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Introduction

Manfred D. Laubichler and Jane Maienschein

Ontogeny and Phylogeny of the Volume

Each summer, starting in 1989, the Dibner Institute has offered a seminar in the history of biology at the Marine Biological Laboratory (MBL) in Woods Hole, Massachusetts. Each year the seminar, founded by Garland Allen and Jane Maienschein, and currently coordinated by John Beatty, James Collins, and Jane Maienschein, is devoted to a different topic in the history of biology. As a rule, the Dibner Seminars in the History of Biology are organized by the coordinators in collaboration with experts in the respective topics and bring together a group of students and faculty for a week of intense discussions. In 2001 the Dibner Seminar "From Embryology to Evo-Devo (Evolutionary Developmental Biology)," organized by Manfred Laubichler and Jane Maienschein, focused on the history of the relations between embryology and evolution. Among the participants exploring the rich and diverse history of the subject were noted historians, philosophers, sociologists, and biologists, including John Tyler Bonner, Evelyn Fox Keller, Rudolf Raff, Sahorta Sarkar, and most of the authors in this volume.

The results of the week-long discussions at the Marine Biological Laboratory encouraged the organizers to convene another meeting with the specific goal of producing a tightly integrated edited volume. The Dibner Institute and its director, George Smith, agreed to continue to fund this project, and in October 2002, Manfred Laubichler and Jane Maienschein convened the Dibner Institute workshop "From Embryology to Evo-Devo." Most of the workshop participants had attended the Woods Hole seminar; a few of the seminar participants were unable to come, and others, such as Everett Mendelsohn and George Smith, joined the group.

The goal of the Dibner Institute workshop was not only further discussion of the work of the participants at the Woods Hole seminar in preparation for the planned volume, but also to have present three of the leading scientists in the current field of evolutionary developmental biology—Brian Hall, Gerd Müller, and Günter Wagner, all of whom have expressed an interest in the history of their discipline. The rationale for inviting scientists to a workshop devoted to the history of science was to break down disciplinary boundaries and to take advantage of diverse perspectives. This was the first time that scientists had participated in a Dibner Institute workshop other than as the subject for inquiry, and it was, by all accounts, a tremendously successful experience.

Discussions at the workshop benefited greatly from these new perspectives, and when Brian Hall, Gerd Müller, Günter Wagner, and Everett Mendelsohn presented their reflections on the papers and discussions, new avenues for thinking about the history of the relations between development and evolution emerged. The authors subsequently revised their papers in light of these ideas and suggestions, and our commentators graciously agreed to produce additional chapters, which accurately reflect the discussion at the workshop.

The initial seminar's venue at the MBL was a fortuitous match for the topic "From Embryology to Evo-Devo." After its founding in 1888, the MBL had been one of the premier research sites for embryology, physiology, *Entwicklungsmechanik,* and comparative biology and evolutionary biology, as well as a key meeting place for many of the leading scientists of those days. Many discussions about the relations between individual development (ontogeny) and evolutionary transformations (phylogeny) took place in this "marketplace of ideas," where people gathered at the Friday evening lectures to hear about the latest discoveries or theories, and continued their discussion in their labs, during collecting trips, and at (frequent) social events. From the beginning of the MBL, embryology has been one of the core areas of research and education.[1]

The seminar's topic, "From Embryology to Evo-Devo," proved to be extremely timely. The major events in biology during the 1990s, such as the announcement of Dolly, the first cloned mammal; the emerging debates about the therapeutic potential of stem cells (and the resulting regulatory and policy confusions); and the completion of the first sequence of the human genome marked the beginning of a new era in biological research. Development (embryology) clearly was to become a major focus in this "postgenomic" period in the history of biology. Focusing the attention of historians of biology on the largely neglected history of twentieth-century embryology therefore was appropriate, even more so because the seminar emphasized one particular aspect of this history, the discussions about the relations between ontogeny and phylogeny.

For many (historians as well as biologists), Ernst Haeckel's biogenetic law, "Ontogeny recapitulates phylogeny," still represents the canonical formulation of this relationship. The fact that even though it has long been disproven, at least in its radical form, the biogenetic law still discussed in textbooks is, at the very least, a testament to its intuitive appeal, if not to a more fundamental recognition that these two temporal processes in biology are in some way linked.

Exploring the various connections between ontogeny and phylogeny is also at the heart of a newly emerging discipline, evolutionary developmental biology. The field is often heralded as the new synthesis of developmental and evolutionary biology, especially since developmental biology (embryology) was not prominently featured in the last evolutionary synthesis, which centered more on genetics, systematics, and paleontology.[2] By the late 1990s evolutionary developmental biology had all the markings of a new scientific discipline. Two new journals were specifically devoted to the field: *Evolution & Development* and an independent section of the *Journal of Experimental Zoology, titled Molecular and Developmental Evolution* (now *JEZ Part B: Molecular and Developmental Biology).* In addition, the oldest journal in the field of experimental embryology (*Entwicklungsmechanik*)—*Roux's Archiv für Entwicklungsmechanik der Organismen*, founded in 1890—has been renamed *Genes, Development, and Evolution,* another reflection of the changed focus in developmental biology. Among granting agencies, the National Science Foundation has established a specific panel devoted to the "evolution of developmental mechanisms"; and professional societies, such as the Society for Integrative and Comparative Biology (formerly American Society of Zoologists), now have specific sections for evolutionary developmental biology. In short, by the time of the 2001 Dibner Seminar in the History of Biology, evolutionary developmental biology (Evo-Devo) had arrived, at least institutionally. As a consequence, the focus of developmental biology has been broadened substantially.

This did not happen overnight. Rather, the relations between development and evolution have been the subject of renewed, intense, and controversial discussions since the 1970s. Recognizing that these developments are an interesting episode in the recent history of biology, one that also had the potential to reconfigure the interpretation of the history of twentieth-century biology, the organizers decided to devote a Dibner Seminar in the History of Biology to this topic. It soon became obvious that while quite a bit was known about the late nineteenth-century discussions on the biogenetic law, comparative embryology, *Entwicklungsmechanik*, and morphogenesis—and several participants in the recent emergence of evolutionary developmental biology had begun to document these events—next to nothing was known of what happened to these questions in the period between the 1920s and the 1970s. This historiographical vacuum provided the stimulus for expanding the topic of the seminar and focusing on a longer period, taking us "From Embryology to Evo-Devo."

Some readers misread the message and jumped to the conclusion that "from" implied direct causal change. For them, "From Embryology to Evo-Devo" seemed to imply a direct lineage of problems, ignoring the inherent complexity of the history. For others, the title evoked the image of a linear and gradual development, as if embryology had become Evo-Devo. Neither interpretation reflects either the organizers' intentions or the actual discussions at the seminar and the workshop. In these contexts embryology and Evo-Devo are merely historical markers that stand for the late nineteenth and the early twenty-first century, respectively. Exploring what happened in between was the goal of both events. Taken together, the contributions in this volume provide a first map of this extremely rich and fascinating part of the history of twentieth-century biology.

Several common themes emerged in the context of these discussions.

1. Development, as one of the central processes as well as one of the theoretical concepts of biology, has continuously been the focus of both empirical and conceptual attention. This in itself is not surprising. However, throughout the historical period covered here development has been studied and interpreted from different experimental angles and the results of these studies have been incorporated into often radically different conceptual systems, ranging from traditional comparative studies of embryology to molecular genetics and computational analysis. Studying the history "From Embryology to Evo-Devo" thus leads one to appreciate the diversity of conceptual interpretations and experimental strategies that characterizes twentieth century biology.

2. Throughout the twentieth century, multiple traditions of developmental biology coexisted; some of them are defined by their experimental strategies, others by their explanatory reference frames. In addition, different local and national traditions have persisted until the present day. These traditions are also reflected in different emphases within current evolutionary developmental biology.

3. Technology played an important role in the history of twentieth-century developmental biology, as it did in the emergence of *Entwicklungsmechanik* in the late nineteenth century (see especially Hall and Gilbert, this volume). In particular with respect to the question of ontogeny and phylogeny, the lack

of an adequate experimental approach is notable during several decades of the twentieth century.

4. Development, even more than physiology, has provided the foundation for an organism-centered perspective in biology. Even the most successful and in a sense most radical, molecular explanations of development, such as reaction diffusion models, lead to a concept, such as positional information, that implicitly refers to the three- and four-dimensional properties of organisms.

5. While the explanatory reference frames for development and evolution are different, roughly reflecting what Ernst Mayr calls proximate and ultimate explanations, at several times since the mid-1850s development has been considered essential to explanations of the patterns of phenotypic evolution. For example, in the context of evolutionary morphology, embryology provided a possible inference about genealogical connections between species (phylogeny); and in the context of developmental physiology and physiological genetics, the developmental and cellular context was considered essential to any mechanistic explanation of the evolution of phenotypes; and currently developmental mechanisms are implicated in discussions about the genotype-phenotype map, the limits of adaptation, and the origin of evolutionary novelties, among other things (see also chapters 15 and 16 in this volume).

6. All these observations contribute to a growing skepticism about what the current emphasis on a "synthesis" of evolutionary and developmental biology actually entails. On the one hand, current evolutionary developmental biology includes more than just developmental and evolutionary biology; on the other hand, it is still unclear whether the Evo-Devo focus can succeed in providing new perspectives that go beyond what would be possible within other explanatory schemata (see especially chapters 15 and 16 in this volume).

Of late, writing the history of science with a long-range perspective in order to get at the underlying persisting traditions, and thereby to be able to recognize and interpret significant patterns of change, has become unfashionable. Recent historiography of science has focused more on the local, immediate, contingent, and particular aspects of the scientific enterprise. The history of science has also matured as an academic discipline in its own right, and no longer sees its primary function as contributing to commemorative occasions and providing a "grand narrative of scientific progress" suitable for the first few pages of introductory textbooks. This new orientation in the historiography of science has led to important new insights, but it has also contributed to a growing alienation between the communities of historians of science and scientists.

In this volume with its long perspectives, we hope to bridge this unfortunate gap by including biologists as well as philosophers and sociologists. Our focus on a period of almost 150 years and our emphasis on a specific scientific problem—the relationship between ontogeny and phylogeny—allow us to analyze simultaneously continuities and transformations as well as discontinuities and novelties. Indeed, one would not be possible without the other, especially in areas of the history of biology where we do not have a commonly known, detailed historical narrative of their development. The chapters in this volume thus emphasize both the continuity of the general problem of defining the relationship between ontogeny and phylogeny, and the diversity of approaches, technologies, and concepts as well as the continuous transformation of the both the question and the scientific disciplines.

Finally, we want to mention one (tongue-in-cheek) observation that emerged during the workshop discussions: that the history of embryology and developmental biology has certain structural affinities with the individual and the phylogenetic history of organisms, and maybe this explains, in part, why among biologists, evolutionary and developmental biologists show the greatest interest in the history of their profession.

Structure of This Volume

This volume collects the papers that were discussed at the 2002 Dibner Institute workshop. In addition, it includes a paper by Scott Gilbert that was presented at the 2001 Dibner Seminar in the History of Biology but not discussed at the workshop and a paper by Stuart Newman that the editors solicited after hearing a version presented at an international meeting.

Following the conceptual and epistemological introduction by Manfred Laubichler, the chapters are organized in three sections: part I, Ontogeny and Phylogeny in Early Twentieth-Century Biology; part II, Roots and Problems of Evolutionary Developmental Biology; and part III, Reflections. This structure reflects the course of the discussions at the Dibner Institute workshop and also broadly represents the chronological sequence of events "From Embryology to Evo-Devo." Everett Mendelsohn's observations were helpful in integrating the discussions at the Dibner Institute workshop and are reflected in several of the papers.

In chapter 2, Manfred Laubichler briefly discusses some of the conceptual and historiographic problems associated with writing the history of evolutionary developmental biology. He argues that the many transformations and discontinuities in that history are best understood if they are seen in the context of a specific scientific problem: defining the relations and connections between ontogeny and phylogeny. As a historical "object" of analysis, or an epistemic thing, this scientific problem has enough continuity that it can serve as a narrative anchor for telling the history "From Embryology to Evo-Devo." The conceptual changes associated with this scientific problem are then used to reconstruct the transformations of the epistemic space associated with the history of evolutionary developmental biology.

The chapters in part I of the volume provide a fresh perspective on events in the history of early twentieth-century embryology and developmental genetics. Fred Churchill discusses the fate of Haeckel's biogenetic law and analyzes several reformulations in major textbooks of embryology during the late nineteenth and early twentieth centuries. The picture that emerges is less black-and-white than many previous characterizations of the biogenetic law, and Churchill opens up new venues for analyzing the "internal critique" and reformulations of the biogenetic law, thus allowing for a careful reconstruction of the epistemic space of early debates about ontogeny and phylogeny. Stuart Newman's chapter focuses on William Bateson and his ideas about the physical determination of organic forms. Newman discusses Bateson's "vibratory theory," an attempt to incorporate physical principles (so-called Chladni patterns) into explanations of segmentation and repetitive pattern formation. Newman situates Bateson's ideas both within turn-of-the-century discussions about the nature of variation and inheritance and within the early twenty-first-century context of system biology. Analyzing the conceptual repertoire of both Bateson and modern system biologists, Newman argues for a broadening of the conceptual (epistemic) framework of explanations of development.

Jane Maienschein's contribution introduces cells and the process of morphogenesis into the discussions about the history of Evo-Devo. She emphasizes the role that cells played as an object of study and, in the form of slime molds in the work of John Tyler Bonner, also as model system for morphogenesis. Maienschein's chapter continues Newman's argument (via Bateson) that the physical and cellular characteristics of developing organisms are an important part of explanations of development.

Where Newman and Maienschein focus on specific objects and morphogenetic processes, Garland Allen takes a more conceptual and dynamic perspective. He presents a detailed account of the dialectics between analytic and synthetic explanations of development. In the interplay between these opposite yet complementary explanations of organic processes, Allen sees the organizing epistemological theme for the history of evolutionary developmental biology. Far from being abstract, his proposal provides a framework for the inclusion of many of the more detailed historical case studies.

Marsha Richmond's study of Richard Goldschmidt's role in uniting development and evolution concludes part I. During the 1920 and 1930s Goldschmidt, who remains an enigma to many even today, developed his idiosyncratic synthesis of ontogeny and phylogeny. Working with a different model organism (*Lymantria*) and beginning with a physiological and genetic account of sex determination, he developed a theory of the gene as a physiological agent. While during his lifetime many details of gene action remained beyond experimental reach, Goldschmidt nevertheless developed a conceptual framework that connected development, genetics, and evolution during a period when the prevailing attitude in science was to keep these domains apart.

Even though the chapters in part I revisit previously studied territory, each author has discovered new interpretative angles as well as new materials. In light of the theme of this volume, the history of the relations between ontogeny and phylogeny, they provide a fresh perspective on the history of embryology, genetics, and evolutionary biology in the first decades of the twentieth century.

The chapters in part II are more diverse. The topics covered here range from the history of comparative embryology in America and morphological and paleontological perspectives in the history of evolutionary developmental biology to a study of how developmental processes have been visually represented, a philosophical-historical analysis of research styles in embryology and genetics, a discussion of recent attempts to integrate development and evolution and the conceptual problems associated with these issues, and, finally, a philosophical-sociological analysis of research styles and conceptual change in biological research during the last few decades of the twentieth century. Most of these chapters focus on events during the period (1920s to the 1970s) that has not received much attention from historians of biology, and all of them provide perspectives that add dimensions to the problem of defining the relations between ontology and phylogeny.

John Wourms's study of comparative embryology in the American context brings to light an almost unknown chapter in the history of biology, especially with regard to the period that he includes. Wourms reminds us that even the most sophisticated conceptual schemata need to be grounded in empirical data, and that in the case of ontogeny and phylogeny, comparative embryology, in both a morphological and a systematic context, provides many of these data. Since during most periods in the history of biology, comparative embryology was not part of mainstream research, we have to look at different institutional settings (such as fisheries) to find the continuity of the work.

Alan Love's chapter similarly focuses on mostly neglected parts of the history of twentieth-century biology. His discussion of morphological and paleontological research by Dwight Davis and William Gregory is informed by the recognition that present-day evolutionary developmental biology is more than just a "synthesis" of development and evolution; rather, it involves the integration of various research traditions, including morphology and paleontology. As Love argues, it is in these fields which have not been part of mainstream twentieth-century biology that we find a closer continuity of the late nineteenth-century problem of ontogeny and phylogeny. His chapter thus opens an important new perspective on the history of midtwentieth-century biology.

William Wimsatt places attention on areas in the history of biology that have not received much attention from historians of biology, even though they are now becoming part of the canonical history of present-day evolutionary developmental biology. He discusses the problem of so-called internal factors of evolution, the idea that the details of the developing organismal system can have a major impact on the course of evolution. Internal factors of evolution are the prime candidates for a mechanistic integration of developmental processes into a theory of phenotypic evolution, and have received considerable attention since the mid-1970s. Wimsatt focuses specifically on the work of Rupert Riedl and Wallace Arthur, and concludes his historical analysis with a brief discussion of his own work on generative entrenchment, which is one of several attempts to model internal factors of evolution.

Scott Gilbert discusses a current problem in developmental biology that has a long history. Since development is a complex process, visual representations of developmental transformations have always been a major conceptual as well as pedagogical tool. Gilbert argues that there is a conceptual continuity between late nineteenth- and early twentieth-century attempts to trace the fate of cells in the developing embryo and modern approaches designed to establish gene expression patterns. He also states that one important aspect of the mapping program in the context of evolutionary developmental biology is to connect new (molecular) evidence with old (traditional) knowledge in embryology. In ways similar to Goethe's *Faust*, a major problem of current molecular approaches in developmental genetics is to reintegrate new molecular data into an organismal whole.

History, as a repository of knowledge, thus becomes an integral part of cutting-edge research in evolutionary developmental biology.

In his chapter James Griesemer uses a well-documented historical case study, the split between embryology and Morgan-style transmission genetics at the beginning of the twentieth century, to develop a philosophical argument about an important aspect of scientific representations and explanations of complex processes. He argues that in all explanations of complex processes, certain elements will necessarily be foregrounded while other will be relegated to the background. His analysis of the consequences of this dynamic contains several important lessons for all those—historians, philosophers, and biologists—who emphasize the synthetic character of modern evolutionary developmental biology.

The final chapter in part II presents an analytic perspective complementary to the ones proposed by Laubichler and Griesemer. Elihu Gerson focuses on the long-term pattern of relationships among lines of research in comparative biology by providing a framework for the inclusion of institutional and technological factors, what he calls a style of research. These factors cannot be separated from the epistemological concerns raised by Laubichler and Griesemer, so that Gerson's chapter (which includes a discussion of the effects of rationalization of work in both science and society) suggests further explorations of the interplay of contextual and contingent factors with epistemological factors in the history of evolutionary developmental biology.

The chapters in part III collect the reflective comments by Brian Hall, Gerd Müller, and Günter Wagner. These papers are expanded versions of the commentaries that these scientists and scholars gave after listening to (and participating in) two days of discussions at the workshop. In his chapter, Brian Hall, author of the first modern textbook of evolutionary developmental biology, who has a "second" career as a historian of developmental biology, reminds us about the many elements that contribute to the Modern Synthesis of Evo-Devo. In Hall's view, Evo-Devo is, and always has been, a model of an interdisciplinary science. To illustrate his point, Hall provides a few historical case studies that demonstrate how the problem of ontogeny and phylogeny has always been approached from a variety of conceptual perspectives and how specific institutions, such as the Naples Zoological Station, and instruments and their associated experimental practices—specifically the Cambridge Instrument Company and the automatic microtome—helped to establish an interdisciplinary environment. Hall's lessons are clear: any reconstruction of the history of evolutionary developmental biology will have to connect questions of conceptual integration with local issues of institutional and technological changes.

In his chapter, Gerd Müller takes the historical lessons of this workshop and volume and applies them to his analysis of the future of the field. His chapter is also a reflection of what he identifies as a phenomenon peculiar to the Evo-Devo discourse: the emphasis on metatheoretical reflections within Evo-Devo and the close collaboration of philosophers, historians, and biologists in shaping the future agenda of the field. He presents six memos that characterize the distinctiveness the Evo-Devo discipline. These memos, which capture the breadth of the Evo-Devo research agenda, are a fitting conclusion as well as a new beginning for the historical work presented in this volume. They show what happened "From Embryology to Evo-Devo," and they also invite the reader, as they did the workshop participants, to look back at the fascinating complexities of this history and ask: How did we get there? And what does it all mean?

Günter Wagner's comments move us forward by addressing the present state of evolutionary developmental biology, or developmental evolution (Devo-Evo), as he refers to it. This nomenclature reflects the internal disunity of present-day evolutionary developmental biology. Currently, several different questions are pursued in the context of this overarching synthesis. Wagner uses an episode in the history of biology—the decline of evolutionary morphology at the beginning of the twentieth century—to warn of the dire consequences for a field that fails to agree on standards of evidence to evaluate its results and interpretations. He goes on to suggest that if Evo-Devo (Devo-Evo) is currently entering its "academic phase," it will have to establish such evidentiary standards. Wagner then briefly sketches how such standards can be developed for evolutionary innovations.

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been at the seminar but could not join us at the workshop were heard as each participant responded to the substance of the seminar. This was truly a collaborative project, and each participant has an intellectual property interest in the product. Finally, George Smith encouraged us to pursue the publication of the collection and patiently waited for revision after revision during the preparation. His enthusiastic encouragement makes this, as well as other recent Dibner Institute volumes, possible.

Notes

1. Jane Maienschein and Ruth Davis, *100 Years Exploring Life, 1888–1988. The Marine Biological Laboratory at Woods Hole* (Boston: Jones and Bartlett, 1989); Jane Maienschein, ed., *Defining Biology: Lectures from the 1890s* (Cambridge, Mass.: Harvard University Press, 1986).

2. Ernst Mayr and William B. Provine, eds., *The Evolutionary Synthesis: Perspectives on the Unification of Biology* (Cambridge, Mass.: Harvard University Press, 1980).

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To Evo-Devo Through Cells, Embryos, and Morphogenesis

Jane Maienschein

Evo-Devo finally brings us a new synthesis, it is claimed, with evolution of development as the central focus. There is a sense of triumphalism in the declarations that this is a much better synthesis than the so-called evolutionary synthesis before it. Discussion has, naturally enough, centered on the question "Why not before, and why now?"

Fans of the evolutionary synthesis have invoked a variety of explanations for why development was left out of the synthesis of the 1940s and 1950s. Yet we can also ask the question rather differently: Why was evolutionary biology so foolishly distracted by philosophy and theology that it failed to do "real" science and missed the boat of experimental progress? We might, with Yale developmental biologist J. P. Trinkaus (known as Trink), hold that far from feeling left out of some important self-declared "synthesis," those concerned with development actually felt sorry for their evolutionary biology counterparts. As Trink put it, "Hell, no, we didn't feel left out of anything. They were just jealous because they couldn't figure how to get the NIH funding!"[1]

In 1884, Karl Nägeli had already noted the tendency of evolutionists to wander away from what he considered the core biological questions. He emphasized the importance of examining physical and mechanical understanding of organic nature. Nägeli complained that

> The theory of evolution touches also philosophy and theology in very sensitive spots and interests the intelligent general public partly for this reason and partly because human vanity has always attached much importance to origin and relationship.
>
> On this account we have seen philosophers, theologians and, in addition, literati of all sorts and conditions take possession of the problem. This too would have been quite in order, if every one had but utilized the established results of scientific investigation for his own field and rendered to his own circle a clarifying and instructive account of them; and if so many had not considered this field of difficult physiological problems to be a free-for-all arena for senseless argumentation.[2]

Citing Nägeli, Ross Harrison echoed this sentiment in 1936, in his address as retiring chairman of the Section on Zoological Science at the American Association for the Advancement of Science meeting in Atlantic City, New Jersey. Discussing "Embryology and Its Relations," Harrison saw evolution as having gone astray because of its engagement with fundamentalist theology and lamented that "The scientific investigation of evolution has suffered severely from this emotional conflict." In particular, he pointed to the failure to achieve scientific—by which he meant experimental—results. He acknowledged that the long time frame required for evolution makes experimental investigation more difficult, but it is nonetheless necessary, for "it can scarcely escape any one accustomed to scientific thinking that the processes of evolution can be elucidated only by painstaking experimental work carried on over a long period of years." Fortunately, Harrison saw "hopeful signs of the applicability of exact methods to the study of evolutionary processes" in the "development of modern genetics, the experimental study of the origin of mutations and the new mathematical theory of natural selection."[3]

Harrison was not alone in his thinking; he represented a community of researchers exploring embryology and its relations to other fields and other processes and patterns of biology. They felt that true science must be experimental and analytical, and must avoid the speculative distractions to which they felt evolution had succumbed.

In the 1920s Harrison had been less sanguine about the prospects for such science and for embryology. In his address as retiring president of the American Society of Zoologists in 1925, he had urged a "Return to Embryology."[4] After a period of quiescence and even depression within the field, he had pointed to what he hoped would soon become a resurgence of embryological study. The concept of the "organizer" had brought promise for analytical approaches to development, and there had been reason to hope that younger researchers would take up the study of embryos again. By 1936, Harrison was clearly pleased to announce, the resurrection had taken place. And even though the organizer theory had given way to concepts of "induction," and to closer and more careful analysis of internal regulation within organisms—and indeed within individual cells within the organisms—this was progress. Embryology had come much farther than scientific study of evolution. For Harrison and his likes, there could be a coming together of evolution and development only if those studying evolution, those studying heredity through genetics, and embryologists all relied on the same experimental scientific approaches.

It was not in the 1930s, or even during the next half-century, that evo and devo began to come together in the new and promising ways that have given rise to today's self-proclaimed "Evo-devo" movement. And that has come, as Harrison predicted, because of technical and experimental advances more than because of additional speculation and theory. Some chapters in this volume explore aspects of these recent advances, while others look at episodes of study of devo and earlier attempts at evo-devo syntheses. In this chapter, I concentrate instead on lines of research that lay within what would have been considered embryology and that largely ignored evolution as a factor to be addressed directly. Yet I contend that these studies that focused on exploring embryos and cells really did seek to address fundamental questions about development in the light of evolution.

I look at studies of morphogenesis. This field focused on the proximate or local and immediate causal mechanisms of the emergence of the parts that make up an individual organism's form. Yet attempts to make sense of morphogenesis also bring together the different time scales of individual development and evolutionary history because "morphogenesis" presumes the development of a particular "morph" that conforms to the form of its species. The question, then, was how an individual comes to acquire the particular form of its species, which is a product of the different long-term time scale of evolution.

Therefore, morphogenesis was at its heart one way of bringing together the devo and the evo, respecting the proximate mechanisms of individual development and also the "ultimate" factors brought by evolution and revealed through systematics. In the twentieth century, fundamental questions about morphogenesis found tractability in study of cells and of the whole, interacting, developing embryos of which the cells are the parts. I therefore concentrate on studies at the conjunction of cells, embryos, and morphogenesis. This allows us to get at one set of ways in which researchers thought they could meaningfully bring together development and evolution, and this historical perspective should illuminate current discussions.

Cells and Morphogenesis in the 1890s

In the 1890s, the development of morphological structures was labeled "morphogenesis." At the same time, because of tremendous advances in cytology during the last quarter of the nineteenth century, researchers had begun to focus on cells and on the ways that cells interact to generate structure. While some researchers moved toward hereditary accounts of development, pointing to the inherited material inside cells as determining what follows, those concentrating on development drew on epigenetic accounts. Cells, embryos, morphogenesis, and epigenesis converged in exciting new research programs.

Years later, the committed agnostic Harrison emphasized the epigenetic outlook that underlay this research by quoting a passage from the Biblical Psalm 139: "And in Thy book all my members were written, which in continuance were fashioned, when as yet there was none of them." Development is not seen as an unfolding of something preexistent, but as a coming into being. Obviously, Harrison agreed and wanted to emphasize that therefore the best approach for understanding the genesis of an individual's life was through embryology as the study of epigenetic emergence, and focused on "Cellular Differentiation and Internal Environment."[5]

The central question was what role cells play in development. Do cells serve as causal agents in morphogenesis, actually bringing about the generation of form and the function that comes with form through the actions and interactions of individual cells? If so, in what way? What is the relative importance of local, proximate, internal environmental factors, and how can the interplay of these factors in shaping each cell give rise to complex, multicellular forms? Or, alternatively, are cells just epiphenomenal results that come only after the real work of development has occurred through other forces? And if they are, what are the forces and how do they do the job of morphogenesis?

One view held that cells do carry significant causal force for development and differentiation. Edmund Beecher Wilson took this view in the first edition of his *The Cell in Development and Inheritance* (1896). He noted that cell theory and evolution provide the two foundations for biology. He asked what cell division does, and how we get from one fertilized egg cell to differentiated cells and eventually to a formed organism. How does development of the form, or morphogenesis, work?

Wilson answered that cell division brings differentiation, and the series of cell divisions leads to the gradual and epigenetic process of morphogenesis. Wilson noted that "for two reasons the cleavage of the egg possesses a higher interest than any other case of cell-division. First, the egg-cell gives rise by division not only to cells like itself, as is the case with most tissue-cells, but also to many other kinds of cells. The operation of cleavage is therefore immediately connected with the process of differentiation, which is the most fundamental phenomenon in development."[6]

Therefore, cleavage and differentiation are connected, with cleavage apparently causing or at least leading to differentiation. There was some "promorphological" arrangement in the segmented egg that brought a sort of "germinal localization," but there was no preformation or even predetermination in any meaningful sense. The form was not there already. Rather, for Wilson there was some "organization" or prelocalization in the segmented egg that established the starting point for and process that gives rise to an individual organism.[7] Then it was the cell division that brings differentiation, and with it morphogenesis. For Wilson, morphogenesis occurred one cell division at a time, against a background of cytoplasmic differentiation.

Wilhelm Roux took a much more extreme version of this cell-division-as-cause-of-developing-form. His mosaic interpretation involved parceling out differentiated inherited material to each cell, so that every cell division brought specialization and localization of differentiated cells and parts. Again, morphogenesis occurred one cell division at a time, very decidedly *because of* the cell divisions. Yet on this interpretation the cells were little more than containers for the hereditary units. In Roux's case, however, the form was effectively predelineated in the inherited units parceled out to each cell.

Alternatively, a second theory held that cells are epiphenomena that follow rather than cause cell division. In this case, some other causes drive differentiation and morphogenesis. For example, Thomas Henry Huxley saw them this way, for cells "are no more the producers of vital phenomena, than the shells scattered in orderly line[s] along the sea-beach are the instruments by which the gravitational force of the moon acts upon the ocean. Like these, the cells mark only where the vital tides have been, and how they have acted."[8] Instead of cells and cell division, properties of protoplasm and evolutionary factors drove development, according to Huxley; cells were simply secondary, or epiphenomenal.

Charles Otis Whitman agreed with Huxley's view in his essay "The Inadequacy of the Cell-Theory."[9] Whitman insisted that Wilson had it backward. Organization was *not* the product of cell-formation; rather, "organization precedes cell formatting and regulates it."[10] He said that "an organism is an organism from the egg onward," and that cleavage simply followed and divided up the material. He explained morphogenesis and differentiation in terms of a predelineation within the egg that provided the "organization" for the future "organism."

Charles Manning Child agreed with Whitman. It must be "the organism—the individual, which is the unit and not the cell."[11] For Child, morphogenesis was driven by internal gradients set up by inherited nuclear and cytoplasmic factors, and responding to external and internal environmental considerations.

If this interpretation that cells are secondary effects rather than causes were right, what causes differentiation and morphogenesis? It cannot simply be genes, since, as Thomas Hunt Morgan liked to remind his colleagues, all the genes seem to be the same in every cell. How, then, can we get difference from the inherited sameness? How does morphogenesis—and with it differentiation—occur? It was the failure to address these questions adequately that kept those most seriously committed to explaining development from seeing genetics or evolution as important for understanding embryology.

"Embryology and Its Relations"

Ross Harrison agreed with Morgan that the answer could not be in the genes, and that this was a central problem of biology. In his 1936 speech to the American Association for the Advancement of Science, Harrison noted: "The prestige of success enjoyed by the gene theory might easily become a hindrance to the understanding of development by directing our attention solely to the genom." Instead, Harrison insisted that "cell movements, differentiation, and in fact all developmental processes are actually effected by the cytoplasm."[12] They are effected through the cytoplasm—that is, through local action and particularly through local chemical action—and not through the action of some remote and distance-inherited material or purported information.

Harrison suggested that morphogenesis involves a sort of crystallization process that brings chemical compositions of parts and differentiation through the relations among them.[13] He lamented that excessive enthusiasm about Hans Spemann's "organizer" had distracted embryologists, as genetics had, and had led them to ignore other important factors in development, especially relations among differentiating parts. Yet embryologists were making great progress by looking at the microstructures of eggs, cells, and developing organic parts. Harrison acknowledged that he had questions with few answers, but that it was very important to work hard—and to continue working hard, using proper scientific experimental analysis—on the hard questions, and not to give in to temptations to unwarranted theorizing or guesswork.

Harrison quoted Max Planck to the effect that "We must never forget that ideas devoid of a clear meaning frequently gave the strongest impulse to further development of science . . . they [can] give rise to thought, for they show clearly that in science as elsewhere fortune favors the brave."[14] The brave included Joseph Needham, with his ideas about chemical morphogenesis through the internal chemical relations of parts and "morphogenetic hormones,"[15] or those offering the mathematical, mechanical models that Evelyn Fox Keller discusses in her book *Making Sense of Life*.[16]

As J. H. Woodger had pointed out earlier, it is especially important to have some brave theorizers or big thinkers when the data and details pile up and threaten to overwhelm our thinking: "The continual heaping up of data is worse than useless if interpretation does not keep pace with it. In biology, this is all the more deplorable because it leads us to slur over what is characteristically biological in order to reach hypothetical 'causes.'"[17]

Morphogenesis

For Harrison, and for many others, biological form and the apparent "organization" of individuals were "characteristically biological" and ought not to be slurred over, no matter how difficult to address. Among the many making scientific sense of the emergence and establishment of form in later decades was another brave man, John Tyler Bonner. Bonner's *Morphogenesis: An Essay on Development* appeared in 1952, roughly a half-century after Wilson's *Cell* and roughly a half-century before our current enthusiasm for Evo-Devo.[18]

Yale biologist John Spangler Nicholas reviewed Bonner's book and wrote that "Bonner deserves our thanks. He makes no pretense of giving the answer to the problem of form. He has, however, placed it succinctly before us and has focused attention on what we do not know but need to know before a more definite answer can be given to the significant factors underlying the formative pattern of development which results in the specific form of the organism."[19]

We still owe Bonner our thanks for keeping a focus on form and pattern, on morphogenesis and internal relations, when so many were rushing to embrace the "modern synthesis" of the evolutionists, or the molecular interpretations brought by DNA and genetics. As they took up other methods and other questions, they set aside and often forgot about scientific efforts to understand these fundamental life processes. Bonner has continued to keep our eye on the "problem of form," especially the question of how form emerges, and, within that problem, on questions about the role of cells and their internal relations in development and differentiation. Bonner retained his focus on the mechanisms and proximate time frame of individual development, while also remaining mindful of the longer time scale and causal shaping of form by evolution. He sought to bring devo and evo together through the study of morphogenesis.

Bonner wrote his *Morphogenesis* in Woods Hole, Massachusetts, at the Marine Biological Laboratory. He worked in the library there, and in Edwin Grant Conklin's laboratory, writing the sort of general, problem-oriented, big-picture book that young biologists at places such as Princeton can no longer afford to write if they hope to remain on a normal track toward tenure. Bonner tackled the tough problems and tried to bring order to our thinking about them. He tried to weigh the range of theories, data, and worries without succumbing prematurely to any one interpretation or to giving up trying to address the big questions.

Bonner set out to consider the "problem of form" in terms of three things—growth, morphogenetic movements, and differentiation. He sought to avoid the "treacherously hypothetical" by including a full range of organisms—animals, plants, and microbes: slime molds (especially slime molds), *Hydra*, sponges, frogs, and ants.

First came growth and the patterns of growth. Growth is a basic process and does not bring about any morphogenesis or differentiation by itself, but it makes these processes possible. Next come the patterns of morphogenetic movements. These are like the actions of a sculptor who has already added the clay, through growth, and now shapes it. But it is the cells, rather than the sculptor, doing the shaping in the biological organism. So, yes, cells are inevitably involved, but the movement comes through groups of cells or cell interactions as they move. Morphogenetic movements lead to differentiation, by which Bonner means differences in parts because of the chemical composition and also because of the positions and needs of the whole organism.

Differentiation very clearly does *not* result from parceling out of genetic information, as Roux and his later genetic determinist followers had suggested. At least for all practical purposes this is true, Bonner was sure. Rather, differentiation can be caused by position in the organism. Bonner cited Henry van Peters Wilson's research on sponges, in which Wilson had separated (disaggregated) cells to discover whether they were all the same or were already differentiated at various points throughout development.[20] That research and other studies on *Hydra*, slime molds, sea urchins, and other organisms showed that cells and groups of cells might be differentiated, but could be redifferentiated by changing position. That is, the role of the individual cell could be influenced by the needs of the whole organism.

There seemed to be internal diffusion gradients and some organized microstructure that functioned as "ultrastructure" to guide the "regulation" of the whole. Bonner saw this regulation of the whole, with its responsiveness to changing conditions and to the internal and external environments, as an important driver for differentiation. Organisms can have gradients or fields that affect the "patterns of differentiation," and these play out in different ways in different organisms. The differentiation and morphogenetic processes of different organisms can be different not just because the organism started differently, or has different heredity, but also because of the particular interactions within each whole.

Bonner clearly saw differentiation as a problem of the whole, living organism and the way the parts interact. Understanding this is a challenge, however, and Bonner was brave enough to insist that we not ignore it. The question was how to make sense of the "wholeness" or "organization." As Bonner put it, we must not "forget the most important fact that the organism always differentiates as a whole, and that the particular cause of the differentiation of a part is determined by its position with respect to the whole."[21] There is indeed a wholeness that begins with "localization of differences in different parts of the egg or sperm."[22] That is, there is some initial structure that provides a starting point, as E. B. Wilson had suggested, though it is not a "promorphological" delineation in Wilson's sense or any sort of preformation or predetermination of form.

Nonetheless, Bonner cautioned that we should not be "overly impressed by the [special] significance of this wholeness."[23] The wholeness is not mysterious, as some would suggest, but is a product of interactions and microprocesses within the context of the initial germ cell that is itself influenced by natural selection. Organisms inherit the tendency for cells "to migrate and [to] respond to the substances given off by the other cells," through a sort of chemotaxis and interactions among the cells.

Bonner constantly tries to find a balance among microexplanations of chemical and mechanical causation, and also attempts to preserve wholeness and a sense of integrated life—whatever that might mean and even when that might seem vague and mushy. It is precisely this grappling with making sense of form and his unwillingness to fall into reductionistic geneticism or to succumb to mysterious organicism that is appealing. Bonner wrote, "There must be some factor which transcends the cell wall and unifies this cottony mass, but what this factor or factors might be is another matter. Already we have come to the deep-rooted sign of the least understood problem of this sort of development that makes us say that growth and development is a problem. Really it is many problems; but this one, the unification of great masses of protoplasm into a oneness, a wholeness, has us more mystified than others."[24]

Yet, "More than anything else, this . . . making of a perfect whole from a small bit of a previous whole, is what seems marvelous to us, so much so that we become, I think, psychologically affected and troubled, and cannot believe that a solution to such a problem would be anything but difficult, if not impossible."[25] Yet difficult—or even apparently impossible—as this "problem of development" might seem, Bonner tried, and felt it vitally important to continue trying.

Surely Bonner's drawing on evidence from diverse organisms and trying to bring together different kinds of evidence shaped his thinking in important ways. It kept his focus on the bigger problems, even when they were difficult to solve. Model, select organisms can work to solve particular problems, but would not have served Bonner's purposes unless he made the a priori assumption that all organisms differentiate in the same way. And he did not make that assumption, that the "evo" affects the "devo." This brings us back to cells.

Each germ cell has an internal arrangement, and every cell division brings new arrangements. The particularities of growth and morphogenetic movements, with regulatory responses to the conditions and needs of the organism, bring differentiation—and the material basis for the mechanisms of morphogenesis. But each set of opportunities and pattern of responses is shaped by evolution as well, and each represents a set of adaptations. For, as Bonner put it: "In each case, there is a . . . unity which comes with the structure, and this we have related to the advantage of functional wholes, for without being functionally cohesive they would either not live, or at least not withstand the rigors of natural selection. The very fact that they are wholes must be adaptively advantageous, and natural selection, by differential reproduction, would tend to keep them that way."[26] Evolution and development, long and short time scales: all there to be studied in cells through morphogenesis.

Conclusion

In sum, for Bonner cells are not the cause of morphogenesis (as Wilson and Roux had suggested in their very different ways). Nor are they mere epiphenomena (or shells on the shore, as Huxley and Whitman held). Rather, cells and cell interactions are primary players in the processes that shape organisms, but the processes are also influenced by genetics and by evolutionary adaptations. Bonner just was not sure how, though he felt it important to try to understand.

Bonner ended his book by declaring that if anyone comes up with a microstructural account of the causes of morphogenesis, "the world will acclaim his discovery as a most satisfying explanation and a great advancement in science."[27] But in 1952, it was clear that Bonner did not expect such an account anytime soon.

Compare Bonner's tone with Wilson's ending of his book in 1896, Wilson wrote:

> I can only express my conviction that the magnitude of the problem of development . . . has been underestimated. . . . Yet the splendid achievements of cell-research in the past twenty years stand as the promise of its possibilities for the future, and we need set no limits to its advance. . . . We cannot foretell its future triumphs, nor can we repress the hope that step by step the way may yet be opened to our understanding of inheritance and development.[28]

For Bonner a half-century later, the problem of development remained, and would not be solved through cell research alone or even primarily. Today, another half-century later, we are swimming in data, yet the fundamental biological problems of morphogenesis and development of form remain as challenging and exciting as ever—in new ways. It is important not to lose sight of the cells or of morphogenesis as we embrace Evo-Devo enthusiasm for other levels of analysis. Joining evo (and with it molecular genetics) with devo surely offers the greatest promise for achieving the greatest advances in understanding the problem of development that Wilson sought, and also in giving us the microstructural account of development that Bonner would still like to see.

Notes

1. J. P. Trinkaus, personal discussion at the Marine Biological Laboratory, Woods Hole, Massachusetts. He thought this was a silly question that missed the point that, as he saw it, developmental biology had been considered a success even when it was not as much advertised or heralded as genetics or evolution. There is, he noted, no Ernst Mayr for developmental biology, and he clearly did not think that was a bad thing.

2. Nägeli, 1884, translated and quoted by Harrison, 1937, p. 371.

3. Harrison, 1937, p. 371.

4. Harrison, 1925.

5. Harrison, 1940, p. 77.

6. E. B. Wilson, 1896, pp. 264–265.

7. Dröscher.

8. Huxley, 1853, p. 243. For discussion, see Richmond, 2000.

9. Whitman, 1893.

10. See Lillie, 1911.

11. Child, 1900, p. 265. Also see Child, 1915.

12. Harrison, 1937, p. 372.

13. Haraway, 1976.

14. Planck, 1936, p. 112, cited in Harrison, 1937, p. 374.

15. See Haraway, 1976, chap. 4, for further discussion.

16. Keller, 2002.

17. Woodger, 1929, p. 318.

18. Bonner, 1952.

19. Nicholas, 1952, p. 492.

20. H. v. P. Wilson, 1907.

21. Bonner, 1952, p. 260.

22. Ibid., p. 201.

23. Ibid., p. 268.

24. Ibid., p. 100.

25. Ibid., p. 241.

26. Ibid., p. 268.

27. Ibid., p. 276.

28. E. B. Wilson, 1896, p. 330.

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