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REVIEW

Developmental plasticity and evolution—*quo vadis?*

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The role of developmental (phenotypic) plasticity in ecology and evolution is receiving a growing appreciation among the biologists, and many plasticity-specific concepts have become well established as part of the mainstream evolutionary biological thinking. In this essay, I posit that despite this progress several key perspectives in developmental plasticity remain remarkably traditional, and that it may be time to re-evaluate their continued usefulness in the face of the available evidence as the field looks to its future. Specifically, I discuss the utility of viewing plastic development as ultimately rooted in genes and genomes, and investigate the common notion that the environment—albeit a critical source of information—nevertheless remains passive, external to and separable from the organism responding to it. I end by highlighting conceptual and empirical opportunities that may permit developmental plasticity research to transcend its current boundaries and to continue its contributions toward a holistic and realistic understanding of organismal development and evolution.
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THE ACCOMMODATION OF PLASTICITY IN EVOLUTIONARY BIOLOGY

Developmental, or phenotypic, plasticity has matured from an embellishment to mainstream thinking in evolutionary biology and ecology and is now a fundamental aspect in our understanding of the genesis of phenotypic variation. It is safe to say that we have arrived at a point where, without explicit consideration of plasticity, our understanding of any trait, any pattern of variation within a population, and any reconstruction or prediction of evolutionary trajectories would be incomplete (Schlichting and Pigliucci, 1998; Pfennig *et al.* 2010).

Developmental plasticity is clearly here to stay, as are the concepts that have matured in its midst. A battle won early in the field's history was the realization that quantitative genetic models are incomplete without explicit recognition of *g x e* interactions, and that reaction norms can evolve independently of trait means within environments (Schlichting and Pigliucci, 1998). Similarly, we now widely recognize that penetrance of mutant phenotypes, trait heritabilities and trait covariance structures are all influenced by environmental conditions, and are thereby able to alter evolutionary trajectories, sometimes in profound ways (Stearns, 1989; Gibson and Dworkin, 2004; Schlichting, 2008).

Other insights, however, have taken longer to solidify and spread: for example, the notion that developmental plasticity acts as a buffer to not only just environmental but also genetic perturbations, and thus can function as a capacitor for cryptic genetic variation, has only more recently gained traction (Gibson and Dworkin, 2004; Schlichting, 2008; Snell-Rood *et al.* 2010; Van Dyken and, Wade, 2010; Paaby and Rockman, 2014). Similarly, it has taken us fairly long to realize that—via the process of phenotypic accommodation—developmental processes self-adjust to novel challenges, producing integrated and functional phenotypes in the process without requiring any genetic changes to do so (West-Eberhard, 2003). And there remains heterogenous appreciation for the notion that phenotypic accommodation can fuel genetic accommodation when environmentally induced phenotypes are subsequently stabilized and fine-tuned across generations by selection on standing genetic variation, previously cryptic genetic variation, or newly arising mutations (West-Eberhard, 2003; Pfennig *et al.* 2010; Moczek *et al.* 2011). However, the growing number of research and review articles, edited volumes, monographs and special issues such as this one attest to the likely staying power of these concepts.

At the same time, research into phenotypic plasticity has identified a wealth of developmental, physiological and behavioral mechanisms that mediate plastic responses depending on organism and context (reviewed in, for example, West-Eberhard, 2003; Nijhout, 2003; Beldade *et al.* 2011). Collectively, this research gradually replaced an abstract treatment of plasticity dominated by statistical approaches, with the biological reality of hormones, cells, genes and methylation patterns. There is no question that research in developmental plasticity has fundamentally enriched the conceptual and mechanistic portfolio of biologists in ways that now enable us to investigate and understand phenomena we previously could not, or were not even aware existed.

Below I argue that despite this progress, several key perspectives in developmental plasticity remain remarkably traditional, and that it may be time to re-evaluate their usefulness in the face of the available evidence as the field looks to its future. I begin with the notion of where, exactly, the ability to be plastic resides.

PLASTIC GENOTYPES

Most text books and reviews explicitly define norms of reaction, and developmental plasticity more generally, as the property of a genotype. Correspondingly, much research in developmental plasticity now focuses on identifying genes and pathways that change expression in response to environmental conditions, or alter their methylation signatures, or modify their interactions with other genes and their products to mediate responses to divergent environmental regimes.

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This trend has become ever more enhanced in recent years as screening technologies are increasingly available and affordable outside traditional model systems.

Viewing developmental plasticity as a phenomenon enabled ultimately by genes and genotypes in response to an external environment, provides a straightforward framework which has helped guide many successful research programs within the field and generated a wealth of interesting data. The question before us now is whether we are done and whether this framework is sufficient to guide the field into the future.

Here it may be useful to examine how far other disciplines have come that have adopted a purely gene- or genome-centric perspective on phenotype formation. For example, a truly massive effort has been devoted to identifying the genetic basis of human diseases and disorders. Yet for many of them, including late onset Alzheimer's disease (Li *et al.* 2008; Bertram *et al.* 2010), schizophrenia (Kato, 2007), depression (Levinson, 2006) or obsessive-compulsive disorder (Nestadt *et al.* 2010) we remain unable to explain more than a few percentage points of the phenotypic variation based on knowledge of genetic variation alone. Another example concerns perhaps one of the oldest quests in evolutionary biology—to understand the genetic basis of evolutionary novelties and major transitions in evolution. Major innovation and transitions in evolution reflect, by definition, significant departures from ancestral variation, yet our search for genes and genetic variants that facilitated the origin of the first eye or wing, or the transition from water to land, have overall been rather frustrating (Moczek, 2008). As before, we are able to associate important genetic contributions to the present day manifestations of each of these major innovations (for example, Shubin *et al.* 2009), but exactly what it took to initiate each of these transitions in the first place, and why they occurred when they did, remains surprisingly poorly understood.

This brief excursion is not meant to deter a search for genes for plasticity, but to emphasize that if we limit ourselves to this approach we may face the same limitations already encountered by other branches of biology. Instead, plasticity research may benefit from (re) emphasizing more strongly that plasticity may be best understood as an emergent property of developmental systems, and one that is enabled by diverse biological mechanisms, at least some of which may not primarily be underlain by differential gene expression or affected by sequence variation. Interestingly, efforts to adopt such a developmental systems perspective have led to some of the most significant recent progress in both the search for the developmental causes of disease (for example, Barker, 2013; McMullen and Swali, 2013) and the developmental basis of major evolutionary transitions (for example, Ledón-Rettig *et al.* 2008, 2010; Standen *et al.* 2014), and there is every reason to believe that such an integrative approach could be similarly advantageous for research programs in developmental plasticity.

PASSIVE ENVIRONMENTS

Even though research in developmental plasticity clearly emphasizes and appreciates the environment as important and critical in organismal development, we continue to view it as separable, external and passive. The field is reaching a point; however, where these attributes are increasingly difficult to reconcile with empirical data.

For example, across diverse taxa, the prevailing sensory environment experienced during development heavily influences synapse formation during nervous system differentiation, yet doing so influences in turn which sensory environment is perceived a later developmental stages (Levitt *et al.* 1998; Kolb and Whishaw, 1998; Rampon and Tsien 2000; Baroncelli *et al.* 2010). Similarly, across phyla gut formation is responsive to dietary conditions, which in turn delineates which future dietary environments the developing organism will experience (Ledón-Rettig *et al.* 2008; Bloom *et al.* 2013; Christeller *et al.* 2010; Saikia *et al.* 2011; Agrawal *et al.* 2002). In these and many other cases, plastic responses to environmental conditions often do not simply adjust aspects of phenotype formation but also modify the selective environmental conditions in which the developing organism finds itself.

This is further enhanced in contexts in which the responses to environmental conditions modify selective environments across generations, for instance via plasticity in habitat conditioning or environment-responsive parental care (Laland *et al.* 2014). At the same time such effects may play out on any level of biological organization, from social groups to maternally transmitted antibodies. As a consequence, at least some, and perhaps most, organismal environments may be better viewed as in part constructed by the organisms themselve, as a type of extended phenotype that is potentially heritable across generations, and thus capable of evolutionary change (Laland *et al.* 2014). In such situations, where plasticity starts, organisms end, and their environments begin, is less straightforward to nail down than we are used to. Luckily, several conceptual frameworks have emerged that may provide useful ways to incorporate the growing complexity of developmental plasticity into meaningful experimental frameworks. Two such frameworks are discussed next.

THE MORPHOLOGY OF DEVELOPMENT AND THE THEORY OF FACILITATED VARIATION

Formulated by Kirschner and Gerhart (2005) and Gerhart and Kirschner (2007, 2010), the theory of facilitated variation represents a conceptual framework for investigating the role of developmental mechanisms in generating viable, functional and novel variants in the face of environmental changes. This framework developed fully outside a developmental plasticity context, but may have much to offer for those interested in trying to understand how plasticity is achieved in development and in turn shapes, and is shaped by, organismal evolution.

Central to this framework is the realization that multicellular organisms rely on a set of highly conserved core processes (for example, transcription, translation, microtubule assembly, synapse formation and so on). Many of these processes share a propensity for exploratory behavior which is then followed by periods of somatic selection of the most functional state. For instance, microtubules initially grow and shrink randomly into cytoplasmic space until polarized by stabilizing intra- and extracellular signals. Similarly, but on a different level of biological organization, muscle precursor cells initially migrate randomly during early development but are maintained into later stages only if they manage to innervate muscles (reviewed by Alonzo *et al.* 2011; Kovach *et al.* 2011; Herring, 2011). The same conserved core processes are also characterized by weak linkage to the signals that regulate their activity as well as other developmental processes with which they interact, causing any specific signal to have only a weak (meaning easily altered) relationship to the specific developmental outcome it solicits. For instance, a great diversity of sensory inputs can bring about, via the same highly conserved neuronal machinery, a great diversity of motor functions. The same, highly conserved cellular transduction pathways connect an enormous wealth of external inputs to internal outputs. Combined, exploratory behavior, weak linkage and other common properties of development enable developmental processes to be adaptably responsive to conditions. As such, development facilitates ontogenetic change because it can adjust to context. Development facilitates evolutionary

change because it enables random perturbations, including those provided by novel mutations or environmental challenges, to give rise to nonrandom, functional, integrated and on occasion adaptive, phenotypic variations. Because of the highly constrained nature of its constituent core processes, their respective specific developmental functions are ensured regardless of the context. But at the same time, because of an exploratory behavior and weak linkage, the emergence of novel and sometimes adaptive phenotypic variation is deconstrained.

The theory of facilitated variation generates important opportunities for a more biologically realistic understanding of the mechanisms and consequences of developmental plasticity in general, and phenotypic accommodation in particular. First, it views plasticity as rooted in development rather than genes and genetic variation. The latter clearly make a difference, but they do not, by themselves, allow plastic responses to emerge. Second, it provides a framework for understanding the mechanisms by which alterations of development brought about by changes in ecological conditions can elicit nonrandom and integrated phenotypic changes, chaperoned by the facilitating nature of development. As such it provides a useful new way of thinking about the mechanisms that allow development to be plastic, and plastic development to evolve.

ENVIRONMENTS AS EVOLVING PHENOTYPES—THE PROMISE OF NICHE CONSTRUCTION THEORY

Niche construction theory (NCT) overturns the traditional dichotomy that separates organisms from their environment or niche and instead posits that organisms actively construct and shape many aspects of their environment, from the alteration of soil chemistry through metabolites to the construction of thermal environments through burrow building and social environments through the choice of partners (Lewontin, 1983; Laland *et al.* 2001). Like facilitated variation, NCT has a matured outside a developmental plasticity context, yet may have much to offer toward a more realistic understanding of organism–environment interdependencies (Saltz and Nuzhdin, 2014). The perhaps most critical contributions of NCT to a developmental plasticity context are twofold. First, NCT allows adaptation to emerge not just from organisms responding to the environment, but modifying their environment in ways that suit their responses (Laland *et al.* 1996). Secondly, NCT extends our notion of what is heritable beyond genotypes toward what we traditionally used to associate as 'only' environmental, from antibodies and symbionts to habitat conditions and ecological legacies (Laland *et al.* 2001).

How does niche construction theory relate to the theory of facilitated variation? On the surface, both appear to exist in separate biological realms and in fact have developed completely independently of each other (for example, Laland *et al.* 1999, but see Laland *et al.* 2008). Yet there is no reason why niches and environments can only exist outside the body or why their construction cannot occur during any stage of development (Laland *et al.* 2008; Moczek, 2012). In fact, it is remarkable how close the active construction of selective environments appropriate for developmental events central to NCT matches the thinking explicit in the exploratory behavior of the core processes and the demand-based nature of development envisioned in the theory of facilitated variation. In both frameworks, either entire organisms or their component parts actively construct environments that enable subsequent adaptive responses, with the only difference being one of scale: facilitated variation focuses on the construction of developmental environments from organelles to organ systems, whereas niche construction theory extends our perspectives toward the environment-constructing abilities of individuals or groups of organisms and their effects on subsequent generations. On either scale, niche construction facilitates the production of adaptive phenotypes by improving the match between developmental outputs and the selective contexts within which they function (Moczek, 2012).

CHALLENGES, OPPORTUNITIES AND THE (BRIGHT) FUTURE OF DEVELOPMENTAL PLASTICITY

I began this essay by highlighting some of the major contributions plasticity research has already made to biology, some of the newer challenges that have emerged in the process, as well as novel conceptual developments that may help research in developmental plasticity deal with these new challenges. But doing so effectively and productively may take additional measures, and perhaps most importantly, may require some adjustment of the current priorities of developmental plasticity research. I would like to end this essay by highlighting three such adjustments that I consider especially relevant.

For starters, researchers in developmental plasticity may benefit from learning more about development itself, how development produces traits in space and time, how it puts them together and how the underlying processes enable each other. Here, the highly conserved nature of core processes emphasized by the theory of facilitated variation may provide a useful starting point. To do so, however, our research must focus more on understanding the nature of development and developmental plasticity and less on cataloging environment-responsive genes. The latter is of course a terrific starting point, but by itself is unlikely to substitute for understanding the mechanisms by which developmental plasticity comes into being.

Secondly, research in developmental plasticity needs to take advantage of quantitative and thus predictive frameworks that have developed elsewhere, but that with modest modifications may immediately be applicable to current challenges. A case in point is NCT, which has already resulted in an expansion of evolutionary theory by modeling selective environments as co-evolving because of the evolution of environment-modifying phenotypes (Laland *et al.* 1996, 1999; Laland and Sterelny, 2006; Saltz and Nuzhdin, 2014). There is no reason why such models could not be coopted into efforts to understand and predict the evolution of developmental plasticity.

Lastly, while evolutionary biology has come a long way in recognizing and incorporating the significance of developmental plasticity, this process must continue, not just within evolutionary biology but in the biological sciences in general. Not only can plastic development no longer be viewed as an embellishment of 'normal' development, an add-on, present in a set of special cases, developmental plasticity instead needs to be recognized as the norm of development and as an important nexus for directing developmental evolution. Developmental plasticity is everywhere, from microtubule and synapse formation to allometries and learning. To develop is to be plastic. To make traits come into being is to utilize developmental plasticity. Research in developmental plasticity thus deserves to be recognized for what it really is—an investigation of phenomena of fundamental importance to the genesis of all traits, in all organisms. It is an exciting time indeed to study the development and evolution of plasticity.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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