Physics, genetics, and investigative reasoning in developmental biology

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Approaches to understanding ontogeny that involve physical factors such as flow or deformation have intrigued biologists for more than a century. Wilhelm His (1831-1904) favored explanations of developing chick embryos based on analogies with mechanical phenomena exhibited by non-living materials, such as the folding of rubber tubes (Hopwood 1999). D'Arcy Thompson (1860-1948) generated iconic examples with hypothetical changes in morphological shape derived from cartesian coordinate transformations based on differential growth rates (Olby 1986). Another famous example is Alan Turing's model of spatially constrained reaction-diffusion mechanisms producing pattern formation, such as differential coloration of epithelia or periodic repetitions in leaf structure (Turing 1952).

In all of these cases, the explanatory reasoning is analogical. If physical forces or mechanisms generate specific morphologies in viscoelastic or chemical materials, then similar morphologies in living species could be explained sufficiently by physical forces or mechanisms operating on similar materials in the developing embryo. The living medusa has a geometrical symmetry so marked and regular as to suggest a physical or mechanical element in the little creature's growth and construction... we seem able to discover various actual phases of the splash or drop in all but innumerable living types of jellyfish ...[these] indicate, at the very least, how certain simple organic forms might be naturally assumed by one fluid mass within another, when gravity, surface tension and fluid friction play their part (Thompson 1942).

It is suggested that a system of chemical substances, called morphogens, reacting together and diffusing through a tissue, is adequate to account for the main phenomena of morphogenesis... certain well-known physical laws are sufficient to account for many of the facts (Turing 1952).

Although physical explanations never disappeared completely, they were eclipsed toward the end of the 20th century due to dramatic experimental successes from molecular genetic approaches that transformed experimental embryology into developmental biology (Fraser and Holland 2000). The sentiment was captured in a NIH proposal review from the 1990s: "The physics of how embryos change shape is neither an important nor an interesting question" (quoted in Keller 2002). "For some researchers, development can now be reduced to the interplay of cell-cell signaling and transcriptional regulation" (Gerhart 2015).

Despite this eclipse, a new dawn of developmental inquiry about physical forces has recently emerged: "There has been a renewed appreciation of the fact that to understand morphogenesis in three dimensions, it is necessary to combine molecular insights (genes and morphogens) with knowledge of physical processes (transport, deformation and flow) generated by growing tissues" (Savin et al. 2011; cf. Miller and Davidson 2013). In light of history, what accounts for this new dawn? Why, after all this time, is physics (seemingly) gaining a place at the high table of developmental biology? I argue that one major factor is the use of physical approaches for investigative rather than explanatory reasoning. The capacity of experimental practice to manipulate physical forces surgically, on par with standard genetic approaches, is relatively new. As has been argued elsewhere (Waters 2004), scientific knowledge is structured by investigative strategies as much as theoretical explanations. The explanatory potential of physical approaches to understanding ontogeny has not changed dramatically in recent years; what has changed is the precision of physical manipulations to investigate properties of developing systems. This has increased practical knowledge about how changes in the values of physical variables affect embryogenesis and created evaluative knowledge about what kinds of physical manipulations exhibit fecundity for ongoing inquiry.

I illustrate this situation with two examples: fluid flow in vertebrate cardiogenesis and bioelectricity in planarian regeneration. The former demonstrates how investigative reasoning using physical approaches yields practical knowledge through experimental manipulation on analogy with mutational analysis in the genetic approach (Hove et al. 2003). Explanatory analogies between physical and living systems largely fell on deaf ears; investigative analogies between physics and genetics turned out to be decisive. The latter example bioelectricity exemplifies a novel form of evaluative knowledge: how physical variables (e.g., voltage gradients) can be manipulated using the genetic approach (e.g., via altered expression of ion channel genes) to yield diverse morphological outcomes (Beane et al. 2013). I close with remarks on how this alignment of investigative reasoning between physics and genetics is nurturing new controversies about the purported genetic control of ontogeny the predominant form of explanatory reasoning in developmental biology (Levin 2014).