

CHAPTER IX

THEORIES OF INHERITANCE AND DEVELOPMENT

“It is certain that the germ is not merely a body in which life is dormant or potential, but that it is itself simply a detached portion of the substance of a preëxisting living body.”

HUXLEY.¹

“Inheritance must be looked at as merely a form of growth.”

DARWIN.²

“Ich möchte daher wohl den Versuch wagen, durch eine Darstellung des Beobachteten Sie zu einer tiefern Einsicht in die Zeugungs- und Entwicklungsgeschichte der organischen Körper zu führen und zu zeigen, wie dieselben weder vorgebildet sind, noch auch, wie man sich gewöhnlich denkt, aus ungeformter Masse in einem bestimmten Momente plötzlich ausschliessen.”

VON BAER.³

EVERY discussion of inheritance and development must take as its point of departure the fact that the germ is a single cell similar in its essential nature to any one of the tissue-cells of which the body is composed. That a cell can carry with it the sum total of the heritage of the species, that it can in the course of a few days or weeks give rise to a mollusk or a man, is the greatest marvel of biological science. In attempting to analyze the problems that it involves, we must from the outset hold fast to the fact, on which Huxley insisted, that the wonderful formative energy of the germ is not impressed upon it from without, but is inherent in the egg as a heritage from the parental life of which it was originally a part. The development of the embryo is nothing new. It involves no breach of continuity, and is but a continuation of the vital processes going on in the parental body. What gives development its marvellous character is the rapidity with which it proceeds and the diversity of the results attained in a span so brief.

But when we have grasped this cardinal fact, we have but focussed our instruments for a study of the real problem. *How* do the adult characteristics lie latent in the germ-cell; and how do they become patent as development proceeds? This is the final question that looms in the background of every investigation of the cell. In approaching it we may well make a frank confession of ignorance; for in spite of all that the microscope has revealed, we have not yet penetrated the mystery, and inheritance and development still remain in their fun-

¹ *Evolution, Science and Culture*, p. 291.

² *Variation of Animals and Plants*, II., p. 398.

³ *Entwick. der Thiere*, II., 1837, p. 8.

damental aspects as great a riddle as they were to the Greeks. What we have gained is a tolerably precise acquaintance with the external aspects of development. The gross errors of the early preformationists have been dispelled.¹ We know that the germ-cell contains no predelineated embryo; that development is manifested, on the one hand, by the cleavage of the egg, on the other hand, by a process of differentiation, through which the products of cleavage gradually assume diverse forms and functions, and so accomplish a physiological division of labour. We can clearly recognize the fact that these processes fall in the same category as those that take place in the tissue-cells; for the cleavage of the ovum is a form of mitotic cell-division, while, as many eminent naturalists have perceived, differentiation is nearly related to growth and has its root in the phenomena of nutrition and metabolism. The real problem of development is *the orderly sequence and correlation of these phenomena toward a typical result*. We cannot escape the conclusion that this is the outcome of the organization of the germ-cells; but the nature of that which, for lack of a better term, we call "organization," is and doubtless long will remain almost wholly in the dark.

In the following discussion, which is necessarily compressed within narrow limits, we shall disregard the earlier baseless speculations, such as those of the seventeenth and eighteenth centuries, which attempted a merely formal solution of the problem, confining ourselves to more recent discussions that have grown directly out of modern research. An introduction to the general subject may be given by a preliminary examination of two central hypotheses about which most recent discussions have revolved. These are, first, the theory of *Germinal Localization*² of Wilhelm His ('74), and, second, the *Idioplasm Hypothesis* of Nägeli ('84). The relation between these two conceptions, close as it is, is not at first sight very apparent; and for the purpose of a preliminary sketch they may best be considered separately.

A. THE THEORY OF GERMINAL LOCALIZATION

Although the *naïve* early theory of preformation and evolution was long since abandoned, yet we find an after-image of it in the theory of germinal localization which in one form or another has been advocated by some of the foremost students of development. It is maintained that, although the embryo is not *preformed* in the germ, it must nevertheless be *predetermined* in the sense that the egg contains

¹ Cf. Introduction, p. 8.

² I venture to suggest this term as an English equivalent for the awkward expression "Organbildende Keimbezirke" of His.

definite areas or definite substances predestined for the formation of corresponding parts of the embryonic body. The first clear statement of this conception is found in the interesting and suggestive work of Wilhelm His ('74) entitled *Unsere Körperform*. Considering the development of the chick, he says: "It is clear, on the one hand, that every point in the embryonic region of the blastoderm must represent a later organ or part of an organ, and, on the other hand, that every organ developed from the blastoderm has its preformed germ (vorgebildete Anlage) in a definitely located region of the flat germ-disc. . . . The material of the germ is already present in the flat germ-disc, but is not yet morphologically marked off and hence not directly recognizable. But by following the development backwards we may determine the location of every such germ, even at a period when the morphological differentiation is incomplete or before it occurs; logically, indeed, we must extend this process back to the fertilized or even the unfertilized egg. According to this principle, the germ-disc contains the organ-germs spread out in a flat plate, and, conversely, every point of the germ-disc reappears in a later organ; I call this the *principle of organ-forming germ-regions*."¹ His thus conceived the embryo, not as *preformed*, but as having all of its parts *prelocalized* in the egg-protoplasm (cytoplasm).

A great impulse to this conception was given during the following decade by discoveries relating, on the one hand, to protoplasmic structure, on the other hand, to the promorphological relations of the ovum. Ray Lankester writes, in 1877: "Though the substance of a cell² may appear homogeneous under the most powerful microscope, it is quite possible, indeed certain, that it may contain, *already formed and individualized*, various kinds of physiological molecules. The visible process of segregation is only the sequel of a differentiation already established, and not visible."³ The egg-cytoplasm has a definite molecular organization directly handed down from the parent; cleavage sunders the various "physiological molecules" and isolates them in particular cells. Whitman expresses a similar thought in the following year: "While we cannot say that the embryo is pre-delineated, we can say that it is predetermined. The 'histogenetic sundering' of embryonic elements begins with the cleavage, and every step in the process bears a definite and invariable relation to antecedent and subsequent steps. . . . It is, therefore, not surprising to find certain important histological differentiations and fundamental structural relations anticipated in the early phases of cleavage, and foreshadowed even before cleavage begins."⁴ It was, however, Flem-

¹ *l. c.*, p. 19.

² It is clear from the context that by "substance" Lankester had in mind the cytoplasm, though this is not specifically stated.

³ '77, p. 14.

⁴ '78, p. 49.

ming who gave the first specific statement of the matter from the cytological point of view: "But if the substance of the egg-cell has a definite *structure* (Bau), and if this structure and the nature of the network varies in different regions of the cell-body, we may seek in it a basis for the predetermination of development wherein one egg differs from another, and it will be possible to look for it *with the microscope*. How far this search can be carried no one can say, but its ultimate aim is nothing less than a true *morphology of inheritance*."¹ In the following year Van Beneden pointed out how nearly this conception approaches to a theory of preformation: "If this were the case (*i.e.* if the egg-axis coincided with the principal axis of the adult body), the old theory of evolution would not be as baseless as we think to-day. The fact that in the ascidians, and probably in other bilateral animals, the median plane of the body of the future animal is marked out from the beginning of cleavage, fully justifies the hypothesis that the materials destined to form the right side of the body are situated in one of the lateral hemispheres of the egg, while the left hemisphere gives rise to all of the organs of the left half."²

The hypothesis thus suggested seemed, for a time, to be placed on a secure basis of fact through a remarkable experiment subsequently performed by Roux ('88) on the frog's egg. On killing one of the blastomeres of the two-cell stage by means of a heated needle the uninjured half developed in some cases into a well-formed half-larva (Fig. 182), representing approximately the right or left half of the body, containing one medullary fold, one auditory pit, etc.³ Analogous, though less complete, results were obtained by operating with the four-cell stage. Roux was thus led to the declaration (made with certain subsequent reservations) that "the development of the frog-gastrula and of the embryo formed from it is from the second cleavage onward a mosaic-work, consisting of at least four vertical independently developing pieces."⁴ This conclusion seemed to form a very strong support to His's theory of germinal localization, though, as will appear beyond, Roux transferred this theory to the nucleus, and thus developed it in a very different direction from Lankester or Van Beneden. His's theory also received very strong apparent support through investigations on cell-lineage by Whitman, Rabl, and

¹ Zellsubstanz, '82, p. 70: the italics are in the original.

² '83, p. 571.

³ The accuracy of this result was disputed by Oscar Hertwig ('93, 1), who found that the uninjured blastomere gave rise to a defective larva, in which certain parts were missing, but not to a true half-body. Later observers, especially Schultze, Endres, and Morgan, have, however, shown that both Hertwig and Roux were right, proving that the uninjured blastomere may give rise to a true half-larva, to a larva with irregular defects, or to a whole larva of half-size, according to circumstances (p. 422).

⁴ *L.c.*, p. 30.

many later observers, which have shown that in the cleavage of annelids, mollusks, platodes, tunicates, and many other animals, every cell has a definite origin and fate, and plays a definite part in the building of the body.¹

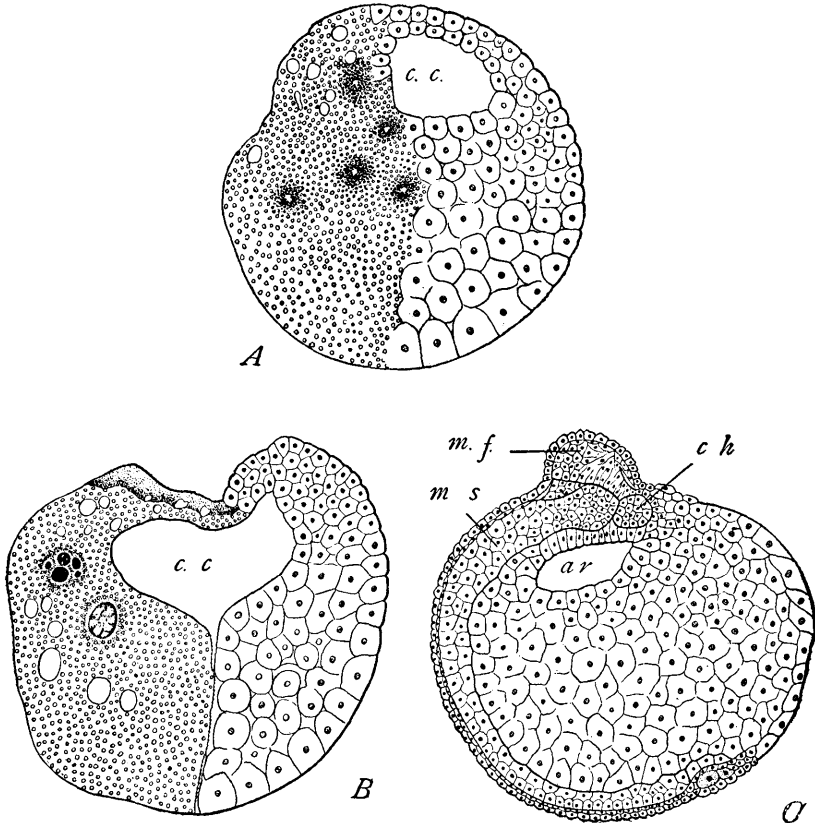


Fig. 182. — Half-embryos of the frog (in transverse section) arising from a blastomere of the two-cell stage after killing the other blastomere. [ROUX.]

A. Half-blastula (dead blastomere on the left). *B.* Later stage. *C.* Half-tadpole with one medullary fold and one mesoblast plate; regeneration of the missing (right) half in process.

ar. archenteric cavity; *c.c.* cleavage-cavity; *ch.* notochord; *m.f.* medullary fold; *m.s.* mesoblast-plate.

In an able series of later works Whitman has followed out the suggestion made in his paper of 1878, cited above, pointing out how essential a part is played in development by the cytoplasm and insisting that cytoplasmic preorganization must be regarded as a leading factor in the ontogeny. Whitman's interesting and suggestive views are expressed with great caution and with a full recognition of the

¹ *Cf.* p. 378.

difficulty and complexity of the problem. From his latest essay, indeed ('94), it is not easy to gather his precise position regarding the theory of cytoplasmic localization. Through all his writings, nevertheless, runs the leading idea that the germ is definitely organized before development begins, and that cleavage only reveals an organization that exists from the beginning. "That organization precedes cell-formation and regulates it, rather than the reverse, is a conclusion that forces itself upon us from many sides."¹ "The organism exists before cleavage sets in, and persists throughout every stage of cell-multiplication."²

All of these views, excepting those of Roux, lean more or less distinctly toward the conclusion that the cytoplasm of the egg-cell is from the first mapped out, as it were, into regions which correspond with the parts of the future embryonic body. The cleavage of the ovum does not create these regions, but only reveals them to view by marking off their boundaries. Their topographical arrangement in the egg does not necessarily coincide with that of the adult parts, but only involves the latter as a necessary consequence—somewhat as a picture in the kaleidoscope gives rise to a succeeding picture composed of the same parts in a different arrangement. The germinal localization may, however, in a greater or less degree, foreshadow the arrangement of adult parts—for instance, in the egg of the tunicate or cephalopod, where the bilateral symmetry and antero-posterior differentiation of the adult is foreshadowed not only in the cleavage stages, but even in the unsegmented egg.

By another set of writers, such as Roux, De Vries, Hertwig, and Weismann, germinal localization is primarily sought not in the cytoplasm, but in the nucleus; but these views can be best considered after a review of the idioplasm hypothesis, to which we now proceed.

B. THE IDIOPLOSM THEORY

We owe to Nägeli the first systematic attempt to discuss heredity regarded as inherent in a definite physical basis;³ but it is hardly necessary to point out his great debt to earlier writers, foremost among them Darwin, Herbert Spencer, and Hæckel. The essence of Nägeli's hypothesis was the assumption that inheritance is effected by the transmission not of a cell, considered as a whole, but of a particular substance, the *idioplasm*, contained within a cell, and forming the physical basis of heredity. The idioplasm is to be sharply distinguished from the other constituents of the cell, which play no direct part in inheritance and form a "nutritive plasma" or *tropho-*

¹ '93, p. 115.

² *Ic.*, p. 112.

³ *Theorie der Abstammungslehre*, 1884.

plasm. Hereditary traits are the outcome of a definite molecular organization of the idioplasm. The hen's egg differs from the frog's because it contains a different idioplasm. The species is as completely contained in the one as in the other, and the hen's egg differs from a frog's egg as widely as a hen from a frog.

The idioplasm was conceived as an extremely complex substance, consisting of elementary complexes of molecules known as *micellæ*. These are variously grouped to form units of higher orders, which, as development proceeds, determine the development of the adult cells, tissues, and organs. The specific peculiarities of the idioplasm are therefore due to the arrangement of the micellæ; and this, in its turn, is owing to dynamic properties of the micellæ themselves. During development the idioplasm undergoes a progressive transformation of its substance, not through any material change, but through dynamic alterations of the conditions of tension and movement of the micellæ. These changes in the idioplasm cause reactions on the part of surrounding structures leading to definite chemical and plastic changes, *i.e.* to differentiation and development.

Nägeli made no attempt to locate the idioplasm precisely or to identify it with any of the known morphological constituents of the cell. It was somewhat vaguely conceived as a network extending through both nucleus and cytoplasm, and from cell to cell throughout the entire organism. Almost immediately after the publication of his theory, however, several of the foremost leaders of biological investigation were led to locate the idioplasm in the nucleus, and concluded that it is to be identified with *chromatin*. The grounds for this conclusion, which have already been stated in Chapter VII., may be here again briefly reviewed. The beautiful experiments of Nussbaum, Gruber, and Verworn proved that the regeneration of differentiated cytoplasmic structures in the Protozoa can only take place when nuclear matter is present (*cf.* p. 342). The study of fertilization by Hertwig, Strasburger, and Van Beneden proved that in the sexual reproduction of both plants and animals the nucleus of the germ is equally derived from both sexes, while the cytoplasm is derived almost entirely from the female. The two germ-nuclei, which by their union give rise to that of the germ, were shown by Van Beneden to be of exactly the same morphological nature, since each gives rise to chromosomes of the same number, form, and size. Van Beneden and Boveri proved (p. 182) that the paternal and maternal nuclear substances are equally distributed to each of the first two cells, and the more recent work of Häcker, Rückert, Herla, and Zoja establishes a strong probability that this equal distribution continues in the later divisions. Roux pointed out the telling fact that the entire complicated mechanism of mitosis seems designed to affect

the most accurate division of the entire nuclear substance in all of its parts, while fission of the cytoplasmic cell-body is in the main a mass-division, and not a meristic division of the individual parts. Again, the complicated processes of maturation show the significant fact that while the greatest pains is taken to prepare the germ-nuclei for their coming union, by rendering them exactly equivalent, the cytoplasm becomes widely different in the two germ-cells and is devoted to entirely different functions.

It was in the main these considerations that led Hertwig, Strasburger, Kölliker, and Weismann independently and almost simultaneously to the conclusion that *the nucleus contains the physical basis of inheritance, and that chromatin, its essential constituent, is the idioplasm postulated in Nägeli's theory*. This conclusion is now widely accepted and rests upon a basis so firm that it must be regarded as a working hypothesis of high value. To accept it is, however, to reject the theory of germinal localization in so far as it assumes a prelocalization of the egg-cytoplasm as a fundamental character of the egg. For if the specific character of the organism be determined by an idioplasm contained in the chromatin, then every characteristic of the cytoplasm must in the long run be determined from the same source. A striking illustration of this point is given by the phenomena of colour-inheritance in plant-hybrids, as De Vries has pointed out. Pigment is developed in the embryonic cytoplasm, which is derived from the mother-cell; yet in hybrids it may be inherited from the male through the nucleus of the germ-cell. The specific form of cytoplasmic metabolism by which the pigment is formed must therefore be determined by the paternal chromatin in the germ-nucleus, and not by a predetermination of the egg-cytoplasm.

C. UNION OF THE TWO THEORIES

We have now to consider the attempts that have been made to transfer the localization-theory from the cytoplasm to the nucleus, and thus to bring it into harmony with the theory of nuclear idioplasm. These attempts are especially associated with the names of Roux, De Vries, Weismann, and Hertwig; but all of them may be traced back to Darwin's celebrated hypothesis of pangenesis as a prototype. This hypothesis is so well known as to require but a brief review. Its fundamental postulate assumes that the germ-cells contain innumerable ultra-microscopic organized bodies or *gemmules*, each of which is the germ of a cell and determines the development of a similar cell during the ontogeny. The germ-cell is, therefore, in Darwin's words, a microcosm formed of a host of inconceivably minute self-propagating organisms, every one of which predetermines

the formation of one of the adult cells. De Vries ('89) brought this conception into relation with the theory of nuclear idioplasm by assuming that the gemmules of Darwin, which he called *pangens*, are contained in the nucleus, migrating thence into the cytoplasm step by step during ontogeny, and thus determining the successive stages of development. The hypothesis is further modified by the assumption that the pangens are not cell-germs, as Darwin assumed, but ultimate protoplasmic units of which cells are built, and which are the bearers of particular hereditary qualities. The same view was afterward accepted by Hertwig and Weismann.²

The theory of germinal localization is thus transferred from the cytoplasm to the nucleus. It is not denied that the egg-cytoplasm may be more or less distinctly differentiated into regions that have a constant relation to the parts of the embryo. This differentiation is, however, conceived, not as a primordial characteristic of the egg, but as one secondarily determined through the influence of the nucleus. Both De Vries and Weismann assume, in fact, that the entire cytoplasm is a product of the nucleus, being composed of pangens that migrate out from the latter, and by their active growth and multiplication build up the cytoplasmic substance.³

D. THE ROUX-WEISMANN THEORY OF DEVELOPMENT

We now proceed to an examination of two sharply opposing hypotheses of development based on the theory of nuclear idioplasm. One of these originated with Roux ('83) and has been elaborated especially by Weismann. The other was clearly outlined by De Vries ('89), and has been developed in various directions by Oscar Hertwig, Driesch, and other writers. In discussing them, it should be borne in mind that, although both have been especially developed by the advocates of the pangen-hypothesis, neither necessarily involves that hypothesis in its strict form, *i.e.* the postulate of discrete self-propagating units in the idioplasm. This hypothesis may therefore be laid

¹ Cf. p. 290.

² The neo-pangenesis of De Vries differs from Darwin's hypothesis in one very important respect. Darwin assumed that the gemmules arose in the body, being thrown off as germs by the individual tissue-cells, transported to the germ-cells, and there accumulated as in a reservoir; and he thus endeavoured to explain the transmission of acquired characters. De Vries, on the other hand, denies such a transportal from cell to cell, maintaining that the pangens arise or preëxist in the germ-cell, and those of the tissue-cells are derived from this source by cell-division.

³ This conception obviously harmonizes with the rôle of the nucleus in the synthetic process. In accepting the view that the nuclear control of the cell is effected by an emanation of specific substances from the nucleus, we need not, however, necessarily adopt the pangen-hypothesis.

aside as an open question,¹ and will be considered only in so far as it is necessary to a presentation of the views of individual writers.

The Roux-Weismann hypothesis has already been touched on at page 245. Roux conceived the idioplasm (*i.e.* the chromatin) not as a single chemical compound or a homogeneous mass of molecules, but as a highly complex mixture of different substances, representing *different qualities*, and having their seat in the individual chromatin-granules. In mitosis these become arranged in a linear series to form the spireme-thread, and hence may be precisely divided by the splitting of the thread. Roux assumes, as a fundamental postulate, that division of the granules may be either *quantitative* or *qualitative*. In the first mode the group of qualities represented in the mother-granule is first doubled and then split into equivalent daughter-groups, the daughter-cells therefore receiving the same qualities and remaining of the same nature. In "qualitative division," on the other hand, the mother-group of qualities is split into dissimilar groups, which, passing into the respective daughter-nuclei, lead to *a corresponding differentiation in the daughter-cells*. By qualitative divisions, occurring in a fixed and predetermined order, the idioplasm is thus split up during ontogeny into its constituent qualities, which are, as it were, sifted apart and distributed to the various nuclei of the embryo. *Every cell-nucleus, therefore, receives a specific form of chromatin* which determines the nature of the cell at a given period and its later history. Every cell is thus endowed with a power of *self-determination*, which lies in the specific structure of its nucleus, and its course of development is only in a minor degree capable of modification through the relation of the cell to its fellows ("correlative differentiation").

Roux's hypothesis, be it observed, does not commit him to the theory of pangenesis. It was reserved for Weismann to develop the hypothesis of qualitative division in terms of the pangen-hypothesis, and to elaborate it as a complete theory of development. In his first essay ('85), published before De Vries's paper, he went no farther than Roux. "I believe that we must accept the hypothesis that in indirect nuclear division, the formation of non-equivalent halves may take place quite as readily as the formation of equivalent halves, and that the equivalence or non-equivalence of the subsequently produced daughter-cells must depend upon that of the nuclei. Thus, during ontogeny a gradual transformation of the nuclear substance takes place, necessarily imposed upon it, according to certain laws, by its own nature, and such transformation is accompanied by a gradual change in the character of the cell-bodies."² In later writings Weismann advanced far beyond this, building up an elaborate artificial system, which appears in its final form in the remarkable

¹ Cf. Chapter VI.

² Essay IV., p. 193, 1885.

book on the germ-plasm ('92). Accepting De Vries's conception of the pangens, he assumes a definite grouping of these bodies in the germ-plasm or idioplasm (chromatin), somewhat as in Nägeli's conception. The pangens or *biophores* are conceived to be successively aggregated in larger and larger groups; namely, (1) *determinants*, which are still beyond the limits of microscopical vision; (2) *ids*, which are identified with the visible chromatin-granules; and (3) *idants*, or chromosomes. The chromatin has, therefore, a highly complex fixed architecture, which is transmitted from generation to generation, and determines the development of the embryo in a definite and specific manner. Mitotic division is conceived as an apparatus which may distribute the elements of the chromatin to the daughter-nuclei either equally or unequally. In the former case ("*homœokinesis*," *integral* or *quantitative division*), the resulting nuclei remain precisely equivalent. In the second case ("*heterokinesis*," *qualitative* or *differential division*), the daughter-cells receive different groups of chromatin-elements, and hence become differently modified. During ontogeny, through successive qualitative divisions, the elements of the idioplasm or *germ-plasm* (chromatin) are gradually sifted apart, and distributed in a definite and predetermined manner to the various parts of the body. "Ontogeny depends on a gradual process of disintegration of the id of germ-plasm, which splits into smaller and smaller groups of determinants in the development of each individual. . . . Finally, if we neglect possible complications, only *one* kind of determinant remains in each cell, viz. that which has to control that particular cell or group of cells. . . . In this cell it breaks up into its constituent biophores, and gives the cell its inherited specific character."¹ Development is, therefore, essentially evolutionary and not epigenetic;² its point of departure is a substance in which all of the adult characters are represented by preformed, prearranged germs; its course is the result of a predetermined harmony in the succession of the qualitative divisions by which the hereditary substance is progressively disintegrated. In order to account for heredity through successive generations, Weismann is obliged to assume that, by means of quantitative or integral division, a certain part of the original germ-plasm is carried on unchanged, and is finally delivered, with its original architecture unaltered, to the germ-nuclei. The power of regeneration is explained, in like manner, as the result of a transmission of unmodified or slightly modified germ-plasm to those parts capable of regeneration.

¹ *Germ-plasm*, pp. 76, 77.

² *Lc.*, p. 15.

E. CRITIQUE OF THE ROUX-WEISMANN THEORY

It is impossible not to admire the thoroughness, candour, and logical skill with which Weismann has developed his theory, or to deny that, in its final form, it does afford up to a certain point a *formal* solution of the problems with which it deals. Its fundamental weakness is its *quasi-metaphysical* character, which, indeed, almost places it outside

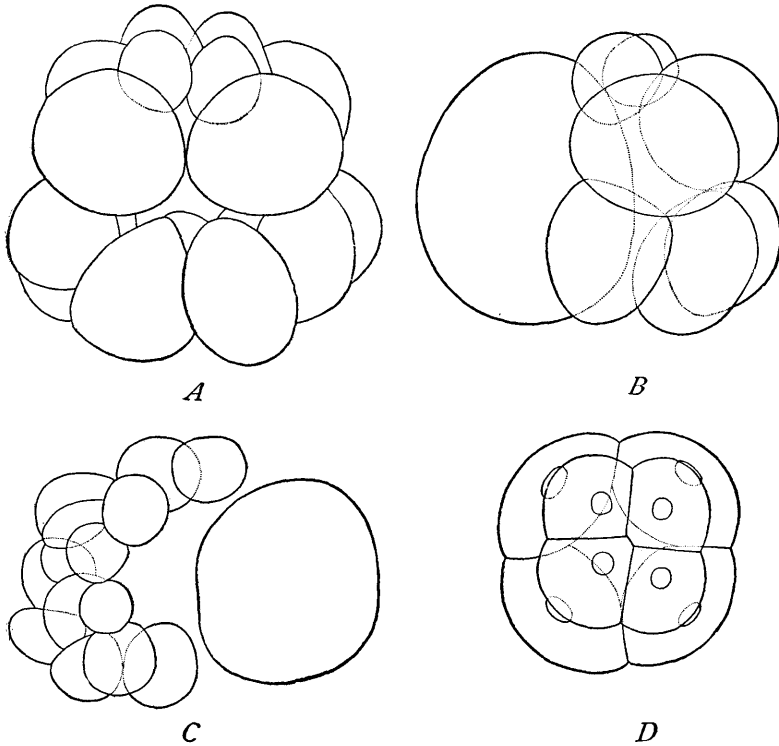


Fig. 183. — Half and whole cleavage in the eggs of sea-urchins.

A. Normal sixteen-cell stage, showing the four micromeres above (from Driesch, after Selenka). B. Half sixteen-cell stage developed from one blastomere of the two-cell stage after killing the other by shaking (Driesch). C. Half blastula resulting, the dead blastomere at the right (Driesch). D. Half-sized sixteen-cell stage of *Toxopneustes*, viewed from the micromere-pole (the eight lower not shown). This embryo, developed from an isolated blastomere of the two-cell stage, segmented like an entire normal ovum.

the sphere of legitimate scientific hypothesis. Save in the maturation of the germ-cells ("reducing divisions"), none of the visible phenomena of cell-division give even a remote suggestion of qualitative division. All the facts of ordinary mitosis, on the contrary, indicate that the division of the chromatin is carried out with the most exact equality.

The hypothesis mainly rests upon a quite different order of phenomena, namely, on facts indicating that isolated blastomeres, or other cells, have a certain power of self-determination, or "self-differentiation" (Roux), peculiar to themselves, and which is assumed to be primarily due to the specific quality of the nuclei. This assumption, which may or may not be true,¹ is itself based upon the further assumption of qualitative nuclear division of which we actually know nothing whatever. The fundamental hypothesis is thus of purely *a priori* character; and every fact opposed to it has been met by subsidi-

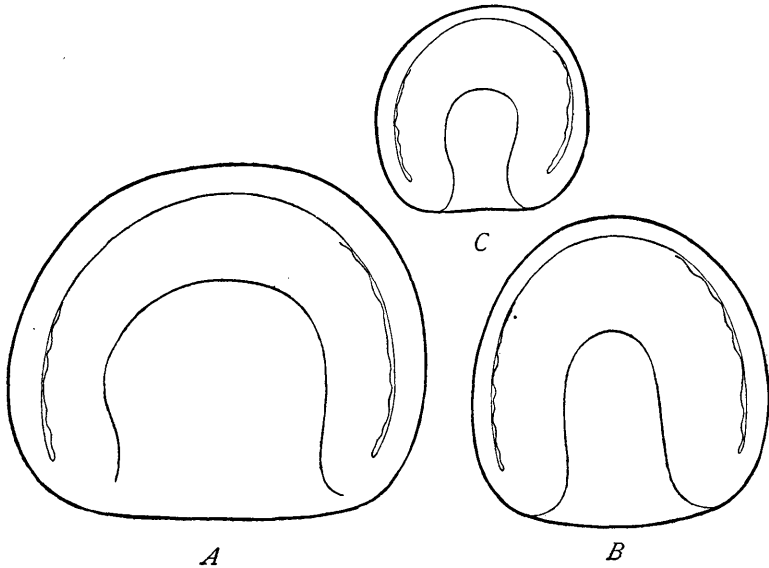


Fig. 184. — Normal and dwarf gastrulas of *Amphioxus*.

A. Normal gastrula. B. Half-sized dwarf, from an isolated blastomere of the two-cell stage. C. Quarter-sized dwarf, from an isolated blastomere of the four-cell stage.

ary hypotheses, which, like their principal, relate to matters beyond the reach of observation.

Such an hypothesis cannot be actually overturned by a direct appeal to fact. We can, however, make an indirect appeal, the results of which show that the hypothesis of qualitative division is not only so improbable as to lose all semblance of reality, but is in fact quite superfluous. It is rather remarkable that Roux himself led the way in this direction. In the course of his observations on the development of a half-embryo from one of the blastomeres of the two-cell stage of the frog's egg, he determined the significant fact that the half-embryo in the end *restores more or less completely*

¹ Cf. p. 426.

the missing half by a peculiar process, related to regeneration, which Roux designated as *post-generation*. Later studies showed that an isolated blastomere is able to give rise to a complete embryo in many other animals, sometimes developing in its earlier stages as though

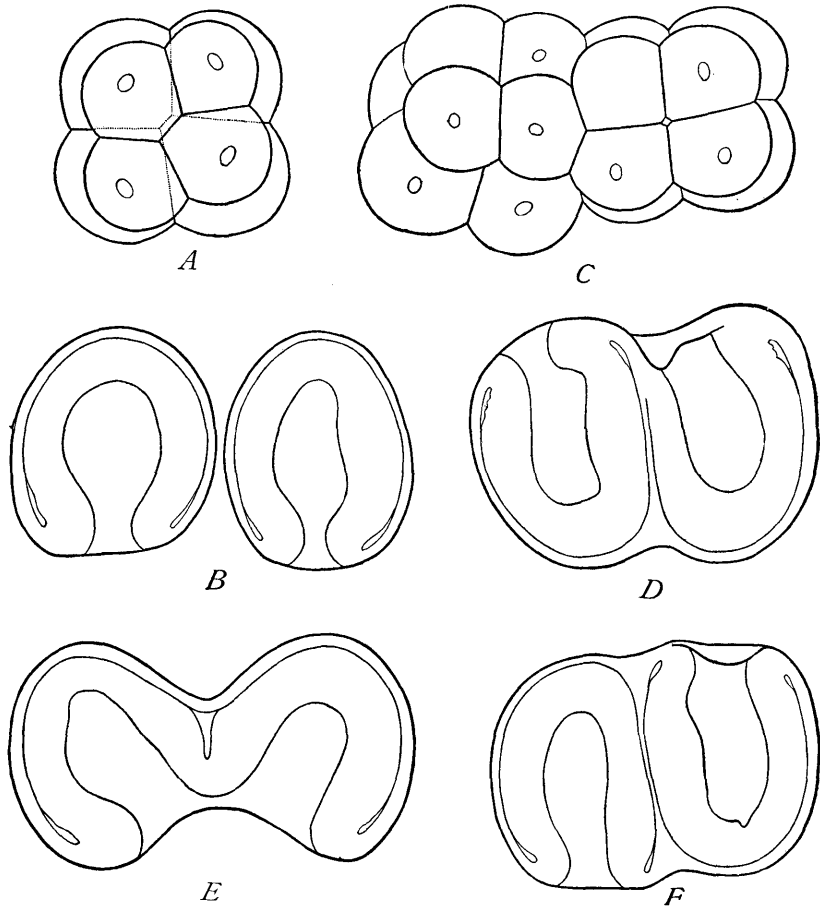


Fig. 185. — Dwarf and double embryos of *Amphioxus*.

A. Isolated blastomere of the two-cell stage segmenting like an entire egg (*cf.* Fig. 183, *D*).
B. Twin gastrulas from a single egg. *C.* Double cleavage resulting from the partial separation, by shaking, of the blastomeres of the two-cell stage. *D.E.F.* Double gastrulas arising from such forms as the last.

still forming part of a complete embryo (“partial development”), but in other cases developing directly into a complete dwarf embryo, as if it were an egg of diminished size. In 1891 Driesch was able to follow out the development of isolated blastomeres of sea-urchin

eggs separated by shaking to pieces the two-cell and four-cell stages. Blastomeres thus isolated segment as if still forming part of an entire larva, and give rise to a half- (or quarter-) blastula (Fig. 183). The opening soon closes, however, to form a small complete blastula, and the resulting gastrula and Pluteus larva is a perfectly formed dwarf of only half (or quarter) the normal size. Incompletely separated blastomeres give rise to double embryos like the Siamese twins. Shortly afterward the writer obtained similar results in the case of *Amphioxus*, but here *the isolated blastomere behaves from the beginning like a complete ovum of half the usual size*, and gives rise to a complete blastula, gastrula, and larva. Complete embryos have also been obtained from a single blastomere in the teleost *Fundulus* (Morgan, '95, 2), in *Triton* (Herlitzka, '95), and in a number of hydromedusæ (Zoja, '95, Bunting, '99); and nearly complete embryos in the tunicates *Asciella* (Chabry, '87), *Phallusia* (Driesch, '94), and *Molgula* (Crampton, '98).¹ Perhaps the most striking of these cases is that of the hydroid *Clytia*, in which Zoja was able to obtain perfect embryos, not only from the blastomeres of the two-cell and four-cell stages, but from eight-cell and even from sixteen-cell stages, the dwarfs in the last case being but one-sixteenth the normal size.

These experiments render highly improbable the hypothesis of qualitative division in its strict form, for they demonstrate that the earlier cleavages, at least, do not in these cases sunder fundamentally different materials, either nuclear or cytoplasmic, but only split the egg up into a number of parts, each of which is capable of producing an entire body of diminished size, and hence must contain all of the material essential to complete development. Both Roux and Weismann endeavour to meet this adverse evidence with the assumption of a "reserve idioplasm," containing all of the elements of the germplasm which is in these cases distributed equally to all the cells in addition to the specific chromatin conveyed to them by qualitative division. This subsidiary hypothesis renders the principal one (*i.e.* that of qualitative division) superfluous, and brings us back to the same problems that arise when the assumption of qualitative division is discarded.

The theory of qualitative nuclear division has been practically disproved in another way by Driesch, through the pressure-experiments already mentioned at page 375. Following the earlier experiments of Pflüger ('84) and Roux ('85) on the frog's egg, Driesch subjected segmenting eggs of the sea-urchin to pressure, and thus obtained flat plates of cells in which the arrangement of the nuclei differed totally

¹The "partial" development in the earlier stages of some of these forms is considered at page 419.

from the normal (Fig. 186); yet such eggs when released from pressure continue to segment, *without rearrangement of the nuclei*, and give rise to perfectly normal larvæ. I have repeated these experiments not only with sea-urchin eggs, but also with those of an annelid (*Nereis*), which yield a very convincing result, since in this case the histological differentiation of the cells appears very early. In the normal development of this animal the archenteron arises from four large cells or macromeres (entomeres), which remain after the successive formation of three quartets of micromeres (ectomeres) and the parent-cell of the mesoblast. After the primary differentiation of the germ-layers the four entomeres do not divide again until a very late period (free-swimming trochophore), and their substance always retains a characteristic appearance, differing from that of the other

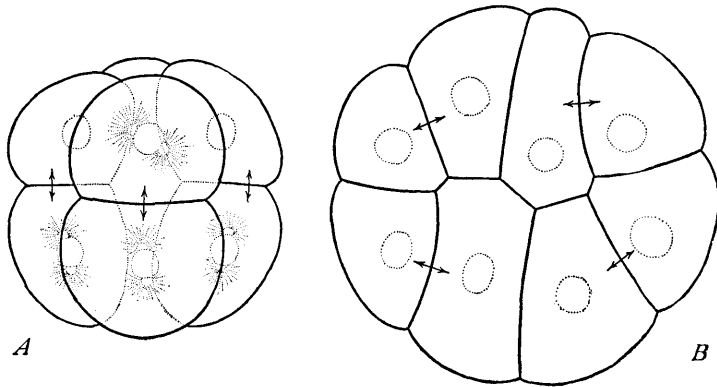


Fig. 186. — Modification of cleavage in sea-urchin eggs by pressure.

A. Normal eight-cell stage of *Toxopneustes*. B. Eight-cell stage of *Echinus* segmenting under pressure. Both forms produce normal Plutei.

blastomeres in its pale non-granular character and in the presence of large oil-drops. If unsegmented eggs be subjected to pressure, as in Driesch's echinoderm experiments, they segment in a flat plate, all of the cleavages being vertical. In this way are formed eight-celled plates in which all of the cells contain oil-drops (Fig. 187, D). If they are now released from the pressure, each of the cells divides in a plane approximately horizontal, a smaller granular micromere being formed above, leaving below a larger clear macromere in which the oil-drops remain. The sixteen-cell stage, therefore, consists of eight deutoplasm-laden macromeres and eight protoplasmic micromeres (instead of four macromeres and twelve micromeres, as in the usual development). These embryos developed into free-swimming trochophores containing eight instead of four macromeres, which have the typical clear protoplasm containing oil-drops. In this case there can

be no doubt whatever that four of the entoblastic nuclei were normally destined for the first quartet of micromeres (Fig. 187, *B*), from which arise the apical ganglia and the prototroch. Under the conditions of the experiment, however, they have given rise to the nuclei of cells which differ in no wise from the other entoderm-cells. Even

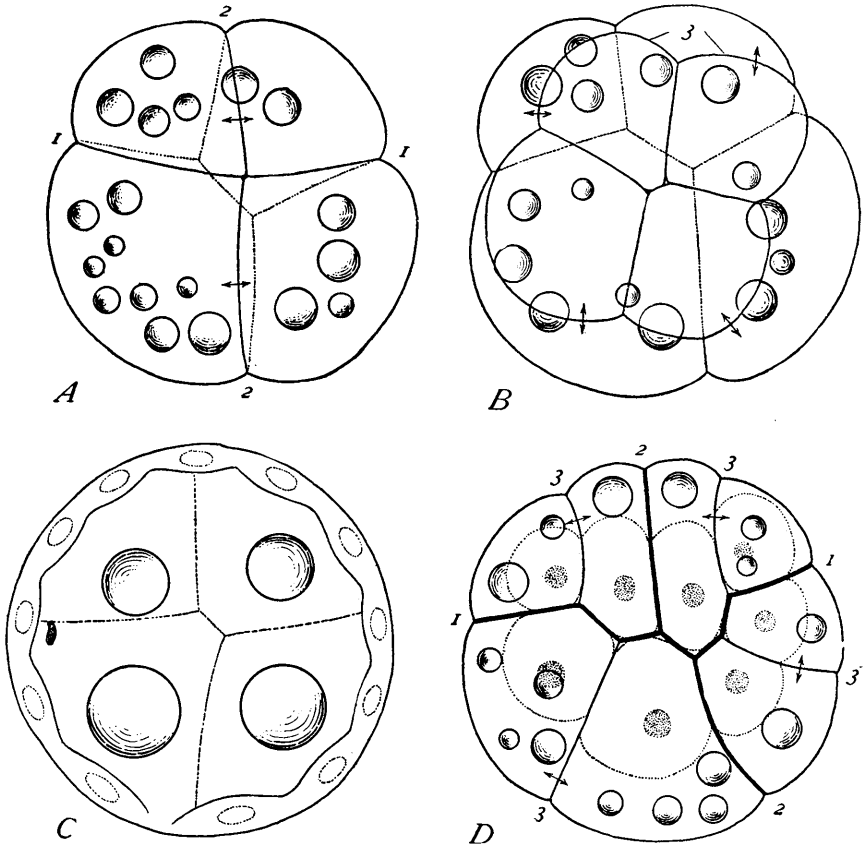


Fig. 187. — Modifications of cleavage by pressure in *Nereis*.

A, B. Normal four- and eight-cell stages. *C.* Normal trochophore larva resulting, with four entoderm-cells. *D.* Eight-cell stage arising from an egg flattened by pressure; such eggs give rise to trochophores with eight instead of four entoderm-cells. Numerals designate the successive cleavages.

in a highly differentiated type of cleavage, therefore, the nuclei of the segmenting egg are not specifically different, as the Roux-Weismann hypothesis demands, but contain the same materials even in the cells that undergo the most diverse subsequent fate. But there is, furthermore, very strong reason for believing that this may be true in later

stages as well, as Kölliker insisted in opposition to Weismann as early as 1886, and as has been urged by many subsequent writers. The strongest evidence in this direction is afforded by the facts of regeneration; and many cases are known—for instance, among the hydroids and the plants—in which even a small fragment of the body is able to reproduce the whole. It is true that the power of regeneration is always limited to a greater or less extent according to the species. But there is no evidence whatever that such limitation arises through specification of the nuclei by qualitative division, and, as will appear beyond, its explanation is probably to be sought in a very different direction.

F. ON THE NATURE AND CAUSES OF DIFFERENTIATION

We have now cleared the ground for a restatement of the problem of development and an examination of the views opposed to the Roux-Weismann theory. After discarding the hypothesis of qualitative division the problem confronts us in the following form. If chromatin be the idioplasm in which inheres the sum total of hereditary forces, and if it be equally distributed at every cell-division, how can its mode of action so vary in different cells as to cause diversity of structure, *i.e. differentiation*? It is perfectly certain that differentiation is an actual progressive transformation of the egg-substance involving both physical and chemical changes, occurring in a definite order, and showing a definite distribution in the regions of the egg. These changes are sooner or later accompanied by the cleavage of the egg into cells whose boundaries may sharply mark the areas of differentiation. What gives these cells their specific character? Why, in the four-cell stage of an annelid egg, should the four cells contribute equally to the formation of the alimentary canal and the cephalic nervous system, while only one of them (the left-hand posterior) gives rise to the nervous system of the trunk-region and to the muscles, connective tissues, and the germ-cells? (Figs. 171, 188, *B.*) There cannot be a fixed relation between the various regions of the egg which these blastomeres represent and the adult parts arising from them; for in some eggs these relations may be artificially changed. A portion of the egg which under normal conditions would give rise to only a fragment of the body will, if split off from the rest, give rise to an entire body of diminished size. What then determines the history of such a portion? What influence moulds it now into an entire body, now into a part of a body?

De Vries, in his remarkable essay on *Intracellular Pangenesis* ('89), endeavoured to cut this Gordian knot by assuming that the character of each cell is determined by pangens that migrate from

the nucleus into the cytoplasm, and, there becoming active, set up specific changes and determine the character of the cell, this way or that, according to their nature. But what influence guides the migrations of the pangens, and so correlates the operations of development? Both Driesch and Oscar Hertwig have attempted to

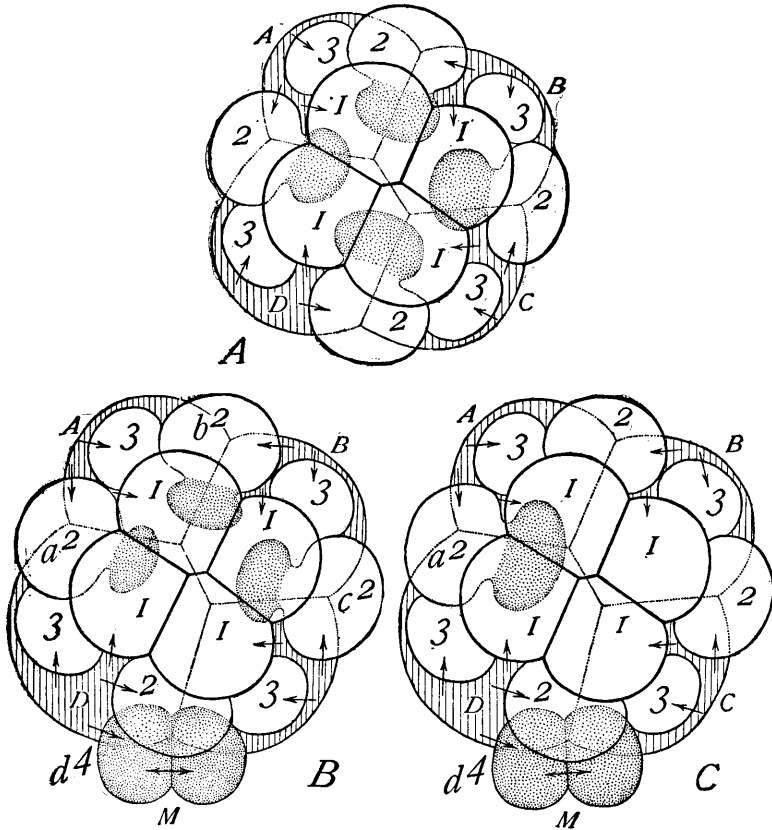


Fig. 188. — Diagrams illustrating the value of the quartets in a polyclade (*Leptoplana*), a lamelibranch (*Unio*), and a gasteropod (*Crepidula*). *A. Leptoplana*, showing mesoblast-formation in the second quartet. *B. Crepidula*, showing source of ectomesoblast (from a^2 , b^2 , c^2) and entomesoblast (from quadrant *D*). *C. Unio*, ectomesoblast formed only from a^2 .

In all the figures the successive quartets are numbered with Arabic figures; ectoblast unshaded, mesoblast dotted, entoblast vertically lined.

answer this question, though the first-named author does not commit himself to the pangen-hypothesis. These writers have maintained that the particular mode of development in a given region or blastomere of the egg is a result of its relation to the remainder of the mass, i.e. a product of what may be called the intra-embryonic environ-

ment. Hertwig insisted that the organism develops as a whole as the result of a physiological interaction of equivalent blastomeres, the transformation of each being due not to an inherent specific power of self-differentiation, as Roux's mosaic-theory assumed, but to the action upon it of the whole system of which it is a part. "According to my conception," said Hertwig, "each of the first two blastomeres contains the formative and differentiating forces not simply for the production of a half-body, but for the entire organism; the left blastomere develops into the left half of the body only because it is placed in relation to a right blastomere."¹ Again, in a later paper: "The egg is a specifically organized elementary organism that develops epigenetically by breaking up into cells and their subsequent differentiation. Since every elementary part (*i.e.* cell) arises through the division of the germ, or fertilized egg, it contains also the germ of the whole, but during the process of development it becomes ever more precisely differentiated and determined by the formation of cytoplasmic products according to its position with reference to the entire organism (blastula, gastrula, etc.)."²

An essentially similar view was advocated by the writer ('93, '94) nearly at the same time, and the same general conception was expressed with great clearness and precision by Driesch shortly after Hertwig: "The fragments (*i.e.* cells) produced by cleavage are completely equivalent or indifferent." "The blastomeres of the sea-urchin are to be regarded as forming a uniform material, and they may be thrown about, like balls in a pile, without in the least degree impairing thereby the normal power of development."³ "*The relative position of a blastomere in the whole determines in general what develops from it; if its position be changed, it gives rise to something different; in other words, its prospective value is a function of its position.*"⁴

In this last aphorism the whole problem of development is brought to a focus. It is clearly not a solution of the problem, but only a highly suggestive restatement of it; for everything turns upon how the relation of the part to the whole is conceived. Very little consideration is required to show that this relation cannot be a merely geometrical or rudely mechanical one, for in the eggs of different

¹ '92, I, p. 481.

² '93, p. 793. It should be pointed out that Roux himself in several papers expressly recognizes the fact that development cannot be regarded as a pure mosaic-work, and that besides the power of self-differentiation postulated by his hypothesis we must assume a "correlative differentiation" or differentiating interaction of parts in the embryo. Cf. Roux, '92, '93, I.

³ Studien IV., p. 25.

⁴ Studien IV., p. 39. Cf. His, "Es muss die Wachstumsregbarkeit des Eies eine Function des Raumes sein." ('74, p. 153.)