

## Short Conceptual Overview

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# Developmental evolution and the origins of phenotypic variation

**Abstract:** Because of the variability of relevant developmental resources across different environments, and because only a portion of the genome is expressed in any individual organism as a result of its specific developmental context and experience, what is actually realized during the course of individual development represents only one of many possibilities. One conclusion to be drawn from this insight is that the origin of phenotypic traits and their variation can be traced to the process of development. In this conceptual overview, I briefly explore how recent efforts to integrate genetic, epigenetic, and environmental levels of analysis through a developmental lens is advancing our understanding of the generation of the stability *and* variability of phenotypic outcomes observed within and across generations. A growing body of evidence indicates that phenotypes are the outcomes of the whole developmental system, comprised of the organism, with its particular genetic and cellular make-up in its specific physical, biological, and social environments. I conclude that the emergent products of development are epigenetic, not just genetic, and evolutionary explanation cannot be complete without a developmental mode of analysis.

**Keywords:** developmental systems; epigenetics; evolutionary innovation; phenotypic variation; probabilistic epigenesis.

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## Introduction

A new perspective on the sources and dynamics of phenotypic variation has taken shape across the life sciences over

the several previous decades (1–3). This new perspective is based on a relatively simple but fundamental insight: given that all phenotypes arise during ontogeny as products of development, it follows that a primary basis for phenotypic variation within and across generations must be the process of development. The thread of this insight can be traced back to several embryologists and evolutionary biologists working in the first half of the 20th century, including Walter Garstang (4), Edward Russell (5), Gavin de Beer (6), Richard Goldschmidt (7), Conrad Waddington (8), and Ivan Schmalhausen (9). Although each of these biologists had a distinctive perspective on how to characterize the links between development and evolution, they all promoted the ideas that (a) changes in individual development were a potentially important basis for evolutionary change and (b) environmental factors could both select among phenotypic variants and contribute to that variation in the first place [see (10) for a recent discussion]. In other words, the environment can be both the agent of selection and an agent of development (11).

Waddington (8) was critical of evolutionary models in which genes were portrayed as directly causing development or were directly acted upon by natural selection. Based in part on his experimental work with fruit flies, Waddington came to question the canonical view of the time that there was a simple correspondence between genes and phenotypic traits and proposed that only an understanding of the interaction of genes with each other and with the internal and external environment of the organism could successfully account for phenotypic development. Schmalhausen (9) was likewise critical of genocentric models of development and evolution and, similar to Waddington, emphasized the importance of non-genetic factors in inducing changes in development. For example, he argued that, “the history or current adaptation cannot be uncoupled from the history of the organism” (9). The views of Waddington and Schmalhausen were well outside mainstream 20th century thinking with regards to evolution, but have been reassessed across the biological sciences in recent years. This reassessment has involved moving beyond the notion of genes as the

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primary cause of phenotypic traits, thereby allowing for a reconsideration of the role of non-genetic factors now known to be at play in the emergence, maintenance, and modification of phenotypes within and across generations (3, 12–14).

As Badyaev (15) recently pointed out, the main conceptual challenge in characterizing the links between development, phenotypic variation, and inheritance has historically centered on how to view the stability of phenotypes across generations in light of the well-documented environmental contingency of within-generation development. Over 30 years ago, Alberch (16) suggested a conception of development that provides some leverage to this enduring challenge. He proposed that development contributes to the evolutionary process in at least two key ways, one regulatory and the other generative. First, the process of development constrains phenotypic diversity by limiting the “range of the possible” in terms of both form and function. Alberch (16) termed this robustness of development, despite genetic or environmental perturbations, as the regulatory function of development [see also (17, 18)]. In the most general sense, developmental constraints result from the physical properties of biological materials and the temporal and spatial limitations on the relations among internal and external factors at play in the developmental process. Developmental constraints operate at multiple levels of the developmental system, including genes, molecular regulatory networks, cellular dynamics, social interaction, and so on. These constraints effectively bias the course of evolution, contributing to the stability of phenotypes observed across generations and limiting the type and range of variation available to natural selection (19).

The process of development also introduces phenotypic variation and novelties of potential evolutionary significance. Alberch (16) termed this the “generative function of development”. For example, many phenotypes show graded responses to factors or events that occur along natural environmental gradients (e.g. temperature, pH levels) and dichotomous responses (polyphenisms) to factors or events that occur in a dichotomous manner (e.g. the presence or absence of predators or particular food items) (19, 20). This variation in phenotypic outcomes in response to variations in or modifications of genetic and environmental factors is often referred to as developmental plasticity (3, 21) or phenotypic flexibility (22), the processes by which organisms adjust their state in response to the conditions of their physical, biological, and social environments.

There has been a growing recognition across the biological sciences of the necessity of considering and

defining the complex transactions among genetics, development, and ecology in order to understand the range of morphological structures, shifts in behavioral repertoires, and other instances of phenotypic variation observed across plant and animal species (11, 23–26). This relational approach views the novelty-generating aspects of evolution as being the result of the developmental dynamics of living organisms, situated and competing in specific ecological contexts, and not simply the result of random genetic mutations, genetic drift, or genetic recombination. This is a paradigmatic shift in emphasis, as genetic factors were argued to be the only evolutionary relevant source of phenotypic variation by the neo-Darwinian or “Modern Synthesis” school of evolutionary thought that dominated 20th century biology (27–31).

A concern with how development contributes to evolutionary change is now evident among biologists and psychologists working in diverse areas of research, including genomics, cellular and molecular biology, developmental biology, evolutionary theory, ecology, and comparative and developmental psychology, as well as philosophers of biology (15, 19, 32–39). In this review, I briefly explore how recent efforts to integrate genetic, epigenetic, and environmental levels of analysis through a developmental lens are contributing to an emerging conceptual framework for how the process of development can generate phenotypic variability (and stability). More generally, I argue that evolutionary explanation cannot be complete without developmental explanation because it is the process of development that generates the phenotypic variation on which natural selection can act.

## Distributed sources of phenotypic variation

Over the last several decades, research across the life sciences has provided a wealth of evidence that phenotypic variability across individuals (the grist for the mill of natural selection) can be generated by genetic *and* non-genetic means. These means are varied, including random mutation, transposons, and other genetic processes. They also include less well studied extra-genetic processes, such as maternal cytoplasmic constituents, mRNA, and chromatin-modifying enzymes, all known to influence changes by which the fertilized egg cell transforms into a complex organism during embryonic development and in later life allows cells to respond to hormones, growth factors, and other regulatory molecules (40–42). As Waddington (8) suggested over 70 years ago, what a gene does

in the sense of what it provides to development depends on the expression and activity of other genes, as well as non-genetic factors internal and external to the organism. Genes interact with other constituents of the cell, which interacts with other cells in the organism, which interacts with other organisms (43). It is out of this dynamic, multileveled process that phenotypes emerge. In other words, phenotypes are the outcomes of the whole developmental system, comprised of the organism, with its particular genetic and cellular make-up, in its specific physical, biological, and social environments.

Research with Darwin's finches (genus *Geospiza*), famous for their role in Darwin's formulation of the principle of natural selection, provides an example of how the complex interplay of molecular, cellular, and ecological factors can result in relatively rapid and dramatic phenotypic change (in this case, the variety of beak shapes observed across the 13 species of finches distributed across the Galapagos Islands). Such developmental plasticity provides a potent pathway for organisms to rapidly change structure and function in response to environmental resources and changes (3, 19, 44). In the case of Darwin's finches, in the time frame of just 1–2 million years, a founding group of finches from South America generated an array of different finch species on the remote Galapagos Islands, including some with large, pliers-like beaks capable of cracking nuts and seeds and some with forceps-like beaks able to extract insects from fruit. Darwin had noted these birds' remarkable differences in beak size and shape on his visit to the Galapagos Islands during his *Beagle* voyage in 1835, but due to the degree of variation across species he did not realize at the time that they were all finches. Further reflection on this variation after his return to England contributed to Darwin's formulation of the critical role of natural selection in the direction of evolutionary change.

The received explanation of the past century on the striking variation in beak size and shape seen across these closely related finch species held that genetic mutation, recombination, and re-assortment of genes in an island's founder population would occasionally result in variant birds that had somewhat smaller and more forceps-like beaks or somewhat larger and more pliers-like beaks than those of the founder population. These individuals would be more likely to explore and exploit different food niches (for example, insects vs. seeds), potentially leading to increasing geographic and behavioral isolation from each other. Morphological change would be gradual in this scenario, but over many generations differential reproduction (based in part on relative feeding success) would eventually result in the selection of several variations of the

original founders' beak type. In this neo-Darwinian view, initiating phenotypic change is dependent on "waiting for a mutation" (24, 45).

More recent molecular, cellular, and ecological research indicates that the pathway to the remarkable variations observed in beak size and shape is more contingent on the process of development and more rapid than traditional views of evolutionary change would suggest (46–48). Current evidence indicates that the size and shape of the finch beak can be traced to the growth and differentiation of neural crest cells that settle around the mouth of the developing bird embryo. These neural crest cells produce a growth factor protein, bone morphogenetic protein 4 (*Bmp4*), which stimulates the deposition of bone and beak materials during embryogenesis. Importantly, this signaling protein is known to be a signal for cell growth, differentiation, or apoptosis, depending on the cells receiving it. It is produced earlier in embryonic development and at higher levels in the finch species with larger and wider beaks than in the closely related finch species with shorter and narrower beaks (46). Further, when *Bmp4* is experimentally introduced into the beak neural crest cells of chicken embryos, they likewise develop broader and larger beaks than those seen in control chicks. Additional experiments that introduced other growth factors did not have this effect. Related work has found that a signaling protein (calmodulin or CaM) that mediates signals of changing calcium concentrations to a variety of proteins and plays a role in cell and tissue differentiation is expressed at higher levels in finch species with longer and narrower beaks than in those with the longer, wider beaks (47).

It appears that a variety of interrelated factors, including the number of neural crest cells, the level of signaling that stimulates or inhibits the production of growth factor proteins (including fibroblast growth factor 8 and transforming growth factor beta) and calmodulin, and the types of signals that induce cell death of the neural crest cells, are all at play in generating the beak shape variation seen across Darwin's finches. How these various factors and their relations are regulated by the birds' experience and ecology (particularly the type of food sources available) are not fully understood, but given the wide adaptability of neural crest cells, it seems that relatively large modifications in beak size and shape have been accomplished with relatively few changes in the developmental process [see (49) for a detailed example from house finches, *Carpodacus mexicanus*]. This potential for rapid phenotypic adjustment to the contextual features of development has important implications for evolutionary change, in that it would increase the likelihood that members of the

population could quickly take advantage of new or changing resources and habitats as they become available (50).

The finch beak example illustrates how a focus on the complexities of the dynamics of development and evolution is bringing together genetics, molecular, cellular, and developmental biology, and evolutionary biology to construct a more comprehensive explanation of the ways and means of the stability and variability of phenotypic development (1, 44, 51, 52). In particular, the finch beak example highlights the highly complex regulatory interactions that direct gene expression and the key role of environmental conditions in influencing development by means of internal and external signals, including diet, hormones, receptor molecules, and physical interactions among cells (24). For all multicellular organisms, there is a hierarchy of integrated levels, including genes – cells – tissues – organs – organ-systems – organism – populations. Genes and all other levels of the hierarchy are part of this complex system, in which the cytoplasm influences the genes, extracellular hormones influence the cell nucleus, external sensory stimulation influences the genes, hormones are influenced by the external environment, and so on. As a result of this bidirectional traffic across levels of the developmental system, the molecular mechanisms of gene regulation, the embryonic generation of form, and environment-induced variation of traits are all linked in complex regulatory networks (26, 53).

The causal interconnections that have been found to underlie the expression of reproductive behavior in the ring dove (*Streptopelia capicola*) illustrate the rich network of internal and external factors that underlie their courtship, nest-building, egg-laying, incubation, and parental care. Our knowledge of ring dove reproductive behavior, based in large part on classic studies by Lehrman (54, 55) and Michel (56), highlights the historical, contingent, and dynamic nature of phenotypic expression by demonstrating that: (a) hypothalamic, pituitary, and gonadal functions, essential for the range of reproductive behaviors seen in ring doves, are largely determined by the social and physical stimuli associated with the reproductive cycle (i.e., the long days of spring, the presence and activities of the mate); (b) changes in levels of circulating hormones influence the dove's sensitivity to specific social and physical stimuli (i.e., the presence of a nest, the activities of the newly hatched young); (c) the dove's prior reproductive experience alters the pattern and regulation of behavior by its influence on the sensitivity of the dove's nervous system to specific hormones and to social and physical stimuli (57).

The bidirectional traffic observed between neural function, hormones, behavior, and environmental stimuli

involved in the reproductive behavior of the ring dove exemplifies the difficult but critically important task of developmental analysis – filling in the bidirectional details among the specific internal and external factors contributing to the generation of any phenotypic trait or character. This is a daunting challenge and will require collaborative efforts across biological disciplines. An understanding of the ring dove's reproductive behavior was not achieved by examining only molecular, neurological, endocrine, or physiological levels of analysis; it also required detailed information about the organism's physical and social milieu. In any given aspect of the dove's reproductive process, some factors might be more central and predominate more than others, but the variety of factors at play always operate in a context in which their effects are dependent upon their relation with other factors of the developmental system.

## The possible and the actual: pathways to innovation

Because of the variability of relevant resources across different environments and because only a portion of the genome is expressed in any individual due to its specific developmental context and experience, what is actually realized during the course of individual development represents only one of many possibilities (32, 58). Some years ago, Atchley and Newman (59) highlighted several types of resources – genetic, maternal, and environmental – that can impact this probabilistic nature of the stability and variability of developmental outcomes. Their dynamic model for integrating genetics with developmental analysis recognized that multiple factors, including contingencies in mating (which create the developing organism's genome) and contingencies of the maternal environment in which the individual develops (including cytoplasmic and uterine in the case of mammals) contribute to the variability and stability in developmental outcomes. As a result, understanding the developmental pathways of morphological, physiological, and behavioral phenotypes requires knowing the dynamic and contingent processes and regulatory networks of internal and external factors operating over the course of individual ontogeny. The range of internal (including genes) and external factors contributing to an organism's phenotype can be characterized as developmental resources (60–63) and the reliability and availability of these resources has been shown to be a source of both phenotypic stability and variation within and across generations (3, 11, 44).



To illustrate, consider the case of cerebral lateralization in precocial birds. During the later stages of prenatal development, the precocial avian embryo is oriented in the egg such that its left eye is occluded by the body and yolk sac, whereas the right eye is exposed to diffuse light passing through the egg shell when the brooding hen is intermittently off the nest during the incubation period. This differential prenatal visual stimulation to the left vs. right eye resulting from the embryo's invariant postural orientation in the egg has been shown to influence the direction of hemispheric specialization for a variety of postnatal behaviors, including visual discrimination, spatial orientation, feeding behavior, and various visual and motor asymmetries (64). Altering the normal pattern of light stimulation available during prenatal development can modify this typical pattern of brain and behavioral development (65). For example, Casey and Lickliter (66) found a left spatial turning bias in a large majority of quail chicks following hatching (>85%). Occluding the right eye and stimulating the left eye with light prior to hatching reversed this species-typical turning bias. Further, the induction of such lateralization was prevented by incubating eggs in darkness or by providing the same level of light stimulation to both eyes in the period prior to hatching (66). In this example, phenotypic variation across experimental groups occurred when different embryos did not have the same developmental resources (patterns of prenatal visual stimulation). Similar types of changes in the amount, intensity, or timing of prenatal sensory stimulation can set up a trajectory of experiential events that can result in modifications to typical patterns of species identification, perceptual learning, habitat preferences, and other key aspects of the organism-environment system (67, 68). Such phenotypic variations provide the opportunity for natural selection to filter out those modifications that are less successful and promote those that provide some reproductive advantage.

The reliable and repeatable features of external stimulation and experience available in an organism's developmental context have been termed the "ontogenetic niche" by West and King (69), which they defined as the set of ecological and social circumstances typically inherited by members of a given species. This ontogenetic niche is available both prenatally and postnatally and provides diverse but dependable resources and influences for the developing individual. The ontogenetic niche can be described in terms of temperature, humidity, salinity, light level and cycle, energy sources and their distribution, diet, patterns of parental care and social interaction, and so on. Every species' ontogenetic cycle depends on the availability of a particular set of these developmental resources,

reconstructed in each generation, and these resources contribute to the stability of phenotypes observed within and across generations (63, 70).

On the other side of the coin, significant modifications in the normally available resources and interactions of an organism's ontogenetic niche are a primary basis for the generation of novel phenotypic outcomes [or *neophenotypes*; (71, 72)]. In other words, the realization of new phenotypes typically requires a change in normal or usual developmental resources and circumstances that ordinarily function to constrain development along species-typical trajectories. The phenomenon of domestication, the process by which organisms change in terms of morphology, physiology, or behavior as a result of the human control of their breeding, feeding, and care (73), provides an informative example of the role of distributed developmental resources in the complex dynamics involved in phenotypic change within and across generations (74–76).

The variance of phenotypes among wild and domestic strains of a single species has long been appreciated. Darwin (77, 78), for example, documented the wide array of alterations in size, shape, coloration, productivity, and behavior evident in domesticated animals and speculated on their possible origin. Following the neo-Darwinian synthesis of the first half of the 20th century and its emphasis on population genetics, most students of domestication assumed that the morphological, physiological, and behavior differences observed between wild and domestic strains of animals could be explained by random and non-random genetic mechanisms associated with captive rearing. These genetic mechanisms include natural and artificial selection, inbreeding, genetic drift, and genetic mutation (79).

Although the importance of genes as sources of phenotypic variation in both wild and domestic animals is indisputable, domestication is certainly not simply a matter of changing gene frequencies. The transition from free-living to captivity is accompanied by many and varied changes in an animal's physical, biological, and social environments and we know that changes in these developmental resources can bring about significant modifications in phenotypic development. For example, Clark and Galef (80) were able to show that specific differences in the morphology, physiology, and behavior of wild and domestic strains of gerbils (*Meriones unguiculatus*) could be traced to relatively minor changes in the developmental resources available in their early rearing experiences. Gerbils reared in standard laboratory cages without access to shelter show accelerated eye opening following birth, earlier sexual maturity, increased docility, and reduced reactivity to humans when compared

to gerbils reared in laboratory conditions that allow free access to shelter, as would normally occur in the wild. Of course, the change from free-living to captivity for most species is typically accompanied by changes in the availability of not only shelter, but also space, food and water, predation, and possibilities for social interaction (76). The influence of such changes on the nature and range of phenotypic change under domestication remains relatively unexplored (75).

One research program that has attempted to address these changes is that of Belyaev and colleagues (74, 81) on the domestication of silver foxes (*Vulpes vulpes*). Selection for tame behavior in silver foxes began in the 1950s and continues to the present. Selection was based solely on behavioral criteria, breeding those foxes that were least timid when humans attempted to handle or interact with them. It is important to note that such selective breeding (common in cases of domestication) is selecting for developmental outcomes (in this case, tameness), not genes. In addition to becoming more dog-like in their behavior over the course of more than 40 generations, the silver foxes quickly showed a number of other phenotypic modifications, including changes in the skeleton (shortened legs, tail, and snout, and a widened skull), hormonal changes, altered tail and ear posture, and decreased sexual dimorphism. Belyaev (74) proposed that the experiential conditions of domestication led to neural and hormonal changes that in turn activated the expression of dormant genes, thereby revealing “hidden variation” previously undetected in wild silver foxes. This idea remains speculative, but Belyaev’s interpretation that certain genes were able to switch from dormant to active states in response to changes in environmental conditions is certainly plausible in light of recent advances in epigenetics and would help explain the rapid rate of phenotypic changes observed across only a few generations. It is certainly the case that genes are not self-expressive, and the presence of a gene as part of the organism’s genotype does not necessarily mean it will be transcribed. Genes are not able to turn themselves on and off; they require intracellular signals, some of which originate from outside the cell and even outside the organism (82).

The more we learn about the mechanisms by which non-genetic developmental resources (both internal and external) can influence the activation and expression of genes (1, 11, 42), the more it becomes clear that relatively small developmental changes can have large phenotypic effects (83, 84). For example, Brylski and Hall (85, 86) investigated the genesis of external cheek pouches in geomyoid rodents (pocket gophers and kangaroo rats). In most rodent species with cheek pouches (for example,

squirrels and chipmunks) they located inside the mouth and are lined with buccal epithelium. In contrast, geomyoid rodents have cheek pouches located outside the mouth, lined with fur. Both types of cheek pouch are used to store food temporarily during foraging. Brylski and Hall showed that the novel external pouch of geomyoid rodents is the result of a shift in the location and magnitude of evagination to include the lip epithelium at the corner of the mouth during embryonic development. As the lips develop with the growth of the snout, the evaginated corner of the mouth is transformed into the external pouch opening. In this example, a small developmental change (the pattern of epithelial evagination during embryogenesis) produced a major phenotypic change (externalization of the cheek pouch).

## The power of youth

The types and degrees of phenotypic plasticity expressed by organisms are known to change over the course of the life cycle. Drawing on decades of work by developmental biologists and psychobiologists (57), it is generally accepted that the conditions that best favor the expression of modified or novel phenotypes are species-atypical alterations in environmental conditions and contingencies that occur early in ontogeny (71, 87–89). Shifts in behavior brought about by alterations to the developmental system can arise at any stage of the life cycle, but are generally more likely to occur earlier in individual development. Several evolutionary biologists made this point over the past century (4, 7, 90), and despite their different backgrounds and perspectives realized the significance of embryonic and neonatal periods of development for the generation of phenotypic novelties. These early periods of development are a time of rapid morphological, physiological, and behavioral change, and modifications to an individual’s developmental system during this time can initiate a host of physical and behavioral changes, and in some cases (given the availability of appropriate developmental resources) persist across subsequent generations (91). For example, variation in the patterns of social interaction between rodent mothers and their offspring can modify pups’ gene expression within a generation, but can also be maintained over subsequent generations (92).

The insight that there is generally a higher degree of malleability during earlier as compared to later phases of development has at least two important implications for understanding evolutionary processes (51). First, in addition to selection acting upon phenotypic outcomes as

they are expressed in breeding age adults, selection can also occur at earlier stages of development, allowing for the potential for the rapid spread of novel phenotypes in response to modified developmental circumstances. In addition, the young of a species frequently have more potential than older members of the species to facilitate or accelerate phenotypic change. Learning mechanisms and developmental plasticity allow the young of many organisms to readily establish novel relationships with their environments (70). Such novelties, once established, can provide the basis for the eventual expression of a host of other novel phenotypic traits.

Johnston and Gottlieb (72) provide a useful overview of this scenario. They describe a population of rodents whose normal diet consists of soft vegetation encounters a new food source of relatively hard but highly nutritious seeds. As young animals in the population learn to sample and eventually increase the representation of seeds in their diet, a number of developmental effects of their new diet become evident, including changes in body size and composition, fecundity, age of sexual maturation, and indirect changes in morphology. For example, as the diet changes from soft vegetation to harder seed items, the mechanical stresses exerted on growing jaw tissues during development change. Given that patterns of bone growth are known to be determined, in part, by forces exerted on the growing bone (93), the skeletal anatomy of the jaw will likely be different in the animals that experience hard vs. soft diets early in life. Such changes in diet have, in fact, been shown to affect the jaw and skull of rats (94). In this example, behavioral change in members of a population (a preference for a new diet of hard seeds) leads to specific anatomical changes (modification of the jaw and teeth). Such changes can endure across generations, and as long as the new diet remains available, may eventually lead to changes in gene frequency as a result of long-term behavioral or geographic isolation among variants within the population.

## Conclusion

Biology has been undergoing a significant shift in how it characterizes development and evolution over the last several decades. Several of the core concepts widely applied during the past century to address the causal source of phenotypic stability and variability have been called into question by empirical and conceptual advances in genomics, cellular and molecular biology, epigenetics, and systems biology. In particular, underlying

assumptions regarding the primary role of genes in development and evolution (i.e., instructions for building organisms resides in their genes, genes are the exclusive means by which these instructions are faithfully transmitted from one generation to the next, and there is no meaningful feedback from the environment or the experience of the organism to the genes) have been seriously challenged by demonstrations of the epigenetic regulation of gene expression and cellular function, in some cases across generations, as well as the varied effects of sensory stimulation and social interaction on genetic, neural, and hormonal responsiveness (95, 96). This body of work strongly suggests that the emergent products of development are always epigenetic, not just genetic.

My focus in this brief conceptual overview has been to explore how a developmental point of view is forging a more complete explanation of the origin of phenotypic traits – one of the most enduring challenges of developmental and evolutionary biology. Much work remains to do on this project, but it now seems clear that a complete understanding of evolutionary change will require understanding development. Callebaut, Muller, and Newman (97) summarized the far-reaching implications of this insight for evolutionary theory and concluded that development is the causal mechanism for the process of evolution. Rather than evolution producing organisms that develop, they propose that “development has resulted in populations of organisms that evolve”, effectively turning 20th century evolutionary thinking on its head and suggesting a new framework for forging a more comprehensive and integrative 21st century approach to the study of developmental evolution [see also, (98)]. From this view, the dynamic stability or variability of phenotypes can be traced to the developmental resources and conditions that gave rise to them in the first place (13, 99). This approach can contribute to a clearer conceptual framework of how genes, development, and the environment coact to produce both stable as well as novel phenotypes.

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