Integrating Evolution and Development

From Theory to Practice

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1 Embryos, Cells, Genes, and Organisms: Reflections on the History of Evolutionary Developmental Biology

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Evolution and development are the two biological processes most associated with the idea of organic change. Indeed, the very notion of evolution originally referred to the unfolding of a preformed structure within the developing embryo and only later acquired its current meaning as the transformation of species through time. It seems, therefore, only logical to assume that the biological disciplines that study these two different phenomena—embryology, later transformed into developmental biology, and evolutionary biology, especially phylogenetics—would be closely related.

From Aristotle until the late nineteenth century, history in the context of the life sciences was always understood as life history. As such, history always stretched across generations. What we today identify as three distinct processes of development, inheritance, and evolution (each investigated by several separate research programs), were previously all part of an inclusive theory of generation. This fact, often overlooked in recent discussions of the prehistory of evolutionary developmental biology, is important, because the conceptual topology and epistemological structure of these earlier discussions is quite different from today's attempts to resynthesize evolution and development (see also Laubichler 2007). This earlier concept of generation conceptualized as organic nature unfolding as one grand historical process is distinctly pre-Weismannian, whereas today's attempts to integrate evolution and development implicitly accept and even reify Weismann's idea of a separation of the soma and the germ line as the respective domains of these divergent research programs (see, e.g., Weismann 1892; Buss 1987). Synthesis in our current context therefore means finding a way to integrate the results from one discipline within the theoretical structure of the other, whether as research into the evolution of developmental mechanisms or as research into the evolutionary consequences of developmental processes. There are a few exceptions to these two paradigmatic cases of integration, but those have not yet become sustained research programs within evolutionary developmental biology.

During the second half of the nineteenth century several attempts were made to hold on to the idea of the unity of generation in light of the growing specialization of research within the life sciences. To be clear, the idea of generation itself had undergone several transformations since its canonical formulation in the eighteenth century, but its main focus on a continuous historical connection through the life cycle of organisms remained intact. Ernst Haeckel's program of evolutionary morphology and phylogenetics with its focus on the biogenetic law provided one such attempt, as did August Weismann's theoretical and Wilhelm Roux's experimental systems. (Neither Weismann nor Roux was as radical as their followers believed they were; both are transitional figures mostly concerned with establishing sustainable research programs within the conceptual topology of generation.) However, at the turn of the twentieth century, with the sustained success of *Entwicklungsmechanik* and other experimental approaches to the study of development and inheritance, the situation began to change. While most late nineteenth-century scientists did not consider the evolutionary process to be truly separate from development, the focus of the next generation was different. Rather than phylogeny and generation together, organisms and cells and their respective properties such as regulation and differentiation provided the frame of reference for new experiments, observations, and theories. This trend, seeking to account for development on the level of its supposed determinants (cells, genes, or molecules, but also organism-level phenomena, such as fields and gradients), continued throughout the twentieth century (see, e.g., Allen 1975; Gilbert 1994; Mayr 1982; Mocek 1998). A similar pattern can be seen in evolutionary biology where, within the emerging disciplines of population and quantitative genetics, evolution was reconceptualized as the change in the frequencies of certain alleles within populations (Provine 1971). In the context of these models the focus of evolutionary biology shifted from an earlier emphasis on explaining phenotypic change to the study of genetic variation within populations. This view of evolution produced operational models and theories, but completely ignored the crucial question of how a genotype produces a phenotype (e.g., Sarkar 1998).

It has been argued that the success of the modern synthesis was based on the exclusion of the messy phenomenon of development and the correlated claim that denies a difference between micro- and macroevolutionary processes (see, e.g., discussions in Mayr and Provine 1980). The tables were turned when, in the early 1970s, several authors argued that there is

something important to be gained by bridging the gap between developmental and evolutionary biology. Initially, these proposals, such as punctuated equilibrium (Eldredge and Gould 1972), developmental constraints (Maynard-Smith et al. 1985), or burden (Riedl 1975), remained minority opinions, but after remarkable new results in developmental genetics showed the widespread conservation of "developmental genes," such "new syntheses" of macro- and microevolution and of evolution and development soon gained momentum (see, e.g., Hall 1992, 1998). This is, at least, the growing myth about the origin of modern evo-devo.

However, despite recent enthusiasm for this "new synthesis" it is not at all clear whether there is enough agreement among the various versions that supposedly fall within this camp to justify such a label of synthesis. Different authors entered the field with different perspectives and from different intellectual traditions. Thus, Brian Hall's recent question "evo-devo or devo-evo?" is more than just an exercise in semantics (Hall 2000). We still find very few universally agreed on concepts or even research questions in evo-devo (e.g., Wagner, Chiu, and Laublicher 2000). Understanding the origins of the different conceptions of evo-devo might thus be a necessary step on the way to a deep synthesis.

Here, we seek to shed some light on the epistemological and theoretical assumptions that lie behind attempts to conceptualize development and evolution and to ask "what is new with evo-devo?", "what are the conceptual resources of different versions of evo-devo?", and "to what extent is evo-devo a continuation of earlier traditions?" Our chapter is decidedly *not* intended as a history of evo-devo, or even as a history of the changing relations between evolution and development. Such a study would require much more space than we have here (for beginnings of a history of evo-devo, see Amundson 2005; Laubichler 2005; Laubichler and Maienschein 2007). Rather, we illustrate through a few short historical vignettes a specific hypothesis related to the conceptual and epistemological shifts that determined the ways researchers have thought about the relationship between evolution and development.

In short, our hypothesis is that there was a crucial conceptual and epistemological break associated with the establishment of several independent and self-sustaining experimental research programs devoted to specific aspects of evolution, development, and inheritance at the turn of the twentieth century. For centuries these phenomena were conceptualized within the single theoretical framework of generation that implied the unity of development, inheritance, and later also of evolution. However, late nineteenth-century adherents of this conceptual framework did not succeed in establishing a sustainable experimental research program, nor could they accommodate all of the new experimental results that emerged within the lines of research made possible by the many technological as well as organizational innovations during that period. As a consequence, the unity of generation disintegrated with the rise of the growing specialization of the experimental disciplines within biology. A small band of theoretical and experimental biologists tried to hold on to the conceptual unity of generation as well as to create a new conceptual structure for biology, but they remained a minority and did not succeed in establishing a conceptual alternative powerful enough to counteract the centrifugal tendencies within experimental biology. As a consequence, the conceptual topology once represented by the idea of generation was transformed into several separate domains represented by the concepts of inheritance, development, and evolution.

For example, embryologists in medical schools focused on "proximate" details of the developing individual human, while the "ultimate" distant evolutionary history seemed of little immediate importance. This lack of attention to evolution persists far outside the world where it is medically explicable, and for a much wider range of related reasons developmental biologists have largely ignored evolution as unimportant to the immediate research at hand. There has been little explicit opposition, but neither has there been a consistent sense of sameness of purpose or a compulsion to bring embryology closer to evolution. From the other side, as both historians and biologists have often noted, embryology was largely not included in the so-called evolutionary synthesis of the 1950s—though whether it was actively left out or just failed to see the point of joining remains an open question. Ron Amundson, for instance, has published his own take on this history, one based on the assumption of an active exclusion of developmental biology by what he calls "synthesis historiography" (Amundson 2005; see also Laubichler 2005 for a critical reading of Amundson).

These separatist tendencies have changed in the last couple of decades, of course, and it is not because researchers have managed to fit embryology belatedly into the now-established synthesis or because development has somehow been tied into the "central dogma" of genetics. Rather, there are new ways of thinking about how to bring the fields together, and new reasons to do so, leading to the search for a new and different synthesis. Hence the perceived need for a lively new name for the integrated field dedicated to stimulating research (and funding), seemingly fulfilled by "evo devo."

However, as our historical reconstruction of the shift in the conceptual and epistemological structure from generation to development, inheritance, and evolution indicates, accomplishing a true synthesis of "evo" and "devo" will actually be quite difficult. This is largely true because, with a few exceptions, most of the current discussion remains within the conceptual topology that separates development, inheritance, and evolution. Furthermore, "evo-devo" or "devo-evo" is already experiencing the same centrifugal tendencies that have led to the earlier separation into different disciplines, and largely for the same reasons of experimental success and the lack of a unifying theoretical structure. Our examples suggest that unless a new conceptual topology is established, within which development, inheritance, and evolution represent different elements of one historical process (as was the case in the earlier conception of generation), a new synthesis of evo-devo might remain elusive.

The Phenomenology of *Entwicklung*

We have stated above that throughout most of the nineteenth century, historical processes in nature were conceptualized as generation. This unified view of generation, or *Entwicklung,* had far-reaching epistemological consequences, especially with regard to the relationship between historical description and mechanical causality. Even though studies of generation had always also referred to mechanical causes (or other forms of the Aristotelian *causa efficiens*), the primary focus of these studies had been historical. *Entwicklungsgeschichte* was foremost a phenomenology of Entwicklung. However, within this framework of Entwicklungsgeschichte the older conception of generation, which focused on the iterative processes of development and inheritance, could be extended to include an evolutionary dimension. In this way it can be argued that the conception of embryology as Entwicklungsgeschichte enabled the formulation of the theory of evolution (see also Richards 1992). The foremost representatives of this trend in the second half of the nineteenth century are Darwin and Haeckel, whereas Weismann and Roux represent transitional figures, who tried to integrate new experimental approaches and results within this conceptual structure of generation and Entwicklungsgeschichte.

Darwin on Development and Generation

Darwin brought development into the foreground of natural history in the first edition of his *Origin.* There he declared his enthusiasm for embryology as providing perhaps the most compelling evidence for evolution by common descent, "second in importance to none in natural history" (Darwin [1859] 1964, 450). He asked,

> How, then, can we explain these several facts in embryology,—namely the very general, but not universal difference in structure between the embryo and the adult;—of parts in the same individual embryo, which ultimately became very unlike and serve for diverse purposes, being at this early period of growth alike;—of embryos of different species within the same class;—of embryos of different species within the same class, generally, but not universally, resembling each other;—of the structure of the embryo not being closely related to its conditions of existence, except when the embryo becomes at any period of life active and has to provide for itself;—of the embryo apparently having sometimes a higher organization than the mature animal, into which it is developed.

The answer lay with evolution, for "I believe that all these facts can be explained as follows, on the view of descent with modification" (Darwin [1859] 1964, 442–443).

Darwin scholars have provided much historical evidence regarding what Darwin knew, when he knew it, how he knew it, and what he concluded, when, and why. Darwin was clearly influenced by German embryological studies, and reinforced by Karl Ernst von Baer's "laws" that embryos remain largely similar for similar types of organisms and only diverge later according to type. Historians have pointed out the irony that empirical reports of what Darwin offered as his best evidence came in large part from those who opposed the idea of evolution. Yet this fits Darwin's pattern of taking what is available (such as William Paley's 1802 argument from design) and brilliantly using it to demonstrate the fit with his theory of evolution as common descent through natural selection. In Darwin's methodological reasoning, if the evidence can be explained by evolutionary theory, it lends confirmation to that theory. Therefore, Darwin had more a devo-evo focus, concerned with taking embryology to inform evolution (or more properly embryo-evo, since what became developmental biology after World War II was called embryology in Darwin's day and "development" often referred to the unfolding that occurs during evolution).

Darwin's focus on evolutionary relationships, especially among embryos, guaranteed that embryology would become a lively subject at the end of the nineteenth century as researchers sought empirical support for evolutionary ideas, or against them. Tracing detailed morphological patterns of development for individual types of organisms provided data, and the apparent ability of embryonic relationships to reveal ancestral and therefore also adult relationships provided work for many embryologists. Darwin had, in effect, issued an invitation to engage in detailed descriptions of embryonic development typical of an individual species. This was not Rudy and Elizabeth Raff's "evolutionary ontogenetics" for the sake of studying development, but rather embryology in aid of constructing evolutionary phylogenies, more devo-into-evo. In other words, Darwin was still arguing within the conceptual framework of generation where embryological data could support claims about descent with modification and the phylogenetic relations between different taxa. While this was not Darwin's emphasis, Ernst Haeckel very quickly provided a most highly visible theoretical structure by which to organize these burgeoning investigations.

Ernst Haeckel and the Biogenetic Law

As Ernst Mayr has explained, Haeckel was practically required reading for intelligent young students early in the twentieth century, and well before. Because of his "monistic materialism," Haeckel was a bit naughty, and public school teachers did not really want their young students discussing such things (Mayr 1999). Yet Haeckel had quickly gained a popularity and credibility that made it impossible to ban him from the classroom. Thus, the clever young student could both annoy the teacher and intrigue other students by quoting Haeckel. Haeckel evidently thus inadvertently helped to start at least one young German man on his way to becoming one of the world's leading evolutionary biologists.

Haeckel built on earlier studies based in a *Naturphilosophie* tradition that stressed the unity of nature. He sought to outline comparisons between the series of changes in the development of individuals (ontogeny) and that of species (phylogeny). Further, he sought to demonstrate the value of comparative ontogeny for revealing otherwise elusive phylogenetic relationships. Haeckel expressed his ideas in different places and in varying forms for both German- and English-speaking audiences, because his major books were quickly translated and published in popular form. Statements of the theory, its corollaries, and implications were often distorted, even by Haeckel himself in some cases. Yet the key principles remained quite clear and consistent, and though familiar to some, Haeckel's views are worth reviewing since they are so often misrepresented.

Most basically, Haeckel saw ontogeny and phylogeny as intimately related, not as separate processes. Indeed, the "fundamental law of organic evolution" was "that Ontogeny is a recapitulation of Phylogeny; or somewhat more explicitly: that the series of forms through which the Individual Organism passes during its progress from the egg cell to its fully developed state, is a brief, compressed reproduction of the long series of forms through which the animal ancestors of that organism (or the ancestral forms of its species) have passed from the earliest periods of so-called organic creation down to the present time" (Haeckel 1876, 6–7). Furthermore, this is a causal relationship in which the phylogenetic changes in one sense cause the ontogenetic series of changes. Therefore, development reveals evolution, or devo takes us into evo. The recapitulation is not perfect, however, but rather ontogeny is the short and rapid recapitulation of phylogeny, "conditioned by physiological functions such as heredity (reproduction) and adaptation (nutrition). The organic individual . . . repeats during the rapid and short course of its individual development the most important of the form-changes which its ancestors traversed during the long and slow course of their paleontological evolution according to the laws of heredity and adaptation." Deviations and specifics make the patterns, so devo illuminates evo and reveals relationships. Or, to put it in modern terms, devo is seen as reflecting evo (Haeckel 1866, vol. II, 300). All this he offered with special emphasis on the role of changes in the germ layers, which provided a convenient starting point for research and raised questions for the theory. Ultimately, however, the earlier stages prior to germ-layer formation did not show the same visual embryonic parallels that had enthused Haeckel. Haeckel did admit that secondary adaptation can cause divergences from the ancestral pattern, but he saw those as only helping to inform our understanding of the evolutionary process. His biogenetic law, or the law of recapitulation, is the most familiar encapsulation of his views.

To reinforce his lengthy and often repetitious tomes, Haeckel typically provided tables of comparative figures to make his point more persuasive. Haeckel's many long volumes were eagerly received in the United States and elsewhere, as well as in Germany. In fact, they appeared in such large numbers from such popular presses that they are still quite easy to find inexpensively in used bookstores.

While Haeckel was a great authority for claims about embryonic parallels and recapitulation, he later became a repudiated figure regarded as a mere popularizer and an intellectual lightweight, and was accused of deliberate fraud. It is not for us to decide Haeckel's scientific reputation here, nor to chronicle his debates with Carl Gegenbaur, Anton Dohrn, and others, but rather to note that by the early twentieth century Haeckel, more than any other single author besides Darwin himself, focused attention on the relations between embryos and ancestors, between development and Darwinism (Laubichler and Maienschein 2003; Nyhart 1995). The fact that the pages of such leading scientific journals as *Science* and *Nature* still carry

notes on Haeckel's contributions (albeit often highly critical) stands as testimony to his impact (see also Richards 1992; Haeckel Haus documents in Jena). By bringing evolution and embryology together in the way he did, however, he also set the stage for repudiation of the particular speculative relationships that the embryological comparisons seemed to suggest. Indirectly, Haeckel's excessive speculation and theorizing helped to stimulate opposition to the goal of phylogenizing, and also led to a rallying to embryology for its own sake separate from evolution. Embryologists increasingly called for exploration of the mechanisms and proximate causes of ontogenies, increasingly pushing evolution into the background. Ironically, this initial interest in development stimulated by interest in evolution helped to drive a sharp wedge between embryology and evolution for most of a century. The connections seemed too weak and strained as biologists called for a stronger, experimentally, and empirically grounded science.

August Weismann and the Gradual Disintegration of "Generation"

Etymology can sometimes lead to interesting insights. It would be a worthwhile undertaking to document all the multiple interpretations of the word *evolution* in the second half of the nineteenth century. This term was still mostly defined in opposition to epigenesis in that it referred to a strictly mechanical theory of development. Development (evolution) was seen as a gradual unfolding of causes (factors) that are already present at the beginning—that is, in the fertilized egg. Epigenesis, on the other hand, implied the gradual emergence of complexity as part of a dynamic process of development. As Weismann, who did more than anybody else to develop this view, stated in the preface to his theory of the germplasm, "So kam ich zuletzt zu der Einsicht, dass es eine epigenetische Entwicklung überhaupt nicht geben kann" ("and thus I finally realized that epigenetic development is impossible"). Weismann, who according to his own admission, had tried to develop several theoretical systems that would include epigenetic processes in development, finally convinced himself that only a strictly deterministic theory of development could account for all the empirical facts and be theoretically satisfactory. The one theoretical problem that Weismann was most concerned with was the causal and material relationships among development (Entwicklungsgeschichte), heredity, and the transmutation of species (Abstammungslehre). The problem, as it presented itself to Weismann, was to find the material cause that would connect all the different elements of generation (including descent with modification).

He starts his discussion of the problem with some remarks about Darwin's theory of pangenesis as well as about Herbert Spencer's notion of "physiological entities," but soon rejects both because of the number of theoretical assumptions that these theories require. Weismann's solution was to focus on the material continuity between the generations (heredity) and separate it from the mechanistic causation of development. This theoretical separation of development from inheritance allowed Weismann to clearly analyze the kind of causation involved in each of these processes and to ask how these chains of causation could be realized materially. His answer was deceptively simple. To account for heredity, Weismann assumed that the germplasm, which contained all hereditary factors, always remains within the germ cells—in other words, that there is a continuity of the germ line. This assumption, for which there was ample empirical evidence, also supported the theoretical separation of development from inheritance. Weismann argued that during development, which represents a differentiation of the zygote into multiple cell types, the material composition of the dividing cells changes; the idioplasm of the differentiating cells is therefore not identical to the germplasm of the gametes. Furthermore, he argued that these changes in the material composition of individual cells are the causes for their differentiation into separate cell types. However, and this was a central part of Weismann's argument, the idioplasm of differentiated cells in the body is completely separate from the germplasm. Weismann did not allow for any form of causal connection that would reach from the differentiated cells of the organism back to the germplasm. This view was the opposite of Darwin's theory of pangenesis (which had already been discredited by Darwin's own cousin, Francis Galton) and also affirmed Weismann's commitment to an evolutionary (unfolding) conception of development.

Conceptually, Weismann's theoretical system introduced a clear distinction between the processes of development and heredity, two aspects of the older concept of generation. However, in his system Weismann still maintained the material unity of generation. The germplasm represents the material connection between generations, and the material changes in the idioplasm provide a mechanical explanation of development as evolution (unfolding). Furthermore, the germplasm contains all the material factors that are needed to build an organism. But the theoretical separation between germplasm and idioplasm also provided the conceptual framework for the emerging experimental research programs in Entwicklungsmechanik and genetics.

The Separation of Entwicklung into Independent Research Programs

By 1900 the conceptual unity of generation had fallen apart. The Haeckel-Gegenbaur program of evolutionary morphology and the biogenetic law could no longer be sustained as a productive research program, largely because it did not solve the fundamental problem of circularity inherent in reconstructing phylogenies based solely on comparative and embryological data (Laubichler 2003; Laubichler and Maienschein 2003; Nyhart 2002). In the meantime, new experimental programs had established themselves as powerful alternatives to earlier descriptive approaches, introducing a conceptual shift from phenomenological Entwicklungsgeschichte to Entwicklungsmechanik and Entwicklungsphysiologie. Consequently, the new focus was predominantly on proximate causes for development (or on the Aristotelian causa materialis and causa efficiens). This was, in a way, inevitable, because the problem of generation was now approached experimentally, and each experimental manipulation defines its own form of causation as correlated changes between measurable parameters. As a consequence, development, inheritance, and evolution were mostly studied as separate experimental problems, soon followed by conceptual developments specific to each of the newly emerging disciplines.

In the context of development the focus was on the causal determinants of differentiation. This required a careful record of cellular differentiation during development and a conceptual reorientation of the question of development from the life history of an organism to the differentiation of cells. Phenomenology was thus still part of Entwicklung, but it was the phenomenology of parts, not wholes, that mattered here. It was studied experimentally through increasingly difficult manipulations, such as selective killing of cells, various forms of constriction experiments, and a whole series of grafting experiments. The conceptual innovations that most characterize this period are the ideas of cell-lineage studies, of tissue cultures, and of the physical-chemical determinants of development, culminating in the idea of the organizer, as well as in the notion of regulation in development.

The study of inheritance took a similar path, focusing mostly on factors of inheritance, although the history of genetics during the first half of the twentieth century is extremely diverse and also includes several research programs that continued to study inheritance and development together as two intricately related biological processes. The most prominent of these alternative approaches were Richard Goldschmidt's program in physiological genetics and Alfred Kühn's related program in developmental genetics (e.g., Geison and Laubichler 2001; Laubichler and Rheinberger 2004). But these locally successful programs were eclipsed by the even greater success of Morgan-style transmission genetics, which established the Drosophila model as the international standard (Kühn and Goldschmidt both used different species of moths as model organisms), the emerging mathematical population genetics, which was soon integrated into the modern synthesis, and, shortly thereafter, by molecular genetics. Besides their experimental work, Kühn and Goldschmidt also made important theoretical contributions that continued to develop the conceptual framework of generation (as well as of epigenetics), but their theories had a similar fate as their model organisms: they were "outbred" by their much simpler and faster reproducing competitors.

An even more ambitious program in experimental biology that explicitly continued within the earlier tradition of the conceptual unity of generation was initiated by Hans Przibram at the Vienna Vivarium. Przibram's program included experimental research into development, regeneration, heredity, and evolution. To that end he and his coworkers developed the most sophisticated techniques to maintain research animals for extended periods and many generations. Research in the Vivarium was explicitly focused on an epigenetic conception of development that included the study of regeneration as well as experiments that investigated the role of the environment in development and evolution. Today, the Vienna Vivarium is mostly associated with the controversy surrounding Paul Kammerer and the final discreditation of neo-Lamarckian theories of inheritance. This is extremely unfortunate, since in many ways, the research program of the Vienna Vivarium is the link between nineteenth-century theories of generation and late twentieth-century attempts to resynthesize evolution and development and lately ecology as well.

But for the reasons sketched above as well as for a variety of others that we could not discuss here, a different set of questions came to dominate the scientific study of development, inheritance, and evolution in the early decades of the twentieth century. Here we will provide two exemplary cases that represent the transition from the earlier focus of Entwicklungsgeschichte and generation to the newly emerging research programs of cell biology, Entwicklungsmechanik, and transmission genetics.

E. B. Wilson

The American biologist E. B. Wilson felt this call to undertake a rigorous study of embryology, in the context of cell theory. Wilson saw evolution and cell theory as the two great foundations for biology, and development

as a central part of cell theory (Wilson 1896, 1). In an essay "Some Aspects of Progress in Modern Zoology," this leading cytologist explained the increasing divergence between those interested in evolution and those interested in embryology. While Darwin concentrated attention on evolution and phylogenetic relationships for a while, soon the "post-Darwinians awoke once more to the profound interest that lies in the genetic composition and capacities of living things as they now are. They turned aside from general theories of evolution and their deductive application to special problems of descent in order to take up objective experiments on variation and heredity for their own sake" (Wilson 1915, 6).

This was certainly not because they rejected evolution. Quite the contrary. Evolution became, in effect, a fundamental background condition, against which individual development and behavior were to be understood. Yet the background faded in immediate importance, as the researchers focused on individual structure, function, and their development. Instead of evolutionary relationships, embryologists and geneticists found new areas to explore, and what they saw as the proper exact science of biology quickly moved in those directions. This was devo in the foreground, with evo essentially in waiting as a background assumption. Evo and devo were not yet connected.

Wilson saw embryologists as able to remain on relatively firm ground, with a "rich harvest" of careful, detailed empirical descriptions of the stages of development. In contrast, he feared that the evolutionist phylogenizers often tread on thin metaphysical ice and narrowly miss entering the "habitat of the mystic" in their speculations. Evolution was just too difficult to study rigorously, he felt (Wilson 1915, 8). Embryology, in contrast, is based on chemistry and physics and the close study of cells, and hence more solidly grounded in empirical science.

Complex epistemological preferences dictated this conclusion, shaped by Wilson's own education at Johns Hopkins, and reinforced by his research at the Stazione Zoologica in Naples and the Marine Biological Laboratory in Woods Hole, Massachusetts (Maienschein 1991). He was a leader among biologists, and typical of the new specialists who decades later were called cell and developmental biologists. We can already see embryology diverging by the first decade of the twentieth century from evolution: different questions, different approaches, different methods, different researchers, and different values. Development might be a foundation for biology, and evolution might be a persistent shaping force, but for those who would study biology, these were two separate cornerstones and not integrated profoundly.

For Wilson, the "exact" (and hence most desirable) biological science for his time already lay with embryology and genetics (or heredity and development). For the time being, he pointed out that we did not understand how the inherited material "of the germ-cell can so respond to the play of physical forces upon it as to call forth an adaptive variation." In addition, the distance from the inorganic to the simplest life seems so large that it is difficult to understand how the gap could be bridged. Therefore, Wilson concluded in 1896, "I can only express my conviction that the magnitude of the problem of development, whether ontogenetic or phylogenetic, has been underestimated" (Wilson 1896, 330). Cell theory had made tremendous advances in understanding the basic phenomena of life, but much remained to be done. Study of development based on cells and evolution remained far apart. Devo sat alongside evo. We had not discovered how to bring the two together and retain the proper epistemic commitments of science.

In large part, Wilson remained focused on morphology. By looking at the structure of cells and cell parts, and their changes through the stages of individual development, this premier cytologist did not see how to connect the developing morphological patterns of individuals and those of the species to which they belong and from which they have derived by evolution. It was by going deeper into the cell, and beginning to see the connections of physical-chemical compositions, which took researchers much of the twentieth century, that we moved toward bridging the gap that Wilson saw at the end of the nineteenth century.

T. H. Morgan

Three decades later, another American (a friend and colleague of Wilson's)—Thomas Hunt Morgan—began to suggest one way the increasingly apparent differences might be bridged. By then, he had already carried out the Nobel Prize–winning foundational work in genetics on white-eyed Drosophila. The eighth chapter of his *The Scientific Basis of Evolution* (1932) considered "Embryonic Development and Its Relation to Evolution." As this architect of genetics put it, "One of the important chapters of the Evolution Theory concerns the interpretation of the evidence from embryonic development." All the discussions of recapitulation sparked by Darwin and Haeckel had led to great debate and much new study, Morgan (1932, 171), acknowledged, but they had not made much progress in their attempt to "unravel the remote past" of evolution. Darwin's assertion that "community of embryonic structure reveals community of descent" did not go far toward explaining how that revelation would occur, or its details.

As he pointed out, it does not get us very far to know whether ape adults or ape embryos were the closest human ancestors. For Morgan (1932, e.g., 177), we were going to need to know a lot more than that to make any progress with the important questions of biology.

That knowledge could only come with close study of chemical and physical details of the egg and the embryo. Specifically, genetics held the key for Morgan. It was genes that would tie together individual development and evolution, since genes underlie heredity that ties individuals together across generations and guides development. Genes could lead to changes in early, embryonic, stages of development and thereby have far-reaching effects later on. The risks involved in making early changes would explain why those early stages are so highly conserved, and why the later stages tend to vary more often. Genetics, in short, could explain why we see the patterns we do in embryology and evolution. Yet for Morgan, it clearly remained more important, more legitimate, and more progressive science to build a strong bridge from the evolutionary past to the present developing individual organism, through genetics. He would surely have been happy with others pursuing "evolutionary ontogenetics" as a goal. But then evolution remained entirely in the background of his own research, which focused on heredity primarily and at times on development.

The examples of Morgan and Wilson and many others that we could not mention here demonstrate how productive research programs all too easily take on a life of their own. "Evolutionary ontogenetics" remained a goal for Morgan, but one that gradually disappeared behind mountains of new data and research questions made possible by the establishment of the successful Drosophila model. However, these new data also needed to be interpreted and organized, which, in turn, required the development of a new conceptual structure, that of transmission genetics and the chromosomal theory of the gene. Heredity was now a problem of transmission rules; genes, still identified by their phenotypic effects, were localized on chromosomes; and complications that arose due to development (the genotype-phenotype mapping problem) were soon hidden behind conceptual innovations designed to insulate the core assumptions of transmission genetics from all potential threats to the theory. Concepts such as "penetrance" and "expressivity" allowed researchers to maintain a simple model of genetic determination, while paying lip service to the intricate process of development.

Experimental embryology (soon to be renamed as developmental biology), which had been a major success story from the early 1890s on, hit a roadblock during the mid-1930s, mainly because it had reached the limits of what was technically possible at that time and with the standard-model organisms. Despite intensive research, the chemical nature of Spemann's organizer remained elusive and the connection of development to the newly emerging genetics was even more difficult to accomplish. It took Alfred Kühn, for example, years of almost industrial-scale research and the help of Nobel Prize–winning chemist Adolf Butenandt to uncover the biochemical pathway of an eye-color mutation in the moth Ephestia kühnellia (Rheinberger 2000). No wonder, then, that problems of gene action were soon studied with simpler organisms, such as Neurospora, E. coli, or even phage. But this shift in experimental methodology and technology also initiated another major conceptual change, that of molecular biology. The subsequent history of molecular biology and molecular genetics has been well documented, but it is also important to remember that it represents a further step away from the initial conceptual unity of generation.

A similar story can be told for population genetics. Originally mired in the controversy between Mendelians and biometricians about the nature of variation in natural populations, it soon emerged as the mathematical foundation of the modern synthesis. This was possible because Fisher, Haldane, Wright, and others managed to establish a system of successful mathematical abstractions that reconceptualized the problem of evolution. Under the assumption that specific genetic factors are correlated with specific genotypes—an assumption seemingly supported by the results of transmission genetics—it was possible to establish an operational mathematical theory for the dynamics of gene frequencies within (similarly abstracted) populations. This mathematical theory then provided the theoretical foundation for the modern synthesis in that it connected, through a successful series of abstractions, such as fitness values, the dynamics of alleles (particles) within populations to such phenotypic phenomena as adaptation and speciation.

The initial unity of generation thus disappeared while evolution (now defined by the assumptions of the modern synthesis), genetics (as population genetics, quantitative genetics, and molecular genetics) and developmental biology (soon transformed by molecular biology), established themselves as the cornerstones of twentieth-century biology. To be fair, quite a number of researchers tried to hold on to more integrative questions—the whole movement of theoretical biology in the first decades of the twentieth century is a case in point—but they remained at the margins and often had to fight hard for their reputation. Goldschmidt, for instance, was long vilified and only recently experienced somewhat of a renaissance, largely due to the efforts of Stephen Jay Gould, and C. H. Waddington had to endure unfounded accusations of being a neo-Lamarckian, because his ideas, such as genetic assimilation did not easily fit within the theoretical structure of population genetics. But those "renegades" were the ones who first saw the importance of new results and methods in evolutionary biology and developmental genetics, and in the early 1970s they began to address the old problem of the relations between development and evolution.

The Emergence of an Evo-Devo or Devo-Evo Synthesis?

Embryology may not have made it into the self-declared "evolutionary synthesis" of the 1930s and 1940s, and it has taken a while for researchers to sort out how to study relationships of evolution and embryology in the context of the conceptual topology of late twentieth-century biology. Yet the current evo-devo enthusiasm provides us with an encouraging major shift in thinking that may actually bring about that "new light" that de Beer foresaw. This synthetic field has the potential to bridge the epistemological, methodological, and theoretical gaps separating development and evolution for the past century.

Over the last thirty years many important contributions shaped the gradual emergence of evo-devo. Scientists working within a variety of different traditions of twentieth-century biology began to address the question of the relation between development and evolution. These diverse perspectives have led to several different versions of the evo-devo or devo-evo synthesis that have not yet been fully reconciled. Some of these differences are merely individual idiosyncrasies, but others are symptoms of a fundamental theoretical rift that divides the evo-devo community. Does one incorporate elements of evolutionary biology to better understand development (evo-devo), or does one integrate the results of developmental genetics and developmental biology into evolutionary biology in order to gain a better understanding of phenotypic evolution (devo-evo)? This theoretical rift is largely a consequence of the current conceptual topology of biology after the original unity of generation has been split into the separate concepts of inheritance, development, and evolution. In particular, development and evolution (the two historical processes of biology), have each acquired their own interpretation of dynamical causality, which roughly fits Ernst Mayr's distinction between proximate and ultimate causes. Without fundamentally changing this framework, one field's explanatory structure will always dominate, whereas the other can only contribute supplementary evidence, or, at most, lead to a modification of some of the basic assumptions about the underlying causes of the respective historical dynamic (of development or evolution).

Yet despite this fundamental rift in the theoretical structure, evo-devo is apparently coming of age, with reports in *Science*, a new professional organization, and new journals. Obviously, this new venture concerns evolution and development, but what is the relationship? Is it simply evolutionary ontogenetics, or something more? Or something different?

In 2001 Michael K. Richardson offered a website for an "Evo-Devo Research Group" (which turned up first with popular Internet search engines under "evo-devo" at that time). Richardson explained that "'Evo-devo' is the nickname for a branch of science which aims to understand how developmental mechanisms are modified during evolution. Evo-devo has its origins in the work of scientists such as von Baer and Haeckel. But it emerged in its modern form with the rise of molecular biology." Wallace Arthur (2002) has advocated a similar view. Such accounts sounds like evolutionary ontogenetics, with the emphasis on bringing evolutionary thinking into developmental biology and developmental genetics. They deemphasize the value of development for evolution, which would be part of a truly balanced interdisciplinary field. In contrast, others do emphasize devo-into-evo, which does recognize the value of developmental patterns for phylogenetics.

This mix of views is not surprising for an emerging field. Wade Roush and Elizabeth Pennisi (1997) brought attention to the "Growing Pains" in their article in *Science*, explaining that "Evo-Devo Researchers Straddle Cultures." Typical evolutionary biologists seek to document the course of evolution across species and across time, while developmental biologists look at the developmental changes in the life of individual model organisms. As developmental biologist Greg Wray put it in that article, "Evolutionary biologists have the conceptual background [on evolution], but a lot of the time they don't even understand these data. Developmental biologists have the data, but they are not really up on what to do with it" (Roush and Pennisi 1997, 38). Ideally, at least, evo-devo researchers combine both the data on individuals, with the perspective and data concerning evolutionary patterns. Genetic and molecular information provide links.

Yet such work is not easy since it is difficult to cross deep and well-established disciplinary boundaries, especially when the data remain incomplete on both sides and it is necessary to make assumptions. Researchers on one side may fear or distrust those on the other, so that those who would straddle both must excel in both to gain credibility. For example, as Günter Wagner points out, evolutionary biology is much more theoretical in focus than molecular biology. The evo-devolutionist therefore must master the molecular details, generate and interpret the developmental data, and also work within the larger theoretical frameworks of evolution. For untenured younger scientists this can be risky.

There are growing pains indeed. As Mark Martindale admitted in 1997, funding at that time remained elusive and limited. "Evo-Devo is what we discuss over Friday beers, but when it comes to paying bills, people are more pragmatic," he reported (Roush 1997, 39). Others manage because as senior scientists they can piggyback this research on their "regular" grants. The situation has reportedly improved since then, and the successes are exciting for those who do succeed. So, only two years later there is growing evidence of that success and of a community of researchers eager to take the risks involved to be part of the efforts to build effective bridges.

The Society for Integrative and Comparative Biology (formerly American Society of Zoologists, now known as SICB, and one of the oldest persisting biological organizations in the United States) announced in its spring 1999 newsletter the formation of a new "Division of Evolutionary Developmental Biology." As the SICB leadership explained, this new field of evo-devo "is attracting growing attention from the life sciences community, academic institutions, funding agencies and major journals" (SICB 1999, 2). As co-organizer with Scott Gilbert, Billie Swalla urged members to attend that first-ever symposium at the annual SICB meeting in Atlanta in January 2000.

That meeting brought together those who embrace evo-devo and those who prefer devo-evo. At times, in the enthusiasms of talking together on the same podium in the course of a day of marvelous papers, the gaps still seemed large, but the will to bridge them is clearly strong and enthusiastic. In the wrap-up session, Rudy Raff called for "new experimental directions" that cooperation between the once-disparate disciplines could bring. And Günter Wagner and his collaborators suggested that the field of evo-devo has moved through what biologist Gunther Stent once called a "romantic" and "enthusiastic" stage to the much more difficult "academic" stage (Wagner, Chiu, and Laubichler 2000). At this more mature point, it becomes necessary to work out what is really at issue and to develop broadly multidisciplinary approaches to evolution, development, and genetics through which the field can make progress. There are methodological,