PART I

THE MATERIAL BASIS OF HEREDITY

CHAPTER I

THE GERM-PLASM

1. The Fundamental Units

Now that the conception of the germ-plasm as the hereditary substance contained in the germ-cells has been fully established, and since it has been shown in general terms that this form of the idioplasm must become changed during ontogeny and converted into the idioplasm of the cells which constitute the mature organism, we must attempt to form some idea of its nature; for it would otherwise be impossible to construct a theory of heredity. In attempting this, we shall for the present entirely neglect the complication due to sexual reproduction, and take as our starting-point a germ-plasm which does not contain the primary constituents of two parents, but those of one only, — that is to say, one which is constituted just as it would be in a species which had at all times multiplied asexually.

Before venturing to express an opinion concerning the constitution of the germ-plasm, and to derive therefrom the phenomena of heredity, I should like to premise that it is not my intention to attempt an explanation of life. It is necessary to distinguish between a theory of life and one of heredity. De Vries has pointed out very clearly that the former is impossible at present, but that it seems by no means impossible to arrive at a satisfactory explanation of the phenomena of heredity if one takes for granted the essential phenomena of life, — nutrition, assimilation, and growth.

These functions, together with the associated ones of sensation and movement, are connected in all organisms with which we are familiar, from the simplest unicellular forms to the highest plants and animals, with at least two different substances, viz., the idioplasm of the nucleus, — *i.e.*, the hereditary plasm in the more general sense, — and the protoplasm of the cell-body. These two differ as regards their functions, though they resemble each other in being composed of living substance: that is to say, the primary vital forces, nutrition and growth, are developed within them. As the term 'protoplasm' is used in a far too indefinite sense, I shall follow Nägeli's example, and call the vital substance of the cell the 'formative plasm' or *morphoplasm* (Nägeli's 'trophoplasm'), in contrast to the *idioplasm*. The latter is the active element in the process of formation, and the former the passive one. As we now know that the idioplasm is situated in the nuclei only, we cannot regard the cell-bodies which determine the form of all parts of the organism as mere 'nutrient plasm.'

Both forms of the living substance are included in the term 'protoplasm,' and we have now to decide how we are to imagine its constitution in detail. 'Protoplasm' has often been conceived as a 'modification of albumen'; till quite recently, in fact, this was the general idea. Brücke, however, pointed out a considerable time ago that albumen does not possess the power of assimilation, and has therefore no vitality; it has moreover been proved by the study of physiological chemistry that other substances besides albumen are also obtained from protoplasm, and that these cannot be assumed to be insignificant without further proof. Although compounds of sulphur and phosphorus, for instance, only exist in protoplasm in comparatively small quantities, we must not infer from this fact that they are of slight importance. In any case, we cannot say that protoplasm is a modification of albumen, because we can only examine it chemically when dead, and in this condition it has lost its most important properties, and has become changed in a manner which we need not here consider further. As de Vries expresses it, protoplasm is not a chemical, but a morphological conception. That is, it does not consist of a confused mass of certain chemical molecules, but of morphological units, which are themselves composed of molecules, or, as Brücke first expressed it, protoplasm is 'organised.' As I have shown in the historical introduction to this book, Herbert Spencer, and more recently de Vries and Wiesner, have assumed the existence of such organic units.

De Vries, moreover, points out that protoplasm possesses certain 'historical' properties besides its physical and chemical ones. It may certainly be doubted, as de Vries states, whether it will ever be possible to produce 'living protoplasm otherwise than in a phylogenetic manner,' that is to say, to make it artificially in the laboratory; but it cannot be admitted that this is so improbable, merely because the conception of protoplasm demands that it should be derived from pre-existing protoplasm. This would exclude for ever not only the possibility of its production in our laboratories, but also its logically inevitable and indispensable primary formation in the great laboratory of Nature. Most, in fact probably all, kinds of protoplasm with which we are acquainted possess historical qualities, not *in addition to*, but *within* their physico-chemical ones; that is, they contain special modifications of construction peculiar to themselves which arose in adaptation to the conditions of life, and have been transmitted for a long period of time. But protoplasm which does not yet possess 'historical' *i.e.*, inherited qualities, does not seem to me to be inconceivable. It would be the simplest form of living matter which, in virtue of its constitution, possessed the primary vital forces,—assimilation, metabolism, and so on. The *historical* qualities of the protoplasm, its special hereditary tendencies, are not connected with these primary vital forces. The latter must exist independently in all protoplasm.

All those writers * who have assumed the existence of units on which the vital forces of protoplasm depend, have pointed out that they are not chemical molecules, for the latter do not possess the power of assimilation and reproduction. Hence it follows that protoplasm is a complex substance which is not homogeneous, but which consists of different kinds of molecules. There is therefore no molecule of protoplasm, but we have to imagine that even in its simplest modifications, protoplasm invariably consists of *groups* of molecules, each of which is

* Brücke, Herbert Spencer, de Vries, and Wiesner.

composed of *different kinds* of chemical molecules. I shall call these units the '*bearers of vitality*' ('Lebensträger') or '*biophors*,' because they are the smallest units which exhibit the primary vital forces, viz., *assimilation and metabolism*, *growth, and multiplication by fission.*

As living protoplasm cannot be subjected to chemical analysis, we cannot describe its chemical constitution more precisely; but what has so far been determined by the analysis of dead protoplasm certainly indicates that the albuminoids are not the only bearers of vitality, as has generally been assumed, but that other substances play a no less important part in living protoplasm,— a fact which has been insisted on by Hoppe-Seyler and Baumann. Besides albuminoids, compounds containing phosphorus, such as lecithin and nuclein, which are not related chemically to albumen, but enter into combination with it, are known to occur in dead protoplasm; and besides these, protoplasm also contains cholesterin, which is probably a product of destructive metabolism, and carbohydrates, such as glycogen, starch, inulin, and dextrine, as well as compounds of potassium.* Although we cannot at present guess from what chemical compounds in living protoplasm these bodies have been derived, there can be no doubt that 'a relation exists between them and the vital processes' (Hoppe-Seyler), and that albumen, or different kinds of albumen, do not alone bring about the vital processes, but that several other substances, such as salts, and compounds containing phosphorus, and more particularly water, are just as essential: in short, life depends simply on the interaction of molecules, differing chemically from one another, but *defined* within certain limits.

After long consideration, I have decided to designate such a group of molecules on which the phenomena of life depend by the special term '*biophor*.' This seemed to be advisable, because the various terms introduced previously by others were either left too vague for these minute vital particles to be identified with them, or if defined more exactly, were used with a different meaning. It would certainly be a mistake to make use of a name already introduced, in another sense from its original one. Herbert Spencer's † 'physiological units' are similar to the biophors,

* Cf. Hoppe-Seyler, 'Allgemeine Biologie,' Berlin, 1877, p. 75 (Part I. of the 'Lehrbuch der physiologischen Chemie').

† Herbert Spencer, 'Principles of Biology,' vol. i., p. 183.

and he looks upon them as being intermediate between the chemical units (molecules) and the morphological units (cells). But he supposes their function in heredity to be different from that which I ascribe to my biophors. Haeckel * understands by the term 'plastidule,' introduced by Elsberg,† the hypothetical ultimate particles of which 'protoplasm' is composed; he regards them as equivalent to the 'molecules' of inorganic matter, but supposes them to possess 'vital qualities' as well. Of course this definition is in itself insufficient proof, as de Vries very correctly remarks, that Haeckel's plastidules are not molecules in the physical sense; these very 'vital qualities' are the point in which they differ from them. I could not adopt Nägeli's term either, because a 'micella' differs essentially in its construction and properties from a biophor. It is defined as 'a minute crystal, microscopically invisible, consisting of a larger or smaller number of molecules, and is, when turgid, surrounded by a layer of water.' ‡ As regards the absolute size of the micella, Nägeli calculates that it may consist of one hundred molecules, or on the other hand, of only a single molecule of albumen. As in the case of Haeckel's plastidules, we have here therefore to deal with a unit the vital character of which does not depend on a peculiar grouping of several or even many different kinds of molecules. Indeed Nägeli draws attention in another part of his book (p. 63) to the unstable chemical composition of the proteids so far as can be made out by analyses, and very correctly considers it extremely probable 'that there are various molecules of albumen which differ from one another in containing unequal quantities of hydrogen, oxygen, &c.' This leads him to the further assumption 'that the micellæ of the proteids consist of a mixture of two or more different kinds of molecules of albumen. In each proteid the different molecules of albumen would be mixed in special proportions, and, further, each would contain special quantities of phosphates, salts of magnesia, lime, and so on.' This conception, however, hardly agrees with that of the 'crystalline'

* Ernst Haeckel, 'Die Perigenesis der Plastidule,' Berlin, 1876.

† Louis Elsberg, 'Regeneration; or, The Preservation of Organic Molecules; a Contribution to the Doctrine of Evolution.'—*Proceed. Am. Assoc. for the Advancement of Science*, Hartford Meeting, Aug. 1874.

‡ Carl Nägeli, 'Mechanisch-physiologische Theorie der Abstammungsehre,' München u. Leipzig, 1884, p. 35.

nature of the micella, for crystals are not 'mixtures,' but chemically pure substances. And apart from this, we should be wrong in inferring from this passage that Nägeli considers the vital properties of a micella dependent on the co-operation of *different* molecules united into a single group; for in the passage quoted above he also states that *one* molecule of albumen is sufficient for the constitution of a micella.

For this reason alone it will be seen that the conceptions of the biophor and of the micella do not coincide. They differ also as regards the mode of multiplication: the fundamental importance of this will become apparent later on. The biophors, as bearers of vitality, possess the power of growth and of multiplication by fission, *just as is the case in all orders of vital units on which direct observations have been made*, beginning with the microsomata, which constitute the chromatin of the nucleus, and passing through the chlorophyll granules, nuclei, and cells, up to the simpler plants and animals. Nägeli's micellæ also multiply, but the multiplication occurs 'by the free interposition of new micellæ, similar to, or identical with, those already present,' in the same manner as he supposed the addition of new particles to take place in a starch grain, or as crystals separate from the mother liquor. These new micellæ would certainly have to be formed by an influence, exerted by those already present, which cannot be further defined.

The 'pangenes' of de Vries correspond almost exactly to my biophors, for they are also accredited with the functions of growth and multiplication by division, and play a similar part in heredity. The biophors, as will be explained in the following pages, only differ from the pangenes in being constituents of higher units of the hereditary substance.

The minute vital particles or 'plasomes,' recently assumed by Wiesner, resemble both pangenes and biophors as regards their properties. The part they take in heredity is, however, only hinted at, and it is therefore better for me to use the special term biophor than to press the plasomes into the service of my theory of heredity.

The biophors play the same part with respect to heredity as that which de Vries ascribes to his pangenes, *i.e.*, they are the '*bearers of the qualities or 'characters'* of the cells;' or more accurately, *the bearers of the cell-qualities*. As all living matter consists of biophors, the differences in it can only depend on the differences in the biophors composing it; an animal cell containing, for example, transversely striped muscular substance, or delicate nervous or glandular structures, or again, a vegetable cell enclosing chlorophyll bodies, must contain several *different* kinds of biophors of which these various cell-structures are composed, and which constitute the germ-plasm of a species.

There must be a great number of different kinds of biophors, for otherwise they could not give rise to so great a variety of cells as exists in the organic world. Nor is it difficult to infer the possibility of an almost unlimited number of different kinds of biophors from their assumed composition.

As the biophors are not individual molecules, but *groups* of molecules, nothing prevents us from tracing a large number of variations in them to the widely varying *number of their molecules*. But even the *chemical constitution of the molecules* is not by any means necessarily the same in all cases, although the possible fluctuations are certainly confined within certain limits.

Numerous facts show that at any rate in the two main divisions of the organic world, the animal and vegetable kingdoms, several of the molecules composing the biophors differ chemically from one another, so that substitutions occur. Whereas glycogen is a constituent which is never absent from animal protoplasm, provided that the latter possesses amœboid movement, this carbohydrate has not yet been discovered in plants, in which, as Hoppe-Seyler suspects, it is probably replaced by amylum, dextrine, or gum. Similarly, the crystalline proteids in plants, which are known as aleurone grains, are chemically different from the yolk-granules in animals.

A difference in the biophors can, moreover, be conceived without a change in their atomic composition, by regarding as possible a *rearrangement of the atoms* in the individual molecules. The molecule of albumen in particular has, according to the conclusions of modern chemistry, a molecular weight of at least 1,000, so that innumerable isomeric molecules of albumen seem to be conceivable. It is, however, impossible to state how many of them actually exist.

In order to give as complete an explanation as possible of the phenomena of heredity with the aid of the biophors, the latter must be invested with the capacity for a further change, namely, *a rearrangement of the molecules*, analogous to the isomeric rearrangement of the atoms in a single molecule. This assumption is not unfounded, inasmuch as several instances of molecular compounds are known in chemistry, *e.g.*, the double salts and the water of crystallisation of salts, in which definite numbers of molecules are always present: this number is even retained in spite of substitution. Thus alum always contains twenty-four molecules of water of crystallisation, and this evidently indicates a degree of affinity between the molecules. We shall have to assume this property for the biophor also, for without it the latter would not be a real unit at all. We shall, moreover, be able to conclude that these degrees of affinity are of various kinds, and that the molecules can combine in many different ways and form groups, so that isomeric molecular compounds are formed. Such isomeric compounds, however, will possess other properties, just as in the isomeric arrangement of atoms in the individual molecule; and thus we conclude that the special properties of a biophor are to be considered dependent not only on the physico-chemical constitution of the molecule, but also very essentially on their position and relation to one another; so that one biophor can be changed into another by an alteration in the arrangement of its molecules.

According to this statement there are several kinds of biophors, the difference between which depends on either the absolute relative number of molecules, their chemical constitution (isomerism included), or their grouping; in fact we may say that the *number of possible kinds of biophors is unlimited*, just as is the number of conceivable organic molecules. We shall, at any rate, meet with no theoretical difficulties on this score, however large the number of different kinds of biophors may be which we require to explain the theory of heredity.

The biophors are not, I believe, by any means mere hypothetical units; they must exist, for the phenomena of life must be connected with a material unit of some sort. But since the primary vital forces — assimilation and growth — do not proceed spontaneously from either atoms or molecules, there must be a unit of a higher order from which these forces are developed, and this can only consist of a group consisting of a combination of dissimilar molecules. I emphasise this particularly, because a theory of heredity requires so many assumptions which cannot be substantiated that the few fixed points on which we can rely are doubly valuable.

These biophors constitute *all* protoplasm — the morphoplasm which is differentiated into the cell-substance, as well as the idioplasm contained in the nucleus. It will be shown subsequently in what manner these two kinds of protoplasm differ as regards their constitution, and I will only remark here that the idioplasm must have a far more complex structure than the morphoplasm. The latter, as the cell-substance of a muscle or gland-cell shows, can assimilate, grow, and also divide, but it is not able to change into anything *different from itself*. The idioplasm, on the other hand, is capable of regular change during growth; and ontogeny, or the development of the individual in multicellular organisms, depends upon this fact. The two first embryonic cells of an animal arise from the division of the ovum, and continually give rise to differently constituted cells during the course of embryogeny. The diversity of these cells must, as I have shown, depend on changes in the nuclear substance.

It now remains to be considered how we are to imagine this capacity on the part of the idioplasm for regular and spontaneous change. The fact in itself is beyond doubt, when once it is established that the morphoplasm of each cell is controlled, and its character decided, by the idioplasm of the nucleus. The regular changes occurring in the egg-cell and the products of its division in each embryogeny must then be referred to the corresponding changes of the idioplasm. *But what is the nature of these changes, and how are they brought about?*

2. The Control of the Cell

In order to answer the question which has just been asked, it will be necessary to consider the manner in which the idioplasm of the nucleus determines the characters of the cell. At present we only know that the idioplasm consists of a large number of different biophors of various kinds. To exert a determining influence on the minute structure of the cell-body and on the chemical composition of its different components, it must either be capable of exerting an emitted influence ('Fernwirkung') or else material particles must pass out of the nucleus into the cell-body.

Strasburger * has endeavoured to prove a dynamical effect of

* E. Strasburger, 'Neue Untersuchungen über den Befruchtungsvorgang bei den Phanerogamen,' 1884, p. 111.

the nuclear matter. In his opinion 'molecular stimuli are transmitted from the nucleus to the surrounding cytoplasm, and, on the one hand, control the processes of metabolism in the cell, and on the other, give a definite specific character to the growth of the cytoplasm, this growth being caused by nutrition.' Although transmission of the molecular stimuli, proceeding from the nucleus to the rest of the cell, is certainly conceivable, de Vries has rightly shown that this is not a sufficient explanation of the phenomena, because it takes for granted the fundamental point of the matter requiring explanation. If the cell of any plant is to acquire the hereditary property of forming malic acid, those pangenes in the cell-body which can produce this acid could, it is true, come into play by molecular stimuli being transmitted to them from the nucleus; but this hypothesis takes their presence for granted, and the main question as to how these producers of malic acid get into the cell remains unanswered.

Haberlandt * has attempted to trace the control of the cell by the nucleus to the enzymatic action of the latter, *i.e.*, to the giving off from the nucleus of certain chemical compounds which cause the cell-substance to become changed in a given manner; but this explanation is regarded by de Vries as insufficient, because here again it is necessary to presuppose a definite differentiation of the cell-body.

De Vries himself gives a solution of the problem, and his hypothesis has, at any rate, the advantage of great simplicity and lucidity. He supposes that some of the pangenes which constitute the nuclear matter pass into the body of the cell through the nuclear membrane, and there form its parts and structures, of the qualities of which they are the special bearers.

Although I formerly inclined towards Strasburger's view, it always appeared to me rather as a formal than as a real explanation of the problem, and I regarded it more as a provisional formulation than as a solution of the difficulty. In my opinion de Vries's idea of the migration of minute, specific, vital particles from the nucleus into the cell-body affords an extremely happy solution of the apparently inexplicable manner in which

* G. Haberlandt, 'Uber die Beziehungen zwischen Funktionen und Lage des Zellkerns,' 1877.

the cell is controlled by the nucleus. It, moreover, fits in very well with my other views.

As long as I was engaged in seeking for an epigenetic theory of heredity, an explanation of this sort was naturally impossible, but as soon as I assumed that the germ-plasm consisted of biophors, the various kinds of which are required for the various characters of the respective cells, it was not only possible to suppose that the particles exerted an influence of this nature on the cell, but such an explanation of the phenomena became the most natural and satisfactory one. Much may of course be urged against this fundamental assumption, and it is not in itself a sufficient explanation; but it is not only fruitless to attempt a satisfactory explanation from the other point of view, but as will appear later on, de Vries's conception alone agrees with certain fundamental biological principles.

If the nuclear substance exerted an emitted influence on the cell-body so as to give rise to the structures characteristic of this particular kind of cell, they would be formed by a kind of '*generatio equivoca*'; they would have arisen by the operation of an external influence on the given substance in the cell, just as would be the case in primordial generation. Particularly favourable influences would have operated on certain combinations of inorganic substances in such a way as to give rise to a vital particle.

We know nothing of such a primordial generation as far as our experience extends, and even if it must be considered to be logically necessary, we have every reason to suppose that it has no share in the origin of those forms of life with which we are acquainted, but that these always arise by division from others similar to themselves. Moreover, what is true of the independent organisms familiar to us must also hold good for *all the different orders of vital units* which have united to form higher organisms, for each of the earliest and lowest organisms must have been neither more nor less than *the equivalent of one biophor*. If, then, in order to explain the presence of life on the earth, we must assume that such individual biophors arose at one time by primordial generation, they must have been capable of reproduction by division immediately after their origin, for such multiplication is caused directly by the primary forces of life, — assimilation and growth. We can only imagine the very simplest biophors as having been produced by primordial generation: *all subsequent and more complex kinds of biophors can only have arisen on the principle of adaptation to new conditions of life;* they must have been developed gradually by the long-continued co-operation of heredity and selection. All these biophors of a higher order, which are adapted to the special conditions of existence and which in endless varieties form organisms as we see them around us, possess '*historical*' qualities; they can, therefore, only arise from others like themselves, and cannot be formed spontaneously. This fact is confirmed by experience. Not only does a cell always arise from a cell, and a nucleus from a nucleus, as de Vries, and more recently Wiesner, have shown, but all the other constituents which occur in the cell-body and determine its structure never arise, so far as we know, by '*generatio equivoca*,' or, as de Vries expresses it, 'neogenetically.' They are always produced by the division of similar structures already present. This is apparently true of the green chromatophores and the 'vacuoles' of plant-cells, as well as of the 'sphere of attraction,' or centrosome, which controls the division of the nucleus: the same must also hold good for those invisible vital units, the various kinds of biophors, which have arisen during the course of the earth's history by gradual adaptation to continually new conditions of life.

If then, each vital unit in all organisms, from the lowest to the highest grade, can only arise by division from another like itself, an answer is given to the question with which we started; and we see that the structures of a cell-body, which constitute the specific character of the cell, cannot be produced by the emitted influence of the nuclear substance, nor by its enzymatic action, but can only arise owing to the migration of material particles of the nucleus into the cell-body. *Hence the nuclear matter must be in a sense a storehouse for the various kinds of biophors which enter into the cell-body and are destined to transform it.* Thus the development of the 'undifferentiated' embryonic cell into a nerve-, gland-, or muscle-cell, as the case may be, is determined in each case by the presence of the corresponding biophors in the respective nuclei, and in due time these biophors will pass out of the nuclei into the cell-bodies, and transform them.

To me this reasoning is so convincing that any difficulties we meet with in the process of determining the nature of the cell hardly come into account. We are still far from being able to describe in detail the entire histological process of the differentiation of a cell. The passage of invisible 'biophors' through the pores of the nuclear membrane is probably just as admissible an assumption as that of the independent power of motion thereby necessitated in these bearers of vitality; but the histological structure of a cell is not completed by the mere emission into the cell-body of a few kinds of biophors with great powers of multiplication. Numerous questions suggest themselves in this connection, all pointing to the fact that forces are at work of which we are at present ignorant. The immigrating biophors are the mere material which forms the histological structure of a cell, only when subjected to the guiding forces — presumably those of attraction and repulsion — which must be located in the biophor.

We can as yet form no more exact conception of this process than we can of the manner in which the biophors already contained in the cell-body behave in respect to those which have migrated into it from the nucleus. Presumably a struggle of the parts occurs, in which the weaker are suppressed and serve as nutritive material for the stronger ones. But although much remains to be decided by future investigation, the main point at issue, at any rate, viz., that the nature of the cell is really decided by the elements of the nucleus, is definitely established. By the nature of the cell must be understood not only the histological structure of the cell as a whole and its mode of reacting to external influences, but more particularly its *mode of division* in respect of time and place. It is true that the cell-*body* itself and its apparatus for division (the centrosome) primarily determine whether a cell is to divide sooner or later, and into equal or unequal parts; but these processes always depend finally on the nucleus, which controls the cell-body and impresses on the latter its definite nature.

The most plausible objection which can be urged against the migration of the particles of the idioplasm into the cell-body is that the substance of the latter is chemically quite different from that of the nucleus. Their behaviour as regards taking up colouring matters is certainly different, as the terms chromosome and chromatin indicate; but even if a difference in their chemical composition could be inferred from this fact, it would still fail to constitute a decisive proof against the hypothesis of migration:

for it is well known that the affinity of the chromosomes for colouring matter varies markedly at different periods, and this indicates that slight changes, which are beyond our control, take place in the constitution of this substance, and are sufficient to cause its most striking reaction with regard to colouring matters to disappear for a time. Chemical analysis of the substance contained in the nucleus has certainly established the presence of 'nuclein'; but although it is probable from Miescher's * excellent observations on the sperm of the salmon that nuclein is derived from the nuclei of the sperm-cells, it is not by any means certain from what part of the nucleus it originates: if one supposes that over 48 per cent. of the dried sperm consists of nuclein, it is doubtful whether this is contained in the small mass of chromatin which we see in the form of chromosomes.

Another recent observation may be mentioned here, which proves at any rate that matter is actually transferred from the chromosomes of the nucleus into the cell-body just at the time when the characteristic structure of the cell-body is being formed. I refer to Rückert's observations on the remarkable *alteration in the size of the chromosomes* of the nucleus during the growth of the ovum of the dog-fish.† One of the youngest ova observed in the ovary — which measured 2 mm. in diameter — contained from 30 to 36 chromosomes, each of which was 12 microns ‡ long, and 2 cubic microns in bulk: later on, in nearly ripe eggs, the length of a chromosome reaches 100 μ, and its cubic contents 7,850 cubic μ, or more accurately, since it has meanwhile become doubled by division, 15,700 cubic μ. Still later, just before the formation of the first polar body, when the ovum is ripe and has attained its full size, the length of the individual chromosome diminishes to 2 μ, and the cubic contents of a double rod to 3 cubic μ. Rückert infers from these facts that the chromosomes give off a great amount of substance to the ovum during the gradual ripening of the latter, and we can only agree with him on this point. But the question arises as to how this transference of substance takes place, —

* Miescher-Rüsch, 'Statist. u. biolog. Beiträge zur Kentniss vom Leben des Rheinsalm,' 1880; Schweiz. Literatursamml. z. internationalen Fischereianstell. in Berlin.

† J. Rückert, 'Anat. Anzeiger,' 10th March, 1892.

‡ A micron (μ) is the $\frac{1}{1000}$ of a millimetre.

whether it occurs in the ordinary way, fluid nutrient material being given off, and then assimilated by the cell-body, or in some other manner. There seems to me to be no reason why we should not assume that *minute, specific, vital particles*, and not merely nutritive substances, are produced by the chromosomes during the growth of the egg, and are then emitted through the nuclear membrane into the cell-body. Further facts must be ascertained before we can attempt to explain the details of the curious morphological transformations which the chromosomes undergo during this period. We are already, however, in a position to state that the extremely interesting processes described by Rückert must have a wide significance, and must occur in all cells which become histologically differentiated as well as in all animal ova. But they cannot appear so distinctly in these other cells, for no animal cell grows to such an enormous size as does the egg-cell. I shall again refer to the process in a later section, in order to emphasise one of the consequences which results from it still more strongly.

Let us now suppose with de Vries that the nature of a cell depends on the extrusion of minute vital particles of different kinds from the nucleus into the cell-body, and that these subsequently multiply and become regularly distributed and arranged in groups according to the forces of attraction and repulsion situated within them. On this supposition, heredity could be simply and easily accounted for in unicellular organisms, for in them multiplication depends on a division of the whole body and of the nucleus into two parts, and thus each product of the division receives a similar supply of latent biophors which form its nucleus, and from which it can then provide the necessary material to the cell-body.

As the influence of amphimixis is not taken into account in the present connection, I may here leave out of consideration the fact that the nucleus may be differentiated into two different kinds of nuclei. This arrangement is practically universal amongst the highest unicellular forms — the Infusoria — and is merely an adaptation for conjugation. In the unicellular forms heredity will therefore depend, firstly, on the fact that all the different kinds of biophors which are required for the construction of the body are present in the nucleus in a latent condition, and in definite proportions — very probably they have also a definite style of architecture; and secondly, on the periodical or occasional migration of these biophors into the cell-body, where they multiply, and become arranged in obedience to the forces acting within them. The difficulty of ascertaining the actual mode of arrangement is nowhere greater than in the case of the higher unicellular forms. How is it possible that the nucleus should always allow only those kinds of biophors to migrate which are required to replace those structures lost by division? And why do these biophors always move either in the direction of the missing oral region, or towards the posterior end of the body, according to which parts are wanting in the two daughter-animals? For the present these questions are unanswerable; and in the meantime we must be content with having shown how the materials for the construction of the cell-substance are transmitted from mother to daughter, and in what way they are placed at the disposal of the forces acting in the cell-body.

The experiments made by Nussbaum * and Gruber † on the artificial division of Infusoria prove that the nucleus really controls the cell-body. These observers found that only those portions which contained a part of the nucleus were capable of giving rise to a complete animal; the other pieces lived for a time, and then perished. One of Gruber's observations also tends to show that when regeneration of missing parts occurs, the nucleus sends out invisible material particles into the cell-body. He cut a large *Stentor* which was preparing for division transversely into two parts, so that the posterior portion contained no trace of the nucleus, and then observed that regeneration of the missing parts nevertheless took place, especially in the oral region. If the control of the cell depended on the emitted influence of the nucleus, this regeneration would be totally inexplicable; if, however, biophors proceed from the nucleus into the cell-body when regeneration is to take place, this might have already occurred in an animal preparing for division, as this one was before it was artificially divided.

The descendants of unicellular animals are similar to their ancestors: two daughter-cells are produced by the division of

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* Nussbaum, 'Ueber die Theilbarkeit der lebenden Materie,' Archiv. f. mikr. Anat., 1886.

† Gruber, 'Ueber künstliche Teilung bei Infusorien,' 'Biol. Centralblatt,' Bd. iv.; and 'Beiträge zur Kentniss der Physiologie und Biologie der Protozoën,' Ber. d. naturf. Gesellsch. zu Freiburg i/Br., 1886.

the mother-cell, and thus the nuclear substance is always composed of different kinds of biophors. But how does this apply to multicellular forms in which so large a number of different kinds of cells, each presupposing a different structure of the nuclear matter, arises from the germ-plasm of the ovum? Thus we find ourselves brought back to the question asked at the end of the last section: — on what do the regular series of changes in the germ-plasm during ontogeny depend?

3. The Determinants

As has just been shown, the nuclear matter of an Infusorian must be composed of a great number of different kinds of biophors, each of which corresponds to the primary constituent of a definite portion of the unicellular organism. If the cells of a multicellular animal were represented in the germ-plasm by all the kinds of biophors occurring in them, such an enormous aggregation of biophors would result that, even if they were extremely small, the minute quantity of matter in the germ-plasm would not be able to contain them. It was this consideration more than any other which for many years made me persevere in my attempt to discover an epigenetic theory of heredity. I thought that it must be possible to imagine a germ-plasm which, although highly complex, nevertheless did not consist of such an inconceivably large number of separate particles, but which was of such a structure as to become changed in a regular manner during its growth in the course of ontogeny, and, finally, to yield a large number of different kinds of idioplasm for the control of the cells of the body in a specific manner.

Hatschek,* too, has recently put forward the view that 'the egg-cell may be supposed to contain a relatively small number of qualities,' and that this number is not larger than that which is to be assumed in the case of any other histologically differentiated cell of the body. The diversity in structure seen in multicellular organisms is due, in his opinion, to the fact that in spite of the limited diversity as regards the qualities contained within a single cell (including the ovum), a far greater complication of the body as a whole is attained by the variation of these few qualities ('des einen Grundthemas').

* B. Hatschek, 'Lehrbuch der Zoologie,' 2te Lieferung, Jena, 1889, p. 232.

If in considering a theory of heredity we had only to deal with an explanation of the transmission of an *unalterable* structure from the parent to the offspring from generation to generation, there would be theoretically no objection to the assumption of such a structure of the germ-plasm. We have, however, to deal with the transmission of parts which are *variable*, and this necessitates the assumption that just as many independent and variable parts exist in the germ-plasm as are present in the fully formed organism. It is impossible that a portion of the body should exhibit an independent variation capable of transmission unless it were represented in the germ-plasm by a special particle, a variation in which is followed by one in the part under consideration. If this were represented, together with other parts of the body, by one particle of the germ-plasm, a change in the latter would be followed by a variation in all the parts of the body determined by it. *The independently and hereditarily variable parts of the body therefore serve as an exact measure for determining the number of ultimate particles of which the germ-plasm is composed: the latter must contain at least as great a number as would be arrived at by such a computation.*

An example may make it clear that the independently variable parts are not identical with those which are merely hereditary.

It is well known that butterflies pass through a metamorphosis in the course of development, the stages of which are independently variable from the germ onwards: that is to say, a variation in the caterpillar is not necessarily followed by one in the butterfly, and *vice versâ*. The caterpillars of a species may be dimorphic, some being green, and others brown, but both of these forms nevertheless give rise to butterflies with a similar coloration. If, therefore, the phyletic modifications depend on changes in the minute structure of the germ-plasm, there must be at least *two* independently variable units in the germ-plasm of such a butterfly; for if there were only one, the butterfly as well as the caterpillar would be affected by a variation in it. But a comparison of nearly related species shows us that the individual parts of the caterpillar or butterfly must also be variable from the germ onwards: the limbs, for instance, of two species may be very similar, while their wings are different, and even the separate parts of the wings may vary independently of one another. We must therefore assume that the germ-plasm contains a large number of units, on the variation of which the independent changes of certain parts of the body depend.

In all the higher animals the number of these units must be very large, because the parts which are independently variable from the germ onwards is large also.

A consideration of the individual and hereditary characters in the human species will show most clearly how great this number may be. I know of a family in which a depression of the size of a pin's head in the skin in front of the left ear has been transmitted through three generations. This slight abnormality must therefore have been contained potentially in the germ-plasm of the respective individuals, and their germ-plasm must differ from that of other people in the slightly abnormal form of the element which determines this peculiarity. We are logically compelled to assume a particular element of the germ-plasm for each peculiarity of this sort, not because heredity may be manifested in details so minute, but because *the transmission of such details may be independent.* If all people possessed such a depression in front of one ear, we could not thereby conclude that it must be represented by a special element in the germ-plasm merely because it is hereditary. It might conceivably be represented, together with the skin of half the face, by *one* element or biophor, which in the course of ontogeny became divided into a number of secondary ones of divers sorts, one of which proved to be abnormal and came to be situated at that particular spot in the skin. What compels us to accept the above assumption is the fact that all people do not possess this depression, and that two persons might conceivably resemble one another in all other respects except in the possession of this abnormality. The germ-plasm of both these persons would be almost identical, but not *perfectly* so, for it would contain a certain element which differed in the two cases. This simply means that *this particular character which is independently variable from the germ onwards is also represented by a special element in the germ-plasm.* It would not have been possible to infer this from its transmissibility alone. A hundred different characters might conceivably be determined by a single element in the germ-plasm; the whole hundred would then be transmitted as soon as the determining element was present in the latter, but not one of them would be independently variable from the germ onwards; but if the determining element varied, all the hundred characters would vary at the same time. The capacity for transmission and that of independent variation from the germ onwards are distinct from one another.

The germ-plasm must consequently be composed of as many units as there are transmissible parts in the body which are independently variable from the germ onwards. Each of these units cannot be smaller than a biophor, and they can therefore not be simple molecules within a biophor; for variation is a biological conception, and a biological element does not presuppose a one that is merely physical.

What parts of the body of a multicellular organism are represented in the germ by special particles of the minimum value of one biophor? Is each cell, or even each part of a cell? Darwin adopted the former, and de Vries the latter of these two alternatives. Darwin's gemmules are germs of *cells*, so that every cell of the body would be represented in the ovum by these units; while de Vries's pangenes are in a sense germs of the characters or structures ('Zellorganen') of the cell. There is no doubt that the hereditary variations in plants and animals manifest themselves in alterations of the individual parts or structures of the cell, and not only in the *number*, relative arrangement, and the changes in the form, size, and nature of the cells as a whole. The variegated varieties of our ornamental plants possess similar cells to those of their ancestral forms, but the green colour of the leaf is absent in certain of the cells: the red tint of the leaves of the copper beech, and other varieties of plants, depends on the red colour of the sap in a certain layer of cells, and this colour is transmissible. The coloured pattern on a butterfly's wing or a bird's plumage depends on cellular elements which were probably all alike in remote ancestors, but which afterwards became gradually changed by hereditary variations in the individual components or in the structure of the cell. Although the entire phyletic transformation of a species does not by any means alone depend on its *intra*-cellular variation, the latter has, nevertheless, constantly accompanied the other variations, and has shared to a greater or less extent in the transformation of the species. Hence it cannot be doubted that even in multicellular forms not only the cells as a whole, but also their parts, are determined from the germ onwards.

It seems therefore impossible to avoid the stupendous assumption that each of the millions of cells in a multicellular organism is represented in the germ-plasm by several or many different kinds of biophors. There is, however, a simple and natural way out of this dilemma, as soon as we inquire whether *every* cell of a plant or an animal is independently variable at all, and whether consequently it must be represented by special elements in the germ-plasm.

I shall designate the cells or groups of cells which are independently variable from the germ onwards as the '*hereditary parts*' or '*determinates*,' and the particles of the germ-plasm corresponding to and determining them, as the '*determining parts*' or '*determinants*.' It is evident that many of the cells in the higher animals are not represented *individually* in the germ-plasm by a determinant. The millions of blood-corpuscles which are formed during the life of a Vertebrate might possibly be controlled in the germ-plasm by a *single* determinant. At any rate no disadvantage to the species would result from this, because the capacity for being independently determined on the part of the individual blood-corpuscles, or even individual thousands of them, would be of no value to the animal. They are not localised: one of them has the same value as another, and their variability therefore might well be controlled from a single point. In conformity with the law of economy, Nature would not have incorporated more determinants than was necessary into the germ-plasm.

Thus there are probably many groups of cells in the higher animals, the constituents of which are not represented individually in the germ-plasm. All the nerve-cells of the brain do, it is true, possess their special determinants, as otherwise the transmission of such fine shades of mental qualities in man would be inexplicable; but it can matter little whether each fibre of a muscle, or each cell of the epidermis or of the epithelial lining of the alimentary canal, has its special determinant: in the last-mentioned cases larger or smaller *groups* of cells are presumably controlled by a single determinant. The manner in which the epithelium of the alimentary canal is renewed amongst insects may perhaps be taken as pointing to this assumption. In flies and butterflies, for instance, as I have proved long ago, the alimentary canal of the larva undergoes disintegration, and that of the imago, which has a very different structure, is developed out of its remains. Kowalewski and van Rees have since shown that the process takes place as follows: — the formation of portions of the new alimentary canal begins in certain cells which are separated by fairly regular intervals; these then spread until they come into contact with one another. The idioplasm of the new intestinal cells is consequently only contained in these formative cells, and it is natural to suppose that each of them contains only *one* kind of determinant.

The same appears to be the case with the hair of mammals. Every hair does not possess a special determinant in the germ, but more or less extensive regions of the hairy covering are represented each by one determinant. These regions are not large, as is shown by the stripes and spots on the coat of such animals as the tiger and leopard. The recurrence in the son, on exactly the same part of the head as in the parent, of an abnormal tuft of white hair, has been observed in the human subject.

Similar hereditary parts or determinates may be observed in butterflies, in which the colours on the wings often form very complicated lines and spots of slight extent but of great constancy. Such regions are often limited to quite a few scales (cells): *Lycæna argus*, for instance, possesses a black spot on a particular part of the anterior wing consisting of only ten scales, while the surrounding parts are blue. In this case we may therefore conclude that the black cells are represented in the germ-plasm by at least one determinant. The determination may possibly be carried out in still further detail in this instance, and each cell in the black spot may be determined from the germ onwards; and possibly it is only the constant intermingling of two hereditary tendencies in sexual reproduction, and the consequent variability in the number of scales, which prevents us from recognising the fact. We can at any rate, however, find instances of the determination of single cells in other species of animals. For example, in many Crustaceans a number of sensory organs are situated on the anterior antennæ: each of these corresponds to one cell. The number, position, and form of these 'olfactory' setæ is determined exactly for each species. The Ostracod *Cypris* possesses only *one* olfactory seta on each antennule, while in the common fresh-water species of *Gammarus*, there are about twenty of these structures, each of which is separately attached to one of the consecutive joints of the feeler. In many blind Crustaceans, which live in the dark, the number of these setæ is greater than in the case of related forms which possess the sense of sight. And though in all these instances individual deviations occur, we may nevertheless suppose them to be hereditary, for otherwise the increase in the number of olfactory setæ incident on a life in darkness, could not have been established as a specific character.

In smaller and simpler organisms each individual cell may well have been determined from the germ onwards, and not merely with the result that the number of cells is a definite one, and the position of each definitely localised: the determination may also have caused individual peculiarities of each cell, in so far as they depend on changes in the germ-plasm at all — *i.e.*, are 'blastogenic,' — to reappear in the corresponding cell in the next generation, just as in the case of a birthmark in the human subject which recurs in precisely the same place on the same side of the body. This may also be true of animals as simple as the *Dicyemidæ* or the *Tardigrada*, although it is not possible to prove it positively.

In all the more highly differentiated animals there can be little doubt that the number of determinants is always very much less than that of the cells which are the factors in the process of ontogeny. If we compare this statement with Darwin's assumption of the presence of a gemmule — or rather of several gemmules — for each cell, it is evident that the germ-plasm is thus to some extent relieved of a burden.

We must not forget, however, that a cell may vary as regards transmission not only as a whole but also in its parts, so that not *one* but several biophors must be assumed for each determinant of a cell or group of cells; we must, in fact, suppose just as many to be present as there are structures in the cell which are variable from the germ onwards. We ought, properly speaking, to speak of these bearers of qualities, which correspond to de Vries's pangenes, as determinants also, for they determine the parts of a cell. As the name of biophor has been given to them, however, it is better to retain this term, and to define a *determinant as a primary constituent of a cell or group of cells*. Thus a determinant is always a group of biophors, and never a single one.

It may now, I believe, be proved without difficulty that the biophors determining a cell not only lie close together in the germ-plasm so as to form a group, but that *they also combine to form a higher unit.* The determinant is not a disconnected mass of different biophors, but *a vital unit of a higher order than the biophor, possessed of special qualities.*

The fact that the determinants must possess the power of multiplication is in itself a sufficient proof of this. We know how greatly the nuclear matter contained in the fertilised egg-cell increases in volume during development, and this can only be due to the multiplication of its vital particles, the biophors. Such a multiplication could never occur with as much precision and regularity as is necessary for the preservation of the character of a certain cell, if the biophors which determine it were scattered at random instead of being definitely separated from those of other cells. Hence the multiplication of the biophors must occur within the fixed limits of the determinant, and must be preliminary to the division of the determinant itself. And consequently the latter is also a vital unit.

In accordance with our assumption, which can scarcely be refuted, a single determinant of the germ-plasm frequently controls entire groups of cells: this is a further proof that the determinants as such must multiply. This is only possible if they do so in the process of ontogeny. It is very probable, moreover, that the nucleoplasm of any cell in the body never contains *one* specimen only of the determinant controlling it, but several; otherwise, how could such a cell be visible at all under our microscopes? Biophors, at any rate, are far beyond the limit of vision, and even determinants can hardly come within it.

Thus the assumption made by the gifted propounder of the theory of pangenesis is so far justified. 'Gemmules' of cells really exist, and multiply by fission; but they are not the ultimate vital units, nor are special gemmules of all the cells of the body already present in the germ-plasm.

We have next to deal with the question as to how these two elements of the germ-plasm, which have now been formulated, are instrumental in the process of ontogeny.

4. The Id in Ontogeny

We can now make an attempt to solve the problem stated at the close of the last section concerning the way in which the germ-plasm is capable of giving rise to the various kinds of idioplasm required in the construction of the organism.

As we have seen, the germ-plasm contains the primary constituents of all the cells in the body in its determinants, and it only remains to inquire how each kind of determinant reaches the right part in the right number. Although we do not know what forces are called into play for this purpose, the elements of the germ-plasm now formulated, and the processes and course of ontogeny, nevertheless enable us to draw certain conclusions as to the structure of the germ-plasm and the nature of the changes it undergoes; and I trust that these conclusions will not lead us too far from the truth.

We can, in the first place, state with certainty that the germ-plasm possesses a *fixed architecture, which has been transmitted historically.* In working out the idea of determinates, it was stated that probably not nearly all the cells of the higher organisms are represented in the germ-plasm by special determinants: possibly all the blood-corpuscles, or the thousands of fibres in a particular muscle, for instance, are represented each by *one* determinant. But it does not therefore follow that all the cells of a similar kind which exist in the body can be represented by *one* common determinant: this would be equivalent to abandoning the conception of determinants altogether. If, for instance, all the transversely striped muscles of a Vertebrate were represented in the germ-plasm by a *single* determinant, each variation in the latter would also produce a corresponding change in *all* the muscles, and the independent variation of which each individual muscle is actually capable would then be impossible.

Several, or even many, similar determinants must therefore exist in the germ-plasm of an animal. Muscle-cells and nerve-cells are repeatedly formed even in the fully developed organism, and, in so far as they can vary individually at all from the germ onwards, will be represented by identical or by very similar determinants in the germ-plasm.

If such *identical* determinants represent a single fixed cell or group of cells, they cannot be situated anywhere in the germ-plasm, nor can they change their position according to varying influences: the determinants must be definitely localised, for otherwise, they would not be certain to reach the right cell and the right position in the course of ontogeny. I have already mentioned the olfactory setæ of *Gammarus*, which are situated individually on particular segments of the feeler. Each of these can vary hereditarily, and thus it is necessary to assume special determinants for them in the germ-plasm; these, however, will all be similar to one another. This is also true of the black spots on the wings of certain butterflies, already referred to. In *Lycæna Argus*, for instance, there is a spot on that part of the wing which is known to entomologists as 'cell 1 b,' and this spot is independently variable: it may be larger or smaller, and the variations in it can be transmitted quite independently of the numerous other black marks on the wing. The particular spot referred to may have disappeared entirely in another species of *Lycæna*, while a precisely similar spot in 'cell 4' has become much larger. We have also decided indications that homologous parts in the two halves of the body in bilaterally symmetrical animals can vary independently of one another. The human birthmark mentioned above was always inherited on the left side, and never on the right.

If each determinant occupies a fixed position in the germ-plasm, *it cannot have an indefinite or variable size and form, but must form a complete unit by itself*, from which nothing can be removed, and to which nothing can be added. In other words, we are led to the assumption *of groups of determinants*, each of which represents a separate vital unit of the third degree, since it is composed of determinants, which in their turn are made up of biophors. These are the units which I formulated on different lines long ago, and to which the name of *ancestral germ-plasms* was then given. I shall now speak of them as '*ids*,'* a term which recalls the 'idioplasm' of Nägeli.

I assume that just as the individual biophor has other qualities than those of the determinant, which is composed of biophors, so also does the id possess qualities differing from those of its component determinants. The fundamental vital properties — growth and multiplication by division — must however be attributed to the id as to all vital units. Several reasons,

* I have already used this term in my essay on 'Amphimixis' ('Amphimixis, oder die Vermischung der Individuen,' Jena, 1891, p. 39). In my earlier essays the ids were spoken of as 'ancestral germ-plasms,' the meaning and derivation of which term will be explained in the chapter on amphigonic heredity.

more especially those furnished by the phenomena of heredity in sexual reproduction, lead us to assume that the germ-plasm does not consist of a *single* id, but of several, or even many of them, and this assumption must be made even in the case of asexual reproduction.

I shall therefore assume that *each idioplasm is composed of several or many ids, which are capable of growth and multiplication by division.* If animals existed, in the whole series of ancestors of which sexual reproduction had never occurred, these ids would be exactly similar to one another. But in all cases every id of the germ-plasm contains the whole of the elements which are necessary for the development of all subsequent idic stages. Theoretically, therefore, *one* id would suffice for ontogeny.

We assume that *the changes in the id of germ-plasm during ontogeny* consist merely in a regular disintegration of the determinants into smaller and smaller groups, until finally only *one* kind of determinant is contained in the cell, viz., that which has to determine it. It is highly improbable that all the determinants in the id of germ-plasm are carried along through all the idic stages of the ontogeny. In discussing regeneration and gemmation later on, I shall have to show that, under certain circumstances, groups of determinants are supplied to certain series of cells, and that these are not actually required for determining the cells; this arrangement, however, depends, I believe, on special adaptations, and is not primitive, at any rate not in the higher animals and plants. Why should Nature, who always manages with economy, indulge in the luxury of providing all the cells of the body with the whole of the determinants of the germ-plasm if a single kind of them is sufficient? Such an arrangement will presumably only have occurred in cases in which it serves definite purposes. The enormous number of determinants contained in the germ-plasm also stands in the way of such an assumption, for in the higher animals they can be reckoned by hundreds of thousands at the very least; and although we may assume that they all remain in a latent condition in every cell, and so need not interfere with the activity of the determinants which control the cell, they nevertheless deprive the active determinants — which we must also suppose to exist in large numbers — of a considerable space.

If we wished to assume that the whole of the determinants of the germ-plasm are supplied to all the cells of the ontogeny, we should have to suppose that differentiation of the body is due to all the determinants except *one* particular one remaining dormant in a regular order, and that, apart from special adaptations, only *one* determinant reaches the cell, viz., that which has to control it. This latter supposition is undoubtedly less likely than the former.

If however we do make this assumption, the question then arises as to what factors can cause the gradual disintegration of the id of germ-plasm into smaller and smaller groups of determinants, — that is to say, into ids which contain fewer and fewer *kinds* of determinants.

This disintegration I believe to be due to the co-operation of three factors: these are — *the inherited architecture of the germ-plasm*, in which each determinant has its definite position; *the unequally vigorous multiplication of the various determinants*; and possibly also, *the forces of attraction* which are situated within each determinant, and result from its specific nature as a special and independent vital unit. The architecture of the germ-plasm has already been discussed in general terms: for the present, at any rate, we can hardly conjecture the actual details of its structure. In order to do so, it would be necessary to suppose that hundreds of thousands, or millions, of determinants, which are all definitely localised, take part in the formation of the higher organisms. The fact that the right and left halves of the body can vary independently in bilaterally symmetrical animals, points to the conclusion that all the determinants are present in pairs in the germ-plasm. As, moreover, in many of these animals, *e.g.* the frog, the division of the ovum into the two first embryonic cells indicates a separation of the body into right and left halves, it follows that the id of germ-plasm itself possesses a bilateral structure, and that it also divides so as to give rise to the determinants of the right and left halves of the body. This illustration may be taken as a further proof of our view of the constant architecture of the germ-plasm. An id is evidently not constituted like the sediment of a complicated and well-shaken mixture, in which the heavier particles come to lie at the bottom and the lighter ones at the top; nor is it constituted in such a manner that the respective positions of the particles are only determined independently by the forces acting on them and between them momentarily. Its structure may be compared to that of a complicated ancient building, the stones of which we may suppose to be alive, so that they can grow and increase, and thus cause displacements and fissures in the walls, in which process the forces of attraction present within these living stones take part. *The historical transmission of the architecture of the germ-plasm forms the basis of the entire ontogenetic development of the idioplasm.*

If however the id has a right and left half in bilateral animals, we must not thereby infer that it is merely a miniature of the fully-formed animal, and that therefore we are once more dealing with the old theory of preformation. Quite apart from all conjectures as to the detailed architecture of the id of germ-plasm, it is at any rate certain that the arrangement of the determinants in it is quite different from that of the corresponding parts in the fully-formed organism. This is proved by a study of development, and need scarcely be treated of in detail here. Any one with a knowledge of animal embryology knows how great a difference there is between the mode of development of the parts from one another in the embryo and their respective relation in the mature organism. The early stages of segmentation of the ovum show that groups of determinants have been formed in the id of germ-plasm, and that these, moreover, correspond to the parts of the body which arise from one another consecutively, though they can have no resemblance to them either in form or in their degree of perfection.

In some worms the two first blastomeres do not give rise respectively to the right and left sides of the body, but to the entire ectoderm and endoderm. In these cases the id of germ-plasm must break up into two groups, one of which contains all the determinants of the ectodermal organs, and the other all those of the endoderm: it is evident that this arrangement has no analogy to that which obtains as regards the organs of the fully-formed animal. If in any species we knew the 'value in primary constituents' ('Anlagenwerth') — if I may use such a term — of each cell in the ontogeny, we could give an approximate representation of the architecture of the germ-plasm; for, beginning with the last formed cells, we could infer the nature of the determinants which must have been contained in each previous mother-cell, passing gradually backwards to the ovum; thus we should reach the two first blastomeres, and finally the egg-cell itself. The groups of determinants which are present at each stage would thus be known, and we might in imagination then arrange them in such a way that it would be possible to picture *their disintegration into the respective series of smaller and* smaller groups.

Such a representation of the architecture of the id of germ-plasm would, however, never be an accurate one, because its parts must be subjected to incessant slow displacement during the growth of the idioplasm and in the course of development.

This brings us to the *second factor* which takes part in the ontogeny of the idioplasm, viz., the uneven *rate of multiplication of the determinants*. An id of germ-plasm composed entirely of *similar* determinants, would have to retain its original architecture even during vigorous growth and continued division; just as would be the case in one of the lowest forms of life — a Moner — consisting of a number of identical biophors, which must remain the same throughout all the divisions which it undergoes. In a germ-plasm consisting of a number of different determinants, a perfectly even rate of multiplication cannot be assumed in the case of all of them. For the difference between two determinants depends presumably on the differences in the nature, number, or arrangement of their constituent biophors, and the latter differ again in their molecular structure, *i.e.* in their essential physico-chemical properties. Hence the determinants will behave differently as regards their reaction to external influences, — more especially in respect of their rate of growth and increase, — according to their constitution. The same conditions of nutrition will therefore stimulate one to a faster, and another to a slower, growth and corresponding multiplication, and thus an alteration in the proportional numbers in which the individual kinds of determinants are present in the germ-plasm must occur continually in the course of embryogeny; for the latter is connected with a constant growth of the idioplasm, and therefore also with a continual increase of the determinants. This must cause a disarrangement in the architecture of the germ-plasm, in which process the third factor concerned in these changes, viz., *the forces of attraction in the determinants*, may take part.

The assumption of such forces can scarcely be avoided. For it is very probable, *a priori*, that vital units do act upon one another in different degrees, and this view is supported by a consideration of the processes of nuclear division, together with the distribution of the primary constituents in ontogeny.

So far I have not touched upon the question as to what observable parts of the idioplasm are to be regarded as ids. This point cannot be decided with certainty at present, but I have elsewhere expressed the opinion that those rod-like, loop-like, or granular masses of chromatin in the nucleus, — the chromosomes, — are to be considered equivalent, not to single ids, but to series or aggregations of ids. I have therefore proposed to call the chromosomes *idants*,[1] in order to keep up a certain uniformity in the nomenclature. It is probable that the ids correspond to the small granules hitherto called 'microsomata,' which are known to form the individual idants in many animals: we may mention as an example, *Ascaris megalocephala*, as in it the nuclear structure is best known. These microsomata, although lying very close together in *one* row, are nevertheless separated by a thin layer of intermediate substance; the whole idant cannot therefore be equivalent to one id, for the latter is a clearly defined vital unit possessing a fixed architecture, and cannot consist of completely separated parts.

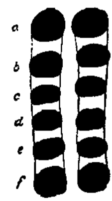

FIG. 2.
Two Idants with their contained Ids of *Ascaris megalocephala*. (After Boveri.)

The great variety as regards size, number, and form of the chromosomes in different species of animals, indicates that they possibly have not always a similar morphological value. As however there is no reason for assuming that the number of ids must always be the same in all species, and as, on the contrary, it is much more probable that their number varies greatly, it is impossible to make use of the above fact as a decisive argument. We can only state that the individual chromosome or idant in all probability represents a different number of ids in different species.

Division of the nucleus depends on the longitudinal splitting of the idants, in which process each of the spherical ids — assuming these to correspond to the microsomata — becomes halved. Each half then becomes rounded off, and passes, together with the idant to which it belongs, into one of the two daughter-nuclei.

In the ordinary process of cell-division in tissues, which results in the formation of daughter-cells similar to those from

[1] 'Amphimixis,' pp. 39, 40.

which they arose, the ids produced by the division naturally contain precisely similar determinants; in embryogeny, on the other hand, divisions occur which ensure that the two daughter-nuclei contain combinations of determinants which are usually entirely different from one another. We have an example of such a nuclear division in the segmentation of the ovum in the case, for instance, of certain worms already referred to, in which two cells are formed by the first division of the egg-cell, one of which contains all the determinants of the internal, and the other all those of the external germinal layer. A division of this latter kind we may speak of as *differential* or *dissimilar as regards heredity* ('erbungleich'), in contrast to the former, which is *integral* or *similar as regards heredity* ('erbgleich'). As in the case of the entire idants, the ids are split by an internal force, and are not pulled apart mechanically by the threads of the 'nuclear spindle' which are attached to them. Flemming has shown that this splitting often takes place long before the spindle-threads become active. The forces of attraction in the determinants must therefore take part in this process, just as they must be assumed to act between the biophors which constitute the body of a dividing cell.

It appears to me, therefore, that the inherited architecture of the id of germ-plasm undergoes a gradual change, owing to the uneven rate of multiplication of the determinants, and that it is further regulated by the forces of attraction which we must suppose to act between them. We might represent the architecture of the id by a very complicated geometrical figure, which gradually becomes changed during the growth of the id; this change does not occur in the first division, the preparation for which has been accurately made in the original figure, but in the subsequent stages of ontogeny. As the greater number of these divisions is connected with a diminution in the number of kinds of determinants, the geometrical figure representing the id gradually becomes simpler and simpler, until finally it assumes the simplest conceivable form, and then each cell will contain the single kind of determinant which controls it. The disintegration of the germ-plasm is a wonderfully complicated process; it is a true 'development,' in which the idic stages necessarily follow one another in a regular order, and thus the thousands and hundreds of thousands of hereditary parts are gradually formed, each in its right place, and each provided with the proper determinants.

The construction of the whole body, as well as its differentiation into parts, its segmentation, and the formation of its organs, and even the size of these organs, — determined by the number of cells composing them, — depends on this complicated disintegration of the determinants in the id of germ-plasm. *The transmission of characters of the most general kind — that is to say, those which determine the structure of an animal as well as those characterising the class, order, family, and genus to which it belongs — are due exclusively to this process.* The slight differences only, namely those which distinguish species from species, and individual from individual, depend partly on the characters of the *individual cells.* De Vries has overlooked this in his attempt to explain all the facts of heredity by the theory of '*intra*-cellular' pangenesis. As was mentioned in the 'Historical Introduction' to this book, it must be borne in mind that most of the 'characters' of any of the higher forms of life result not from the characters of the individual cells, but from the way in which they are combined. On the other hand, the construction of a living organism is not conceivable unless we presuppose the determination of the characters of each cell.

We have therefore to give an explanation of this concluding part of the process of ontogeny; this has already been done to a great extent above, in the section treating of the control of the cell by the idioplasm. I there assumed, as de Vries has also done, that this determination depends on the migration of minute vital particles from the nucleus into the cell-body. We have now seen by what means the biophors characteristic of any particular cell reach that cell in the requisite proportion. This results from the fact that the biophors are held together in a determinant which previously existed as such in the germ-plasm, and which was passed on mechanically, owing to its ontogenetic disintegration, to the right part of the body. In order that the determinant may really control the cell, it is necessary that it should *break up into its constituent biophors.* This is an inevitable consequence of the assumed mode of determination of the cell. We must suppose that the determinants gradually break up into biophors when they have reached their destination. This assumption allows, at the same time, an explanation of the otherwise enigmatical circumstance, that the rest of the determinants, which are contained in every id except in the last stages of development, exert no influence on the cell. As each determinant consists of many biophors, it must be considerably larger than a biophor, and is probably therefore unable to pass out through the pores of the nuclear membrane, which we must suppose to be very small and only adapted for the passage of the biophors. Although it is *impossible to make any definite* statement with regard to the internal structure of the determinants, it must be owing to this structure that each determinant only breaks up into biophors when it reaches the cell to be determined by it. We may suppose that, just as one fruit on a tree ripens more quickly than another, even when the same external influences act on both, so also one sort of determinant may mature sooner than another, although similar nourishment is supplied to both.

It must not, however, be overlooked, that a difference in the time of maturation of the determinants in the embryogeny of animals is chiefly to be assumed only in the case of the actual embryonic cells; for the histological differentiation of the cells of the body, and the differentiation of the parts of the latter, occur at about the same time; that is, not until the organs already exist as definite groups of cells. This is equivalent to saying that the disintegration into biophors occurs when the *id only contains the single determinant which controls that particular* kind of cell. It is well known how suddenly the histological differentiation of the cells occurs in the embryogeny of an animal. For a long time the various parts and tissues are very similar to one another, though not perfectly so, and then histological differentiation suddenly sets in. This is very markedly the case as regards the transversely striped muscles of Arthropods and Vertebrates, in which the contractile substance is first seen as a mere narrow ring around the cell, and then gradually becomes thicker, so as to replace the greater portion of the cell-body, — just as one would expect if it were caused by muscle-biophors which had migrated into the cell-substance and there multiplied.

The assumption of a 'ripening' of the determinants, which though not simultaneous, is yet exactly regulated, nevertheless remains indispensable; or, to express it differently, we must assume that the determinants pass through a strictly regulated *period of inactivity, at the close of which the disintegration into* biophors sets in. The determinants certainly continue to grow and multiply without interruption during this period, as may be deduced from the fact that the amount of the nuclear substance in the individual cell does not decrease during embryogeny, although such an enormous increase in the number of cells takes place. No accurate and methodical observations have at present been made with regard to the comparative size of the chromosomes in the various stages of development and in the different organs of the body, but it may nevertheless be taken as certain that the entire mass of the nuclear substance grows considerably during embryonic development. It appears to me, however, to follow from the observations of Rückert I have already referred to concerning the chromosomes of the ovum of the dog-fish,* that *the most marked growth of the determinants takes place immediately before, and during, their activity.* During the period of growth and histological differentiation of the egg in this fish the idants grow enormously, and towards the completion of these processes they gradually decrease in size, until finally, when the ovum is ripe, they have become almost as small as they were originally.

This may be expressed, in the terms we have adopted, as follows: *the determinants which control the histological structure of the egg*† *multiply enormously during the growth of the ovum, into the body of which they transmit their numerous biophors.* After this has occurred, only those determinants of the germ-plasm are left which have in the meantime been inactive, and which have only increased to a slight extent; these are thus contained in those idants which are not much larger than they were in the young egg-cell. From the beginning of ontogeny and onwards, one determinant after another becomes active, and during their activity they also multiply. It has for a long time appeared to me probable that the determination of a cell does not take place, as one might suppose, by the agency of a single determinant, but by that of many determinants of

* Anat. Anzeiger, 10th March 1892.

† These determinants of the ovum correspond to the 'oogenetic nucleoplasm' of my earlier essays, and constitute the substance which determines the growth and histological differentiation of the egg. For a long time I believed that this substance was extruded from the ovum at the close of the period of maturation by means of the polar bodies. We now see that such an extrusion is not required, as this substance is used up in the differentiation of the egg.

a similar kind; and I imagine that that kind of determinant which has to control a particular cell, multiplies considerably by division before—and perhaps even during—the process or determination. This view is completely borne out by Rückert's interesting observations.

Every cell during the whole period of ontogeny is, however, controlled—not only as regards its structure, but also in respect of its mode of division—by a *single* determinant only. The inactive determinants remain without exerting any influence on the cell-body; they however determine the architecture of the id, and therefore the further formation of the embryo also. For, indeed, the mode of disintegration of the id into smaller groups of determinants is necessitated by its architecture.

I have above attributed to the determinants forces of attraction which take part in the configuration of the structure of the ids. Such forces must be present, for otherwise the id could not possess a definite architecture; but I do not wish it to be understood that these forces are the principal factors in the arrangement of the determinants. They are concerned in connecting together the parts of which the determinants are composed, and not in their continual rearrangement during the course of ontogeny. It is primarily always the inherited definite architecture of the id of germ-plasm which results mechanically in the idic figure of the subsequent stages; disarrangements in this architecture are due to the unequally vigorous increase of the various kinds of determinants, all of which naturally are definitely determined beforehand. The arbitrary or accidental action of the forces of attraction takes no part at all in this process.

I must emphasise this view particularly, in contrast to that of Galton, who speaks of 'repulsions and affinities' of the gemmules which compose the 'stirp.' He compares the masses of these gemmules, which undergo active and incessant changes of their mutual positions owing to attraction and repulsion, to a swarm of flying insects, in which 'the personal likings and dislikings of an individual may be supposed to determine the position that he occupies in it.' With this view I can by no means agree, for it rests on the assumption that the germ-substance is composed of many *homologous* gemmules ('competing germs') which struggle for the supremacy, only those which are successful determining the character of the future organism. From the very first Galton takes into consideration the complications or the germ-substance caused by sexual reproduction, which, as will be shown subsequently, are due essentially to the fact that *the germ-plasm contains many, and not a single specimen of* each primary constituent, and that these are present in various modifications. It is this struggle between the *homologous* primary constituents which Galton refers to in the passage just quoted, which indicates that first one, and then another, reaches the desired spot, without any definite order being observed. This conception appears still more plainly in another passage, in which he compares the germ-plasm (the 'stirp') to a nation, and those gemmules 'that achieve development,'—*i.e.*, become transformed into the corresponding parts of the body—'to the foremost men of that nation, who succeed in becoming its representatives.'

Excellent as these similes are in themselves, I cannot help thinking that they lead to error if intended as an explanation of ontogeny. If we take up the position which Galton occupies with regard to the essential part of the theory of pangenesis, we must suppose that a large number of gemmules—many more than are necessary for the construction of the body—are contained in the stirp; that is, in the germ-substance of the fertilised egg. For only *one* gemmule is required for each cell of the body, but nevertheless a large number are present; and these, so to speak, struggle for the precedence, the successful gemmule alone becoming converted into the cell which is to be formed. In this conception the fact is entirely overlooked that ontogeny itself cannot possibly depend on this struggle, but would take place just the same if only *one* gemmule were present in the 'stirp' for each cell, and that the cause for the progress of development must therefore be sought elsewhere than in the rivalry between homologous gemmules: it must be due to the right *succession* of the gemmules. Galton considers that the 'purely step-by-step-development' assumed by Darwin in his theory of pangenesis is insufficient, but I think, nevertheless, that Darwin's opinion is the more correct one.

Neither does Galton's simile of the swarm of insects seem to me to be appropriate as an explanation of the struggle between homologous gemmules derived from different ancestors. Even if the gemmules in the 'stirp' were in perpetual motion, and if on this depended the decision as to which of them obtained the privilege of taking part in the formation of the organism, how could one explain the existence of identical twins, about which we have received such valuable information from Galton himself? How would it be possible for the *exactly* corresponding gemmules in two individuals in the flying and ever-changing swarm always to reach the most favourable position, even if the 'stirp' contained precisely similar gemmules?

In a subsequent section I shall attempt to show that this struggle between homologous but individually different primary constituents can be proved in quite another manner in connection with the idioplasm. It was necessary to mention Galton's view here, in order to show that the forces of attraction and repulsion, assumed by him, are introduced for an entirely different purpose from that which I have stated with regard to the similar forces in connection with the biophors of the idio-plasm.

Two physiological conditions of the elements of the idioplasm exist, — an active and an inactive. In the former, these elements become disintegrated into their constituent parts; while in the latter, they remain entire, although they are capable of multiplication. When determinants are active, they become disintegrated into biophors, and are then capable of controlling the cell in the nucleus of which they are situated. The activity of entire ids depends on a disintegration into determinants, which, though certainly successive, is often very slow; it must be contrasted with the inactive state, which in both elements of the idioplasm depends on the fact that their constituent parts do not become separated from one another, but remain in their primarily entire condition. In the immature ovum, for instance, only *one* kind of determinant — the 'oogenetic' determinant — is active, and this controls the growth and histological differentiation of the egg; all the other kinds remain inactive, as do also the ids which are formed from them. Only when fertilisation has occurred do they become active, — that is to say, one kind of determinant after another begins to separate itself from the entire id. We shall see later on, however, that ids of the germ-plasm also exist which remain inactive even after fertilisation has occurred, and are passed on from cell to cell in what we may call an *unalterable* ('*gebundenem*,') condition, so as to form subsequently the germ-cells of the embryo. We know as little about the cause of this condition as we do about that of the state of the brain during sleep, or of the latent period of certain fertilised animal eggs, which, after beginning to undergo development, remain inactive at a certain stage for months. The facts with which we are acquainted, however, render the assumption of an active and an inactive state of the ids and determinants unavoidable, as will become more evident in the course of this book. A similar assumption has been made by all those who have formulated vital units: thus Darwin has assumed these conditions in connection with his 'gemmules,' and de Vries with regard to his 'pangenes.'

Two forms of heredity, which we call homotopic and homochronic, may be deduced from the theory given above. As the individual determinants — from the germ-plasm onwards, throughout all the stages of ontogeny — take up a definite position in the id, they must reach the right place in the body, and there cause the development of a structure corresponding to that of the parent. As, moreover, the period of maturation of each determinant is decided by the nature of the latter, the determinant will become active in the individual and will cause the formation of any particular part of the body at the same stage of development as in the parent. Exceptions to this rule occur in the case of abnormalities, and also in that of phylogenetic displacements.

5. Summary of Sections 1–4, relating to the Structure of the Germ-plasm

According to my view, the germ-plasm of multicellular organisms is composed of ancestral germ-plasms or *ids*, — the vital units of the third order, — each nuclear rod or *idant* being formed of a number of these. Each id in the germ-plasm is built up of thousands or hundreds of thousands of *determinants*, — the vital units of the second order, — which, in their turn, are composed of the actual bearers of vitality ('Lebensträger'), or *biophors*, — the ultimate vital units. The biophors are of various kinds, and each kind corresponds to a different part of a cell: they are, therefore, the 'bearers of the characters or qualities' ('Eigenschaftsträger') of cells. Various but perfectly definite numbers and combinations of these form the determinants, each of which is the primary constituent ('Anlage') of a particular cell, or of a small or even large group of cells (*e.g.*, blood-corpuscles).

These determinants control the cell by breaking up into biophors, which migrate into the cell-body through the pores of the nuclear membrane, multiply there, arrange themselves according to the forces within them, and determine the histological structure of the cell. But they only do so after a certain definitely prescribed period of development, during which they reach the cell which they have to control.

The cause of each determinant reaching its proper place in the body depends on the fact that it takes up a definite position in the id of germ-plasm, and that the latter, therefore, exhibits an inherited and perfectly definite architecture. 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, so that in place of a million different determinants, of which we may suppose the id of germ-plasm to be composed, each daughter-cell in the next ontogenetic stage would only possess half a million, and each cell in the next following stage only a quarter of a million, and so on. 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. This gradual disintegration of the id of germ-plasm into smaller and smaller groups of determinants in the subsequent idic stages does not consist in a mere division of the id into portions, but — as occurs in all disintegrations of vital units — is accompanied by displacements in the groups of these units, brought about by the unequally vigorous multiplication of the various individual determinants, and regulated by the forces of attraction acting within them. In spite of all the alterations in the arrangement of the determinants which must occur, owing to the differential nuclear divisions together with unequal growth of the various kinds of these units of the second order, the original position of each determinant in the extremely complex structure of the id of germ-plasm renders it necessary that it should take up a definite and fixed position in each idic stage; and also that it should traverse the precisely regulated course from the id of germ-plasm, through perfectly definite series of cells, to the cell in which it reaches maturity in the final stage of development. In this cell it breaks up into its constituent biophors, and gives the cell its inherited specific character. *Each id, in every stage, has its definitely inherited architecture; its structure is a complex but perfectly definite one, which, originating in the id of germ-plasm, is transferred by regular changes to the subsequent idic stages.* The structure exhibited in all these stages exists potentially in the architecture of the id of germ-plasm: to this architecture is due, not only the regular distribution of the determinants, — that is to say, the entire construction of the body from its primary form to that in which its parts attain their final arrangement and relation, — but also the fact that the determinant, of a small spot on a butterfly's wing, for example, reaches exactly the right place; and that, to take another instance, the determinant of the fifth segment in the feeler of a *Gammarus* reaches this particular segment. The determination of the character of the individual cell depends on the biophors which the corresponding determinant contains, and which it transmits to the cell.

6. The Mechanism for the Phyletic Variations in the Germ-plasm

The *causes* of phyletic development will be treated of in the chapter on Variation: the present section merely gives an account of the mechanism existing in the idioplasm in connection with this process. I shall here attempt to show how the phyletic changes in the idioplasm follow mechanically from its assumed ultimate structure.

Since all parts of the organism are determined from the germ onwards, permanent variations in these parts can only originate from variations in the germ. Each phyletic variation must therefore be due to a variation in the structure of the id of germ-plasm. If we suppose, with Darwin, that the transformation of species is a gradual one, originating in individual variations which become increased and directed by selection, it follows that the corresponding process in the idioplasm cannot be due to a sudden and complete variation in the entire id, but must begin with changes in the individual biophors or in individual determinants and groups of determinants also, and must then extend gradually to more numerous groups, until finally the nature of the id becomes entirely, or to a great extent, changed.

The basis of the process must be sought in the variability of the biophors, which is followed in turn by that of the units of a higher order, — the determinants and ids. These variations are not by any means confined to the *structure* of the individual cell, but concern primarily the *number* of cells of which an organism consists. A leaf of a plant, or a bird's feather, may increase considerably in size during the course of phylogeny, without a change necessarily occurring in the cells which form these parts. The variation will depend primarily on a multiplication of the respective determinants. If the primitive eye of a lower animal consisted of a single cell, constituting a visual rod, and the power of multiplication of its determinants gradually increased in the course of phylogeny, the number of identical determinants which would arise during development by the multiplication of the *single* determinant in the germ-plasm would gradually increase so as to suffice for two cells instead of one. The eye would then possess two visual rods, and if the power of multiplication increased still more, a whole group of visual rods would be controlled by *one* determinant. We are unable to conjecture on what internal variations in the determinant such an increase in the power of multiplication depends; but the fact that every individual cell in the body does not possess a special determinant, while large groups of cells are controlled by a single one, proves that such variations must be possible.

Such a very simple phyletic variation, resulting in the local increase of the number of cells, will be followed by a further variation as soon as the multiplication of the determinant of, *e.g.*, an undifferentiated sensory cell, is not confined to the later stages of ontogeny, but occurs also in the germ-plasm itself; that is, when the doubling of the determinant has already taken place in the id of germ-plasm. For in this case the group of sensory cells, which have become developed phyletically from the originally single cell, will now be controlled by two determinants, each of which can vary independently of the other, and can transform the group of cells under its control. Thus one of these groups might give rise to auditory cells, and the other to gustatory or olfactory cells.

Thus the increase in the differentiation of the body depends primarily upon the multiplication of the determinants in the id of germ-plasm, but this differentiation is only rendered complete by variations in the determinants of similar origin taking place in different directions. The mere addition of a new ontogenetic stage can very easily be conceived without an increase occurring in the determinants of the id; but as soon as the double number of cells which are present in the new idic stage have to become differentiated in various ways, the differentiation must be preceded by a doubling of the determinants in the id of germ-plasm. A higher degree of differentiation will therefore be primarily connected with an increase in the number of cells of which the organism is constituted. It is known that the extreme prolongation of development, due to the constant addition of new generations of cells at the end of ontogeny, can be neutralised by the abbreviation and reduction of the ontogenetic stages: this process may be also to some extent understood if we trace it to its origin in the structure of the idioplasm. The reduction in the number of generations of cells from two or more to one, depends on the fact that the process of multiplication and rearrangement of the determinants takes place more rapidly during these particular stages, than does that of cell-division; so that several idic stages, each of which formerly characterised a *particular* stage of the cell, pass into one another during the *same* stage of the cell. The respective idic stages have not here disappeared completely: they only follow one another more rapidly, and therefore disappear as recognisable stages in development.

In lowly organised beings the differentiation of the body may become increased by a simple *reduction of the hereditary parts or determinates*, without an increase taking place in the cell-generations. If a determinant which controls a region consisting of a hundred cells divides into two, each of which only controls fifty cells, the two resulting groups of cells can vary independently of each other from this point onwards, and may give rise to very different structures. In this way a continued division of the determinants, and consequently also a constantly increasing differentiation of the species, may occur, without necessitating an increase in the total number of cells present in ontogeny.

Each additional differentiation denotes an increase in the degree of organisation. But the phyletic development of the organism is by no means invariably connected with an increase, or, in fact, with any other change in the degree of organisation.

The species of a genus, and often the genera of a family, cannot be distinguished from one another by the number of cells composing them, nor by an increase in the variety of these cells, but only by qualitative differences in the structure of the various parts. Hence the phyletic development of living beings cannot simply be due to the augmentation of the number of determinants in the id of germ-plasm, but must also be attributed to a change in the *nature* of the determinants and in that of their component biophors.

The structure of the idioplasm which we have here assumed, also offers an explanation of the phenomena of *parallelism between ontogeny and phylogeny*, which depend on the law of biogenesis as well as on *the relegation of the final characters* to earlier and earlier ontogenetic stages in the course of phylogeny. Let us first consider the former of these phenomena. We have assumed that each ontogenetic stage is characterised by a definite 'determinant figure,' *i.e.*, a sort of geometrical structure composed of the determinants. The nature of each individual cell is certainly controlled by those determinants in the nucleus which have reached maturity,—that is to say, have arrived at the stage in which they break up into biophors and migrate into the cell-body. But the manner in which the embryonic development of an animal occurs does not by any means depend only on the histological structure of the individual cells in each stage,—it rests to a much greater degree on the manner in which these cells divide and on the rate of their division, and also primarily on the way in which the 'unripe' determinants of the nuclear substance, which are still latent, are grouped together and distributed by means of the cell-divisions. *This distribution of the primary constituents* among the different cells is of the first importance in determining the character of the ontogeny; and one could easily imagine a case of animal embryogeny in which ten or twenty generations of similarly constituted 'embryonic cells' followed each other, and in which a perfectly definite distribution of the primary constituents (determinants) had nevertheless occurred, although only now apparent for the first time. It is well known how close a resemblance exists between the cells of the embryo in various stages in the case of the higher animals.

The regular distribution of the determinants which are still latent or 'unripe' must therefore decide the course of ontogeny;

and the manner of this distribution finds expression in the architecture of each idic stage, or, as I have expressed it, in each 'determinant-figure.'

It is obvious that the same geometrical figure may be constructed out of different elements, just as the same form of crystal may be produced from molecules of a different nature. Thus the resemblance between the ontogenetic stages of nearly allied species is to be explained by the degree of similarity between their respective 'determinant figures,' which persists although the individual determinants constituting the figure differ more or less from one another. As the study of development shows, an explanation is thus offered of the fact that the earlier ontogenetic stages are so very much alike in allied species, and that the differences only appear later on; for in the early idic stages, the differences as regards the nature or power of multiplication of single determinants, or groups of determinants, can exert no marked influence, because the entire number of determinants is still very large, and thus the architecture of the id will be practically the same in corresponding stages. But the further ontogeny advances, and the smaller the groups become into which the determinants separate, the greater also will be the diversity in the architecture of the id, and in the further distribution of 'unripe' determinants resulting from this architecture. Thus a certain part will be longer or shorter, a spot of colour larger or smaller, and the final stages of ontogeny — in which the cells possess only *one* determinant — will differ according to the degree of difference which obtains in the respective determinants. This explains the fact that the segmentation cells in allied species are frequently exactly alike, and also that the resemblance between many mammalian embryos in their earlier stages, though not complete, is nevertheless a very close one.

The law of biogenesis, as far as it applies at all, depends on the fact that phyletic development is partly due to new ontogenetic stages being added at the end of ontogeny. In order that these new stages may be reached, the stages which were previously the final ones must be passed through in each ontogeny. This may be expressed in terms of the idioplasm as follows: — the determinants of the id of germ-plasm become endowed with a greater power of multiplication, so that each one of them causes the addition of one or more cell-generations to the end of the ontogeny. At the same time, the determinants in the germ-plasm increase in number, and each of them becomes differentiated in a fresh manner. As, however, every two new determinants always follow the same course from the id of germ-plasm to the final stage in ontogeny as was taken by the single original determinant, they will pass through the same determinant figures as before, and only lead to the formation of new structures in the final stages, when they become separated from one another.

The ontogenetic stages of the ancestors will be repeated less accurately the nearer development approaches its termination.

The disappearance of a character or of a part which has become useless, may also be traced to the mechanism of the idioplasm. The group of determinants which gives rise to a particular character, will have to be removed entirely from the germ-plasm if the corresponding part is to disappear completely. But this is a very complicated process, and one of long duration as regards more complex organs, such as, for instance, the limbs of Vertebrates. For the determinants which take part in the formation of an extremity are very numerous, and of many different kinds; and moreover, they cause the rudiment of the limb to appear very early in ontogeny. Hence the determinants will have to suffer successively many retrogressive and simplifying changes before a noticeable reduction of the organ occurs. The functionless and rudimentary wings of the Australian Kiwi (*Apteryx*), which are concealed by the plumage, possess all the bones of the perfect wing, though these are very much reduced in size. This is to be explained by supposing that the entire group of determinants for the wing still remain in the id of germ-plasm, but that it has decreased in strength, — that is to say, its elements no longer increase so rapidly, — and they therefore can only control smaller groups of cells. If the process of degeneration continued, the organ would not only grow smaller and smaller, but its component parts would also disappear at different rates, and, losing their characteristic form, would appear as indistinguishable rudiments. Such a degeneration has occurred in certain species of whales, in which the rudiments of the posterior extremity lie concealed beneath the skin; while in other species, the form of the separate bones has been to some extent preserved, and those of the thigh and shank can still be plainly distinguished. In these cases, many of the determinants which were formerly present must have disappeared entirely from the id of germ-plasm, and the remainder must have lost the power of multiplication to a greater extent than has occurred in the case of the wing of *Apteryx*.

We know, however, that even in such animals as snakes, in which the extremities have in most cases disappeared completely in previous geological periods, the rudiments of the limbs arise in the form of 'muscle-buds' in the earlier stages of development, and then disappear very shortly afterwards.* This fact may be expressed in terms of the idioplasm as follows:—the power of multiplication in the small remnant of the group of determinants of the extremity which still exists in the id of germ-plasm, has decreased so considerably that it only suffices for these early embryonic stages. The youngest determinants, and consequently the most recent hereditary structures, are the first to disappear, the loss of the older ones taking place gradually, until even the oldest of all are no longer present. This must be due to the manner in which the determinants increase, although the actual connection between the two phenomena is not apparent. It may perhaps be traced to the fact that those determinants which are the youngest phyletically are destined for the latest ontogenetic stages, in which only therefore they become 'ripe,' and undergo disintegration into biophors. If then, their power of multiplication decreases considerably during the process of degeneration, the number of determinants required for the control of any particular group of cells will not be reached, nor will the determinants even become ripe. Although still present, they are unable to exert any influence; whereas the determinants of the older phyletic stages which are still passed through, ripen in the earlier stages of ontogeny.

The process of degeneration of an organ may be represented as depending on the fact that the determinants first become changed in such a manner as to cause a decrease in their power of multiplication, and this then leads to a very gradual reduction affecting an increasing number of determinants belonging to the group in question. At the same time, the power of mul-

* *Cf.* J. van Bemmelen, 'Over den oorsprong von de vorste ledematen en de tongspieren bij Reptilen.' Kon. Akademie de Wetenschappen te Amsterdam, 30th June 1888.

tiplication in the remaining determinants also diminishes, so that the groups which they constitute gradually extend a less distance into the ontogeny, until finally they drop out of it altogether.

It must not be understood that I have given a mechanico-physiological explanation of the process of degeneration because I have connected it with the theory of determinants. As long as we know practically nothing about the forces which act within and among the biophors, it will be impossible to offer an explanation of this kind. I have only attempted to show that this doctrine does not contradict the facts, but that, on the contrary, it agrees with them up to a certain point. The phenomena of degeneration have not hitherto been considered from this point of view. When a deeper insight into the actual phenomena has been obtained, we may perhaps be able to make further theoretical deductions, and it would then be possible to develop the theory of determinants more fully.

A few words may now be said as regards *correlated variations*. Darwin has shown what an important part these variations play in the transformation of species, and how changes which we must consider to be primary are followed by a number of others in various parts of the organism. Thus an increase in size in a stag's antler necessitates a thickening of the skull, and a strengthening of other parts, viz., the muscles of the neck, the spines of the cervical vertebræ, the ligamentum nuchæ, and even the thoracic skeleton and fore-limbs. Referring all these variations to the processes which take place in the idioplasm, they will be seen to depend on changes in the corresponding groups of determinants in the id of germ-plasm, which cannot be due *directly* to the change and increase in the group of determinants of the antler: they must have arisen secondarily, owing to the occurrence of variations in the determinants upon which selection could act. There is also an entirely different kind of correlation, in which the variation in one part is accompanied by that in another, the latter having no anatomical or functional connection with the former. Thus Darwin states, for instance, that cats with blue eyes are generally deaf, and that pigeons with feathered legs have a web between the outer toes.

I do not think such correlations can be traced to a connection of the parts by means of the nervous system: it is perhaps more likely that they are due to *the contiguity of the determinants* *in the id of germ-plasm* of those parts which vary correlatively. It will be shown later on that local differences in nutrition occur in the id, and that these may cause changes in the determinants affected by them. If, now, the determinants controlling regions of the body which are far apart, are situated close together in the id, they might easily be affected simultaneously by influences producing variation. But the perfectly definite architecture of the id of germ-plasm, on which we base our argument, does not only permit of a vicinity of the determinants of parts of the body far removed from one another, but actually requires it. For, according to our assumption, the id of germ-plasm is not a representation of the body in miniature, but a structure of a special kind, in which the individual component parts are arranged in the order in which they are passed on subsequently in the process of ontogeny to their final destination, viz., to the determinates or hereditary parts. This however requires that the determinants of the ectoderm should be closely adjacent to those of the endoderm in the id, if they are to be distributed to a primary ectoderm and a primary endoderm cell in the first division of the ovum. A cell-division which leads to the separation of widely differing groups of determinants, admits of a close aggregation of these different groups in the id of the mother-cell. This may give some slight insight into the above-mentioned phenomena of correlation.

7. The Magnitude of the Constituents of the Germ-plasm

The assumption that the germ-plasm is composed of biophors, determinants, and ids, implies the existence within a narrow space of a large number of ultimate vital units (biophors) in all the higher organisms. The question arises whether a sufficient number of these units can be contained within an id. Although I believe it is at present quite impossible to obtain anything like a reliable answer to this question by calculating the relative sizes of the elements of the germ-plasm, it may perhaps not be uninteresting to attempt to make such a calculation.

In order to solve the problem with any approach to accuracy, it would at least be necessary to know the sizes of a biophor and of an id, and also the number of determinants in a given species. Unfortunately, however, we are completely ignorant on these points, nor do we even know how many molecules take part in the construction of a biophor: even the computed size of the molecule is somewhat uncertain.

The diameter of a molecule has been estimated at between the $\frac{1}{1,000,000}$th and the $\frac{1}{10,000,000}$th of a millimetre by four different lines of reasoning, 'founded respectively on the undulatory theory of light, on the phenomena of contact electricity on capillary attraction, and on the kinetic theory of gases.' * O. E. Meyer has calculated the size of a molecule 'from the properties and behaviour of vapours. From the constant of friction and the comparison between the space occupied in the liquid and gaseous conditions, together with the deviations from Boyle and Mariott's law, we can approximately calculate, firstly, the volume of all the particles contained within a given space; secondly, that of a single particle; thirdly, the number of particles; and finally, the weight of a single particle.' The result of such a calculation agrees with that given above.

If we take the average diameter of a molecule to be $\frac{1}{2,000,000}$th mm., and reckon that each biophor, which we will suppose to be a cubical structure, is composed of 1,000 molecules, the biophor would measure 10 molecules in length. A row of 200 biophors would therefore measure 1 μ, and 8,000,000 biophors would occupy the space of 1 cubic μ. A human blood-corpuscle measures 7.7 μ. in diameter; if we imagine it to be enlarged so as to form a cube of 7.7 μ. in diagonal length, this space would contain 703,000,000 biophors. Let us further assume that those portions of the cell which, according to the facts at our disposal, must contain the idioplasm, viz., the chromosomes, are mostly a great deal smaller than the nucleus in which they are situated, and that the germ-plasm is composed not of *one* but of several ids, each of which contains all the biophors required for the construction of the entire body, it will then be evident that only a limited number of biophors can be contained in one id.

The chromosomes in the germ-plasm of *Ascaris megalocephala* are the largest which are at present known to us. Each

* Sir William Thomson, 'Popular Lectures and Addresses,' Vol. I., 1889, p. 148.

nucleus in this animal contains two or four rod-like chromosomes (see fig. 2), each of which is composed of 'six thickened granular or disc-shaped portions, which become deeply stained with colouring matter, and which are separated by portions staining less deeply' (Boveri). If we connect this fact with the hypothetical composition of the germ-plasm out of ids, it follows that an id cannot in any case be larger, and is probably smaller, than one of these granules or microsomata. It cannot be larger, because the id is a unit which is capable of division into two daughter-ids, but which cannot remain permanently separated into several parts by a different kind of intermediate substance. If we suppose the id to be as large as it can possibly be, — that is to say, to correspond in size to a microsome, — it will measure, according to Boveri's drawing and scale of enlargement, .0,008 mm., or not quite 1 μ in diameter. Only the terminal granules of the rods, however, are as large as this; the greatest diameter of those in the middle measures .0,006 mm., while their shorter diameter is about .0,003 — .0,004 mm. The terminal granules, looked upon as spherical bodies, would be capable of containing about two million biophors of the size given above.

This number is certainly a very considerable one, and it would apparently be sufficient to make up the number of determinants in such a lowly organised animal as *Ascaris*. But even in Arthropods the number of determinates, and therefore that of the determinants also, is considerably greater. Each of the olfactory setæ on the feelers of Crustaceans, which were mentioned above, must be capable of being determined from the germ onwards; and this is also true of the spots and lines on a butterfly's wing, each of which represents at least *one* determinant, and in case of all the large markings several, or even many, of these units. If we consider that the pattern on the wing is often very complicated, and frequently differs on the under and upper surfaces, it is evident that hundreds of determinants must exist for this pattern alone. But there are, again, several peculiarities in the structure of the wing-scales, and thus it is probable that almost every scale can vary independently from the germ onwards. In some males of the family *Lycaenidæ*, *e.g.*, *Lycaena adonis*, small guitar-shaped odoriferous scales (the 'androconia' of Scudder) are distributed regularly amongst the colour-scales, while these are entirely absent in other nearly allied species, such as *Lycaena agestis:* hence we must conclude that these androconia have arisen by the transformation of ordinary scales. This, however, presupposes the independent variability of the scales which are to become changed phyletically, and consequently also their capability of being determined from the germ onwards. Were this not the case, a single scale could never have varied from the others *hereditarily*. In *Lycaena adonis* there are 30,830 scales on the upper surface of the wing.* If each of these is to be looked upon as corresponding to a determinate, the enormous number of about 240,000 determinants of the germ-plasm would result merely from the scales covering the wings, provided that the upper and under surface of the four wings possess each about the same number of scales.

I have endeavoured by direct experiment to ascertain the lowest limit to the size of a determinate, — that is to say, the size of the smallest determinates for a particular character of a certain species. For this purpose I selected one of the Ostracoda, *Cypris reptans*, which multiplies parthenogenetically, and in which it is easy to compare the different green spots on the shell in the mother and daughter. It appears that the larger spots are strictly transmitted, though this is not the case as regards the very small ones, which consist of only one or two pigment-cells. The form of these larger spots, which consist of fifty or a hundred pigment-cells, also varies to some extent, so that the number is here also somewhat inconstant. If parthenogenetic reproduction could be looked upon as being *purely uniserial*, it might be inferred that the determinates are not in this case single cells, but groups of cells. Unfortunately, however, this experiment cannot be considered conclusive, for — as will appear later on — the germ-plasm is here composed, just as in the case of sexual reproduction, of dissimilar, and not of *similar* ids, and consequently variations in heredity may thus arise.

We must conclude, even from the external coloration, that a very considerable number of determinates exists in the case of the higher Vertebrates. Thus most, if not all, of the contour-feathers of a bird must be controlled by special determinants in the germ-plasm, for they are independently variable hereditarily.

* My assistant, Dr. V. Häcker, was good enough to make this calculation for me.

The number of wing- and tail-quills is nevertheless definitely fixed for every species of bird, and each of these feathers possesses a definite form, size, and coloration. We must assume that *more than one* determinant is necessary for an entire feather, for a feather is formed from thousands of epidermic cells, which are not by any means all similar to one another, either as regards form, mode of combination, or colour. Many feathers are striped, while others have a brilliant ornamental spot at the tip; as in the case, for instance, of the peacock, many humming-birds, and certain birds of paradise. The cells to which these stripes and spots owe their origin, must contain determinants which differ from those of the rest of the cells which take part in the construction of the feather. We must therefore conclude that at least *one*, and often several, determinants of the germ exist for each of these two kinds of cells; for, as is well known, ornamental spots of this kind are often formed of several colours, and are very complex.

It would be erroneous to suppose that the contour-feathers are not determined individually in such birds as the raven, in which the plumage is all of one colour; but in such cases the qualitative differences refer less to colour than to form and size. The fact that each part of the feather is determined hereditarily, even as regards its colour, is proved by the variation which occurs, and which in individual species has resulted in certain feathers being partially or entirely white, or being brilliantly coloured, as in the case of the bird of paradise, which is allied to the raven. One need only look through a collection of humming-birds, and compare the females, which are so often plainly coloured, with the wonderfully variegated males, in order to become convinced that almost every contour-feather can vary in almost any direction as regards coloration, form, size, and minute structure.

As has already been remarked, the internal organs are apparently by no means so specially determined from the germ onwards as are the external parts: their determinants must therefore control larger regions of cells, as in the case, *e.g.*, of blood-corpuscles and epithelial cells. The number of determinants in the germ-plasm of the higher animals is nevertheless an enormous one, and it might certainly be doubted whether such a large number of biophors as must be required for the construction of an id of the germ-plasm could be contained within a single id.

It is impossible, as we have already seen, to obtain a satisfactory answer by means of a calculation. But let us assume for the moment that we possess reliable data as to the number of determinants and the size of an id in a particular species. We will further assume that each determinant is composed of, let us say, fifty biophors, and each biophor of a thousand molecules, and that the average diameter of a molecule is $\frac{1}{2,000,000}$th mm. Supposing we found that all these units could not be contained within an id of the size we have assumed, we should be forced to conclude that one or more of these quantities had been overestimated. This result would not weaken the theory of determinants, for minute particles *must* exist in the germ-plasm for each hereditary and independently variable part of the body. I therefore consider it fruitless to attempt a more accurate estimation of the number of determinants in individual species, and to endeavour to find a support for this fundamental theory by means of such calculations. The theory is correct in any case, although our conception of the structure of the germ-plasm may be very incomplete.

The object of making the above calculation was simply to arrive at this result. The germ-plasm is an extremely delicately-formed organic structure, — a microcosm in the true sense of the word, — in which each independently variable part present throughout ontogeny is represented by a vital particle, each of which again has its definite inherited position, structure, and rate of increase. *A theory of evolution appears to me to be only possible in this sense.* The constituents of the germ-plasm are not miniatures of the fully-formed parts, or even particles existing solely for the formation of the corresponding parts in the body. But each of these particles (the biophors and determinants) has a definite and important share in the preceding stages of development, for it takes part in determining the architecture of each idic stage, and consequently also assists in the further ontogenetic disintegration and distribution of the determinants amongst the subsequent cell-stages. All the more essential differences in the structure of organisms depend on this fact. The determinants are particles on whose nature that of the corresponding parts in the fully-formed body depends, whether the latter consists of a *single* cell or of several or many cells. The assumption of such particles is inevitable in a theory of heredity, and it alone necessitates an almost inconceivable complexity in the architecture of the germ-plasm. But if we suppose that the number of ultimate particles of which the germ-plasm is composed is less than the number of parts in the body which are independently variable hereditarily, it would then follow that several minute parts of the body must become changed simultaneously with the variation of *one* of these particles, — that is to say, the number of determinants then become too small theoretically.