INTRODUCTION

A. — Historical Part

HERBERT SPENCER was practically the first in the present generation to attempt a theoretical explanation of heredity when he propounded his theory of 'physiological units.' The regeneration of lost parts, *e.g.*, of a leg or the tail of a salamander, led him to the conception of these units, 'in all of which there dwells the intrinsic aptitude to aggregate into the form of that species; just as in the atoms of a salt there dwells the intrinsic aptitude to crystallise in a particular way.' He calls this aptitude the 'polarity of the organic units,' and defines the latter as being intermediate between the 'chemical units' or molecules and the 'morphological units' or cells. They must be 'immensely more complex than the chemical units,' and must therefore correspond to groups of molecules. It is very interesting at the present day, now that we have advanced somewhat further towards a theory of heredity, to summarise the various aptitudes and forces which Herbert Spencer thought it necessary to ascribe to his 'physiological units,' in order to arrive at an explanation of the phenomena. Although the sections on Heredity and Regeneration constitute only a small portion of his great work on the 'Principles of Biology,' and cannot therefore contain a detailed treatment of the phenomena of heredity, his opinions on this subject are evident.

Spencer considers, on the one hand, that the whole organism is composed of these units, which are all alike in kind, and on the other, that the germ-cells also contain small groups of them. The former supposition makes regeneration possible to each sufficiently large portion of the body, while the latter gives the germ-cell the power of reproducing the whole: inasmuch as the 'polarity' of the 'units' leads to their arrangement in such a way that the whole 'crystal'—the organism—is restored, or even formed anew. The mere *difference in the arrangement* of units alike in kind determines the diversity of the *parts of the body*, while the distinction between different species and that between different *individuals* is due to a diversity in the constitution of the units.

The units of an individual are therefore to a certain extent protean. They are capable of arranging themselves in an immense variety of ways, and so form the most diverse cells, tissues, organs, and parts of the body. But they only do this under the directing influence of the whole, in such a way that the whole forces the units of one part to arrange themselves in just such a way as is necessary for the perfection of that part,—a perfection required for the harmony of the whole. Spencer himself says very rightly, 'It seems difficult to conceive that this can be so, but we see that it *is* so.' As a matter of fact, groups of units removed from an organism possess the power of constructing the whole anew; and we are thus obliged to admit that the tendency to take a specific form is present in all parts of the organism. The 'units' are *physiologically variable* quantities, which in every case act in such a manner as the whole demands.

The assumption of these 'physiological units' does not suffice as an explanation of heredity: it proves insufficient even as interpreting the differentiation of organs in simple ontogeny, quite apart from the question of amphigonic heredity. But it has the merit of having utilised the smallest vital particles as constituent elements of the organism, and of having made them the basis of a theory of heredity.

Ernst Brücke was the first to admit the existence of small vital particles of this kind, and to give cogent reasons for so doing. Although he did not denote them by any special name in his extremely important paper entitled 'Elementar Organismen,'* he was the first to oppose the old theory of the cell, especially with regard to its fluid contents, and to show that its body must possess an *organisation*, quite distinct from the molecular structure of the organic compounds.

Darwin's theory of 'pangenesis' was stated in the final chapter of his great work on 'The Variation of Animals and Plants

* 'Wiener Sitzungsberichte,' Oct. 10, 1861, Bd. 44, ii., p. 381.

under Domestication,' which appeared only a few years after Spencer's 'Principles of Biology.' The enormous wealth of facts bearing on heredity which is accumulated in this book is in itself sufficient to show how the gifted author felt himself urged on all sides to consider this extremely difficult and complicated problem. For although Darwin modestly described his theory as a provisional hypothesis, his was, nevertheless, the first comprehensive attempt to explain all the known phenomena of heredity by a common principle. The theory has so often been discussed and is so well known that a brief account of its substance will suffice here.

A multicellular organism, whether animal or vegetable, is gradually built up by cell-division: but it is assumed that this method of multiplication is not the only one. Each cell possesses in addition, at each stage of its development, the power of giving off invisible granules or atoms, which, at a later period and under certain conditions, can develop again into cells similar to those from which they originated. Numbers of these 'gemmules' are being given off continually from all cells of the body and conveyed into the blood, and thus circulate through the body, finally settling down in some part, principally in those regions in which the development of offspring will take place later on, *i.e.*, in buds or germ-cells. As gemmules from all the cells of the body are aggregated in these cells, they invest the latter with the power of developing into a new and complete organism. This occurs as follows: — each gemmule reproduces the cell from which it is derived, and the gemmules of the different cells become active in the same order as that in which the corresponding cells followed each other in the ontogeny of the parent.

The germ is not by any means composed exclusively of gemmules which have been derived from the organism in which they were formed, but consists, at the same time, of a very large number of gemmules which are derived from parents and ancestors even of very remote generations; and hence a great many more gemmules take part in each case of ontogeny than there are cells formed. Each cell and each part is represented by a great variety of gemmules. A selection must therefore take place, as only *one* gemmule can form the required cell, and the rest must remain dormant. In this way a number of gemmules, which have been hitherto dormant, are transferred from one generation to the next: they may, under certain conditions, become active, and thus again bring into existence ancestral traits which had disappeared in the parents.

This is, in brief, the theory of pangenesis. It does not take into account the physical nature of the gemmules. They are capable of multiplying, and do so continually: but the question as to whether they have any definite arrangement, and if so, what the nature of that arrangement is, is not touched upon; nor is any mention made of the causes and mechanism by which it comes about that they are always in the right place and develop into cells at the right time.

I do not say this by any means as a reproach, but only to bring out clearly the speculative character of the whole hypothesis. Darwin did not go on to inquire whether all these assumptions were possible: he only asked what it was necessary to assume in order to explain this or that fact of heredity, without troubling himself to consider whether the assumption were borne out by facts or not. And he was right in doing so, for at the time when he propounded his hypothesis it was not possible to found any theory of heredity on the only sound basis, — that of a knowledge of the most minute cell-structure. I have already pointed out how extremely important and fruitful his theory of pangenesis has been: it drew attention for the first time to all the phenomena that needed explanation, and showed what assumptions must be made in order to explain them.

It will be shown later on that, in spite of the fact that a considerable number of these assumptions are untenable, a part of the theory still remains which must be accepted as fundamental and correct, — in principle at any rate, — not only now, but also for all time to come. I refer to the most general portion of these assumptions only, namely, that presupposing the existence of material particles in the germ which possess the properties of the living being, and each of which is to be regarded as the primary constituent ('Anlage') of one portion of the organism. I must honestly confess to having mentally resisted this fundamental point of the Darwinian doctrine for a long time. It appeared almost impossible to me that such an enormously large number of individual primary constituents as we must suppose to exist, according to Darwin's view, could be contained in the minimum of substance which, as will be shown hereafter, we have to regard as the actual bearer of heredity. I tried in several ways to arrive at a satisfactory epigenetic theory,* which, starting *from a germ-substance of comparatively simple structure*, should exhibit the various differentiations of the organism as due to regular changes brought about by the division of this primary structure. But the more I considered the problem as time went on, the more I was convinced that such a solution was impossible. And in this book I trust that I shall be able to give a satisfactory proof that only one theory of evolution in Darwin's sense, *i.e.*, the assumption of minute primary constituents in the germ, is in accordance with the facts; and the objection which for a long time prevented me from accepting this very simple assumption, disappears with the discovery that what is apparently impossible does really occur.

I certainly consider even now that Darwin's theory must be looked upon, and that he probably considered it, rather as an inquiry into the problem of heredity than as a solution of the problem. His assumptions do not, properly speaking, explain the phenomena. They are to a certain extent a mere paraphrase of the facts, an explanation of a purely *formal* nature, based on speculative assumptions, which were made not because they seemed possible, or even likely, but because they provided a formal explanation of all the phenomena on one principle. If we suppose that each cell arises from a special gemmule, and that these gemmules are present wherever they are wanted, it is easy to see how that structure, the origin of which we wish to explain, may appear in any given position. Further, when a large number of cells is to arise in regular succession from *one* egg-cell, the desired sequence of cells must of course result if we assume that the gemmules present become active in the required order. But this supposition does not really explain the phenomena. Even at the present day our explanations are imperfect enough, and are far from going to the bottom of the matter, but they differ from Darwin's provisional hypothesis in that they attempt to find out the actual facts concerned in the processes, and to arrive at a *real*, and not merely a formal, solution of the problem. *The great naturalist's merit in having at* once found the right foundation on which to base a real solution

* The indication of such a theory is given, *e.g.*, in the essay entitled 'Die Continuität des Keimplasma's,' Jena, 1885, p. 38 *et seq.* (pp. 207 *et seq.* of the English translation).

is not diminished by the fact of his having been less startled by the consequences of his 'gemmule'-hypothesis when seeking for a purely formal explanation, than he would have been had he tried to adapt his hypothesis to the facts. The hypothesis, as stated by him, could not be regarded as a real solution of the problem of heredity, if only because it leaves unexplained the giving off of the gemmules into the blood, their circulation through the body, and intrusion into the germ- and other cells. All these are assumptions without a basis in fact. This is evidently the reason why modifications of the theory of pangenesis were repeatedly made very soon afterwards.

Before considering these modifications, I should like once more to state clearly the relation of Spencer's 'physiological units' to Darwin's 'gemmules.' Darwin himself considered the former to be closely related to his gemmules; and, in fact, he would have regarded Spencer's ideas as essentially coinciding with his own, had he not noticed certain passages in Spencer's book which seemed to point to something quite different.*

It will be apparent, I think, from what has already been said, that these two views are entirely different. What is common to both is that they assume the existence of minute living units, multiplying by fission: but the part taken by them in the constitution of the body is quite differently conceived. Spencer's units are the elements which exclusively compose the living body; while Darwin's gemmules only give rise to cells, *i.e.*, they are elements which are present for the special purpose of bringing about heredity, without anything being specified as to their share in the composition of the living body. As will be shown more clearly later on, Spencer's hypothesis is superior in this respect to Darwin's. On the other hand, Spencer's similar units are the bearers of all the characters of the species, owing to their complex molecular structure; while the Darwinian gemmules are primary constituents of individual cells, which are to be considered as differing in a manner corresponding to the difference of the individual cells. Spencer's theory is epigenetic, Darwin's evolutionary; in this respect the latter is, in my opinion, superior to the former.

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* Charles Darwin, 'The Variation of Animals and Plants under Domestication,' 2nd ed., vol. ii., London, 1888; note on p. 371.

Galton* was the first to make an attempt to improve on the theory of pangenesis. In a short but suggestive essay he accepted the hypothesis of the gemmules, but rejected the doctrines of their circulation through the blood, and of the aggregation in the germ-cells of gemmules given off by the body-cells. Now as the gemmules which have been converted into body-cells are used up, it follows that the germ-cells can only contain those gemmules which are left — those, out of the enormous number contained in a germ-cell, which have not developed further. For each germ-cell, as both Galton and Darwin assume, contains each kind of gemmule in many modifications, originating from the different ancestors of the organism. The theory of the origin of the germ-cells from the remains of the germ mass not used up in ontogeny ('the residue of the stirp') has been compared to, and regarded as the precursor of, the conception of the continuity of the germ-plasm which I originated long afterwards. A certain resemblance does, it is true, exist between the two conceptions, but it will be shown in the section on the continuity of the germ-plasm that the similarity is only a superficial one.

Herbert Spencer defines heredity as the capacity of every plant and animal to produce other individuals of a like kind, and states expressly that in this fact, which is perfectly familiar to us, and for this reason seems to be a matter of course, lies the real essence and principle of heredity, 'the phenomena commonly referred to it being quite subordinate manifestations.' Thus the *blending of the individual 'characters' of the parents* in the children has, as a rule, been placed in the foreground in considering questions of heredity, and it has been overlooked that this is quite a secondary phenomenon, — important no doubt in many respects, and interesting in a high degree, but still only the result of a certain mode of multiplication, *i.e.*, sexual reproduction, and by no means an essential phenomenon of heredity. Darwin recognised this distinctly, and concerned himself primarily with the theoretical explanation of individual development (ontogeny). But the majority of writers on heredity, including Galton, have turned their whole attention to the blending of the qualities of the parents

* Francis Galton, 'A Theory of Heredity,' *Journal of the Anthropological Institute*, 1875.

in the children, — a problem which is doubtless well worthy of investigation, but which, at the same time, deals only with a side issue of the processes of reproduction. How little I underrate the significance of amphigonic heredity, even in its theoretical relations, will be evident in a later part of this book, in which I attempt to derive the existence of the germ-plasm from the phenomena of this form of heredity; but to me it seems dangerous to investigate heredity theoretically from the point of view of amphigonic descent exclusively, because one has here to deal with the most complex of all the phenomena, and the main point may easily be overlooked in a mass of confusing secondary considerations. Even Galton, in my opinion, allowed himself to be too much influenced by this aspect of the question. Excellent as are his later researches on the laws relating to the blending of characters of the parents in the children, I consider his theoretical deductions on the fundamental phenomena of heredity unsatisfactory. The few hints that he gives as to the cause of ontogeny seem to me by no means equal to Darwin's simple but truly penetrating and accurate deductions. It is quite conceivable that the phenomena of the blending of the characters of the parents in the children would be the most interesting to a statistician and anthropologist like Galton, but they have kept him within the limited range of these phenomena, and have prevented him from arriving at really general principles and at a comprehensive theory of heredity.

Galton has, however, the merit of having been the first to deny the circulation of the gemmules, and, in connection with this, to cast doubt upon the general validity of the doctrine of the transmission of acquired modifications. He certainly believes the latter to be 'faintly heritable,' and assumes, in order to explain this transmission, that no general 'circulation of the gemmules' takes place, but that each cell sets free some gemmules which get into the circulation and eventually penetrate into the sexual elements.

Galton's essay was published only a few years after the appearance of Darwin's theory of pangenesis; but it cannot be said that it exercised any influence on the subsequent development of the theory of heredity. Apparently it was not much noticed even in England, and on the Continent it remained unknown for a long time. This must be my excuse for being ignorant of the existence of this paper, and consequently for not referring to it in my essays which appeared nearly ten years later.* In one of these essays 'On Heredity' (1883), I contested at first in general terms not only the existence but also the theoretical possibility of the transmission of acquired characters, and tried to release the theory from the necessity of an explanation which deprived it of any further development. In this essay I further assumed the existence in the germ-cell of a reproductive substance, the *germ-plasm*, which cannot be formed spontaneously, but is always passed on from the germ-cell in which an organism originates in direct *continuity* to the germ-cells of the succeeding generations. The difference between the 'body' in the narrower sense (soma) and the reproductive cells was also emphasised, and it was maintained that the germ-cells alone transmit the reproductive substance or germ-plasm in uninterrupted succession from one generation to the next, while the body (soma) which bears and nourishes the germ-cells, is, in a certain sense, only an outgrowth from one of them.

A second attempt to improve upon the theory of pangenesis must be considered here. I have already referred elsewhere † to the interesting and ingenious book on 'The Laws of Heredity,' ‡ by W. K. Brooks. The author retains the fundamental points of this theory, viz., the formation of gemmules in all the cells of the body, their circulation through the latter, and their aggregation in the germ-cells or buds: he differs, however, from Darwin principally in ascribing to the male germ-cell a particularly strong power of attraction for the gemmules, so that it collects a special mass of them and stores them up. As this assumption is made chiefly for the purpose of explaining varia-

* These essays first appeared separately in the years 1881–91. The only complete edition of the collected essays which has hitherto appeared is the English translation, 'Essays upon Heredity and Kindred Biological Problems' (edited by Poulton, Schönland, and Shipley, Oxford, 1889), containing Essays I.—VIII. A second edition appeared in 1891 as Vol. I., and Essays IX.—XII. follow this year as Vol. II. A French translation of all these essays, with the exception of the last on 'Amphimixis,' &c., has also appeared with the title, 'Essais sur l'Hérédité et la Selection Naturelle,' traduits par Henry de Varigny, Paris, 1892.

† 'The Significance of Sexual Reproduction in the Theory of Natural Selection.'—'Essays upon Heredity,' p. 326.

‡ W. K. Brooks, 'The Laws of Heredity, a Study of the Cause of Variation and the Origin of Living Organisms,' Baltimore, 1883.

tion, I shall postpone any further consideration of it to the section which treats of this subject.

In the following year, Nägeli's 'Mechanico-physiological Theory of Descent'* appeared. This book, which abounds in ingenious deductions and important suggestions, doubtless exercised a great influence on the views of that time. Its importance cannot be denied, even if, as I believe to be the case, only a small portion of its theoretical propositions can be retained. Many as are the fruitful ideas and anticipation of facts afterwards proved which we owe to Nägeli, his own theory of heredity has already become untenable. For this reason, and also because the theory is so well-known, I will not describe it fully here, but will only refer to the remarks which I made on the subject some years ago,† and to the recent detailed criticism by Wiesner.‡ Although I do not consider that Nägeli's hypothesis leads us towards a true theory of heredity, it nevertheless contains an important suggestion, that of the *idioplasm*, which gives us a further insight into the problem. I had already assumed the existence of a special reproductive substance — the germ-plasm — on the changes of which development depends, while heredity rests on its continuity: and now Nägeli independently postulated a special reproductive substance, an 'Anlagenplasma' or 'idioplasm,' which although much smaller in bulk than the rest of the living substance of the body — the trophoplasm ('Ernährungsplasma') — determines the detailed construction of the latter. The correctness of this conjecture has not as yet, so far as I know, been disputed, although it was very soon shown that Nägeli was wrong as regards the form in which he imagined the idioplasm to exist. He represented it as consisting of very fine parallel fibres which, by uniting into bundles and crossing each other so as to form a network, traverse the substance of the cell, and being continuous from cell to cell, pervade the whole body as a connected network.

At the time when Nägeli's book appeared, it was already suspected that the reproductive substance is not contained in

* C. v. Nägeli, 'Mechanisch-physiologische Theorie der Abstammungslehre,' München and Leipzig, 1884.

† *Vide* 'The Continuity of the Germ-plasm,' 1885 (pp. 180 *et seq.*, 192, &c.).

‡ Julius Wiesner, 'Die Elementarstructur und das Wachsthum der lebenden Substanz,' Wien, 1892.

the *body* of the cell but in its *nucleus*, and several discoveries were made shortly afterwards which rendered it certain that the idioplasm is to be looked for in the 'chromosomes' of the nucleus, — those rod-like, coiled, or grain-like structures which are distinguished by their remarkable affinity for certain colouring matters. I shall return to the proof of this fact in the following section.

From this time onwards each subsequent theory of heredity was based on a firm foundation of fact. It was now not only known that the phenomena of heredity among the higher organisms are connected with a definite substance, but the seat of the latter had also been ascertained. I now therefore adopted this firm basis for my theory of the germ-plasm, if I may call the imperfect form in which it then existed by such a name: I localised the germ-plasm in the nuclear substance of the germ-cell, and supposed that ontogeny was due to a qualitative change in it, which hands the idioplasm on from one generation to the next by means of nuclear- and cell-division. But I soon went further. From the fact of sexual reproduction, which brings together equal amounts of paternal and maternal germ-plasm at each fertilisation, I inferred not only the composition of the germ-plasm out of a number of units, the '*ancestral germ-plasms*' ('Ahnenplasmen'), but also the necessity of *a reduction of the germ-plasm* each time to one-half of its bulk, as well as a reduction of the number of the ancestral germ-plasms contained in it.* The hypothesis of the 'reducing divisions of the germ-cells' has been thoroughly substantiated by subsequent observations: in fact it has even been proved that in many cases this reduction occurs exactly as I had foretold and had represented in a diagrammatic figure; † that is to say, by the non-occurrence of the longitudinal division of the chromosomes which occurs in the ordinary nuclear division, and by the distribution of these in the daughter-nuclei. This holds good for the ovum as well as for the sperm-cell in animals, and, as far as is known, in plants also. The germ-cell must in all cases by division get rid of half of its nuclear rods, — that is to say, of its germ-plasm, — in order to become capable of fertilisation. This fact supports the other assumption of the construction of the germ-plasm from ancestral germ-plasms, which are not minute vital particles — analogous to Spencer's

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* '*On the Number of Polar Bodies*,' *&c., 1887.* † *Ibid.*

physiological units — but rather bodies of a highly complex constitution, each containing all the primary constituents which are necessary to the formation of an organism. Each ancestral germ-plasm seemed to me to be of a 'special kind,' and just as many 'different kinds of idioplasm' are removed by the reducing division 'from the ovum as are afterwards introduced by the sperm-nucleus' on fertilisation. It will be seen that I retain this essential basis of the theory of the germ-plasm in its further development as presented here, and I trust that I may now succeed in refuting the objections which have been urged against the 'ancestral germ-plasms,' or, as I now call them, the '*ids.*' In any case it cannot be denied that they help to throw an important light on the subject.

De Vries has so far been my most powerful opponent as regards the ancestral germ-plasms, but his opposition is founded on the misunderstanding I have already referred to, for he looks upon them as the ultimate vital particles — an idea which was foreign to me from the beginning. Of this, however, I do not complain, as at that time I had left the question as to the construction of the ancestral germ-plasms unanswered.* This omission is supplied in the present book, and it will be shown that, although each ancestral germ-plasm is in my opinion a bearer of all the primary constituents required for the construction of an organism, my assumption does not exclude the possibility of its being composed of these constituents in the form of minute vital particles. The 'ancestral germ-plasm' is indeed a unit, but one of a higher order. For this reason alone it cannot be compared with Spencer's 'physiological units,' because the latter, as ultimate vital particles, compose the whole body; while the ancestral germ-plasms only form the nuclear matter, and merely serve the mechanical purpose of the processes of heredity.

De Vries has in a significant manner developed a theory of

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* De Vries is also mistaken in ascribing to me the opinion that 'there is only one hereditary substance — only one material bearer of the hereditary tendencies in each individual.' The sentence quoted by him ('On the Number of Polar Bodies,' p. 355) does not deal with this question; it runs as follows: — From several reasons already stated 'at least one certain result follows, viz., that there is an *hereditary substance*, a material bearer of hereditary tendencies, and that this substance is contained in the nucleus of the germ-cell,' &c.

heredity in his essay on 'Intracellular Pangenesis.'* The opinions there expressed really contradict the title of the paper; for pangenesis, in Darwin's sense, means the development of gemmules throughout the body, — the composition of the hereditary substance from gemmules which are derived from all the cells of the body. This very point in Darwin's hypothesis is set aside completely by de Vries: the most characteristic part of it is removed, and what remains is of a more general nature, consisting of principles which, in one form or another, must form the basis of every theory of heredity, at the present day at any rate. Some ideas of his own, however, are then added, and it is these which give a characteristic stamp to his whole series of conceptions. If we regard his hypothesis, as de Vries himself does, as an alteration of the Darwinian theory of pangenesis, it is certainly a radical one, and is of such a kind as at one stroke to infuse new life into the latter, which had become untenable in its original form.

De Vries distinguishes two parts in Darwin's theory of pangenesis, one of which he rejects, while he retains the other. He calls the former portion the 'transport hypothesis,' meaning thereby the assumption of the origin of the gemmules in all the cells of the body, their separation from the cells, circulation in the blood, and ultimate aggregation in the germ-cells. And relying on my rejection of the heredity of 'somatogenic' characters, he shows that the assumption of the transportation of the gemmules from all the cells of the body to the germ-cells is superfluous. He thus does away with that portion of the hypothesis of pangenesis which makes it unacceptable to most people, and places the theory on a new and firmer foundation on which it is capable of further development.

De Vries nevertheless goes too far if he looks upon the 'transport hypothesis' as necessary only for explaining the transmission of somatogenic qualities. It must not be forgotten that the idea of the continuity of the germ-plasm did not exist in Darwin's time. How could the gemmules of all the cells of an organism enter its germ-cells unless they are formed in the body-cells, migrate therefrom, circulate through the body, and come together in the germ-cells? A direct connection between the fertilised egg-cell and the germ-cells of the organism

* 'Die Intracellülare Pangenesis,' Jena, 1889.

arising from it was not supposed to exist by any one at that time, nor does it do so except in isolated cases. The 'transport hypothesis' was therefore also necessary in order to explain the production of germ-cells of each kind, which must again contain the gemmules of the parents. Galton, who also rejected the 'transport hypothesis,' thus found himself in the peculiar position of being obliged to suppose that the germ-cells which the organism produces can only contain the unused remainder of the gemmules and their successors, *i.e.*, those gemmules which had been unable to take part in the construction of the organism, and which had remained dormant and were individually of a different nature from the other gemmules. He made use of this supposition to explain the difference between children of the same parents, but found himself obliged to resort to a very artificial assumption to account for the main problem of the resemblance between such children and their parents.

That part of Darwin's theory which de Vries retains is the existence of an hereditary substance composed of 'gemmules,' or minute vital particles which are capable of growth and multiplication by fission, and which become active consecutively in ontogeny, and so build up the organism. The theory is thus deprived of its merely speculative elements, and by transferring the gemmules, in accordance with the most recently ascertained facts, to the germ substance, which, as we know, is passed on by division from cell to cell, the theory of pangenesis is placed on a firm footing.

De Vries, however, was not content with simply modifying Darwin's theory of pangenesis in a negative manner, by doing away with one — almost the greater — portion of it; he also reformed it positively by giving a new meaning to the 'gemmules.' There is an essential difference between Darwin's gemmules of *cells*, and de Vries's pangenes, which are gemmules of elements much smaller than cells — that is to say, of the smallest parts of which a single cell is composed. These pangenes are the bearers of the individual qualities or 'characters' of the cell.

The train of thought which led de Vries to imagine the construction of the hereditary substance from such 'bearers of the qualities' ('Eigenschaftsträger') of the cells is too interesting to be passed over. He bases this idea on the assumption of '*a mutual independence of the hereditary qualities*.' According to his view, all species consist of a sum of 'hereditary qualities'; very few, or none of these, are peculiar to any one species, the character of which is determined by the way in which they are combined. The *same* quality recurs in many species, but in different combinations. 'We constantly see how one and the same hereditary quality, or how a definite small group of such, may be combined with all kinds of other hereditary qualities; and how the different characters of individual species are due to the extreme variety of these combinations.' The different organs of a species stand in the same relation to one another in this respect, as do the different species themselves. They exhibit the same qualities, but in different combinations. The individual qualities which constitute a species 'can almost all vary independently of each other,' and can therefore be increased even by artificial selection according to the fancy of the breeder, without requiring a corresponding change in the remaining qualities of the species. But the qualities too are 'miscible in almost any proportion,' as experiments in hybridising are intended to show: 'in no other way can we so clearly demonstrate the secondary importance of a specific type ('Bild'), regarded as a whole as opposed to the independent factors which constitute it.' The qualities, or rather their material substratum, are therefore independent of one another, and miscible to almost any extent.

Those ultimate vital particles or pangenes, which de Vries substitutes for Darwin's gemmules, are therefore the bearers of constituent qualities of the species.

The fundamental idea of de Vries's whole deduction is doubtless perfectly correct. Some ten years ago, when I first began to devote my attention to the problem of heredity, I fully believed in the possibility of an epigenetic theory, but, as will be seen in the course of this book, have long since given up this idea as untenable. I too now believe that the hereditary substance is composed of primary constituents, and even trust that I can prove this assumption to be not only sound, but inevitable. But, at the same time, I do not imagine that it suffices as an explanation of the phenomena of heredity. According to de Vries, the germ-substance is formed of a number of different kinds of pangenes, of which as many are present as there are qualities in the species. He does not consider these pangenes as arranged in any definite grouping, but as freely miscible, in accordance with the assumed 'free miscibility of the qualities.' He contests as superfluous the assumption of *higher* units, such as might be formed by a certain number of pangenes in a definite order; and this view seems to me to be the weak point in his argument.

In the section on the control of the cell by the nuclear substance, I shall adopt what seems to me to be a remarkably happy idea on the part of de Vries, who supposes that material particles leave the nucleus, and take part in the construction of the body of the cell. These particles correspond to the 'pangenes,' they are the 'bearers of the qualities' of the cell, the specific character of which I believe to be stamped upon it by the nature, the different varieties, and the proportional numbers of these particles.

But does the character of a species depend only on these primary qualities of the cell? Are there not qualities of various degrees — primary, secondary, and so on? The pangenes are *primary* 'bearers of qualities'; their mere presence in the hereditary substance gives no indication, or at most, only a very slight one, as to the character of a species. If, for instance, 'chlorophyll-pangenes' are present in the egg-cell of a plant, the only conclusions we can draw as to the specific character of the latter are that it will have green cells of some sort: but we cannot thereby determine where they will be situated, or which portions of the plant will be green, and which variegated; or again, whether its flowers will be green, white, or of some other colour. Not until we were able to find groups of pangenes in the germ-substance, some of which were destined to give rise to leaves, and others to flowers, should we be able to say whether the latter will be green or otherwise.

In the course of his remarks, de Vries mentions the stripes of a zebra. How can these be hereditary if the different kinds of pangenes merely lie close together in the germ without being united into fixed groups, *hereditary as such?* There can be no 'zebra pangenes,' because the striping of a zebra is not a cell-character. There may perhaps be black and white pangenes whose presence causes the black or white colour of a cell: but the striping of a zebra does not depend on the development of these colours *within a cell*, but is due to the regular alternation of thousands of black and white cells arranged in stripes.

De Vries, in another place, refers to the long-stalked variety of the alpine *Primula acaulis*, which is due to reversion to a remote ancestral form of the species. In this case, again, the special peculiarity cannot depend on 'long-stalk pangenes,' because the possession of a long stalk is not an intracellular character. The specific form of the leaves and other parts of a plant is likewise not due to the character of the individual cells composing them: the serrated margin of a leaf, for instance, cannot depend on the presence of 'serration-pangenes,' but is due to the peculiar arrangement of the cells. The same argument would apply to almost all the obvious 'characters' of the species, genus, family, and so on. For instance, the size, structure, veining, and shape of leaves, the characteristic and often absolutely constant patches of colour on the petals of flowers, such as orchids, may be referred to similar causes: these qualities can only arise by the regular co-operation of many cells. The characteristics of the human race may be taken as another illustration. The peculiarities as regards the shape of the skull, nose, &c., cannot depend on the mere *presence* in the germ of pangenes, which are destined to form the hundreds and thousands of different cells constituting the respective qualities; but they must be due to a *fixed grouping of pangenes*, or some other primary elements of the germ, which is *transferable from generation to generation*.

The character of a species cannot depend only upon the number and relation of the pangenes in the germ. It is quite possible to conceive of two different species of totally different structure in which the pangenes of the germ were alike in nature and amount, the difference being solely due to the grouping of the pangenes in the germ. De Vries, it is true, traces 'systematic difference to the possession of *different kinds* of pangenes,' and considers that 'the number of similar pangenes in two species is the real measure of their affinity;'* but this statement seems to me to be somewhat at variance with his fundamental view, according to which 'a number of hereditary qualities constitute the character of each individual species, *though by far the greater majority of them recur in innumerable other species*.' Does he not, in so many words, emphasise the fact that the almost formidable number of different pangenes which are required for 'the construction of a single species' does not necessitate the existence of an inconceivably large multitude of

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* *Loc. cit.*, p. 73.

different pangenes in the entire organic world, because 'the number of individual hereditary qualities required for the construction of the latter is relatively small when compared with the number of species'! Each species appears to us as an extremely complicated structure: the whole organic world, however, seems to be the result of innumerable different combinations and permutations of *relatively few factors*.

The idea which is here so clearly and decidedly expressed of the construction of innumerable species by various combinations of relatively few pangenes, shows that, even from de Vries's point of view, it is not the 'pangene *material*' as such, which is the main factor in determining the character of the species, but rather its *arrangement*, or as I shall afterwards express it, *the architecture of the germ-plasm*.

De Vries certainly speaks frequently of 'groups of pangenes,' but he only just touches upon this idea, and postpones entering into details until further discoveries are made with regard to the mechanism of nuclear division. Important as his fundamental view as regards the composition of the germ substance out of primary constituents undoubtedly is, it may easily seem to explain more than it really does; without assuming the formation of groups of such primary constituents for a number of orders each included in the other, even the simplest case of ontogeny cannot be explained, quite apart from reversion or any other complicated phenomenon of amphigonic heredity. Darwin's theory of pangenesis accomplishes more in this respect than does de Vries's modification of it, inasmuch as the former at least deals with the primary constituents of *cell*-structures. The mere presence of a certain collection of pangenes in the germ does not necessitate the formation in the offspring of similar cells to those which existed in the parent; for the character of the individual cell is determined by a definite selection of pangenes. If, indeed, it be assumed that the required pangenes always lie close together, and are always ready at hand whenever they are wanted, an explanation of any particular phenomenon of heredity is no longer difficult, but it seems to me that it would then be necessary to show how the nature of the germ can determine that the right primary constituents are always at the right spot.

As already stated, de Vries occasionally speaks of *groups* of pangenes, but, at the same time, he looks upon the view of there being any 'higher units' in the germ as a superfluous one. I can only explain this inconsistency by supposing that he regards the 'qualities' as independent and perfectly freely miscible, and, in fact, postulates a germ-mechanism which admits of their separation in any manner required. If this were really the case, and the primary constituents were not combined into fixed groups in the germ, how could composite characters composed of many different kinds of cells with a definite arrangement,—*e.g.*, the eye-like spot on a certain feather of a bird,—become a fixed specific character? I am of opinion that the view which entails an independence and uncontrolled miscibility of the qualities is a fallacy, originating in the conception of amphigonic reproduction as a necessary element in heredity. The chapters on amphigonic heredity, reversion, &c., will show how I imagine the idea of the uncontrolled miscibility of the separate qualities to have arisen.

It will frequently be apparent in the course of this book that my point of view is identical with that of the Dutch botanist in many of the most important particulars. I believe, however, that his 'pangenes' or similar minute elements do not suffice *in themselves* for the construction of a theory of heredity, but that something more must be added to make the phenomena comprehensible at any rate in principle.

The manuscript of the present book had already been written for some time when Wiesner's work on the elementary structure and growth of living substance * appeared. Although this monograph does not contain, and is not intended to offer, a theory of heredity, it is nevertheless of great importance in this respect, for it treats of the fundamental points of such a theory, viz., *the composition of living matter out of very small units.* Wiesner remarks that theories of heredity have hitherto always adopted units invented for the purpose, whereas the same units which make life possible at all, and which control assimilation and growth, must also be the agents in bringing about the phenomena of heredity. Spencer's 'physiological units,' Darwin's 'gemmules,' Haeckel's 'plastidules,' and my 'ancestral germ-plasms,' are all, in fact, elements of this kind, assumed for the explanation of the problem of heredity. De Vries stands

* J. Wiesner, 'Die Elementarstruktur und das Wachsthum der lebenden Substanz,' Wien, 1892.

alone in considering all living matter to be actually composed of his 'pangenes,' though I have already indicated that my 'ancestral germ-plasms' are also composed of similar primary units, which do not exist in them alone. The minute vital particles or 'plasomes,' adopted by Wiesner from Brücke, correspond in all essential points to the 'biophors' or bearers of life assumed by myself.

B.—Descriptive Part

By the term heredity is simply meant the well-known fact that living organisms are able to produce their like, and that the resemblance between a child and its parent, although never perfect, may nevertheless extend to the most minute details of construction and functions.

The fundamental phenomena of heredity are familiar in all existing organisms: the transmission of the character of the species from parent to offspring results whether the multiplication takes place by the halving of a unicellular organism or by the process which occurs in multicellular organisms, which consists in a complex succession of continually increasing groups of cells, *i.e.*, in development. These fundamental phenomena of heredity are, however, complicated in all the higher organisms by the connection of reproduction with that process which may be described as amphimixis.* This consists in the mingling of two individuals or of their germs, and owing to its constant connection with reproduction in multicellular organisms it is usually spoken of as 'sexual reproduction.' As will be shown in greater detail further on, the various phenomena, such as the blending of parental characters in the offspring, and reversion, depend exclusively on the hold which amphimixis has taken on the life of the species. Similar phenomena must occur amongst unicellular organisms, in which amphimixis is widely spread if not universal, in the form of conjugation, and is, therefore, not directly connected with reproduction. At present, however, we are ignorant of the details of heredity in these forms, and are therefore compelled to base our conclusions entirely upon what we know to occur in multicellular organisms.

* August Weismann, 'Amphimixis, oder die Vermischung der Individuen,' Jena, 1891. *See* 'Essays upon Heredity,' vol. ii., 1892.

These phenomena have only been observed in detail in the higher plants and animals, more particularly in man. In the case of the higher forms of life a large number of facts have now been accumulated which can be used for the purpose of theoretical analysis.

Although the study of heredity is greatly complicated by amphimixis, this mingling of the hereditary tendencies of *two* parents, and even the process of sexual reproduction which accompanies it, afford us a much deeper insight into the actual processes of heredity than we could ever have obtained in any other way. We may thus hope in time to penetrate further into its nature by carrying out more detailed investigations of the phenomena.

In order to do so, however, we must not forget that this form of reproduction is neither the only nor the original one, and that even in multicellular organisms reproduction is not necessarily connected with amphimixis; it must also be borne in mind that so-called asexual (*monogonic*) reproduction forms the basis of the amphigonic method. The fundamental phenomena of heredity had already shaped their course in the living world before the introduction of amphimixis, and have, therefore, no connection with amphigonic descent and the complications arising from it. This fact has often been overlooked or left out of consideration, and thus the solution of the problem of heredity has been rendered much more difficult. A whole series of the phenomena of heredity can be investigated theoretically without considering the complications arising from amphimixis, though, in point of fact, it is always a factor, and thus the problem to be solved is very considerably simplified.

The natural course of such an investigation would be to pass from the simple to the complex, but it is not advisable at present to begin the study of heredity by a consideration of the simplest beings, and to ascend from the unicellular to the multicellular organisms. For besides the fact that we know nothing of the individual phenomena, — such as the transmission of the individual characters, — in the lower forms, the principal reason for not following the ordinary course in this case is the fact that amphigonic reproduction, or the processes of fertilisation and the complicated development of multicellular organisms, affords us, as already stated, a deep insight into the processes of heredity. The same is true in this case as in almost all physiological processes, — investigation cannot proceed from the simple to the more complex without taking into consideration the objects and processes for which it was first undertaken. It must, on the contrary, avoid the densely overgrown path and skirt the hedge which surrounds the enchanted castle of the secret of Nature, in order to see if there be not somewhere a gap through which it is possible to enter and obtain a firm foothold.

Such a gap in the hedge which encloses the secret of heredity may be found in the processes of fertilisation, if we connect them with the facts of heredity as observed in the organisms which have adopted sexual reproduction.

As long as we were under the erroneous impression that the fertilisation of the ovum by the spermatozoon depended on an *aura seminalis* which incited the egg to undergo development, we could only partially explain the fact that the father as well as the mother is able to transmit characters to the children by assuming the existence of a *spiritus rector*, contained in the *aura seminalis* which was transferred to the ovum and united with that of the latter, and thus with it directed the development. The discovery that development is effected by material particles of the substance of the sperm, the sperm-cells, entering the ovum, opened the way to a more correct interpretation of this process. We now know that fertilisation is nothing more than the partial or complete fusion of two cells, the sperm-cell and the egg-cell, and that normally only *one* of the former unites with *one* of the latter. Fertilisation thus depends on the union of two protoplasmic substances. Moreover, although the male germ-cell is always very much smaller relatively than the female germ-cell, we know that the father's capacity for transmission is as great as the mother's. The important conclusion is therefore arrived at that only a small portion of the substance of the ovum can be the actual hereditary substance. Pflüger and Nägeli were the first to follow out this idea to its logical conclusion, and the latter observer stated definitely that it is impossible to avoid the assumption that no more hereditary substance is contained in the egg-cell than in the male germ-cell, and that consequently the amount of the substance must be infinitesimal, for the sperm-cell is, in most cases, many hundred times smaller than the ovum.

The numerous and important results of the investigations of many excellent observers on the process of fertilisation have now rendered it almost certain — in my opinion, absolutely so — that by far the larger part of the egg-cell does not consist of hereditary substance, and that the latter only constitutes a small portion even of the sperm-cell. From his observations on the egg of the star-fish, Oscar Hertwig had suspected that the essential part of the process of fertilisation consists in the union of the *nuclei* of the egg- and sperm-cells, and as it is now known that the hereditary substance is undoubtedly contained in the nucleus, this view has, in this respect at least, proved to be the right one. It is true that the nucleus of the male cell is always surrounded by a cell-body, and that Strasburger's opinion to the contrary is incorrect. We now know, through the researches of Guignard, that even in Phanerogams a small cell-body surrounds the nucleus, and that a special structure, the 'centrosome,' — which is absolutely essential for the commencement of development, — is contained within it. This structure will be treated of in further detail presently, but I must here lay stress upon my view, that *the 'centrosome' with its 'sphere of attraction' cannot in any case be the hereditary substance*, and that *it is merely an apparatus for the division of the cell and nucleus.*

Both in animals and plants, however, essentially the same substance is contained in the nucleus both of the sperm-cell and egg-cell: — this is the *hereditary substance of the species.* There can now be no longer any doubt that the view which has been held for years by Strasburger and myself is the correct one, according to which *the nuclei of the male and those of the female germ-cells are essentially similar, i.e.*, in any given species *they contain the same specific hereditary substance.*

The splendid and important investigations carried out by Auerbach, Bütschli, Flemming, and many others, on the detailed processes of nuclear division in general, and those dealing more particularly with the fertilisation of the egg in *Ascaris* by van Beneden, Boveri, and others, have given us the means of ascertaining more definitely what portion of the nucleus is the substance on which heredity depends. As already remarked, this substance corresponds to the 'chromosomes,' those rod-like, looped, or granular bodies which are contained in the nucleus, and which become deeply stained by colouring matters.

As soon as it had been undoubtedly proved that the nucleus, and not the body of the cell, must contain the hereditary substance, the conclusion was drawn that neither the membrane of the nucleus, nor its fluid contents, nor the nucleoli — which latter had been the first to attract attention — could be regarded as such, and that the 'chromatic granules' alone were important in this respect. As a matter of fact several investigators, — Strasburger, Oscar Hertwig, Köllicker, and myself, — reasoning from the same data, arrived at this conclusion independently, within a short time of one another.

It will not be considered uninteresting or superfluous to recapitulate the weighty reasons which force us to this conclusion, for it is clear that it must be of fundamental importance in a theory of heredity to know for certain what the substance is from which the phenomena which are to be explained proceed.

The certainty with which we can claim the 'chromatin granules' of the nucleus as the hereditary substance depends firstly, on the process of amphimixis; and secondly, on that of nuclear division. We know that the process of fertilisation consists essentially in the association of an equal number of chromatin rods from the paternal and maternal germ-cells, and that these give rise to a new nucleus from which the formation of the offspring proceeds. We also know that in order to become capable of fertilisation each germ-cell must first get rid of half of its nuclear rods, a process which is accomplished by very peculiar divisions. Without entering into further particulars here, amphimixis may be described as a process by means of which one-half of the number of nuclear rods is removed from a cell and replaced by an equal number from another germ-cell.

The manner, however, in which the chromatin substance is divided in nuclear division strengthens the above view of its fundamental nature. This method of division leaves no doubt that it is a substance of the utmost importance. I need only briefly recapitulate the main points of the wonderfully complicated process of the so-called mitotic or karyokinetic cell-division, which follows a definite law even as regards the most minute details.

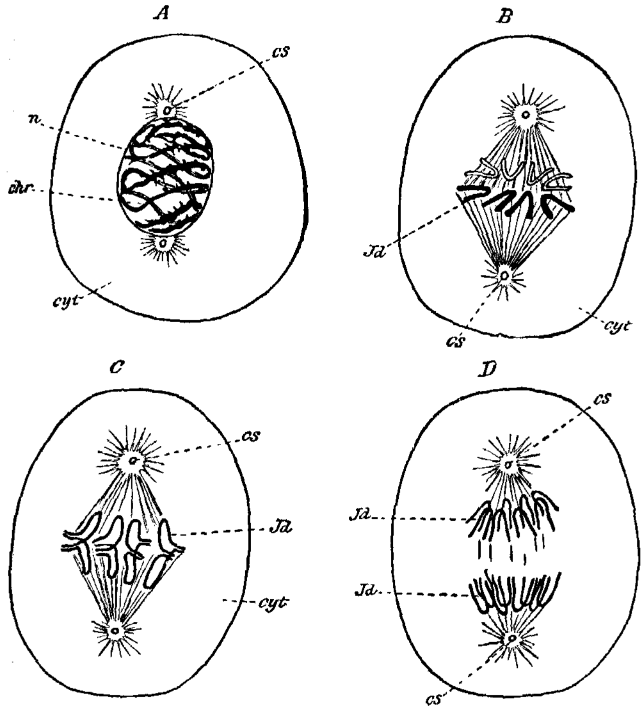
When the nucleus is going to divide, the chromatin granules, which till then were scattered, become arranged in a row, and form a long thread, which extends through the nucleus in an irregular spiral, and then divides into portions (*chromosomes*) of fairly equal length. The chromosomes have at first the form of long bands or loops, but afterwards become shortened, thus giving rise to short loops, or else to straight rods or rounded granules. With certain exceptions, to be mentioned later, the number of chromosomes which arise in this way is constant for each species of plant or animal, and also for successive series of cells. By the time the process has reached this stage a special mechanism appears, which has till now remained concealed in the cell substance. This serves to divide the chromatin elements into two equal parts, to separate the resulting halves from one another, and to arrange them in a regular manner. At the opposite poles of the longitudinal axis of the nucleus two clear bodies — the 'centrosomes,' each surrounded by a clear zone, the so-called 'sphere of attraction' — now become visible. The importance of these was first recognised by Fol, van Beneden, and Boveri. They possess a great power of attraction over the vital particles of the cell, so that these become arranged around them like a series of rays. At a certain stage in the preparation for division, the soft protoplasmic substance of the cell-body as well as of the nucleus gives rise to delicate fibres or threads: these fibres are motile, and, after the disappearance of the nuclear membrane, seize the chromosomes — whether these have the form of loops, rods, or globular bodies — with wonderful certainty and regularity, and in such a way that each element is held on either side by several threads from either pole. The chromatin elements thus immediately become arranged in a fixed and regular manner, so that they all come to lie in the equatorial plane of the nucleus, which we may consider as a spherical body. The chromatin elements then split longitudinally, and thus become doubled, as Flemming first pointed out. It must be mentioned that this splitting is not caused by a pull from the pole threads (spindle threads), which attach themselves to the chromatin rods on both sides; the division arises rather from forces acting in the rods themselves, as is proved by the fact that they are often ready to divide, or indeed have already done so, some time before their equatorial arrangement has taken place by means of these threads.

The splitting is completed by the two halves being gradually drawn further apart towards the opposite poles of the nuclear spindle, until they finally approach the centre of attraction or centrosome, which has now fulfilled its object for the present, and retires into the obscurity of the cell-substance, only to become active again at the next cell-division. Each separated half of the nucleus now constitutes a daughter-nucleus, in which it immediately breaks up, and becomes scattered in the form of minute granules in the delicate nuclear network, so that finally a nucleus is formed of exactly the same structure as that with which we started. Similar stages to those which occur in the aggregation of the chromatin substance in the mother-nucleus preparatory to division are passed through during the separation of the daughter-nuclei, but in the reverse order.

It is evident, as Wilhelm Roux was the first to point out, that the whole complex but wonderfully exact apparatus for the division of the nucleus exists for the purpose of dividing the chromatin substance in a fixed and regular manner, not merely quantitatively, but also in respect of the *different qualities* which must be contained in it. So complicated an apparatus would have been unnecessary for the quantitative division only: if, however, the chromatin substance is not uniform, but is made up of several or many different qualities, each of which has to be divided as nearly as possible into halves, or according to some definite rule, a better apparatus could not be devised for the purpose. On the strength of this argument, we may therefore represent *the hereditary substance as consisting of different 'qualities.'* The same conclusion is arrived at on purely theoretical grounds, as will be shown later on when we follow out the consequences of the process of amphimixis.

For the present it is sufficient to show that the complex mechanism for cell-division exists practically for the sole purpose of dividing the chromatin, and that thus the latter is without doubt the most important portion of the nucleus. Since, therefore, the hereditary substance is contained within the nucleus, *the chromatin must be the hereditary substance.*

De Vries's objection to this view is, in my opinion, only an apparent one; for it has not been asserted that 'the nucleus alone is the bearer of the hereditary characters,' as de Vries thinks, but that the nucleus alone contains the *hereditary substance,* or that substance which is capable of determining not only the character of a particular cell, but also that of its descendants. This is never contained in the cell-body, but always in the nucleus in multicellular organisms, and doubtless the same holds good for unicellular beings. It is quite possible that in certain lower Algæ a few of the structures in the cell—such



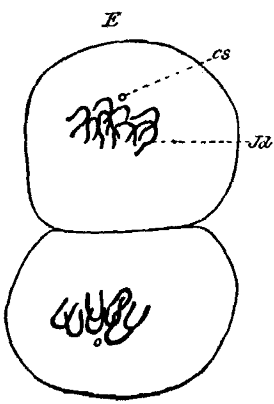


FIG. I.—DIAGRAM OF NUCLEAR DIVISION.

A.—Cell with nucleus—*n*, and centrosomes—*cs*, preparatory to division. The *chromatin* has become thickened so as to form a spiral thread—*chr*.

B.—The nuclear membrane has disappeared. Delicate threads radiate from the centrosomes, and form the 'nuclear spindle,' in the equator of which eight chromosomes or nuclear loops (*chr*) are arranged: these have been formed by the spiral thread of chromatin in A becoming broken up.

C.—The chromosomes have each become split longitudinally into two, and are about to be drawn apart by means of the spindle-threads. (For the sake of clearness only four of the eight chromosomes are indicated.)

D.—The daughter-loops pass towards the poles of the spindle.

E.—The body of the cell has undergone division; each of the resultant cells contains a centrosome and eight nuclear loops.

as vacuoles and chlorophyll bodies—pass directly from the egg-cell into the daughter-cells, although this cannot by any means be considered as proved. In any case such a *direct* transmission plays only a very insignificant part in plants, and practically none at all in animals, for specific structures are not present in the egg-cells of animals: there may at most be deposits of nutrient material. These, however, are not living structures of the cell, but only passive chemical substances. So far from denying that the nucleus contains the hereditary substance, de Vries bases his whole theory on this incontestable fact. The last doubts on this point were dispelled by the experiments of Boveri,* who, after artificially removing the nucleus from the eggs of a species *A* of sea-urchin, and then pouring over them the sperm of another species *B*, found that these eggs developed into larvæ of the latter species. In this case therefore the substance of the maternal germ-cell acted as nutrient material only, whilst the paternal germ-cell impressed the character of the species on the larva. None of the maternal specific characteristics were transmitted, and in this case, at all events, the question of any 'heredity apart from the nucleus' is therefore excluded.

Several objections have been recently raised to my view that the nucleus is the seat of heredity. Verworn,† for instance, repeats the opinion, previously expressed by Whitman, that the cell-body, quite as much as the nucleus, must be looked upon as the hereditary substance, because the nucleus cannot exist without the cell-body; and also because, in his opinion, which is undoubtedly a correct one, the life of a cell consists in a continual interchange of substance between the cell and the nucleus. But is the question as to whether the closest physiological relations exist between the nucleus and the cell, so that neither can exist apart from the other, synonymous with that as to whether the hereditary substance is contained in the nucleus or in the cell-body? We must at least be allowed to make the hypothesis that the 'store of the primary constituents' ('Anlagenmagazin') of the hereditary substance is contained and preserved in the

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* Boveri, 'Ein geschlechtlich erzeugter Organismus ohne mütterliche Eigenschaften.' Gesellsch. f. Morph. u. Physiol., München, 16 Juli 1883.

† Max Verworn, 'Die physiologische Bedeutung des Zellkerns,' Bonn, 1891 (Archiv. f. ges. Physiol., Bd. 51).

nucleus; for, as has already been indicated, and will subsequently be shown more clearly, this substance can hardly be stored up in two different places, seeing that a very complicated apparatus is required for its distribution: a double apparatus would certainly not have been formed by nature if a single one suffices for the purpose. Only as long as the phenomena of heredity and the meaning of these phenomena are still far from being known, is it possible to hold such opinions as that which presupposes the distribution of the hereditary substance amongst both cell and nucleus. As soon as a further insight into these processes is obtained, it will no longer be possible to doubt that the structure of the hereditary substance must be so complex that we can only wonder how it could ever have been developed at all. We know that the nucleus contains a substance which, even with the imperfect means of observation at our disposal, is seen to be extremely complex, and that it becomes modified in a very remarkable manner after every cell division, only to be again transformed at the approach of the following division. We can, moreover, observe that the cell is provided with a special apparatus which evidently enables it to halve this substance very accurately. The statement that *this substance is the hereditary substance* can, therefore, hardly be considered as an hypothesis any longer.

It has also been supposed that fresh evidence against the view that the chromosomes are the hereditary substance, has been furnished by the recent observations of Fol * and Guignard,† which prove that the centrosome and its 'sphere of attraction,'— which belong to the cell-body, and constitute the apparatus for division,— pass into the ovum along with the sperm-nucleus in the process of fertilisation. Suppose I take two heaps of grain from different places, and load them on two carts, harness a horse to each cart, and drive them to the same place; does this prove that the horses consist of grain? They are merely the means by which the grain is transferred from one place to another, just as the centrosomes are the means whereby the sperm-nucleus is transferred to the ovum: whether they are any-

* 'Le Quadrille des Centres,' Archiv. Sc. Phys. et Nat., Genève, 15 Avril 1891.

† 'Sur l'Existence des Sphères Attractives dans les Cellules Végétales,' Compt. Rend. Sc., 9 Mars 1891.

thing more than this, — *i.e.*, whether they contain hereditary substance, — still remains to be proved, and such a conjecture is hardly more probable than that the horses, besides being the means of transport of the corn, should actually consist of corn!

It might, however, be urged that the transference not only of the hereditary substance or *store of primary constituents*, but also of the centrosome or *means of transference* of this substance, implies the transference of the rate of cell-division, which is regulated by the centrosome and essentially decides the cell-sequence in the offspring, and which consequently also takes part in heredity. But I consider this also to be an incorrect deduction, because the periods of activity of the apparatus for division must obviously be dependent on the conditions of the cell itself; these conditions, however, apart from nutrition, depend on the ultimate specific structure of the cell. As, according to my view, this structure is impressed on the cell by the nuclear substance, the periodicity of cell-division must also be dependent on the nucleus. The law that *only a certain part of the nuclear matter is to be regarded as the hereditary substance appears to me to receive fresh support from all the more recent observations.**

Chromatin substance is not only contained in the nucleus of the germ-cells and of the fertilised ovum, but also in all the cells

* Many seem inclined to regard the process observed by Fol, which he described as 'Le quadrille des centres,' as a proof that the centrosomes nevertheless must — or at any rate might — contain a kind of hereditary substance. I believe, however, that this process is quite similar to that which occurs in every nuclear division, except that in fertilisation, — owing to the fact that the first segmentation nucleus receives a centrosome from each of the two conjugating cells, — it is a double, and not a single process. Each of these centrosomes divides and passes to the region of the two poles of the future spindle, just as would occur if only a single centrosome were present in the cells. I should be surprised if this were not the case, and if the centrosome of the egg-cell passed to one pole, and that of the spermatozoon to the other! Guignard is of the opinion that even if the nucleus is of great importance as regards the transference of transmissible qualities, we must nevertheless attribute to the 'sphères directives,' 'le rôle primordial dans l'accomplissement de la fécondation.' This is true if it only indicates that the beginning of embryonic development depends — as does every nuclear division — on the presence of the *apparatus* for division. But the view is not thereby refuted that fertilisation consists in the union of two nuclear substances.

of the entire organism in each phase of its development, at any rate as long as they are capable of multiplying, and are possessed of vitality. The chromatin in all the cells of the body is derived from that in the fertilised ovum, while the development of the body from the egg-cell is effected by a series of cell-divisions, each of which includes a division of the nucleus in the manner just described. In the process of ontogeny the chromatin of the first nucleus undergoes repeated subdivisions into two parts of equal volume, and it would very soon become so small as to be invisible even under the highest powers of the microscope, if it did not continue to grow, as does the cell-body. This occurs just as much in the case of numerous animal eggs to which no nutrient material is supplied during the development of the embryo, as in that of those which are nourished from the beginning, or of plants which as a rule begin to obtain their own nutriment at a very early stage. The chromatin, or hereditary substance of the fertilised ovum, enters upon a long and complex process of growth, which only ceases when no new cells are produced either for the formation of new parts, or to replace old ones, — that is to say, at the end of the life of the individual. This growing hereditary substance may be compared to a tree whose branches arise in strict dichotomy, except for the fact that the chromatin does not consist of *one* continuous mass, but of a number of separate particles not actually contiguous with one another; for at each cell-division the two halves of the chromatin rods separate never to unite again in *one* nucleus. Each is finally contained in a special nucleus, which is separated from the rest by being enclosed in a special cell-body. The question now arises as to whether all these fragments of the hereditary substance which compose the chromatin 'tree' of an organism are similar to, or different from, one another, and it can easily be shown that the latter must be the case.

In order to prove this, we take as our basis the well-grounded assumption that the chromatin in the nucleus of the fertilised egg is the substance on which heredity depends. Thus we know that the possibility of the offspring resembling its father, for example, in a thousand different physical and mental characters depends on the minute mass of a few chromatin granules in the nucleus of the sperm-cell, and that the characters of a fully formed organism depend as a whole, as well as in detail, on the arrangement, number, and nature of the cells which compose it. The influence therefore which the minute mass of paternal chromatin in the nucleus of the fertilised egg-cell exerts on the course of development, can only be such as to regulate the nature and the rate of multiplication of the cells in the body of the offspring in such a manner as to cause them to resemble the cells of the paternal body. *The chromatin is therefore in a condition to impress the specific character on the cell in the nucleus of which it is contained.*

As the thousands of cells which constitute an organism possess very different properties, *the chromatin* which controls them *cannot be uniform; it must be different in each kind of cell.*

The chromatin, moreover, cannot *become* different in the cells of the fully formed organism; the differences in the chromatin controlling the cells must begin with the development of the egg-cell, and must increase as development proceeds; for otherwise the different products of the division of the ovum could not give rise to entirely different hereditary tendencies. This is, however, the case. Even the two first daughter-cells which result from the division of the egg-cell give rise in many animals to totally different parts. One of them, by continued cell division, forms the *outer* germinal layer, and eventually all the organs which arise from it — *e.g.*, the epidermis, central nervous system, and sensory cells; the other gives rise to the *inner* germinal layer and the organs derived from it, — the alimentary system, certain glands, &c. The conclusion is inevitable that the chromatin determining these hereditary tendencies is different in the daughter-cells.

This holds good in all subsequent stages of ontogeny; the difference between the developmental tendencies of the cells resulting from the division of the ovum is in exact proportion to that between the chromatin substance of their nuclei. *Ontogeny, or the development of the individual, depends therefore on a series of gradual qualitative changes in the nuclear substance of the egg-cell.*

The fundamental principle of the view which has just been briefly sketched was put forward by me some years ago, and I then made use of the term *idioplasm* to represent the substance which is contained in the chromatin bodies of the nucleus, and which determines the nature of the whole cell. Oscar Hertwig also independently adopted this term, which had first been introduced by Nägeli with a somewhat different meaning. As stated in the first section of this book, Nägeli defined idioplasm as the guiding and controlling substance of the body, in contrast to the more passive and controllable trophoplasm. It is open to doubt whether the latter term should be retained, but the former is certainly happily chosen. It is true Nägeli did not mean to indicate any definite substance visible under the microscope when he used the word idioplasm, for the facts of nuclear division and fertilisation were then unknown. But these facts are so convincing that no doubt as to what is to be regarded as the idioplasm is any longer possible, and Nägeli's conception of an idioplasm forming a network, traversing and connecting the contents of all the cells in the organism, may be regarded as abandoned. We are therefore justified in transferring the term introduced by him to the nuclear substance which determines the nature of the cell.

We now therefore understand by the term idioplasm the nuclear substance controlling any particular cell. This is at the same time the hereditary substance, for it is never formed afresh, but is always derived from the idioplasm of another cell; moreover, it not only determines the *actual* characters of the particular cell, but also those of all of its descendants.

Hence we must assume a difference in the idioplasm not only in dealing with two cells differing in structure and functions, but also in all cases in which we know that different primary constituents are contained in two cells. This has often been overlooked in using the term 'embryonic cells' merely in the sense of equivalent elements 'which may give rise to any parts,' simply because they frequently resemble one another, assuming that they must therefore always be actually equivalent. It is quite true that the idioplasm of such cells appears similar, at least we can recognise no definable differences in the chromatin rods of two cells in the same animal. But this is no argument against the assumption of an internal difference. The perfect external resemblance between two eggs is not a sufficient reason why two identical chickens should be hatched from them. The eggs may have been produced by different mothers, or they may have been fertilised by two different males. We cannot perceive these slight differences in either case, and we could not even do so by attempting to analyse the idioplasm concealed in the nuclei of the two eggs by the aid of our most powerful objectives. Theoretical considerations will show later on that it must be so, and that the units of the idioplasm on which the nature of the latter depends are far too numerous, and therefore far too small, to be visible.

If therefore the two halves into which the chromatin rods are split in karyokinesis look exactly alike, and even if the divided portions of the granules (microsomes), of which the rods often visibly consist, resemble each other exactly, there is still no reason why they should not be different in their nature; in some cases one, and in others another occur.

We shall consequently in this connection have to assume two kinds of nuclear division which are externally indistinguishable from one another, in one of which the two daughter-nuclei contain similar idioplasm, while in the other they contain different kinds of idioplasm. These kinds of division we may speak of as *homœokinesis* and *heterokinesis*, that is, as a division into parts similar or dissimilar to each other with regard to the hereditary tendencies they contain ('erbgleich' and 'erbungleich'). The former must depend on a perfectly uniform distribution of the primary constituents in the two halves of the rods, and will consequently have been preceded by a duplication in the process of growth; in the latter this growth will be connected with a heterogeneous grouping of these constituents.

Although we cannot ascertain anything directly about the forces which cause this splitting of the chromatin rods, it may at any rate be asserted that they must be contained within the substance of the latter, and be connected with the actual development of the qualities of the idioplasm: for otherwise it could not be understood how the qualities, which are changed during the division of the nucleus, become separated sharply from one another and arranged in the two daughter-nuclei. And yet this must be the case if different cells with different kinds of idioplasm can all arise from *one* mother-cell, which is an undoubted fact.

It appears to me, therefore, that the regular ontogenetic changes of the idioplasm, as they begin with the division of the egg-cell and cease with the natural death of the organism, depend on purely internal causes, which lie in the physical nature of the idioplasm. In obedience to these, a division of the nucleus accompanies each qualitative change in the idioplasm, in which process the different qualities are distributed between the two resulting halves of the chromatin rods. I shall speak of the different kinds of idioplasm arising in this way as the *ontogenetic stages of the idioplasm*, or shortly, *the onto-idic stages*.

Hereditary substance, in the full meaning of the term—*i.e.*, that substance which contains all the primary constituents of the whole organism, is merely the idioplasm of the germ-cell, and it is advisable for practical purposes to denote this first onto-idic stage by the short term *germ-plasm*, which I suggested for it at a time when the idea of idioplasm had not been introduced. At that time I meant by the term 'germ-plasm' the hereditary substance of a germ-cell capable of development, without expressing any opinion as to its position or nature. We can now state that *the germ-plasm is the first ontogenetic stage of the idioplasm of an animal or a plant*, whether the cell, in the nucleus of which it is contained, is sexually differentiated or not.

We must next attempt to form an idea of *the constitution and nature of the germ-plasm*, and of the ontogenetic stages of the idioplasm, or onto-idic stages.