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SOME CURRENT CONCEPTIONS OF THE GERM PLASM[1]

It is a commonplace of observation that the first decade of the present century has been, so far as the study of heredity and the germ plasm is concerned, a period of observation and experimentation, rather than of theorizing. The speculations as to a physical basis of heredity and its ultimate structure, which began with Naegeli's conception of the idioplasm and micellæ and culminated in Weismann's elaborate system of ultra-microscopic bearers and determiners of heredity and development, have given place to a renewed activity of observation on the structure and functions of the cell in reproduction and especially to experimentation in hybridizing and all forms of plant and animal breeding. We need not go so far as to say that evolution was on its death bed before the Mendelian revival. The study of the ultimate structure and processes of the plant cell has gone on from Von Mohl's time at least without much regard to such highly speculative disciplines as natural selection, Neo-Lamarckianism, neo-vitalism, etc.; still there can be no question that with the rediscovery of Mendelism and the possibility of bringing a great mass of both breeding and cytological data, as to unit characters, gametic purity, segregation and germinal variation and the behavior of the chromosomes in nuclear division and fusion, synapsis and reduction, into one harmonious theory of development, a great impetus has been given to the study of the funda-

[1] Address of the vice-president and chairman of Section G, Botany, American Association for the Advancement of Science, December, 1911.

mental problems of cell behavior and heredity.

The relative share in this stimulus to renewed and hopeful study of the facts which is to be assigned to the older theories of the germ plasm and to the new observations of mutation, dominance, segregation, synapsis, etc., is a question which may be left to the historian of biological science in the future to determine. There can be no question that De Vries's theory of pangenesis has guided in large degree his experimental studies in mutation.

It will certainly be of interest to attempt to discover how the new observations are related to the older theories of the germ plasm and especially to try to learn how the numerous experimenters and breeders who are putting forth such a flood of data on hybridization, pure-line breeding, bud variation, graft hybrids, etc., find it necessary to modify or discard and replace the terms and conceptions of the older theories in order to give an intelligible account of their observations.

The theories of Naegeli, Darwin, Weismann and De Vries can all be characterized as Detto and others have made clear, as corpuscular theories of heredity and organization more or less frankly based on an assumed analogy between the ultimate constitution of matter as given in the atomic theory and the grosser mechanical organization of living plants and animals. The fate of this assumption in the hands of experimental breeders and students of the cell is certainly a matter of great interest.

We may first note that the outcome of all this activity of research, both in cytology and breeding, has made it increasingly certain that we do have in the permanent structural constituents of the nucleus a real physical basis of heredity. The evidence available ten years and more ago, that the chromosomes transmit the hereditary characters of the adult organism in so far as they are directly transmitted, which is based on the permanence of the chromosomes through successive generations, due to their method of reproduction by equational division, their constancy in size, number, shape and position in the germ cells, however the latter may differ in shape, motility, cytoplasmic mass, etc., has been continually strengthened as the result of a more careful analysis and interpretation of results.

The attack on the specific character of the chromosomes and their reproduction by splitting, which has been made in the contention repeatedly appearing from both botanists and zoologists, that nuclei may divide by so-called direct division, that is, simple constriction, and still continue capable of perpetuating the species, has in every case on more careful study been found to be due to faulty interpretation or inadequate methods of observation. Only a passing reference to the exploded notions of Pfeffer as to *Spirogyra* and Child as to certain flat worms is necessary in this connection. Cases of apparent preponderance of the female, such as the echinoderm hybrids, in which the enucleated egg cytoplasm determines the type of cleavage and early embryonic development, are always those in which the egg has become a highly specialized cell by reason of the accumulation of yolk stuffs, etc. That a cell so enlarged should have also developed what has been called a promorphology is natural enough. That this preconjugation organization is that of the species to which the egg belongs is inevitable, but such cases can have no final significance in determining the question of the relative functions of nucleus and cytoplasm in heredity. Perhaps the best recent evidence that elements of the cytoplasm may also belong specifically to the germ plasm is found in Meves's observation of the so-called chrondriosomes which he finds widely distributed in the tissues of the embryo chick and so evenly scattered in the cytoplasm of each cell that they are somewhat equally allotted to the daughter cells in division. That these bodies may be concerned in heredity is however hardly more than an interesting suggestion. That any considerable portion of their material is really derived from the male gamete is certainly not proven. In sexual reproduction they are as yet to be classed with the ordinary cytoplasm. That they are, however, widely distributed cell organs seems probable. Unpublished observations in my own laboratory show that they are present in the embryonic muscle, connective tissue, cartilage and nerve cells of trout embryos with the same appearance and apparently the same relation to the formation of muscle and nerve fibrils, etc., which has been described by Meves for the chick. That similar structures are also present in embryonic tissues of plants seems probable from the recent preliminary announcement and figures of Guilliermond showing their appearance in the embryonic cells of the kernels of the cereal grains thus confirming the still earlier observations of Bigaud and Lewitsky. That they are in reality *anlagen* for the cell plastids needs further proof, of course, but that we have in them an important and widely occurring stage in the differentiation of embryonic cytoplasm into the characteristic organs of specialized cells in both animals and plants is strongly suggested. Their study may be expected to throw further light on the methods by which the material transmitted by the germ cells comes to its expression in the structural features of the adult tissues.

Other minor objections are being urged repeatedly against the doctrine, but in my opinion it must be taken as one of the best established facts of cytology to-day that there is a specific germ plasm differentiated from the general protoplasm of the cell, and that this specific plasm is at least carried by and continuously present in the stainable materials of the nucleus. From the cytological side, evidence has continually increased that we have in the chromatin of the nucleus a physical basis of heredity in a very specific sense.

When we turn to the interesting question as to how far the laborious and widespread cytological studies of the past decade have gone toward confirming the earlier corpuscular theories as to the ultimate structure of this germ plasm, we are confronted for the most part as yet with negative results. It can be claimed by no one that there is any substantial agreement among students of the cell to-day as to the existence even of any visible organized structure in the chromosomes themselves. Heidenhain is the most effective recent defender of the theory of an ultramicroscopic organization of the cell and nucleus, but his arguments for the existence of a bio-system below the grade of the chromosome represented by chromioles and centrioles has met with no general acceptance. As Haecker affirms, there is no agreement as to any facts of structure in the chromosomes themselves. The existence of the chromioles as specific units has not been confirmed. Errera has made it clear that bodies of the size of the chromomeres could contain only some thousands or less of proteid molecules, according to the chemical evidence, and it is hardly possible that an organization of any significance could be achieved with so few units. It is not impossible that in the chromosomes we have reached the ultimate units in the organization of the cell, themselves not organized, but purely chemical aggregates. Certain it is that the strands and granules and the spongy, knotted structure shown in the drawings of the chromosomes by the best cytological students of the day agree superficially in some respects at least with the descriptions of the colloid chemists of the structure of two-phased colloidal systems.

On the other hand, our knowledge of the chromosomes as independent continuously perpetuated organs of the cell has been enlarged and confirmed from many sources.

The extreme form of the doctrine that the chromosomes are independent individual organisms, cells within the cells, is probably an exaggeration, but evidence has continually accumulated that the chromosomes are specific and permanent parts of the cell which are formed only by the division of already existent chromosomes and which are nourished and grow after division so as to maintain within certain limits a size and number characteristic for each species. From the cytological standpoint also the argument for the significance of the serial arrangement of the chromosomes in the splitting spirem has lost none of its force.

The importance of the conclusion that each species has its constant number of chromosomes has only been emphasized by the discovery of cases in which such differential qualities within the species as distinctions of sex are found to be accompanied by a corresponding difference in the number of chromosomes in the two sexes. To be sure, such an extreme germinal difference as the presence of an additional chromosome in the female is probably a rare case found so far chiefly among insects. But the fact that in these cases the structural and functional differences between the sexes in the adult form are correlated with specific differences in chromosome number in the germ cells must be regarded as strong evidence that the chromosomes represent in some fashion the hereditary characters in the germ cells.

It may well be expected that other slight differences in chromosome number which have been observed within the species will be found to have quite as rational and natural an explanation as have the sex chromosomes. Other forms of dimorphism may perhaps be dependent on corresponding variations in chromosome number or size.

In the case of the sex-chromosomes the question as to how the organs and characteristics of the adult can be represented in the germ plasm is raised in a very concrete form. If the presence of an extra chromosome determines the female sex, it must apparently not only represent the specific female sex organs of the adult, but also a series of secondary sexual characters belonging to the other organs and tissues. The difficulties involved in any corpuscular theory of heredity become conspicuous in such a case. That a series of granules representing *anlagen* for all the various characteristics of the female sex should be brought together in a single chromosome, being thus apparently separated from all the other *anlagen* for the organs which show secondary sex characters, and should still be able to determine the development of the individual in all these respects, is scarcely conceivable. The discovery of the sex chromosomes must be regarded as evidence against the corpuscular theories of heredity.

The view that characters that are sex-limited in heredity must also be determined by materials which accompany or are included in the sex chromosomes makes the situation still more difficult, being quite inconsistent with even a serial arrangement of the elements of the germ plasm such as the cytological facts as to the longitudinal splitting of the chromosomes seem to demand, and shows how inconsistent with the assumption of even the simplest form of determinate arrangement of elements in the germ plasm Mendelian conceptions are. It is obvious that the couplings seen in sex-limited inheritance suggest the connection of the factors representing them with a sex chromosome. That is why such characters are called sex-limited. But to actually imagine such diverse and easily transferred characteristics of color, etc., affecting such widely separated parts of the adult organism as inhering in or connected with a single sex-chromosome is just as obviously opposed to the common interpretation of the serial arrangement of the chromosomes and their parts. Other cases of Mendelian couplings, such as that of long pollen and purple flower color, are just as inconceivable on the basis of a serial corpuscular representation of genes in the chromosomes. To be sure, Bateson is now inclined to give up the conception of gametic coupling, but the idea has been widely taken up and seems fairly well established among Mendelian conceptions. It differs little, of course, from the older ideas of correlation in heredity. The factors in heredity in such cases are certainly more easily conceived as due to the characteristic constitution of the germ plasm, as a whole, than as represented by unit corpuscles.

One of the strongest pieces of cytological evidence that the number of the chromosomes is due to their own specific and individual characters, rather than any mere mechanical necessities in the cell organization, such as Fick assumes in his maneuver hypothesis, is found in the work of the Marchals on aposporous mosses. By regenerating the gametophyte directly from the sporophyte without the intervention of the reduction division (apospory) they have produced diploid gametophytes. These in turn in fertilization have produced tetraploid sporophytes, and these by regeneration again tetraploid gametophytes. No stronger evidence for the permanence and independence of each chromosome could be produced. An excess of chromosomes can only be gotten rid of by a specific reduction division, that is, by separating them without the splitting of each into two. Some of the diploid gametophytes seemed vigorous, the tetraploid gametophytes were weak, and the physiological limit for the number of chromosomes in one cell was probably reached in them. These cases, along with those in ferns, show that an excess in the amount of the germ plasm doubling or trebling the representation of each hereditary quality need not necessarily affect the morphological characteristics of the organism, and are in strong contrast with such cases as that of *Œnothera gigas* and certain races of bananas, in which a doubling or trebling of the chromosome number is associated with marked structural changes in the plant. When the excess number of chromosomes fails to produce visible effects, the condition is perhaps analogous to that of ordinary latency. The condition of ineffectiveness of the excess chromosomes in these diploid and tetraploid gametophytes of the mosses, so far as their relation to morphogenetic processes is concerned, also seems analogous to that of the chromosomes of the recessive parent in the F_1 generation in cases of Mendelian dominance. Cells containing two complete sets of chromosomes may show complete resemblance to one parent or mixed, mosaic and intermediate resemblance, depending on the degree of prepotency or latency represented by the conflicting sets of chromosomes. Mendelian dominance and recessiveness represent the extremes of prepotency and subordination in the relations of the diploid germ plasm.

Such evidence as this suggests that the germ plasms are related to each other much as competing races of organisms are. The evidence here may be said to favor the idea of the germ plasm as a mass of independent individual corpuscles competing with each other for their existence. One of the most obvious ways in which Mendelian concepts have influenced the idea of the germ plasm is in the emphasis which the idea of Mendelian dominance gave to the conception of antagonistic relations between its elements. Of any two characters present in the parents, one may dominate the other in the offspring without destroying it. These facts are obviously opposed to a chemical theory of the germ plasm. If the union of the two factors is chemical it should result in some new compound with properties in some degree different from either. As has been pointed out by Friedmann on chemical analogy, the product of the union of two germ plasms would not necessarily be intermediate in its properties between those of the two combining elements, especially in its form and spatial configuration. The angles of a crystal made of a mixture of two isomorphic salts are not the average of the angles of the two components. Such so-called chemical theories of dominance as assume the existence of regulative enzymes influencing the rate of morphogenetic processes by their relative concentration seem to me to beg the whole question by assuming in the appearance of the regulative enzymes at the critical point the element of organization which they start out to deny.

Not only the facts as to constancy and variation in the number of chromosomes, but also our knowledge of their constant arrangement and position in the cell nucleus, has been greatly strengthened by the critical study of recent years. The accumulating evidence for the constant position of each chromosome in the resting nucleus as it reappears after the disturbance of nuclear division is most suggestive of mechanical organization in the nucleus as a whole, whether or not there be an ultramicroscopic organization of the chromosomes themselves.

Boveri has shown for *Ascaris* that the long chromosomes of the embryonic nuclei reappear at each cell generation in the same position and determine the configuration of the young resting nuclei. In certain fungi at least there is permanent connection between the chromosomes and centrosomes, thus determining the polar organization of the cell as conceived by Rabl. These conditions give strong evidence for a mechanically organized, rather than a mere chemical cell and nuclear structure.

No more important question confronts the students of the cell to-day than the determination of the relative positions of the paternal and maternal chromosomes in the diploid vegetative cells. Evidence that the serial arrangement found in all spirems is maintained in the resting condition and in the equatorial plate of a species of *Carex* will be presented at this meeting. Strasburger, Overton and others find that the chromosomes are paired throughout vegetative development, the members of the pairs representing respectively maternal and paternal elements. If these results are confirmed and found to be general, we have a further vantage point from which to attack the question as to the method by which the parental germ plasms are not only transmitted but come to expression in the offspring.

It is fairly well established that homologous chromosomes are paired in synapsis, and the prophases of the reduction division. The evidence from cases of chromosomes of unequal length in both animals and plants seems convincing on this point. The determination of the relative position of the parental elements in the vegetative cell generations would go far to settle the vexed question of whether this pairing is side by side or end to end. Without going into the evidence on this point, so many times reviewed in recent years, I may express my opinion that it favors the side-by-side conjugation and, further, indicates that the union of the two parental germ plasms is, in many cases at least, a very intimate one, so that in the pachyneme spireme the visible identity of the two parental elements completely disappears. The discovery that this intimate union of the germ plasms comes at the close of the F_1 generation in the preparation of the germ cells for the F_2 generation forms perhaps one of the closest points of contact between the results of cytological study and experimental breeding. The long-known relative constancy of the first hybrid generation contrasted with the breaking up in the succeeding generations has here its counterpart in the relations of the germ plasms in the reproductive cells.

It seems plain to me also that the behavior of the chromosomes in thus uniting so intimately that their visible identity is lost in the pachyneme spirem, is strongly opposed to the conception of universal and absolute gametic purity and unit characters. It is a very obvious suggestion that the elements of the gametes should not be pure after this union. This obvious suggestion from cytology may clear up the behavior of the offspring from many crossings better than the assumption of more unit factors. The behavior of the parental chromosomes in synapsis and the following stages is well calculated to provide for just such fluctuating variability as well as a certain degree of stability as the breeder unbiased by Mendelian preconceptions finds. It is quite possible that in some cases pairs of parental characters may separate or interchange without a trace of mutual influence, but the close union found in the synaptic knot and the succeeding spirem certainly seems adapted to provide the opportunity for a vast amount of modification and interaction between the parental germ plasms.

At this stage again we are confronted in very concrete form with the alternatives of a chemical and mechanical organization of the chromosomes and the difficulties involved in the corpuscular theories become very conspicuous. There is no visible provision in synapsis for maintaining any such space relations between the determinants as Weismann's theory requires, and if we consider the case of the more vaguely arranged pangens of De Vries, it is still at least very possible that chemical reactions might occur between these minute proteid masses so intimately associated as they are.

In the phenomena of reduction, on the one hand, and segregation, on the other, the work of the cytologist and experimental breeder finds a most intimate point of contact, and the results of studies on these phenomena from both standpoints must have the most profound and far-reaching effects on our theories of heredity. The facts of synapsis are even more opposed to complexity of organization in the germ plasm than are the facts of nuclear division which have been so much emphasized.

To understand the present point of view of cytologists and breeders more clearly we must briefly examine the current corpuscular conceptions of the germ plasm. Detto's analysis and criticism of these views seem to me most suggestive. In his attempts to explain the heredity of form, Weismann conceives a so-called heteronomic structural preformation of the adult plant or animal as existing in his determinants and their architectural arrangement in the germ cell from which it arises. The development of the individual is epigenetic in a sense, but the corpuscular *anlagen* determine the outcome of the series of epigenetic changes. The assumption of all those who hold to a representation of the adult organism in the egg seems to be that if development is really to be explained a complicated spatially differentiated organization must be supposed to exist in the fertilized egg. Hertwig, in his doctrine of epigenetic cellular interaction, also assumes a complicated qualitatively differentiated germ plasm, but these heteronomic preformed structures develop and differentiate themselves under the influence of intercellular and environmental interactions.

Weismann's material determinants are to be described as heteronomic, because there certainly is no visible resemblance between their organization and that of the adult body. It is held that the tissues of the adult body are not to be considered as especially preformed, but that they may be represented in the egg not as formed parts, but as particles in which inhere particular qualities and capacities of the protoplasm. These particles are not identical in organization with the adult characteristic which they determine, but they necessitate the development of that particular adult structural quality. It would seem that the important thing here is the quality or potency rather than the particle, and the difficulty is in assuming complex potentialities as inhering in particles of simple structure. Detto has proposed to call certain of these *anlagen* metidentical, to indicate that they are heteronomic as regards the actual adult characteristics, but identical with the protoplasmic qualities which are assumed to cause them. Regulative *anlagen* are also assumed which, acting catalytically, perhaps, produce their effects in such fashion that basic protoplasms may be worked out into a product of specific type. It is assumed to be conceivable that form may be due to regulative form *anlagen*. Elements of the cytoplasm forming an internal environment for the germ plasm may act as regulating factors of this sort.

Such doctrines of qualitative preformation aim to explain the architectural arrangements of the adult organism, but as Detto points out, we really explain nothing by simply assuming in the egg a so-called metidentical and heteronomic representation of the structure of the adult. Any organization in the egg which will help to explain the complex and adaptive spatial configuration of the adult organs and tissues must be assumed to possess a similar spatial configuration in three dimensions. In a word, we can explain by our *anlage* no greater degree of spatial complexity than we put into it.

A most striking feature in the assumptions of present-day experimenters is their thoroughgoing break with the conceptions of Weismann as to the existence of germinal elements representing tissues or organs of the adult plant, and in definite space relations with each other in the germ plasm. Many of the factors of the Mendelians have no particular space relations in the adult. Tall and dwarf habits are diffuse characters of the plant, as a whole. Hairiness may be on stem, leaves, calyx, part or all of them. Mendelian hereditary units are not leaves, petioles, stamens, etc., but qualities of these organs or still more diffuse qualities of the whole plant. Fixed space relations between elements of the germ plasm are quite unnecessary in the heredity of such qualities.

With the disappearance of Weismann's conception of definite and complex space relations between the elements of the germ plasm, we perhaps see the last of the old doctrine of formal preformation. And yet it is a curious fact that one of the most important influences which Mendelian studies have exerted on our conceptions of the germ plasm seems to be in the stimulus which they have apparently given to all corpuscular theories of heredity. The doctrine of unit characters is the real gist of Mendelism, and it seems obvious to associate these unit characters of the plant, as a whole, with the theoretically postulated determinants, granules, etc., of the corpuscular theories of heredity.

The relative popularity of De Vries's conception of the *pangens* is due to the emphasis he lays on the conception of units representing diffuse characters of the plant as a whole rather than organisms or tissues. De Vries's *pangens* are assumed in many cases to represent just such qualities and characteristics of color, size, etc., in the plant as are found to show the Mendelian behavior most perfectly. It is certainly a striking fact that Mendel and De Vries independently reached the conception of the importance of such characters in an analysis of heredity. That De Vries should regard them as units is due to the influence of his corpuscular theory of the germ plasm. They are more properly described as diffuse characteristics of the plant or its organs, as wholes, as De Vries has so strongly emphasized in relating them to the origin of his mutants which differ from their parents in general features affecting the whole organism.

It must be remembered also, that while De Vries makes his *pangens* stand for characteristic features of the plant or its organs as wholes rather than for specific organs or tissues, and rejects Weismann's and Naegeli's conception of a mosaic combination of the units in a germ plasm, yet he is not free from the feeling that a definite spatial relation of the *pangens* in the germ plasm is necessary. The *pangens* must be in smaller and larger groups and these groups so arranged that the members of a group may become active at the same time at least. The arrangement must also be such as to provide for their proper distribution at each cell division. This sounds as if a relatively simple serial arrangement were all that is necessary, but as noted, the coupling of *pangens* representing all the secondary sex and sex-limited characters affecting widely distributed organs of the body, which in many respects are otherwise determined, with a single sex chromosome or group of *pangens,* is not a simple matter. The doctrine of intracellular pangenesis, with its storage of *pangens* in the nucleus and their migration into the cytoplasm, provides for the behavior of the Mendelian factors hardly better than the formal unfolding of the architecturally prearranged corpuscles of Weismann's theory.

That the harmony in underlying assumptions between the Mendelians and the adherents of corpuscular theories of heredity is only apparent seems to me the inevitable conclusion of any careful analysis. A list of the characters associated by De Vries with his *pangens* is itself suggestive of difficulties. The first character he mentions in his intracellular pangenesis is the green color of plants. That this is a characteristic of plants which have a certain unity of behavior in heredity may be true, but to see how it can be represented by a *pangen* granule in the germ plasm so as to appear in just the proper tissues in just the proper degree is not so obvious. Other *pangen* characters, such as those for the production of specific alkaloids, oils, tannin, etc., involve the same difficulties, and this is no less true for morphogenetic *pangens* of leaf form, etc. To speak with Klebs, such *pangens* should be potentialities rather than material granules.

The failure of the experimental breeders to characterize more exactly the hypothetical units, genes, etc., in the germ plasm which represent their factors is not all due to a desire for absolute freedom from prejudice in matters of theory, but rather to an inability to identify the behavior of their factors with that of any such units in the germ plasm as the older theories have assumed. Johannsen gives a name to the units of which his germ plasm is composed, the genes, but he defines genes and genotype strictly from the visible behavior of the different characters of the many-celled plant. The genotype is the specific germ plasm, each of the genes represents a unit character. How they are situated or related in the egg is unspecified, though it is suggested they probably have only a chemical constitution.

The Mendelian unit characters are, as noted, most typically generalized qualities of the plant or organ as physiological wholes. They are very diverse in their character and there is little attempt as yet to classify them. We have quantitative characters of weight and measure in fruits, stems, etc., superficial factors of color, which palpably depend on nothing more fundamental than a slight change in the degree of oxidation of a by-product of the protoplasm or a variation in the alkalinity or acidity of the cell sap.

We have factors for annual and biennial habit, as well as the more fundamental factors for form and tissue differentiation which are essential to the every-day existence of the organism. These heterogeneous factors show couplings, repulsions, etc., without regard to any, at present, explainable relationship between them which would make it possible to associate them with any definite spatial distribution of *anlagen* in the germ cells.

It may be found to be one of the most valuable results of Mendelian experimentation that it has helped to destroy the last vestiges of preformationist ideas which inhered in the prearrangement of the hereditary corpuscles assumed in the theories of Weismann. It is certainly impossible to imagine where a corpuscle should be placed in the egg or what it should do to change a plant from an annual to a biennial, or a crenate to a serrate leaf.

It is sufficiently clear that the results of Mendelian and mutational breeding from the standpoint of the kind of unit factors observed and their behavior in cases of so-called coupling and repulsion are opposed to the doctrine of a spatially organized germ plasm made up of corpuscular units. The doctrine of the fixity of the unit characters and their segregation as pure elements seems still, however, to harmonize well with the conception of *pangens*, perhaps not so definitely related to each other, spatially, in the germ plasm. If there are fixed elements, unit characters, which are transmitted in reproduction, this is certainly strong ground for the assumption of the existence of corresponding corpuscular units in the germ plasm. The experience of experimental breeders with the doctrine of segregation must be examined critically as to the evidence it gives on this point. It is a fundamental assumption of Mendelism that the characteristics of the parents behave in fertilization, whether hybrid or normal, as unit characters, and that hybridization and the phenomena of segregation which follow give the best possible means of recognizing and identifying them. Still there can be no question that the doctrine of segregation and alternative inheritance no longer has the clear and simple form in which Mendel proposed it. It is equally certain that the changes which have been made were necessary in order to bring the theory into harmony with the vast mass of new facts which breeding on a large scale has brought to light.

These modifications have largely been in the direction of providing for a greater degree of variability in the F_2 and succeeding generations than is provided for by the doctrine of segregation. Pre-Mendelian views held to a general breaking-up and tendency to vary in hybrids after the first generation. It was Mendel's great contribution to apparently discover in this multiplicity of forms a real simplicity in fundamental features. Recent workers have, however, found it increasingly difficult to interpret their results within the limits of the Mendelian formulæ.

One of the first steps in the modification of Mendel's views was to admit greater variation in the first generation. It is generally agreed now that there is no law of dominance, that the first generation may be intermediate, or a mosaic of the parental characters, and the possibility is present that there may even be di- or poly-morphism in the first generation. Practically all the pre-Mendelian conceptions as to the character of the first generation have now been confirmed and generally admitted.

An important step toward the modification of the Mendelian account of segregation in the second and following generations was in the introduction of the presence and absence hypothesis as a substitute for the Mendelian doctrine of pairs of positive visible characters. The presence and absence hypothesis when applied to simple Mendelian pairs of contrasting characters seems perhaps to have a sort of explanatory value. To be sure, the case is somewhat as if a geologist should explain a given hill as due to the absence of a mountain, failing to suggest anything as to the forces and conditions concerned in the production of both hills and mountains. There can be no question that Mendel's doctrine of segregation assumed the probable occurrence of alternative inheritance for all homologous differential qualities in the parents of hybrids. It was the task of the breeder to discover such pairs of opposite characters and operate with them. This has been found to be impossible in many cases, and the presence and absence hypothesis is advanced as an expression more nearly in accord with the facts as found in practical breeding work. The facts that have necessitated this change show that not all apparently homologous contrasting characteristics form allelomorphic pairs. When two contrasting flower colors are found not to form an allelomorphic pair, the pairing may sometimes still be discovered by operating with groups of characters in the formation of allelomorphs, such as pigmentation against white or albinism, and here again albinism is by no means always found to be the same thing in heredity.

In other cases the presence and absence hypothesis is introduced as a concession to the fact that the second and following hybrid generations are much more variable than the Mendelian doctrine allowed. On the Mendelian hypothesis of allelomorphic pairs and their segregation, two individuals differing in a single character, such as flower color, could produce but two kinds of gametes and four groups of offspring. On the presence and absence hypothesis we can assume at once four elements, a factor for the presence and absence of each of the two colors. To take the stock illustration: fowls with pea and rose combs when crossed are found to produce two further new comb types, walnut in the F_1 and single in the F_2 generations. The whole result harmonizes with the assumption that we have here two allelomorphic pairs—rose present and absent and pea present and absent—the absence in each case resulting in single comb.

The real discovery here is that two birds visibly differing in the one feature of comb character do not produce monohybrid offspring, as in the case of the green and yellow peas, but show on breeding that the qualities pea and rose comb belong to separate allelomorphic pairs. This permits of four kinds of gametes and sixteen different combinations in the F_2 generation. That is, the result resembles that of a dihybrid rather than a monohybrid combination.

It is really a case of the assumption of two factors as responsible for a single unit character. And the use of the presence and absence hypothesis perhaps tends to obscure the real facts. Single comb is superficially at least just as positive a character as pea or rose comb. Single comb is found to occur in the absence of either pea or rose comb. If the absence had not happened to have the same result in both cases—if, for example, absence of pea comb had meant no comb, then the cross would have had a still different result. Stated in plain terms, the experiment shows that in applying Mendel's principles to a wider and wider range of experimental material we find it necessary to provide for a much greater degree of variability in our results than was anticipated. The pre-Mendelian dogma of the breaking-up of the F_2 generation is to this degree vindicated.

This adoption of the presence and absence hypothesis and of additional factors is probably an entirely correct method of procedure as far as it goes, and allows much more fully for the real variability which we find in heredity.

That the increase of diversity with added pairs of differentiating characters in the parents should follow just this Mendelian law is, of course, only necessary on the assumption of fixed unit characters. It is a question whether it is sufficiently obvious that we need just twelve more groups in which to place our phenomena when we pass from the results of crossing parents with one visible difference to those with two visible differences. Perhaps some other number of groups would really classify the results of such a cross just as well as sixteen.

It is to be remembered that the biometrician dealing with symbols can proceed with perfect certainty that his results will be mathematically correct without troubling himself in the least as to whether his series of symbols corresponds to any realities. Handling a series of the combinations of numbers or letters from one to ten is very elementary mathematics, but to hold in mind and be able to visualize from day to day with certainty of a constant result ten related colors and their combinations in a bed of snap-dragons is, as can be shown by appropriate tests, a matter of expert training and considerable uncertainty. When we realize further that unit characters are not conceived as hard and fast categories, but as each having an allowed range of fluctuating variability, we can see that the chances of mistake in estimating the sixty-four classes of offspring which might come from a pair of parents differing in three characters are very great. It is a matter of difficulty for the student of the problem and it is almost impossible for any one who reads of such results to pass any critical judgment on their probable accuracy.

Formally the presence and absence

hypothesis is perhaps consistent with the corpuscular theories of heredity but the necessity of its introduction arising from the variability of the products of hybridization must be regarded as seriously affecting the basal conception of segregation of fixed unit characters.

Perhaps the most important modification of Mendelian theories is in the continuous discovery of further cases in which single visible characteristics as conceived by Mendel or De Vries may be dependent for their realization on from two to several factors, or may arise in more than one way. Nilsson-Ehle tells us that the black color in oats and the red color in certain wheats may each be produced in different ways. Shull finds that two separate genes may be responsible for the common form of capsule in *Capsella bursa-pastoris.* Bateson and Saunders tell us that certain white varieties of peas and stocks when crossed give purple. This is because the colors in question are due to two factors instead of one. These two factors are not members of one allelomorphic pair but must be assumed to be the members of two distinct pairs, each from different parents. Hoariness in stocks is dependent on four factors, two for hoariness and two for flower color, not compounded in one unit but distributed in four allelomorphic pairs. Reversion is the reappearance of a character because of the reunion of the two necessary factors which had become separated.

An extreme of this tendency is found in Tammes's recent paper on heredity in flax in which she has worked with three types and apparently has used all possible precautions as to control, etc. Tammes finds that the results of her study of seed size, petal size, petal color, etc., can only be brought into harmony with Mendelian ratios by assuming that each of these visible characters is dependent on from one to several factors in the germ plasm. For the length of the seed at least four factors must be assumed. For length and breadth of petal three factors must be assumed in one cross and at least four in others. For flower color three factors were found; for dehiscence of seed pod three or four factors; for hoariness of seed pod alone one factor. Tammes finds in crossing two individuals differing in a single visible character where Mendel would expect to find a monohybrid giving four combinations in the F_2 generation that the results are those which should be expected in the case of a di- or poly-hybrid. In plain terms this merely states that the F_2 generation is, as the older views of hybridization held, vastly more variable than the ordinary Mendelian expectation permits.

It is probable that Tammes and the others who are assuming a multiplicity of factors as necessary to the production of a single visible character are giving the facts as they find them, but the doctrine of fixed unit characters represented by pangens or genes in the germ plasm certainly shows itself inadequate to account for such facts. These results attack the doctrine of the *pangen* at its very foundation. According to De Vries the multiplicity of plant and animal forms is due to the large number of combinations possible with relatively few unit characters. We are now given multiplicity in the germ plasm to account for apparent simplicity in the organism. On Johannsen's view also each factor must be represented by a gene in the germ plasm.

Furthermore, as noted, the unit characters are diffuse characteristics of the plant taken as a whole. Each hereditary factor responsible for this diffuse character may influence many parts of the plant. We have thus a most complex overlapping of functions among the factors, one character being dependent on several factors and each factor affecting a number of parts and even qualities of the plant.

Even the most thoroughgoing Mendelian must admit that a unit character made up of four fractions or assumed to be dependent for its realization on four factors has lost something of its unity. What the student of the germ plasm wants to know, of course, is the nature of these fractions or the ultimate elements in heredity, whatever they may be. The breeder may perhaps properly, as Baur does, relegate all questions as to the nature of the representation of the hereditary qualities of the many-celled organism in the egg to the future as outside the scope of his immediate experiments. The cytologist dealing directly with the germ plasm in the chromosomes is confronted directly with the question of their ultimate constitution and must attempt to connect any discoverable units in the make-up of the adult in some way with the structure and properties of the germ plasm itself. It is obvious that visible characters which may arise in more than one way or that require the combination of from two to several factors for their production can hardly be represented in the germ plasm by the *pangens,* determinants or other corpuscular units of the older theories. To call a visible character which depends on four hereditary factors for its production a unit character is certainly not conducive to clearness of thought. To attempt to find fixed units in the maze of fluctuating colors, forms and physiological processes of multicellular plants looked upon as wholes is perhaps a hopeless task. Much more is it inconceivable that such diffuse fluctuating characteristics are represented by specific corpuscles in the germ plasm.

We have noted that Mendelian breeding, emphasizing as it does the existence of characteristics belonging to the organism as a whole and their couplings and repulsions in inheritance may have a most important result in the elimination of the last trace of the doctrine of preformation from our conceptions of the germ plasm. It seems to me also probable that the consistent study of the so-called unit characters is tending rapidly to the overthrow of all corpuscular theories of heredity, and that with a proper understanding and interpretation of the Mendelian factors we may finally be freed from these confusing molecular chemical analogies in the study of the germ plasm.

There are certain broad inconsistencies in the doctrine that the characters of the whole organism as such are represented in any fashion by units of the germ plasm, which should always be borne in mind. Most conspicuous of these is the fact that there is no proportion between either the number of the chromosomes or their mass and the complexity of the organism to which they belong. The simplest algæ and fungi may have as many chromosomes and, proportionally to the size of the cell and nucleus, as large chromosomes as some flowering plants. Allowing for a large amount of possible ultra-microscopic organization, such disproportions are not consistent with any corpuscular theory of heredity. It may well be that just as many of the so-called unit characters of Mendel and De Vries relate to the diffuse properties of the organism, as a whole, so the hereditary factors representing them depend on diffuse qualities of the cells as wholes in their interactions with each other. Such a view is not inconsistent with the doctrine that the chromosomes are the physical basis of heredity. We should perhaps, with Hertwig, more clearly distinguish between the heredity which determines the characters of the cells, epidermal, mesophyl, vessels, etc., and the determination of the qualities of the organisms as wholes which depend upon the interaction of these cells and which only indirectly represent and are represented by the organization of the cell and germ plasm. A leaf can not be represented directly in a cell, but the color of the leaf may be represented in the color of the cell, and its size may be determined by the capacity of the cell to divide and grow. Such Mendelian unit characters as color, length of life, etc., are properties of individual cells and agree with Detto's conception of metidentical characters which become by multiplication of the cells more or less diffuse properties of plants as wholes or organs as wholes.

It is easy to distinguish the heredity of the cell form as such from the heredity of the form of the many-celled colony. No one thinks now of asserting that the organization of the cell is identical with that of the many-celled individual. That dogma of the old preformationists disappeared with the improvement of the microscope. If we can, however, fix clearly in mind that such representation of the adult organism as is present in the egg in no way resembles in space configuration or in complexity the arrangement of organs and tissues in the adult animal or plant, we can attack the problem of form development as it really exists, and free from many encumbering traditions of preformation and epigenesis.

There can be no doubt that the cell and nucleus have a highly complex mechanical organization. It is a commonplace of histology that cell and tissue structures are relatively constant through genera and families—regardless of variation in the size and form of organs and of the plant as a whole. Cell size is also relatively constant through genera and even families. Quantitative variations in the size of leaves, seeds, etc., are due to the number of cells they contain, and this, of course, depends on the number of times the cells have reproduced themselves by division. In some cases Mendelian characters can thus be identified with qualities of the cells.

The attempt from the standpoint of Mendelian conceptions of dominance and segregation to analyze the behavior of the generalized qualities of plants and their parts in development and heredity has been stimulating to research in a high degree, but the attempt to express the results of such analyses in terms of unit characters may be found to be only a relic of the preconceptions of the earlier corpuscular and preformational theories of heredity. Many Mendelians are inclined to think of their germ plasm as merely chemical in its essential constitution and I have referred above to the uncertainty of the evidence as to any ultramicroscopic organization of the nuclear chromatin of the cell. With the clarification of our conceptions in the domain of colloid chemistry we may hope to gain new viewpoints which will be more serviceable in the interpretation of biological facts than the conceptions of atoms and molecules which have so far dominated the corpuscular theories of protoplasmic structure. But we must also expect, perhaps, that the real distinctions between the organization of protoplasm with its long history of slow evolution and the *in vitro* aggregates of the chemist will be emphasized rather than obliterated.

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