
Towards a Theory of Development

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CHAPTER 14

Towards a theory of development through a theory of developmental evolution

Armin P. Moczek

Overview

This chapter explores the relationship between a theory of development and a theory of developmental evolution, in three parts. The first part reviews points of tension between different perspectives on the importance of understanding development in order to understand organismal form, function, and evolution, and highlights persistent empirical roadblocks within sub-disciplines that could potentially be resolved through contributions from companion perspectives. In the second part I ask if a theory of development could be formulated that could serve as a conceptual mediator to revise existing disconnects. I posit that to achieve this goal a theory of development should be nested within a theory of developmental evolution. Specifically, I propose a two-step approach to construct a scaffold along which a theory of development could be built. Step 1 would accumulate the knowledge base of development, focussed on identifying and linking developmental products and processes. Step 2 would then organize this information using a three-layered approach, focussed on the development of homologues (layer 1), a nested hierarchy of homologues (layer 2), and a description of patterns and causes of variation within homologues (layer 3). I argue that by nesting a theory of development within a theory of developmental evolution, we will be able to go beyond understanding the nature of development and towards a historic and phylogenetic understanding of this nature. The strategy outlined here would allow a conceptualization of

development that (i) is biologically realistic, (ii) refineable alongside a growing knowledge base, (iii) flexible to incorporate both homology (descent) and variation (modification), and (iv) capable of bridging to relevant conceptual frameworks that are developing in adjacent biological fields. Examples of such frameworks, the bridges they provide, and future challenges are discussed in the third and last part.

Stepping back: what needs to be explained?

Before I embark on the main objectives of this essay, at least two terms require clarification. The first is development. For the purposes of this essay, I would like to define development as the sum of all processes and interacting components that are required to allow organismal form and function, on all levels of biological organization, to come into being. Components are defined to specifically include all the products of developmental processes (from nucleic acids and morphogen gradients to tissues and organ systems) that influence subsequent developmental outcomes, whereas form and function are defined broadly, including morphology, physiology, behaviour, and the complex phenotypes that emerge through their interactions.

If this is how I conceptualize development, what then would I consider a theory of development? I would consider a theory of development any conceptual framework that is applicable to a wide range

of organismal diversity and across levels of biological organization and which would allow us to identify, understand, analyse, and derive predictions about the nature of development. In other words, a theory of development should allow us to generalize features of organismal development (what is development like?), understand the forces that shape development (why is it the way it is?), and provide starting points for further expanding and applying this framework to new organisms and traits (given what we know about development, what hypotheses can we generate to explain the developmental origins of previously unexplained organismal diversity?).

In this essay I will focus in many ways on the relationship between development and evolutionary biology. Specifically, I will argue that, to maximize the usefulness of a theory of development, it should be nested within a theory of developmental evolution, and that doing so will not diminish our understanding of the principles of phenotype construction but will instead ensure that one of the dominating forces that has shaped the way present-day organisms build themselves, decent with modification, is adequately incorporated as we further analyse and begin to derive predictions regarding the nature of development in as-of-yet unexplored phenotype space. I argue in favour of such an approach, despite the historically rather heterogeneous appreciation that evolutionary biology has harbored for development (Amundson, 2005; Gilbert & Epel, 2009). What do I mean by that?

Population geneticists, for instance, frequently define evolution as a change in the genetic composition of a population, enabling a corresponding change in the population-wide distribution of a given phenotype of interest. Describing such changes and identifying the relative contributions of different evolutionary mechanisms (selection, drift, recombination, mutation) to the process represent key objectives. Such efforts depend on a close association between the occurrence of specific phenotypic variants in a population and some marker linking them to the assumed genetic basis of different variants, such as alleles, quantitative trait loci, single nucleotide polymorphisms, etc. As long as such associations exist, traits and variants, and their genetic proxies, can be counted in populations, their changes

in frequency can be traced across generations, and the nature of change can be compared to model predictions. Importantly, as long as such associations exist, it is secondary exactly how a given trait or trait variant of interest comes into being through ontogeny. Instead, the evolutionary process is studied through the methodologies of *transmission genetics*, and heredity can be studied without reference to ontogeny. Consequently, traditional population genetics does not have to draw from developmental biology in order to answer the questions it poses, and a theory of development may seem of little value.

Embryologists, comparative morphologists, and practitioners of evo-devo are also interested in phenotypic changes over time, but the starting point of their investigation is different (Gilbert & Epel, 2009; Minelli, 2003). Traits are generally viewed as the products of development. To change these products over evolutionary time, aspects of their development must change. To understand phenotypic evolution thus requires an understanding of the evolution of developmental properties, which in turn requires an understanding of development. To the extent to which such an investigation is carried out on the level of genes and pathways, *comparative developmental genetics* takes the place of transmission genetics as an important means of inquiry into the evolutionary process. Rather than divorced from it, heredity emerges through ontogeny, and a comprehensive theory of development may constitute a key resource to advance the field.

Given the uneven relationship between developmental and evolutionary biology, why then do I advocate nesting a theory of development within a theory of developmental evolution? The most important reason is that, given the role of phylogeny in shaping organismal development, this simply makes a lot of sense. But an important second reason is that doing so would enable both developmental and evolutionary biologists to go beyond where each discipline has been able to go thus far, and to approach areas in which fundamental problems have remained stubbornly resistant to resolution because appropriate empirical and conceptual tools are missing within disciplines and points of exchange across disciplines have not yet been cultivated. One of the most productive contributions

of a theory of development that is explicitly integrated into a theory of developmental evolution may thus lay in providing opportunities for such cross-fertilization.

For example, the origin of phyla and *Bauplan* diversity is a fundamental question in evolutionary biology (Raff, 1996), but one that population-genetic approaches are unable to address because they lack the necessary phenotypic variation accessible via the methods of transmission genetics (Amundson, 2005). *Baupläne*, while highly diverse among phyla, are nearly invariant within them; thus, no variation exists that could be marked, followed across generations, or artificially selected upon. The same problem arises for any highly canalized, phenotypically invariant trait. Not that these traits do not (or did not) evolve in natural populations or that they are somehow less relevant—on the contrary. But unlike bristle patterns or eye color, their respective patterns of variation simply render them difficult to study through traditional population-genetic means.

A similar problem arises in the study of novelty and innovation in evolution, one of the oldest, most fundamental, and still largely unresolved questions in evolutionary biology (Moczek, 2008). Population-genetic approaches allow an investigation into how and why the composition of trait variations within a population changes over time, but provide no satisfying understanding of how novel traits come into being in the first place beyond postulating the occurrence of key mutations that must somehow have enabled a particular phenotypic transformation. In contrast, comparative developmental and developmental-genetic approaches can overcome these limitations, because in this case, evolutionary insights derive from the comparison of phenotype construction during development across taxa, rather than following the differential spread of variants across generations. The resulting efforts have permanently enriched evolutionary biology by contributing fundamental new concepts such as co-option, deep and partial homology, and developmental systems drift (Abouheif, 1997; Shubin et al., 2009; True & Haag, 2001).

Inversely, developmental biologists and evo-devo practitioners have encountered their own persistent empirical roadblocks. For example, comparative

embryologists have known for a long time that life stages differ dramatically in the degree to which they have diversified across taxa, giving rise to the concepts of the hourglass of development and the phylotypic stage (Raff, 1996). Several hypotheses have been advanced to explain these patterns, arguably without resolving the issue in any satisfying manner. Recent genomic and population-genetic approaches have now provided important new considerations, suggesting for instance that relaxed selection on strictly maternally acting genes (such as those guiding much of early embryonic development in many organisms) may be sufficient to explain their elevated accumulation of sequence variation within, and differential divergence among, species (Cruickshank & Wade, 2008; Demuth & Wade, 2007). While these results do not yet resolve the issue of the developmental hourglass, they nevertheless highlight how population-genetic approaches can contribute relevant and novel insights beyond where comparative developmental approaches have been able to go on their own.

Thus, integrating a theory of development into a larger theory of developmental evolution may benefit all involved, regardless of their initial perspectives on exactly what matters in development or evolution and what deserves explanation. The remainder of this chapter seeks to explore how a theory of development, and what kind of a theory, may be most conducive towards that goal.

How to build a productive theory of development—a two-step proposal

A productive theory of development in most general terms should provide a meaningful framework for understanding the nature of development. But to do so, as a first step, we must agree what we mean by the nature of development and what it is that is worth explaining and generalizing about development. What should be the foci around which a theory of development should be structured to be most useful to developmental biology itself and to other disciplines with which it interacts?

I posit that, to be most useful, a theory of development should have three foci. First, it should focus on the outputs of development, across all levels of

biological organization, from bona fide traits (e.g. cells, tissues, organs) to more transient products (e.g. expression domains, gradients, thresholds). Second, it should focus on the developmental processes that generate these products, across the domains of molecular and developmental biology as well as physiology. Third, and most importantly, it should focus on linking products to processes, recognizing that this relationship is not linear: developmental processes generate many products, products require many processes, and frequently the product of one developmental process itself constitutes a critical component of another process generating yet another developmental output. Clearly, this is not a simple and straightforward starting point for a theory. But it has several key advantages that may make it worth the effort. By identifying, and linking, developmental products and processes, this strategy allows us to begin to organize the complexities of organismal development, to make room to accommodate the self-constructing nature of ontogeny (more on this in the next section), and to facilitate an understanding of development across levels of biological organization.

Next, to be meaningful, a theory of development must provide opportunity to conceptualize the diversity of development across the enormity of organismal diversity, to discover general rules and principles, should they exist, and to connect to relevant conceptual frameworks that are developing outside its area of focus. To do so I propose as a second step to organize and expand the knowledge base accumulated during step 1 using a three-layered framework to begin constructing a theory of development, with the goal to simultaneously incorporate homology and diversification, developmental descent and developmental variation.

The first, foundational level of a theory of development would catalogue the developmental means by which homologous traits come into being. The use of homologous traits allows us to draw from all of organismal diversity while simultaneously reducing this diversity to a more manageable level, namely that of homologs. As such it establishes homology as a structuring principle of a theory of development (for a contrasting view, see Vervoort, this volume). The second level then establishes a nested hierarchy of homologues and their developmental

basis, from genes, to pathways, to networks, and to cell and tissue types, organs, and bodies. This effort facilitates immediate recognition of where developmental processes are reused to generate diverse products, how similar products are made in diverse ways, and on what level of biological organization any of this is occurring. Collectively, this permits co-option and convergence, as well as partial and deep homology to emerge naturally from within the approach (Shubin et al., 2009). The third and last level then focusses on the patterns and causes of variation inherent in the development of each homologue on a microevolutionary level, i.e. among populations and closely related species.

Combined, steps 1 and 2 thus catalogue the genesis of form and function across the diversity of developmental products and processes and their various homologous manifestations. Steps 2 and 3 then expand this framework for understanding the nature of development into a framework for understanding the nature of developmental evolution by (i) providing a deeper appreciation of how development has (or has not) diversified at different levels of biological organization and in different lineages; (ii) identifying patterns and mechanistic causes of variation available in natural populations; and (iii) doing all of this in a framework of homology and descent with modification. Thus, by nesting a theory of development within a theory of developmental evolution, we can go beyond understanding the nature of development and towards a historic and phylogenetic understanding of this nature; moreover, we may be able to connect such a theory to existing, independent frameworks in ecological and evolutionary genetics.

How to build a productive theory of development—an example

Let's now try to implement the strategy sketched out above in the concrete example of appendage development in insects. Specifically, as posited above, a theory of development should begin by focussing on identifying and linking products and processes. With respect to insect appendage formation, we can identify many concrete products, such as segments,

joints, spines, bristles, cuticle, tissue types, attachment sites, etc., but also proximal–distal and anterior–posterior axes or sizes of parts, in absolute terms as well as relative to other traits. And we can identify a diversity of processes that underlie their production, from gene expression, paracrine signaling, and pattern formation to the behaviour of cells and the interactions among tissues (e.g. Angelini & Kaufman, 2005; Kojima, 2004; Snodgrass, 1935). Accumulating this information across as much of insect diversity as possible, we are essentially building an ever-growing knowledge base of everything it takes to build an insect appendage, no matter what the appendage, or the insect, at least for starters.

With this raw material as a starting point, we can begin to organize and expand this information using the three-layered approach proposed above. On the foundational level our understanding of insect appendage development would be organized according to the developmental means by which homologous appendages (and their component parts) come into being, as well as the processes that underlie their formation. For example, we would note that all insect appendages are of epidermal origin, that most emerge late in larval development as epidermal outbuddings while others derive from early developing imaginal discs, that distal identity in all but the mandible requires the correct expression of the transcription factor *Distal-less*, that programmed cell death plays a key role in delineating the exact final shape of at least some appendages, etc. On the second level, homologous relationships would be refined further by nesting them within each other: for example, *hedgehog* expression and function would be nested within the *hedgehog* pathway, which in turn would nest within anterior–posterior axis formation and growth regulation, etc., which would be nested within the particular appendage types and regions to which we know this applies (Angelini & Kaufman, 2005; Kojima, 2004). The third and final layer would then add information regarding variation in product and process homologues present in natural populations or among closely related species. In the context of insect appendage development, we would note, for example, that all appendages of adult fruit flies form from imaginal discs specified during late

embryonic development, which then grow during most of larval development as two-dimensional invaginations into the larval body, and of which at least the legs functionally require the expression of the morphogen Decapentaplegic for initial specification (Kojima, 2004; Ober & Jockusch, 2006). We would further note that a subset of this machinery is also involved in the making of genital claspers in sepsid flies, highly modified serial homologues of traditional appendages, even though they derive from histoblasts rather than imaginal disks (Bowsher & Nijhout, 2007, 2009). This would be in contrast to the homologous appendages of adult beetles or butterflies which either derive from early developing imaginal disks, or more frequently, from late-forming, three-dimensional evaginations which—at least in part—do not require Decapentaplegic for normal development (Švácha, 1992;). This view could then be expanded to the horns of beetles, which, unlike sepsid claspers, lack even remote homology to traditional appendages, but like sepsid claspers, exhibit in their development a certain degree of partial, and deep, homology to that of legs and antennae (Moczek, 2009). Current understanding of beetle horn development then also allows us to contrast the degree of variability that exists in their development on a microevolutionary level as a function of sex, population, or species, providing starting points to link such variation to the evolutionary processes that might shape it in natural populations (Kijimoto et al., 2012).

Combined, this approach offers several key opportunities: first, there is no predefined starting point or directionality. Instead, investigators can begin *anywhere*, with *any kind of trait on any taxonomic level*, to contribute specific observations towards an eventual, general understanding of the nature of development. For our example above, any insect, any appendage, any aspect of appendage development, and any kind of comparison is relevant. Second, using homology as an organizing principle (levels 1 and 2) immediately identifies the presence or absence of correspondence between homology across products and across processes and whether this correspondence changes as a function of the level of biological organization or phylogenetic distance that is considered. On one side, whatever patterns emerge can then be compared to other efforts

elsewhere in phenotype space (e.g. appendages, anterior–posterior axes, or growth control), providing deep resolution to identify general principles by which development enables its products, and vice versa. On the other, such patterns of variation can be compared to those present among populations and closely related species, providing insights into where and how micro- and macroevolution of development might intersect.

Strengthening the model and building bridges

I will end this chapter by highlighting several problem areas associated with the framework sketched out above. If overcome, however, these problem areas transform into key opportunities to build bridges between a theory of development and recent expansions of adjacent areas of biology.

The nature of nurture

Our understanding of the developmental basis of traits is rapidly advancing, including homologous and partially homologous traits across an ever-growing diversity of organisms. At the same time developmental genetics and evo-devo in general remain steeped in rather traditional perspectives on the causes of traits. In many ways, we continue to assume that traits and organisms essentially pre-exist their development and are programmed somehow in the genome, ready to unfold if the right opportunities present themselves. Moreover, we remain convinced that organismal development can be partitioned into genetic and environmental contributions and their respective interactions. But the metaphors of genes and genomes as blueprints of development, and the separability of genes and environment as contributors to trait formation, have outlived their usefulness: instead it is becoming increasingly clear that while genes and genomes matter enormously in development, they neither suffice to make traits nor organisms. Similarly, while both genes and environmental conditions interact in their contributions to trait formation, it has become clear that describing their relationships as merely interactive is insufficient. Yes, both contributors do interact, but more often than not they are

both *cause and effect* of each other: genes and their products help generate environmental conditions within which the next round of gene expression can contribute to shaping subsequent developmental outcomes. Thus, traits and organisms need to be viewed as the products of developmental *systems* to which genes contribute important interactants. Or put another way: the development of a trait of interest begins with a gene *only* if this is where our investigation starts (Moczek, 2012; Oyama, 1985).

As ongoing efforts in developmental biology provide much of the knowledge base that would allow us to form a theory of development, the way we think of the genesis of traits must therefore become more biologically realistic. In particular, we need to arrive at a deeper appreciation of the contingent nature of developmental processes, and the interdependencies of genetic, developmental, and environmental contributions (Gilbert, 2002; Gilbert & Epel, 2009; Keller, 2010; Moczek, 2012; Oyama, 1985). Several interrelated conceptual frameworks already exist that could facilitate such a process.

For example, the *theory of facilitated variation* as formulated by Kirschner and Gerhart (2005) and Gerhart and Kirschner (2007, 2010) proposes that the combination of exploratory behaviour and weak linkage (between inputs and outputs) inherent in core developmental processes enable developmental systems to be adaptably responsive to conditions. Developmental processes therefore facilitate ontogenetic changes, because they enable adjustments to developmental context, and facilitate evolutionary change, because they enable random genetic variation to give rise to non-random and functionally integrated phenotypic variants. The theory of facilitated variation makes several important contributions towards a theory of development. For instance, it emphasizes that traits and trait variation do not pre-exist in genes and genetic variation but instead emerge through development. Genes and genetic variation are key contributors but by themselves do not suffice to understand the genesis of traits. The theory of facilitated variation thus provides important opportunities to fill (or replace) an abstract, assumed genotype–phenotype map with biological reality. Similarly, this theory provides a framework for understanding the mechanisms by which random and modest genetic

changes can elicit substantial and well-integrated phenotypic changes, guided by the facilitating nature of development (Moczek, 2012).

The *theory of evolution by genetic accommodation*, developed by West-Eberhard (2003, 2005a, b), similarly explores the interplay between environmental conditions and developmental processes in the expression of phenotypic variation. In particular, it emphasizes that environmental changes can elicit, through the condition-sensitivity inherent in developmental processes, phenotypic transformations that can subsequently be stabilized genetically through selection operating on genetic variation present, or newly arising, in a population. As such, genetic accommodation theory critically extends the roles of development and environment in the evolutionary process by emphasizing that the interactions among them determine which genetic variants will be phenotypically expressed and thus selectable and which will remain cryptic (reviewed by Moczek et al., 2011; Pfennig et al., 2010).

Lastly, *niche construction theory* (Lewontin, 1983; Odling-Smee, 2010; Odling-Smee et al., 2003) focusses on the interplay between organisms and their niche, which we generally tend to view as existing separate from each other, i.e. without the organism, the niche should still be there. Niche construction theory challenges this dichotomy and argues instead that organisms actively construct their niches, which in turn affect their development and fitness, with effects often extending across generations (Lewontin, 1983; Odling-Smee et al., 2003). Such niche construction is perhaps most obvious in the manufacturing of shells, cocoons, casings, and nests but also in the alteration of soil properties by fungi or earthworms, the alteration of fire regimes by plant communities, and in fact any kind of parental care. Niche construction theory thus makes room to understand the immediate developmental environment experienced by individuals not as separate from them but instead as being constructed, shaped, and modified by their actions as well as those of their ancestors. Because the environment is now in part generated by the organism itself, it too has a heritable component and can evolve. Most importantly, this allows environmental factors to be incorporated into population-genetic models and predictions even if the environment has no genes

that can be passed on to the next generation. Instead what is passed on is the selective environment as generated by individuals and as experienced by descendant generations. More generally, much like the theory of facilitated variation and genetic accommodation, niche construction emphasizes how the contingent nature of development (and physiology and behaviour) facilitates the production of adaptive phenotypes by improving the match between phenotypes and the selective contexts within which they function.

Collectively, the three theories summarized above provide a rich, interlocking construct within which to begin frame a more realistic understanding of the genesis of form and function in development and evolution beyond the persisting—yet useless—‘blueprint’ and ‘program metaphors’ for development. We should not let this opportunity pass us by.

The Lego fallacy

Above, I proposed to organize developmental products and processes by utilizing a nested hierarchy of homologies. Implicit in this approach is an assumption of modularity: distinct sets of developmental processes work together to generate a developmental product, which differs distinctly from other such products. Processes and products can then be compared, homologized, and related to each other. Furthermore, we should be able to divide both processes and their products into their component parts, allowing further comparison. One major advantage of this approach is that it allows partial and deep homology as well as developmental systems drift to emerge from within the framework as we document the differential reuse of component parts and processes. But such an approach can quickly exhausts its usefulness if we do not recognize the limits of modularity in development. Organisms and their traits are not like Lego bricks, with all parts separable and recombinable in the precise same way. Neither are the developmental processes that produce organisms and their parts. Instead, module boundaries may be more or less definable depending on ontogenetic timing and level of biological organization. Moreover, the relationship between products and processes in development is complicated: a single developmental process generates (or

interacts with a varying cast of other processes to generate) many products, a single product requires many interacting processes, and the same thing can both be product and part of a process. Furthermore, developmental products and processes influence other products and processes, reciprocally inducing, shaping, and modifying phenotypic outcomes and properties. Where one trait ends and another begins is often remarkably difficult to assess. Thus, as we organize organismal development into nested hierarchies of homologues, we must be mindful that modularity and homology are matters of degree and that we may learn much from shifting, loosening, or otherwise adjusting how we subdivide the developing organism into parts and processes (for detailed discussion of these and related topics see Minelli (1997) and Moczek (2008)).

Conclusion

Nesting a theory of development within a theory of developmental evolution offers the opportunity to acquire an understanding of the nature of development alongside a historic and phylogenetic understanding of this nature. Here I have proposed a framework by which the growing richness of our understanding of organismal development could be organized to structure the formulation of a theory of developmental evolution in a way that is biologically realistic and meaningful, able to incorporate both homology and variation, and capable of linking to important conceptual developments in adjacent biological fields. Further refinement and application of such a framework may hold the key for diverse biological disciplines to grow together and to facilitate the resolution of long-standing, fundamental challenges in a productive manner.

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