SCIENCE

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MSS. intended for publication and books, etc., intended for review should be sent to Professor J. McKeen Cattell, Garrison-on-Hudson, N. Y.

THE BASIS OF INDIVIDUALITY IN ORGANISMS[1]

INTRODUCTORY

To enter upon the "higher criticism" of the concept individuality, is far beyond my powers. Even the humble attempt to think of it, in the organic realm, in what I conceive to be the simplest terms, offers difficulties most of which must be bequeathed in their entirety to future generations. Yet to point these out and to take a few soundings, unsatisfactory though they be, may not prove entirely futile even at this time.

For me, the basis of individuality in organisms is the mechanism by which living things, despite profound and constant change, keep themselves capable of identification. Some of the changes through which organisms pass are so radical that by common consent we treat them separately under the head of development, but since there is no evidence that living things become individuals at a particular point in their history, we may expect to find anywhere in the life-cycle the mechanism upon whose workings the possibility of identification rests. For obvious reasons the arrangements that make for constancy must occur in their least complicated form in the simplest of all the stages of development.

Fortunately, since it forces us at once to engage with fundamentals, the beginnings of development offer no refuge from our most insistent problem. We habitually identify a given organism at two more or

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[1] Read at a joint symposium of the American Society of Zoologists and Section F of the American Association for the Advancement of Science, Columbus, Ohio, December 30, 1915.

less remote points of time, but no biologist limits himself to this relatively simple pursuit, since every living thing can be, at least partly, identified also with the better known portions of its ancestry. Indeed, these so-called genetic similarities are so striking and constant that one generation can be inferred from another with considerable precision.

If there is a substantial basis for the resemblances between parents and offspring, it must be the chromatin, for this is the only material capable of being contributed to each generation in essentially equivalent values by all the members of a given lineage. But if chromatin is responsible for the partial identifications possible between the individuals of two or more generations, we must also suspect that the specific recognition of a given individual at any of the numerous phases of his life is traceable to the same source.

THE SYNTHESIS OF CHROMATIN

Strictly speaking, ''chromatin'' is a morphological concept. Chemical analysis shows that it contains a conjugated phospho-protein provided with a nucleic acid group, the latter a complex of phosphoric acid and a nuclein base. During the so-called resting state of the cell, this material appears segregated in the nucleus.

We must attach to this substance a degree of specificity not less exact than the specificities we are seeking to explain. In this we have ample encouragement from cytologists and geneticists. But the question at once arises how chromatin can increase in quantity during more than one life cycle and yet lose none of its original characteristics. Brothers, who in the one-celled state derived from their mother the kind or arrangement of chromatin which in her father was associated with color-blindness, not only exhibit this defect in their own persons, but between the ages of 25 and 55 produce each some 169,692,750,000 examples of the same factor, all traceable to their own original endowment.

Compared with cytoplasm, the nucleus seems meager in the diversity of its chemical make-up. It is free from salts; it is devoid of fats and carbohydrates. Moreover, iron and phosphorus, easily demonstrable in the cytoplasm, are present in nuclei in forms difficult to detect and for that reason spoken of as masked or organic. These facts are not altered by doubting the localization of the iron in chromatin[2] or the accuracy of the tests for organic phosphorus.[3]

From the constancy of their occurrence we must conclude that both elements, as nuclear constituents, are essential. However, their absence in inorganic form, coupled with the general chemical poverty of the nucleus, indicates that simple raw materials for the synthesis of chromatin are excluded by the nuclear membrane (Macallum).

This conclusion is out of harmony with prevalent interpretation. Yet no one need be misled. That nuclei are rendered conspicuous by staining, are scrupulously divided in cleavage and maturation, and combined with equal exactitude in fertilization, are all beside the point. Further, though no cell devoid of a certain proportion of nuclear material can live, it is no less true that a nucleus embarrassed by the loss of cytoplasm also fails to maintain itself. Chromatin, moreover, is present in the bacteria, but not in the form of a nucleus. Here its complete cytoplasmic synthesis is not open to doubt. We are ready enough to admit that the cytoplasm of nu-

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[2] References in Aristides Kanitz, ''Handbuch d. Biochemie,'' etc. Herausgegeben von Carl Oppenheimer, pp. 253–254, Bd. II., Teil 1.

[3] R. R. Bensley, *Biological Bulletin*, Vol. X., pp. 49–65.

cleated cells can synthetize fats, carbohydrates, and proteins in general, including the most complicated compound forms. What real evidence have we that nucleoproteins constitute the sole exception?[4]

If we reckon with the synthetic powers of the cytoplasm as a possibility, we must next inquire how these can be influenced by the presence of a specific nucleus. That cytoplasmic response, in general, is dependent on the chemism of the cell, and that these activities are specifically and profoundly modified by changes in the variety of nuclear material present, are well-known facts shown nowhere more clearly than in the structural differentiations called forth in hybrids. These, especially, are important for us since the introduction of nuclei into foreign cytoplasm demonstrates most strikingly their ability to regulate syntheses so that more nuclei like themselves are produced. In what terms are we to conceive this regulation?

The influence of a specific chromatin on cellular processes can be directly attributed to the samples which are known to leave the nucleus and come directly into the cytoplasmic reaction-sphere. But the details of their activity there remain obscure. Autocatalysis, suggested on quite inadequate grounds, is not necessarily excluded by the recent work of Conklin[5] and other effects are also thinkable. A fitness, chemical or physical in nature, between the liberated chromatin or its products, on the one hand, and certain of the reaction-products of cytoplasmic synthesis on the other, leading to the formation of different, or larger, non-reacting aggregates, would automatically increase the production of such substances, provided always the machinery necessary for their production is given at all. Very possibly the reciprocal relation suggested here is one of the keys to successful hybridization.

It is useless to hope for intellectual satisfaction in this matter at the present time. We can, however, assert with confidence that a cell is viable and assured of the possibility of offspring, essentially like itself, if it contains, at the beginning of its life-cycle, samples of all the various kinds of chromatin possessed by its immediate parent, and moreover, contains these in quantities sufficient to influence cytoplasmic syntheses so that they shall ultimately yield a chromosomal complex in which the original proportions among the several variants are quantitatively preserved.

THE SYNTHESIS OF CHROMOSOMES

If chromatin or its immediate forerunners are cytoplasmic in origin, how do they get into the nucleus? The impermeability of nuclear membranes for most constituents of the cell is probable; likewise, their permeability for nucleins, since these, even in the form of visible aggregates, seem to pass freely into the cytoplasm. If they can get through the membrane, going out, they can also get through, going in. The nucleus, therefore, is to be thought of as a kind of sanctuary into which certain proteins may enter, and, so long as they remain behind their wall, be free from the influence of other substances (Macallum).

These considerations are only an entering wedge. We infer a specific chromatin for each race, for every individual, and even for particular cells of the individual. More than this, in its intranuclear state, the chromatin is organized, in all likelihood, permanently, into chromosomes which

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[4] For a fuller discussion of the methods, evidence, and conclusions, see the articles by A. B. Macallum in Abderhalden, "Handb. d. Biochem. Arbeitmethoden," and in Ascher-Spiro "Ergebnisse d. Physiol.," VII.

[5] E. G. Conklin, *Journal of Experimental Zoology*, Vol. 12, pp. 1–98.

exhibit symptoms, increasingly serious, of linear differentiation.[6]

If we admit the permeability of the nuclear membrane for chromatin or its immediate forerunners, we can with equal justification attribute the exact character of this membrane to the quantities and qualities of the substances enclosed. Specific permeabilities at once suggest themselves and so, by selective exclusion, any elements not true to one or the other of the types already present within the nucleus may, conceivably, be warded off (Macallum).

Having admitted only specific elements to the nucleus, it becomes our duty to attach them to particular places in specific chromosomes. Here we are, necessarily, thrown on our resources in analogies.

Most suggestive is the behavior of optically active substances in various degrees of dispersion. The common Japanese camphor, dextro-rotatory in alcoholic solution, is also dextral in gaseous as well as solid form. A property therefore which in the highest and intermediate states of dispersal must be attributed to the configuration of individual molecules, is preserved in aggregates of these. This can only result from specific orientation.

Taken alone, this analogy is too simple. It may enable us to form some notion of the terms in which differentiation among the chromosomes is conceivable; but each chromosome, instead of being homogeneous, is, if we can trust ourselves, a system of heterogeneous complexes definitely arranged in space.

Our starting point may again be a relatively simple analog. The hexoses are also systems of heterogeneous complexes definitely arranged in space. While the actual form of the hexose molecule is unknown, the carbon atoms are distributed in a manner conceivable as a linear series in which aldehyde and ketone groups occupy the only positions possible.

Chromosomes, of course, are not large molecules, but aggregates of complexes of these. While the chemical forces determining the specific structure of the individual molecules may be precisely analogous to those which account for the nature of the hexose molecule, aggregation into linear series, in the case of the chromosomes, very likely involves elements not strictly molecular. There is one suggestion, however, that is bodily transferable to the situation presented by the chromosome, namely: factors, in the Mendelian sense, may occupy certain positions because these are the only loci possible.

In this connection, the temporary unions between enzymes and their specific substrates are especially interesting because they depend on the stereo-relations of large complexes of molecules. Conditions, generically similar, may play a determining rôle in the formation of more permanent unions even though these are not chemical. Stereometrically determinable fitness, degrees of fitness, or possibilities of fitness, between various regions of persistent differentiated chromosomes and the newly synthetized elements by the lateral accretion or incorporation of which, these regions grow, enable us to visualize not only the periodic restoration of chromosomes to full size, but even the physical requirements for such phenomena as the single and double cross-over.

THE DIVERSITY OF DESCENDANTS

We can hammer out, on the lines suggested, a provisional interpretation of that constancy in organisms which makes us

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[6] This evidence has been brought together conveniently by T. H. Morgan and others, in "The Mechanism of Mendelian Inheritance." The Macmillan Co., 1915.

call them individuals. But no two descendants of either compound or unicellular organisms are strictly alike. Each maintains an individuality of its own different from that of its immediate forerunners. This diversity must also be accounted for.

The differences between parents and offspring are adequately explained by the details of maturation. Why, however, do the units derived from the fertilized egg differ? This question is the inevitable consequence of our inability to consider more than one thing at a time. As yet we have neither reckoned with the differential distribution of cytoplasmic substances nor with the intimate history of the chromosomes during and after division.

Students of embryology are familiar with the distribution of "organ-forming" substances. These have been convincingly traced in a number of eggs (Conklin). The remarkable homologies found in the early development of molluscan and annelidan eggs of various types can be understood only as expressions of the accuracy with which these materials manœuver.

The visibility of an "organ-forming" substance is the merest accident. In the egg or cell from which an individual comes there may be and probably are materials whose accurate but uneven distribution during cleavage has not been noticed. Obviously there may be many occasions on which the cytoplasmic composition is changed during development.

Differential localization of itself indirectly increases the possibilities of further differentiation. With increase in the number of cells come purely physical and mechanical disturbances of equilibrium. In the readjustments that follow, changes of relation, themselves certain to influence the greatest variety of subsequent events, are inevitable. A crisis like gastrulation can not but affect, directly or indirectly, every cell in the system.

I am not forgetting the work of the Drieschian school of experimentalists. They have sinned abundantly in this field for the origin of two or four individuals from an egg whose blastomeres are separated at the appropriate moment by no means demonstrates a harmonious equipotential system. Harmonious it probably is, but equipotentiality is proved by meridional divisions only to those who consider them identical with equatorial or latitudinal cleavages. The production of viable organisms from blastulæ has been misinterpreted in the same way.

Differentiation may also be nuclear in origin. Not only are we unable to exclude the possibility of qualitative and quantitative disparities in ordinary mitosis, but we know positively that differences in nuclei may come about after division. We should recall the somatic cells of *Ascaris* and especially the differential growth of chromosomes.

As Conklin has pointed out[7] the chromatin mass does not necessarily double with each doubling in the number of cleavage cells, since growth is not shared proportionately by all the chromosomes. This fact, which very likely does not apply to the divisions of the sex cells, has been observed in the mitoses of early development, divisions which have been but little studied in detail. Such diminutions in the relative sizes of chromosomes may be accompanied by changes in the chromosomal balance and, through this, bring on changes of equilibrium among cytoplasmic processes. Some chromosomes may, in one respect or another, become ineffective, or in their altered circumstances may have effects qualitatively different from their earlier ones.

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[7] *Loc. cit.*

CONCLUSION

From the standpoint here adopted, differentiation is the expression of internal as well as external specificities. It is a cytoplasmic reaction and when it occurs denotes that something is not as it was before. Here as elsewhere, we do not deal with isolated events, but correlative changes with specific antecedents and specific consequences. This linkage of specified happenings persists through the entire life-cycle but in the adult, having few or relatively unimportant morphogenetic results, constitutes the basis for a physiology of maintenance.

In development as well as maintenance, that which constitutes our problem is a harmonic relation among all the processes whose net result makes possible the identification not only of an organism at any stage of life, but also of its ancestors. Such constancy, maintained despite the bewildering complexity and multiplicity of processes, is thinkable only in terms of the most rigid determinism.

The results of destroying portions of an embryo, the restoration of lost parts, heteromorphoses, the development of entire organisms from egg-fragments, grafting, the reorganization of an individual from its disjointed cells, and the fluidity of certain types of behavior, are in no sense counter arguments. All that these show is that the equilibria within which specificity is possible, have a certain range. When the eye-stalk of a crustacean regenerates, not an eye, which it does only under certain circumstances, but an antenna, the antenna is species-true, and when the stump grows an eye, which it does under circumstances of a different sort, but no less specific, the eye is not that of a man or an octopus.

If the developmental history of an individual yields a result from which his ancestry can be inferred, what other proof is needed for the accuracy of all the underlying processes? And what need have we who can think through our problems in materialistic terms for regulatory interference by metaphysical vapors? Far from making these things easier to understand, the table-rappings of the vitalist only withdraw attention from the one basis on which we can hope, at present, for a scientific account of the individual at all.

O. C. Glaser

University of Michigan

THE NECESSITY FOR BIOLOGICAL BASES FOR LEGISLATION AND PRACTISE IN THE FISHERIES INDUSTRIES

It is lack of knowledge of the world he lives in that makes civilized man an actual catastrophe to nature's resources and methods.

In this, as in every new country, earlier generations began a series of stupendous economic blunders of turning into cash every natural asset available, blindly regardless of future necessities. Public assets have been, and in some instances are still, legitimate private booty for those whose imagination may be sufficiently keen to see the gold dollar hidden there. It is only within recent years that evidence has accumulated of the imperative necessity of developing the converse method of solving the economic problems of how best to transform free public goods, *e. g.*, lands, minerals, forests, water power, aquatic life, wild birds and quadrupeds, and scenery, into private property or adequately safeguarded public assets. The problem itself is of huge proportions and extensive in its ramifications. We are only beginning to grasp its fundamentalness and to awaken to the extent of our failure to find the correct solution. We still need a system of education which enables the child, the teacher, the parent, the state and federal legislator better to acquire the fundamental facts and their bearings upon human life and human progress. This alone would have made improbable, if not impossible, the present status where in some respects, in any