genes are expressed." West-Eberhard then extends and reinforces this idea (pp. 93–94):

> "Exquisite precision in the timing of gene expression should not be taken as evidence for the genetic orchestration of development. Rather it should be taken as evidence of the enslavement of the genome by the phenotype…the predictable effects of genes depend as much on the specific organized flexibility, modular differentiation, and local conditions within a preexisting structure as they do on the specificity of the genes themselves."

Contrast this to my development of the same analogy in the context of the genome as a coadapted genetic templet derived by holistic selection at the phenotypic level—one of West-Eberhard's problematic metaphors (Rollo 1994, p. 121):

> "The wondrous degree of integration revealed in the developmental genetics of *Drosophila* resoundingly validates the intuition of numerous evolutionary biologists that the genome represents a highly coadapted complex…Rather than being free-ranging selfish outlaws, most consolidated genes probably reside in rather cramped organizational prisons. Selfish DNA…and viruses, if they have not coevolved with their hosts, might be viewed analogously as rats scurrying from cell to cell. The existence of free-ranging rats, however, in no way obviates the reality of incarceration for the inmates."

Natural selection at the level of phenotypes screens through numerous organizational levels down to the genome (otherwise there is no evolution). Developmental unzipping of the genome (from genes to phenotype) traverses the same levels of organization according to previous evolutionary success. Whether genes are selected through or developmentally act through numerous levels of phenotypic organization does not detract from their importance in either top-down evolution or genes-up development. A single mutation in the Ames dwarf mouse results in failure to differentiate pituitary cells that secrete growth hormone, prolactin, and thyrotropin-releasing hormone. These higher order control systems are tightly linked to the genome and globally impact development and adult functioning. Knockout of the leptin receptor or inserting extra growth hormone genes in mice further reinforces that transcription factors, cell transduction networks, and hormones are messengers to and from the genome. To my mind the fact that such proteins are extragenomic or environmentally sensitive or even that cell–cell interactions are involved in morphogenesis does not diminish the reality of genetic orchestration.

Core mechanisms are elaborated in Chapter 6 (Adaptive Evolution). Three classic phenomena, genetic assimilation, neutralization of harmful mutations, and the Baldwin effect, are elaborated, synthesized, and extended under the new umbrella of "genetic accommodation." The classic example of Waddington's genetic assimilation was the fixation of lines of four-winged *Drosophila* (*bithorax*) by selecting flies that so responded when egg development was derailed by an environmental insult. The importance of the concept has paralleled the rise of evo-devo. My favorite example of Schmalhausen's "neutralization of harmful mutations" was a line of "*eyeless*" *Drosophila* that regained their eyes in freely breeding cultures via segregation of modifiers that neutralized the presence of the mutation. Such examples led Schmalhausen (I believe rightly) to his recognition of stabilizing selection as an important evolutionary mechanism, and one closely allied to Waddington's ideas of canalization. West-Eberhard deemphasizes both concepts (as they suggest developmental inflexibility) while adopting both mechanisms. The Baldwin effect proposes that phenotypic traits expressed in novel or extreme environments may precede genetic accommodations that may improve, stabilize, or extend such expression. Waddington considered that this referred to fortuitous mutations, but West-Eberhard clarifies that mutation need not be involved. Such ideas reflect West-Eberhard's view that phenotypic variation necessarily precedes genetic changes. As have others (e.g., Hall 1992), I too have argued that phenotypes may lead evolution (e.g., Rollo 1994, p. 228, Lake Victoria cichlid fish):

> Given a range of different feeding niches that represent alternative adaptive peaks, a generalized cichlid ancestor could chase its own plasticity across the regulatory maze of epigenetic organization.

That genetic change may follow environmental alterations in phenotypes is no problem; it is the apparent deemphasis of genetics as playing an important initial role or in providing selectable phenotypic novelty (other than for mutations) that rings too extreme.

The validity of "genetic accommodation" will require the test of time. Although nicely capturing the theme of this book, in application better clarity might be obtained by reference to the explicit mechanisms. Placing environmental impacts and mutations in one box does not create fusion but quite possibly an ambiguous metaphor. This was highlighted by a discussion of maize evolution where genetic mechanisms were abutted to genetic accommodation (p. 268), and I found myself asking, what is the difference?

Mutations pose a serious problem for the claim that genes always follow phenotypes and treating them as a special case sets off alarms. There are indications that mutations of large effect are meant (pp. 104–105), but this then creates an artificial dichotomy. Although circulating alleles likely represent consolidated mutations (even if transcending speciation events), genetic variation due to sexual reproduction is dismissed as a source of phenotypic novelty by West-Eberhard (p. 145):

> I know of no evidence that genetic recombination is an important source of adaptive phenotypic novelties in sexually reproducing organisms, as important as recombination may be in the spread of alleles and their testing in different conditions.

Surely the uniqueness of most individuals in sexually reproducing populations constitutes important phenotypic/genetic novelty, and the fact that individuals are transient in no way hindered classical geneticists from selecting traits expressed in constant environments—often to profound effect. All the mechanisms representing genetic accommodation require recombination/segregation to work, and West-Eberhard herself notes (p. 506) "Individual differences in response to unusual extremes may be due to genetic differences among individuals and this would hasten their genetic accommodation." Selection of a phenotype as extreme as *bithorax* without new mutations highlights sexual recombination, segregation, and initial genetic variation as critical to generating phenotypic shifts in response to the environment, but the importance of these aspects is largely restricted to the movement of alleles among bodies by West-Eberhard. Alternatively, her point that environment can impact entire populations whereas mutations must spread is well taken.

West-Eberhard does not disappoint with respect to fully developing and exploring her theories of "alternative phenotypes" (four chapters in section 3). Here many novel and powerful ideas are driven home with a host of examples, making this perhaps the most useful and interesting section of the book.

Darwin considered that species diversity reflected the availability of niches. West-Eberhard criticizes the empty niche theory (p. 610) and even apologizes for using the term niche (p. 507). Discussion focuses on niche shifts that may induce phenotypic novelties and genetic accommodation, which is appropriate for the book and well done (Chapter 26, Environmental Modifications). I was surprised, however, to find little substantial discussion of convergent evolution. Chapter 25 devoted to homology (similarity due to common descent) is certainly appropriate for a focus on developmental plasticity, but there are arguments that common descent extends very deeply (e.g., to homologous genes in the eyes of insects and vertebrates; p. 492). The chapter is a thoughtful consideration concluding that terms like parallelism and convergence are only approximate and potentially misleading. In Chapter 28 on adaptive radiations (also very well done), we are referred elsewhere for consideration of the "ecological theory of adaptive radiation" which is criticized for not considering that ancestral phenotypes must influence the nature of radiations (p. 565). To me, phenotypic convergence in distantly related species occupying similar niches emphasizes the ecological shaping of developmental flexibility (e.g., parallel radiations in marsupials and eutherians; fish-like designs in fish, reptiles, and mammals; insect versions of hummingbirds and moles). That whales and ichthyosaurs may share homologous fin genes means little because these would also occur in a plethora of terrestrial and aerial modifications in both reptiles and mammals. Convergence on fins and fish-like bodies reflects hydrodynamics and not necessarily common descent at all. Convergence emphasizes the magnitude of developmental flexibility whereas the ecological underpinnings highlight niches, adaptive suites (which do not exclude plasticity), coadapted genomes, stabilizing selection, and canalization (neither of which excludes multiple canalized morphs). Although there is plenty of ecology in this book, it does not conform to conventional evolutionary ecology.

With regards to sexual reproduction, Chapter 15 extensively covers cross-sexual transfer of traits, and mate choice is considered in Chapter 23 (Assessment). Chapter 27 (Speciation) is an important discussion suggesting that phenotypic divergence may precede assortive mating. I read Chapter 31 devoted to sexual reproduction first as I expected that recombination and segregation would be highlighted in any evolutionary theory of phenotypes. Instead, the chapter is largely restricted to arguments that sex may be maintained (despite its twofold disadvantage to individuals) because of developmental constraints or traps, even though most of the book argues otherwise. The discussion of female mate choice as a possible factor maintaining sexual reproduction was a nicely honed gem, whereas suggestions that constraints may arise from the donation of mitochondria by males (p. 632) and genomic imprinting (which apparently is developmentally reprogrammed for the appropriate gender) seem to be particularly unconvincing. What I expected here was discussion of things like that touched on in Chapter 26. Here (p. 506) West-Eberhard argues that environmental extremes (like temperature) may expose variation in reaction norms or even extensions of these norms not previously exposed to selection. I outlined this same model using the hypothetical evolution of short tails in northern rodents (Rollo 1994, p. 224). The naked tails of mice and rats serve as radiators, and a developmental program adaptively modifies tail length in response to ambient temperature. Temperature exposes a reaction norm for building tails that would increase penetrance of relevant genetic variation over that visible to selection in optimal conditions. Although probably heretical, this suggests that the variation exposed may also be adaptive to the stressor.

Consider further that successful selection on tail length can invoke more than one solution, even among lines derived from the same initial population (e.g., more or longer vertebrae to obtain increased tail length) (Hall 1992). In fact, regulation of features like temperature, growth, and mouse tails involves a plethora of possible regulatory variants (e.g., hormones, receptors, cell transduction elements, transcription factors, alternative splicing, protein assembly, degradation machinery). Sexual reproduction among selected parents could assemble suites of regulatory modifiers in offspring, all predisposed to act in the appropriate direction. Such theory requires balanced consideration of development, phenotypic plasticity, genetic variation, environmental impacts, and sexual reproduction as important evolutionary mechanisms (E^3 in the title). Consequently, I see West-Eberhard's call to dismiss the dichotomy between regulatory and structural genes as a step backward, even if some structural genes indeed provide signals. That 99% of mouse genes have human counterparts (Gunter and Dhand 2002) and that regulatory sites in *Drosophila* developmental genes can comprise 95% of sequences reinforces gene regulation as paramount to developmental divergence (Rollo 1994). Even small changes in regulatory sequences can potentially rewire developmental circuitry.

Clearly, new (and nongenomic) information is unzipped as development proceeds. Chapter 17 explores how combinatorial evolution at the molecular level can contribute to increasing higher order information and attests to West-Eberhard's deep knowledge of modern genetics and genome organization. This is nicely done, but what ultimately is regulating things like splicesomes? The fact that there is an unfolding of information does not discount genomic regulation. On pages 327–328 West-Eberhard argues that changes in gene expression can represent evolution, and this is contrasted to "conventional" evolution representing gene frequency changes or "genomic change." The purpose is to point out that a change in environment can alter patterns of gene expression. She does not seem to consider here that mutations in regulatory (rather than coding) sequences may explain most changes accounting for differences in mice and men. Both species are environmentally cosmopolitan, but phenotypic variation is generally modest. Environmentally induced change in gene expression is physiology or plasticity to me—not evolution. Consequently, I have trouble with West-Eberhard's arguments that phenotypic diversity does not reflect genomic information (p. 334): "Evolved phenotypic diversification is not likely to be limited by the variety of genomic information—by the mutation rate."

If genes were overemphasized by previous paradigms, West-Eberhard's enthusiasm may swing the pendulum a little too far in other directions. Ultimately, a balanced synthesis is required (E^3), although that may be a singular opinion. Regardless, this book represents an intellectual blitzkrieg worthy of careful consideration and respect. This is certainly one of the best books I have seen in 20 years, and one can benefit from the full range of content, regardless of whether West-Eberhard's perspective is fully accepted or not. Every reader will find their own ideas altered and expanded by at least some of the examples and arguments representing the lifetime gestalt of this exemplary scientist. The scope and scholarship are truly awe inspiring. I recommend it to all without reservation.

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