The Historiography of Embryology and Developmental Biology

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Abstract

Embryology is the science of studying how embryos undergo change over time as they grow and differentiate. The unit of study is the unfolding organism, and the timeline upon which embryology is focused is brief compared to the life cycle of the organism. Developmental biology is the science of studying development, which includes all of the processes that are required go from a single celled embryo to an adult. While embryos undergo development, so to do later stages of organisms. Thus, development is broader than embryology, and it focuses on the processes more than on the entities being developed. The fields overlap, and in some senses embryology gave way to developmental biology as new techniques

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and new questions, in particular genetic analyses and methods, allowed researchers to "see" more inside of organisms and manipulate the processes that are required for their unfolding. This article examines the ways in which developmental biology manifested from embryology, while also retaining aspects of the scientific goals and approaches of the earlier field of embryology. It also looks at the ways in which the study of both embryos and their processes of development have intersected with evolution, both in the nineteenth century and throughout the late-20th century emergence of the field of evolutionary developmental biology.

Introduction

"Developmental biology" became a field by that name only in the 1960s, and at the same time, it became a complex cluster of often uncoordinated questions and methods. Before that time, researchers who studied the development of individual organisms tended to call themselves embryologists and to focus on the ways embryos arise and change over time. Historians have largely muddled the two together, though embryology involved different questions, methods, and interpretations focused especially on morphological change rather than the later more molecular and genetics-driven developmental biology. Some historians and biologists have assumed that the field only emerged when it was called "developmental biology" and that no serious research took place before. We show that this is not the case and that it is important to explore how researchers have for millennia sought to understand how individual organisms come into existence, grow, and become the appropriate kind of living thing.

As a result of the complexity of the topic of developmental biology, in this essay we look at selected episodes to explore the history of understanding how organisms develop, and we set aside plants to focus on animal development. We largely skip the early modern period when curious people began looking through microscopes and applying a scientific method to their studies and focus mainly on the nineteenth and twentieth centuries.

For the late eighteenth into the nineteenth century, much of the historical work was carried out by embryologists seeking to present and interpret their own predecessors (e.g., Needham 1934; Russell 1916, and others we discuss below). Their histories reflect their own predispositions about what was most important for embryology. More recently, historians have provided broader overviews to help illuminate some of the themes, questions, and methods involved in this earlier work. For the late nineteenth-century period, more historians have taken up the study of embryology as it relates to evolution in particular. Those historical interpretations reflect a recent resurgence in interest in connections between "evo" and "devo," as evolution and development have been represented in the "evo-devo" movement.

Study of development in the twentieth century has had much more attention, both recently and in previous decades. We explore the major themes that emerge from that study, including the importance of experimental methods and analytical approaches. As “embryology” became known as developmental biology in the second half of the twentieth century, molecular and genetics approaches took on a dominant role and brought new questions and methods that gave developmental studies a new focus. To some extent embryos largely disappeared from the story. They reappear at the end of the twentieth century, with *in vitro* fertilization, cloning, stem cell research, and most recently gene editing. We end this essay with some twenty-first-century topics to show how diffuse the study of development has become.

Embryos and the Enlightenment of the Eighteenth and Early Nineteenth Centuries

General histories of science largely ignored embryology and development, but several review articles provide a useful overview of the themes. This section points to some of the leading thinkers about the history of embryology. Because these historians focus on different themes, and do so in different ways, we point to the most significant contributions as a way to get at how the topic has been interpreted. Historians Tim Horder and Nick Hopwood offer recent valuable overviews, while embryologists looked at their own history in many of the earlier studies of the period.

A summary article by Tim Horder on “History of Developmental Biology” reviews the early science and provides references that we need not repeat here (Horder 2010). He noted the contributions of Aristotle, Leonardo da Vinci, William Harvey, Marcello Malpighi, and other later luminaries as well. Horder succinctly pointed out that “Of progress in the eighteenth century, it is easy to conclude simply that theory ran ahead of data.” (p. 3) In contrast, later work became more based on observation, description, comparison, and eventually experimentation.

While theory played a leading role in investigations of embryos, the early period through the eighteenth century was not devoid of empirical contributions to understanding organismal development. One line of research involved examining how the contributions of male and female parents come together to make one individual or how sexual reproduction occurs. Aristotle had considered this problem but was only able to conclude that the fluids from male and female combine – through the action of the four kinds of causes (material, formal, efficient, and final) that he thought operated on all phenomena. The question of just how fertilization and reproduction work only received close attention starting in the late eighteenth and nineteenth centuries.

Another insightful review article, “Embryology” by Nick Hopwood (2009), shows the rich diversity of research into development that falls under the broad umbrella of that title. Medical study of reproduction and development, comparative embryology, and evolutionary questions all brought different sets of questions and methods. There was, Hopwood showed, no one clear discipline or established institutional home for embryology or development. This complexity has affected the historical research as well, as historians have concentrated on particular areas and ignored others (Hopwood 2009). Looking back to the earlier twentieth century, the history of reproductive research gained the attention of zoologist Francis Joseph Cole. He became fascinated by the history of protozoology and of sexual reproduction, and his 1930 volume *Early Theories of Sexual Generation* provided a starting point for generations of biologists and those interested in history of biology. In his own research as well as his historical studies, Cole showed that the process of development of an individual animal has a starting point, namely, with the coming together of the egg and sperm, and that there is a regular and predictable process of generation that occurs as a result. His focus on the early history of understanding that early development revealed the importance of microscopic observations and materialistic thinking in order to see the processes involved. By the mid-nineteenth century, the early ideas had led to an understanding of the process by which a sperm cell fertilizes an egg cell to produce a fertilized egg and thus an embryo. Historian John Farley (1982) picked up on that theme and carried it forward into the early twentieth century with his *Gametes and Spores: Ideas about Sexual Reproduction 1750–1914* that introduced the variety of different ways of thinking about germ cells and reproduction during that period.

At about the same time that Cole published his historical study, embryologist Joseph Needham published his own detailed three-volume study, *Chemical Embryology*. His work on that massive project led him to reflect also on the historical study of embryos, and he included chapters on the topic. At the same time, he delivered a series of historical lectures at the University of London. A few years later, in 1934, he published those lectures as *A History of Embryology*, which he revised for a 1959 edition (Needham 1934). There he looked at themes in embryological research up to the end of the eighteenth century, which provided a background for the way researchers in the early twentieth century were approaching problems of development.

Needham showed that the study of embryos had a rich history and had long raised curiosity among leading and less well-known researchers. Careful observation and experimentation in order to create new conditions, which expanded the range of what could be seen, added to the theoretical background that Horder noted. After giving us rich descriptions of a sequence of observations, in the last section of the book, Needham pointed to themes that continued into the nineteenth century. In particular, competing theoretical frameworks for the research started from competing assumptions about whether development of an individual from its earliest starting point occurs gradually, with form and function emerging over time out of unformed matter in motion (the epigenetic view) or whether the earliest stages were already laid out in some way and simply grew larger (the preformationist view) (Maienschein 2005; Roe 1981; Bowler 1971 on preformation and epigenesis). Needham noted that he had initially titled his lecture series "Speculation, Observation, and Experiment," but he realized that experimentation did not really come to embryology until the end of the nineteenth century with Wilhelm Roux. He suggested that he would hold a discussion of that period for a second volume to appear later, though he apparently did not publish such a book (Needham 1934, p. 230).

Around the same time that Needham was working out his ideas about the history of embryology, Edward Stuart Russell was also thinking about how life develops.

Trained as a classicist and zoologist, Russell turned his attention to philosophy of biology and especially to questions about what organisms are and how they develop. His *Form and Function* appeared in 1916 and his *The Interpretation of Development and Heredity* in 1930 (Russell 1916, 1930). This second book asked how an individual develops from an unformed material into a complex and organized organism. And to what extent, Russell asked, is the result an organized whole that is more than or different from the sum of the parts? His questions and his approach involved reviewing ideas of the past and examining current discussions, including explorations of the idea of an "organism as a whole" that had become popular with Jacques Loeb, William Ritter, Charles Manning Child, and others of the time.

Another contribution from the 1930s that also focused on earlier periods of embryology is embryologist Arthur William Meyer's 1939 volume *The Rise of Embryology*, which focuses especially on the contributions of early embryologists up to the work of the epigenesist Karl Ernst von Baer (Meyer 1939). As Meyer noted, the 1930s had attracted considerable attention to embryology, but the historical growth of the ideas remained largely unexamined and unfamiliar. Perhaps in part because of the increased interest in developmental questions and research, a few scientists such as Meyer and Needham turned their attention to reviewing and interpreting the historical study of embryos and development as well.

Though Meyer continued his study of von Baer and von Baer's contemporaries, which led to the 1956 volume *Human Generation: Conclusions of Burdach, Döllinger and von Baer*, it was not until the 1960s that we again see such concerted attention to the history of studies of development (Meyer 1956). At that point, embryologist Jane Oppenheimer led the way to serious scholarly study of the history of embryology. While Cornell zoologist and historian Howard Adelmann spent much of his career focusing on the publications and correspondence of Italian embryologist Marcello Malpighi (Adelmann 1966), which resulted in the definitive study of this outstanding Italian anatomist's meticulous anatomical studies, Oppenheimer looked at embryology more broadly.

Some of the essays that Oppenheimer collected into an important volume signaling the new field of history of embryology include essays on the classic early figures: William Harvey, William Gilbert, Sir Thomas Browne, John hunter and his brother William Hunter, and Karl Ernst von Baer. One essay focuses on Ross Granville Harrison, who headed the department at Yale where Oppenheimer had studied and whom she shows as having established an experimental program of research that provided an exemplar for what embryology had become by the twentieth century. Other chapters look at crosscutting themes, assessing what questions embryologists were asking and with what methods. These works offer descriptions of central ideas and contributions in understanding development and also provide historical interpretations that begin to place the biological research in the context in which it developed. As Oppenheimer noted: "a number of us who are working embryologists feel that our life in the laboratories is made more meaningful to us when we know something about our intellectual forebears" (Oppenheimer 1966, p. v).

While Meyer and then Oppenheimer did an excellent job of first interpreting and then making von Baer's work available to twentieth-century English-reading audiences, later generations of professional historians of science looked at von Baer and the early nineteenth-century period in which he worked in different ways (Oppenheimer 1986). Timothy Lenoir's study of different forms of vitalism and teleological thinking, including the work of Friedrich Blumenbach, Karl Friedrich Kielmeyer, and von Baer, emphasized their search for laws and explanations about fundamental issues concerning life (Lenoir 1989). While not everyone accepted his interpretation, Lenoir certainly opened a discussion about central questions related to biology.

More recently, Sabine Brauckmann has been working through von Baer's published work and his archives with meticulous care to explore his ideas about development and also about evolution (e.g., Brauckmann 2008). In collaboration with embryologist and historian Scott Gilbert, Brauckmann has looked at von Baer's descriptions and understanding of gastrulation (Brauckmann and Gilbert 2004). And others, such as Brian Hall and Fred Churchill, have looked more closely at the emergence and understanding of germ layers in development (Churchill 1991; Hall 1998). As MacCord explains (MacCord 2013), embryologists began to understand the importance of germ layers in defining the appearance of form from what starts initially as unformed material. For most animals, the process of gastrulation, which initiates the formation of germ layers, marks a change that leads to visible differentiation and begins a period of growth. It also, developmental geneticists realized later, comes along with increased gene expression, but that is another story.

Embryos and Evolution in the Late Nineteenth Century

Von Baer remained focused on embryos and did not accept the idea of evolution by natural selection. Yet he and other embryologists recognized that the development of individual organisms is shaped by history in some way, if only because a past creator set out the way individuals develop. That simplistic account did not provide sufficient explanation for most researchers interested in development through the middle and second half of the nineteenth century, and they had at least to think about what evolution might mean for development. Biologists who studied development after Darwin at least placed evolution in the background of their study of embryos, and some tried in various ways to bring embryology and evolution more closely together. Those attempts tended to focus on morphological change, and they ran up against limitations in the methods available. It was only in the later twentieth century that researchers sought explicitly to bring development and evolution into the same explanatory framework through "evo-devo" or "devo-evo," as we discuss later.

Darwin's theory of evolution changed the thinking about biological organisms in general, and he also gave embryology a special role in providing information about evolutionary relationships. Yet he had little to say about the developmental process itself. In Chapter XIII of his *On the Origin of Species*, Darwin pointed to embryos as especially valuable. He had observed a variety of embryos in different species and was aware of some of the contemporary work such as von Baer's.

Pointing to what seemed to him clear similarities among embryonic forms of different species, Darwin concluded that "the leading facts in embryology, which are second in importance to none in natural history, are explained on the principle of slight modifications not appearing, in the many descendants from some one ancient progenitor, at a very early period in the life of each, though perhaps caused at the earliest, and being inherited at a corresponding not early period. Embryology rises greatly in interest, when we thus look at the embryo as a picture, more or less obscured, of the common parent-form of each great class of mammals" (Darwin 1859, pp. 432–433). To reiterate, embryology was thought to be important for understanding evolution and in particular the relationships among organisms. By implication, knowing those evolutionary relationships might help illuminate why embryos were similar, but Darwin's evolution did not provide any explanation for why embryological development occurred as it did nor information about the processes involved.

Ernst Haeckel provided the strongest claims that the results of evolutionary history actually define and direct development. For this outspoken German zoologist, "ontogeny recapitulates phylogeny." In other words, the developmental process of an individual organism will repeat or "recapitulate" the developmental process of the phylogenetic group to which that organism belongs. Evolutionary history started to provide an explanation for embryology, according to Haeckel. Yet his evidence remained largely theoretical and based on the apparent similarities that Darwin had also observed. Only recently have professional historians of science turned their attention to Haeckel, and Robert Richards and Nick Hopwood in particular give us very vibrant views about this larger-than-life zoologist, his work, images, and impact (Richards 2008; Hopwood 2015).

In his day, Haeckel was reviled or revered, largely depending on the reviewer's own theoretical leanings. Those inclined toward the social implications of Haeckel's world view, grounded as it was in materialism and a sense of progress for individuals as well as species, praised his work and its popular impact. Researchers immersed in the details of meticulous study of cells and processes of development, such as Wilhelm His, were appalled by Haeckel's tendencies toward bold and expansive conclusions. Much of the historical study of Haeckel and his recapitulation ideas are concerned with the social impacts of his theorizing.

One result of Haeckel's popularity and accompanying controversy was a shift to marine studies. Haeckel himself studied a variety of marine organisms, seeking to get at the "Urform" that Haeckel believed to be the earliest form of animal life and from which all subsequent forms arose. He was confident that these would be found in the sea and therefore observed, drew, and compared a variety of marine invertebrates. As a result, he gathered his collecting buckets, waders, and other equipment and headed off to the seaside to collect organisms in jars and study them at the tables of the rooms he rented. His critics began to do the same, sometimes also looking for evolutionary relationships and sometimes looking instead at fundamental biological descriptions of form and function.

Especially important for marine studies was Anton Dohrn, a graduate from the University at Jena where Haeckel taught. Dohrn heard about evolution and became an enthusiastic convert. He also became convinced that studying marine organisms would help reveal both fundamental living phenomena including embryonic development as well as evolutionary relationships. Thus, marine studies would illuminate both ontogeny and phylogeny. And so Dohrn used his tremendous energy to attract the funding and moral support that led to founding the Stazione Zoologica in Naples in 1872. Longtime Stazione archivist Christiane Groeben has given us many historical resources, cited in her 2013 summary, to help understand the importance of that special place and the kinds of work done there (Groeben 2013). The earliest work started with natural historical descriptions of development of different organisms and comparison across them.

Haeckel inspired and was inspired by another German zoologist, August Weismann. As a passionate naturalist, Weismann studied a wide diversity of living organisms in his efforts to understand how they work. In his masterful book, *August Weismann: Development, Heredity, and Evolution*, historian Frederick Churchill discusses of Weismann's interactions, friendship, and frustrations with Haeckel and most other leading figures in zoology of his long life. Churchill spent 50 years in careful study of Weismann's research and shows us that leading nineteenth-century biologists did not think of either genetics or embryology or evolution as separate. Rather, the phenomenon of development and life in general intertwines all those factors, and the goal for the science of life should be to interpret the interconnections. Churchill also showed that Weismann kept one foot in the conceptual traditions of the nineteenth century and another in the experimental and analytical traditions that came to dominate the twentieth century (Churchill 2015).

Experimental Embryology

It is not the case that the period around 1900 brought experimentation to biology for the first time. Yet the push for "Entwicklungsmechanik," or developmental mechanics, in particular made experimental approaches and mechanistic interpretations the norm for developmental studies. In 1964 with a first edition, and then in 1974 with a second and expanded edition of *Foundations of Experimental Embryology*, Jane Oppenheimer and fellow embryologist Benjamin Willier provided a set of classic papers that they felt helped define experimental work in embryology. The first of these came from Wilhelm Roux and was his 1888 manifesto for experimentation (Willier and Oppenheimer 1964).

In introducing the Roux article, the editors explained that when comparative and descriptive methods had become inadequate for explaining the development of individual organisms, Wilhelm Roux led the way when he "founded a new discipline, causal analytical embryology, which he called developmental mechanics" (Willier and Oppenheimer 1964, p. 3). Roux also founded a new journal for the field and expected leading embryologists to publish their work there. Most did, but Roux proved himself such a heavy-handed editor that other journals arose as alternatives, including the *Journal of Experimental Zoology* with Harrison as the managing editor.

Willier and Oppenheimer explained the way Roux had punctured one of two cells in a developing frog embryo to determine whether each cell could develop on its own or only as a part of the whole. Roux had concluded that the embryo acts as a mosaic of differentiated cells, each with its own "fate." Though it turned out that Roux's theory overreached his empirical data, this experiment nonetheless has remained an important introduction for students of embryology. In part, this may be because of the way that Willier and Oppenheimer introduced the work to a wider readership. As embryologist turned historian, Oppenheimer especially looked closely at the ideas and methods of the embryologists she studied. The esteem in which she was held by professional embryologists gave her an authority that other historians might not have had. It took a few more decades for professional historians of biology to emerge and become accepted, at least among historians of science even if not always among the embryologists themselves.

The professionalization of the history of biology as a new academic field within the history of science brought additional perspectives. In particular, Garland Allen and William Coleman, two graduate students working with Harvard historian of science Everett Mendelsohn, suggested that the late nineteenth century might be viewed in terms of a "revolt from morphology." Coleman introduced the idea at the end of his 1971 book, *Biology in the Nineteenth Century: Problems of Form, Function, and Transformation*. Intended as an introductory volume in a series for students and nonspecialists, the volume became a starting point for students in the history of biology. Coleman emphasized what professional historians were coming to see as a distinct break at the end of the nineteenth century, namely, as a move away from the reliance on historical methods and toward experimentation as the new ideal for biology. "To the embryologist, the bacteriologist, or the student of heredity and variation," Coleman wrote, "the model was truly the new ideal. In its name – experiment – was set in motion a campaign to revolutionize the goals and methods of biology" (Coleman 1971, p. 166).

Following Coleman, Garland Allen, took the turn to experimentation theme further in his contribution to the same introductory series in his 1975 book, *Life Science in the Twentieth Century* (Allen 1975). For Allen, the turn of the twentieth century saw a "revolt from morphology" that was truly revolutionary and that cast out the earlier morphological, descriptive, and historical approaches. According to Allen's interpretation, a younger cohort of embryological researchers, including Thomas Hunt Morgan, Edwin Grant Conklin, and Edmund Beecher Wilson, rejected the natural historical traditions of the past and pushed for experimentation. Experimental embryology provided Allen's central case for this revolt. Although other historians questioned aspects of Allen's interpretation, especially the notion of a revolt or clean break between historical or morphological life sciences and experimental sciences (Benson 1981; Maienschein 1981; Rainger 1981), it was clear that the study of development had begun to change in important ways around 1900 (Maienschein et al. 1981).

Early Twentieth-Century Understanding of Embryos and Development

The 1980s brought increased attention to the history of embryology from embryologists and historians alike. Timothy Horder, Jan Witkowski, and C. C. Wylie edited *A History of Embryology* (1986), a volume for the British Society for Developmental Biology that both reviewed older themes and introduced many new ones. Though the title includes "embryology," the set of essays included analysis of biochemical, molecular, morphological, physiological, and other perspectives on the understanding of development. The focus remained largely on early twentieth-century themes, and the editors brought together biological, historical, philosophical, and sociological points of view. In his review of the volume, Gilbert noted that, "There is a great need for a major new history of embryology, as developmental biology, the anagenic descendant of embryology, is becoming pivotal to all areas of biology. It is in a remarkable period of growth, expanding in one direction into the molecular basis of gene regulation and in another direction into the developmental basis of evolutionary change" (Gilbert 1987).

The edited volume and other work of the time pointed to a number of themes emerging among historians by the 1980s that deserve a closer look, including among many others: the role of research institutions like the Marine Biological Laboratory (MBL) and Stazione Zoologica and University of Chicago, the importance of cells, regeneration, the organizer, metaphors and interpretation, and social views of embryos. While the earliest historiographic approaches, often by biologists reflecting on their own work, had emphasized the role of individuals and the ideas and interpretations, professional historians increasingly adopted a wider range of questions and methods. Individual scientists and their ideas remain important, of course, but often as part of larger institutions, changing scientific practices, and social influences.

Indeed, historians have come to recognize the importance of particular people, places, methods, organisms, concepts, and other choices in the history of embryological work. Social factors, metaphors, ethical worries, and other considerations outside the parameters of laboratory work, some historians have argued, have helped to shape the study of development. We can see the diversity of historical approaches with some examples.

In efforts to identify institutions important for the emergence of professional biology, historians have looked especially at the Stazione Zoologica in Naples (Groeben 2013) and the MBL in Woods Hole, Massachusetts (Maienschein 1985, 1989). As historian of science, Philip Pauly put it, "By the middle of the 1890s, an important group of American scientists and academic administrators, centered around such leading universities and colleges as Johns Hopkins, the University of Chicago, Columbia, Bryn Mawr, and Harvard, believed in the existence of a science of biology" (Pauly 1988, p. 121). Increasingly, these scientists went to the seashore to explore life and to carry out their biological research, with embryology as one of the core fields of study (Lillie 1944; Maienschein 1989; Benson 2001). They also found new research-oriented universities like the University of Chicago especially welcoming, and Chicago has had close ties with the MBL since its beginning (Maienschein 1988). These institutions provided a place to train graduate students by letting them jump in and carry out research themselves, embracing the importance of “learning by doing” and engaging in “hands-on discovery.” They also allowed biologists from different institutions and different specialties to come together in the summers and learn from each other, often developing long-term friendships and research collaborations.

Marine biology lent itself to studies of developing individuals, through embryology, and also to study of cells as a way of studying, step-by-step, the processes of individual development. Embryologists at the end of the nineteenth century observed and compared many different types of embryos to observe the emergence of form. They saw patterns repeating regularly in different organisms, and they described in detail what they came to call the developmental stages (Hopwood 2007). In addition to the marine invertebrates and more accessible species of amphibians and such favored by zoologists, medical researchers had a fascination with human embryos. The Carnegie Institution of Washington Embryology Department gathered human embryos and fetuses in a collection that was later housed at the Walter Reed Army Medical Hospital and then also digitized and made available virtually through several venues (Maienschein et al. 2004). Such stages and collections remained a standard for those studying development until the advent of photography, films, and other technologies became the standard for displaying what counts as normal or pathological in development.

Around 1900 cell lineage studies brought together study of cells with study of development to trace how cells change and give shape to embryos and organisms. Comparing these changes in cells across different organisms provided a source of information about development and possibly also about evolution, though it soon became obvious that the cells vary widely and the approach had limitations. The close examination of cells by Oscar Hertwig and Theodor Boveri in Germany, and Edmund Beecher Wilson and his colleagues such as Edwin Grant Conklin and Charles Otis Whitman in the USA, provided excellent observations and interpretations of what was happening as one cell divided into two, into four, and so on. Only recently have historians begun to look more closely at the history of cell biology in its own right, and the ways that study of cells and study of development were connected remains a largely untapped field.

Almost a century since cell lineage research connected the study of individual cells to organismal development, human embryonic stem cell research opened new doors and new questions for biologists and for historians and led to regenerative biology as a hot topic, starting in 1998, and the first human stem cell research. Regeneration was not a new topic, but it gained new attention. In fact, Thomas Hunt Morgan had carried out a number of studies on regeneration in the 1890s, and in 1901 he published a volume that summarized research to date that showed a strong fascination among biologists for the powers of regeneration. The questions for Morgan and his predecessors were: Which organisms could regenerate, under what conditions, and how did regeneration work? (Morgan 1901). Almost a century later, biologist Charles Dinsmore enticed a set of biologists and historians to explore the history of studies of regeneration, with much of the discussion focused on the periods leading up to Morgan's work (Dinsmore 1991). Stem cell research has since added to this discussion by directing thinking about regeneration into the context of often-exaggerated hopes for regenerative medicine. We are likely to see more historical work on the topic in the future as the science develops further.

As those studying regeneration raised questions about how organisms could respond to changing conditions to regenerate missing parts, others used experimental methods to create new conditions in order to discover the effects of disturbing development. Perhaps the most important of these methods for the first half of the twentieth century was transplantation. Hans Spemann in Germany and Ross Harrison in the USA (after he received a medical degree in Germany as well as a Ph.D. in the USA) each used amphibians for their transplantations. Spemann cut out parts that would normally give rise to eyes or ears or limbs in one individual; then he transplanted them to another individual to see what would happen. Would they develop as normal eyes or ears or limbs, but in the new place? Or would they adapt to their new surroundings and blend in with the local tissue? The pieces had a strong tendency to retain their initial capacity, and yet they also adapted significantly – or else they would not have developed at all. This suggested a combination of intrinsic capacity to become a particular part, along with a strong ability to adapt to changed conditions. Development, clearly, is a complex process. Spemann's work was well-known, and in 1935 he received a Nobel Prize for the work the he had begun with his student Hilde Proescholdt (later Mangold); unfortunately she died before the Prize was awarded (Hamburger 1984; Horder 2001; Sander and Faessler 2001).

Meanwhile, Harrison was also transplanting cells and tissues. In 1907, he transplanted nerve cells (neuroblast cells) completely out of a frog and into a dish with frog lymph. The cells kept differentiating as they would have done normally inside the organism, with the fibers reaching out to make neural connections. With this work, Harrison showed the power of tissue culture and also of apparent self-determination of cells under some conditions.

The work of Spemann and Harrison led Spemann to hypothesize the existence of a process of induction, through which an "organizer" induces surrounding cells to begin differentiation at the appropriate times and under the appropriate conditions. The search for the organizer and resulting experiments led to what Harrison referred to as a "gold rush" for embryological research (Hamburger 1988; Maienschein 2010). Such work dominated embryology through much of the 1930s, despite the fact that Johannes Holtfreter challenged the concept of a specific organizer and showed that many different kinds of tissue, including inert material, could stimulate the same result. Holtfreter's questions strengthened calls by others for more sophisticated biochemical studies. By the 1950s, the gold rush of morphological experimentation gave way in part to molecular approaches and developmental genetics (Hamburger 1996).

Despite the great enthusiasm for experimental embryology, and despite the prominence of Spemann and Harrison in the field, little historical analysis of the period appeared until Jane Oppenheimer identified it as an important topic.

Then Horder, Allen, Maienschein, Gilbert, and others undertook historical explorations from different perspectives (Oppenheimer 1967; Horder 2001; Allen 1975; Maienschein 1991; Gilbert 1991). Yet the most important historical study of Spemann and his approach is surely by distinguished neuroembryologist Viktor Hamburger. Late in his career, Hamburger turned his considerable talents to history, in particular examining the lab and director under whom he had received his Ph.D. Few scientists have so successfully carried out such a challenging professional project, including discussions of the personal side while also developing a critical distance for the historical analysis. Hamburger's use of two different type fonts throughout his volume allows him to maintain two different voices (Hamburger 1988).

While Hamburger's approach is grounded in close study of the science itself and the people involved in carrying out research, other historians have adopted alternative views. Donna Haraway, better known for her later, more socially oriented studies, wrote her dissertation and first book about three efforts to interpret developmental processes. Her *Crystals, Fabrics, and Fields* looked at the use of three different metaphors by, respectively, Harrison, Needham, and Paul Weiss. Inspired by Thomas Kuhn's ideas of paradigm shifts in science, Haraway shows how each of the chosen metaphors both reflected and helped shape the research approach of the proponent (Haraway 1976).

Embryologist Scott Gilbert received his Ph.D. from the Johns Hopkins University in biology, and he also received a master's degree in History of Science while working with Haraway. His own historical and social studies of metaphor usage in biology complement his scientific use of metaphor in his own work. Gilbert's *Developmental Biology* textbook, first published in 1985 and now in its tenth edition, has introduced generations to the field, including its theoretical and metaphoric side (Gilbert 1985, 1991).

A number of insightful social scientists have pointed to other ways that social factors impact science. For example, Emily Martin has shown that the apparently straightforward understanding of fertilization is highly gendered. After examining a wide range of descriptions of the process by which sperm and egg combine, she noted that most describe a very traditional "boy meets girl" story. Both scientists and those writing about the science invoke a kind of triumph of the male in penetrating the female myth. She pointed to these stereotypical male-female roles in 1991 and challenged writers to be more aware and more accurate in their descriptions (Martin 1991).

More recently, Lynn Morgan pointed to another social side of studying development, namely, censorship. At her own Mt. Holyoke, she discovered that a once well-used collection of human embryos and fetuses had been removed. Institutions became concerned that antiabortion politics had created such a heated social environment that these embryos were no longer seen as neutral scientific objects but as something ethically tainted. In her *Icons of Life: A Cultural History of Human Embryos*, Morgan lays out a number of examples of the cultural role and meaning of human embryos (Morgan 2009).

Evelyn Fox Keller has contributed extensively to our understanding of the history of biology, including especially the history of genetics and development. Her 2002 text, *Making Sense of Life: Explaining Biological Development with Models, Metaphors and Machines* looked at another side of developmental studies. And her more recent look at the persistent disputes about whether life results from "nature" or "nurture" in *The Mirage of a Space Between Nature and Nurture* shows ways in which cultural and social values shape biological thinking about life (Fox Keller 2010).

Science and its intersections with society and cultural values play out especially in evolutionary work. Even researchers focused on developmental biology bring in their own convictions about the relative importance of historical evolutionary factors and local embryological factors in shaping the processes and patterns through which the individual organism becomes organized and differentiated.

From Embryology to Developmental Biology

Decades before historians started to explore the social aspects and impacts of embryos (and embryological research), embryology witnessed its own social upheaval. In the wake of World War II, the field of embryology was transformed into a new field called developmental biology. This transition was replete with journals and society name changes. For example, the first issue of the US journal *Developmental Biology* came out in 1959, along with statements of unity from leading scientists like Weiss (Hopwood 2009; Oppenheimer 1966; Pradeu 2016). Despite appeals of unity within the field, historians have pointed to this as an era of "fragmentation," where the old recourse of studying embryos as whole organisms was pushed to the boundaries as the field experienced increasing diversification in terms of research questions, fields of influence, and methods (Crowe et al. 2015; Hopwood 2009; Horder 2010). Historians who have dealt with this shift and its subsequent history have tended to privilege the biochemical and molecular aspects of the emerging field, focusing on narratives that centralize the molecularization of developmental biology (Burian and Thieffry 2000; Crowe et al. 2015; de Chadarevian 2000; Gilbert 1996; Hopwood 2009; Morange 2000; Oppenheimer 1966). Molecularization in this context designates the "substitution of molecular level analyses of biological problems for traditional cellular, tissue, or organism-level analyses" (Burian and Thieffry 2000, p. 316).

Bridging her career as an embryologist and as a thoughtful historian, Oppenheimer (1966) contributed the introductory chapter to the 25th Symposium of the Society for Developmental Biology (previously the Society for the Study of Development and Growth). This chapter, which was praised by the conveners of the symposium, deals with "The Growth and Development of Developmental Biology" and traces the historical unfolding of this field starting with the first symposium on development and growth held in 1939 (Oppenheimer 1966). At that time, the study of genetics and heredity remained largely separate from the study of development. Embryology included the work of Harrison on tissue development, Spemann on the organizer and induction, Holtfreter on the developmental potential of isolated pieces, and so on. All this work ignored genetics, largely because researchers did not see how to connect the study of heredity and development. Oppenheimer concluded that recently the two had converged and transformed biology.

Following along the lines that Oppenheimer laid, Hopwood has further highlighted the importance of molecularization for the field of developmental biology. “Developmental biology was a joint initiative of self-consciously ‘modern’ embryologists and geneticists, biochemists, cell biologists, and molecular biologists who saw a field ripe for their skills. . .the new field’s key generalization was development as differential gene expression” (Hopwood 2009, p. 309). In addition to the overviews provided by Oppenheimer and Hopwood, historians interested in the molecular aspects of developmental biology have focused on the works or research programs of individuals and, particularly, on molecular biologists who crossed the boundary into developmental biology. Historians of genetics Michel Morange and Soraya de Chadarevian have given us glimpses into the shifting research programs during the 1960s of Francois Jacob and Sydney Brenner, respectively, each of whom left a bacterial model in order to apply gene regulatory questions to eukaryotes (mice, in the case of Jacob, and *C. elegans*, in the case of Brenner) (de Chadarevian 2000; Morange 2000).

While Morange’s work explores in detail the *T*-complex model and the metaphor of “program” that surrounded Jacob’s work, de Chadarevian’s focuses on the tools that molecular biologists (e.g., Sydney Brenner) brought with them as they moved to developmental questions. The topic of genetics is covered elsewhere in this volume (see ► Chap. 6, “Gregor Mendel and the History of Heredity”), and so we do not address the intersection of genetics and development in further detail here.

Nonmolecular Narratives in the History of Developmental Biology

While genetics has had an undeniable impact on the field, a great deal of research within developmental biology has not utilized molecular techniques (Sunderland 2011). Following from a computational study of the General Embryological Information Service, Crowe et al. (2015) have recently pointed out that genetics cannot account for the diversification of topics that came along with the advent of developmental biology. If it is the case that genetics cannot account for the diversification of topics within developmental biology post-1945, what can? That is, what does a focus on the molecularization of developmental biology leave out?

We can look to a dizzying array of research problems, such as morphogenesis or regeneration, for example, where molecular methods were not co-opted for the study of developmental processes along the same timeline that can be applied to the phenomena of differentiation. This is a research area poorly populated by historians of science but immensely rich in subject matter and different stories. Here we focus on just one topic, morphogenesis, and a few scientists whose work has proven hugely influential.

Those few who have focused their historical lenses outside of the molecular (or chemical/biochemical) trend in developmental biology have tended to focus on individuals and localized research programs, preferring to trace the conceptual and practical work embedded in the science rather than broader networks of individuals or the social settings of the research. Looking back in 1996, developmental biologist Viktor Hamburger provided an overview of the work of his close friend and colleague, Johannes Holtfreter, whose work never included molecular or even biochemical methods (Hamburger 1996).

Holtfreter started out in Spemann's laboratory, receiving his Ph.D. in 1925. His work over the next 15 years produced impressive insights into the determination of different parts of the embryo during different stages of development, answered the question of whether induction was mediated by a chemical or physical force, and even investigated the dynamic morphogenetic movements and properties (e.g., cell motility and cell adhesion) that shape the embryo.

Holtfreter's research was guided by a search for the mechanisms of development, to the extent that when, at a conference in Utrecht in 1931, he heard Spemann speak about the "metaphysical concept" of the organizer and its "vitalistic agency," he set up a series of experiments to test the organizer's capacity for neural induction himself (Holtfreter 1991, p. 117). His results dealt a blow to Spemann's vitalistic concept of the organizer, showing that the organizer was "merely the source of certain chemical substance(s) that initiated neural differentiation in the responding ectoderm" rather than some metaphysical entity (Holtfreter 1991, p. 117).

With regard to Holtfreter's research on morphogenetic movements, Hamburger tells us that it was his "seminal contribution to envision these processes as the manifestations of inherent properties of cells and cells assemblies, and, furthermore, that these dynamic properties are inseparably connected with the histological and organological fate of the different regions" (Hamburger 1996, pp. 215–216). Holtfreter's approach to morphogenesis was a radical departure from the tradition of the time because it extended analytical embryology to the cellular level and one that greatly impacted future morphogenetic research (Hamburger 1996; Dietrich 2007; also see Gilbert 1991 and elsewhere for more extensive discussion of Holtfreter's work).

In his autobiography, *Embryologist*, developmental biologist John P. Trinkaus traces his own research program in morphogenesis from the 1930s through the 1990s. *Embryologist* is a very personal history of Trinkaus's research, combining anecdotes and stories about his life with detailed conceptual and practical aspects of his research (as well as the research of those colleagues that he admired).

Trinkaus describes being so inspired by Holtfreter's work on cell motility and adhesion that it directed his career, noting, "Here was a subject of outstanding developmental importance whose mechanism was poorly understood but which was definitely attackable, as Holtfreter had so brilliantly demonstrated" (Trinkaus 2003, p. 89). Trinkaus' career was spent understanding the mechanisms of cell motility and adhesion during epiboly in *Fundulus* – work for which he received the first ever Edwin Grant Conklin Medal from the Society for Developmental Biology in 1995. Also notable about Trinkaus for our purposes was his aversion to genetics, "The morphological beauty of embryology won out over the logical beauty of genetics" (Trinkaus 2003, p. 56), and his reflection on a general trend in developmental biology that, ". . .the bulk of research in developmental biology in recent decades has concentrated on cytodifferentiation, leaving somewhat to the side the equally important problems of how the cells got there in the first place, how they change form, and how they arrange themselves into different tissues and organs" (Trinkaus 1984, p. 3).

Trinkaus's friend and fellow graduate student at Johns Hopkins University, John Saunders, similarly embarked on a nonmolecular career track with a focus on tissue and cellular interactions. Trinkaus discusses briefly in his autobiography Saunders' discovery during his graduate studies of the apical ectodermal ridge (AER), the thickening of ectoderm on the developing vertebrate limb bud that directs limb outgrowth (Trinkaus 2003). Saunders continued work on the AER but also looked at other problems of vertebrate limb development, including cell death and the formation of digits. It was through his investigations of cell death that he discovered, along with his colleague, the zone of polarizing activity (ZPA), a region on the outgrowing limb that is central to limb patterning (Tickle 2002). Developmental biologist, Cheryll Tickle, whose own research on avian limb patterning led to the discovery that retinoic acid could mimic the effects of the ZPA, has shown that Saunders' work on the ZPA was the result of grafting experiments and that, while his work to uncover the role of the ZPA was molecule-free, his discovery spurred a long debate over competing models of limb patterning and a search for chemical and molecular mechanisms (Tickle 2002).

John Tyler Bonner, often referred to as one of the "grand old men" of the *Dictyostelium* community, similarly pursued questions of morphogenesis that focused on organisms rather than genes or molecules. Historian of science Mary Sunderland (2011) has shown both that Bonner's investigative pathway fell outside of the traditional molecular narrative, due both to his emphasis on applying an array of experimental strategies to a range of organisms and the intractability of *Dictyostelium* as a genetic model at the time and that he conceptually laid the groundwork for evolutionary developmental biology. In his 1952 text, *Morphogenesis: An Essay on Development*, which was written in the Woods Hole, MA, laboratory of famed cell biologist and embryologist Edwin Grant Conklin, Bonner laid out an argument for uncovering shared developmental principles by studying organismal diversity in a theoretical context (Bonner 1952; Sunderland 2011). Unfortunately, not much heed was taken of Bonner's arguments for studying development across the animal kingdom at the time of publication.

Evolutionary Developmental Biology

In the field of evolutionary developmental biology (or "evo-devo"), Bonner's vision of scouring organismal diversity for mechanisms of developmental change has been achieved. The field of evo-devo is broad, encompassing many organisms, techniques, goals, and theoretical and epistemic frameworks. It is a field bound together by the tenet that understanding development gives the best insights into understanding organismal evolution and one in which no unifying theoretical framework has emerged.

The twentieth-century concrescence of evolutionary and developmental biology into evo-devo has been traced back to several key events: Stephen Jay Gould's publication of *Ontogeny and Phylogeny* (Gould 1977), the 1981 Dahlem Conference on "Evolution and Development" organized by John Tyler Bonner (1982), and the discovery of the universality of Hox genes (See Carroll 2005). Each of these moments spurred the broader scientific community to reclaim an evolutionary perspective for developmental biology – a field that had largely been left out of the Modern Synthesis.

The history of evo-devo has been told along two separate, yet complementary, narrative arcs. In the first arc, which has been called "the standard narrative" (Laubichler and Maienschein 2013), a direct conceptual lineage is traced from Darwin, through the Modern Synthesis, to an "expanded evolutionary synthesis" in which development is incorporated into the evolutionary theoretical framework that the Modern Synthesis provided (Carroll 2005, 2008; Raff 2000). The evolutionary framework of the Modern Synthesis is one tied to genes, particularly population genetics, and the role of natural selection in guiding evolutionary processes. Studies of development are seen in this evo-devo narrative as providing insights into the limitations of natural selection, i.e., the developmental constraints that affect the direction of evolution. As evolutionary developmental biologist Rudy Raff put it, in modern evolutionary theory, "Micro-evolutionary processes are considered sufficient to explain macro-evolutionary history. However, developmental processes are emergent, and not predictable from the properties of genes or cells; therefore, starting with a particular ontogeny, some phenotypes might be readily achieved and others impossible. Developmental mechanisms are crucial, both to large-scale evolutionary changes, and also to small scale evolutionary processes" (Raff 2000, p. 78).

The standard narrative is neat and tidy, but as Laubichler and Maienschein (2013) point out, there is "an implicit progression of ideas, with inclusion of new empirical facts and methodological approaches within the general framework of Darwinism leading to an increasingly more complete understanding of the evolutionary process" (2013, p. 375). The problem with the standard narrative is that it leaves out several traditions that have played a major role in conceptually shaping evo-devo and, in doing so, gives the impression that it is a unified, theoretically coherent field. Unfortunately, this is not the case at the present time. A precursory look at current publications in the field or attendance at an evo-devo conference shows just how theoretically and epistemically diverse the field is. In fact, at the inaugural meeting of the Pan-American Society for Evolutionary Developmental Biology in August 2015, one of the main talking points for the "Future of EvoDevo" session was how to form a more (theoretically) unified field so that funding bodies would continue to recognize the research (MacCord was in attendance).

Laubichler and Maienschein (2007, 2013) offer an alternative narrative arc that complements the standard narrative by filling in the history with an understanding of traditions that focused on the origins of variation, rather than the inheritance of them. In an edited volume that arose from the 2001 Dibner Seminar at the MBL "From Embryology to Evo-Devo (Evolutionary Developmental Biology)" and a follow-up workshop the next year, Laubichler and Maienschein (2007) brought together historians, philosophers, and scientists to explore the historical trajectory of research that joined together evolution and development. While contributors like Scott Gilbert, Brian Hall, and Alan Love had previously made contributions to this problem space (see, for instance, Gilbert 2003; Hall 2000; Love 2003), it was a singular accomplishment to unite a group that could both broadly survey evo-devo history and use these historical insights to analyze the future of the field. Topics in this volume range from understanding the modern significance of research programs of historical figures like William Bateson (Newman) and Richard Goldschmidt (Richmond) to tracking the contributions of different fields outside of evolutionary biology and developmental biology (Love).

As broad a perspective as Laubichler and Maienschein offer, there remains a great deal of territory for historians to cover. In light of the current theoretical and epistemic disunity of the field, historical and philosophical investigations can only serve to benefit any future synthesis of evo-devo. Thus, this is an area where young historians of science can both carve out their own niche and have a tremendous impact on shaping the future of a scientific field.

Conclusion

Developmental biology (formerly and sometimes still known as embryology) has a long and rich history, and scientific research in this area is unfolding at a growing rate. Despite the centuries of theoretical, empirical, and, more recently, experimental investigations of the phenomena and processes that shape life, this is an area of inquiry that is only sparsely populated with historical analyses. The future of historical work (which sounds a bit like an oxymoron) in this area is wide open for fresh, young historians of biology to dig in and offer new perspectives.

In closing, we point to some forward-looking techniques and areas where contextualized understandings of development offer an excellent place for an intersection between academic and public knowledge. Instead of focusing on particular topics that could benefit from more historical attention, we note that there are so many theories, practices, and discussions ripe for study. Throughout, we have noted a number of them, and there are many, many others.

There is a huge potential in the historical study of developmental biology for new digital and computational approaches and techniques that bring new questions and new discoveries of patterns worth exploration. These techniques also enable historians to reach a broad, public audience like never before. Digital publications, such as the online, open access *Embryo Project Encyclopedia* (EPE), edited at Arizona State University, have enabled publically oriented scholarship that is approaching one million page views a year. The project welcomes submissions of shorter and longer articles and can be accessed through http://www.embryo.asu.edu.

The EPE, along with the MBL History Project (a digital project that preserves and communicates the history of science at the Marine Biological Laboratory in Woods Hole, MA, at http://history.archives.mbl.edu), is also starting to integrate computational approaches, which will allow both scholars and the public to query data harvested from digitized content of the MBL archives. As these projects expand, computational methods like citation analyses, topic modeling, and semantic network analyses will become available, allowing all users to explore the connections between researchers, institutions, and concepts in new ways. Software for such analyses is currently being developed in places like Manfred Laubichler's Digital Innovation Group at Arizona State University through http://diging.asu.edu.

Such new approaches, new studies of existing topics, and also studies of emerging areas within the rapidly growing field of developmental biology make this an especially dynamic area for historians. In fact, we hope that we have missed other intriguing areas for research, because that just means the field is even richer.

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