Introduction to the Special Section
"From Embryology to Developmental Biology"

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Three of the four papers contained in this special section are revised versions of papers delivered at the 1999 meeting of the International Society for History, Philosophy, and Social Studies of Biology in Oaxaca, Mexico. They were presented in a pair of symposia that we co-organized under the overarching title "From Embryology to Developmental Biology".[1] The fourth paper was invited for the Oaxaca symposia, but due to schedule conflicts, could not be presented on that occasion. In organizing these symposia we sought, in part, to help foster three lines of historical-methodological work:

- studies of the transition from embryology to developmental biology,
- studies of the impact of the molecularization of biology on developmental and embryological studies, and
- studies of the interactions among embryology/developmental biology, biochemistry, evolutionary biology, genetics, and other cognate fields.

The present group of papers thus represents a small part of a large enterprise that reaches far beyond the confines of any symposium or special section of a journal. In this introduction, we will present a brief orientation to the contributions put forward on this occasion, with some indication of questions that remain to be faced in dealing with the larger domain in which this project is embedded. We also provide an appendix listing some of the work on the history of embryology and developmental biology published since about 1970.

Starting around 1890, a major reorientation of biology began that continued until about 1940. In some respects, this reorientation, which, of course, proceeded very unevenly in different places and in different disciplines, received its ideological formulation in the work of Wilhelm Roux. His manifesto for a new science of development, put forward in 1885 in rather florid German under the title '*Beiträge zur Entwicklungsmechanik des Embryo*',[2] provides a useful introduction to the papers in this special section. He held that the ultimate goal of descriptive embryology is a complete particle-by-particle description of the trajectories of the particles of the egg from fertilization to adulthood. But such a ‘kinematic’ description (a term he borrowed from Ampere) is unachievable. Indeed, Roux claimed, because of the inaccessibility of the particles in question, the available techniques prevent a closer approach to such a description than was already available. He suggested working with an alternative ‘kinetic’ science of development, based on the dynamics of particle movement even though the ideal it proposed was also unachievable. He reasoned that working from dynamics would offer a better opportunity for experimental progress. By combining the available descriptive knowledge with the experimentally ground dynamics, one could hope to create a new science, an Entwicklungsmechanik [developmental mechanics] of the embryo. And it was realistic to go further, seeking to go beyond the restriction to the embryo, aiming at a ‘general Entwicklungsmechanik’. This term would designate “*the science of the composition and functioning of the combinations of energy that bring about development*” (p. 413, Roux’s emphasis). “Entwicklung” [development or unfolding] here has its conventional meaning, “the origination of perceptible diversity (wahrnembarer Mannifgaltigkeit),” which is, in turn, divisible into “production of diversity” and “mere transformation of imperceptible into perceptible diversity” (p. 414). Once these could be experimentally distinguished from one another, one would be able to settle disputes over epigenesis vs. predetermination. Since, at just about this time, new experimental questions and techniques (especially in cytology and microscopy) were yielding important new knowledge, the reorientation of biology was also driven in part by the drive to make biology into an experimental discipline, coping with more manageable problems, producing clear-cut results, and generating practical applications.[3]

The reorientation of biology begun in the 1890s was also driven by the difficulty of resolving evolutionary questions. In that decade biologists began to recognize that they had no adequate way to determine the requirements for species formation or for establishing the validity of putative phylogenies. Of particular importance for present purposes is the long string of unsuccessful attempts to employ descriptive embryology as a tool for determining phylogenies and clarifying the course of evolutionary history. Around this time it slowly became clear that attempts to use embryology in this way resulted in futile debates with no prospect of a definitive outcome.

Over the next fifty years or so, this complex reorganization resulted in a major restructuring of the disciplinary organization, concepts, and tools of major parts of biology. It resulted in reduced emphasis on the traditional disciplines of botany and zoology. They were often displaced by work in new, more experimentally oriented, disciplines such as experimental embryology (Entwicklungsmechanik)[4] and genetics. Functional disciplines, such as physiology (which was typically located in medical schools), developed in close interaction with new (inter)disciplines such as biochemistry, which eventually interacted closely with both genetics and developmental biology.[5] It is important to repeat that the changes took place unevenly and in different ways in different places. For example, in Britain the development of biochemistry was fairly separate from that of physiology and embryology, while in Belgium the development of physiology and embryology played a major role in the development of biochemistry. But, in any event, the process of setting up new disciplines also created barriers between disciplines – as happened between genetics and embryology and between evolutionary biology and most of the new experimental disciplines. Thus, partly because of the emphasis on experiment as the basis for new biological disciplines, evolutionary biology did not, as such, acquire the sociological trappings of a separate discipline (separate journals, departments, and meetings) until about the time of World War II – except, perhaps, in Russia.[6]

The first reorganization of biology was quickly followed by a second, equally drastic, reorganization, considerably influenced by developments in the Second World War and their aftermath. Well begun by 1950, and also lasting about a half century, for shorthand purposes this reorganization can be labelled "the molecularization of biology." Conventionally, 'molecularization' designates the substitution of molecular level analyses of biological problems for traditional cellular, tissue, or organism-level analyses. Biochemical treatments of the products and chemical cycles within cells occupy a boundary region. But because of the differences between the techniques, experimental tools, and the problem formulations posed by biochemists and early molecular biologists as of, say, the early 1950s, it is common to distinguish the biochemistry of this era from molecular biology and treat it as less reductionist in spirit than molecular biology. However, as nicely emphasized by de Chadarevian and Morange, these distinctions are quite problematic, especially in the field of developmental biology, as "molecular" analyses have to be articulated to more "traditional" approaches in order to generate, stepwise, a consistent account of embryogenesis. (See below for further discussion of this point in the context of the presentation of Morange's and de Chadarevian's papers.)

The first two papers of this special section touch on aspects of the first reorganization. They both are concerned primarily with the period when experimental embryology had already been stabilized as a discipline, and genetics was already well established, at least in the United States, as part of the effort to make biology more experimental and to avoid sterile evolutionary debates. These two disciplines, though, had gone in quite different directions, and they could not wholly avoid evolutionary issues. Notoriously, by the 1930s, they offered conflicting accounts of the means by which key features of organisms are produced and of the factors that should be accorded the greatest importance in organismic evolution. Ronald Amundson's paper is one of a number of recent papers and books that elaborate on the conflict between embryology and genetics.[7] To put it crudely, geneticists were, by and large "friends of the nucleus," seeing nuclear genetic factors (eventually localized on the chromosomes and relabeled 'genes') as the primary determinants of the structure, organization, and functional capacities of organisms. In contrast, embryologists were by and large "friends of the cytoplasm". They held that the cytoplasm contains the key structures and/or process that determine the organization and fundamental features of the organism. As Amundson explains in some detail, they argued that genetics could not account for differentiation, cell movements, and the formation of one Bauplan rather than another. Amundson develops some of the issues involved in order to investigate the extent to which embryologists, perhaps influenced by the old links of their discipline to evolution, might have been inspired by the development of the evolutionary synthesis to rework the relationship between their discipline and genetics in the 1930s and 1940s. His argument provides powerful evidence that the evolutionary synthesis, as such, did not play an important role in leading to a *rapprochement* between embryology and genetics or to the reworking of embryology into developmental biology and/or developmental genetics.

Bernardino Fantini's contribution touches on events contemporaneous with many of those discussed by Amundson, but with historically very distinct roots. He examines the growing influence of (initially British and European) chemical embryology within embryology, even claiming that cytochemical techniques and theories graduated from a means of supporting and developing experimental embryology to being a privileged provider of key concepts to experimental embryology, cytology and even genetics [**MS p. 5**]. Thus, on his account, work of people like Joseph Needham and Jean Brachet in chemical embryology was influential in leading to the molecularization of embryology. Yet he also holds that the developments in chemical embryology were unable to force the transition to a full-fledged molecular developmental biology in the absence of the sort of molecularization that took place in genetics. This suggests that it is worth exploring the extent to which biochemical and molecular tools (and, perhaps secondarily, theories about the roles played by specific classes of molecules) led to the convergence of some embryological findings with those of genetics, thus providing an opening for the transformation of embryology into developmental biology. Relatively speaking, this is a pathway that has been little explored by historians of biology, and it is clearly worth considerably more investigation.

Fantini's analysis thus deals with a major pathway leading toward the molecularization of embryology and, ultimately, to direct contact among biochemists, embryologists, and geneticists. There is some overlap between the investigative worlds examined in his paper and that of Amundson, most prominently in the person of C. H. Waddington, who worked with Needham and Brachet on the evocator in the 1930s and who was perhaps as well placed as anyone to establish a synthesis among biochemistry, embryology, evolution, and genetics in the 1950s and 1960s.[8] But Fantini's topic is different than Amundson's. He is concerned with technical developments within chemical embryology in order to understand the interactions of the techniques and choice of technical tools within that discipline with embryological theory. Michel Morange and Soraya de Chadarevian touch on closely related issues in their papers.

Fantini's perspective is internal to embryology and, to a lesser extent, biochemistry. He considers the role played by techniques for characterizing the composition and distribution of key biochemicals, especially the nucleic acids. In light of developments after the Second World

War, it is obvious that investigations into these topics came to play an unexpectedly crucial role in the interactions among the disciplines in question. Fantini avoids excessive influence from subsequent developments by restricting his study to an investigation of the resources and findings employed within the domain of chemical embryology at the time. In the process, he uncovers important details affecting the interpretation of a major pathway leading to molecular-level analysis of the composition and organization of the cell and the processes by which proteins are synthesized, a pathway that has received increasing attention in the last few years.[9] Biochemical and embryological approaches to the ways in which nucleic acids in the nucleus yield and/or control the synthesis of proteins in the cytoplasm and the ways in which embryos interchange regulatory molecules and pattern-forming cues between cytoplasm, nucleus, and back to cytoplasm deserve considerably more study than they have yet received.

Yet, as is clear in reading Fantini's article, the work in chemical embryology was only one step among many, often pulling in different directions, toward the 'molecularization' of biology in the sense now employed when speaking about 'molecular biology'. The work of Brachet and colleagues on the one hand, and Caspersson and Schultz and colleagues on the other from, say, 1938-1952, did not lead directly yield to the formation of fields like developmental genetics, or developmental biology that began to take shape some twenty years later. In some places, there was a fairly direct pathway (e.g., in Brussels, thanks to the influence of Brachet and his school;[10] the path followed by Eric Davidson at Cal Tech would also deserve exploration on this issue). Both Soraya de Chadarevian's and Michel Morange's contributions address important work that followed a different pathway during the transition that took place at this later date. De Chadarevian examines some of Sydney Brenner's and Morange some of François Jacob's contributions to the study of development in metazoans. Both of these men are founders of molecular biology who turned from work with microorganisms to the study of development in eukaryotes. Both of them applied molecular tools to problems of cellular commitment, competence, and differentiation – phrased more generally, to development and its regulation.

To help the reader think about the challenge raised by de Chadarevian and Morange, it may help the reader to think back to Roux's manifesto. Once one removes the archaic language and Roux's commitment to energetics, his description of general Entwicklungsmechanik – which we certainly think of as 'old time biology' – is a useful foil for comparison with de Chadarevian's and Morange's independent descriptions of what Sidney Brenner and François Jacob were striving to accomplish in the 1970s. Both of them make it clear that the task of characterizing the role of 'molecular tools' and 'molecularization' in the entry of molecular biologists into developmental biology is not simple. Both Jacob and Brenner drew heavily on traditional pre-molecular descriptive techniques. De Chadarevian's description of the Brenner laboratory's work on *C. elegans* fits Roux's account of the ambitions of general Entwicklungsmechanik quite well, especially in light of the eventual attempt to achieve a 'complete solution' of *C. elegans*. Even where the work of Jacob's and Brenner's laboratories focused on molecules, they typically aimed at what Roux called *kinematic* descriptions, often carrying out the familiar tasks described by Roux by use of new techniques and on newly characterized or visualized entities, some of them at the molecular level. In general, neither Jacob's nor Brenner's group worked directly from molecular findings about nucleic acids or proteins to key features of their organisms as had become common in work on prokaryotes.

In light of their detailed examination of the work in the two laboratories, de Chadarevian and Morange both argue against exaggerating the special role of molecular commitments and findings in the work that they describe – and similarly for some of the concepts, such as that of a genetic program and even of the operon, that had seemed promising in dealing with procaryotes. Put generally, the turn to eucaryotes required a return to traditional descriptive tools and techniques, plus the incorporation of new technologies to increase the power of older tools to yield findings, many of which, at least in principle, could have been produced by older techniques. Thus, for example, Jacob's work on mice did not involve direct study of DNA or the genetic regulatory scheme of the operon, either as an investigative tool or in articulating findings about the development of mice. And, as Morange argues, a major difference between Jacob's mouse work and his work on *E. coli* with Monod is that he makes no use of the concept of a closed genetic program, i.e., one that could be gone through sequentially without much dependence on the inputs affecting gene expression. In particular, interactions at and across cell membranes, which became a major focus of research, were seen to play a major role in development. These interactions entered into steps taken by the developing organism that could not be 'read out' of the program or decoded by reference only to the circuitry built into a (genetic) program within the cell.

This change in the character of the work and the key findings is deeply connected to the biological issues of concern in studying development, as reflected in a saying employed in variant forms by both Boris Ephrussi and Jean Brachet: the proper way to study embryology is on embryos.[11] The complexities of development are not just those of eukaryotic (as opposed to prokaryotic) cells, though that is certainly involved, but also those of the integration of development in multicellular organisms. A major change in the issues addressed and the style of work was required in order to bring the findings of molecular biology, as developed in prokaryotes, to bear on the problems of development in eukaryotes. And the beginning of that change (at the very least) required doing quite a bit of traditional biology on the organism(s) being studied.

These considerations make evident the need for careful integration of molecular work with basic biology in turning to development – an integration that involved an unpredictable transformation of both sorts of study and an expansion of molecular biology from the narrowly reductive programs with which it began. De Chadarevian speaks of the ways in which complete maps of the sort achieved in Brenner's lab "allowed new levels of intervention ad opened up new avenues of research" – but also of the melting of the boundaries between molecular and 'old-time biology' mapping projects. Morange speaks of Jacob's "disillusionment" during this phase of his career, as reflected in the contrasting philosophical images of science presented in *The Logic of Life* (1970) and *The Possible and the Actual* (1981). We believe that the issues alluded to in this paragraph have something to do with the hidden crisis that Morange mentions at the beginning of his paper – and that the way out of the crisis depended critically on integrating new techniques and concepts with molecular biology as practiced on eukaryotes. Such techniques (e.g., autoradiography, immunolabeling, etc.) were needed to allow one to follow events *in situ* in ways that could not be readily exported from prokaryotes to eukaryotes. The concepts were needed to handle the multiple levels of integration that are involved in the development of multicellular organisms.

Morange also complains of the relative paucity of historical and philosophical studies of the difficulties encountered by molecular biologists, particularly those who turned to eukaryotes, during this period. We are confident that there will soon be more studies of these issues, both because there is a large budget of further topics for investigation here and because we have achieved sufficient historical distance from the events involved to begin to assess the work that was then on the forefront of research and in an unsettled state. We hope that this small group of papers, along with many others elsewhere, will help spur others to join into the examination of the issues raised here.

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Footnotes

[1] Several of the papers delivered in these symposia are already published or in press elsewhere (Galperin 1998, Gilbert in press, Rheinberger in press).

[2] See (Roux 1885). The German title translates as "Contributions to the mechanics of development."

[3] The experimental turn taken by biology near the beginning of the last century has been the subject of considerable debate ever since the *Journal of the History of Biology* published a special section on 'American Morphology at the Turn of the Century (Maienschein *et al*. 1981); See also (Allen 1979, Maienschein 1981).

[4] Experimental embryology never fully succeeded in its program of research or in displacing traditional descriptive embryology. An interesting boundary region between the two, worth exploration in this connection, concerns cell lineage studies, especially in their connection with exploration of the effects of ablating cells, deforming eggs or blastulae, and subjecting eggs and zygotes to various mechanical and electrical forces, chemical insults, and the like.

[5] The complexities of discipline formation go far beyond the scope of our discussion here. Many sociological factors are, of course, involved, including patronage, the formation of academic departments, and the development of specialized journals and societies. By these measures, a large number of new biological disciplines and interdisciplines arose 1890-1940, most of which are not discussed here – e.g., bacteriology (with strong medical affiliations), biochemistry (with multiple affiliations and forms), and ecology. Our concern for this period is primarily with embryology and genetics, but also with evolutionary biology, which did not acquire the sociological trappings of a discipline to the same degree as these other two at that time, even though evolution *did*, in many places, come to be thought of as a distinct biological specialty long before 1940.

[6] See (Mayr & Provine 1980, Cain 1993 and 1994, Smocovitis 1992). For Russia, see, for example, (Todes 1989) and Part I of (Adams 1994).

[7] E.g., (Maienschein 1986 and 1987, Sapp 1986). One under-appreciated aspect of the differences in the practices of genetics and embryology that deeply influenced the differences between the disciplines is the choice of experimental organisms to suit the goals of the disciplines. For this topic, see (Burian 1992, Lederman & Burian 1993, and Kohler 1994).

[8] For further information on Waddington's connections, see (Gilbert 1988 and 2000, Robertson, 1985). Another candidate for accomplishing a synthesis between genetics and embryology is Boris Ephrussi. See, e.g., (Burian, Gayon & Zallen 1991, Burian 1999). Amundson is clearly right, however, in arguing that Ephrussi was not driven by an interest in evolution or particularly well placed to develop a synthesis that included evolution.

[9] See (Brachet 1987, Burian 1997, Fantini 1978, Rheinberger 1995 and 1997, Thieffry & Burian 1996).

[10] See, e.g., (Burian & Thieffry 1997) and the references therein.

[11] Both men were pressured by Monod to switch to the use of bacteria as model organisms for differentiation and/or development, and both self-consciously chose not to do so. See (Sapp 1997, Ephrussi 1953; see also Lederberg 1956).