1.02 The Epigenetic Problem

"The one great exception was Aristotle, whose genius foresaw what [William] Harvey [1578-1657] more explicitly declared two thousand years afterwards. Harvey quotes a sentence from Aristotle which deserves to be remembered: 'All living creatures, whether they swim, or walk, or fly, and whether they come into the world with the form of an animal or of an egg, are engendered in the same way'. And one of the most scholarly of embryologists, Prof. [C.O.] Whitman [1893, 1896a], has said 'that part of Harvey's theory which affirms that the parts of the future organism do not pre-exist as such, but make their appearance in due order of succession, and which is so often cited as the essence of epigenesis, was all clearly stated by Aristotle'" (Thomson, 1910).

The fundamental question of developmental biology is: How do cells differentiate in the right place, at the right time, into the right kinds (Driesch in Reid, 1985)? This question of epigenesis became acute in biology when Driesch (1891a,c) (cf. Driesch, 1892a, 1929; Ravin, 1977; Khaner, 1993) discovered that when he shook apart the two cells in a sea urchin embryo just after the first cell division, both cells formed whole sea urchin larvae:

"The strict atomistic, mechanistic paradigm applied to organisms led Driesch in 1891 to expect the echinoderm egg to behave like a good machine.... Driesch formed his expectations in such allegiance to the paradigm that he was certain his experiment of [separating]... the first two blastomeres resulting from the first cleavage of sea urchin eggs would result in half-embryos. The appearance of whole little animals in his dish precipitated a practical and philosophic crisis of the first rank in embryology" (Haraway, 1976).

("This work impressed me profoundly as a young biologist, and it still does": Sinnott, 1966.) Driesch's observation contradicted an earlier result by Wilhelm Roux in frogs (Roux, 1888a, translated in Willier & Oppenheimer, 1964; cf. Morgan, 1895a; Maienschein, 1991c; Papaioannou & Ebert, 1995), that one cell of a two cell embryo produced a half embryo, when the other cell was killed (Oppenheimer, 1967; cf. Spemann, 1938). Roux's conclusion was, in retrospect, premature, as Driesch (1891c) anticipated:

"Compared with Roux's results, my findings show a difference between the behavior of the sea urchin and the frog. Still. this difference may not be so fundamental. If the blastomeres of the frog were really isolated and removed from the other half - which was probably not dead in Roux's experiment - might they not behave like my echinoid cells?... I have tried in vain to isolate amphibian blastomeres; let those who are more skilled try their luck at it" (Driesch, 1891c).

"Although [Driesch]... was the initial challenger of Roux's half-embryo experiments, his opposition to Roux seems quite benign, and his regeneration experiments on more advanced stages of development supported Roux's notions of a *Mosaikarbeit* [mosaic process] and of the specificity of the germ layers, which is seldom mentioned in histories that wish to emphasize the dramatic contrast between their famous blastomere experiments.... Driesch used to stay at Roux's home when he passed through Halle" (Churchill, 1991b).

"Not only in the egg of the sea urchin and *Triton* [a newt], but also in that of the frog, a whole embryo originates from a completely isolated blastomere. That same blastomere, however, forms - at least at first - a half embryo when the other blastomere, although destroyed, remains in connection with it. This is the case not only in the frog's egg, but also in the egg of the axolotl, as we know from the work of D. Barfurth (1893).... When the isolation is absolute, a change toward the 'whole,' a regulation, takes place. When the isolation is incomplete this change does not occur" (Spemann, 1938).

"Morgan [1895a]... shocked his European colleagues by showing that the mutilation of one cell of a two-celled frog embryo does not lead inevitably to a deformed half-embryo, as they had thought. Rather, if the remaining live cell were turned upside down, a normal embryo ['*of half-size* ': Morgan, 1897a] would form!" (Carlson, 1981).

The 'shock' is a bit difficult to understand, given the first result of this kind by Chabry (1887) in ascidians (Dalcq, 1957; cf. Churchill, 1973; Fischer, 1991; Wolpert, 1991b):

"A paper of Chabry which has not become generally known is the only other investigation of this kind known to me. With a very refined apparatus constructed for the purpose, Chabry killed individual blastomeres - among others one of the first two cells.... The French investigator nowhere refers to the fundamental result of his experiment: namely, that from the unoperated blastomere there developed *not a left or right half-embryo, but always an entire embryo of half size*, from which, to be sure, certain organs of minor importance (otoliths, suckers) were missing.

"His exposition and illustrations make this certain: The result *is essentially contradictory to that of Roux*. I must note that I became aware of Chabry's work after completion of my own experiments" (Driesch, 1891c).

We also now know that Roux's form of the experiment involving incomplete separation of the two halves (when applied to sea urchins) does not yield a half embryo (Khaner, 1993).

Driesch could not see a solution to this question of how a whole could split into two wholes, and was driven towards espousal of vitalism, which had come to mean that there is a mysterious essence of life, the entelechy, which is not reducible to, but exists mingled with, physical and chemical phenomena (cf. Rádl, 1930; Schubert-Soldern, 1962; Mayr, 1976; Freyhofer, 1987; Sander, 1993a):

"Vitalism is easiest to take seriously when science is ignorant of what lies behind various biological processes. For example, before the physical basis of respiration was understood, it was possible to suggest that organisms are able to breathe only because they are animated by an immaterial life principle. Similarly, before molecular biology explained so much about the physical basis of heredity, it was possible to entertain vitalistic theories about how parents influence the characteristics of their offspring. The progress of science has made such claims about respiration and inheritance wildly implausible...

"The area of development (ontogeny) is full of unanswered questions. How can a single-celled embryo produce an organism in which there are different specialized cell types? How do these cell types organize themselves into organ systems? No adequate physicalistic explanation is available now, so why not advance a vitalistic claim about ontogenetic processes? The point to recognize is that vitalism does not become plausible just because we currently lack a physical explanation.... Although there is no reason to doubt that these phenomena *are consistent with* our current best physical theories, no one has the slightest idea how the physics might be put to work" (Sober, 1993).

Supplying the beginning of that physical theory is what this book is about. Here, in Driesch's own words, is what turned him to vitalism:

"The experiments of several years upon the power which organisms possess of regulation of form, and continual reflection on the collective results of experiments on the physiology of development, upon which I had been working since 1891, combined with a logical analysis of the concepts of 'regulation' and 'action,' brought about an entire change of my opinions and the gradual elaboration of a complete system of Vitalism....

"Analytic experimental embryology - Entwicklungsmechanik, as Roux has called it [cf. Maienschein, 1991b] - has been able to show that there are many kinds of embryonic organs or even animals which, if by an operation deprived of part of their cells, behave in the following way: of whatever material you deprive these organs or animals, the remainder, unless it is very small, will always develop in the normal manner, though, so to speak, in miniature. That is to say: there will develop out of the part of the embryonic organ or animal left by the operation, as might be expected, not a part of the organisation *but the whole*, only on a smaller scale. I have proposed the name of *harmonious-equipotential systems* for organs or animals of this type; they are 'equipotential,' because all their elements (cells) quite evidently must possess the same morphogenetic 'potency,' otherwise the experimental result would be impossible; and their elements work 'harmoniously' together in each single experimental case....

"...Take from the blastula of a sea-urchin whatever you like (but not more than three-quarters) and the rest will always develop into a very small *but complete* 'Pluteus.'

"...Experiments now show that any part of the system, however large and wherever taken, may be cut away from it without disturbing proportionate development. This proves that a 'machine' cannot be the basis of harmonious-equipotential differentiation: for a 'machine,' *i.e.* a specific arrangement of physico-chemical things and agents, *does not remain itself, if you take from it whatever you please....*

"The harmonious system, then, is not a 'machine'; it is, in fact, as it seemed from the beginning, a something that is governed by Individualising Causality. 'Entelechy,' as a non-mechanical agent of nature, is at work in the harmonious-equipotential system" (Driesch, 1914).

What we need to come to grips with is how to have our whole, harmonious equipotential system without invoking a mystical entelechy.

1.03 Wholeness and the Symmetry of the Early Embryo

One way of looking at wholeness is in terms of the symmetry properties of the early embryo. Wilson (1925) tried to dismiss Driesch's findings on the