The long road to theoretical synthesis

Review of: *Embryogenesis Explained*
written by Natalie K. Gordon and Richard Gordon

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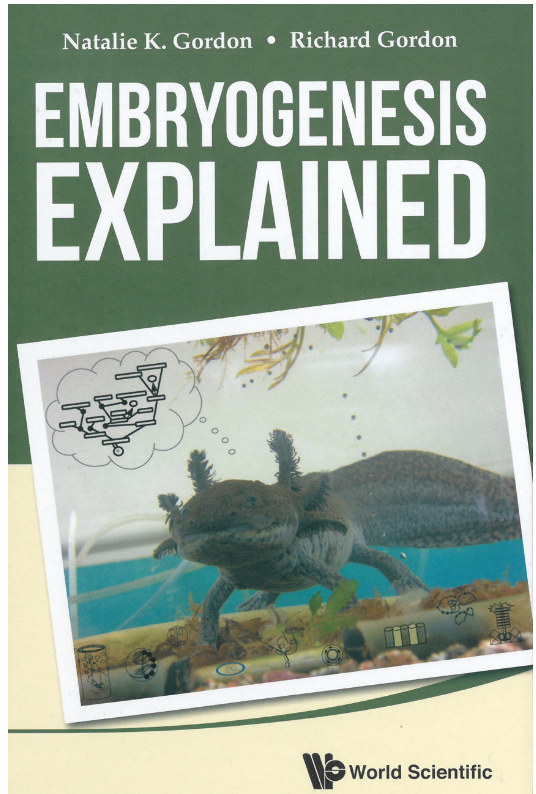

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Much of contemporary biological research is strictly reductionist, being focused on the level of experimental manipulations, gene function, and ultimately mechanism. There is of course a practical reason for decoupling evidence and broader theory in this way: experimental work is the most empirically direct and informative way to learn about biology. Yet these results are always contingent on other findings or the next set of investigations. An over-emphasis on empirical flow locks us into approaching biological phenomena such as development and disease with a limited technical and statistical vocabulary. It is therefore refreshing when a book comes along that challenges this approach and provides us with a big-picture synthesis. This is at least one reason why *"On the Origin of Species"* is a perpetual scientific classic. Charles Darwin not only got the phenomenology correct, but also offered myriad robust examples in support of these contentions. Works like this require a lifetime of observation and reflection, and perhaps that is why they are so rare. Such long roads to theoretical synthesis require large amounts of dedication, with the potential for large scientific payoffs.

Richard Gordon has taken such a quasi-Darwinian methodological approach to his life's research. Trained as a biological physicist and having spent much of his career as a theoretical developmental biologist, Richard has devoted much energy to interpreting the empirical outcomes of embryogenesis. A central finding in this respect is the existence of differentiation waves. Differentiation waves occur as the consequence of producing asymmetrically sized daughter cells during the process of morphogenetic differentiation. While the direct observation of differentiation waves is limited to a few Metazoan species (such as the Axolotl), the theoretical construct is consistent with developmental processes in a wide range of animal species. The book "*Embryogenesis Explained*" is a semi-technical follow-up to a previous book "*The Hierarchical Genome and Differentiation Waves: Novel Unification of Development, Genetics and Evolution*". In the previous book, Richard set out to establish the theory of differentiation waves in embryogenesis and proposed a large number of theoretical predictions in the areas of development and evolution. While new theoretical ideas often come and go, particularly those that invoke "waves", the burden is always on theorists to empirically support what are at times extraordinary claims. With "*Embryogenesis Explained*", Richard and Natalie (his co-author) take the next step of presenting the concept of differentiation waves in a less technical manner, but also with respect to modern cell and molecular biology. This leads to the philosophical implications of looking at the big biological picture.

In the interest of comprehensive coverage, "*Embryogenesis Explained*" is 784 pages long. Yet this length serves Gordon and Gordon well, as they are dealing with a conceptual area that is difficult to communicate. With this book, their intended audience seems to range from literate non-scientists to scientists with little to no prior knowledge of developmental biology. To ease the audience into formidable scientific territory, the authors provide many technical and analogical figures that serve a general pedagogical function. In choosing between the two books, those who prefer parsimony and occasional levity in their theories should read "*Embryogenesis Explained*" before "*The Hierarchical Genome and Differentiation Waves*". As the authors' theory exists in a greater biological milieu, their choice of how to present material in "*Embryogenesis Explained*" is more straightforward and thus more effectively communicates their ideas. On the other hand, the earlier book provides details on how characterizing differentiation waves can lead to greater theoretical constructs such as differentiation trees and differentiation codes.

"*Embryogenesis Explained*" has three major sections: five chapters on the biological background and support for differentiation waves, five chapters on the cell and molecular mechanisms of differentiation waves, and two final chapters on the philosophical implications of differentiation waves. This structure is particularly helpful in understanding the biological underpinnings of differentiation waves, as it eases readers into the theoretical claims through an assessment of currently understood biological facts. The philosophical implications in the last section seem at times to indulge the authors' personal interests; nevertheless, the last chapter (on wholeness) seems to provide momentum for future work.

The first section focuses on the biological underpinnings of differentiation waves, and moves from macroevolution to the developmental biology of a model organism (Axolotl), and finally onto intracellular components (cytoskeletal filaments). While this is a somewhat audacious agenda for only five chapters, Gordon and Gordon use this space to set up the story of a possible mechanism for differentiation waves. This requires some selective presentation of the available data, but also balances biological reality with the book's main message. In the next five chapters, a formal mechanism for differentiation waves is proposed. While it may seem somewhat *ad hoc* to an experimentalist, this mechanism is a refinement of a previously published model (Lu, Cao, and Gordon, 2012). The approach taken can best be described as a "biologically plausible abstraction", where an abstraction is a theoretical construct that describes the essential function (if the not complete structure) of the proposed mechanism within its biological context. For example, while the authors define a cell state splitter as a binary switch, the proposed switch actually describes actions the cell must make to decide between one state and another. Such abstractions are commonly found in the systems biology literature, and in these cases rely heavily on computational analysis. Gordon and Gordon approach their theoretical propositions in a qualitative fashion, but present the concept of biological switches in a more empirical fashion. Also to their credit is the inclusion of diagrams that demonstrate developmental scenarios that lead to their expected outcomes.

The final section provides quite a bit of speculation, and in some ways seems disconnected from the rest of the book. It is worth noting, however, that many of these ideas are sketched out in more detail within "*The Hierarchical Genome and Differentiation Waves*" amongst its many propositions. It is also worth noting that ideas such as progressive evolution and implicate wholeness are either controversial or not typically thought of as relevant biological problems. In particular, the last chapter (implicate wholeness) relies on insights from fields such as physics and philosophy of science. Perhaps this is a flight of fancy, yet we can also learn something quite profound from these two chapters. One is that we often do not fully appreciate the limits of natural language (and sometimes mathematics) in describing scientific phenomena. The discussion of progress in evolution exposes this quite well: while something may look progressive to the observer, it may not possess a truly progressive set of origins. Progress may also be simply in the mind of the observer, and thus characterizes a subjective observation. While counterfactual arguments might help to overcome these limitations, it is the underappreciated biases of the observer that shape the way we think about biological systems. The role of the scientific observer is also discussed in detail while discussing the implicate wholeness of embryos. As with the notion of evolutionary progress, the observer's context and their partial ability to describe the whole beyond the sum of its parts limits current empirical and theoretical approaches.

In terms of future work, it should be noted that the last chapter could be spread out over three or four chapters to really do justice to these concepts. Of these, the concept of wholeness is probably the most relevant to the practice of developmental biology. The definition of wholeness as presented in this chapter is similar to another elusive topic: weak and strong emergence (Chalmers, 2006). Weak and strong emergence are relevant to the effects that synergistic interactions between individual cells have on the embryogenetic process. In weak emergence, these interactions result in unexpected outcomes at the embryogenetic level. By contrast, strong emergence produces an embryogenetic process that is not deducible from cellular interactions. One consequence of viewing the embryo holistically is that the analysis of a synergistically produced whole embryo provides information that is not available through tools such as pathway analysis or meta-analysis of studies. For example, observations of contraction waves that occur during neural induction formed the initial basis for the differentiation wave theoretical construct (Brodland et.al, 1994). Is one concrete benefit of a holistic approach the ability to discover larger-scale mechanisms from such reductionist observations by using a broader conceptual framework? Read the book and judge for yourself.

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