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**A HISTORY OF REGENERATION RESEARCH**

**Milestones in the evolution of a science**

*Edited by*

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## T. H. Morgan's regeneration, epigenesis, and (w)holism

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Those who know Thomas Hunt Morgan primarily as a well-established geneticist, and those who value the successes in twentieth-century reductionist programs in genetics, will be surprised to learn that Morgan began his career as a wholist.<sup>1</sup> In fact, Morgan clearly did deny the efficacy of reductionism. Indeed, his first two decades of research exhibit a concern with the organism as a whole that has come in more recent decades to be associated with fuzzy thinking and sloppy vitalism. Textbooks often ridicule such biologists gone wrong as Hans Driesch, who finally turned to philosophy rather than biology to support his vitalistic and wholistic position. Modern biology tries to convert such biologists as Morgan, Charles Manning Child, J. S. Haldane, and Jacques Loeb into something other than they were by omitting discussion of their wholistic inclinations.

It is worthwhile to explore such wholistic ideas and to attempt to understand why in the early part of this century they seemed both consistent with good science and necessary. This, in turn, should help to illuminate the perpetual discussion of whether biology should be in some interesting way considered a unique science or whether it is just

<sup>1</sup> Key terms such as "wholism," "holism," and "materialism," will be defined in the course of the chapter. These terms have been given a widely varied range of meanings by different writers, which has created and continues to create a great deal of confusion. Garland Allen, for example, insists that Morgan was a "dialectical materialist." For Allen, such materialists are "concerned with the complex interactions between parts in a whole. They see the whole as equal to more than the sum of its parts (i.e., to the sum of the individual parts plus their interactions). They reject the simplistic billiard-ball model of physical processes. They see all processes in the world undergoing constant change, motivated by the interaction of various contradictory (dialectical) elements within the systems themselves." Garland E. Allen, *Thomas Hunt Morgan: The Man and His Science* (Princeton: Princeton University Press, 1978), p. 327. I do not agree that Morgan fits this description, and I offer an alternative interpretation, using the term "wholism" to emphasize the distinction.

like physics and chemistry. Focusing on Morgan, who should prove noncontroversially respectable to all parties, rather than on a "suspect" individual like Driesch or a less well-known figure like Child, should demonstrate the pervasiveness of wholistic thinking.<sup>2</sup> It should also reveal the central role that regeneration played in establishing respectability, however fleeting, for that position.

### Morgan on development

During the 1890s, Morgan explored a wide range of questions about embryological development of a variety of organisms. Among other projects, he began a survey of studies of frog development, which had become a popular subject in recent years. Europeans in particular had been centrifuging frogs' eggs, putting them under pressure, rotating them within gravitational fields, killing blastomeres, and otherwise subjecting them to various sorts of manipulations. The result was a plethora of data and interpretations. All assumed that the frog's egg is essentially a material thing, with no special vital forces involved in directing its production or development. None of the leading researchers invoked special vital forces or entities to account for embryonic action. All assumed that some combination of motions and forces, either internal or external to the egg, direct development. But not all agreed as to the relative importance of the various possible forces. Nor did all agree that development could be explained simply by reducing the developmental phenomena to the actions of matter in motion. Morgan examined the subject and surveyed the literature in his book *The Development of the Frog's Egg*.<sup>3</sup> Not surprisingly, the project took him longer than he had expected and carried him into a consideration of larger questions about the nature of development and to a level of detail that he had not anticipated. He went to Europe in 1894-5, in part to complete the book.

Inspired by Jacques Loeb, his colleague at Bryn Mawr College in 1891-2, and by his friends from the Johns Hopkins University graduate school and the Woods Hole Marine Biological Laboratory, including Edmund Beecher Wilson, Morgan also began by 1893 to carry out an experimental study of the development of marine invertebrates. He read about the experimental studies of development emerging from laboratories in Germany (which Wilson had just visited for a year

<sup>2</sup> Sharon Kingsland, on Child and Herrick, in progress.

<sup>3</sup> Thomas Hunt Morgan, *The Development of the Frog's Egg: An Introduction to Experimental Embryology* (New York: Macmillan, 1897).

and from which Loeb had come to the United States), and he began to explore the same sorts of questions using the same kinds of techniques. His own visit to the Naples Zoological Station in 1894–5 reinforced his interest and directed him also toward new techniques and questions. There he became good friends with Hans Driesch, who had a provocative point of view and a high level of energy that promoted eager discussion among the young embryologists gathered in Naples.

By 1894, when Morgan met him, Driesch had moved from the strict mechanistic and reductionistic position he had originally held. He had begun to suggest that although an analytic, or mechanistic, account of development was appropriate, perhaps that account need not be reductionistic.<sup>4</sup> Such a distinction calls for clarification of terms.

In the context of this discussion, materialism and mechanism are taken to be primarily ontological positions. They assert that the nature of what exists in the world is material or a combination of matter and motion. Materialists hold that there is no special vital something that exists in addition to matter and motion. There are no vital forces or vital entities in the world. Yet a materialist need not be a reductionist. Instead the materialist might adopt the wholist position that what exists in the world is complex, interactive wholes; alternatively the materialist might insist that what exists is really parts, which have reality of their own. For "reductionism" is taken here as an epistemological position, referring to the reduction of theories, explanations, or sentences.<sup>5</sup> The reductionist biologist claims that all of life's phenomena can be reduced to – that is, explained in terms of – physics and chemistry. Yet others might hold that there is something about living phenomena that goes beyond the basic properties and laws of physics and chemistry. In particular, the whole might be more than the sum of the parts; that is, there might be something about the nature of the whole organism that makes it act in a way that cannot be explained in terms of the sum of the actions of the parts. This view is generally labeled "holism." Driesch was beginning to explore this holistic position by 1894, as well as a wholistic ontology. So was Morgan.

<sup>4</sup> For example, Hans Driesch, *Analytische Theorie der organischen Entwicklung* (Leipzig: Wilhelm Engelmann, 1894).

<sup>5</sup> There is a vast literature on mechanism, vitalism, and reductionism, much of it quite unilluminating and confusing. In large part this stems from the varied and contradictory use of the terms by different writers, or even by the same writers. I use the terms in a way that seems to make sense, coincides with their meanings in embryology around 1900, and remains consistent with the major historical and philosophical discussion of the subject.

### Morgan's move to regeneration

By 1895, Morgan realized that it was difficult to get at the basic processes of normal development simply by peering at developing embryos. Yet radical, highly interventionist experimentation raised the question of whether the resulting process remained sufficiently like normal development to provide any useful information. Regeneration experiments, however, seemed to mimic natural conditions and could therefore provide information about normal developmental processes.

In a paper of 1896, Morgan began thinking about regeneration. He first reported on his own and other studies of partial embryos.<sup>6</sup> In 1888, Wilhelm Roux had stimulated a succession of explorations of the frog's egg in which one of the first two, or four, or eight blastomeres was pricked with a hot needle and thereby, evidently, killed.<sup>7</sup> The resulting partial embryo could still develop, Roux showed, but only into the part that it normally would have become. The part could not compensate for the absence of the rest of the material. Or so Roux had believed at first. Yet time produced conflicting results, and Roux later concluded that the part is capable of a process of "postgeneration" that resembles the normal regeneration process and by which the part "re"-generates the whole.

In contrast, Driesch's study of sea urchins, initially intended to support and extend Roux's results for frogs, had shown clearly by 1892 that partial embryos can indeed develop into whole larvae.<sup>8</sup> The part is capable of producing the whole and actually does so. This suggested that something about the nature of the whole was available in the part, or at least that the wholeness could be regenerated after injury. But how? And was a certain minimal size of material or minimal number of cells required before regeneration could occur? Driesch, Wilson, Morgan, and a handful of others took on these questions in the 1890s.

<sup>6</sup> Thomas Hunt Morgan, "Studies of the 'Partial' Larvae of *Sphaerechinus*," *Archiv für Entwicklungsmechanik der Organismen* (1895) 2: 81-126.

<sup>7</sup> Wilhelm Roux, "Beiträge zur Entwicklungsmechanik des Embryo. Über die künstliche Hervorbringung halber Embryonen durch Zerstörung einer der beiden ersten Furchungskugeln, sowie über die Nachentwicklung (Postgeneration) der fehlenden Körperhälften," *Virchow's Archiv* (1888) 114: 113-53; partly translated in B. Willier and J. Oppenheimer, eds., *Foundations of Experimental Embryology* (Englewood Cliffs, N.J.: Prentice-Hall, 1964), pp. 2-37.

<sup>8</sup> Hans Driesch, "Entwicklungsmechanische Studien. I. Der Werth der beiden ersten Furchungszellen in der Echinodermentwicklung. Experimentelle Erzeugen von Theil- und Doppelbildung," *Zeitschrift für wissenschaftliche Zoologie* (1892) 53: 160-78 and 183-4; translated in Willier and Oppenheimer, *Foundations*, pp. 38-50.

Morgan concluded, after carefully surveying the literature and his own accumulating results, that partial larvae of sea urchins behave like the material in normal and familiar cases of regeneration. The whole is regenerated from the part, just as surely as a worm can regenerate its tail or a crab its leg. Furthermore, it must be conditions internal rather than external to the organism itself that drive development, despite the pressures from outside the egg that have caused the artificial condition.

But the process of regeneration is not just a simple mechanical or chemical playing out of preexisting directions, Morgan concluded. Rather:

In much the same way, an animal or plant tends in many cases to replace a part of itself that has been lost or injured by external agencies; i.e. we say the whole is regenerated from a part. We can find no chemical or physical explanation for any of these phenomena. It does not make our problem any easier to admit the possibility that factors may be present in the ontogeny that are dependent on principles unknown and unrecognized by the chemist and physicist. We call these "vital" factors and in many of the fundamental problems of Biology, such as development, cell-division, and regeneration these vital processes come to the front. So far as we can see at present the vital factors that control the development do make use of many known chemical and physical properties of matter, but it seems to me that it is very rash at present to conclude therefore that the vital processes of living things are necessarily only the complex of known physical and chemical processes.<sup>9</sup>

There was no legitimate reason to assume that special vital somethings exist, but the living phenomena might be the product of something more than the sum of known physical and chemical processes. Morgan certainly left the door open to vitalism, although he inclined more to a materialistic wholism. As yet, however, he sought to remain agnostic. He simply did not think there was sufficient scientific evidence to permit researchers to determine either the ontological or the epistemological question definitively one way or the other.

By 1897, Morgan had read August Weismann's theoretical explanation of regeneration as a process derived from evolution by natural selection, had decided that it was entirely unsupported, and had turned directly to investigating regenerative phenomena himself.<sup>10</sup>

<sup>9</sup> Morgan, "The Number of Cells in Larvae from Isolated Blastomeres of *Amphioxus*," *Archiv für Entwicklungsmechanik der Organismen* (1896) 3: 269-94 (quoted from p. 292).

<sup>10</sup> Morgan, "Regeneration in *Allolobophora foetida*," *Archiv für Entwicklungsmechanik der Organismen* (1897) 5: 570-86. Weismann then responded to Morgan in a paper widely available to his English-speaking audience: "Regeneration: Facts and Interpretations," *Natural Science* (1899) 14: 305-28.

Following up studies by Loeb and Driesch on planarians, Morgan discovered the animals' ability to regenerate the normal parts under a wide variety of complicated conditions. This showed that they did not just add on new material after an injury in order to replace the missing old material. Rather, they actually had the power to transform the old material into a new part. "We see here not only a power of regeneration," Morgan concluded, "but also a subsequent self-regulation, and by means of the latter the normal relations of the parts, characteristic for the species, are regained." Surprisingly, the body material of the already formed planarian remains "almost as plastic as that of an undivided or dividing egg."<sup>11</sup> Something about the nature of the whole made it possible for the individual to transform material and regulate the characteristics of the whole. Morgan called this process "morphallaxis."

In another paper of 1898, Morgan took on Weismann's theory directly. Weismann had argued that certain parts of an organism are more susceptible to injury than others. These, influenced over the course of time and by the constant action of evolutionary forces, gain a power to regenerate because of a built-in set of auxiliary inherited materials that guide the reconstruction of the part in question. Thus, according to Weismann, ability to regenerate is correlated with liability to injury. This view was particularly appealing because it implied that an injured organism only needed to kick into action a preexisting and inherited capacity for regenerating a missing part. It did not have to go through a complex epigenetic process of determining what part was needed and then generating it anew. Yet this predeterministic interpretation did not appeal to a committed epigenesist like Morgan.

In a series of studies, Morgan sought to establish that this view is false and that regeneration is akin to the normal developmental processes, rather than a special ability adapted for special cases. By showing in hermit crabs, for example, that the parts most likely to be injured are not those most able to regenerate, he undercut Weismann's theory.<sup>12</sup> If Weismann was wrong, however, the question remained, What does cause regeneration? And this is really the key. For Weismann's preformationist account could easily explain regeneration if the injured organism simply grows the right sort of part by adding new material as directed by hereditary information. Morgan

<sup>11</sup> Morgan, "Experimental Studies of the Regeneration of *Planaria maculata*," *Archiv für Entwicklungsmechanik der Organismen* (1898) 7: 364-97 (quoted from pp. 389, 396).

<sup>12</sup> Morgan, "Regeneration and the Liability to Injury," *Zoological Bulletin* (1898) 1: 287-300.

did not accept that idea, and he therefore had to provide a much more difficult, epigenetic account of regeneration, as well as of generation in the first place.

Morgan spent part of the summer of 1898 in Europe, visiting Naples and elsewhere. On his return trip to the United States in September, he found himself with time on his hands in London when his ship was delayed. He went to the British Museum and read classic eighteenth-century regeneration studies, particularly those of Trembley and Bonnet. As he wrote to Driesch, he found these works much more interesting than contemporary work on the subject.<sup>13</sup> These eighteenth-century theories became the starting point for Morgan's systematic treatment of regeneration.

In lectures he gave at the Woods Hole Marine Biological Laboratory in Massachusetts in 1898 and 1899, Morgan considered the various alternative theories and the available data about regeneration. The fact that a part can regenerate a new whole in a way parallel to the action of normal development raised a most interesting problem, namely to explain how that epigenetic response to abnormal conditions is possible. Morgan concluded that

something more is included in these phenomena . . . than can be explained by simple physical interaction or by chemical influences. The process that takes place suggests that something like an intelligent process must be at work — I mean that what we call correlation of the parts seems here to belong rather to the category of phenomena that we call intelligent, than to physical and chemical processes as known in the physical sciences. The action seems, however, to be intelligent only so far as concerns the internal relations of the part, i.e., it acts rather as a "perfecting principle" than as a process of adaptation to external needs (adaptation).<sup>14</sup>

Morgan realized that to account for this "perfecting principle" in a way that was not vitalistic but that provided a real — that is, a legitimate — scientific explanation was the central problem for the study of embryology and regeneration.

Furthermore, not only might an extraphysical, intelligent process be at work, but normal reductionist methods from the physical sciences might prove inadequate to the biological task. Morgan explained:

<sup>13</sup> Morgan to Driesch, September 13, 1898, cited in Allen, *Morgan*, pp. 86–7.

<sup>14</sup> Morgan, "Some Problems of Regeneration," *Biological Lectures Delivered at the Marine Biological Laboratory of Woods Hole* (hereafter cited as *Biological Lectures*), (1899) 1898: 193–207 (quoted from pp. 205–6).



In much of our biological work we have been guided by methods derived from the physical sciences, and most fortunately so, for perhaps only in this way can we hope to reduce living phenomena to simpler terms. But sooner or later we meet with a factor that defies further physical analysis, and this factor seems to be present in all biological phenomena. We gain nothing by calling it a vital force, unless we can define what we mean by vitality. Whether or not this factor\* [Morgan's footnote: "It is simpler to speak of it as one factor, but it may equally well be true that there are many factors."] is only a complex of physical forces that we cannot unravel, or whether there exists something that cannot be expressed in terms of physics and chemistry – that is the question!

We err, I think, in going at present to either extreme, i.e., either in ignoring this something that has been called a vital force and pretending that physics and chemistry will soon make everything clear, or, on the other hand, in calling the unknown a vital force and pretending to explain results as the outcome of its action.

In our studies of the development of form we meet most often with this factor. Are we at bottom trying to give a causal explanation of form itself, and, if so, is not our problem insoluble? Can we hope to do more than determine under what internal and external conditions a given form appears? If we limit our researches to this problem we can hope to succeed. But can we go back of this and explain the reaction itself? At present we have not succeeded in doing so, any more than has the mineralogist explained the form of the crystal. It may be that what we call a formative force or a vital force is the property of living things to assume a given form under certain conditions. If so, is there here legitimate ground for investigation, or rather let me ask, can we hope to extend our investigations beyond the knowledge of the internal and external conditions within which new forms arise. It is this uncertainty in regard to the problem of vitality that we need first to clear up, and it seems to me that this is the cardinal point for us to examine at present. It is possible, I think, by means of experiment alone, to determine how far and in what sense we can pursue the investigation of the causes of form. In this regard experimental studies on the regeneration of animals and plants offer a most admirable field for future work.<sup>15</sup>

And so Morgan launched into an experimental study of regeneration, seeking a "verifiable hypothesis," since he felt that only in this way could progress be made in science.<sup>16</sup>

Experiments with hydromedusae, earthworms, more with planarians, studies of frogs (including grafting of pieces between two different species, to determine which tissue gives rise to the regenerated part) – all contributed to Morgan's suggestions in his 1899 Woods Hole lecture. There he discussed earlier theories of regeneration, considered the alternatives in more detail than during the preceding summer, addressed current work on the subject, and formulated what

<sup>15</sup> Ibid., pp. 206–7.

<sup>16</sup> Morgan, "Regeneration in *Hydromedusa*, *Gonionemus vertens*," *American Naturalist* (1899) 33: 939–51, p. 950, calls for such a hypothesis.

he described as a tentative and temporary working hypothesis. What we call "regeneration" involves many different phenomena, he had concluded, and this makes any theory of regeneration difficult to achieve. In particular, the phenomena of "morphallaxis," as Morgan called it, or the remodeling of existing material into new parts, caused problems for a simple interpretation. It would be far easier to explain how the organism might add on new material of the proper sort than to account for how already existing and already differentiated material parts become transformed in some coordinated way that retains the organism as a whole.

The central phenomenon, Morgan suggested, was the way in which an injury, however it is caused, stimulates molecular changes within the whole body of the injured organism. "It is this molecular change that, dominating the subsequent development, seems to control it, and gives us the impression of formative processes at work." This might sound mystical, he realized, and yet "the formative processes are only the expression of the physical, molecular structure that has been assumed by the piece."<sup>17</sup> Although a full theory remained to be developed, he felt that the molecular (and hence physicochemical) nature and the organization of the whole seemed crucial to explaining development. He had made progress toward a mechanical account since the previous talk of a vague "perfecting principle," but he was no closer to a reduction of the explanation to physical and chemical terms.

The next year brought further results and further suggestions. Perhaps the physical or chemical structure of the original part is carried directly over into the new material that is bringing about the regeneration; perhaps there are formative "stuffs" or "actions" of some sort. But Morgan rejected this view because the material retains its plasticity and therefore cannot have been so completely specified that the specification alone could explain its subsequent development into a particular part. The new material remains too "omnipotent" for such an account to work. Vague as the conclusion necessarily remained, Morgan felt that he must "suppose that there is something in the structure or composition of the head and tail, that may act as a determining factor in the production of heteromorphic regeneration."<sup>18</sup> The organization was key.

Yet the nature of this structure or organization remained the critical point, and Morgan continued to attack that problem. In a more gen-

<sup>17</sup> Morgan, "Regeneration: Old and New Interpretations," *Biological Lectures* (1900) 1899: 185–208 (quoted from p. 207).

<sup>18</sup> Morgan, "Regeneration in Planarians," *Archiv für Entwicklungsmechanik der Organismen* (1900) 10: 58–119 (quoted from p. 113).

eral article of 1901, he compared the phenomena of regeneration in the egg, the embryo, and the adult. All exhibit parallel processes, he concluded, and all show that some organization of the whole organism lies behind and directs development.

Somehow a piece of an egg, for example, which can have no inherited or preestablished bilateral symmetry, since it is only part of a normal whole, nonetheless manages to give rise to a properly bilateral embryo. Since it clearly cannot have relied on a preestablished symmetry, it must have assumed that symmetry. Regeneration must have been epigenetic, rather than preformed, and cannot have resulted from any simple inherited structure or stuffs. Yet this "gives us one of the most interesting and also important problems with which the student of experimental embryology has to deal. We know of nothing similar taking place in inorganic nature."<sup>19</sup>

Crystal formation is not parallel, since the crystal never has to reorient and rearrange itself in this way. Nor is the way in which pieces of a magnet reorient themselves analogous, for, Morgan continued,

our conception of the polarity of the magnet rests on the idea that it is the sum total of the polarities, or, perhaps, of the orientation of the minutest elements, the molecules, of which the magnet is made up, while our conception of the organization of the egg is exactly the reverse (or at least I shall try to show that we must really believe this to be the case), and we must think of the entire egg as a whole and not the sum total of an infinite number of smaller wholes. We may claim, I think, that this property of the egg substance of forming itself into a new whole is peculiar to the living protoplasm and is a property that we do not find, or have not found as yet, in inorganic, or perhaps we may go further and say in dead, matter. If we choose to call this property of living matter a vital factor in the sense that it is not found in matter that is dead there can be, I think, little objection to so doing. If the statement seems to be arguing in a circle, we may state more simply that those properties of living things that are not shown by non-living things we shall call vital properties. We may add that we cannot be sure, at present, whether these vital factors will conflict with our present ideas of causality or not; they seem rather to be, however, new causal phenomena peculiar to certain organic substances or compounds, but it would be out of place here to examine further into these difficult questions.<sup>20</sup>

And further:

We are therefore, I believe, also justified in calling the organization of living things a vital property in the sense, to repeat what I have just said, that it is

<sup>19</sup> Morgan, "Regeneration in the Egg, Embryo, and Adult," *American Naturalist* (1901) 35: 949-73 (quoted from p. 956).

<sup>20</sup> *Ibid.*, p. 957.

peculiar to this kind of substance or structure, and not the result of a complex of known physical principles; or, in other words, it is a physical phenomenon as fundamental as the polarity shown by crystals or the magnetism of the magnet, and just as the latter are associated with certain kinds of matter, so is the organization associated with the substance protoplasm.<sup>21</sup>

This emphasis on organization and the nonphysical nature of that organizational property did not mean that Morgan had succumbed to vitalism, however. He remained strongly inclined to a materialist ontology even though he recognized the difficulty of supporting this point of view. He wrote to Driesch, in response to a paper of Driesch's on vitalism:

I had intended reading again your paper on vitalism in order that I might write to you more specifically about it. I do not dare begin, however, for my letter would never come to an end. I follow you a long way, but cannot truthfully say that I consider you have "proven" the existence of a principle of vitality — except insofar as there is much that we cannot explain. Loeb thinks, and I am almost prepared to follow him, the idea is a sterile one in regard to its value as a working hypothesis; at any rate, it comes dangerously near to metaphysics in our present state of knowledge. That, however, is only a matter of opinion.<sup>22</sup>

### *Regeneration*

In 1900, Morgan was invited to deliver a set of lectures at Columbia University. He later expanded those five lectures into a book, *Regeneration*, where he maintained the conclusion that he had been developing throughout his regeneration studies. The factor that allows the injured part of an organism to undergo reorganization and make up a new, functioning organism of the right sort is the internal organization of the whole. The key question, then, must still be "what is organization." Yet: "This it must be admitted is a question that we cannot answer. Looked at in this way the problem of development seems an insoluble riddle; but this may be because we have asked a question that we have no right to expect to be answered."

If the physicist were to ask what gravity is, he would ask just such a question and would likewise have no right to expect an answer. But he can ask other, more accessible questions about gravity, such as what its effects are. So with embryonic development and organization. Yet there is still something about organic organization that seems not

<sup>21</sup> Ibid., p. 973.

<sup>22</sup> Morgan to Driesch, September 13, 1899, quoted in Allen, *Morgan*, pp. 321–2.

parallel to the case of gravity, he argues: "The action of the organism is sometimes compared to that of a machine, but we do not know of any machine that has the property of reproducing itself by means of parts thrown off from itself."<sup>23</sup>

The organization of the developing organism is more complex and demands more study. That study must remain the very center of embryology. For:

It can be shown, I think, with some probability that the forming organism is of such a kind that we can better understand its action when we consider it as a whole and not simply as the sum of a vast number of smaller elements. To draw again a rough parallel; just as the properties of sugar are peculiar to the molecule and cannot be accounted for as the sum total of the properties of the atoms of carbon, hydrogen, and oxygen of which the molecule is made up, so the properties of the organism are connected with its whole organization and are not simply those of its individual cells, or lower units.<sup>24</sup>

Morgan realized that getting at just what this organization means, what causes it, and what effects it brings was basic to embryology. He also recognized the difficulty of that central task. He acknowledged toward the end of the regeneration volume that "there must be a certain amount of vagueness connected with our idea of what the organization can be." It is the structure of the organism "to which are to be referred all the fundamental changes in form" but about which we admittedly know little. In fact, "we know this organization at present from only a few attributes that we ascribe to it, and we are not in a position even to picture to ourselves the arrangement that we supposed to exist."<sup>25</sup>

Morgan accepted Du Bois-Reymond's "Ignorabimus," according to which he acknowledged that there are things in science that we do not now know and things that we shall probably never know. Morgan clearly preferred not to think that this organization was one of the unknowables, but he was prepared to accept that conclusion if forced to do so. In the meantime, he proposed to continue seeking experimental evidence from regeneration studies and elsewhere to provide insights into just what this organization is and how it works.

In the course of his next decades of research on embryology, Morgan discussed the process of differentiation in terms of tensions and pressures within the organism. He suggested, as a working hypothesis, that these mechanical forces might account for organization, although he recognized the rather unspecific nature of the hypothesis.

<sup>23</sup> Morgan, *Regeneration* (New York: Macmillan, 1901), pp. 358-9.

<sup>24</sup> *Ibid.*, pp. 278-9.

<sup>25</sup> *Ibid.*, p. 288.

### The epigenetic perspective

During the early decades of this century, a number of embryologists – particularly the Americans – joined Morgan in calling for an epigenetic and wholistic view of development. Frank Lillie, for example, urged that embryologists consider the “properties of the whole” that produce a “principle of unity of organization.”<sup>26</sup> Scripps Institution of Oceanography director William E. Ritter urged study of the unity of the organism.<sup>27</sup> Charles Otis Whitman insisted many times that the cell could not be considered the fundamental unit of life, if that is taken to mean that understanding the cell will explain all phenomena of life; instead, the interactions of cells are essential and demand an organizing principle.<sup>28</sup>

Edmund Beecher Wilson remained more ambivalent. His specialization in cytology tempted him to view the cell as the basic life unit, yet even Wilson urged that the connections among cells in the organism are crucial and that “the life of the multicellular organism is to be conceived as a whole.”<sup>29</sup> He continued: “The only real unity is that of the entire organism, and as long as its cells remain in continuity they are to be regarded, not as morphological individuals, but as specialized centres of action into which the living body resolves itself, and by means of which the physiological division of labor is effected.”<sup>30</sup> By 1923, however, Wilson acknowledged that when we invoke the action of the “organism as a whole” or some “principle of organization,” in fact we mean that “we do not know.”<sup>31</sup>

Jacques Loeb held to a strictly mechanistic interpretation of life and denied the existence of a special “directive force” that explains organization. Yet he concerned himself with the organism as a whole and sought to account for the interactions of the various parts in terms of chemical reactions and interactions. Like Morgan, Loeb saw regeneration as a central problem for embryology. Asking what causes injured parts to regenerate only when injured and not otherwise – in other words, asking how the part knows to regenerate – Loeb concluded

<sup>26</sup> F. R. Lillie, “Observations and Experiments Concerning the Elementary Phenomena of Embryonic Development in Chaetopterus,” *Journal of Experimental Zoology* (1906) 3: 153–268, especially the section “Properties of the Whole.”

<sup>27</sup> William E. Ritter, *The Unity of the Organism* (Boston: Badger, 1919).

<sup>28</sup> Charles Otis Whitman, “The Inadequacy of the Cell Theory of Development,” *Journal of Morphology* (1893) 8: 639–58.

<sup>29</sup> E. B. Wilson, *The Cell in Development and Inheritance* (New York: Macmillan, 1896), p. 41.

<sup>30</sup> E. B. Wilson, “The Mosaic Theory of Development,” *Biological Lectures* (1894) 1893: 1–14 (quoted from p. 9).

<sup>31</sup> E. B. Wilson, *The Physical Basis of Life* (New Haven: Yale University Press, 1923), pp. 45–6.

that "certain substances" were involved. These "certain substances" circulate throughout the organism. They accumulate and prevent further growth when the organism is completely developed. Then injury can cause them to flow into the hurt part and to stimulate regrowth or regeneration. Thus, according to Loeb, it is "utterly unnecessary to endow such organisms with a 'directing force' which has to elaborate the isolated parts into a whole."<sup>32</sup> The movement of chemical substances can explain all.

Charles Manning Child developed a different point of view, but one responding to the same impulses. Individuality of the whole organism is achieved through the establishment of a system of gradients in the individual. The gradients develop, become more strongly established, and eventually gain virtual permanency. At that point, in conjunction with other, related changes, the parts of the organism have been made into an interacting whole. "From this point of view," Child concluded, "the assumption of a mysterious, self-determined organization in the protoplasm, the cell or the cell mass as the basis of physiological individuality becomes entirely unnecessary."<sup>33</sup> For Child, the internal structure determined by the set of gradients and the responses to the external world can explain normal development and regeneration alike.

A host of others made similar calls for an epigenetic interpretation of development, in which no appeal was to be made to the preexistence of inherited units of information that simply unfold or grow up to bring into existence the adult differentiated being. This emphasis was accompanied by other demands to understand epigenetic development in terms of the whole organism, rather than simply as the sum of the individual parts. The fundamental nature of life seemed, to many biologists in the early decades of this century, to require such epigenetic and wholistic thinking.

The next decades brought new lines of research trying to get at the same phenomenon of organization. Carl Vogt's use of advanced vital staining techniques established a detailed fate map for the frog's egg, for example. This showed that normal eggs are already highly specified, so that materials from different locations in the egg become particular germ layers and particular parts of the embryo and adult with great regularity. Normal development is highly directed by the structure and materials of the egg. This made the phenomena of

<sup>32</sup> Jacques Loeb, *The Organism as a Whole from a Physicochemical Viewpoint* (New York: Putnam, 1916), pp. 9-10.

<sup>33</sup> Charles Manning Child, *Individuality in Organisms* (Chicago: University of Chicago Press, 1915), p. 41.



regeneration all the more puzzling and all the more important, for discovering how the egg regenerates in response to disruptions might well reveal the developmental processes by which it became so highly directed in the first place.

Hans Spemann's work on tissue transplantation also held significant promise for explaining both normal development and regeneration. By 1918, Spemann had begun adapting Gustav Born's technique of transplanting pieces of embryonic tissue from one individual to another. With differently pigmented members of different species, the experimental technique allowed the observer to watch the relative contributions to the resulting embryo from each of the pieces of tissue. For example, suppose one takes a piece of tissue that would normally give rise to limb, removes it from the host, and grafts it onto a donor. Does the developmental process that occurs involve tissue from the host, the donor, or both – and how so? The fact that tissue from both host and donor contribute and yet the result is a normally structured and functioning individual shows that the development is not simply predetermined. A fairly sophisticated regulation of the whole must occur.

Spemann also experimented with eggs and with early embryonic tissue. The results of his and others' work showed that the dorsal lip of the blastopore was especially "potent." In 1921, Spemann suggested to his student Hilde Mangold that she should try transplanting pieces of the dorsal lip of the blastopore into a host gastrula. The resulting induction of a secondary embryo at that point suggested that the development worked through a kind of chemical action, not unlike Child's gradients. Spemann developed the concept of the "organizer," which "creates an organization field of a certain [axial] orientation and extent, in the indifferent material in which it is normally located or to which it is transplanted."<sup>34</sup> Spemann certainly emphasized organization of the whole as a responsive and interactive unit, yet he avoided vitalism.<sup>35</sup> He also held an epigenetic view of development.

<sup>34</sup> Hans Spemann, "Die erzeugung tierischer Chimären durch heteroplastische Transplantation zwischen *Triton cristatus* und *taeniatus*," *Roux's Archiv für Entwicklungsmechanik der Organismen* (1921) 48: 533–70 (quoted from p. 568); translated in Viktor Hamburger, *The Heritage of Experimental Embryology: Hans Spemann and the Organizer* (New York: Oxford University Press, 1988), p. 45.

<sup>35</sup> Hamburger, *Heritage*, pp. 65–7; T. J. Horder and P. J. Weindling, "Hans Spemann and the Organizer," in T. J. Horder, J. A. Witkowski, and C. C. Wylie, eds., *A History of Embryology* (Cambridge: Cambridge University Press, 1985), pp. 183–242.



Eventually the concept of the organizer proved problematic, for it was found that a wide variety of substances could induce embryonic change. After the apparent triumph of genetics in the 1950s, embryologists tended to view development in terms of genetics, stressing the action of genetic messages, through developmental genetics. Few researchers have persisted in searching for explanations of how the whole organism maintains its individuality and its ability to regulate and regenerate. Reductionism has come to appear more promising.

As Wilson said, talking about organization amounts to admitting that "we do not know," but scientists always desire to advance knowing rather than deal with not knowing. Increasingly, science has come to be judged in terms of its products – bits of knowledge yielding definite and practical results. Morgan himself accepted this as the goal for science and set off on his productive research program in genetics, which did yield answers.

Yet Morgan remained committed to studying development in terms of epigenesis and of at least whole regions of the organism, if not the whole organism. In his *Embryology and Genetics* (1934), for example, he considered regeneration and asked how we can explain how cells with identical genetic makeup undergo regeneration and reorganization into the appropriate sort of new tissue and thereby allow regeneration into a full organism. He concluded: "The old act as the determiners or organizers of the new, and we can perhaps assume that this is a chemical influence. It is not safe, however, to push such comparisons too far." Induction or action of organizers or determinants was apparently at work; yet just how was not clear. He admits: "The nature of these prospective influences is entirely unknown at present, and may be very different in kind and degree in different parts of the embryo."<sup>36</sup> By 1934, Morgan was focusing more on regions than whole organisms, but he clearly maintained his emphasis on the whole and on epigenesis and resisted the move toward reductionism in embryology.

### Conclusion

Despite the accelerating move away from wholism and toward reductionism in embryology, and in biology in general, questions remain, and the issue has not yet been settled for all time. We still cannot fully account for the remarkable ability of the organism to regulate and

<sup>36</sup> Morgan, *Embryology and Genetics* (New York: Columbia University Press, 1934), pp. 169, 198.

regenerate during development. We may eventually find an explanation in terms of the chemical makeup and physical processes in the organism. Certainly studies on cell-cell interactions, for example, hold promise. Whether we can in fact achieve this reduction remains an open question, and whether we can do so in principle remains a matter of conviction rather than rigorous logical demonstration.

There was something about the ability of the organism to regenerate that led most American embryologists around 1900 to believe in an organization of the whole that amounted to more than the sum of the parts. There may also be something about the nature of our nervous system that, as gestalt psychologists suggest, inclines us to think synthetically rather than analytically and therefore to see the world more easily in terms of wholes than in terms of parts. At any rate, the current bias toward reductionism has not settled the issue, any more than has the morass of writing on reductionism by philosophers of science, especially during the 1960s and 1970s.

Ernst Mayr argues that biology is an autonomous science, in part because living things act as wholes ("as if they were a homogeneous entity") rather than as sums of parts; "their characteristics cannot be deduced (even in theory) from the most complete knowledge of the components, new characteristics of the whole emerge that could not have been predicted from a knowledge of the constituents."<sup>37</sup> Morgan would have neither agreed nor disagreed absolutely, but he would have been sympathetic, as would generations of embryologists. Clearly there is still room for epigenesis and wholism in biology, and it may well be phenomena of regulation in regeneration that best show how they fit.

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<sup>37</sup> Ernst Mayr, *Towards a New Philosophy of Biology* (Cambridge, Mass.: Harvard University Press, 1988), p. 15. For responses, see, for example, Alexander Rosenberg, *The Structure of Biological Science* (Cambridge: Cambridge University Press, 1985), pp. 21-5.