MODERN THEORIES OF DEVELOPMENT

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AN INTRODUCTION TO THEORETICAL BIOLOGY

By

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PREFACE

THE present work is identical in subject-matter with a book which has already been published in German under the title *Kritische Theorie der Formbildung*. It now appears, however, almost as a new book, because, in the first place, the treatment of the material has been adapted to the interests of the English biological public, secondly, the results of investigations published since the completion of the German edition have been included, and thirdly, as complete a picture as possible of the standpoint of the author is here presented in a concise form. For a fuller treatment of problems which are here dealt with briefly the reader may be referred to the German book which appeared in the well-known series of 'Abhandlungen zur theoretischen Biologie'.

It will be advisable to state the aim of the book in a few words. The book deals with *theoretical* embryology, i.e. it is not a summary of investigations on the physiology of development. Experimental embryology stands to-day at the focus of interest. This is evident from the fact that even in the last few years nearly a dozen books have appeared which summarize recent work in this branch of biology. We have the larger works of Morgan (1927), Korschelt (1927), Dürken (1928), Schleip (1929), Przibram (1929), smaller books by Brachet (1927), and Schleip (1926), and recently the excellent book by P. Weiss (1930). The reader is especially referred to the admirable little book by Mr. de Beer, *An Introduction to Experimental Embryology*, published by the Clarendon Press, which will serve as a companion volume to the present work. There is thus no lack of monographs of experimental embryology, and no occasion to add to their number. In consequence of its special standpoint the arrangement of the material in the present work departs considerably from that in books on experimental embryology. The simplest arrangement for a theoretical embryology seems to be one which describes and evaluates the principal current theories.

And although a description of experimental results is avoided by reference to the existing monographs, yet—if our book is not merely to appeal to a narrow circle of specialists—the most important of these results must be described. Consequently those results which are most essential from the theoretical standpoint must be described in order that the reader who is not familiar with this branch of biology will be in a position to follow the theoretical discussion. If he has also read the little book by Mr. de Beer above mentioned he need find no difficulty in understanding what follows.

The fact that the German book has enjoyed a very friendly reception—of which the desire for an English edition is evidence—seems to suggest that our undertaking in supplementing the usual works on experimental embryology corresponds to a real need. For this reason we have not thought it necessary to alter its general aim and standpoint, in spite of a good deal of rewriting in detail.

But beyond giving an account of the present state of theoretical embryology, the book has yet a second object, namely, to establish and describe the 'organismic' point of view which the author supports. For this reason Part II, which deals with the embryological theories, is preceded by a more general Introductory Part. The presence of this part appears to be a necessary presupposition of the second; for the clarification of the general theoretical foundations of biology must precede the building up of theories in the special branches. Epistemological and logical problems have, as far as possible, been avoided; the attempt being made to give a formulation of the views presented which is independent of particular philosophical points of view. On the other hand, theoretical embryology forms the application and the test of the views obtained in the more general part. From considerations of space, this introduction must be short, and what is here offered is an extract from a work by the author entitled *Theoretical Biology*, recently published, with the assistance of the Österreichisch-Deutsche Wissenschaftshilfe.

In view of the increasing growth of 'organismic' views, we may perhaps point out that the German book appeared in 1928, and thus before Dr. E. S. Russell's *The Interpretation of Development and Heredity*, and about simultaneously with the excellent account by W. E. Ritter and E. W. Bailey, *The Organismal Conception*. We do not doubt that in the striking parallelism which exists between Russell's book and the author's *Kritische Theorie der Formbildung*, the famous 'Law of the Series' exhibits itself; or, better, this correspondence is a sign that this way of thinking is 'in the air', and is forcing itself upon the attention of independent authors.

In connexion with this publication we have to thank the Österreichisch-Deutsche Wissenschaftshilfe which, in spite of the difficult conditions in Austria and Germany, enabled the author to devote himself to the above-mentioned book, and so at the same time promoted the present work. We have also to express our warmest thanks to Dr. J. H. Woodger, who not only undertook the English translation, but has whole-heartedly placed his understanding of the questions here discussed at our disposal, and given us many valuable suggestions, references, and criticisms. We have further to thank Professor Schaxel, the editor, and Dr. Thost, the publisher, of the 'Abhandlungen zur theoretischen Biologie' who have kindly permitted the use of the German work for the present English publication. Our thanks are due, finally, to the Clarendon Press for their readiness to publish this English edition.

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PRINCIPLES OF THEORETICAL BIOLOGY

I

BIOLOGICAL METHODOLOGY

1. The Crisis in Biology

IN the natural science of the present day we are witnessing a strange and disturbing spectacle. It is as though the grand sweep of its historical development, stretching from its beginnings in early Greek times up to the turn of the twentieth century, had to-day received a check. The foundations of our thought and investigation, hitherto regarded as assured, have collapsed. In their place new ways of thought, often paradoxical and apparently contradictory to the plain man, have appeared in bewildering variety, and among these still hotly contested ideas it is not yet possible to discover those which are destined to win an enduring place in our view of the world. Some years ago this state of affairs could be regarded as the break-down of Western science. But the remarkable developments which have recently been coming to fruition in physics suggest a totally different interpretation: we can see in the present state the raw and as yet unsettled early phase of a new step in scientific thought—the fruitful chaos out of which a new cosmos, a new system of thought will develop, albeit a view which will differ in essential points from that which we owe to Galileo, Kepler, and Newton.

In this place we need not describe the powerful revolutions which have occurred in mathematics and logic through the non-Euclidian geometries and the theory of aggregates, in physics through the Relativity and Quantum theories, and in psychology through the *Gestalttheorie*. The mere mention of these transformations suffices to indicate the place in the whole contemporary picture of the critical condition which we also find in the biology of the present day. When we speak of a crisis in biology it will be understood that we are not in any way saying anything prejudicial to its value. These general transformations in modern science signify rather the most powerful forward development which it has experienced since its foundation at the Renaissance. But it is at the same time essential that this state of affairs should be clearly reviewed, and that no attempt should be made to conceal it by entrenching ourselves behind theories which are now no longer tenable, or by shutting our eyes to the difficulties of our science.

> 'Modern biology is not in a position to display the results of systematic research in a system of concepts, or to represent the orderly behaviour which is common to its objects in a general theory. The place of theoretical science is taken rather by a heterogeneous multitude of facts, problems, views and interpretations. . . . Such a state of affairs cannot be improved upon by the piling up of new facts and opinions upon the old ones, but only by a fundamental re-organization after a process of careful sifting of those we already possess.'

These assertions of Schaxel (1922, pp. 1 and 298) admirably express the present position of biology and its primary task. We find in biology a bitter dispute between spheres of investigation, opinions, and principles. In their methods and fundamental concepts the various branches of biology are extraordinarily diverse and disconnected, and occasionally even in direct opposition to one another. The physico-chemical investigation of the vital process has given us, from the time of Harvey's fundamental discovery up to the most modern results of colloid-, ion-, and enzyme-chemistry, an uninterrupted chain of important discoveries—and yet there are good grounds for the belief that they still scarcely touch the essential problems of biology. The physiology of development and of behaviour work with systems of ideas which, at least at present, show only superficial relations to physics and chemistry. In genetics we have the most developed branch of biology, the only region in which we have an insight into the real biological laws, but we are still far from possessing a satisfactory theory of phylogenetic development, the fundamental idea of which is the most comprehensive that has so far appeared in the biological sphere. Attempts to master biology philosophically and theoretically are common enough outside the science, and stand in emphatic contradiction to its mechanistic point of view.

Whilst the majority of investigators find only physical and chemical processes in the object of their study, others find problematic metaphysical entities at the bottom of the vital phenomena. Between physico-chemistry and metaphysics biology pursues a strange and crooked path. Because there is no generally adopted theory of the organism, a thousand different individual opinions, personally coloured in varying degrees, confront one another, among which a given worker will choose according to his personal taste and the requirements of his special sphere.

It is not our intention to describe in detail in this place the numerous controversies underlying the great biological theories of the last century, such as Mechanism, Vitalism, Selection Theory, Lamarckism, and Theory of Descent.[1] Under the influence of these theories, doctrines once belonging to the 'assured acquisitions' of biology were established but have since been as much shaken as the seemingly 'matter of course' ideas of space and time, of mass and causality, in physics. The above remarks will perhaps suffice to justify us in some measure in speaking of a state of crisis in biology.

But how can we speak of a crisis in this science when our knowledge of vital processes is being increased every year by a multitude of publications? It might be said that all such general conceptions are more or less fragile: let them go. We need not waste regrets over philosophical or semi-philosophical constructions. True science consists only in the knowledge of

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[1] A review of these controversies is given in our *Kritische Theorie der Formbildung*, 1928.

facts, and even the bitterest opponent of science cannot deny that this grows daily or even hourly.

Many investigators will perhaps adopt this attitude towards the state of uncertainty regarding fundamental doctrines in biology to which we have alluded. The empirical investigator is apt to look down upon 'theory' with more or less disrespect, and therefore may not feel much distress at the uncertainty of the great theories.

But the empiricist is apt to forget two things. He forgets, in the first place, that a collection of facts, be it never so large, no more makes a science than a heap of bricks makes a house. In his scathing *Schöpfungsliedern* Heine makes God say: 'Allein der Plan, die Überlegung, da zeigt sich's, wer ein Meister ist.' Only if the multiplicity of facts is ordered, brought into a system, subordinated to great laws and principles, only then does the heap of data become a science. Secondly, he forgets that no empirical science is even possible save on a basis of theoretical assumptions. Schaxel remarks very appropriately that 'The empiricist moves hesitatingly between different attitudes. He wants to seem free, and yet is dependent upon ideas adopted at second hand with insufficient understanding.' (1922, p. 5.) Thus the procedure of the biology of yesterday has failed: on the one hand 'theory' has been looked down upon, and on the other, fact and theory have frequently been confused in an arbitrary and subjective manner.

A resolution of the present critical state of biology can thus only be sought in a theoretical clarification. Theoretical thinking must be recognized as a necessary ingredient of science. In biology until to-day such recognition has been rare, but in physics—which is taken as its model—it has always been a generally adopted demand. So much for criticism. Our critique will consist rather of construction, since we shall try to show a way to a new organization of biology which, we believe, will permit the present difficulties and contradictions—or at least many of them—to be overcome.

2. The Tasks of Theoretical Biology

If biology is to emerge from the crisis of its foundations and the accumulation of unrelated facts, as a critically purified exact science, the attainment of an assured theoretical biology will be necessary. But the term 'theoretical biology' has two meanings denoting two different, but not completely separable, spheres of knowledge.

Theoretical biology in the *first sense* is the logic and methodology of the science of organisms. It establishes the foundations of biological knowledge and thus forms a branch of general logic and epistemology, whilst it may also be important for biological investigation. Problems requiring logical investigation, e.g. that of teleology, of the relation between fact and theory, of the significance of experiment in biology, &c., may be of the greatest importance for the whole direction of research in biology. Critical methodological clarification may constitute an active protection against the fallacies of hurried hypotheses.

But theoretical biology in the *second sense* signifies a branch of natural science which is related to descriptive and experimental biology in just the same way in which theoretical physics is related to experimental physics. That is the task of a theory of the various single branches of the vital phenomena, of development, metabolism, behaviour, reproduction, inheritance, and so on, and, in the last resort, of a 'theory of life', in just the same sense in which there is a 'theory of heat', a 'theory of light', &c.

Since what has hitherto been called 'theoretical biology' has consisted in great part of philosophical speculation, and since theoretical biology in the 'first sense' consists of logical investigations, something must be said in clarification of the relations between theoretical biology and philosophy. As we have already mentioned, theoretical biology ('second sense') is just as much a branch of natural science as theoretical physics, i.e. it deals exclusively with the exact theoretical systematization of facts, and has no place for speculations. This point requires emphasis because voices are often raised in biology in rejection of theoretical biology as 'merely philosophical' or 'speculative' and superfluous. Such objections are entirely justified against many 'theoretical biologies', especially those of a vitalistic character, which, however, are to a great extent 'philosophical' and speculative and do not constitute scientifically applicable theorizing. But such objections are totally unjustified against theoretical biology conceived as a legitimate branch of natural science in the manner described above.

Naturally, it is not suggested that theoretical biology in the first and second senses, logic of biology and theory of life, should be regarded as totally unrelated to one another. Such a view would rather misrepresent the nature of theoretical science. Just as it is scarcely possible, in relation to the fundamental questions concerning space and time, action, deterministic or statistical law, &c., to draw a sharp line between physical theory and theory of knowledge, so will it also be the case in biology, in which the most general concepts (first of all that of 'organism') on the one hand require logical clarification, and, on the other, form the foundation of biological explanations and theories. Such general scientific assumptions must be clarified in close connexion both with logical and epistemological considerations and with the empirical study of the relevant phenomena. It need hardly be mentioned that, like the fundamental questions of physics, those of biology, such as Vitalism and Evolution, touch upon philosophical and cosmological problems of the most important kind.

If we are to overcome the state of crisis in biology which we have discussed above, we require theoretical biology in both the 'first' and in the 'second' senses. We must first of all make clear to ourselves the methodological principles which must be applied in the different branches of the system of biological sciences. In doing this we shall be carrying out the task of theoretical biology in the 'first sense' (Chapter I, 3–4). Then we must endeavour to reach a sound basis for a theory of life (Chapter II); and finally (in the main part of this book) we shall try to carry through the proposed programme of theoretical biology in a particularly suitable example, the phenomena of development. We shall endeavour to sift the current theories in this sphere and bring into application the theory we have traced in the general considerations.

3. The System of Biology

The attempt to arrange the various spheres of biology in a general system can be carried out in the following way.[1] We distinguish three stages in the system of biology.

1. Every science begins with an exact description and classification of its objects. Hence at the beginning of biology stands *systematics*, the aim of which is to give a catalogue, as complete and exact as possible, of all kinds of animals and plants. Related to this is the exact description of the different living forms, or *anatomy* (including microscopical anatomy). *Comparative anatomy* and *morphology* result from the comparison of the structure of different organisms. Finally, in addition to classification in a system, in addition to simple and comparative description of living forms, the description of their distribution in space and time is necessary. In this way we have *bio-geography* and *palaeontology*. These two sciences are—to use Meyer's expression—not logically pure, but logically complex, since they involve oecological and phylogenetic problems, in addition to simple description of distribution in space and time.

2 *a*. After the objects of biology have thus been described and classified there remains the demand for a description of organic *processes*. It is clear that every vital process must first be *causally* described, and, if possible, by the method of causal explanation employed in the more advanced sciences of physics and chemistry. This is the method of investigation followed in

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[1] For other systems of biology see the discussions of Tschulok (1910), Meyer (1926), and Bertalanffy (1928, chap. ii).

physiology. About the conceptual methods of the physico-chemical investigation of life little need be said. It is clear that 'the methods of the physiological chemist are peculiar only in very few cases. They are almost exclusively taken from the neighbouring sciences of chemistry and physics' (Abderhalden). It is also widely believed that since biology in general coincides with the physical and chemical investigations of vital processes there is no necessity for peculiarly biological points of view, or for a special theoretical biology.

2 *b*. We believe that this view is not correct, since there are vital phenomena for the description of which other points of view are required. The first of these special biological points of view is the *organismic*.[1] We can undoubtedly describe the organism and its processes physico-chemically *in principle*, although we may still be far removed from reaching such a goal. But as *vital* processes they are not characterized in this way at all, since what is essential in the organism—as will be shown later (cf. p. 33 f.)—is that the particular physico-chemical processes are organized in it in quite a peculiar manner. We need not delay by entering into details in this place, and the reader may be referred to the discussions of Ungerer (1919, 1922, 1930), Rignano (1926, 1930–1), Sapper (1928), and Bertalanffy (1929). Whether we consider nutrition, voluntary and instinctive behaviour, development, the harmonious functioning of the organism under normal conditions, or its regulative functioning in cases of disturbances of the normal, we find that practically all vital processes are so organized that they are directed to the maintenance, production, or restoration of the wholeness of the organism. On that account the physico-chemical description of the vital processes does not exhaust them. They must also be considered from the standpoint of

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[1] This word replaces the old term 'teleological'. It will be seen in what follows that 'teleology' as we conceive it has nothing to do with any psychological or vitalistic assumptions which were often confused with this point of view.

their significance for the maintenance of the organism. And we see that in fact—in spite of the postulate that science must only proceed physico-chemically—biology has at all times applied organismic ideas, and must apply them, and that whole spheres of investigation are concerned with the establishment of the significance of the organs and of organic processes for the whole.

The notion of 'organ', of visual, auditory, or sexual organ, already involves the notion that this is a 'tool' for something. As soon as we say that an animal has legs 'in order to' run, the giraffe a long neck 'because' it browses on the leaves—modes of expression which cannot be avoided in biology—we have already introduced a point of view which characterizes the significance of the organ for the maintenance of the organism—an organismic point of view. This point of view cannot be avoided so long as we cannot exclude the notion of an organ as 'serving' some definite purpose. Similarly, the concept of 'function' has an organismic sense: it only has significance within an organism, to the maintenance of which the function is exerted. We thus find *physiological anatomy* to be the first branch of biology which investigates the organs in connexion with their functions, in their so-called 'purposefulness' for the maintenance of the organism. Physiological anatomy furnishes a continual demonstration of the necessity of an organismic point of view in biology. As a second such branch we have *oecology*, which investigates the organic forms and functions as adaptations to their inorganic and organic environment. But since such concepts as disease, norm, disturbance, &c., are only significant in reference to the maintenance of an organism, *pathology* also belongs to the sphere of organismic branches of biology, but it is a logically complex discipline, since simple description and physiology have an important place in it.

For us there is no doubt that an organismic point of view of this kind is unavoidable. Organisms, as Kant knew, force this point of view upon us. It provides 'a means of describing the organism and the vital processes from an aspect which is not touched by the causal standpoint' (Ungerer, 1919, p. 250). Indeed it might be said that the real biological problem lies just in this question of the significance of organs and vital processes for the organism. The best proof of the necessity of organicism and the insufficiency of the purely causal point of view is that mechanism also, contrary to its express declaration that only the physico-chemical causal standpoint is scientific, nevertheless cannot escape the use of 'teleological' notions (cf. pp. 35 ff.). Thus the mechanist Plate, in reply to the objection that 'the purposefulness of the organic is not a problem for research' and that 'exact investigation is only concerned with the search for causes', rightly says:

> 'The attempt to disavow the purposiveness of the organic as a problem for investigation leads to an arbitrary restriction of biology; for the latter must investigate and explain *all* relations of organisms, and hence one of its chief tasks must be to analyse and explain causally the great difference which exists between living and non-living natural objects.' (1914, p. 31.)

In modern biology there is, however, a strong movement in favour of excluding the 'teleological' point of view as unscientific. In the first place the occurrence of dysteleology is brought forward as an objection. It is pointed out that even in organic nature by no means everything is 'purposeful' or teleological. From the dystelelogical occurrences it is concluded that teleology only represents a subjective and anthropomorphic point of view and that, in consequence, the physico-chemical causal procedure is the only legitimate one in biology as well as in physics. This is the attitude of such authors as Goebel, Rabaud, B. Fischer, Needham, &c., who declare war upon the teleological point of view, whether it be Darwinistic, vitalistic, or purely methodological, and seek, or believe themselves to have already found, an ateleological standpoint.

Now, the refutation of this ateleological position has already been given in our foregoing discussions: we see that such a view would uproot whole branches of investigation, such as physiological anatomy, oecology, and pathology. We shall not here enter upon a detailed discussion of the problem of dysteleology (cf. 1928, pp. 83 ff.; 1929). In any case it may be asserted that the attempt to refute the general 'teleology' of the organic realm by picking out a dysteleological organ or process here and there is to pursue an 'ostrich policy'. There is a whole series of considerations by means of which dysteleology may be reconciled with teleology in general. In the first place the apparent uselessness or purposelessness of organic structures or processes may simply rest on the fact that so far no one has succeeded in discovering their 'purpose', as was the case with the ductless glands before the discovery of internal secretions. Further, we cannot expect—even if we go so far as to assume that a purposive principle is active in the organism—that this is omnipotent. Even man, with his certainly 'purposive' behaviour, is only able to guide matter for his use within certain limits. If, further, the organism is helpless before certain injuries—e.g. a minimal dose of prussic acid—this by no means represents a contradiction of organic teleology; for it is obvious that every system—including the organism—is only capable of existence in a definite environment. The possibility of an injury through unnatural interference no more refutes the 'maintenance as a whole' of the organism than the fact that it cannot be filled with sulphuric acid destroys the 'purposiveness' of a steam-engine. Moreover, ateleological reactions almost always occur—e.g. in the tropistic movements of animals—under experimental conditions which seldom or never occur in nature. That the teleology of the reaction is frustrated by the artifice of the experimenter is no more to be laid to nature's door as a defect, than intellect is to be denied to man because in a particularly difficult situation he does not choose to his best advantage. Finally, attention should be given in cases of dysteleology to the feature which Heidenhain has called 'Encapsis' (see below, p. 111): a process (e.g. suppuration of the brain) may be quite 'purposeful' for a subordinate system of the organism, and yet destroy the system to which it is subordinate (as in the example mentioned, in which the skull prevents the escape of the pus), or we may have a situation in which the reverse is the case. At all events the most convinced representative of an ateleological point of view must admit that actually an enormous preponderance of vital processes and mechanisms have a whole-maintaining character; were this not so the organism could not exist at all. But if this is so, then the establishment of the significance of the processes for the life of the organism is a necessary branch of investigation.

The second main objection against the organismic standpoint goes deeper than the one just mentioned. It is said that only the causal point of view is strictly scientific, whilst 'teleology' always involves the introduction of a mode of thought which is anthropomorphic and contradictory to the principles of science. Every 'purpose' presupposes a striving, willing being, and to regard the mechanisms and processes in the organism teleologically means to assume a mystical anthropomorphic vital principle.

We can, however, say that the modern study of biological knowledge has succeeded in giving to the organismic point of view a formulation which avoids these objections. For this clarification we have chiefly to thank E. Ungerer (1919, 1922, 1930) who replaces the biological 'consideration of purposes' with that of 'consideration of wholeness'. Applying the organismic method means in this sense investigating the vital processes with a view to discovering how far they contribute to the maintenance of organic wholeness. Ungerer points out that the so-called 'purposefulness' of organisms is a pure fiction; it is 'as if' a 'purpose' were followed in organic processes, namely, the maintenance of the organism in function and form. This means nothing more than: it is 'as if' this preservation was willed or intended; but in the 'as if' there lies also the implication that nothing is or can be known of the 'willing' and 'intending' nor of a willing or intending subject. Since only the maintenance, production, and restoration of the organism as one whole in function and form appear as 'purpose' in the organic, or the special relation of a partial function to the total function of the whole, the 'consideration of purpose' is to be replaced by that of 'wholeness'.

> 'The teleological point of view in the sense here intended is quite free from hypothesis. It cannot be sufficiently emphasized that nothing mental is presupposed nor is a law of the purposiveness of reactions put forward, nor is it even asserted that the vital process must in all cases proceed in such a way as to attain the highest degree of purposiveness. . . . The confusion of the notion of wholeness with vitalism, which has done so much to prevent the attainment of a clear grasp of the present problem, must be fatal and lead to a disregard of the progress made so far, when such confusion is found in the works of one of the most important defenders of vitalism (Driesch!). It is therefore important to work out clearly the non-hypothetical, purely descriptive concept of wholeness and to show that it is the kernel of all "teleological" concepts of botany. The prejudice which sees in all teleology a concession to vitalism, the one-sidedness which overlooks an essential and fundamental feature of all living things and presents the shield of Darwinism to every true "purposiveness", must be just as strongly opposed as the unjustified attempt to seek a *deus ex machina* behind all "phenomena of adaptation". Quite apart from all controversies about mechanism it must be shown that the facts relating to organisms cannot be represented with purely causal concepts alone, and never were so represented, since a scientific elaboration of facts has always involved and still involves the use of the notion of wholeness. It remains to show what the "teleological point of view" means when freed from all admixtures, and how its use is unavoidable and free from danger.' (1919, p. 39, f. iv.)

The strict mechanist Winterstein (1928) is of the same opinion.

> 'When we attempt to conceive the vital occurrences of an organism we are at once confronted with the fact that we shall not succeed if attention is confined to the single processes going on in it at a given moment. We can only reach a satisfactory understanding if we consider them as partial processes in relation to the whole "vital

> mechanism". This inner connexion of the particular processes with the working of the whole gives the impression that the former are related to a total idea in a manner analogous to the way in which our own purposive behaviour appears to be guided by a preconceived plan. It is, however, possible to give a clear meaning, free from all subjective interpretation, to the originally anthropomorphic notion of purpose: "purposive" is nothing else than a short expression for all phenomena upon which the maintenance of an observed state or process depends.'

Zimmermann (1928), Jordan (1929), Bertalanffy (1927, 1928) have reached views similar in principle to the above.

We thus see that organismic description of vital processes does not in any way constitute an 'explanation'; it leaves the question open of how the maintenance of organic wholeness is achieved. The organismic standpoint neither asserts nor denies that the processes through which this is brought about are reducible to the phenomena of inorganic nature. Vitalism has erred in hypostasizing the concepts necessary for the teleological description of vital processes into active natural factors or entelechies.

The organismic point of view prejudges nothing regarding the theory of life, but every theory of life must of course give account of those features of organisms which this point of view reveals. On the other hand, the assertion that the organismic approach is incapable of leading to positive results is erroneous. In the first place, the teleological judgement of functioning organs or vital processes does not consist of popular wonderment—how beautiful and purposeful are all organic processes—but, like physics and chemistry, it promotes a thorough and, where possible, experimental study; on the other hand, as Winterstein rightly points out, the *a priori* assumption of the existence of regulations (thus the organismic point of view) has proved itself to be a principle of research of great heuristic worth: we may, for example, recall the fundamental ideas of Bier on the therapeutic value of fever, or Abderhalden's conception of defensive enzymes regulating the constancy of chemical composition.

In any case organismic description in the realm of the organic is just as necessary as the causal and physico-chemical; there is no sense in attempting to dispute away the organic character, the proper procedure is first to investigate, and secondly to explain it.

2 *c*. Alongside the causal and organismic there is yet a third form of description necessary in relation to organisms. This third form is the *historical*, which describes the organic forms and processes as products of an historical development. It is the business of *phylogeny* to provide such a description by establishing lines of descent. This historical point of view also represents a non-physical principle which forces itself upon us in the organic realm. On the other hand, in the sense here intended it only signifies a point of view and not a hypothesis. In order fully to understand organisms it is just as necessary to regard them as members in a process of historical development as it is to treat them as physico-chemical systems and as organic unities. And this general historical standpoint also is free from hypothesis, for, if we arrange organisms in phylogenetic series and so regard the organic event as an historical process, we do not need for this purpose any assumption regarding the nature of life and its development.[1] Moreover, the

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[1] We say: the historical *point of view* is free from hypothesis. That many, probably most, of the ancestral series set up by its aid are extremely hypothetical is indeed obvious. Logically, we must, however, sharply distinguish two kinds of hypotheses. First, those which serve to bridge the gaps in our incomplete knowledge of facts; such are especially noticeable in phylogeny in consequence of the fragmentary nature of our fossil material, but they naturally occur also in the physico-chemical and organismic procedures. Our ideas about the stages of assimilation of carbon dioxide, or about the significance of the Golgi apparatus in the cell, are still hypothetical in character. But the student of phylogeny hopes sooner or later to be able to demonstrate those members of the developmental series of man, for example, which are still lacking, just as the biochemist hopes to fill in the gaps in our knowledge of carbon assimilation, and the physiological cell-anatomist hopes to demonstrate visibly the secretion of the Golgi apparatus. But if the physicist

historical standpoint serves to acquaint us with organisms from an aspect which is not touched by physics and chemistry; hypotheses only begin when we reflect upon the *causes* of development, upon the nature of historical accumulation, &c. (pp. 41 ff.).

. . . .

From the comparison of the multiplicity of living forms and processes certain uniformities result which are the same in all, or in very many, organisms. The bringing together of these uniformities is the task of *general biology*. Or, we can say: general biology is the collection of general rules which can be derived from the consideration of the multiplicity of vital phenomena. Such rules issue both from the comparison of forms in morphology, and from the description of vital processes from the causal, organismic, and historical standpoints.

2 *d*. We have now indicated the necessary presuppositions for an adequate description of the vital processes. All these points of view—the physico-chemical, the organismic, and the historical—represent, as we have said, exclusively methodological assumptions. We remain in the domain of the establishment of empirical facts just as much when we study the vital phenomena physico-chemically, as when we investigate them organismically or historically. In neither case is anything hypothetical asserted about the nature of life when we apply these standpoints. The domain of hypothesis is theoretical biology, which is necessary on the one hand for the general explanation of great spheres of fact, and on the other for making a science of law possible.

introduces the 'hypothesis' of material waves, or the biologist assumes that development occurs through the mutation of genes, he does not attempt to fill in gaps in our knowledge of matter of fact, but hopes to explain the facts themselves. To use an expression to be introduced later (p. 20): the 'complemental' hypotheses express expectations about future experiences in the 'first world' of sensible reality, the 'explanatory' hypotheses belong to the 'second world' of theoretical science. Such explanatory hypotheses are not involved in the mere setting up of ancestral series.

But since the physico-chemical point of view does not suffice in biology, but must be supplemented from the organismic (physiological anatomy, oecology) and historical (phylogeny) standpoints, the necessity of biology as an independent science —at least as far as its descriptive stages are concerned—is proved. For even a complete physico-chemical description of the organic processes would not—as we have seen—render the organismic and historical points of view superfluous. They would always remain necessary avenues of approach for the description of vital phenomena.

These views are, however, in opposition to a widespread opinion which—supporting itself on an assertion of Kant[1]—only regards the causal and, in the last resort, mathematical study of phenomena as 'scientific'. Against this it must be urged that science must always relate itself to the facts, and is not in a position to prescribe to reality what can or must be the case. If organic 'teleology' and history represent essential features of reality, then science must take account of them, and, in order to do this, it does not need the permission of a dogmatic epistemology. To forbid the investigation of certain features of reality is to set up a wholly inadmissible restriction of science. If the vital phenomena present features which do not lend themselves easily to theoretical treatment by the means which have been devised in other branches of natural science, the proper procedure for biology would seem to be to devise its own technique for dealing with them; not to ignore them or to restrict itself by arbitrary definitions based too naïvely and exclusively on traditional models. It is naturally impossible to 'refute' a definition. Every one is at liberty to define 'science' as he pleases. But the least requirement which can be expected of a definition is that it does not fly too much in the face of the actual state of affairs. But this is precisely what is done by a definition of science which makes it equivalent to mathematical physics. According to this definition

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[1] For a criticism of misunderstandings of Kant's assertion see the pertinent remarks of Woodger, 1929, p. 234.

not only are the 'mental sciences'—psychology, sociology, history, &c.—not sciences, and never can be such, but the same will be true of large branches of natural science as well. If this programme is to be realized it will be necessary to displace the majority of professors of zoology and botany, the systematists, anatomists, morphologists, physiological anatomists, oecologists, and students of phylogeny, because they do not pursue physico-chemical, and hence 'scientific', investigations at all. In any case, besides the causal and physico-chemical investigations of living things, morphology, oecology, and phylogeny represent legitimate branches of science, and the equating of 'science' with mathematical physics seems in any case, in the light of the actual state of affairs, to be absurd. In this connexion we may quote the comments which a supporter of our view, the distinguished physicist and natural philosopher Bavink, has made on the views of the author given in the foregoing paragraph.

> 'In my opinion they finally and irrefutably dispose of the fatal error, which has injured an epoch of scientific thinking, of equating science in general with mathematical physics. . . . Science is any attempt to bring facts into logical order. Mathematical physics is only one special aspect of this activity. That the mental sciences do not proceed in this way has long been clear. Now we see that such a narrow definition does not even suffice for natural science.' (1929, p. 340.)

3. But the task of scientific biology is not yet exhausted by the topics so far mentioned. In them it is only a question of the establishment of relations of facts, whether these are of causal, organismic, or historical nature. We remain at the 'descriptive' level of science. The regularities among events established here find their expression in 'rules' or 'empirical' laws. Such empirical laws are unrelated among one another; they are not deducible from higher principles; we can state no necessity for the occurrence of just these regularities and no others. If we wish to bring such empirical laws into relation, if we wish to 'explain' the particular occurrences and the rules they exemplify,

we require hypothetical ideas for this purpose. A strict system of law signifies a logical connexion of conceptual constructions. On that account they cannot—as we shall see in the next section—be simply read off from experience. As relations within a conceptual construction the natural laws are deducible from laws superior to them and admit of subordinate laws being deduced from them; as such they possess logical necessity if the premisses from which they are deducible are agreed to.

A brief consideration may be in place here concerning the question of the relation between 'description' and 'explanation', and here we may refer the reader to the admirable discussion of Bavink (1930, pp. 23 ff.). According to this author's definition, a hypothesis is 'the supposition of a general state of affairs as underlying certain special phenomena occurring in experience, from the presence of which and its assumed laws the phenomena of the region of fact concerned can be deduced'. If this is the case it must be the aim of science to establish hypotheses directly whence the original hypothesis becomes a proved fact, as was the case with atoms and light waves which thereby have come to have the same 'reality value' as 'stones and trees, plant-cells and fixed stars'. With the aid of this definition we can express the relation between 'description' and 'explanation'. If description is the simple assertion of facts, explanation signifies the logical subordination of the particular under the more general, the systematization of the given facts by means of general connexions. This also means that every explanation again demands a new explanation, i.e. the search for still more comprehensive connexions, in relation to which it appears as 'description', as the establishment of a matter of fact.

The first task of theory is thus to give a common explanation for a series of otherwise unconnected facts. Secondly, the hypothetical ideas which theoretical science elaborates make possible the setting up of a system of strict natural laws. We see this double significance in the most fully extended theorems we possess, those of physics; for example, the electron theory makes possible an explanation of an extraordinary number of single phenomena, and on the other hand it has led to the establishment of laws for these phenomena.

Thus in addition to the realm of perceptions there is in theoretical science a second realm of hypothetical structures between which the relations of the natural laws hold. In what relation this 'second realm' stands to the 'third realm' of metaphysical reality is a question which the scientist need not answer, but may leave to the general theory of knowledge; modern physics, however, may be able to give some hints in this direction (see below, pp. 55 ff.):

> 'In opposition to a widespread view it is without significance for physics whether we call the content of the first realm (sense-data), e.g. the perceived colour blue, mere phenomena, and that of the second, e.g. the corresponding electromagnetic vibrations, "reality" in the realistic sense, or whether, on the other hand, in the positivistic sense, we call the first the "really given", and the second as only consisting of conceptual complexes of those sense-data. On that account physics does not say: "where this blue appears there is, in reality, such and such an electronic process", nor "in the place of this blue we conceive such an electronic process in order to make calculation possible", but physics expresses itself quite neutrally with the help of purely formal co-ordinating relations, and leaves the question of further interpretation to a non-physical investigation.' (Carnap, 1923.)

In any case the theoretical constructions must be so constituted that they are, in Schlick's phrase, 'unequivocally co-ordinated' with the perceptual world. If that is achieved, the fulfilment of the principal task of science—the exact prediction of future events—is made possible with the help of natural laws. If our conceptual constructions, the theoretical structure and laws, are unequivocally co-ordinated with the phenomena, it is then no wonder that they not only fit the past but also future events, and hence enable us to 'prophesy' the future.

Scientific law does not consist, as is often said (Dubois-Reymond, Sigwart, Roux, and others), in an insight into the 'causal necessity' of the events. The striking refutation of this definition is provided by modern physics, which recognizes the impossibility of a causal determination of the ultimate intra-atomic processes, and regards all natural law as purely statistical. It is not an insight into the *causal* necessity of the processes which gives physical laws their strict character, but rather the insight into the *logical* necessity of those laws; in fact, according to Bavink (1930, pp. 60 ff.), the causal relation is itself reducible to logical necessity.

It thus comes about that theoretical science is at the same time science of law, and only as such is science of law possible at all. In physics and chemistry this has long been attained, but in biology, on account of the widespread aversion for theoretical thinking, we are very far from such a state of affairs. Nevertheless, or just for that reason, we must also demand a *theoretical biology* as the crown of the whole structure of the science of life—it being presupposed that the biological happenings are not exhausted by the simple physico-chemical description of the individual processes into which, in a given case, it is analysable—an assumption which we can without difficulty prove to be incorrect (cf. p. 37). The chief task of theoretical biology will be to explain the general, organismic, and historical character of biological events from general assumptions. The great systems of mechanism and vitalism represent such theories of life, but we shall see that in their place a more satisfactory foundation must be sought for biological theory.

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In this way we have reached a survey of the chief directions of biological investigation. We see that biological knowledge operates at three levels: in the first level it deals with the ordering, the simple and comparative description, of its objects. In the second the causal, organismic, and historical connexions of the organism are investigated, and—in 'general biology'—rules are set up for the uniformities which here present themselves. The third stage—that of theoretical biology—yields, with the help of hypothetical suppositions, the laws of biological processes.

It need not be emphasized that in the foregoing analysis we have not indicated branches of science which in practice are strictly separable, but rather various attitudes. Consequently a given piece of scientific work rarely belongs to only one of the spheres distinguished but usually embraces several of them. But these attitudes must be clearly distinguished from one another from the logical standpoint. If this is not done we have 'romantic biology' (Schaxel), in which organismic descriptions masquerade as causal explanations, a supposed mechanism will appear in spite of continued use of non-mechanistic teleological and historical notions, and theory and fact will be inextricably confused.

4. The Method of Theoretical Biology

To-day biology is still in its *pre-Copernican* period. We possess an enormous mass of facts, but we still have only a very incomplete insight into the laws governing them. Apart from genetics, which approaches most closely to the goal of theoretical science, the most superficial glance serves to show that whilst in physics we speak everywhere of 'laws', in biology this is the case only in rare and isolated instances. The absence of laws rests on the fact that although we have had numerous biological theories we have so far had no theoretical biology. Theoretical science and science of law are one and the same, and the lack of theoretical biology prevents us from taking the step from a purely empirical descriptive science to one of exact laws.

We must therefore consider the important question: by what means is an assured theoretical biology to be reached? A further comparison with theoretical physics will again serve to throw into relief the peculiar state of theoretical biology. For whilst theoretical physics is a completely developed science, in fact the most highly developed one, theoretical biology has not emerged from its swaddling clothes. For this reason the latter is still faced with a task which for physics has long ceased to be of great importance. This first task of theoretical biology is the *critical analysis of the various theories* which have hitherto been put forward in relation to the various vital phenomena, in order to discover which may claim the title of exactitude. We already have such a multitude of hypotheses and theories—often in all thinkable logical shades—that it seems desirable to make a critical survey of these first before attempting to add new ones to them. To establish what we already possess by way of really firm general knowledge about organisms is the first task of theoretical biology, which we can call 'analytical' theoretical biology.

But naturally the task of theoretical biology is by no means exhausted by such a sifting of theories. Its last aim is to establish a unitary *system*. And in order to be clear about what this entails, it is necessary to inquire into the way in which a scientific theory is built up. For this purpose we can make use of the excellent account given by Kraft (1926).

'It is a common opinion that the principles underlying scientific theories are to be derived "from experience". But a closer study of highly developed theoretical systems shows the complete falsity of this view. The principles of mechanics, for example, cannot be empirical propositions because they involve relations which, in such a form, are never met with in experience. The fall of bodies in accordance with the law of gravitation is an ideal process. If we make cinematograph films of falling bodies and measure from them the time and space involved we could only find an approximate conformity to law, never an exact one. Scientific theory, as exemplified by mechanics or theoretical physics, has the character of a *hypothetico-deductive system.* Freely chosen ideal assumptions are first clearly stated, and then, by the introduction of special conditions, consequences are deduced with logical rigour from these, and such consequences are then compared with experience and, if the premises have been suitably chosen, are thereby verified. The rigorous character of the scientific theory rests *only* on this procedure.

'The antithesis to theory is inductive science. But all inferences from experience, since they rest on particular facts showing only an approximate regularity, can never be more than "assumptions". All general knowledge about reality is rational construction, and theory and induction are distinguished only by the fact that the latter proceeds from the facts and the former is verified by them.'

An insight into the essential nature of scientific theory is of great importance from the biological standpoint. We see how completely untenable, both logically and psychologically, is the view that natural laws can simply be read off as a result of recording as large a collection as possible of empirical data. This view is logically untenable because natural laws are not found running about wild in nature, but must be reached by a process in which abstraction is made from all 'perturbations'. Psychologically this is only possible by means of a happy intuition which is able, with the eye of genius, to discern the essential features of an event behind the complex multiplicity of phenomena and produces the hypothetical statement which brings the facts into order as it were at one stroke. This is true whatever view we may take in regard to the status of the 'second realm' of theoretical science, i.e. whether we regard it as establishing real relations, or as merely a set of conceptual constructions in the positivistic sense. We do not wish to burden the present study with this question, but will refer the reader again to the excellent discussion given by Bavink (1930).

Newton saw the famous apple fall from the tree. Here, if anywhere, we can speak of an intuitive grasp of the general law in the particular case, of a 'Wesensschau' in the sense of Husserl. But this primary intuition is necessary for the setting up of *every* law. Many apples fall from trees, but only rarely is there a Newton to apprehend the laws of the world in such events. Hundreds of thousands of apples, registered with every possible accuracy, would never yield the great law of gravitation.

It is a foolish hope to suppose that by the accumulation of innumerable single cases great laws will finally emerge, like Venus from the nebulous sea.

The significance of all this for biology is obvious. It is not true that empirical knowledge, however extended, suffices for the foundation of a well-systematized science. The latter can only be reached by the close co-operation of experience and deductive-hypothetical thinking.

We are indebted to Kraft for another important notion. He rightly points out that mathematics (as ordinarily understood) is by no means the only possible foundation for a strict theory, i.e. a hypothetico-deductive system, but such is always present when we have deduction from idealized conditions, as is the case, e.g. in Menger's deductive economic theory. It is not impossible to suppose that in biology, in which deductive theory in the mathematical form is as yet scarcely possible, such a system would be appropriate in a non-mathematical form, leaving open the possibility of subsequently fitting such a theory into the system of mathematical logic to be extended in the future.

At the present day, however, the necessity of theoretical biology is by no means generally recognized. The view that experimental investigation alone can claim the title of 'scientific' still reigns. For this reason a few words about the functions of theoretical biology in its two chief aspects will not be out of place.

The importance of its first task—the critical analysis of existing theories and concepts—should be sufficiently obvious. All the critical phenomena in biology which are brought to light in the course of this discussion—the intermingling of contradictory points of view and theories, the lack of a generally accepted theoretical system, the survival of theories which have long become obsolete, the muddles and contradictions involved in many biological concepts—all these can only be overcome by means of analytical theoretical biology.

Not less important is the second, constructive function of theoretical biology. From what has been said in this section, it follows—as Physics shows so clearly—that theoretical and experimental science are necessary complements of one another. A systematic science can only be constructed by their mutual co-operation. A science only becomes a science of exact laws when it becomes theoretical. The ideal of 'science without hypothesis' is quite justified if it means the rejection of superfluous speculations, but it is a mere phantom if it intends to suggest that any science is possible without a framework of theoretical concepts. (Cf. also Schaxel, 1922, pp. 234, 298, &c.)

A majority of biologists at the present day profess to reject 'theory'. Nevertheless, while paying every respect to the importance of experimental investigation, we cannot wholly agree with the frequently repeated demand for more experimentation and less theorizing. When we open one of the biological reviews, and glance at the thousands of experimental investigations which are published yearly, we cannot avoid the heretical opinion that it is perhaps not so necessary to add another dozen or so to these as seriously to set about the task of theoretically exploiting the mountain of raw material we already possess. It may be objected that biology is not yet 'ripe' for such an undertaking. On the contrary it is essential to understand that empirical investigation and theory can only grow properly in correlation with one another, and that the assumption that theory is only possible and necessary when the collection of data is finished is quite erroneous.

We must not conclude this defence of theory in biology without admitting that of course biologists have had many good grounds for their distrust of 'theory'. Nothing is so dangerous as the groundless speculation and theorizing in vogue among biological outsiders, but unfortunately this is not unknown even in the science itself. There is also another ground for the anti-theoretical attitude of contemporary biologists which is not difficult to understand and agree with. Only too often do we see the theorist leave the solid ground of experience and experiment and disappear into the blue mists of metaphysical speculation. When once the aversion to *this* kind of theoretical biology has seized biologists, it may easily happen that *every* kind of 'theory' comes to be regarded as a departure from his proper scientific business. Here, then, is another point where there is a need for change in contemporary attitude, a change which ought not to consist in the rejection of theory in general but in taking seriously the need for a scientific theoretical biology, whilst at the same time declaring war upon all such light-minded speculation as has been responsible for the mistrust of 'theory' in biology.

II

FOUNDATIONS OF THE ORGANISMIC THEORY

1. Mechanism

DURING the centuries of controversy about the problem of life two fundamental theories have emerged of which now one, now the other, has had the upper hand. These theories are called mechanism and vitalism. According to the mechanistic theory, biological phenomena are only highly complicated constellations of physical and chemical processes. The methods of the biologist are thus, generally speaking, just the same as those of the physicist and chemist. By a consistent application of the mechanistic postulate biology will, in the future, become simply a department of physics and chemistry. We can only speak of an independent biology in so far as this resolution is not yet complete.

In contrast to this the vitalistic theory denies the possibility of such a resolution of the vital processes into physical and chemical ones. Special 'principles', different from all physical and chemical ones, are held to be 'active' in living organisms, guiding and organizing the vital processes which for that reason can never be resolved into a mere play of physico-chemical forces. Driesch calls this principle 'entelechy', Reinke speaks of 'diaphysical forces', Bergson of 'élan vital', whilst among psycho-vitalists it is simply 'soul'.

Any attempt to judge this controversy is greatly complicated by the fact that the expressions 'mechanism' and 'vitalism' cover a number of very different meanings and points of view. Regarding the term 'mechanism' we can refer the reader to the excellent analysis of Woodger (1929, chap. v). At least four meanings of this word can be distinguished: 'mechanical explanation' in the narrow sense (e.g. mechanics in the sense of Newton or Hertz); 'physico-chemical' explanation; 'the machine-theory', and 'causal explanation'. This ambiguity of the word and the confusion of its meanings have together been responsible for a monstrous amount of misunderstandings and false problems. Into these we cannot enter here, and must refer the reader to our *Theoretische Biologie*. In what follows we shall use the term 'mechanism' for the physico-chemical interpretation of vital processes.

A circumstance which has still further contributed to complicate the situation is the frequency with which the standpoints of natural science and metaphysics are confused. For the scientist the only question is what principles of explanation are necessary and sufficient for vital processes; in other words, whether the hypotheses and laws of physics suffice in principle for the explanation of biological facts. According to whether we answer this question with yes or no we can call ourselves 'methodological' mechanists or non-mechanists. But very often this question is mixed with the questions about the ultimate metaphysical reality. For 'metaphysical' mechanism the 'blind play of the atoms' appears to be the final reality, the innermost kernel of both organic and inorganic occurrences. Mechanism becomes thus a metaphysical realism, almost a materialism of a very primitive kind. On the other hand, the vitalist assumes his 'purposive vital factors' in opposition to the 'blindly running physico-chemical processes'; indeed, the vitalistic assumption seems to be intelligible only in this 'metaphysical' sense (see below, p. 56). Hence, vitalism constitutes the logical antithesis to 'metaphysical' mechanism. From the methodological standpoint, however, we see that 'mechanism' and 'vitalism' by no means form the mutually exclusive disjunction they have been supposed to do. If a 'non-mechanist' wishes to deny the assumption of methodological mechanism that biological explanations must also be physico-chemical ones, it is obviously by no means intended that the required explanation must be 'vitalistic', i.e. involving the assumption that in living organisms factors analogous to psychical ones are 'at work'. A 'non-mechanistic' theory which is not at all 'vitalistic' thus appears to be logically possible, and if we make a critical study of mechanism and vitalism this possibility will be seen to be of special importance.

It is easy to see that the investigator of nature has nothing to do with metaphysical formulations because, according to the common view, natural science is exclusively concerned with the establishment of the laws of natural processes and rightly leaves the question of the 'third world' of metaphysical reality to philosophy, or to those branches which deal with theory of knowledge and metaphysics. In what follows we shall deal solely with the 'methodological' aspect of mechanism and vitalism.

We may emphasize, first, that a dogmatic decision of this controversy is not admissible. The successes of mechanism are obvious, and it is equally obvious that it has not yet reached its final goal. The dogmatic mechanist will always be able to say that the peculiarities which are not physically or chemically explicable will at some distant date prove to be purely physical or chemical processes. On the other hand, the vitalist will have little difficulty in pointing to certain very complicated features of living organisms for which it seems hopeless to seek a physical or chemical analysis. Both views rest upon prophecy, the justification of which can only be decided by some remote future state of biological science (cf. Woodger, 1929, p. 230 f.).

One fact, however, is very unfavourable to the claims of vitalism, namely, its continual retreat with the progress of research. Again and again it confuses the temporary lack of a physico-chemical explanation of particular vital processes with their inexplicability in principle. For example, the irreversibility of the vital process, the production of optically active compounds, the dependence of the vital process not only on the initial but also on the final state, the so-called 'nostalgia' of the living thing, and many others have been regarded as specifically vital peculiarities. But every time we find that sooner or later physico-chemical explanations for such phenomena offer themselves, or analogies in the inorganic are demonstrated. Needham (1927, pp. 31 ff.) has emphasized this point well. Moreover, a further difficulty for vitalism lies in the fact that the opinions of vitalists are widely divided regarding what phenomena are 'still mechanistic' and what are so no longer (cf. Sapper, 1928, pp. 62 ff.).

The sober critic can do nothing with vague prophecies about whether it will or will not be possible to understand this or that peculiarity of organisms from the physico-chemical standpoint. The problem can only be treated profitably by examining the modes of explanation so far elaborated and discovering whether they are able to yield useful foundations for a theory of life. The answer to this question is that the modes of interpretation still commonly employed in 'mechanism', i.e. the 'additive point of view' and the 'machine theory', prove to be inadequate in certain directions. It turns out that not only are there certain vital processes for which a physico-chemical explanation is still lacking, but that these mechanistic modes of explanation are in principle unsuitable for dealing with certain features of the organic; and it is just these features which make up the essential peculiarities of organisms. Vitalism is equally incapable of offering a satisfactory theory for dealing with them. If this point can be made clear we shall be given important indications of those directions in which we must look in order to reach a satisfactory theory of the organism, which we shall call the 'organismic' or 'system' theory. This does not, of course, mean that we have yet reached a final decision regarding the mechanism versus vitalism controversy. For even if it can be shown that the modes of interpretation hitherto employed under the title of mechanism (additive point of view and machine theory) are not capable of dealing with the characteristic organic features, yet it will not follow that *every* form of 'mechanism', i.e. of chemical or physical theory of the vital process, is impossible. For in physics and chemistry new points of view have emerged (the so-called Gestalt theory) on the basis of which the problems presented by organisms which have resisted the older modes of mechanistic thought may prove to be soluble. But from a closer investigation there results a surprising clarification of the relation of the foundations of biological theory to physics, so that—if not with certainty, at least with considerable probability—the question of the autonomy of biology can be answered. Moreover, even the conflict between metaphysical mechanism and vitalism ultimately seems to be soluble in this way in a very striking manner, because, on the basis of modern physics, from which standpoint this whole investigation must be carried out, this controversy proves to be one about a false problem. This, in broad outline, is the path we shall follow in the subsequent pages.

(*a*) *The 'Additive' Point of View.*

A fundamental principle of mechanism in its commonly applied form is the 'additive' point of view. Chemistry analyses bodies into simple constituents, molecules, atoms, electrons; the physicist regards the storm which uproots a tree as the sum of the movements of all the particles of air, the heat of a body as the sum of the kinetic energy of the molecules, and so on. In the same way the physico-chemical investigation of organisms has consisted in the attempt to analyse them into elementary parts and processes. The once common notion of 'living substance', for example, expresses the view that the material basis of life is an analysable chemical compound, or group of compounds, and that a complete chemical knowledge of this 'living substance' would enable us to understand the properties of organisms. The additive standpoint is expressed most clearly in the theory of the 'cell-state', the attempt to resolve the living body into an aggregate of independent constituents, its total activity into cell-functions. It found its classical expression in the machine theory of Weismann (see below, p. 73), in which it was assumed that the egg contains a collection of developmental machines for the various organs which unfold themselves independently of one another and in this way form the mature organism. In the last resort, mechanism must try to resolve the action of the organism as a whole into single physico-chemical processes. The belief is widespread that with a complete knowledge of the materials and processes in the organism the 'problem of life' is, in principle, solved, and hence that a special biological theory is made superfluous.

But organisms and biological processes have obstinately resisted this point of view. The physicist begins with the various components, but the biologist can only begin with the individual whole organism. This is true, in the first place, of the material basis of life. There is no 'lion substance', or 'dog substance', and no 'hand substance', or 'gut substance', in the sense in which there is water or sodium nitrate, &c., as homogeneous chemical substances. What people call 'living substance' is an endlessly complex system of chemical combinations. Even if we understood and could synthesize all the constituent materials of the organism, we could not obtain the vital properties of metabolism, irritability, locomotion, &c., from the properties of the compounds into which the organism is analysable and which do not themselves exhibit the vital properties but are 'dead'.

Following Woodger (1929, p. 263), we can shortly and simply denote this limit of current mechanistic explanation by the term 'organization'. A lump of iron is adequately defined by its chemical formula, but if it is wrought into a machine it can no longer be adequately described by means of chemical concepts although it is still chemically analysable in just the same way. It now has an 'organization' above the chemical level. The same applies to the case of living organisms.

It is evident that we have not excluded thereby the assumption that this 'organization' is at bottom a provisionally unanalysable combination of physical and chemical factors. But one thing we can confidently assert: namely, that a chemical investigation of the various single materials in the organism can never bring us any nearer to a solution of this problem.

Analogous remarks also apply to the vital processes. No one doubts that the various single processes in organisms are susceptible of physico-chemical explanation. We need only recall that such seemingly specific vital activities as fermentation or breathing can not only be physico-chemically analysed but even imitated in dead models. This is well illustrated by the great insight given by the isolation of enzymes which we owe to Willstätter and his school, and by the imitation of breathing by the models of Warburg. Nevertheless, there remains even for a superficial view an obvious difference between living and dead, between living processes and processes in dead material.

> 'The processes which go on in the corpse of a dog are not only different from those which occur in the living animal. Together they are more than a certain particular aggregate or totality of processes within a body which we call *one* only because it happens to be distinctly marked off from its environment, and comparable with a stone which lies on the road (e.g. a piece of granite) in which also a certain aggregate of chemical processes (weathering) occurs. The processes in the body of the living dog form a wholeness to which every process contributes by the fact that it occurs in this particular way.' (Ungerer, 1922, p. 75.)

The characteristic feature of life is thus to be sought not in some one peculiarity of the particular vital processes, but in the special organization of all these processes among one another. This organization of the processes (the description of which is the concern of a special branch of biology, as we have already emphasized) is not a vitalistic hypothesis nor an apparent problem, but a simple fact which gives us the right and lays upon us the duty of seeking an explanation for it. But it is logically impossible to comprehend it by means of the chemical formulae or the physical explanations which we give for the *single* partial processes into which it is analysable. By these means we learn nothing about the characteristically vital order, any more than the bare energy equations tell us anything about the purpose of an engine, or than a symphony of Beethoven can be known in its essential nature by the quantitative methods of the physicist, e.g. by measurements of the pitch of the single notes.

In this sense, the question of vitalism is incorrectly put when it is asked: 'Whether life is only a combination of chemical and physical occurrences or whether it has its own elementary laws.' (Driesch, 1928, p. 11.) If we investigate vital processes physically and chemically we shall never reach a process which runs contrary to the laws of physics and chemistry. In this sense life is only 'a combination of physical and chemical processes'. But it is possible that such a point of view does not touch at all the real biological problem—and in *this* sense life *is* more than a mere heap of physical and chemical processes and has its 'own laws'.

The physico-chemical explanation of the single phenomena in the organism does not, therefore, suffice for the foundation of theoretical biology. For the essential characteristic of living things as such—the arrangement or organization of materials and processes—it gives no explanation, and offers no possibility of setting up laws for this characteristic. The view that simply by means of a knowledge of the physics and chemistry of the materials and processes of the organism biology will become a branch of physics and chemistry, and so render a theory of the organism superfluous, is thus quite untenable.

(*b*) *Self-contradictions in Mechanism.*

All critics of mechanism have rightly objected that, especially in its popular Darwinian form, it has employed concepts which fundamentally contradict its own demand that the same concepts should hold in both the organic and inorganic realms. Schaxel (1922, p. 156) and Ungerer (1919, p. 246) have pointed out that such notions as adaptation, purpose, regulation, activity, autonomy, compensation, pathology, &c., really give to the organism a special place in contrast to the inorganic world.

Thus the investigator works on the one hand with concepts which are foreign to the physical sciences, and at the same time insists that in the vital process only physico-chemical laws are to be discovered and that no other scientific investigation is allowed. The fact that concepts creep in which give a special place to organisms which they cannot have according to its own principles constitutes a striking refutation of mechanism in its traditional forms.

(*c*) *The Machine Theory.*

We have seen that a simple physico-chemical explanation of the single processes leaves us in the lurch in the face of the fundamental biological problem—the organization of materials and processes in the organism. In order to deal with this we are driven, whether we like it or not, to introduce a theory of the structure of living things which surpasses the mere physico-chemical analysis. There was, up to recent times, only one theory which mechanism possessed for this purpose, namely, the machine theory. Now a machine is, as we have already noted, an 'organized thing'. Just as the working of a machine is ordered and guided by its construction, although all the various processes are purely physical or chemical, so it may be also in the machine 'organism'.

In the history of science and philosophy there is hardly a less happy expression than that of the *bête machine* of Descartes. No concept leads to such a distorted view of the problem underlying it or so greatly falsifies its proper meaning. It might even be said that, in spite of its heuristic success, the notion of the machine has had a destructive effect on the development of biological theory. It has entangled the investigator even to-day with scholastic artificial problems, and at the same time has prevented the clear discernment of the essential problem of organic nature. Only the displacement of the machine theory which is now gradually taking place will put an end to the paralysis of biological thinking for which this Cartesian expression has been responsible.

What makes the machine theory useless is the fact that it is unsuitable for the very purpose for which it was introduced, namely, the physico-chemical analysis of vital processes. In the *first* place, the notion of a machine is only apparently mechanistic and actually crypto-teleological. The 'machinists' forget that every machine is where and what it is for a definite purpose, and that it presupposes the engineer who has conceived and constructed it. The application of the notion of the machine cannot be carried out thoroughly and consistently in biology without leading to nonsense. With regard to every machine it is significant to ask its purpose—the very point of which is considered to be the antithesis of causal physical explanation, and is supposed to be overcome by the help of this problematic notion of the organic machine. Energetics deals with the working of machines, but not with their origin: it does not deal with the question of the builder and tender of the machine. For Descartes the idea of the *bête machine* was simple enough. Animals and plants, he believed, are little machines wonderfully devised by the divine reason. Modern natural science has put aside the dogma of creation: what, then, becomes of the organic machines if we have no engineer who has made them? Locomotives and watches do not grow of themselves in nature; is this, then, the case with the endlessly more complicated organic machines? There is no escape for the machine theory from this 'conclusion to the engineer' as Schultz (1929) calls this argument. It is worthy of note that this most subtle and ingenious of all modern mechanists fully recognizes this, and saves his theory only by the assumption of the cosmic eternity of the 'living machines'. On the other hand, the assumption that organisms are machines is often used by vitalists for the proof of their own theories (see below, p. 44).

But the machine theory is not only logically contradictory, it is, in the *second* place, untenable in the face of the actual data. There is no doubt, however, that there are in organisms innumerable fixed arrangements by means of which a stereotyped response is made to a given influence, and which can be called, metaphorically, 'machine conditions'. Nevertheless, we can no longer regard this fixed 'machine structure' as fundamental for life because modern investigation has demonstrated such an abundance of regulations in the organic world. The untenability of a machine theory of biological processes has been established once and for all by Driesch's 'proofs of vitalism', the most important of which we shall study in the chief part of this work. Meanwhile, it should be noted at this point that the refutation of the machine theory by no means excludes *every* physico-chemical explanation of life.

From the foregoing it is clear that we cannot speak of a machine 'theory' of the organism, but at most of a machine fiction. It can mean nothing to say that an organism 'is' a machine in the sense in which the physicist—without saying anything metaphysical—asserts that bodies 'are' constructed of atoms. We could at most say that organisms can be regarded 'as if' they were machines. We do not at all wish to underestimate the value of picturable fictions in science, but we cannot remain satisfied with the one offered in the present case. If biology is able to offer us no hypothesis for dealing with its most fundamental problem—the organization of materials and processes—but only a doubtful metaphor, then we can only regard this as a declaration of intellectual bankruptcy. Moreover, even as a fiction the machine idea does not attain its goal, because, as we have said, it proves to be inadequate in the face of a large and important section of biological data.

(*d*) *The Selection Theory.*

Mechanism answers the question about the origin of the organic 'machine' by means of Darwin's Selection Theory. Without undertaking a detailed criticism here, we need only point out that the attempt made by this theory to explain the origin of organic contrivances mechanistically, i.e. objectively and scientifically, actually sets out from an uncertain subjectivity. For there is no objective criterion by which we can rationally decide, with regard to a particular case, whether, e.g., a small deviation possessed selective value or not in the evolution of a given organ or character; the decision depends on personal opinions. A review of the Darwinian and anti-Darwinian literature shows clearly how dialectic everywhere takes the place of exact decision. Weismann himself has admitted that a direct control of natural breeding is never possible, and that no one can prove that a given particular change possesses survival value (1912, i, pp. 20, 115). Moreover, the Selection hypothesis does not even do what it set out to do, since it is itself only 'pseudo-mechanistic' in character. It certainly excludes purposive forces, but it is a great misunderstanding to suppose that for that reason the selection principle possesses any sort of similarity to the laws found in physics.

'Purposefulness' is the guiding notion of the supposedly mechanistic Darwinism, but what physicist ever uses this notion? Whilst biology professes to be mechanistic, it still persists in the utilitarian standpoint of Darwinism, i.e. in a low form of teleology. The existence of a naïve value judgement, so different from the point of view of physics, is revealed, for example, by Plate when he gives, as a reason why we cannot speak of 'adaptation' in relation to the inorganic, that 'with the word adaptation we connect a judgement of value. The notion of advantage or use cannot be applied to lifeless matter because one state cannot be regarded as higher than another' (1914, p. 102). But even if we avoid this anthropomorphic notion of 'purposefulness' and with Roux substitute 'capability of maintenance' in its place, we still have an element which is foreign to physical events, at least in the additive sense in which they have hitherto been considered. Were the organism simply an aggregate of physico-chemical processes, 'capable of maintenance' would certainly not be 'life' representing a physically highly improbable state, but would only be a stable physico-chemical equilibrium to which the system would tend as the most probable distribution. In the 'capability of maintenance' of the living state the assumption of an organization at the biological level is thus already presupposed, and thus an element which goes beyond additive mechanism.

We can express this by saying that selectionism does not explain organic wholeness at all but presupposes it. Only if we have 'wholeness-preserving' entities can we have a 'struggle for existence'. Hence we cannot be said to possess in Selection a 'mechanical explanation of organic purposefulness' (Plate).

This brings us to the empirical critique of selectionism, and we shall chose only one decisive point. It is impossible to base the construction of a mechanism which is more complicated and more purposeful than all our machines on the play of accidental variations. Even if selection explained the origin of morphological characters it would surely not suffice for the physiological ones. Consider, for example, the liver-cells, in which, according to our present-day knowledge, some ten, probably many more, chemical processes—all absolutely necessary for life—take place, in a space no greater than about one hundred-thousandth part of a pin's head. 'Is it credible that such a chemical laboratory, in comparison with which our chemical laboratories are the merest child's play, can be accidentally thrown together by the accidental play of molecules and atoms?' (Sapper, 1928, p. 37.) Lack of space forbids a further elaboration of this argument; the interested reader will find all that is essential in the work of Sapper and Jordan (1929, pp. 351 ff.).

(*e*) *The Historical Character of Organisms.*

There is finally one more fundamental feature of the organism in regard to which mechanism fails us, namely, its historical character.

'Whereas in the case of the reactions of inorganic things questions about their origin are, to a large extent, irrelevant because there is no possibility of discovering anything about the history of the elements composing them from a study of their present structure and behaviour, the organization and reactions of living things, on the other hand, are clearly stamped with traces of their historical development.' (Ungerer, 1930.)

We must assume that, in the course of their evolutionary development, living things have amassed *Anlagen*, which progressively unfold in the course of embryonic life in accordance with the 'biogenetic law' of Haeckel which, in spite of its difficulties, still contains a kernel of truth (see below, p. 173). This characteristic is also recognized by mechanists. Weismann, for example, speaks of the ' "Anlagen-substance" which can only have an historical origin, and can never arise suddenly after the manner of a chemical compound' (1912, ii, p. 317). But the mechanist does not notice that with this historical character a fundamental antithesis between chemistry and organism is set up. An essential feature of the organic world is admitted for which the classical system of physical concepts possesses no possibility of interpretation, since for that system the event is determined only by the 'initial state', the 'previous history' being indifferent.

It is usual, however, to bring forward the phenomenon of hysteresis, e.g. the dependence of the behaviour of colloids on their previous history, as an analogue of the historical character of organisms. But it should be noted that even here it is possible to define the initial state independently of the previous history. Certainly, for the prediction of the behaviour of a colloid a knowledge of the actual temperature, &c., no longer suffices, but the micro-structure must also be taken into account. But how this micro-structure has been established is without significance for the further course of events. In this way, what is specific in the past is even here extinguished. In the organic world, however, we have a sharp contrast to this because in the initial state (e.g. of an egg just beginning its development) what is specific in its past (the phyletic development of the species) is not blotted out but is progressively re-awakened. For this reason the double process of phyletic accumulation of *Anlagen* and their ontogenetic unfolding is not comparable with inorganic hysteresis. The classical physics has no means of dealing with such behaviour (the so-called 'biological memory'). We may even venture a little farther and assume that this peculiar character of organisms is also connected with that same supramolecular organization which, in our critique of the additive point of view, we have already recognized as the essential characteristic of living things.

We believe that yet another very important character of organisms is connected with the above behaviour. The inorganic processes tend always towards decreasing complication or disintegration, as we see in the decaying of elements in chemistry and in the dissipation of energy in physics. In contrast to this the tendency in organisms seems to be in the direction of increasing complication—a passage from the simple to the more complicated. We believe that 'biological memory' is essentially responsible for the last-mentioned characteristic of organisms which is very mysterious from the standpoint of traditional physics. If in the inorganic we see statistical probability tending towards the levelling down of differences (e.g. the production of heat equilibrium in accordance with the second law of thermodynamics through the chaotic play of molecules), how, in the organic, can it have tended towards a continually higher complication and differentiation?

. . . .

We thus come to the conclusion that mechanism (at least in the forms so far considered) has not succeeded in showing that the physico-chemical explanation of organisms is able to embrace the whole problem. The essential objection to it is not that the physico-chemical explanation of vital processes has not yet been brought to a conclusion, but that there are fundamental biological problems which cannot possibly be dealt with by the traditional mechanistic explanatory principles.

2. Vitalism

Having seen the difficulties which confront the application of the mechanistic postulate in the biological sphere, we shall now turn to the second theory, Vitalism, to see whether it is able to offer us a more satisfactory basis.

The chief objection to vitalism is that its ideas are so extremely deficient in explanatory value. Driesch has repeatedly been charged with the purely negative characterization of his entelechy. The *entelechia morphogenetica* is neither substance nor energy, nor a constant; it is not spatial but acts into space; it is said to be 'unimaginable', it can only be 'conceived'. The *entelechia psychoidea*, which is involved in instinct, is an entity which, although not a psyche, can only be discussed in psychological analogies. Driesch himself must admit that the definition of entelechy is merely a complicated system of negations.

It is clear that such a vital principle makes no scientific explanation possible. The vitalists explain the vital phenomena by means of an unknown vital principle—just as Molière's celebrated physician explained the action of opium by means of a *vis soporifera*. It is evident that in both cases we are only given an explanation *ignotum per ignotius*. The interpretation of the puzzling purposefulness of life by a still more puzzling active entity offers merely a mythological treatment of biology. Psycho-vitalism, which attempts to give a concrete content to the vital principle as 'soul', suffers from the same weakness. For a sub-human *psyche* is equally unimaginable: we shall not claim to call the organo-genetic and instinctive mental life conscious; but if we call it unconscious we have assumed a mental entity to which is denied the fundamental character of the only mental life known to us, namely, our own consciousness. Hence we are again given a word instead of an explanation.

It is important that we should understand why vitalism comes to an explanation at once so strange and so unacceptable to the investigator of nature.

It is said that vitalism is the antithesis of mechanism, and from one point of view this is correct, but from another it is false. It is correct in relation to the first meaning of mechanism, since vitalism stands in contradiction to the monism of physico-chemical laws. But there is no such contradiction if we mean mechanism in its second sense, namely, the machine theory.

Paradoxical though it may seem, the machine theory is the foundation of both biological mechanism and vitalism. Driesch begins with the problem of organic development. He finds that the machine theory elaborated by Weismann and Roux breaks down in the face of certain regulative processes. But instead of freeing himself from the machine theory he introduces the notion of entelechy to support it. According to him the egg itself is not an organic 'whole', but a multiplicity of developmental mechanisms which are independent of one another, and are guided in their development by the entelechy (cf. below, p. 84). Similarly Reinke introduces his 'Dominanten' as the engineers of the organic machines.

We thus have the following strange position which perhaps shows better than any other the state of our contemporary biology. It is the fundamental defect of mechanism that it admits unclear concepts which savour of vitalism, and it is the defect of vitalism that it does not properly free itself from mechanism. Driesch and Reinke do not begin with an unprejudiced view of the organism but with the notion of the machine. They then see that this view breaks down. But in order to *save* the machine theory they introduce guiding forces to build up the machine in the first instance and restore it when it goes wrong. The mechanistic machinists, on the other hand, have no other resource for dealing with regulations than the 'postulation' of as many subsidiary machines as may be necessary to meet all contingencies. Thus both mechanism and vitalism rest on the machine theory, they only differ in the kind of hypothetical entities they choose to assume in order to meet its deficiencies. The only way out is by rejecting this analogy as a sufficient basis for biological theory.

The source of every vitalism is intuition; for a satisfactory explanation the observer of living things must feel himself into an inner being which he conceives according to the image of his own active ego. The original source of the vitalistic view thus lies not in the intellect but in the realm of feeling. In 'intuitive vitalism' this origin is plain and unconcealed, but it is demonstrable even in the theory of entelechy. For in this theory, although psychological interpretations are avoided, every attempt to give the entelechy principle a concrete content can only lead to psychological analogies.

The historical merit of vitalism has been its recognition of the unity, harmony, regulation, and 'wholeness' of life which, as we have seen, is misunderstood and suppressed in the mechanistic view. The fundamental objection to it is that it bars the way to an investigation of these basic features of organisms by means of natural science, because it bases organic wholeness on transcendent factors which in the last resort are analogous to the psyche.

Vitalism means nothing less than a renunciation of a scientific explanation of biological data. As soon as the possibility is admitted that non-spatial principles 'interfere' in the organic event we render biology as an objective science impossible, and must content ourselves with an intuitive or speculative understanding of biological data, with a mystical feeling or a metaphysic of life. But there is no necessity for any such resignation since no vital process has so far been discovered which unequivocally justifies the 'proofs' of vitalism as contrasted with the refutation of the machine theory. We can therefore agree with the pregnant words of Schaxel when he writes:

> 'For natural science the "psychical components" of vital processes are epiphenomena lying outside its sphere. Biology ranges itself on the side of natural science by virtue of the choice of its object. The

first step of biology is of great consequence. There is no place in scientific biology for whatever in the vitalistic view and its manifold extension relates to non-spatial phenomena, entelechies, psychoids or psychical entities. It is erroneous to see in what is established in natural science a concession to the circle of ideas which is included in the fundamental standpoint of energetics. With the handing over of mental entities to psychology only an explanation of vital processes is demanded of biology. That is to say, we are not required immediately to undertake the quantitative analysis of "life", leaving no remainder. In this way recognition is given to the fact which the mechanistic view in its dogmatic form overlooks: that living processes and living materials as such simply do not exist save as parts of single whole organisms.' (1922, p. 308.)

3. Foundations of Organismic Biology

We can briefly summarize the problematic position of the two fundamental views in biology as follows: Mechanism (at least in the form so far considered) provides us with no grasp of the specific characteristics of organisms, of the organization of organic processes among one another, of organic 'wholeness', of the problem of the origin of organic 'teleology', or of the historical character of organisms. It is a self-contradictory conceptual system, because it can deal with the undeniable 'wholeness' of life only by means of notions which contradict its own fundamental principles. Vitalism, on the other side, recognizes the characteristic of organic order and wholeness, but refers it to a metaphysical or psychical factor and consequently renounces the possibility of a natural scientific explanation. We must therefore try to establish a new standpoint which—as opposed to mechanism—takes account of organic individuality and wholeness, but —in contrast to vitalism—treats it in a manner which admits of scientific investigation. This view, considered as a method of investigation, we shall call 'organismic biology', and, as an attempt at explanation, 'the system-theory of the organism'.

The first step in the direction of our new standpoint has already been indicated by our consideration of the mechanism versus vitalism controversy. We saw that this has its basis not in nature but in the machine fiction which underlies both views. If we begin with the machine analogy we shall wander eternally between the two poles of vitalism and mechanism. We must therefore avoid this fiction and begin with a plain statement of the actual biological data for whose explanation a theory is to be sought.

(*a*) *Life as a System-property.*

The essential feature of vital phenomena, which has still not received sufficient attention, is that the processes of metabolism, of development, of irritability, &c., occur exclusively in relation to well-individualized natural objects with a definite organization which we call 'organisms', and which occur in extremely diverse forms: *myxomycetes*, amoebae, oak-trees, fishes, men.

There is no 'living substance', but only living organisms. Even the slime-fungus is not a 'droplet of protoplasm', or a 'drop of living substance', but already a highly complicated organism. This is shown by the well-known experiment of rubbing lightly in a mortar the plasmodium of a slime-fungus which is about to form the *sporangium*. Although the substance remains quantitatively unchanged, the organization is irrevocably destroyed by this ill-treatment. And whilst under normal circumstances the plasmodium becomes converted into *sporangia* forming innumerable spores, after the injury it changes, in dry air, into a horny structureless mass. If drying is prevented, it decomposes under the influence of bacteria, a change which does not occur in the 'living protoplasm' (Reinke, 1912, p. 250 f.). Thus the basis of life rests on something quite different from the chemical properties of the compounds found in the plasma. This simple experiment shows that destruction of the organization means at the same time destruction of life. It is the same with the living thing as it is with the watch, which has often been used as an analogue. The chemical composition in both remains qualitatively and quantitatively the same when they are pounded in the mortar,[1] but both are irrevocably destroyed. The vital properties are system-properties arising out of the arrangement of the materials and processes, and must therefore disappear when this arrangement is destroyed. The compounds of the organism, which we analyse, are not distinguished by any fundamental differences from 'dead' compounds. Organisms exhibit the properties of life not because of some special peculiarity of these compounds, but on account of the heterogeneous system into which these compounds are articulated. There is no 'living substance' because the characteristic of life is the organization of substances.

> 'This consideration shows unequivocally that even the best chemical knowledge of the bodies occurring in the protoplasm no more suffices for the explanation and understanding of the vital processes, than the most complete chemical knowledge of coal and iron suffices for the understanding of a steam engine.' (Pfeffer, 1897, i, p. 3.)

The same holds for the vital processes. We have already seen that the single processes in the living organism exhibit no fundamental peculiarities as opposed to those in 'dead' material. The chief contrast between living and dead only comes to light when we no longer consider the single processes but the totality of all processes within an organism or within a relatively independent partial system of one. We then find that these processes do not proceed arbitrarily and independently, but are organized and harmonized in a definite way. This organization of the processes is the clearest, and indeed the only decisive distinguishing feature between the vital happenings and the ordinary physico-chemical processes. It is in this way that the events in the living organism are essentially distinguished from the reactions which occur in a weather-beaten stone or in a corpse.

Because the nature of the vital processes depends on their occurrence in an individualized organism, no success can attend the attempt to analyse the vital event without remainder into

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[1] We abstract from the autolysis occurring later.

partial processes occurring in independent units into which the organism is supposed to be analysable (e.g. cells in cellular pathology and physiology, separate developmental machines in Weismann's theory, &c., and, in the last resort, single chemical compounds, in accordance with the customary demand for a resolution of biology into physics and chemistry). It is the property of 'regulation' which is opposed to such an attempt. The reactions in a given part depend to a large extent not only upon what is going on in it but also on the state of the whole organism. For this reason we are driven to regard the organism as, within wide limits, a unitary system, and not merely as an aggregate of individual machines.

By way of summary we can give the following definition of 'living organism':

> 'A living organism is a system organized in hierarchical order (cf. below, p. 129) of a great number of different parts, in which a great number of processes are so disposed that by means of their mutual relations within wide limits with constant change of the materials and energies constituting the system and also in spite of disturbances conditioned by external influences, the system is generated or remains in the state characteristic of it, or these processes lead to the production of similar systems.'

In our *Theoretische Biologie* it is shown in detail that this definition suffices for all the requirements that can be expected of a definition of life. It gives the necessary and sufficient conditions which a natural entity must satisfy if it is to be called 'living', and from it the fundamental principles of organic nature can be derived.

In this sense we may say that the concept of organism occupies an analogous central position in biology to that which the concept of energy occupies in physics. This proposition does nothing more than state the demand already formulated, which, however, stands in sharp contrast to current views, that for an understanding of life the most exact knowledge of its ingredient materials and processes does not suffice. We can only speak of such an understanding when we know the laws which govern the organization of these materials and processes.

From this it becomes clear in what sense we can distinguish biophysics and biochemistry from theoretical biology. If we define the former sciences as the physico-chemical investigation of the ingredient materials and processes in the organism, then it is clear that they cannot constitute a 'theory of life', i.e. a theory of the organization of such materials and processes at the biological level. A theoretical biology is only possible by the aid of definite theoretical ideas capable of dealing with the features of living systems embraced by our definition.

(*b*) *'Gestalttheorie', Organic Mechanism and, Emergent Evolution.*

Perhaps nothing illustrates better the chief trend of modern thought than the fact that we find the same type of development from mechanistic atomism and beyond vitalism to an organismic or system standpoint not only in biology but also in quite different sciences, in psychology and even in physics.

The 'Gestalt theory' originated in psychology, where it was elaborated in opposition to the now obsolete atomism of the associationist theories. According to von Ehrenfels, 'configurations' (*Gestalten*) are psychical states and processes, the characteristic properties and effects of which cannot be obtained by putting together the properties and effects of their so-called parts. A visual figure, a melody, or an intelligible sentence is more than the aggregate of the coloured points, sound impressions, or significant words, concerned. The same spatial 'configuration' can be carried out in other colours, and in other places in the visual field; the same musical *motif* in other pitches, the same meaning in other words. Thus 'configurations' are 'transposable' in accordance with the so-called 'second Ehrenfels criterion'. Wolfgang Köhler (cf. also 1930) next considered the question whether 'configurations' do not also occur in the realm of physics, and showed that in fact physical systems are not merely additive, but that they also satisfy the Ehrenfels criteria.

Generally in physical systems the state (e.g. the distribution of charge on an electrical conductor) or the process (e.g. a stationary electric current) depends on the conditions in *all* regions of the system. Such systems can therefore properly be called 'configurations'. In this way it may be hoped that it will be possible to regard the physiological correlates of the psychical 'configurations' as special cases of the physical ones. In the second part of this work we shall see how Köhler has applied the Gestalt theory to the special problems of embryology.

Pütter (1923, pp. 117 f., 543 ff., 563 f.) emphasizes the *Gestalt*-character of the cell: it is more than an aggregate of its parts, because its individual parts are not capable of independent existence, but change in respect of the state which they exhibit as elements of the *Gestalt*. When we think of the ingredient compounds of the cell as isolated we find in them nothing which renders the vital processes comprehensible. We also recognize the transposability of the *Gestalten* in the cell, since the vital properties of life remain the same in cells which are of extremely different size. It is a consequence of the nature of the cell as a *Gestalt*-bearing event that it cannot be understood as the aggregate of its composing parts. It is for this reason, too, that we cannot find, in any of the groups of material which go into its composition, any one special peculiarity which renders the organism intelligible, or any single physical property which distinguishes living systems from non-living ones, and for the same reason we cannot expect any new physical or chemical discovery suddenly to provide us with the key to the secrets of life. Strictly speaking, it is the particular manner of composition of the materials and processes, their spatial and temporal organization which constitutes what we call life. What physiology teaches in addition to the physics and chemistry of living systems, is the theory of the *Gestalt* properties of these systems. We must, however, confess that at present we have taken only the first feeble steps in the direction of such a further development of the science of life.

One of the most noteworthy features of the history of present-day thought is the fact that—quite independently of these developments in Germany—scientific development has taken an exactly similar course in the 'splendid isolation' of England (cf. e.g. Needham, 1928). Like Driesch in Germany, Haldane in England has insisted on regarding 'wholeness' as the essential feature of the organism. Nothing can be learnt about the organism as such from its parts in isolation; but in its natural totality it shows phenomena which are so different from physical ones that physiology requires entirely new concepts to deal with them. Although without the logical equipment of Driesch, Haldane has sought to show that the 'nostalgia' of the living thing cannot in principle be described by the aid of physico-chemical concepts. The structure of a living organism has nothing in common with that of a machine because the parts of the latter can be separated without change of their properties, whilst in the case of the living organism this is not the case. But it is not quite clear from the works of Haldane, any more than from those of Driesch, what is to take the place of the machine theory. Like the notion of *Gestalt* in Germany, the concept of 'organism' has been extended to the inorganic world by Lloyd Morgan (1927) and Whitehead (1925). What Morgan calls 'emergent' and 'resultant evolution' corresponds to the German concepts of *Gestalt* and aggregate. In emergent evolution every step: atom, molecule, colloidal unit, 'biokyl', cell, cellular organism, colony of organisms, marks the attainment of new peculiarities which, in contrast to resultants, cannot be derived from the subordinate elements. The new view of the world has received its subtlest expression in Whitehead's 'organic mechanism', which goes beyond both the assumption of the 'blind running' of the molecules and vitalism. The true enduring entities are 'organisms' in which the plan of the whole influences the characters of the various subordinate organisms. But this principle is quite general and in no way a special peculiarity of living bodies. It will perhaps interest the English reader to know that ideas closely related to those of emergent evolution and organic mechanism were expressed in Germany by Carus seventy years ago (cf. Meyer, 1929), but naturally without arousing much attention at that time. The excellent views of Ritter and Bailey (1928) stand in less close connexion with this development. They show, in a comprehensive study, the inadequacy in all branches of biology of the 'elemental conception' that parts, regarded as independent entities, can completely explain their wholes. This view must be supplemented by the organismic hypothesis that the living body is just as capable of influencing the inorganic elements which compose it as these elements influence the body into which they enter.

(*c*) *Organicism and Physics.*

In what relation do Gestalt theory and organicism stand to physics? Different authors have come to quite different conclusions on this question. If we apply the Gestalt theory to the organism, the latter represents, according to Sapper (1928, pp. 84 ff.), a system of 'configurations' in which every higher group in the ladder of levels: electron, atom, molecule, cell, tissue, organ, organism, exhibits specifically new modes of action which cannot be understood as mere additive phenomena from the previous ones. It thus seems that wherever a higher specific organic group, e.g. a cell, comes into action as such, the physico-chemical interpretation which works with atoms and molecules must break down, and new concepts will become necessary. On the other hand, 'neo-mechanists', e.g. A. Meyer in Germany and Needham in England, have drawn, from the demonstration of *Gestalten* in the inorganic world, the conclusion that the autonomy of biology can no longer be based upon organic wholeness, and that by means of the *Gestalt* point of view the reduction of biology into physics and chemistry is rendered possible.

Each of these opposed conclusions seems plausible, and we must therefore try to overcome this dilemma. For the present we shall leave on one side the question whether and how far the physical *Gestalten* actually bring us closer to an understanding of organic events (cf. Chap. VII) and only deal here with the logical problem.

Obviously the dilemma has its origin in the question: in what sense can we say that 'the whole is more than the sum of its parts', that *Gestalten* 'cannot be conceived additively'?

This question is very easy to answer (although very strange and contradictory opinions regarding it are to be found in the literature). The characters or modes of action of *Gestalten*—of electrical charges, atoms, crystals, &c.—cannot be interpreted by the summation of the properties or modes of action of their parts *as studied in isolation*. In this sense *Gestalten* are 'non-additive'. But if we know the *totality* of the elements or parts united in the system, and the *relations* existing between them, then the behaviour of the 'Gestalt' can be interpreted by that of the parts, and lastly in terms of the ultimate physical parts and elementary laws.

What consequences follow from this decision for biology? Obviously two. First, that the *additive* form of mechanism is shown once more to be inadequate. If the organism is an 'organism', a *Gestalt*—and is it too much to claim this character for it when it is granted even to atoms, crystals, and electric charges?—then it follows that a knowledge of the parts in isolation does not suffice. And it will also be impossible—on account of the dependence of the single processes on the whole—to resolve the organic event completely into single causal chains which take place in independent component 'machines' (cf. also p. 48).

On the other hand, however, the Gestalt theory, in the form so far considered, constitutes a support for mechanism in the sense of a physical analysis (for which the additive point of view and the machine theory represent only one possibility). If the organism is a *Gestalt* only in that sense, like the electric charge, the atom, and the crystal, then we can hope in the remote future to be able to interpret it in terms of the basic assumptions of physics, i.e. to interpret first the 'organismic' combinations by which organic compounds, colloidal micellae, &c., are built up into the higher components, cell-parts, cells, and organisms, as well as, secondly, the laws of biological systems by which the individual processes harmonize to constitute the totality of the organic event. The demand for a final reducibility of biology to physics would thus be justified, although by a far more difficult path than 'additive' mechanism supposed.

But is there, perhaps, still a fallacy in this inference? We have to emphasize that a complete discussion of these extremely difficult and comprehensive problems in the space available is quite impossible. We can mention only a few important points.[1] For further clarification it is essential to take into consideration the newer ideas in physics. Hitherto the Gestalt theory has stood on the basis of the classical deterministic physics which can now no longer be regarded as final. We must therefore consider the significance of the modern physical ideas for organicism.

In the first place we may point out—and thereby fulfil a former promise (p. 32)—that in the light of contemporary physics the antithesis between metaphysical mechanism and vitalism in a certain sense evaporates. The new wave mechanics has extruded the notion of 'substance' in the most radical manner. At the same time, waves and vibrations in modern physics mean

> 'only "periodic changes" in a given magnitude irrespective of what kind this may be. But now if *all* that is to be said about the processes concerned depends only on the form of these processes whilst the nature of the magnitude itself which is changing in accordance with the wave formula is quite indifferent, then even for physics only the process is significant, and it is quite indifferent on or in what "something" this process occurs. . . . "Materialism" in the narrow sense, i.e. the belief in an "eternally indestructible material", or in atoms as "little hard lumps of reality", is thus finally *ad acta* set aside'. (Bavink, 1930, p. 182 f.)

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[1] A full discussion is given in our *Theoretische Biologie*.

Now the antithesis between metaphysical mechanism and vitalism is significant only on the basis of the materialistic and deterministic metaphysics of the older physics. Only on this basis can we speak of a 'blind play' of atoms, or of their being guided by souls and entelechies. If modern physics presents us with a dynamical resolution of matter, and sees its final task only in the discovery of the formal relations in an otherwise undetermined 'something', and if, finally, it only sets up statistical laws for the average (see below), then there is no longer any support for the metaphysical assertion of mechanism that the 'true reality' is matter and physical forces, since in the last resort—from the standpoint of metaphysics with which physics, of course, is not concerned—we may very well regard every electron or quantum as a freely acting 'entelechy'.[1] But on the other hand the assertion of vitalism that 'the entelechy guides the blind play of the molecules or physico-chemical forces in the organism' becomes equally senseless. Thus the world no longer appears as a machine rolling on with blind necessity after once being set in motion. The ultimate physical processes show—within the limits of the Heisenberg relation—a certain freedom which is only accessible to a statistical treatment. Thus modern physics does not forbid us to regard the world—metaphysically—as an organic becoming. We thus have a surprising resolution of this ancient quarrel in the sense that the antithesis between 'metaphysical mechanism' and 'vitalism' proves to be a false problem, and at the same time the difference between the 'methodological' and 'metaphysical' attitudes is set in the right perspective.

In close relation to the foregoing stands the second fundamental feature of modern physics: the recognition of the

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[1] Of course, the above proposition does not at all mean that the problem of 'freedom of will' is resolved in such a simple way. We do not forget that the indetermination of casual events according to the principles of physics is something other than 'freedom' in the philosopher's sense. We are here concerned not with scientific theories but with metaphysical assumptions, and in *this* sense the above may stand.

statistical character of natural law. We can only briefly sketch the historical development of the problem (cf. Bertalanffy, 1927 *b*., Bavink, 1930, where further reference will be found). Classical physics has already recognized the statistical character of the second law of thermo-dynamics: all directed energy is an improbable state in comparison with the chaotic molecular movements which represent heat. The passage to heat, the increase of entropy, signifies the transition to more and more probable states. It was probably Nernst (1922) who first stated that 'on various grounds we may suppose that the second law of thermo-dynamics does not occupy an exceptional place, but that all our natural laws are of the same nature'—that they also are thus only statistical propositions. The new wave mechanics has taken the problem out of the realm of speculation into that of experimental verification. The Uncertainty Principle of Heisenberg states that the place and momentum of an electron cannot be exactly determined simultaneously. In order to determine the place of an electron it must be illuminated. But this means that a light quantum hits it, and then its momentum is altered. The more accurately its position is determined the less accurately can its momentum be measured, and vice versa. Thus from the Heisenberg-relation it follows: 'In the exact formulation of the causal law "if we know the present exactly we can calculate the future" it is not the conclusion but the assumption which is false. We *cannot* in principle know the present in all levels of determinateness.'

A third feature which is important for us is the recognition of the admirable unification which is attained in modern physical thought. If we ask what elements the modern physicist requires for his unitary picture of the world, we find the proton and electron with their masses M and m, the quantum of action h of Planck, and the field laws of Maxwell or Einstein with their constants c and κ at present regarded as ultimate. The number of fundamental assumptions made by contemporary physics has already become very small; this is true both of 'substances' and of fundamental laws. Perhaps even this number of fundamental assumptions will be capable of still further reduction. From the quantum of action h, and the field laws (eventually also M, m, and c), the whole physical world can be built up. From these the periodic system of the atoms results, from these again one and a half millions of different kinds of molecules, from the combinations of which we obtain innumerable natural materials in increasing complication up to the cosmos of fixed stars and still higher units.

At first sight it seems presumptuous to assert that this prodigious synthesis of physics, reaching as it does from the smallest to the largest in the cosmos, will remain permanently unrelated to that thin layer of strange phenomena on a heavenly body of lower order which we call 'life'. But the question has a somewhat different complexion if we ask, not whether other laws reign in the living thing than in the inorganic world, but whether it is really possible to resolve the laws of biological systems into those of physical ones.

In the light of the foregoing we must formulate our fundamental question as follows: Is it probable that biological law can be reduced to the statistical laws of physics? Without wishing to prejudge the further development of this extremely difficult question—rendered doubly difficult by the fact that at present we have only the vaguest notion regarding what those biological laws may be—we believe that there are still some aspects which render an affirmative answer improbable.

In the first place we have to consider the immense complexity of the organism. If we have to establish system laws for the organism—and this is necessary for its full explanation—then these laws, physico-chemically formulated, would be of stupendous complexity. And just as, in Boltzmann's deduction of the second law of thermo-dynamics, although it is not denied that the paths of the single molecules follow strictly the laws of mechanics, yet in practice these are not determined but we have to content ourselves with a statistical law dealing only with the average behaviour of an immense number of molecules, so in like manner we think that, even assuming that all organic happening is strictly determined physico-chemically, yet it is not possible, owing to the immense number of the component processes involved, to formulate the organic event physico-chemically, but that we must introduce bio-statistical laws of 'higher order'. That is to say, they would not be statistical laws of the behaviour of molecules, atoms, or electrons, but of such biological entities as cell-parts, cells, &c.

A second point also presents difficulties to a complete physico-chemical determination of the vital processes. All biological methods—sero-diagnosis, transplantation, genetics, the study of behaviour—show us that perhaps no two metazoan or protozoan organisms are exactly alike. We might perhaps say that in the metazoa probably no two cells of the same tissue are exactly alike, although the establishment of such differences is at present far beyond our methods of analysis. We may never be able to characterize the behaviour of 'a Paramoecium cell', or 'a nerve-cell' simply by means of a complicated system of physico-chemical equations because such a system would probably only provide a *general* law for the behaviour of cells: a comprehensive law allowing a more or less wide degree of play to the physico-chemical events.

Perhaps a further step is admissible. According to the modern view, 'macroscopical' physical events appear to be strictly deterministic because a practically infinite number of elements is involved so that the statistical 'fluctuations' cancel each other. Appropriately minute particles (e.g. colloids and fine suspensions) are set in Brownian movement, visible under the ultra-microscope, by the fluctuations of the pressure exercised at various points by the molecules in irregular heat-motion. On the ground of these fluctuations of the molecular movement it might also happen that a brick would fall upwards; but since the number of constituent atoms is of the order of 10^{26}, we should, according to Perrin, have to wait some $10^{(10^{10})}$ years for this remarkable event (a number with 10 milliards of zeros!). The objection has been raised to the author (Gross, 1930) that on the same grounds only the deterministic macroscopic laws are applicable to biological events. In general this is quite right, and on it depends the wide possibility of applying physical and chemical methods and laws to organisms. But Niels Bohr (1930) himself has raised the question whether account must not be taken of the limits of causal explanation in relation to the deeper biological problems. We might here consider the possibility that in organisms the (physical) 'microscopical' fluctuations do not cancel one another, but that they are transferred to more and more extensive regions of the system, and so lead to macroscopical departures from the physical, statistical probability of the events. Lillie (1927) has suggested that perhaps the molecular variations within the nervous system are passed on to the whole organism, and so give rise to an apparently 'free' behaviour of the latter. This would mean that the behaviour, and perhaps to a large extent 'organismic' laws in general, could no longer be dealt with by means of physical statistical laws, that they are physically improbable and can only be dealt with by means of a statistics of 'higher order'.

We therefore believe that there are good grounds for supporting the view that organic laws as contrasted with physical require a statistics of 'higher order', which, in the first place, cannot be resolved into the ultimate assumptions of physics because in the organism the complication and individuality of the physical relations becomes predominant, but which, secondly, do not require this resolution, because the biologist is not interested in this individuality, but in the uniformity which is manifest in spite of it. A third level of statistics would probably be required in sociology. The exact treatment of this problem will presumably require totally new forms of logico-mathematical technique.

Perhaps there will be, in the biological realm, an 'Indeterminacy Principle' similar to that of Heisenberg in the realm of intra-atomic events. Physical law can only be statistical—not because Heisenberg may have proved that strict causality breaks down in the intra-atomic events (this is a matter of taste, since we can, like Planck, defend a strict causality even here in principle)—but because even if deterministic dynamical laws held in the realm of quanta we could not discover them from the nature of the case, i.e. on account of the circumstance laid down in the Heisenberg Relation. Similarly, it may be the case that biological law can be only a specific biological statistic, not because it might be shown that physical law breaks down in the organism, but because we cannot reach a complete physico-chemical determination, either because the complication and individuality becomes so predominant as to frustrate its practical establishment, or because 'fluctuations' occur here so that the physical averages are no longer characteristic; thus, we must content ourselves with a statistic of living organisms as wholes. Or, more exactly expressed: Heisenberg's Indeterminacy Relation asserts that physical law can only be statistical because we cannot determine both momentum and place of the electron simultaneously. Similarly, in biology we should say: in order to determine an individual biological process completely we must know *all* the partial processes in the organism concerned upon which the former is dependent. This, however, is impossible, because just the same holds for each of the other partial processes, and our procedure becomes circular. Consequently we can determine the individual events only approximately. We can, therefore, in the *first* place, treat the individual process in isolation physico-chemically—which is the usual procedure in physiology.[1] This, however, on the one hand only determines

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[1] The relation of the 'organismic' conception in the sense explained above to the usual practice of physico-chemical investigation of life processes is analogous to the significance of the modern points of view in physics as expressed by Mises (1930): now, as before, the earth remains a disk, and the proposition—that every change has a cause—is still useful, not only in daily life, but also in *nearly* all situations in science. Only in rare cases in which especially comprehensive or profound problems are involved is the improved

what happens in the organism to varying degrees of approximation (the more 'mechanized' the process the closer the approximation), and, on the other hand, gives us no explanation of the biological problem—the mutual inter-dependence of the partial processes. Or we might, *secondly*, define the total event in the organism with one stroke by means of an integral law (this, in our opinion, is the essential biological problem). But we should then have to renounce the physico-chemical determination of the partial processes, because the integral law would become endlessly complicated if we attempted to fill it in in detail with physico-chemical constants. And even physical probability would not fit, in certain cases, for the biological events.

In this way we should have a peculiar solution of the question of the relation of the organic to the inorganic. On the one hand there is no essential dualism, since no vitalistic factors are involved in the organic realm. The series of *Gestalten* passes continuously from electrons through the atom and molecule to cells and cellular organisms. But biology would, on the other hand, represent a turning-point of the curve, since a level of complication and individuality is reached here which can no longer be dealt with under physical law, and for which a statistic of higher order must be introduced. At the sociological level there is perhaps a second turning-point.

It seems to us that these abstract deductions agree tolerably well with the actual procedure of biology. The only properly worked out system of biological law, namely, modern genetical theory, corresponds closely to such a 'statistic of higher order'. If the chromosomes or genes separate according to Mendel's

conception to be used. In the same way, the point of view developed above leaves the usual physico-chemical investigation of life processes almost unaltered. It need only be taken into consideration where it is a question of the general theory of life. This must be emphasized in order to guard against the mistake that the new conception represents an absurd revolution in methods which have been repeatedly proved, or that it is in opposition to the methods and results of the physico-chemical investigation of biological processes.

laws in meiosis, it remains to be seen whether this represents anything more than statistical probability, or how far this distribution of chromosomes and genes is to be interpreted physico-chemically. Here we have a statistic of biological complexes, in this case of genes.

(*d*) *Summary of the Organismic Position.*

We have made an attempt to think out the implications of the organismic view in the light of modern physics. It need scarcely be said that, in view of the extraordinary difficulty and newness of this problem, we do not wish to defend the foregoing discussion of it in any dogmatic spirit. Our chief aim has been to draw attention to the problem and to urge others to investigate it. We would, in any case, point out that as a *method of investigation* organismic biology is quite independent of those ultimate decisions which we discussed in the last section. We cannot indicate this pragmatic attitude better than has been done by Woodger (1929, pp. 273 ff.):

> If the organism is a hierarchical system with an organization above the chemical level, then it is clear that it requires investigation at all levels, and the investigation of one level (e.g. the chemical) cannot replace that of higher levels. This remains true quite apart from the remote future possibility of expressing the properties of all higher levels in terms of the relations between the parts of the lowest level.

Woodger gives an excellent summary of the reasons why an exclusive attention to physico-chemical explanation is not desirable in biology. To this the reader may be referred for a supplement of what has been said above. The question whether physical concepts *at present* suffice for scientific biology must be answered in the negative, because neurology, experimental embryology, and genetics—to mention only the more important branches—employ purely biological concepts. To the question whether these concepts will be replaced by physical ones in the future, we must answer: wait and see.

It has often been objected against organicism (e.g. Needham,

1929) that the organismic point of view—although of philosophical value—is of no importance for the work of natural science. The organism is something with which the method of natural science cannot work—a hard, smooth, round nut which experimental analysis can neither crack nor lever open at any point without it exploding and vanishing like a Prince Rupert drop. Now, it is quite true that the non-additive character presents great difficulties to scientific treatment. But precisely the same difficulties are confronting certain branches of physics —and are here successfully overcome. Köhler (1924, pp. 92 ff.), for example, points out the difficulties of a mathematical treatment of the structure of electric charges, since it is impossible to determine the charge first in this place and then in that, because the charge at any given place depends upon that at all the others. Consequently, with the usual additive methods of physics we cannot deal with the problem. The problem must be solved at one stroke as a *whole*, and this physics has done in an admirable way by means of the theory of integral equations. 'No one who has closely studied this part of mathematical physics will ever assert that all physical structures have a purely additive character.' It cannot therefore be said that the 'concept of organism' is opposed to scientific treatment. On the contrary we might say that physics has already been dealing with 'organisms', with *Gestalten*, although of a low degree of complication. All that remains of this criticism is the assertion that biology has not yet regarded the organism as a system (as contrasted with an aggregate), and that this is forbidden also for the future. But this is a dogmatism on the side of mechanism which is no better than that of vitalism, when the latter declares that science will 'never' be able to explain this or that property of living things.

We can therefore summarize the demands of organismic biology as follows:

Since the fundamental character of the living thing is its organization, the customary investigation of the single parts and processes, even the most thorough physico-chemical analysis, cannot provide a complete explanation of the vital phenomena. This investigation gives us no information about the co-ordination of the parts and processes in the complicated system of the living whole which constitutes the essential 'nature' of the organism, and by which the reactions in the organism are distinguished from those in the test-tube. But no reason has been brought forward for supposing that the organization of the parts and the mutual adjustments of the vital processes cannot be treated as scientific problems. Thus, the chief task of biology must be to discover the laws of biological systems to which the ingredient parts and processes are subordinate. *We regard this as the fundamental problem for modern biology.* Since these laws cannot yet be formulated in physical and chemical terms, we are entitled to a biological formulation of them. In our view, the question of a final reducibility of such biological laws is of subordinate importance in view of the foregoing demand. Even without this final decision, the antithesis between mechanism and vitalism ceases to be a troublesome problem. The mechanist who believes in the possibility of such a reduction, and the vitalist who denies it, can join forces in an attempt to solve this great problem: the establishment of the laws of biological systems.

The investigation of these laws must proceed in two directions. On the one hand, the empirical rules of organic systems must be obtained from the concrete, especially experimental, data. And on the other hand, it must be the final aim of biology to derive the laws of organisms deductively from general assumptions—a task which will probably be aided by the new mathematical logic and to-day can only be undertaken in a fragmentary form.[1]

With this our brief survey of 'organismic biology' is completed. In this introductory part we have tried to describe its

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[1] See the papers by Woodger (1930–1).

general principles. In Part II we shall follow a different procedure. We shall, from the standpoint of analytical theoretical biology, examine one important problem, passing in review the principal phenomena and theories in this region, in order to see whether the patient study of this problem will lead us to the same conclusions as we have reached from general considerations.

PART II

THEORETICAL EMBRYOLOGY

III

THE PROBLEM OF DEVELOPMENT AS A FOUNDATION OF THEORETICAL BIOLOGY. DEFINITIONS

IF we turn to consider which vital phenomenon is to be chosen to exemplify the programme of analytical theoretical biology, the process of the development of organic forms at once urges itself upon us. For, of all the wonders which life presents to us in such plenty, that of development is surely the greatest. Let us recall what it means: on the one hand we have this little drop of jelly which, as a fertilized ovum, represents the germ of an organism; on the other is the wonderful edifice of the complete living creature, with its myriads of cells, its endlessly complicated organs, characters, and instincts. When we compare the beginning with the end of this process it is easy to understand why it is that in all attempts to solve the great riddle of life, scientifically or philosophically, this cardinal problem of development has been preferred as the starting-point.

Thus the study of developmental processes has greater advantages for the founding of theoretical biology than any other branch. In the first place we are presented with a greater variety of elaborated theories here than in any other branch, with all shades of belief from mechanism to vitalism—theories which exhaust all logical possibilities, so that by means of a critique of these the way to the solution of the problem, at least in its general direction, can be indicated. Moreover, we move in an entirely 'objective' region, and are not compelled, as in the study of behaviour for instance, to touch upon the difficult philosophical problems of the relation between the physical and psychical. And—last but not least—the most important advantage is that we are not driven to speculative discussion in order to decide between rival theories, as would so largely be the case were we to choose phylogenetic problems as our starting-point; we are able to decide between the theories on the ground of experimental investigations. We seem, therefore, to be justified in regarding the problem of development as a *paradigma* of the problem of life in general. In studying it, we shall discover in detail in one important branch the state of contemporary biology which our general discussion has depicted to some extent only *al fresco*; on the other hand we shall try to penetrate to the fundamental problems of the organism by means of this weightiest of all biological problems.

But before we pass to the criticism of the theories we have to explain some important concepts which, at the same time, indicate the main problems to be explained. First, in what does the essence of *development* consist in metazoan organisms (only these will be considered here)? Development has often been described as an 'increase of the degree of visible complexity from internal causes'. As Woodger (1929, pp. 339 ff., 372 ff.) rightly points out, this expression is not quite adequate. As our starting-point we have the fertilized egg, a structure which possesses an organization above the chemical level, namely, that of the cell-level. By means of the very first cleavage, through which the blastomeres thereby arising no longer form a whole organism but parts of such, and later by means of gastrulation, through which the germ-layers as the first 'tissues' are formed, the germ passes over to a level of organization beyond that of the cell. The characteristic feature of development is thus 'a gradual rise in the level of organization'; in this sense development is certainly 'epigenetic' (see below), since in the later stages we have a type of organization which was in no sense given at the beginning, since it contains cellular parts, and in the latter there was no such thing.

It is, moreover, evident that the essential causes of development are situated in the germ itself. We may here recall Roux's discrimination between 'determination' and 'realization factors'. Pflüger once assumed that gravity determined the direction of the axes in the development of the frog (1883, 1884). But Roux, in a classical experiment, in which he slowly rotated an egg on a vertical disk (whence the direction of gravity, light, heat, &c., were continually changed), showed that normal development is independent of such external forces, and hence that the typical formative powers are contained in the egg itself. Development is, therefore, according to Roux, *self-differentiation* of the egg in relation to outer factors, which latter merely yield the material and energy for carrying out development, whilst the determination of form development and its proper causes are enclosed in the developing organism (1895, pp. 17, 44, 423, 777, and elsewhere); in this sense he distinguished the 'determination factors' lying in the germ itself, and determining development qualitatively, but which alone are not sufficient for development, from the 'factors of realization', as he called them, for beginning and maintaining its activity, i.e. such factors as heat, light, nutrient materials, &c., introduced from without.

Such a discrimination is, however, scarcely to be carried through in any absolute manner. Inner as well as outer conditions can be realization factors in Roux's sense, for instance the quantity of an embryonic part or temperature; exterior factors, on the other hand, may determine development qualitatively. The typical example of this is still the exo-gastrulation of the lithium larvae according to Herbst. An important chapter of experimental embryology deals with the action of outer factors, light, heat, electricity, radium radiation, gravity, centrifugal force, chemical substances, &c., on the course of development. It is to be conceded that the external factors may alter the quality of development; but the efficient causes for the occurrence of development at all, lie, of course, not in the temperature, light, gravity, &c., of the environment, but in the germ itself. In this sense, development is an 'immanent' process; this does not mean that the environment can be ignored, but only that since development can occur in a temporally uniform environment, the changes in the organism cannot be interpreted as resulting from changes in the latter (Woodger, 1931, p. 185).

Yet a third essential feature of development is to be emphasized. If we adopt the doctrine of descent—and how are we to reject it without returning to a dogmatic childish belief?—then we have to regard the germ as the result of a process of historical becoming. However unfortunately Haeckel's 'biogenetic fundamental law' may be formulated, we cannot escape from this fact. In the germ lies the whole past of the species, which must develop from it until the adult organism, as the concluding stage of development, is reached.

Some other concepts in general use for the description of certain aspects of development remain to be defined. First the notion of 'potency'. It is a fundamental fact of developmental physiology that the parts of an embryo are, in general, not only capable of one particular contribution to the course of normal development, but also of others as well. The 'possible' contributions which an embryonic part may make under various conditions may be called its 'potencies'.

Since the parts of the embryo possess in general several or many 'potencies', something must decide which of them, in the course of development, is realized. The establishment of the contribution of a given part is called 'determination'.

These definitions of the concepts of "potency" and the closely related one of "determination" are in conformity with the use of these notions in experimental embryology and also in the theories which we shall review. There is no objection to the use of these notions so long as we bear in mind that they only have a "descriptive" and not an "explanatory" character. Thus stating the "potencies" of an embryonic part is simply a convenient way of describing what it furnishes under various conditions. It would be quite beside the point to use the concept of "potency" in an explanatory sense, i.e.

to regard the potencies as mysterious entities, and the embryo as—in the words of Woodger—a "mystery bag of potencies", of which the one or the other is "unfolded". There are no "potencies" or "possibilities" existing as "entities" which may be activated or extinguished, but only reactions which in fact occur when certain conditions or complexes of causes are given. In modern embryology the concept of potency is naturally used in the theoretically neutral sense above explained.

Differentiation means the origin of differences in the various parts of the embryo.

This survey of the chief concepts has emphasized for us some important features of the developmental process. They will help us to understand the following descriptions of theories in which they are often used. The task of experimental and theoretical embryology is the analysis and explanation of the developmental processes. To show how far this has been carried at the present day will be the object of the following pages.

There are two traditional ways of explaining the problem of development, which are characterized by the expressions 'preformation' and 'epigenesis'. The meaning of these expressions has certainly become refined since their origin in the seventeenth century, but even to-day they still express the fundamental antithesis confronting an explanation of development, which we can characterize with Roux as 'transformation of invisible multiplicity into visible', and 'creation of new combinations'. The old preformationists believed in a microscopical structure of the egg or sperm, so that in the ovary of Eve were contained all the innumerable generations of future human beings which only need to grow to become adult men and women. The old epigeneticists spoke of a *nisus formativus*. In modern times, the theory of preformation, under the pressure of microscopical data which show that the organism as such is not preformed in the germ, has taken the form of assuming that not the finished creature, but only the *Anlagen* (rudiments) for all of its parts are already in the egg. The new epigenesis, however, rejects the pre-existence of the individual organ rudiments and assumes that the germ parts are determined by the 'whole' to form certain structures. What this somewhat vague expression may mean will only become clear in the course of our investigations.

IV

THE MACHINE THEORY AND THE FOUNDATION OF DEVELOPMENTAL MECHANICS

In the year 1882 Wilhelm Roux plunged the point of a hot needle (not, as he tells us, without a secret feeling of dread) into one of the blastomeres of a frog's egg at the beginning of cleavage. Roux was well aware of the crudity of this attack upon the mysterious workshop of the organism, and compared it himself to throwing a bomb into a newly-founded factory (1895, p. 154). This classical experiment marked the hour of birth of a new branch of biological science, *developmental mechanics*, which attempts to establish the causes and laws of development by experimental methods.

The result of this experiment, in which one of the blastomeres was thus killed—Vintemberger, 1928, has repeated it with the modern technique of X-ray radiation—was noteworthy enough. From the remaining living cell there developed a half-embryo, either the right or the left half of a tadpole, which only later became a complete animal through a peculiar 'post-generation'.

This experiment formed the starting-point of the first of modern theories of development, the machine theory of Roux and Weismann. We could assume that, just as in this experiment, in which the one blastomere is excluded, in undisturbed development also the two halves of the body develop independently of one another. Each of the two cleavage cells contains all the essential formative and differentiating powers for the development of one half of the cerebral vesicle, for one auditory vesicle, and the remaining organs, each develops independently of the other (or of the complex derived from the latter) in 'self-differentiation' to form a normal lateral half of the body (1895, pp. 448, 775). 'The development of the frog gastrula, and of the embryo immediately arising from it, is, from the second cleavage onwards, a mosaic-work, and is composed of at least four vertical pieces developing independently' (p. 781). With Weismann we must then assume further that in the egg nucleus there are contained 'determinants' for every single organ of the animal body; the differentiation of the organs and tissues results from the separation of the totality of these rudiments—the idioplasm—into single determinants in the course of development, since these are distributed among the descendants of the egg-cell by means of 'unequal nuclear division', as though by a delicate machinery; until finally there remains only one kind of determinant in every cell, and this gives to the cell or cell-group its character. For 'atypical' development in regulation and regeneration, however, a reserve idioplasm was assumed, in which the totality of the determinants persists.

The reviewer of the modern theories of development cannot avoid a description of the Roux-Weismann theory; for this will always retain its historical value as the starting-point of all further theories, and also as a consistent working out of one of the logical possibilities. But the next steps of experimental embryology soon began to show the complete impossibility of this theory.

Driesch, in his epoch-making experiments, worked with the eggs of the sea-urchin. He did not, like Roux, kill one of the blastomeres, but separated them by various methods, e.g. by shaking. The result of these experiments was especially striking because it formed a complete contradiction to that of Roux's work. From a half-germ, even from a quarter or an eighth, was obtained not a half, quarter, or eighth larva, but a whole one, which, however, remained relatively smaller than the normal. But it is not only possible to obtain two larvae from one germ; the opposite is also possible. Driesch was able to unite two sea-urchin eggs or germs together and from them to obtain a single giant larva. Mangold (lately Mangold und Seidel, 1927) has carried out a similar experiment with newt germs.

In contrast to these 'regulative' eggs of the sea-urchin, the

Amphioxus, the newt and others, in which normal organisms develop from divided and fused germs, there is another class of eggs, in which defective organisms arise if single cleavage cells are killed or separated. These are the so-called 'mosaic eggs'. In these, 'organ-forming areas' are already found in the cytoplasm of the unfertilized egg. According to Conklin the egg of the Ascidian *Cynthia* contains no fewer than six different kinds of cytoplasm, which correspond to organs which develop later. The egg of *Dentalium*, according to Wilson, shows three layers which are marked out by a pigmented ring in the middle. In the first cleavage, the polar lobe characteristic of gastropods is formed which is similar to a nucleus-free cell attached to one of the two blastomeres. If the polar lobe is removed, the resulting larva lacks the post-trochal region and the ciliated organ. In the egg-cytoplasm of the ctenophore *Beroë ovata* a region is present which is destined exclusively for the formation of the locomotory ciliated bands. The normal number of these bands is eight; from separated blastomeres develop individuals with a smaller number of bands such that the sum of the bands of all animals resulting from one divided germ together amount to eight.

The difference between regulative and mosaic eggs is only one of degree; there is scarcely a single case of an ideal regulative or mosaic egg, and both extremes are connected by every conceivable transitional form. Even the best examples of regulative eggs, sea-urchin and newt, are only equipotential (see below, p. 78) along the axis passing through the vegetative and animal poles, so that if a separation takes place in this direction both parts yield whole embryos, but if the egg is cut through across this axis, then usually only the vegetative part is capable of yielding a whole. Moreover, even the 'classical' examples of mosaic development are not devoid of all regulative ability; the partial embryos of *Beroë*, for instance, have altogether only eight bands, but each forms a normal gut, a sense organ, &c., thus even if the bands are preformed in the shape of an organ-forming area, this does not hold for the remaining organs, in regard to which therefore regulation is possible.

It is easy to see that both classes of animal eggs contradict the Roux-Weismann hypothesis. The fact that from parts of regulative eggs whole embryos develop shows that every blastomere still contains the whole material of 'determinants' and therefore there can be no question of a mosaic development or of a separation of determinants. But this theory is no less contradicted by the mosaic eggs: for here also there is no unequal division of the material of determinants supposedly localized in the nucleus, but merely an unequal division of cytoplasmic organ-forming regions in the blastomeres. Moreover, Roux never should have drawn the conclusions from the frog experiment which he actually drew, since the development of half-embryos here is only conditioned by its connexion with the dead blastomere; if this is removed, regulation occurs and a whole is formed (O. Hertwig).

For the sake of completeness, we may mention the classical refutation of Weismann's theory of unequal nuclear division. Driesch (and also Hertwig in the case of the Frog, and Wilson in the case of *Nereis*) compressed dividing sea-urchin eggs between glass plates; if the pressure was maintained, for instance, until the completion of the eight-cell stage, he obtained a plate of eight cells lying in one plane, instead of two rings of four cells lying one upon the other, furnished by normal segmentation; the next cell-division occurred at right angles to the preceding, and the result was a sixteen-cell stage, consisting of two plates of cells of eight cells each. The distribution of the blastomeres and the division of the nuclei were thus quite different from the normal. If the cleavage process be a distribution of determinants, then this distribution would be quite different from the normal in the compressed eggs, and monsters must therefore arise. But after releasing the pressure at the right time, normal embryos were obtained, which shows that a splitting of determinants, an unequal nuclear division, cannot occur. Still more convincing is Spemann's recent refutation (1928). He tied a thread round the middle of a newt's egg, so that through the small bridge between the halves instead of a derivative of the first division of the nucleus only one of the second up to the fifth division was allowed to pass into the nucleus-free half, and thus 1/4, 1/8, 1/16, or 1/32 of the original nucleus. It was found that 1/16 suffices to produce, with the cytoplasm, a normal *Triton*. Thus there can be no hereditary unequal division, since, did this occur, the 1/16 nucleus would only contain what was requisite for 1/16 and not for a whole organism.

The multiplicity of regulatory phenomena which we have already mentioned or shall mention later—from the regulation of the cleavage stages up to the results of modern transplantation experiments—all show that cells even of a late generation after the ovum cannot be diminished in their 'determinants'. The cunning hypothesis of the reserve idioplasm, which smuggles into the cells by a back-door the total idioplasm removed from them by unequal division (and which is really nothing less than a relinquishment of the original theory), is totally insufficient to do justice to the multiplicity of these phenomena.

V

VITALISM

WHILST Weismann and Roux have thus regarded development as a process which was carried out by means of a fine machinery contained in the germ, an investigator soon appeared on the scene who approached the question in quite a different way. This was Hans Driesch.

The so-called regulatory eggs of the sea-urchin show, as we saw, that it is not the case that the single cells are determined or preformed for a single developmental function by means of the unequal division of their germ plasm. If we call the actual fate of a part of a germ its 'prospective significance', and its possible fate its 'prospective potency'—all that it is capable of becoming—then we see that the prospective potency of the sea-urchin blastomeres is far greater than their prospective significance. The final fate, the prospective significance, of every blastomere is a function of its position in the whole. The sea-urchin germ is therefore an 'equipotential system', i.e. every single part of the germ can furnish any part of the organism. In the shape of the regulatory egg of the sea-urchin Driesch believed he had found objects in which this proposition was completely realized. Other equipotential systems are certain Ascidians, *Clavellina*, *Tubularia*, which can be cut in any direction and in which, nevertheless, a whole organism can be obtained from every piece.

In these equipotential systems Driesch thought he had found the first and most important proof of vitalism. One might, he thought, quite well explain development by means of a machine-like structure if there were only normal development to be considered, and if the removal of parts led to fragmentary development. But from equipotential systems a whole is obtained, whatever may be removed, and in whatever direction or position this is done. But this is inexplicable on the basis of a machine; for a machine which is differently constructed in the three dimensions of space cannot remain complete when parts are removed or when they are displaced. What is furnished by every part of the germ in regulatory development is, according to Driesch, dependent upon the whole to be reached in the future. According to him, a factor is at work which 'carries the goal in itself', a vitalistic agent, the entelechy.

The second proof is logically similar to the first: development takes its starting-point from the egg, which with a thousand other eggs arises from a primitive germ-cell. According to the mechanistic view the latter is a machine, which can be divided many hundreds of times and nevertheless remains a whole. The idea of such a machine is obviously absurd.

After what has been said in the introductory part (p. 43) we need not here enter into a logical criticism of vitalism, and will therefore restrict our remarks to the criticism of its experimental foundations. The cardinal question is this: Is development really something which 'carries its goal in itself', and must therefore be considered as guided by a purposively working entelechy? Roux (1915, p. 60) has here referred to a very illuminating example, which shows that this is not the case, but that the developmental process is a purely causal one, namely, super-regeneration. One can imagine that a purposeful agency, like the entelechy, may be restrained and baulked in its activity; for the means of such an agency may be restricted and alterable. But that a purposive agency newly creates what is typical, and thus in itself purposive, in places where it is superfluous, and can only do damage, as in Tornier's toads with up to six legs, or lizards with double tails, that cannot be ascribed to a purposive agency. Such activities are unworthy of it. If an agency does this it is not a purposeful one. Super-regeneration is therefore, according to Roux, 'a strong argument for the ateleological, purely mechanical nature, not only of super-regeneration itself, but also of properly regenerative processes'. For that regenerative and super-regenerative processes are identical in their nature there can be no doubt, since all thinkable combinations of the two are found.

The vitalist can, of course, say that in the developmental process a number of subordinate entelechies work together which occasionally, as in super-regeneration, work independently without reference to the whole (1928, pp. 94, 286, 323, 384 ff.).[1] But it must be admitted, even by Driesch himself, that such ideas are very difficult. On the one hand, entelechy is to be a non-spatial 'principle' which governs the material; but on the other hand, it is dependent upon the material, not only in its mode of action which would be understandable, but obviously also in its existence, to such an extent that a cut of the experimenter suffices to make two entelechies out of one.

We come to the proof of vitalism based on the phenomena of regulation. It is indeed completely correct to say that the development of regulative eggs is contrary to the machine theory; the facts of regulation cannot be explained by means of an absurd self-dividing machine which nevertheless remains a whole. But—as has always rightly been pointed out against Driesch—the proof is not furnished that the machine theory is the only possible physico-chemical explanation. The germ is not a rigid apparatus of determinants, but a movable colloidal system which, after displacement, division, or fusion with like systems (likewise after natural division in the second argument), returns again to its proper equilibrium.

In any case we find in the disturbed regulative germ that the course of development is in no wise (as Driesch assumed) dependent on the whole to be reached which it strives as far as possible to produce. On the contrary it is here also dependent throughout on the material conditions of the system. Schaxel (1915) has carried out this proof in detail.

Driesch has displaced, dissected, and united germs and,

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[1] (If this were the case we should require, for normal cases, a 'super-entelechy' to 'guide' the surbordinate ones!) J. H. W.

according to his reports, obtained from all these cases harmoniously developed organisms. From this he concluded that regulative occurrences supervene upon the developmental processes, which still reach typical results by atypical routes—equifinal regulations by means of entelechy, which leads the arbitrarily combined elements to final harmony! Thus in development it is not the preceding stages which determine later ones, but all stages are guided by the goal to be reached—by the entelechy.

This assertion that by means of equifinal regulations typical ends result from atypical beginnings, is, however, false. As regards displacement, in many cases the atypical spatial relations are not maintained, since the displaced blastomeres run together according to Plateau's law. If, however, the displacement persists, then the atypical development leads to the formation of monsters. Boveri (1902, p. 184) says:

> 'The assumption, that in the young germ the protoplasm can be displaced without damage, rests on insufficient experience. I have already shown, and since then can establish more exactly, that slight cytoplasmic displacements at the vegetative pole lead to double monsters, and I have meanwhile also obtained larvae with double, even treble archenterons, and some with strong deformations and skeletal abnormalities from displaced heaps of blastomeres in cases in which the displacements remain and are not undone as so often happens.'

Similarly, Schaxel obtained from eggs of *Strongylocentrotus* maintained long enough in a compressed state, totally atypical structures like stereoblastulae, which neither gastrulate nor yield pluteus larvae, and in which processes which could lead to a typical result are absent (1915, p. 110 f.). Where regulation occurs it is not guided by secret purposive directive forces, but comes about as an accidental result through physico-chemical factors.

Isolation experiments yield similar results. Schaxel tested Driesch's sea-urchin experiments on Asterid eggs. He regularly obtained wholes, atypical and stationary structures. For example, wholes were obtained from isolated blastomeres of the two- and four-celled stages. The four apical cells of the eight-celled stage were stationary as blastulae, and did not gastrulate, the four anal cells became wholes. The eight apical cells of the sixteen-celled stage form stationary blastulae, the eight anal cells wholes. The cells of the thirty-two-celled stage form stationary blastulae, only the eight anal cells yield wholes, and so on. How does the production of wholes come about? If a blastomere is isolated it must behave like the egg, if it has lost nothing through previous divisions, and if it can restore its particular form. The same holds for the isolation of groups of blastomeres; two blastomeres, for example, of the four-celled stage after isolation take up an arrangement corresponding to that of the blastomeres of the typical two-celled stage. At the same time its content is carried over from the arrangement of the quarter-spherical form to the hemi-spherical form. A two-celled stage in typical proportion but of half-size is thus produced and a typically proportioned whole develops from it. Corresponding remarks hold for all cases of typical whole-formations from isolated blastomeres, which always occur if the cell material and the cell displacements lead to a grouping of the blastomeres, and an arrangement of its content thus brought about, which is proportional to a stage of the typical development.

In the case of fusion experiments, finally, we know, since Boveri's experiments, that unitary formations result if the axes of the germs to be united are parallel, otherwise double formations result.

The error which Driesch committed lies, according to Schaxel, in the fact that he simply attributed primary importance to the result of typically proportioned wholes when he obtained them, and regarded the other formations as approximations to the ideal whole formation. With the same strict necessity wholes, stationary structures and atypical ones, all proceed from the starting-point. From typically proportioned initial material typical wholes arise. Thus the formation of typical embryos is not the work of regulations striving towards a goal, but the necessary result from the original constitution. If, however, the beginning is atypical, so must the end also be atypical. The entelechy is not a natural factor *sui generis*, not because other, e.g. physico-chemical, factors yield what the former is supposed to yield, but because the function ascribed to it is not exhibited at all. The problem of atypical regulatory development is a pseudo-problem raised on the ground of insufficiently elaborated experimental results, and hence neither requiring or admitting of a solution.

In a similar manner recent investigations on the sea-urchin egg have demonstrated the strict dependence of developmental results on the constitution of the isolated part, and above all have shown that the sea-urchin egg is equipotential in a far more restricted degree than Driesch assumed. According to the careful investigations of Hörstadius (1927, 1928), purely vegetative halves yield larvae without ciliated tuft, stomodaeum, or ciliated band, purely animal halves cannot gastrulate. Also, in the case of transplantation, gastrulation is only possible in the presence of vegetative material (fusion of two animal halves). As a whole the sea-urchin egg is not an equipotential system, although the ectoderm and endoderm are.

This refutation of vitalism must not be misunderstood: various authors, Bavink (1929, cf. also my reply, 1930 *a*) among others, have objected that the critique here given does not do Driesch justice. The limits which are set to the powers of the entelechy, e.g. in incomplete regulation, the stupidities which it sometimes exhibits, as in the formation of super-regenerates, cannot refute its existence—just as it is no disproof that man possesses understanding because he is not omnipotent or because he sometimes exhibits stupidities in difficult situations. Now, the results mentioned certainly do not show that no entelechy can be present in the germ; what they show is something quite different: namely, that this assumption is superfluous, since the entelechy does nothing that exceeds the functions of the immanent forces of the living system (which yield atypical results in the case of other initial conditions). But as a natural scientific theory vitalism remains condemned: if the course of regulative as well as of atypical development depends completely on the material conditions of the system, then the investigator will not introduce superfluously into his working hypothesis a factor which, as we see, destroys it from the bottom.

The deepest consideration against vitalism consists in the remark that it represents just as much an additive point of view as does the machine theory. According to Driesch it is a fundamental feature of development that it proceeds 'along separate lines' (1928, p. 86); for him the germ is a 'summative conglomerate' (1919, 1923) of independent parts developing in strict self-differentiation. The transcendent entelechy enters into a mere sum of cells developing in separated series. Just because Driesch does not recognize an organic totality he is compelled to assume a metaphysical totalizing factor, the entelechy. Vitalism as well as the machine theory dissolves the organism into atomistic single parts and processes, and they differ only in so far as the latter adds a transcendent purposeful principle. But so soon as we regard the germ as a unitary material system, regulatory development in no way compels us to introduce such a factor; although naturally the question remains, whether and how far we are in a position to explain its working by physico-chemical concepts. This question will be considered more closely in the following chapters.

VI

GOLDSCHMIDT'S PHYSIOLOGICAL THEORY OF INHERITANCE

SINCE neither the machine theory nor vitalism gives a satisfactory explanation of the developmental process, we must look round for further possibilities. The view which undoubtedly has most affinities with contemporary ideas is that which regards the developmental process as a chemical one.

A few years ago it was still possible for Driesch (1921, p. 125) to say that one of the logical possibilities for a theory of development—the chemical theory—was still not yet systematically worked out, although such a view had been hinted at by very many authors. But now the situation is quite changed, for in Goldschmidt's *Physiological Theory of Inheritance* (1927) we possess a theory of this kind, which is, in fact, since the systems of Weismann and Driesch, the greatest, broadest established, and most comprehensive modern theory.

Goldschmidt's starting-point is genetics. Genetical research has found the bearers of heredity in the form of the factorial genes localized in the chromosomes. It has discovered the *mechanism* of heredity. But the Mendelian factorial analysis gives no account of the occurrences which fill the interval between the genes as starting-point and the different inheritable characters as end-point; about the *physiology* of the developmental processes in which the inherited dispositions are realized it says nothing.

Development means the origin of 'patterns'. Between a pattern of markings on the surface of an animal and, say, the differentiation of a strip of ectoderm into medullary tube, between the striping of a hair by pigmentation and the segmentation of the mesoderm, between the development of notches in an insect's wing or on the edge of a leaf, and the formation of the border of a flattened organ, say, of a crustacean extremity, of a fish's wing or of a muscle-bud, there exists no fundamental difference—all these processes mean the formation of a 'pattern'. Now we know that the processes named first in the above pairs of developmental phenomena—patterns of markings, pigmentation, formation of borders—are conditioned by Mendelian genes. We may assume, on account of the essential similarity of both kinds of developmental processes, that the phenomena named second in the above pairs, e.g. formation of medullary plate, segmentation of mesoderm, formation of extremities, are conditioned by genes in exactly the same manner, even although, for obvious reasons, these are not accessible to Mendelian analysis.

When we consider which set of data is likely to offer the best insight into the physiology of developmental processes, those relating to the *determination of sex* suggest themselves. We know that the determination of sex rests on the transmission of chromosomal genes. Sex behaves like a Mendelian backcross, since one sex is homozygous, with two X-chromosomes, the other heterozygous, with one X-chromosome. In every individual genes are present for the development of both male and female characters. In the butterfly, for example, the female has one X-chromosome and the male two. The effect of the male factor contained in the one X-chromosome is overcome by that of the female situated in the autosomes or in the Y-chromosome. Only when two male factors come together do they attain the preponderance. The empirical starting-point for the whole theory was furnished by Goldschmidt's experiments with *Lymantria dispar*. By crossing European and Japanese races of the Gypsy moth sexual intermediates, the so-called intersexes, were obtained. Goldschmidt interpreted their origin by distinguishing between 'strong' and 'weak' races. For example, if a female of a 'weak' race is crossed with a male of a 'strong' race, female intersexes arise, since the inherited 'weak' female-producing factor is not able completely to overcome the 'strong' male-producing factor, over which it should dominate in the production of a normal female. Analysis shows that there are different degrees of 'strength' and 'weakness'. But since, in the normal case, it is a quantitative relation, i.e. two X-chromosomes determine a male, and one X-chromosome a female, which is decisive, so it may be concluded that in the relation of the 'strong' and 'weak' races it is again the *quantity* of the sex-genes which is decisive. Closer investigation shows that an intersex is an individual which up to a certain moment develops according to its gametic sex, but from this moment, the 'turning-point', its sex changes and development ends in the opposite sex. If the turning-point is late, we have a weak, if it is early, we have a strong intersexuality. Since genes for both sexes are present 'determination' means that the chain of reactions proceeding from one of these genes overcomes the other. If the genes in normal mating within a given race are quantitatively adapted to one another, then the sex reaction of the opposite sex which is always present is eliminated, and we obtain normal males and females. If, however, the quantities of the genes in crossing a 'weak' with a 'strong' race are not in the right proportion, if, say, we bring the female factor of a 'weak' race into relation with the male factor of a 'strong' one, then we obtain a genetic female, but from the turning-point onwards the strong male factor gains the upper hand, and from this point onwards we obtain an intersex.

When we ask ourselves what the nature of the genes may be, we find (1) that they must exert their extraordinary effects in extremely small quantities; (2) that they are capable of restoring their quantity more or less after every cell-division; and (3) that the quantity of a gene is proportional to the speed of a certain reaction. These facts agree with the assumption that the genes possess the properties of a catalyst, especially of an autocatalyst. Since the chromatin substance is supposedly of almost the same nature in the whole organic realm, it is assumed that this is not identical with the genes themselves, but that the latter are only situated in the chromosomes.

From the activity of the genes proceed the substances which determine development. These formative substances are subsumed under the concept of hormones. The action of hormones in the old sense is characterized by three features: they are not species-specific, they are distributed in the last resort by diffusion through the body, and their action presupposes the presence of a *substratum* in the right state capable of reacting. That the assumed developmental hormones agree in the second and third points with the 'true' hormones, results from the whole analysis (see under chemo-differentiation). As regards lack of specificity the experiments of Geinitz are cited, in which a toad's organizer exerted its effect on the embryo of a newt. In view of this, application of the concept of hormone to the formative materials appears permissible.

These results on sex determination are now generalized by Goldschmidt over animal development in general, and thus, from the experiments on *Lymantria*, we obtain three consequences of general significance. *First*, the velocity of the sex determining, and of every developmental reaction, is proportional to the quantity of the genes present. *Secondly*, the male and female sex-determining reaction, and in general all developmental reactions, run alongside one another, and the faster reaction controls differentiation. *Thirdly*, sex determination—and every developmental process—is conditioned by determinative stuffs which proceed from the genes.

The developmental process is thus analysed into a series of processes running simultaneously in which the typical succession of the single reactions is rendered possible by the proper dosage of genes. Thus, Goldschmidt points out that the 'quantity of the genes at the beginning' is determinative not only in the case of sex but in inheritance generally. This holds, for example, for the different grades of melanism in *Lymantria* larvae which are conditioned by multiple allelomorphs, for the bar-mutations in *Drosophila*, and finally for Mendelian dominance in general, as well as for polyploid mutations, gene-mutations, &c., most of which are to be regarded as quantitative. We shall not enter into more detail regarding these important considerations since we are not here concerned with inheritance but with development, and pass on at once to Goldschmidt's investigation of 'co-ordinated reaction velocities' as the basis of development.

As the starting-point we have the egg, which experiences its 'primary chemo-differentiation' in part in consequence of its relation to the maternal organism, and partly by means of a reaction starting from the genes, and this differentiation is characterized by the appearance of 'organ-forming materials'. (That the pro-morphology of the egg also depends on the genes is shown by the fact that certain egg-structures, e.g. the egg-shell, show Mendelian inheritance; as well as the right and left twisting of the snail which manifests itself at the beginning of cleavage.) In this way Goldschmidt skilfully circumvents the opposition of genetics and experimental embryology, of which the first regards the characters as dependent upon chromosomal genes, whilst the latter finds them to be dependent on cytoplasmic organ-forming materials, an opposition which, as is well known, led Boveri, Conklin, and Loeb to the assumption that only racial and individual characters are dependent on the nucleus, but the higher systematic characters on the cytoplasm.

The organ-forming materials are then *localized*—the first example of the formation of a pattern in the domain of ontogeny. Localization is a process of *stratification* on the basis of the physico-chemical conditions of the system. In the polyphasic system constituted by the organ-forming materials a condition of physico-chemical equilibrium is necessarily produced. The stratification is thus independent of cleavage, as is shown by the example of 'differentiation without cleavage' (Lillie, *Chaetopterus*), and also by the mosaic eggs.

Mosaic and regulative eggs are distinguished by the difference between them in the time of localization of the organ-forming materials, these being already produced in mosaic eggs before, in regulative eggs only during, segmentation. Up to the conclusion of the primary chemo-differentiation the germ is a unitary physico-chemical system. This system possesses a state of equilibrium for each of its phases, the qualitatively different materials. If the whole system changes, say through reduction to one-half (isolated 1/2 blastomere), then a new state of equilibrium is produced. In this way a physico-chemical explanation of regulation is obtained, and the supposed proofs of vitalism based on the occurrence of such processes fall to the ground. In the case of the extremely regulative eggs, e.g. the newt with its organization centre, the germ remains a long time a chemical unity, from the organization centre a stream of determinative materials ('hormones' in wider sense) proceeds. With the organ-forming substances later, perhaps at the time of gastrulation, other gene-catalysts react and now cause the formation of organs. In every organ the same game of the catalysts proceeds, continually new genes begin to work as soon as their specific substratum has appeared. In such a way, a relatively small number of gene-catalysts and of organ-forming materials may, by their various interactions, yield an infinite number of reactions, and, in consequence, of developmental processes.

In detail, development is guided by means of the principle of harmonized reaction velocities. A disturbance of these, e.g. a retardation of a reaction in consequence of a quantitative insufficiency of the relevant formative materials, means a pathological delay in the development of an organ, which, in many cases, is regarded incorrectly as atavism. The correct harmonization of all reactions among one another guarantees normal development.

In like manner the problem of regeneration may be solved. The pre-requisite of regeneration is that the stump should return to the same initial chemical state which, in normal development, introduced the chain of reactions leading to the formation of the organ concerned.[1]

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[1] How and why wounding re-establishes the chemical initial state of the tissues remains a problem.

In this way the phenomena of regulation and regeneration, which form the foundation of vitalism, receive a chemical explanation. By means of the principle of harmonized reaction velocities an explanation is provided for the harmony, control, and co-ordination of the developmental processes; the theory is strictly mechanistic, although not a machine theory, but a theory of polyphasic chemical systems.

How, by means of the principle of harmonized reaction velocities, the origin of all 'patterns' of form in the organism can be explained, Goldschmidt has shown in an ingenious and profound investigation of the pattern of butterflies' wings. The latter pattern of markings is already preformed in the quite embryonic wing, since in certain places the scales are still soft sacks, whilst in others they are already chitinized. The different areas of the pattern are thus distinguished by different velocities of reaction. The cause of the pattern must therefore be a process which gives to the different epithelial regions different rates of differentiation. The latter then conditions further the different deposition of colour materials in the scales, their different form and surface-structure, &c. Relatively simple quantitative processes are thus able to produce a great multiplicity in the pattern. The different distribution of the determinative stuffs in the wings which forms the foundation for the different rate of differentiation is, however, itself conditioned by a process of stratification, resembling Liesegang's figures, i.e. by a process of stratification, in the same way as the distribution of organ-forming materials in the egg is brought about. As colour mutations show, the wing pattern is dependent upon genes, whence the dependence of pattern upon genetic constitution is once more proved.

We must bear carefully in mind that the assumption that *every* developmental process is determined by determinative materials, plausible though it may seem, nevertheless far oversteps the limits of present-day knowledge. In the mosaic eggs, chemically different areas seem to be really demonstrated, but in the more ambitious attempts at explanation along these lines we come to chains of hypotheses which are not at all free from arbitrariness. Suppose it is a question of interpreting Harrison's results, in which transplanted limb-buds become right and left legs according to the place of their transplantation, not according to that of their origin, whilst the determination of the antero-posterior axis has already occurred in the bud. Goldschmidt (pp. 159 ff.) interprets this by means of the following determinative materials and processes, which are simply 'postulated' *ad hoc* and for the existence of which we possess very little evidence: *First*, the hypothesis of organ-forming substances for the buds in general, whose existence is not at all demonstrated since at present such materials are only definitely known in the mosaic eggs; *secondly*, the stratification process, which is to effect the localization of these materials in the buds —this is a process which we know in inorganic phenomena but the significance and action of which in the organic sphere is again entirely hypothetical; *thirdly*, a determining effect of the whole on the bud; *fourthly*, a dorso-ventrally running stream of determination, in the shape of a formative material which effects the dorso-ventral determination; *fifthly*, another stream which is responsible for the antero-posterior direction, and is just as hypothetical as the former one.

Nevertheless there can be no doubt that the description of chemo-differentiation put forward by Goldschmidt is quite right in essential points—although at present it represents merely a general scheme which must later be filled out with concrete data. We think that, so far as the first stages in the development of the germ are concerned, the formation of chemically different regions, their localization, and the distinction between mosaic and regulative eggs, are explained in a very satisfactory manner in Goldschmidt's theory. The explanation of germ regulation is completely convincing. We see here the great progress of the physico-chemical theory of 'polyphasic systems' as contrasted with Weismann's rigid germ machinery, a progress which disposes of the vitalistic arguments of Driesch Goldschmidt does not say too much when he emphasizes, as against Child, that his 'purely mechanistic' theory, which, however, is not a machine theory, explains the order, co-ordination, and control of development—features which remain inexplicable for the machine theory and the atomistically conceived genetics and therefore lead to the introduction of vitalistic entelechies.

One requisite is, however, presupposed, namely, the existence of this unbelievably complicated chemical mechanism itself, this cosmos of chemical compounds in which every substance appears just when it is wanted for the production of an organ, under normal conditions just in the quantity requisite for the development of an harmonious organism and not a monstrosity, and just at the place, moreover, where that organ belongs, and at the time when this organ must begin its development in order to fulfil its place at the conclusion of ontogeny. The problem of organization is not exhausted by calling the germ a polyphasic chemical system. We must not forget that this chemical system, adjusted internally to bring forth a definite organic form, is not in any way comparable with any chemical system which is known to us in the inorganic world. It is equally certain that the selectionist's rigmarole does not suffice for the explanation of this chemical cosmos.

The primary chemo-differentiation, the separation of the organ-forming regions, can doubtless be interpreted as a process of stratification. The next question is whether this explanation is also sufficient for the further progress of development.

Goldschmidt himself has not the least doubt on this point:

> 'At a certain moment a certain part of the germ is so determined that it will provide, say, the dorsal half of the embryo. Then, after a certain time, there appear in this part also secondary determinative points, say for the epidermis and primitive gut, in the manner already described. Then comes a third system of determinative points, e.g. the neural tube within the epidermis-system. Upon this there follow

the determinative points of the fourth degree, for optic vesicles, medulla, and so on. And so the process goes on, the whole development dividing into a system of determinative points fixed according to their succession, time, and place, and these, as already explained, serve to show that development is explained in essence by means of the gene-conditioned system of co-ordinated reaction velocities.' (1927, p. 147.)

Now there can be no doubt that this description of development is in essentials quite right from the standpoint of the chemist. The latter finds in this process a progressive chemical differentiation, and this at the same time signifies determination. But the question still remains whether this chemical formulation exhausts the process: development is chemo-differentiation—but is that its only, its essential characteristic?

When the gene-enzymes encounter the organ-forming materials, it may well be that here skin and there nerves or muscles are formed. But that these organize themselves into endlessly complicated structures—what has that to do with a chemical reaction? If the theory gives an explanation of the *chemical* problem of development, it gives so far no explanation of the problem of form production.

But wait! For one particular morphogenetic process, for one 'pattern' as he calls it, Goldschmidt does give a comprehensive explanation: for the pattern of the butterfly's wing. This pattern depends upon the unequal differentiation velocity of the single parts of the wing, and the latter depend upon the unequal distribution of the determinative materials according to the principle of Liesegang's rings or some similar physical analogy. Here we have an ingenious attempt to explain the real problem of form. But let us ask the question whether it is applicable to morphogenesis in general.

From the few hints which Goldschmidt gives on this point it is clear that he proposes to interpret the development of every other form, e.g. the limb-buds, in the same manner: by means of the system of harmonized reaction velocities which is set in action by means of the unequal distribution of the determinative stuffs. This would involve, roughly, the following interpretation of morphogenesis: the development of the form of the organ is conditioned by unequal growth, spreading of the cells, invaginations, &c. Cell-division is conditioned by determinative materials in the manner of Haberlandt's cell-division hormones, the resulting differential velocity of cell-division being brought about by their unequal distribution. But the latter is the consequence of the formation of a 'pattern' in the polyphasic system which constitutes the developing organism, namely, of a stratification after a manner comparable to Liesegang's rings.

The problem nevertheless does not appear to be solved in this way. For we have no ground for assuming that every developmental process must go hand in hand with chemical differentiation. The fundamental difficulty which confronts the chemical theory is that presented by the question of the production of organs in their proper 'place and form', a problem to which Driesch long ago called attention (1928).[1] We can here bring forward an example described by Gurwitsch for another purpose, namely, that of the developing mushroom.

[1] 'In the first place, a chemical theory would not be able to explain the fact that in the finished organism there are not as many different combinations as there are particular constituent organs, but that, on the contrary, it consists of a certain fairly restricted number of true chemically different elements of form which, for their part, e.g. nerves and muscles, are repeated again and again, and each time typically as regards place, size, and form. Secondly, the form of the elementary organs as such does not go hand in hand with chemical differences: that alone would exclude every *purely* chemical theory of development which attempts to explain the problem of localization. . . . When we consider the various kinds of skeleton, in the Radiolaria, in starfishes, or in vertebrates, we see true form, but form which is always expressed in the same material. What is typical here is not only the *arrangement* of the constituents of form, e.g. of the single bones of the hand or foot, but also the *particular* form of every single bone constituent is typical, e.g. that of every single bone of the foot. A purely chemical or colloidal theory of development could never give the sufficient reason for typical development in this sense.' (1928, p. 114.)

A mushroom consists of a material growing irregularly at the circumference of the hat-like form, the felt-work of the fungal threads. Here we find no chemo-differentiation, no separation of organ-forming materials, no unequal distribution of determinative substances, which must be the foundation of all development according to the chemical theory; instead we find a wholly homogeneous material which nevertheless attains a definite form. Moreover, there is at least the appearance that the same holds for all cases of organogeny. The endlessly complicated system of bones, the elaborately arranged muscles of the arm or leg, consist—so far as we know—of fairly uniform cells, not much different from the case of the mushroom. Chemically homogeneous material, muscle-, bone-cells, reaches an organization endlessly complicated in form. Thus it seems that, in embryonal development, in addition to chemical differentiation, there is yet another factor, a particular formative factor. (As regards morphogenesis in the Fungi, see also the new investigations of Hein, 1928, who comes to the conclusion —quite similar to our own—that the cause of form development of the fungi is a 'morphaesthesia' in the sense of Noll.)

We do not wish to attach too much weight to the subsumption of the formative materials under the concept of hormones as urged by Goldschmidt. Meanwhile, it may be pointed out that the action of true hormones produced by the glands of internal secretion is not directly comparable with that of the hypothetical stuffs which are regarded as arising from the genes and as the prime movers of development. The essential objection is this: the action of the hormones is *not* a localizing one, they cannot in an indifferent tissue determine the place of origin of a new organ. Take, for example, the famous tadpole experiments of Gudernatsch: feeding with thyroid substance naturally did *not* determine that at a definite place legs were formed, &c., but it only accelerated their development. In contrast to this the action of the formative substances must be supposed as a localizing one: they are required to determine the place of new differentiations. The transplanted organizer, for example, excites the development of a secondary neural system in places where is it never normally formed, and, similarly, the organ-forming materials of the egg represent new rudiments whilst hormones only *stimulate* already existing ones.

This distinction suffices, for the purposes of a general discussion, to show the deepest difficulty which a purely chemical theory of development has to encounter. If this is correct, can the comparison of the developmental processes with the action of hormones be a support of the chemical theory of development? A hormone requires 'rudiments' (*Anlagen*) which it stimulates into development. A hormone, i.e. a fluid with a definite chemical composition, cannot, by reacting with another chemical compound, produce beards, or breasts, or fore-legs of a tadpole. It can only act by stimulating some embryonic rudiments to further development. But the theory requires that in the egg-cell there are only chemical materials (e.g. gene-enzymes and organ-forming materials) which, by acting upon one another, are capable of accomplishing the unheard-of wonder, namely, of crystallizing out of themselves the whole elaborated organization of the living being. Here we see the great paradox of every chemical theory of development. Weismann was perfectly aware why he must distinguish his determinants from all chemical compounds. There is no escaping from the fact that embryonic *Anlagen* are more than chemical compounds.

In other words, merely by drawing a parallel between 'true' hormones and formative stuffs we cannot conceive development as a *purely* chemical reaction. We must not only take into account chemical reactions which would only yield chemical stuffs, never a gradually increasing organization; we must consider too the specific vital organizing relations. A chemical reaction-system, which is what the germ is according to Goldschmidt's theory, does not execute that 'rise in the level of organization' which we found to be the essential feature of development. Whether these vital relations themselves are to be resolved physically is another question; but we cannot abstract from them without leaving the essentials of development unaccounted for. Development cannot be interpreted as though it were *only* a phenomenon of colloidal chemistry.

There are two fundamental developmental problems. The one is the problem of organization; the other the problem of evolution, i.e. the assumption that the organism is developed from an accumulation of deposits formed in the course of geological epochs, from which it goes on increasing in multiplicity. Neither problem can be exhaustively dealt with from a purely chemical point of view. We have just seen that this is so as far as the problem of organization is concerned. The same holds for the double problem of accumulation and evolution; for in the realm of chemical combinations we find no analogue either for phylogeny, the historical accumulation of deposits, nor for their progressive change in visible multiplicity of organisms. That is the great unbelievable wonder: in every human germ lies the whole past extending over millions of years—protozoon, worm, fish, amphibian, reptile, primitive mammal—and is now repeated in the nine months of individual development. Since the ontogenetic repetition of ontogeny (or however we may choose to formulate it, the fact itself cannot be denied) has no analogue in those processes which we know in the domain of the inorganic we cannot resolve development into purely chemical reactions.

Here we are confronted with the two fundamental problems of the organism of which mechanism for the most part takes no heed, whilst vitalism touches only the first, the problem of organization, by starting from a false statement of the problem. We cannot abstract, as does mechanism, from what is the essential characteristic of life; equally we cannot, with vitalism, transfer the problem into metaphysical regions; we need to investigate these fundamental problems with scientific methods. The future path for biological investigation is marked out by these two problems; in them—not in metaphysical spectres—the problem of the *autonomy of life*, resisting solution as it does by our current conceptual methods, appears in all its force.[1]

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[1] For further discussions of Goldschmidt's theory see also Baltzer, 1928; van Bemmelen, 1928; Morgan, 1926; Spemann, 1924.

VII

ORGANIC AND INORGANIC FORM

1. The Crystal Analogy

OUR previous discussions have led us to the view that in organic development there is the question of organizing relations which the chemical theory is not able to explain, and which vitalism wrongly conceives as a supermaterial entelechy. Now we may either seek in the realm of the inorganic sciences for possibilities of explaining it, or we may try to explain it by specific biological assumptions.

The crystal analogy belongs to the considerations of the former kind. The idea of interpreting development, nutrition, growth, and movement of organisms by analogy with crystals is not new. Spencer had already compared the development of organisms with the process of crystallization. Rauber (1909) among others pointed out the parallel between the replacement of damaged crystalline form and the regenerative processes of organisms. H. Przibram has developed the crystal analogy into an extensive theory.

By regarding both crystals and organisms as equilibrium-systems on the basis of a space-lattice structure it is possible, according to Przibram, to apply the unitary causal point of view to organisms (1926, p. 9). The comparison of the form and energy changes in living and lifeless systems allows the 'establishment of the essential subordination of living things under the laws of the inorganic world' (p. 147). The chief objection to the crystal analogy was that whilst crystals consist of homogeneous material, organisms are composed of heterogeneous parts. In answer to this Przibram points out that crystals themselves are not strictly homogeneous since, according to the newer ideas, they are constituted by interpenetrating space-lattices of the various kinds of atoms (p. 200). On the contrary, there is an essential identity between them since both in crystal and organism vectorial potentials are given which determine the form of both. Organic regeneration, especially, finds its prototype in crystals. If we remove the point from an alum crystal, and then return it to the mother liquor, it first regenerates the point before it continues to grow. Or if we break a haemoglobin crystal into small splinters each fragment will transform itself into a complete small crystal—in a manner resembling the dissected *Tubularia* of which every piece becomes a small complete organism by morphallaxis. Regeneration and morphallaxis of crystals present the same achievement for which according to Driesch a mystical entelechy is necessary: namely, after any arbitrary injury to be able to reproduce the whole.

The weak points of the crystal analogy are not difficult to discover. As regards the material aspect the contrast between homogeneous crystals and non-homogeneous organisms is not set aside by Przibram's formulation. For in the interpenetrating crystal lattices the chemically homogeneous substance is distributed in an orderly way, whilst it is the essence of the organism to represent an arrangement of different substances. Just the essential feature of the organic, that there is no sea-urchin or human substance, as there is alum or copper sulphate, is entirely lost in the crystal analogy. As regards the problem of development Driesch has said all that is essential:

> 'Organisms arise from beginnings which possess less visible manifoldness than the end, namely from eggs. Crystals are always themselves and properly only possess the property of growth. A third difference can be found in the fact that crystals, during their growth, make use of the specificity of the medium, whilst to organisms the medium is only a means to growth, and their specificity lies in them themselves.' (1921, p. 404.)

No one will wish to deny that a difference exists between the regeneration of an alum crystal occurring in mutual action with the mother liquor and the regeneration of a lizard's tail resulting from organizing potencies situated in the organism itself, or equally between the transformation of a broken-off piece of a haemoglobin crystal consisting of a single substance, and the redifferentiation of a piece of a *Tubularia* consisting of the most diverse tissues, into a whole organism. If, however, the general analogy is freely admitted, yet the forces at work in the two cases are certainly quite different. Przibram's hope of being able to bring the organic occurrences under the laws of the inorganic by means of crystal analogy can thus scarcely be said to be fulfilled.

2. The Gestalt Theory

Now we come to the most general attempt to deprive the organic wholeness, not only of development, but of vital regulation in general, of its apparent autonomy. This is the Gestalt theory, mentioned already in the first part.

Köhler has applied this new point of view especially to embryological problems (1922, 1927). He begins with the assertion that the reactions in the organism do not proceed arbitrarily but are co-ordinated both in the healthy and diseased organism in accordance with the requirements of the whole. This problem is not satisfactorily dealt with by assuming that all the various processes occur in accordance with laws; forces independent of one another do not lead to an ordered result. The question why the reactions are always suited to the state of the whole cannot be set aside as 'philosophical', since it is a question of objective fact and perhaps the most striking one in the whole sphere of vital phenomena. Moreover, the objection that we can only deal with this 'causal harmony' when we know more about the nature and laws of the particular processes does not hold, because, according to the foregoing view, the problem will still remain unsolved, however well we know the particular reactions in isolation. An important biological point of view is therefore absent which must be provided for. Alongside that of the 'vitalists' who invoke supermaterial powers for the interpretation of the mutual co-ordination of the organic processes, and that of the 'mechanists' who believe this to be guaranteed by a preformed machine-like construction, yet a third view is possible. Mechanism fails because it has no explanation for the origin of the assumed mechanisms. The

Darwinian selection theory breaks down before the multitude of repair-mechanisms which have to be supposed to exist already preformed in regulative eggs in anticipation of possible injuries. But although Driesch's arguments based on regulation of the germ are convincing enough against the machine theory they do not constitute proofs of vitalism. For, that the properties and functions of a part depend on its place in the whole, is not a privilege of organic germs, but rather is a fundamental property of all structures with which the Gestalt Theory deals. A similar 'wholeness' is found in psychology: visual percepts cannot be atomistically and mechanistically explained. But here we do not need to enter into the physical explanation of 'psychical *Gestalten*' (configurations) which Köhler has attempted. His biological conclusions are as follows. In machines the co-ordination of the processes is not entrusted to the forces and energies which work in them, but to the particular arrangement of the parts or its fixed structures. The theory of physical 'configuration', however, deals with the organization of processes which proceeds from the internal forces themselves. Every system to which the second law of thermodynamics applies reaches sooner or later a state of equilibrium. This 'stationary distribution', arising spontaneously from inner dynamic conditions, is—in contrast to 'mechanical distribution' by means of fixed structures—characterized by the fact that the momentary state of every part of the system determines that of the other parts. An example is furnished by electrostatic equilibrium: the charge, which, in a system of condensers connected by fine wire, must be carried by *one* condenser, if the whole is to be in equilibrium, is, apart from its capacity, dependent upon that of all the others. Thus that the parts behave in correlation with the whole is not, as Driesch believes, a fact inexplicable by natural science, but quite a general phenomenon. Organic processes are explicable by means of two assumptions: (1) that the internal forces of living systems are directed towards states of equilibrium, and (2) that this direction holds for the system as a whole. This self-regulation of the organism is wonderful enough in its details, but, in principle, every connected system of the inorganic world in which the grouping of internal forces is directed towards equilibrium, behaves in the same way (Principle of Le Chatelier, which says that if *one* parameter of the system is altered all the others change in such a direction that the first change is counteracted, and the system is again brought to the stationary state). In this way Driesch's paradox is elucidated. Because the organism is a unitary system, what happens at a given place is determined according to its relations in the whole. If, for example, it is found that an egg which has been artificially compressed is able, subsequently, to reach its normal developmental goal, then we cannot—as Driesch rightly says—interpret this by analogy with a machine, because a machine, having a fixed structure of parts, cannot perform such a regulation. But in a system with several degrees of freedom, even in an inorganic one, the occurrences in every partial region will be directed by the whole. Admittedly the organic system can impose fixed structures on itself, e.g. in the mosaic eggs the organism approaches to a very large extent to the condition of a machine with a fixed mode of action. We can, however, suppose that the 'purposefulness' and 'striving towards a goal' of organic processes is nothing else than the outcome of communicating systems of causally determined processes, the inner dynamical conditions of which tend towards equilibrium.

In a more recent investigation (1927) Köhler has worked out his point of view in more detail. The more we learn about 'regulation' in the organic world the clearer it becomes, as Köhler says, that biological theory is approaching a critical turning-point. The machine theory can no longer be regarded as sufficient, since the capacity for regulation of organic processes proves itself to be so universal. The only escape from the present impasse in the controversy between mechanism and vitalism is provided by a system-theory which seeks among inorganic processes for the principles which are relevant to the understanding of the phenomena of regulation. Regulation concerns the direction of natural processes. We have to find a principle according to which systems under a multiplicity of conditions may exhibit a multiplicity of different processes through which in the end the same or essentially the same total state is reached as is ordinarily reached 'without disturbance'. At the present day in physics only the second law of thermodynamics is regarded as a statement about the direction of the changes in a system. But the specific state in which equilibrium consists, e.g. the specific distribution of equilibrium on an electrically charged conductor, cannot be conceived by means of the second law alone.

We therefore require a directive principle for the reversible processes, which Köhler formulates as follows: 'The forces tend to maintain the potential in the whole at a minimum', or—since minimum potential means the state of equilibrium—'the action of the forces is directed towards the approximation of the system as a whole to its condition of equilibrium'. Since it relates to the forces, this principle of direction may be concealed since the movements of parts of the system may take place contrary to the meaning of the law. E.g. the movement of a pendulum after passing the position of equilibrium is opposed to the direction of the force of the earth's gravitation. This rests on the inertia with which, having reached the lowest point, it moves through the position of equilibrium. Systems of this kind show no capability of regulation. But regulation is possible when a system is not conservative but follows the second law, when the persisting velocities of the parts of the system disappear so far as the macroscopic behaviour is concerned and pass over into disordered 'microscopical' heat movements. The slow processes involved in morphogenesis, at least, can be said to happen with strongest 'friction'; all such enduring velocities therefore are absent, and the principle of direction for the totality of the forces becomes entirely a principle of direction of the actual movements. Thus it is a general property of such systems that they 'regulate' themselves. From different initial conditions they always pass into the same final state. If a change of the *conditions* of the system occurs, then for such a disturbance there will in general be no regulation; the *processes* will then take another course and lead to another final state. If, in a cylindrical vessel, materials of different specific gravity are mixed, they will arrange themselves in horizontal layers according to their specific gravities. If, however, we have some grains of shot, and at some height above the floor a sieve is placed, through which they cannot pass, then the final state is dependent upon whether the grains of shot at the beginning were above or below the sieve. In such cases a part of the conditions of the system makes certain regulations impossible. Such restrictions can come about, however, in the processes of the system itself. Considerations quite similar to those just mentioned for mechanical systems also hold for systems in which different kinds of forces are active. Among the processes in such systems we may find such which constitute irreversible changes, e.g. chemical reactions, which lead to the precipitation of certain substances, so that new, unchangeable conditions of the system are produced. If now a disturbance occurs the new condition may stand in the way of the attainment of equilibrium. The system will come as near as possible to the 'normal' final state but without actually reaching it. In this way we should have incomplete regulation.

After having stated and treated, in our first part, the question of physical reducibility in its general aspect, we now have to examine the possibilities of such a reduction from the special standpoint of the developmental processes. Ungerer (1930, cf. also Driesch, 1925, 1927) formulates as follows the chief objection to be raised against a comparison between physical *Gestalten* and organic wholes:

'The difference between the "configurations" chiefly dealt with by Köhler, e.g. the distribution of charge on a condenser, and biological "wholeness", lies especially in the fact that in the former the physical *form* (e.g. of the conductor) is something given from the beginning and the configuration concerns only the physical *state*. "It is not the physical form which is produced or restored after injury, the parts do not order themselves into a whole in dependence on an event, but a state as a whole is dependent on the 'rigid' form, a state which cannot be obtained by putting together independent parts just because it depends on that form." We cannot speak, therefore, of a "wholeness of form" in the biological sense, i.e. of the persistence of the total form in spite of change in the partial processes and even in spite of changes in the single components of that form. As regards "wholeness of process" the physical configurations (Gestalten) are rather more relevant—although even here we do not have a total event happening in the sense of a succession of different single processes belonging to a whole, but a state within a process persisting uniformly under constant conditions. If, in the case of configurations, we are to speak of "relations of wholeness", then we have to deal with examples which are of very simple type, a mere "wholeness of states" which is clearly distinguished from the wholeness of the organic processes as seen, for example, in the process of assimilation and dissimilation which maintains itself as a whole. The preservation of total form which we see in solid and fluid crystals and is manifested in their regeneration stands somewhat closer to the wholeness of organic form. But even this, in consequence of the uniformity of the law of their construction, and the absence of complicated metabolic processes, is something much simpler than the maintenance of the wholeness of the living organism. In the latter "wholeness", as the wholeness of a process, means the maintenance of a great number of different simultaneous or successive processes connected with one another under changing conditions of the system, and, in addition, a production of previously non-existent conditions for the maintenance of the system by means of the system itself. Wholeness as wholeness of form of the system means the production and maintenance of the structural relations conditioned by the processes in the system itself, in a direction which is such that, under various conditions, the system diverts the energy-intake from its environment to the establishment, and reproduction after inquiry, of a typical structural multiplicity of relatively high degree. The physical configurations of inorganic nature do not, so far as we know at present, show anything corresponding to this "wholeness of process" and "wholeness of form". But in comparing organisms with crystals it is especially noteworthy that for every living organism a co-existence of wholeness of process and wholeness of form in the same system holds good, and that it is this co-existence which, in general, constitutes the essential nature of organism.'

These objections do not seem to us to be completely conclusive. That the wholeness of inorganic configurations is enormously simpler than that of organisms is admitted by every supporter of the Gestalt Theory; the question remains open whether a reduction of the latter to the former may be possible. Raschevsky (1929 *b*) has recently shown theoretically that the problem of form is in no way foreign to physics. In diffusion equilibria form plays a decisive part, especially when polyphasic drops are considered. In the case of certain forms, the system concerned being in equilibrium, this form will always be reproduced if it is changed by some passing influence. Again, if external materials diffuse into a jelly the system will grow, not necessarily in a simple spherical form, but, according to the concentration of the diffusing materials, even an originally spherical system can gradually elongate itself. If such a system which, in consequence of growth, has become elongated, be cut into two parts transversely, and so 'rounded off', then in the course of time the elongated form will be reproduced. Raschevsky's investigations show that the capacity of reproducing injured form occurs not only among crystals in the inorganic world, but also in much more complicated and heterogeneous systems. Thus we see that the production and maintenance of wholeness of form, which, however, does not occur in Köhler's 'configurations', is not confined to crystals but occurs in more highly elaborated systems. Let us think of such a system as being composed of materials which are constantly being decomposed and recomposed in a particular environment (such systems also occur in the inorganic world, e.g. nitric acid, which constantly gives up oxygen to sulphur dioxide and which, on the addition of water and air, is reformed again)—then such a combination would come very close to the union of form- and event-wholeness which, according to Ungerer, is the special characteristic of organisms.

The Gestalt Theory has the great merit of recognizing that an organization of processes is possible not only on the basis of fixed structural conditions, but may also result from dynamic interactions within the total system. This is of fundamental importance for 'organismic' biology whose business it is to discover the laws governing the dynamic organization of vital processes. It is, however, not to be forgotten that the organic 'configuration' has essential features which are quite different from the inorganic ones hitherto known. We have formulated as such the 'rise of the level of organization by causes immanent to the system', and the 'historical character of the germ'. For these features we have no analogue in inorganic systems, and they do not seem to be explained merely by an application of 'Gestalt Laws' found in the inorganic realm. It remains to be seen, therefore, how far the *Gestalt* principles known from inorganic systems will suffice for biological ones.

VIII

THE ORGANISMIC THEORIES

In view of the fact that, in the present state of science, a physico-chemical reduction of organic development does not appear possible, it will be desirable to turn to those attempts which deal with development by means of specifically biological concepts, i.e. the 'organismic' theories.

The first duty of an 'organismic' theory is to put aside both the mechanistic and the vitalistic assumptions, to delimit itself from both, and to build upon a sure empirical basis which is not falsified by any superfluous presuppositions. Among recent investigators this task has been carefully and consistently carried out by J. Schaxel. He recognizes a 'formative element' which may be regarded as specifically organic. He says: 'Elimination, deposition, removal, introduction and replacement of parts are the indications that form is present in the material.' (1922 *b*, p. 523.) This organic 'formative element', 'the element of order in the formative processes', is, however, based on material parts which are discoverable for every phase of development, and are given in the constitution of the cells, in the spatial relations of the cell-structures, and their mutual co-ordination. Development is a process restricted to definitely limited paths and, beyond its fundamental determination, its accomplishment is not ensured by any incomprehensible regulation. (1922, p. 98.) A regulation superior to the determination of the partial processes, a regulation in the sense of a return to the normal by atypical paths, does not occur. (1915, p. 190; 1922, p. 31.) From an analysis of embryonic development it results that:

> 'There is a discernible limit in a given case to the typical specific form which cannot be exceeded without serious consequences if the typical is to persist. . . . If this limit is exceeded, if the bearer of the form is changed, the change proceeds necessarily. The atypical

developmental process proves itself to be just as persistent as the typical. From this it results that the type is nothing absolute, it is neither spatially nor non-spatially persistent. . . . The organization of many developmental states tolerates passing disturbances because properly speaking it is not affected by them. Examples of this are furnished by those deformations of the egg which result from artificial pressure, and which disappear as soon as the pressure is removed. In such cases, as far as the essential organization, the constitution, is concerned no disturbance occurs at all. Or, the disturbance is tolerated, as is the case after removal of substance from the vegetative region of the egg or blastula.' (1922 *b*, p. 524.) Disturbances exceeding the foregoing lead to an atypical result. 'What is interpreted as regulation is restricted to the facts of persistence of form, or results from an insufficient clarification of the facts on account of a biased approach to them.' Consequently 'the puzzle and the supposed proofs of vitalism from the occurrence of regulation consist solely in the persistence of organic form. The puzzles of this persistence constitute definite problems the solution of which is a task for empirical investigation after an adequate sifting of concepts with a view to obtaining a suitable point of approach.' (1922 *a*, p. 190.)

The essentials of Schaxel's view can be summarized by saying that in the concept of 'persisting organic form' a specifically organic developmental element is given, but that this principle is immanent to the system, depending on the mutual relations of the material parts. Every process, therefore, of both typical and atypical development is strictly determinate, and nowhere leaves a loophole for the entry of a transcendent regulative principle. Schaxel's assertions exclude a vitalism with an entelechy enthroned above and outside the material basis of development and capable of inhibiting the strict determination of the developmental process which, once started, follows a determinate direction, irrespective of whether the final result is purposive or not. But an immanent organismic developmental principle, which is expressed in the concept of 'persistence of form', is by no means excluded.

If we are to regard the factor which is characteristic of developmental processes as specifically organic two possibilities of interpretation present themselves. In the *first* place we may seek it in the mutual dependence or correlation of the cells. While biology has hitherto sought to conceive the body as an aggregate of cells whose total function is to be regarded as a sum of cell-functions, and so leaves out of account the problem of how the unity of the body can result from a mere sum of cells, Heidenhain (1923, 1929) has rejected the tyranny of the cell theory. Even Driesch's 'analytical theory of development' resolved the totality of the germ into a sum of equivalent cells, which he believed to develop, without synthesis, 'in separate lines'. Therefore, in absence of true correlations entelechy must be introduced as a directive factor, which, in the case of any disturbance of the normal, connects the independent developmental processes together in order to reach the goal of a whole organism. Heidenhain's 'synthetic theory' is based on the proof that many of the components of form ('histo-systems') situated between the cell and the whole body are divisible in a regular manner and are arranged in an increasing series, so that, from the hypothetical smallest elements ('protomeres') up to the whole organism a given superordinate system always includes smaller ones ('Encapsis'). In the muscle, for instance, fibrillae, columns, muscle-fibres, muscle-bundles, finally the macroscopic muscle, are the 'histo-systems', each of which consists of 'encapsulated' histo-systems of the order next below. The division of histo-systems is, in ontogenesis, at the same time a synthesis; for the act of division leads usually not to a complete separation of the descendants, but these remain connected to form a system of higher order which is able again to divide as such. The outer form is the expression of the structure, the inner construction of 'histo-systems'. This 'histomere theory' is proved by Heidenhain by means of a rich histological material, especially based upon the development of glands. The rhythm of the developmental process, which rests on the function of division, is repeated in organs of the most diverse kinds, and belonging to the most diverse levels of life, so that quite different organs—e.g. the glands of animals and the leaves of plants—become comparable from this point of view. The dynamic foundation of development is furnished by the correlation, the 'histo-dynamic interaction', the paradigma of which is the karyoplasmatic ratio. In nerve-cells, for example, there is a dynamic interaction between cytoplasm and chromatin so that if the peripheral nerve is cut Nissl's bodies disappear from the cell. This tonic interaction, named 'syntony' by Heidenhain, also holds good not only within the cell, but also within the tissues; syntony is a natural force, developing from the specific organization of living matter; it can be suppressed (in the division experiments, for example) as well as instituted experimentally (in the fusion experiments).

But we may also try, *secondly*, to conceive the 'organizing factor' as lying outside of the developing system, and then we come to the 'field theory' of A. Gurwitsch.

We have seen that the point of view of chemical determination does not suffice to exhaust the developmental process, and that the development of complexity of form, which is highly independent of the former, apparently demands a specific organic formative principle. We have Gurwitsch to thank for an important clarification of this question and for an original hypothesis about the action of that organic principle which has not been dealt with by previous theories. In 1914 Gurwitsch had already introduced the hypothesis of an organic formative factor under the name of 'Morphe'. In his newer writings he has abandoned the Morphe concept for that of the 'field' (1921, 1927, 1930).

Driesch had shown that the fate of a part is determined by its place in the whole. Nevertheless on account of his purely embryological approach to the question it resulted that no favourable prospect of a deeper insight into the properties and functions of the factor of the 'whole' was opened. This factor must be demonstrable not only in exceptional objects under complicated experimental conditions, but also on the most banal objects and processes and those which have been best studied descriptively.

Two such objects have been thoroughly analysed by Gurwitsch: the development of the flower head of the camomile and the mushroom (1921). The heads of *Matricaria chamomilla* possess a paraboloid form. In older, completed specimens this form is developed throughout their whole extent up to the base, whilst in younger ones it is restricted to the upper sections, deviating, towards the base, more and more from the paraboloid form. The strikingly regular form is therefore not given from the beginning but represents the completion of a complicated developmental process. The paraboloid arrangement is reached by the working together of two loosely co-ordinated processes, namely, by the growth of the common flower-cushion and that of the single flowers themselves. In so far as the florets of a specimen which is still young lie on the paraboloid surface they might all grow equally with the uniform growth of the whole structure. But since the growth of the cushion is irregular, being greater in width than in length, the growth in length of the basal flowers must be accelerated in order that they may take their places in the paraboloid cup. The situation is naturally still more complicated for the basal sections of the bud which originally were not situated on the paraboloid.

There thus exists a state in space distinguished by the fact that it constitutes a 'direction field' for flowers, forming them into paraboloid cups. In this way is reached the notion that the site of the developmental process is a 'field' whose limits do not, in general, coincide with those of the embryo, but extend beyond it. What is presented to us as a living system consists accordingly of the visible egg or embryo and a field. To the field is ascribed sometimes a complicated anisotropy, but the question of its origin and localization is left open, although the latter is in no way confined to definite material components of the germ (e.g. particular cells or chromosomes). This field is not a physical field of force, but rather a 'stimulus field'—as is, for example, a vessel containing micro-organisms which is lighted only from one side: the organisms themselves possess freedom to move in all directions, but the light stimulus limits these directions to one. What is essential in the action of the field is that it is not an 'external field' (e.g. produced by the earth) but one belonging to the germ itself. We may assume that (e.g. in *Matricaria*) the field factor signifies an impulse proceeding from the depths of the plant to the flower bud and influencing cell-division and cell-growth.

The development of the mushroom is interpreted in a similar manner. 'The absence of all internal differentiation, apart from the hymenial lamellae, renders the fundamental problem of the production of form, which is here stripped of all complicating ingredients, all the more difficult.' (1921, p. 404.) Any view based on cellular determination is, in this case, excluded from the beginning. The fate of the fungal hypha is determined by its relation to the whole. Here again the field represents 'so to speak a barrier for the growth of the points' of the otherwise irregularly interpenetrating growth of the hyphae.

Gurwitsch has thus drawn attention to a new feature in development which—although the relevant facts have naturally long been known—has not hitherto been taken into consideration by previous embryological theories. The phenomena of development described by Gurwitsch—phenomena long known descriptively which will serve as a model for most of the others—are insoluble on the basis of previous theories. It requires no elaborate consideration to see that the development of the form of the mushroom cannot be conceived as a splitting up of determinants. Apart from the fact that the material involved is quite homogeneous, growth takes place quite irregularly inside the hat-shaped form, and a mechanical splitting up of determinants is excluded from the outset. The vitalistic explanation of these processes will be the same as that offered for all developmental processes, namely not by means of a scientific type of 'explanation'. But the chemical theory is also confronted here by an obstacle which it cannot encompass. It may enable us to understand why a separation of the organ-forming regions occurs, why the three primitive germ layers, or epidermis and medullary plate, are distinguished. But in the above cases there is no chemo-differentiation at all, no separation of organ-forming materials, no separation of differentiated tissues. Instead, a uniform material, in the case of the fungus, produces a structure of exactly defined form without any separation of tissues. Even if we admit further accessory hypotheses for the interpretation of development—e.g. cell-division hormones and their differential distribution—the theory nevertheless breaks down on logical grounds. Differential distribution of division hormones might determine that an originally simple—say spherical—rudiment should grow unequally in different directions, and so give rise to a structure of complicated form. But here exactly the opposite occurs: an originally irregular growing material takes on a simple geometrical form. We cannot understand how this can come about by a distribution of division hormones.

> 'Many hyphae stand with their ends perpendicular to the surface, others are oblique, yet others bend inwards parallel to the surface when they approach it. The whole looks like shaggy uncombed hair. . . . The smoothing of the contour results from the fact that a progressively smaller number of hyphal ends project from it and more and more threads fuse with the contour. . . . We might summarize the state of affairs by saying that the regular and typical configuration of the mushroom only arises secondarily from less organized parts, and that it cannot in any way be a consequence of correspondingly arranged internal relations of parts.' (1921, p. 406.)

It is clear that no chemo-differentiation, no distribution of cell-division hormones, can bring about a combination of irregular threads into a regular form, e.g. the fusion of threads to form a contour.

In these cases, then, we have the formative action to some extent in 'pure culture', separated from the chemical differentiation which otherwise goes hand in hand with it. But when once our attention is drawn to it we recognize it in *every* developmental process, and in processes with which the chemical theory can only deal by means of complicated and improbable accessory hypotheses. We shall therefore agree with Gurwitsch that 'interconnexion of a normalizing kind is the predominant one for the majority of animal and plant tissues' (p. 413). 'Normalizing'—this is the formative action which joins to the (perhaps chiefly chemical) determination of development, and not conceived as a super-material entelechy, but as a principle anchored in the organization, though perhaps extending beyond the spatial limits of the germ.

In recent years Gurwitsch and his co-workers have developed and deepened the Field Theory. The foundations of Gurwitsch's construction rest, first, on the contention that development is never a pure self-differentiation, that, secondly, the dependence of the elements is not exhausted in mutual action, and that, thirdly, the relations appearing in development must admit of representation in analytical formulae, which contain time as the only independent variable. Finally, in order to carry out this last requirement the hypothesis is introduced that there are realities corresponding to the systems of relations which appear in the formulae. The postulate mentioned and the introduction of the hypothetical field concept have been suggested by the need for making the fundamental discovery of Driesch, that the fate of a part depends in general on its relation to the whole, a fruitful principle for investigation. If we construct a physical model for embryonic development, into the equation of which a constant force enters as parameter, time is taken as the variable, and the points are regarded as mass-points, then we come to the construction of a field which exerts a pondero-motor effect on certain material elements in its sphere of action. By calling the field-construction a 'postulate' the conviction is expressed that the difficult problem of embryogenesis can only be overcome, in its most general form, by the introduction of the notion of a 'field'. For the essential advantage of the field idea does not lie in a merely general and therefore empty assertion that, for example, the fate of a regenerating part is determined by a 'regeneration-field' or a 'determination-field', for that would be a mere tautology. When we assume a field we express the conviction that a unitary law is discoverable, namely the field-law, which connects the variations of the vectors controlling the spatial transformations. If there is any occasion to assume a field in this way, then the field may be regarded as 'actual' or 'real'.

Gurwitsch and his pupils have recently applied the field idea, formulated in the above way, to the following further groups of facts: (1) The results of Spemann and Harrison and others; early embryonic transplantation results in an 'ortsgemäss' behaviour of the transplanted region, and is thus governed by a 'place-field' belonging to the host embryo, older transplanted parts behave 'herkunftsgemäss' and thus carry their own field with them. This is explained by supposing that the originally unitary field of the egg is divided into single fields (1927). (2) The origin of wholes from parts of the embryo is referred by Gurwitsch to a 'radial' constitution of the field. It must be further assumed that in morphogenesis the field action relates only to the surface of the developing complex, as Gurwitsch has already pointed out in connexion with the mushroom. There is a kind of 'dynamic barrier' by means of which the configuration of the hat-shape is formed. Gurwitsch asserts that in relation to such early developmental processes as folding or invagination, &c., we can say without exception that the typical form of the structure concerned is determined by the contours of its external surface and not by means of its internal structural composition. This at the same time constitutes a refutation of a purely chemical theory of development. (3) Gurwitsch has tried to analyse the transformation of the spherical nucleus into a cone- or hook-shaped structure, as it occurs in the development of the heads of certain spermatozoa. By treating it from the standpoint of the field-construction the question of the evolution of the field is transformed into a 'concrete geometrical problem', it appears to be 'not entirely hopeless to attempt to bring the difficult problem of the relation of the whole to its elements in the sphere of embryo-genesis into a relatively simple and clear geometrical form' (1927). (4) The field principle, originally introduced for the analysis of the production of external form, was applied by Lydia Gurwitsch (1924) also to processes of internal differentiation. If we try to depict the spatial distribution of the differentiating elements, e.g. by connecting the neuroblasts in the central nervous system by lines, we obtain a kind of space-lattice, the nodal points of which are occupied by neuroblasts. Now since the mosaic principle is untenable we have to make a choice between two alternatives: either differentiation is a result of the mutual action of elements which are in themselves equivalent, or it is a product of an elementary superimposed field. It should be possible to construct a field radiating out from a source and in which interferences might arise, the nodal points of which must yield 'distinguished points'. How far such an assumption, as opposed to that of differentiation by means of mutual interaction, holds good is shown in the histogenesis of the retinal epithelium. Against the assumption of a differentiation through mutual action it may be urged that, whilst such a hypothesis would enable us to conceive how insignificant differences between the elements involved could produce a wonderful multiplicity in the total structure (e.g. in the formation of snow-flakes, or in the artificial vegetation of Leduc), in the case of the retina just the opposite happens. In the finished retina of the frog the rods are extraordinarily uniform although different ones pass through very different processes of histogenesis, depending on their distance from the oldest regions, i.e. the papilla of the optic nerve. Thus in this case although there may be a far-reaching multiplicity of mutual interaction between an enormous number of parts, yet the outcome is a product which is in essentials uniform. (5) Fields which determine the *direction of growth* of embryonic elements were first introduced by A. Gurwitsch; then *differentiation-fields* by L. Gurwitsch, and finally fields which determine the development of form in a unitary structure (*morphotropic fields*) were introduced by A. Gurwitsch in his analysis of the sperm head. A fourth kind of field has been added by Anikin (1929), the *tactic field*, which governs the displacement of cells, and was applied to the analysis of the grouping of cells in the cartilaginous primordium of the skeleton in the Urodele extremity. In so far as the cell-nuclei lie exactly in the axis they all exhibit a circular shape in transverse section. The more peripheral ones, arranged in a rosette, take on bean-shapes or half-moon-shapes. In order to discover the field law governing the grouping of the nuclei Anikin makes the following assumptions: the source of the field is situated approximately linearly in the long axis of the cylindrical primordium; the field is isotropic about this axis; the field-vectors act centrifugally at the equator of the cell-nuclei resulting in displacements of the nuclear points concerned. On the basis of these assumptions Anikin constructed the deformations to be expected at different distances from the axis, and these corresponded strikingly to those actually observed.[1]

Another theory of a 'biological field' has been put forward by P. Weiss (1926 *a*, 1928 *a*). Weiss transplanted regenerating buds from the newt's tail to the neighbourhood of the leg. In this situation there developed not a tail but a leg. Formative influences belonging to the new site determine the direction of development of the transplanted material. If, however, the 'tail-determining' influences have been active for some time on the original bud, then influences working in other directions in the new site have no effect on the transplanted part. A tail-bud from then onwards develops into a tail, and not into a limb. Now since limb and tail are in no way related morphologically the assumption that the tail possesses so to speak an 'extremity reserve' becomes untenable. We see that the cells involved in the regeneration of various organs may be completely equivalent in respect of their possibilities of differentiation, and yet may differentiate into quite different forms. It is the play of forces acting on the material at the place of development which turns the scale in one direction or another. There is thus both unorganized and organized living material, in which, however, the organization may be completely latent. The difference may be compared with that between electrically charged and electrically uncharged bodies. The system of organizing actions which proceeds from an organized material to its own and to foreign parts Weiss calls a 'field'. An important character of fields is that they break up in the course of development into smaller and smaller partial fields, which gradually become more and more independent of one another, like whirlpools in a fluid stream. Thus in the course of development a mosaic of 'spheres of

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[1] A more detailed summary of Gurwitsch's field theory is given by Gurwitsch (1930), Rudy (1930).

action' arises. The scientific applicability of the field concept is proved by the fact that precise 'field-laws' can be drawn up, of which we may mention the most important:

(1) If material is split off from a field-bearing system the remainder contains the field in its typical structure and distribution. (This holds, for example, for the divided equipotential systems of Driesch, or for those described by Weiss himself—'whole regenerations from half-stumps of extremities' (1926 *b*). (2) If unorganized, but organizable, material enters the field it becomes included in it. The field spreads over the whole of the material at its disposal, preserving the same structure as before (a regenerating part, when enlarged by added material, produces a whole). (3) A field has a tendency to take up and include within itself equivalent fields from its environment (e.g. whole embryos formed from two fused eggs).

The main result of the field theory is, in our opinion, to have drawn attention to the fact that in development not only material but also purely energetical modes of action are to be considered. When we say this or that embryonic process is produced by 'forces' or 'a field' the causes of the process are not thereby 'explained'—as some biologists seem to believe—but only *named.* Even Gurwitsch's formulation is not free from ambiguity. We should conceive the field concept as a comprehensive expression for the general direction of the forces in the germ. The latter can be regarded as the bearer of fields of force of the most diverse physical kinds which—acting through the whole developmental system—may restore themselves (within limits) even when the material is disturbed, and which—being different in the different directions of space—lead to the formative processes by movements and directed growth. In this sense the notion of a field seems to be useful, for it permits, as Weiss has shown, the establishment of comprehensive rules relating to the action of such determinative factors.

IX

SPEMANN'S DOCTRINE OF DEVELOPMENTAL ORGANIZERS

THERE is no doubt that among the results of recent experimental embryology those of Spemann and his school deserve the place of honour. Working without any theoretical encumbrances these investigators have reached results which nevertheless contain the greatest theoretical possibilities, and offer solutions of many ancient problems. Let us recall briefly the main points in the history of Spemann's investigations.

Spemann (1919, 1921) first exchanged small pieces of the outer germ-layer in newt embryos in the gastrula stage. By performing the exchange with differently coloured specimens belonging to different species of newt he was able to follow the fate of the transplanted parts exactly. For example, he implanted a little piece from the region of a Striped Newt gastrula which would later become epidermis (hence called 'presumptive epidermis') into a gastrula of the Crested Newt in the region of the future brain, and vice versa. If this exchange is carried out at the beginning of gastrulation the transplanted epidermis becomes a part of the medullary plate, the transplanted presumptive medullary plate a part of the epidermis. Thus as a result of such an experiment we may have a Striped Newt whose brain consists in part of tissue from a Crested Newt which normally would have become Crested Newt skin, and yet this brain functions quite normally. Thus at the beginning of gastrulation the tissue is still relatively indifferent, so that there are two possibilities: the formation of either medullary plate or epidermis. What the tissue actually becomes depends on its place in the whole. But the result is quite different when the same experiment is performed on a gastrula of a later stage. Presumptive medullary plate now becomes medullary plate, or some derivative of it, even when it is transplanted to the region of epidermis. For example, we may obtain an eye directed towards the body cavity and hence one which is quite useless. In this stage the fate of the tissues of the outer germ-layer is already determined. This determination proceeds outwards from the region of the blastoporic lip which is therefore called the 'organization-centre' by Spemann.

The great problem of determination appears to be solved in principle by Spemann's experiments. Two important principles result from these experiments:

> 'The capacity of regulation of a germ decreases during its development in the same proportion as the determination of its parts progresses. . . . The determination of a group of cells occurs in relation with the whole. But when once this has occurred development continues in this direction independently of the environment' (i.e. of the surrounding parts of the germ).

These assertions from the classical *Rektoratsrede* of Spemann (1922/3, p. 10) summarize the two fundamental principles of development.

Hilde Mangold (1924) next added the proof that certain parts of the young amphibian germ possess the capacity of determining the development of other parts. She transplanted a piece of dorsal blastoporic lip from a gastrula into the presumptive ventral epidermis of another germ, and in this displaced situation there arose a secondary embryonic primordium with chorda, somites, auditory vesicles, and pronephric ducts. Only a very small part of this secondary structure consisted of the implanted material, the bulk of it was derived from material of the host embryo. The boundary between induced *Taeniatus* and inducing *Cristatus* cells passed through the somites, the chorda, &c., as was made visible by the different colour of the implanted tissue. Parts such as the dorsal lip of the blastopore which possess this 'inductive' property are called 'organizers' by Spemann, and the germ-regions in which these organizers lie in the earlier stage of development he called the 'organization-centre' of the germ.

We cannot attempt to give here a complete survey of the investigations of Spemann and his co-workers (cf. Spemann's summary, 1927, and that of Mangold, 1929 *b*, with complete bibliography). We shall merely summarize the most important information that has been obtained regarding the organizers.

These investigations have already clarified a number of important questions concerning the action of organizers. First, as regards the extent of the centre of organization, Bautzmann (1926) has shown that its area is the same as that part of the germ which is to be invaginated in gastrulation, according to the observations of Vogt by means of vital staining, and is found to become chorda and mesoderm. This result is an extension of the data obtained by Marx (1925) showing that a piece of the archenteric roof, when placed into the blastocoele of a gastrula, there induces medullary plate. This procedure, on account of its simplicity, has since played an important part in testing the organizer.

Secondly, regarding the origin of the centre of organization, it is probably situated in the 'grey crescent' already visible in Amphibian larvae before cleavage. An older experiment of Spemann's bears upon this question. If a hair is tied round a newt's egg in the two-celled stage the result varies according to the plane in which the hair is tied. If this coincides with the median plane two whole embryos develop, if with the frontal plane a complete embryo and a ventral piece result. Thus the ventral cells are incapable of yielding an axial system. The same conclusion can be drawn from the experiment which we have cited as a refutation of Weismann's theory in which the undivided egg is tied in such a way that a retarded distribution of nuclei occurs. The result shows that it is not the different constitution of the nucleus in different cells but that of the plasma which is responsible for the result, even 1/8 nucleus in the dorsal half, but not even 15/16 or 31/32 in the ventral one yielding a complete embryo. But that the inability of the ventral half to form an axial system rests on the lack of an organizer, and not on the absence of the materials for the formation of a whole, has been shown by Bautzmann (1927). He implanted pieces of organizer into isolated ventral halves of the gastrula, in which situation they produced a secondary axial system; and at the same time it was shown that such a primordium can develop successfully in complete absence of primary axial organs of the host.

The results of uniting two whole germs also favour the assumption that the place of the organizer is already laid down in the undivided egg. Mangold and Seidel (1927) united whole newts' eggs in the two-celled stage by applying them to one another crosswise. The resulting single embryos, double and multiple monsters, can be interpreted on the assumption that the organization centres are already localized in the two-celled stage, and are distributed between the two blastomeres in different ways by means of the different directions of the first cleavage plane.

The temporal relations involved in the inductive process have recently been investigated. H. Bautzmann (1926, 1928) investigated the particular regions into which the dorsal lip falls (chorda and mesoderm) with reference to their inductive capacity. The result shows that the presumptive archenteric roof possesses inductive capacity before gastrulation: perhaps even in the undivided egg, the rudiments of the notochord preserves this power beyond the neurula stage, whilst the mesoderm has already almost completely lost its much smaller inductive capacity at the beginning of neurulation. Bautzmann's results are completed by those of Mangold (1928 *b*). The induction capacity, whilst it is lost by the chorda rudiment, is got by the medullary plate. The medullary material acquires its inductive capacity during gastrulation when the archenteric roof is extending under it. It retains it for a long time, although the inductive capacity of the differentiated brain is less than that of the medullary plate. The induced medullary plate is formed synchronously with that of the host, however old the inducing implant may be. Thus the ectoderm of the newt's germ can form medullary plate only during a restricted period of development. Speaking generally, to each period there belong definite developmental processes.

Thirdly, a complicated structure probably exists, according to Spemann's opinion, in the organization centre. The presence of a longitudinal structure may be assumed from the fact that the induced embryonic system may be differently orientated to the axial organs of the host embryo. It may actually lie transversely to the primary axis, and if it carries auditory vesicles at its anterior end these lie symmetrically on both sides, and thus from the standpoint of the axis of the host one will be in front and the other behind the secondary medullary tube. A lateral structure of the organization centre is suggested perhaps by the investigations of Goerttler, who replaced a lateral piece of the dorsal lip by a corresponding piece from the opposite side of another germ, and so obtained two left halves of the medullary plate and two left medullary folds running parallel with one another. Finally, a regional structure may be assumed from the fact that different results of induction (e.g. medullary tube with or without brain and optic vesicles) arise which may result from a difference in the inducing organizers. With reference to the inductive capabilities of the medullary plate Mangold (1929 *c*) has recently found that this yields, in addition to 'homoiogenetic induction' (see below), also complex inductive results, since it conditions the origin of the balancer (a thread-like organ on the head of newt larvae), pigment, eyes, lens, nose, auditory vesicles, sense-organ of the lateral line, and tail-formation, whence we may assume that the inductive capacities of the various regions of the medullary plate are different. The organizer (and the inducing medullary plate) is, however, capable of inducing more than it actually does in a given case; it behaves like a harmonious equipotential system. That is suggested also by the results of Bautzmann which demonstrate the co-operation of the structure of the host in cases of inductive action. A certain degree of assimilation shows itself between the parts induced and those of the host, so that posterior fragments of the chorda in the anterior region of the host do not yield posterior but anterior parts of the medullary rudiment.

These influences of the host have recently been investigated in detail by Spemann (1929), for the direction of the induced medullary plate, the invagination tendency of the implanted organizer, different according to the implantation direction, is co-determining, whilst the actions of the host germ tend to rectify the secondary primordium to the primary one. The implanted organizer as well as the host participate in the regional articulation of the induction product: 'head organizer' induced the head region, even if it was transplanted backwards; 'trunk organizer', inducing otherwise spinal cord, also induces the head regions, if implanted close by the head. In the latter case, the influences of the host seem to preponderate. We have a case of 'double assurance' (see below), the tendency of the head organizer to induce the head regions collaborating with the tendency of the (animal) material to form the anterior end.

The two questions concerning the action of the organizer which are theoretically most important may be treated more fully, i.e. that concerning the nature of this action, and that regarding its significance for development. The inducing agent seems not to be of a quite general nature, for example, a stimulus of contact: otherwise a piece of presumptive epidermis would likewise exert organizing action. The inducing stimulus, on the other hand, is not organ-specific. Presumptive chorda, medullary plate, functioning brain, are all capable of inductive action (Mangold, 1928 *a*, pp. 165 ff.). The same is probably true also of limb-buds but not of gill-rudiments and pieces of gut. There is also a direct connexion between the size of the implant and that of the product of induction (Mangold, 1928 *b*). The inducing stimulus is not even species-specific. It is exerted in a tissue belonging to a different animal order. According to Geinitz even the organizer of a toad (*Bombinator*) is capable of producing a secondary embryonic rudiment in a newt embryo. We are still uncertain about the most general question: whether induction is material or dynamic. 'Homoiogenetic induction' favours the first alternative: medullary plate, placed under young ectoderm, again induces medullary plate, even the brain of the swimming larva still possesses this property, according to Mangold and Spemann (1927). Thus in this case the agent inducing medullary plate seems to be transmitted from the organizer to the medullary plate material, and redistributed from the latter. Moreover, the awakening of organizing capacity in previously indifferent material described by Geinitz, through its transplantation into the environment of an organizer, might favour such an interpretation.

In addition to 'homoiogenetic' induction, in which an embryonic part induces its like, Spemann and Mangold distinguish two others kinds of induction: (1) 'heterogenetic induction' when the organizer induces something other than itself, e.g. when by means of an implanted optic vesicle formation of a lens is induced, or when medullary plate formation is induced by means of archenteric roof; and (2) 'complex induction' when the inductive function extends to numerous formations, e.g. when an organizer calls forth a whole axial system. If we are to maintain the chemical interpretation, we must naturally assume 'hormones' for the formation of every single organ, the notochord, the optic vesicle, the otic vesicle, &c. But it is difficult to see how, in the case of heterogenetic induction, formative materials for the formation of organs can be transmitted by an organizer which does not itself give rise to such organs at all. Moreover, how, in the case of complex induction, shall all these stuffs diffusing from the organizer into the host embryo be so disposed that all the organs arise in the induced part in their typical form and localization? Another aspect of the problem is yielded by recent results which suggest that the organizer is distinguished from the rest of the germ not qualitatively but only quantitatively. Such a supposition would bring the organizer into relation with the axial gradients of Child. We shall discuss this possibility later.

The experiments of Marx (1930) also point to a material interpretation of the organizer action. He found that narcotizing does not abolish the organizing capacities, these being unaltered even when the organizer decays in the host germ. But Marx also points out that the totalizing character of the organizer action is difficult to explain on the basis of material assumptions.

Spemann has developed a unitary conception of the significance of the inductive capacity for normal development. Organizing actions similar to the above also occur in later embryonic development, e.g. the optic-cup can excite development of a lens in foreign epidermis, and thus acts as an organizer; but this embryonic organ itself probably receives its organizing ability from the underlying mesodern, and thus is an organizer of the 'second order'. Such a second-order organizer has been produced experimentally by Spemann and Geinitz (1927). Mangold (1925) had shown that even the germ-layers have only a topographical significance, and do not represent a level of determination in the development of the newt's embryo. He produced mesoderm from presumptive epidermis by transplanting the latter in such a way that it became invaginated in the process of gastrulation; i.e. skin material can in the early stages become chorda, somites, or pronephros, according to its position. On the other hand, Marx showed, by putting a piece of archenteric roof into the blastula cavity of the gastrula, that the mesoderm (archenteric roof) was able to induce medullary plate. Spemann and Geinitz now combined both experiments: they converted ectoderm into mesoderm by transplantation, removed it some time after invagination and then placed it into the blastocoele of a young gastrula, where it then induced medullary plate. In this way, then, the whole process of development, at least in the amphibian embryo, can be conceived as put together of single processes connected by organizers of different order.

X

THE PRESENT-DAY PICTURE OF THE DEVELOPMENTAL PROCESS

We have now completed our sketch of the more important of the modern theories of development. The reader will hardly fail to be impressed with the extreme heterogeneity of this theoretical material. The puzzling territory of life and development is brightly illuminated by the various theories in much the same way as a piece of unfamiliar country might be illuminated by a number of searchlights placed at different points on its boundary. First one, then another strip of ground is brilliantly clear, although no one searchlight is able to light up the whole region, and even their combined use does not enable us to obtain a general view of the country as a whole. After the merits of each individual 'searchlight' have been reviewed, the final and most important task of a critical study of theories of development will therefore be to consider how far the developmental process as a whole can at present be interpreted by these various theories. After what has been said we can hardly escape the impression that no single one of the theories reviewed gives a complete explanation, although almost every one is able to contribute something towards such an explanation in the future.

Such a view is in harmony with the latest studies in developmental physiology. We may say that the most important result of the investigations of recent years is the recognition of the fact that 'development' is not simply a unitary process, but rather a complex of relatively independent (but not unrelated) component processes, which can, to a large extent, be experimentally isolated and cannot be reduced to the same terms.

An analysis of the primary developmental processes has been given by Woodger (1930/1) in a study of the relation between embryology and genetics. Making use of the notion of hierarchical order it is possible to describe certain aspects of development in a precise manner and so to avoid some confusions which are apt to be concealed by current language. We shall give a brief account of Woodger's work so far as it concerns purely embryological problems.[1]

It will be easier to grasp the abstract notion of hierarchical order if a few words are first devoted to the simpler and more familiar type of *serial* order. This type is exemplified by such sets of things as a row of palings in a fence, a string of beads in a necklace, the stations of a simple railway system with no branch lines, as well as by the series of cardinal numbers and the points on a line. The essential feature of a series is that all the terms belonging to it are connected by some relation possessing the formal properties known as symmetry, transitivity, and connectivity. Thus suppose we have a simple railway system running north and south, with six stations a, b, c, d, e, and f. Then there will be a relation which we can call 'north of', such that (1) if x and y are *any* two of the six stations, if x is north of y, y cannot be north of x (asymmetry); (2) if x, y, and z are *any* three stations such that y is north of x, and z is north of y, then z is north of x (transitivity); (3) if x and y are *any* two stations of the system, then *either* x is north of y, *or* y is north of x (connectivity). These are the three fundamental properties of any series. But the railway system also has features which are not shared by all series, e.g. it has a first and last term. A necklace of beads does not share this property but is a 'closed' series. The series of cardinal numbers has a first but no last term. But there is another feature which is common to all these three examples although not common to all series; it is common only to *discrete* series. If we regard the most northerly station in the railway system as the last term, it will be seen that every other term has one and only one station which is *immediately* north of it; and every term except the first has one and only one

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[1] We are indebted to Dr. J. H. Woodger for help in preparing the above summary.

term immediately south of it. For this reason the relation 'immediately north of' in this series belongs to the class of relations known as 'one-one' relations. Now suppose *a* is the most southerly station (first term) and *b* the one immediately north of it, and *c* is that which is immediately north of *b*; then *c* is north, but not immediately north, of *a*. If we denote 'immediately north' by N, then the relation of *c* to *a* will (in the logistic notation) be denoted by N^2, and if *d* is immediately north of *c* its relation to *a* will be denoted by N^3. Thus every successor of *a* stands to it in a relation which is *some* 'power' of N; and we can now see that this more general relation (of being related by *some* power of N, which is the ordering relation of the series) will be the relation between any term (except the first) and any term which precedes it. This relation is denoted by N_{po}. It is asymmetrical, transitive, and connected, but not one-one, whilst N is asymmetrical, intransitive, and connected but one-one.

Now a system of entities in hierarchical order is one ordered by a relation which shares with the series generating relations the properties of asymmetry and transitivity but *not* connectivity. Moreover, the relation between two 'neighbouring' terms, corresponding to 'immediate successor', is many-one, not one-one, and there is the further characteristic that there is only one term which is the 'first term', i.e. has successors but is not itself a successor. This will be most easily understood if we now consider two important biological exemplifications of this type of system described by Woodger.

The first example is the system of *cells* resulting from the division of a zygote and its cell-descendants. Every cell (excluding zygotes) stands in the relation of 'immediate division product of' to one and only one cell which is also *before* it in time. But there is always at least one cell which also stands in this relation to the same parent-cell. Hence this relation (which may be denoted by D) is not one-one but many-one, and so gives rise to a branching or tree-like system. Such a system of cells Woodger calls a *division hierarchy*. It consists of a four-dimensional array of cells of which one and only one member (the zygote) is before all the other members in time, and is the only one to which every other term stands in a relation which is some power of D (i.e. the relation D_{po}). Every cell (except the zygote) will stand in D to some one other cell which is a member of the same system, and no cell which is not a member of a given system will stand in this relation to a cell which *is* a member of that system. If x and y are *any* two members of a division hierarchy either x stands in D_{po} to y, or y stands in D_{po} to x, or there is some third cell to which both x and y stand in D_{po}. In consequence of this third alternative D_{po} is not connected, and so not serial. We only obtain a series if we limit the field of this relation to those cells to which some one given cell stands in D_{po}; these constitute a series.

A second example of a hierarchical system is given in the way in which certain spatial parts of organisms (and some inorganic systems) are ordered. Such systems are called *spatial hierarchies*. Woodger points out the ambiguity of the word 'part'. He distinguishes first 'arbitrary parts', i.e. parts (like a piece of 'meat') taken without regard to the organization. Secondly, such parts as the matrix of bone or cartilage or the blood-plasma which are not terms in the hierarchical system and are called constituents. Finally, we have the parts standing in hierarchical order which are distinguished as *components*. Of these there are three major classes: (1) cellular components, (2) cells, and (3) cell-components. The endoderm of, say, the gastrula of *Amphioxus* is a cellular component. But one of its cells will not be a part of the whole in the same sense in which the endoderm itself is a part of the whole gastrula: it will be a part *of a part* of the whole, and the nucleus of this cell will be a part of a part of a part of the whole. This relation 'part of' (in this sense) corresponds to the relation D in a division hierarchy and is denoted by S. The relation of being related by some power of this relation (corresponding to D_{po}) is denoted by S_{po}. A spatial hierarchy is thus a system of spatial components in which the ordering relation is S_{po}, the 'first term' being the spatial whole to which certain of its spatial parts stand in the relation 'part of' in the sense denoted by S, whilst these have parts standing in S to them and in S^2 to the whole, &c. A 'level' (in the case of a spatial hierarchy) is defined as the class of components all of which stand to the whole in the same power of S. The 'first' level consists of the parts standing in S to the whole, the second of those standing in S^2 to the whole, and so on.

There is nothing peculiarly biological in this notion of a spatial hierarchical system, since it is exemplified also by such inorganic systems as crystals and molecules. But we have to distinguish different *orders* among spatial hierarchies. An order may be defined as a class of hierarchical systems all members of which have *the same number of levels*. If all atoms are analysable into electrons and protons, and if these are not themselves analysable, then the class of atoms will constitute an order—the lowest order. If all molecules are analysable into atoms as their first-level components, then the class of molecules will constitute the order next above that of atoms.[1] Similarly, if all cells have the same number of levels the class of cells would constitute an order, but we do not know at present how many levels there are in a cell. It is thus essential to the notion of an order that an entity of a given order is not analysable into components of the same order as itself. In a spatial hierarchical system the components standing in the relation S to a given whole will thus belong to a different order from the latter, and in respect to those of their properties (if any) which are a function of the order to which they belong wholes and parts of different orders will differ. For this reason we have to distinguish different

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[1] It should be mentioned that components are recognized which are not known to exist independently of the systems of which they are components, e.g. the 'radicals' or 'groups' of chemistry ($-$ OH, and $-$ COOH groups) and the chromosomes of biology.

orders of both cell-components and cellular components. Thus the nucleus of a given cell and one of its chromosomes are both cell-components but of different orders. Similarly, the entire ectoderm of an amphibian neurula is a cellular component, and so is the medullary plate, but they are of different order, since the first-level components of the former are themselves cellular, whilst those of the latter are cells. For biological spatial hierarchies we can thus set up a *series* of orders as follows: cellular systems of the nth order, cellular systems of the $n-1$th order, . . ., cellular systems of the second order, cellular systems of the first order, the cell-order, cell-components of the first order, . . ., cell-components of the nth order, . . . and so on through an unknown number of terms until we come to cell-components of the molecular and atomic orders. (Whether we regard the properties of atoms and molecules as differing or not according to whether they are or are not components in biological systems depends only on which assumption best agrees with the requirements of empirical data.)

Now in thus conceiving an organism as a system of spatial components in hierarchical order we are conceiving it in abstraction from time. We must therefore consider its relation to the division hierarchy in which this aspect is included. There are two classes of division hierarchies: (1) those in which the members (i.e. the cells) are always whole organisms (e.g. Protozoa and single-celled plants), and (2) those in which only one member (the zygote) is a whole, all the remaining members being components of one organism (Metazoa). Thus in Metazoa the division hierarchy is also the history of one organism throughout its temporal extent, the earlier temporal parts of which exhibit the changes which we call 'development'. A given 'stage' of development will be what Woodger calls a 'short temporal slice' of the division hierarchy, i.e. the class of cells all of which belong to the same division hierarchy and are contemporaries of one another, or, in other words, a class of cells all standing in the relation D_{po} to the same zygote and all 'existing at the same time'. But this will also be an ordered class or system because, being components, these cells will stand in the relation S_{po} to a spatial whole, as well as standing in definite spatial relations to each other. The cell-order is thus the only order the members of which belong to the fields of both these relations (D_{po} and S_{po}).

We can turn now to the analysis of developmental processes. A division hierarchy (metazoan) is such that if we take any two short temporal slices we find that they differ from one another (provided the temporal interval between them is not too short). Embryology is concerned with the interpretation of such differences as occur between the earlier slices of division hierarchies. Now in natural science if two entities are different the interpretation of the difference always takes the form of assuming that they are analysable into parts which differ (i) in number, or (ii) in kind (in the case of *corresponding* parts), or (iii) in the relations in which the parts stand to one another in the two cases. Now in development a given slice is frequently distinguished from some previous slice by the fact that it has components which were not present in the previous slice. There is a gradual production or *elaboration* of components. Thus, from one point of view at least, the 'problem of development' reduces to the interpretation of the modes of elaboration of components in successive spatial hierarchies which are 'short slices' of the same division hierarchy. Now, as there are three main types of component, so there will be three main types of elaboration of components according to whether these are (1) cellular (of various orders), (2) cells, or (3) cell-components (of various orders).

The elaboration of cells is accomplished through the process of division, i.e. in virtue of the peculiar property of cells of dividing, not into two half-cells, but into two entities both of which are cells. The elaboration of cell-components is exemplified in the formation of myofibrillae, secretion granules, yolk-spheres, and other special cell-components, but it may also occur in much earlier slices. Woodger calls this histological elaboration, but does not confine the term to cases in which there are microscopically recognizable differences between cells.

Most of the special difficulties of embryology centre round the analysis of the third type of elaboration, namely the elaboration of cellular components. It must be remembered that we should expect many different types of process to be covered by this term on account of the existence of cellular components of different orders. (Similarly the term 'differentiation' must cover a great range of very different processes according to the order of the parts concerned.) It must also be remembered that, just as the whole organism is temporally extended and diversified, so also are its cellular (and other) components. And just as the notion of the division hierarchy gives expression to this aspect of the whole organism, so Woodger's notion of the 'cell-cone' helps us to bear in mind this aspect of cellular components. A cell-cone is defined as an ordered class of cells consisting of any given cell (other than a zygote) together with all the cells which stand in D_{po} to it. It is thus a sub-system of a division hierarchy. The first cell, which is before all the others in time, is called the 'apical cell', and all the cells belonging to a given spatial hierarchy which also belong to a given cell-cone (which has its apical cell in some earlier slice) are called the 'basal cells' of that cone in that spatial hierarchy. Thus the simplest cellular component of the first order would be one formed from the basal cells of a single cone, and this same component, considered throughout its temporal extent, would be this cell-cone itself. Actually, of course, cellular components usually consist of contributions from many cell-cones, some or all of the basal cells of which in successive slices of the division hierarchy become interrelated in various ways by movements of their individual cells or by movements of the components to which, in a given slice, they may belong. The analysis of the elaboration of cellular components of the different orders is a major problem still awaiting solution, but Woodger has drawn attention to one or two points which bear on this problem, so far at least as the component cells are concerned. He points out that there are two theoretically possible types of cell-division: (1) divisions in which the resulting cells are different in consequence of the mode of division and are therefore called differentiating divisions, and (2) those in which the resulting cells are not different (although they may become different subsequently), and hence called non-differentiating divisions. The first type is illustrated by the mosaic eggs. If division of type (2) occurred throughout a cell-cone all its basal cells in a given slice would be alike. But if, by folding or some such process, different members of the same cell-cone come into different relations with some other cellular component (e.g. an 'organizer') we shall have the possibility of different changes being set up in the differently related cells which may lead to different histological elaborations occurring in them (e.g. in the case of differences between lens-cells and epidermis-cells according to their relation to the optic cup). Differentiating divisions and different histological elaborations depending upon different relations in a given slice may thus prove to be two important factors in the diversification of cell-cones, and hence in the elaboration of cellular components. But it is doubtful whether these two factors, coupled with the consequences of different rates of division in different cell-cones, will cover all the factors involved in the elaboration of cellular components, as we are reminded when we recall such cases as the development of the hat-shaped form in the mushroom, and the elaboration of cellular components in the seemingly chaotic mass of cells of the stump of a regenerating appendage. Nevertheless Woodger's analysis represents the first attempt to express embryological ideas on a logistic basis and thus provides a number of clear ideas for further work and for the understanding of the relation between embryology and genetics. For this aspect of his work the reader is referred to Woodger's paper.

P. Weiss (1930, p. 20 f.), in a lucid review of recent developmental physiology, has distinguished the following component processes of development:

'Various component processes have been analysed out of the developmental process originally regarded as single, and it has been found that these components cannot all be reduced to the same terms. Under the general notion of "development" four kinds of processes have been concealed:

'1. *Tactical Displacements.* Movements of embryonic parts relatively to one another, resulting in definite distributions and formations of the germinal material.

'2. *Internal Organization.* The passage from the original unitary condition of the embryo into a mosaic of partial regions in some degree independent of one another.

'3. *Histological Differentiation.* The passage of the individual cells from an original state of uniform appearance into the various states of morphological and functional specification.[1] The process of separation of rudiments must be sharply distinguished from that of histological differentiation, and it only leads to misunderstandings if both are simply called differentiation. In order to recognize this we need only recall that certain histological differentiations, such as gland-, sense-, muscle-, connective-tissue-, cartilage-, and pigment-cells, recur in a number of different organs, and that consequently organ-formation and differentiation must be two different processes.

'4. *Growth.* The enlargement and multiplication of cells. The formation of metaplasms (fibrillae, cartilage matrix, &c.) is better treated under histological differentiation.

This fourfold nature of the developmental process has not usually been recognized, and, in consequence, only "the" prospective potency has been considered. Meanwhile it has become clear that a definite necessary connexion between the four partial processes does not exist; i.e. each of the four phenomena (formation, separation, differentiation, and growth) can occur in isolation from the others, and it is thus demonstrated that they must be regarded as real, and not merely as conceptually constructed, components.'

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[1] It is clear that in this connexion the word 'differentiation' is used in a narrower sense than we have hitherto given to it (according to the definition on p. 71).

A. Formation[1]

The independence of formation of the other developmental processes has been demonstrated in the development of the higher metazoa. In his famous analysis of the early development of the amphibian embryo with the help of the vital staining method, Vogt (1929) has closely investigated this process as exemplified by 'formative movements' depending on the spatial displacement of the formative material (in contrast to the developmental processes which depend on growth at different rates in different parts). Among 'fundamental movements of primitive development' are invagination, extension of the roof-region of the archenteron (epiboly), stretching of the peripheral-zone region, and dorsal convergence and ventral divergence of all three germ-layers. We might, with Vogt and Dürken (1928, 1928 *b*), actually speak of 'amoeboid' movements not only of the individual cells, but of the whole embryo. Earlier ideas about morphogenesis were concerned chiefly with cell multiplication, growth pressures, and differential rates of cell-division. But according to the results of marking experiments the *tempo* of division is of little importance, the direction of division almost insignificant, for the formative processes of primitive development.

Goerttler has, however, attempted to demonstrate an essential connexion between formative movements and the determination and differentiation of the medullary plate. We have learnt above that the medullary plate in the urodele embryo is regarded by the school of Spemann as induced by the organizer which underlies it. Under certain circumstances (to which we shall return in more detail later) it is possible to obtain development of medullary plate without such underlayering. Goerttler first showed this by his experiments with so-called 'ring embryos' (1926) and later by the following experiment (1927). He transplanted a piece of presumptive medullary plate into the ventral

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[1] German: *Gestaltung*.

epidermis of a neurula. If the piece is so implanted that its own tendencies of movement are not hindered by its new surroundings it develops into medullary plate. But if its developmental movements are restricted, then (as in Spemann's experiments) a development in accordance with the new site (*ortsgemäss*), i.e. into epidermis, takes place. These experiments seem to indicate that cellular differentiation depends upon the formative movements. Goerttler assumed, therefore, that material differentiation is, in general, a consequence of the formative processes.

This attempt to demonstrate such a connexion between formation and determination has, however, already been abandoned. First, as Marx (1930, pp. 334 f., 379) points out, it is not justified by the actual situation in experimentally produced induction, in which the organizer cannot have carried over its movements on to the induced tissue, since it need not be transplanted in close connexion with the superficial tissue, but only pushed into the blastocoele. On the contrary, in Goerttler's experiments with ring embryos extensive normal medullary plates arise, although the formative movements proceed atypically. Moreover, the newer experiments show more and more that differentiation and formation are to a large extent independent processes (cf. below, the results of Bytinski-Salz, Dürken, Kusche, Bautzmann). Lehmann (1929) removed a rectangular piece of ectoderm from the border between presumptive epidermis and medullary plate, and reimplanted it after it had been rotated through 180°. The piece developed in accordance with its origin (*herkunftsgemäss*) without typical formative processes. We may also mention Ranzi (1928) who, on the basis of his experiments on Sepia (inhibition of normal organ-formation by chemical means), comes to the conclusion that the histo-genetic processes are largely independent of the organo-genetic ones.

If, now, we consider the question how far the theoretical interpretation of the formative processes in development has progressed, we must answer that at present we are only at the beginning of understanding this problem.

Regarding the possible physico-chemical factors which may possibly contribute to formation the most important is surface tension and the related principle of least surface. D'Arcy Thompson (1917) has not only shown how a great many forms among the Protozoa may result from the laws of surface tension, but has also employed the principle in connexion with the formation of tissues and even of the honeycomb, and has attempted to explain quite complicated many-celled forms by the same means, e.g. the forms of Hydroid polyps. The last strikingly resemble the waves which arise when a body falls on to the surface of a fluid. But a detailed reference to this work of genius will not be necessary for English biologists.[1] Naturally, there is the obvious objection that the resemblance between those relatively simple, inorganic structures and organic forms constitutes a problem rather than an explanation. The resemblance between the hydroids and wave-forms is certainly striking, but the question remains upon what this resemblance rests, since hydroids are certainly not falling drops, and their forms are not conditioned *only* by simple surface forces.

We come closer to the real embryonic formative processes with the gastrula models of Spek (1919), composed of two halves which swell in water to different degrees. The 'ectoderm' was formed of a double layer consisting of agar gelatine and more strongly swelling gelatine, the other half from agar gelatine alone. When placed in water this undergoes 'gastrulation'. Spek comes to the conclusion that the outgrowths and foldings of embryos are brought about by differences in the degree of stretching of the plates of cells, produced by different degrees of water absorption. For that reason, materials capable of

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[1] Przibram's book (1922), affords a valuable supplement to Thompson's work. See also the investigation of Hatschek (1927) suggested by Thompson. He obtained structures resembling medusae, blood-corpuscles, &c., from drops and vortices of gelatine in coagulating fluids.

powerful swelling, like lipoids, are of great importance in the formation of folds, and actually organs formed by folding, such as the central nervous system and the liver, are distinguished by their high lipoid content. The action of lithium is similarly explained by the more powerful swelling of the outer surfaces of the ectoderm cells than the inner, so that the invagination of the primitive gut occurs in the opposite direction from the normal.

Thus for the explanation of formation by means of the notion of formative movements (and the same holds for directed growth, see below) we are referred to specifically biological conceptions. The Field theory of Gurwitsch may be regarded as the first step towards such an explanation. According to our view, the 'field laws' so far established for the objects already mentioned, and the generalization of them to be expected from future investigations on other objects, represent statistical laws of 'higher order' in the sense explained in Part I. That is to say, they would give the behaviour of the total systems in question where a physico-chemical analysis of the process is not attainable. The geometrical formulations which Gurwitsch seeks might provide completely adequate forms for such biological laws, whilst the physical interpretation, as mentioned above, and as Gurwitsch expressly emphasizes, leads to misunderstandings. We believe that this interpretation of Gurwitsch's Field theory leaves its comprehensive and well-grounded programme of research quite untouched, and, on the other hand, the paradoxes which arise with the question of the 'reality' of the fields disappear.

B. **Segregation**

As the second fundamental developmental process we now have to consider 'organization of the embryo', or 'autonomizing' (Weiss, 1930), or 'segregation' (Lillie, 1929). A developing system possesses at first a wide range of possible courses for its various parts, i.e. the internal conditions of development can still be restored to the arrangement typical for the whole system if they are disturbed, so that neither disturbing their relations nor diminishing their amount affects the course of development. Gradually, however, the independent developmental conditions for the various partial systems segregate themselves, and thenceforward appear as 'self-differentiating'.

This process of segregation is independent of the remaining component processes; it is, moreover, no more than merely a part of the developmental process. Although, for example, in the *Triton* embryo, after the original segregation of the region of the organizer, for a long time no further segregation occurs (as is shown by those transplantation experiments in which presumptive ectoderm may become epidermis, medullary plate, or mesodermal organs, according to the place of implantation), nevertheless the process of blastula formation and gastrulation takes place. Segregation is, moreover, not confined to cell-division, it can occur as well in a single cell, e.g. the zygote (mosaic eggs), as in cell-complexes (regulative eggs).

The so-called mosaic and regulative eggs are distinguished by the time at which segregation occurs in them. In the mosaic eggs it occurs before cleavage, so that through the latter process what is segregated is distributed to the various cells. In the regulative eggs cleavage occurs before segregation, so that every blastomere still contains the requisites for the formation of the whole organism. For this reason after injury we obtain partial embryos from mosaic eggs and whole embryos from the regulative ones. As we have already reviewed the classical examples of mosaic and regulative development we need only give a brief account here—following a survey by Schleip (1927)—of the series of 'determining plasma regions'—thus the steps of segregation according to our terminology. *First*, we have the 'organ-forming plasma regions' already mentioned, as they occur, for example, in the polar lobe of molluscs. A recent example is furnished by *Tubifex* (Penners, 1926) in which pole-plasms appear at both poles of the egg and later pass over, in the course of cleavage, into a single cell (*D*) of the four-cell stage.

With the help of the X-ray method it can be shown that after destruction of blastomeres *A*, *B*, and *C* a complete embryo develops from *D*, whilst none of the remaining cells are capable of furnishing a whole embryo on isolation. A *second* stage of segregation is given by the organizer of amphibian development. If—as we shall see later—the organizer region is only quantitatively distinguished from the rest of the embryo, there will then be a continuous transition to a *third* class, namely, to the mere quantitative difference in the egg-plasma. In the sea-urchin determination proceeds from quantitative differences—according to the old experiments of Boveri and the more recent ones of Hörstadius (1928). Gastrulation occurs at what is at first the 'most vegetative' place. In the normal egg this is the vegetative pole. A purely 'animal' part contains in general no quantitatively active animal plasma. Hence there exists no fall of potential and no separation of organ rudiments occurs (except in cases of lithium treatment, see below). Any arbitrary detached piece of egg which contains a piece of the vegetative half invaginates at the most vegetative place.

We come now to a question which at present stands in the focus of interest in developmental physiology. It is the question of the scope of Spemann's principle of induction, or, what amounts essentially to the same, the question of 'predetermination'.

Spemann's investigations on the newt's egg have, before all others, forced into the foreground the idea that the regions of the germ are only created by means of organizers and the process of induction. It must be admitted that these experiments have only shown that the parts of the germ before the action of organizers are 'relatively indifferent' or 'capable of transformation'; that they are totally indifferent is not proved by them. Newer investigations show rather that there exists in them a determination which is still reversible: a 'labile determination' (Spemann), 'predetermination' (Goerttler), 'Bahnung' (Vogt), 'institution' (Graeper). Transplantation in indifferent regions will show to what extent such material is already disposed towards a determinate developmental direction; but in regions which are determinatively strongly active this tendency is extinguished, and replaced by one which conforms with the influences of the surrounding parts (induction).

Vogt (1928) has drawn attention to a point of view which has been almost forgotten in the recent prevalence of epigenetic ideas. He described inhibition of development in one half of a frog's embryo owing to lack of oxygen, and obtained the same result by introducing the germ into a close-fitting cavity in a partition wall between two vessels, one of which was perfused with cold and the other with warm water, thus producing a localized cooling. Each half yielded a half-structure of a different stage of development from the other. Vogt concluded from the absence of regulative processes in these and other cases, that there exists from the beginning a far-reaching 'facilitation' (Bahnung) of the developmental processes, so that embryonic development proceeds (1) as a mosaic-work, i.e. a direct origin of each element in its place, and (2) as a regulative process governed by organizers. (A similar experiment, with results also similar to those of Vogt, but with continuous temperature gradients instead of a sharp limit between warm and cold, has been reported independently in England by Huxley; cf. also Dean, Shaw, and Tazelaar (1928).)

Most of the German investigators try to decide the problem in question in a more special form, namely by examining the significance of the underlying organizer in the development of the medullary plate in the newt's germ. We have already learnt that, in certain experiments, the organizer may induce the development of a medullary plate; it is, however, clearly another question whether the underlayering by an organizer is, especially in normal development, absolutely necessary for the medullary plate's development. The significance of the underlying organizer, also in normal development, is supported, for instance, by the experiments of Lehmann (1928), in which defects of the underlying archenteric roof are always followed by defects of the medullary plate. But on the other hand, especially by Goerttler's results, it is proved that medullary plate may also develop without underlayering. The experiments of Bytinsky-Salz point in the same direction. He (1929) introduced ectoderm of different developmental stages and of different urodeles and anurans into the gastrula cavity of embryos of *Triton taeniatus*. In addition to many cases of development according to the new site (*ortsgemäss*), there also occurred development according to origin, in presumptive medullary material which had not been undergrown by organizer, and even in presumptive epidermis. Brachet (1927 *b*) concluded from experiments on anurans (in which the determinative process, however, occurs more rapidly than in urodeles) that the medullary primordium has a fixed determination before undergrowth occurs.

Spemann has attempted to accommodate Goerttler's results to his own views by the notion of 'double assurance' (*doppelte Sicherung*). Certain as it is that the optic cup is able to induce a lens in foreign epidermis, yet it is also certain that the proper lens-forming cells can also develop into lens without the optic cup; in *Rana esculenta* at least, both capabilities occur. A similar 'double assurance' might also be present in the formation of the medullary plate. It might be further assumed that labile determination of the medullary plate already occurs in connexion with the organizer (the presumptive mesoderm); when the latter region is invaginated and brought under the medullary region in gastrulation, the medullary plate is induced definitively. The cases in which only relative self-differentiation is proved, and the widespread actual known functions of induction, as these are shown in Spemann's fundamental experiments, would favour such a unitary view of development.

Thus, there is the question whether the organization of the germ in general starts from the inducing organizer, or whether segregation is essentially an autonomous process in the entire germ which may be supported, however, in a very energetic manner by the organizer. Present investigation seems not to be in a position to allow a definitive answer of this question. It may be mentioned, however, that simply conditioned development, in which the organizer is to be localized, is very rare; it is, in the amphibian germ, demonstrated only for medullary plate and lens, whilst the development of the other germ parts, connective tissue, blood-cells, heart, liver, &c., shows the signs of a multipally conditioned development. We may perhaps conclude, therefore, that segregation is never exclusively performed by means of induction by neighbouring parts, but almost always in dependence upon the entire germ, the organizer exercising, however, by far the strongest action of all germ parts.

In any case, the principle of progressive segregation remains the most fundamental result of modern experimental work. That this progressive segregation holds not only for Amphibia, but also for warm-blooded animals, has been made probable by experiments of many authors (Hoadley, Murray, Corinaldesi, Selby and Murray), in which parts of the young blastoderm were transplanted on to the allantois of incubated fowl embryos. From the observation that the capabilities for differentiation of the transplanted part are greater the later the time of the operation, Hoadley concluded that the 'pre-primordial segregates' are divided up through a process of 'progressive differential dichotomy' into the rudiments of the organs and later of the organ parts (see the tabular summary of Hoadley's results in Mangold, 1928*a*, pp. 179 ff.). Hoadley (1928) has recently drawn similar conclusions from experiments with *Fundulus* embryos, in which after production of local injuries in the early stages about 90 per cent. of the embryos develop normally, in somewhat later stages at least 70 per cent. show quantitative abnormalities, and later still localized defects persist and a lack of definite organs or parts of organs is observed, so that the progressive 'autonomizing' of the embryonic regions seems clear.

In a special case, not only the temporal, but also the spatial progression of determination is rendered probable. After tying off with a thread, in the egg of the dragon-fly *Platycnemis* (Seidel, 1926, 1928), only the posterior parts of the germ-primordium develop. If a complete separation is not effected by tying, two primordia develop, the one before, the other behind the place of tying. By means of localized defects brought about by cautery it was shown that the determining influence progressed from behind forwards. The limits up to which a defect may reach without preventing the formation of an embryo advances with increasing age of the embryo towards the anterior end. Seidel thus concludes that at the hinder end of the egg of the dragon-fly there is a centre from which a determining influence proceeds forwards.

It would lead us too far afield, while providing nothing new from the theoretical standpoint, were we to describe the further course of development in the same fullness. We need, therefore, only say shortly that the processes described hold not only for the germ as a whole, but also for the partial systems into which it breaks up, and hence it applies to the organ rudiments into which the embryo breaks up and which develop independently of their surroundings.

For our knowledge in this field we are indebted to the investigation of limb-buds. For a detailed description we can refer the reader to the comprehensive review by Mangold (1929 *a*) and need only mention a few principal points.

The limb-bud is equipotential along the polar axis, like the regulative egg as a whole; from half-buds, from two whole buds brought together, from two halves with like antero-posterior axes, &c., whole limbs may arise.

Here also the induction principle applies. It must be admitted, however, that between the different kinds of induction there are, at least apparently, very considerable differences. Let us remind ourselves, first, that the organizing action of Spemann does not appear to be merely a releasing one. This is clear from Spemann's result (1927, p. 947, recently confirmed by Bytinski-

Salz) that very diverse orientations of the secondary embryonal rudiment result from the implantation of the organizer, according to accidental changes of the orientation of the latter. Thus it is not something already preformed in the material that is awakened, but something is prescribed to the latter. But we now have to consider the 'induction' of the limbs in Amphibia. A 'homoiogenetic' induction of these, in material which has otherwise not developed, can, according to G. Hertwig (1927), be shown by the implantation of a haploid limb-bud, in which cases, among others, diploid and hence induced extremities appear. The implanted part is derived from haploid larvae obtained by artificial fertilization with sperms irradiated by radium. 'Heterogenetic' induction, however, seems definitely to indicate that only an 'extremity field' is activated. By implantation of auditory vesicles (Balinsky, 1926) or even of pieces of celloidin (Balinsky, 1927 *b*), and hence by a quite unspecific stimulus, it is possible to release the development of limbs. Similarly, Filatow (1927) has observed how auditory vesicles, implanted into the region of the eye, induce the formation of auditory capsules (similarly Balinsky, 1927 *a*), whilst if implanted on the abdominal side they produce supernumerary extremities. Moreover, foreign bodies such as paraffin or celloidin in the place of the auditory capsule previously removed yield auditory capsules. The induction of the development of an extremity by means of a dislocated nerve conducted to it, according to Locatelli and Guyénot, may likewise depend on such a non-specific stimulation.

The contrast between this induction of limbs and the inductions in Spemann's experiments is sufficiently obvious. In the latter, the organizer itself—if we may use the terminology of Weiss—brings its own field with it; in the former a field already existing at the place of reaction is merely set into activity. Probably, the implantation with its operative consequences (wound, inflammation, vaulting) calls forth first a quite unspecific proliferation, which later is taken over by the latent 'organization potency' of the region concerned (Weiss, 1930, p. 51). This induction of limbs, in which proliferation, at first unspecific, becomes a formative centre, is perhaps comparable with the observation of Child that a star-shaped wound conditions the production of a supernumerary head in *Corymorpha*. We might agree with Weiss (1928 *c*, p. 95) who has warned us against speaking here of organizers, since precisely the essential character of the organizer action, namely its qualitatively specific character, is absent—were it not that, on the other hand, transition stages between both kinds of 'induction' exist. Consider the experiment of Gilchrist (1929), in which by local warming—and thus a very non-specific stimulus—doubling of the medullary rudiment was obtained, and thus a result which otherwise is brought about by a true 'organizer'.

The law of progressive determination in the case of limb-buds is especially well illustrated in the fundamental experiments of Harrison and his school. First the antero-posterior axis (the direction of out-growth of the limb) is determined in the Axolotl, next the dorso-ventral axis, and finally, soon afterwards, the medio-lateral (proximo-distal axis of the adult limb, which characterizes the lateral direction right or left). For example, a young left limb-bud, when transplanted, before determination, to the right side develops into a right leg in accordance with its site, but if transplanted after determination it develops into a left limb in accordance with its origin. As Detwiler (1929) has recently established, the polarity of the anterior limb-bud in the antero-posterior direction is already determined immediately after the end of gastrulation.—The noteworthy phenomenon of rotation may also be noticed here, in which abnormally oriented extremities regulate themselves by the shortest route into positions most closely resembling the normal.

In the above-described break-up into single 'spheres of action' (Weiss) or 'elementary unities' (Mangold) it is natural that the organ complexes and organs developing are dependent not simply on the whole, but rather on the next highest region of organization. In this sense Nicholas had shown the influence of the surroundings on the orientation of the limbs. He transplanted a circular disk, which bore a limb-bud in the centre. After healing the latter was turned round in a definite way, and a normal extremity developed, the orientation of which was directed not according to the whole organism, but according to the surrounding ring of transplanted tissue.

We shall not neglect to point out that for other organ rudiments also just the same equipotentiality of the parts with the establishment of a polar axis has been demonstrated as for regulative eggs and limb-buds. This holds especially for the heart rudiment. Corresponding to the experiments of Harrison on limb-buds, Copenhaver (1926) has tested the self-differentiating and equipotential functions of the heart rudiments of the Axolotl. As regards self-differentiation it was found that the various sections of the heart and its antero-posterior axis are determined. After turning the rudiment round through an angle of 180° the sections develop in a reversed order. On the other hand equipotentiality was shown by the fact that two hearts placed one upon the other, a single divided heart, and a partly extirpated heart (in which regenerative ability is lost at the stage of pulsation), two anterior, posterior, right or left halves, put together, can all form normal hearts. Thus a far-reaching correspondence between limb-bud and heart rudiment seems to be demonstrated: the antero-posterior axis being established there is complete equipotentiality of the parts. (It should be added that Stöhr, 1927, in opposition to this, has rejected the concept of the harmonious equipotential system for the heart rudiment, in regard to the fact that from parts no *typical* heart arises.) According to Pasquini (1929) the eye rudiment is also an equipotential system, since after transplantation of the eye rudiment near to that of the host animal the two unite to form one eye-vesicle of large size. The eye rudiment can be cultivated *in vitro* (Strangeways and Fell, 1926; Filatow, 1926), in which case it develops further almost normally, and also, according to the latter author, from an explanted distal half, as well as from the proximal half remaining in the animal, a complete but small cup arises. Also the auditory vesicle rudiment (Fell, 1928) and heart rudiment (Ekman, Olivo, 1928) are capable, after determination, of differentiation *in vitro*. Goerttler (1928) has shown that the heart rudiment in Urodeles is already determined in the open medullary plate stage, and when isolated can develop into a rhythmically pulsating tissue (although without further development of form), in which case only material taken from the left side shows the ability to pulsate, which indicates the 'developmental lead' of this side, and throws light on the asymmetry of *situs viscerum*. The result obtained by Federici (1926) is interesting, according to which the blood of the tadpole is a real organ, possessing, in the blood islands, its determinate and irreplaceable rudiment.

What, then, is the present position regarding the explanation of segregation? We can at least say that by means of the new results the theory of 'preformation' is refuted and that of 'epigenesis' is confirmed. In the egg and embryo only the totality of all species-specific developmental possibilities are 'preformed'. The developmental direction of the individual parts of the embryo has not yet been established; there are no preformed rudiments for the various organs; the individual embryonic parts are only gradually forced into definite paths of development. This establishment of the course of development of these embryonic parts occurs within the organization of the total system by the mutual interaction of such parts, and thus 'epigenetically'. In other words, a real increase of the degree of multiplicity takes place; the multiplicity of the finished organism is not already predelineated in the egg. Some measure of internal differentiation—in the extreme case perhaps mere quantitative differences along a polar axis—we must certainly ascribe to the egg. Both on empirical and *a priori* grounds we cannot regard it as completely homogeneous. Even in the extreme case of regulative eggs we find empirically some axial differences. But a completely homogeneous germ which, as a whole, constituted an equipotential system, would not be susceptible of causal analysis, if different formations arose subsequently from its parts, and these were not correlated with environmental differences.

Nothing stands in the way of our regarding segregation as a 'chemo-differentiation'. We have, however, expressed the conviction that the term 'chemo-differentiation' is not capable of covering the whole problem of development. The results obtained with mosaic eggs, however, and especially some recent investigations on the variations of the colloidal state of the germ, do suggest that the appearance of material differences is at least an *index* of segregation. By means of the centrifuge the lipoid granules in the cytoplasm of the sea-urchin egg were displaced outwards and collected in the future ventral region. It was thus possible to establish a dorso-ventral axis experimentally, and also to prove the influence of the distribution of cytoplasmic colloids (Runnström, 1926 *b*). The polar differentiation of the cytoplasm of the sea-urchin egg (which was first studied by Boveri) has recently been studied by Runnström (1928) under dark-ground illumination. In the fertilized egg an orange-yellow coloured illuminated ring appears—the 'dark-field ring'—the rest of the surface being silvery white. This dark-field ring is not identical with the orange pigment in the sea-urchin egg, and probably corresponds with the part which, in gastrulation, is invaginated. After treatment with lithium the upper limit of the dark-field ring extends into the animal half of the egg. In this way an indicator for the effect of lithium treatment is obtained which is immediately perceptible. These observations of Runnström enable us to understand the paradoxical results of v. Ubisch (1929), according to which even animal halves of the sea-urchin egg may gastrulate after treatment with lithium.

It has already been suggested that the process of regulation presumably represents a special case of the restoration of an equilibrium. But it is easy to see that this does not yet provide a 'physico-chemical explanation' of regulation. The principle of regulation, for example in the form preferred by Köhler, naturally says nothing at all about the nature of the system governed by it. It holds equally for mechanical systems (the formation of layers in fluids of different density), for electrical ones (Köhler's system of condensers), or for chemical ones (chemical equilibrium); and it can also hold for embryos if they are systems with quite special kinds of 'forces' governing them, i.e. if they form specifically biological systems. The process of regulation would only be 'physico-chemically explained' if we could show that regulation means nothing more than the formation of layers of fluids of different density, or the restoration of disturbed concentration-relations in accordance with the law of mass action, &c. Such an interpretation—if we follow Goldschmidt—is more or less plausible for the regulation of experimentally injured embryos, although naturally no exact proof has been given. But belonging to the same series as regulations of divided, fused, and injured embryos, we have the analogous experiments with organ rudiments, regenerating blastemas, and whole lower organisms (e.g. the 're-integration' of artificially produced planarian monsters, Steinmann, 1927). In all these cases it seems hopeless to discuss physico-chemical speculations about the nature of the 'equilibrium' which is supposed to be restored by regulation.

Since, then, a physico-chemical explanation of the process in question is certainly impossible in the present state of our knowledge, and may be impossible in principle, we must meanwhile use for the purpose specific biological concepts like 'field', 'induction', 'organizer', and others of like nature, and thus deal with entities and relations of 'organismic' order.

C. **Differentiation**

Segregation is normally followed by differentiation. After definite developmental directions are established in the various parts of the embryo—either by the autonomous break-up of the whole system, or under the influence of definite localized organizers—the processes of differentiation now proceed in the individual parts of the embryo, or their cells, independently of one another. If segregation is a process which is completed in the system as a whole, the differentiation following it is a matter of individual parts, especially of cells. When segregation is complete there is no longer any 'regulation'; development of the parts follows the path now laid down, in 'self-differentiation', without respect to the environment—indifferently whether this leads to a functional or to an abnormal structure.

The reaction of segregation to the 'differentiation potencies' of the cells manifests itself firstly in a reversible *Bahnung*: under sufficiently indifferent conditions, they differentiate *herkunftsgemäss* (cf., for instance, Holtfreter's interplantation experiments, see below, also Goerttler's results); but under the influence of a determining region, the developmental direction may be changed, and differentiation *ortsgemäss* takes place (thus, for example, the presumptive epidermis and medullary plate-cells of the early stage of the gastrula in Spemann's fundamental experiment, p. 121; in Mangold's experiment the transplanted material enters even into the formations of another germ-layer). In a later stage, however, development occurs *herkunftsgemäss* in any case (Spemann's transplantations of pieces of the later gastrula). This falling off of 'differentiation potency' is especially clarified by a newer experiment of Lehmann (1929).

He took rectangular pieces from the region between presumptive medullary plate and presumptive epidermis, reversed them, and then replaced them so that the half consisting of presumptive medullary plate came to lie in the epidermis region, and the half consisting of presumptive epidermis in the medullary plate region. The experiment was carried out on germs of different developmental stages. As a result it was found that before the archenteric roof comes to underlie the ectoderm the developmental direction is changeable in all cases, but this is so only in some cases during the process of underlayering with archenteric roof, and shortly after the completion of this process only in a few cases. It is then found that development according to origin (*herkunftsgemäss*) cannot be stopped.

We have already demonstrated that 'differentiation' and 'segregation' are to be regarded as different processes. Newer experiments seem to indicate that differentiation may occur independently of segregation or of organizer action.

Dürken (1926) introduced animal material of the blastula and gastrula of *Rana fusca* into the empty eye-cavity of older larvae, and observed that these developed into chorda, cartilage, ganglion cells, and even into central nervous system and labyrinth. Thus tissues and organs may arise without the normal course of gastrulation, although it is difficult to exclude here the possibility that organizer material was introduced with the rest. Dürken has sought to bring his results into relation with the theory of tumours of Cohnheim. Holtfreter (1929, *a*, *b*) introduced embryonic parts into the body cavity and lymph spaces of older larvae: presumptive epidermis yielded epidermis, corium, connective tissue, and sense-buds; presumptive medullary plate before undergrowth yielded structures resembling neural tube, complexes resembling ganglia, and also nerve-fibres. In this way the capacity for self-differentiation is proved for presumptive epidermis as well as for presumptive medullary plate.

Bautzmann (1929) by means of interplantation experiments similar to those of Dürken (but performed on *Triton* embryos) obtained self-differentiation in a direction other than that corresponding to the prospective significance of the part. Material from the boundary between medullary region and ectoderm (and thus far removed from the ectoderm-mesoderm region) developed into chorda and musculature. Kusche (1929) found that—whilst cells of the region of presumptive organizer always develop *herkunftsgemäss* into chorda and muscles—from all other regions of the early *Triton* gastrula chorda and muscles arise; medullary plate and epidermis material of the late gastrula, however, differentiate always *herkunftsgemäss*.

This 'self-differentiation contrary to the prospective significance' (*bedeutungsfremde Selbstdifferenzierung*) may be interpreted on the assumption

> 'that the cells may possess from the beginning various differentiation possibilities. In cases where the cells are in an organization area, a definite typical one of these possibilities is activated. But it may also occur that any indefinite one of these possibilities is activated by means of *unspecific* influences'. (Weiss, 1930, p. 57.)[1]

Differentiation may be regarded as the visible result of 'chemo-differentiation' occurring in segregation. This chemo-differentiation may be interpreted by assuming that in different regions different reaction-chains proceed; so long as only a small advantage is reached by certain reactions, it may, unhindered, progress farther, but it may be overtaken by the slower reactions, if these are favoured by new conditions. In this way 'labile determination' or 'facilitation' may be conceived. We can assume, for example, that there are going on, in the ectoderm cells belonging to presumptive epidermis, the reactions leading to the formation of 'epidermis' as well as those which lead to the formation of 'medullary plate'. Normally, the 'epidermis reaction' progresses faster than the 'medullary plate reaction'. But after implantation of an organizer which transmits 'medullary plate substances' the 'medullary plate reactions' attain the preponderance—and medullary plate develops (cf. also Marx, 1930, pp. 368 ff.). If, however, certain reaction-chains have attained a considerable advantage, later influences cannot suppress it; further development goes on in 'self-differentiation', and the 'differentiation pluripotence' given at the beginning is 'extinguished'.

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[1] It may be mentioned, however, that this explanation of Weiss's is not the only possible one. We could assume also, with Huxley (1930), that every cell in the interplantated parts becomes a 'dominant region', an 'organizer' yielding mesodermal material, by means of a 'physiological isolation' in Child's sense; in the same manner as in the regeneration of planarians, coelenterates, &c., every isolated piece becomes a 'dominant region'.

D. **Growth**

We only have to consider growth in so far as it constitutes a component process in development, i.e. we are concerned neither with the problem of cell-division as such, nor the laws of growth as quantitative increase. The form of an organ or part—e.g. the formation of an extremity—is essentially determined by different growth-rates in different directions. When tissue fragments are explanted they show in general a disorganized and chaotic growth. In the organism, on the other hand, growth is organized in a definite manner, and is anisotropic in different directions. The fundamental problem is thus to discover the factors which condition the direction of growth in the organism. We are at present very far removed from an insight into this question, and only possess some first hints towards an answer to it.

A first possibility of interpreting the organization of growth is through the orientation of the cells by the medium which surrounds them. Weiss investigated the problem whether the chaotically growing material of a tissue-culture might not be forced experimentally into a definite structure. He cultivated tissues in freely hanging membranes, which were stretched between simple geometrical figures (rectangle, triangle), and was able to show that growth takes place in the direction of maximum tension. Thus in a triangle, for example, it occurs in three ray-like tufts towards the corners. The effect is in the first place directive, because the direction of growth seems to be guided into the chief directions of tension, and secondly it is intensive, because in these directions the strongest growth takes place. A closer analysis shows that heterogeneous growth is referrable to a primary structure arising in the medium in such a way that its mycellae are oriented in the direction of the tension. Thus cell-growth follows, as it were, the path marked out for it by the directed mycellae of the medium. As regards the intensity effect, this is conditioned by the fact that in the fibrillae water is more easily available to the cells. On the other hand, the removal of fluid not only occurs in the direction of the fibrillae, but, as a consequence of this, further fibrilla-formation is organized in the same direction, so that an effect which is weak at first increases of itself. Presumably in the organism also the ground-substance first becomes organized, and the growth of the cells follows its colloidal organization. This also makes possible a causal explanation of the seemingly so remarkable teleology of functional adaptation. But the most manifold physical and chemical actions also have an influence on the structure of colloids, and may, in this way, indirectly affect the direction of cell-growth.

A *second* possibility regarding the regulation of growth is offered by cell-division hormones. It has been shown that materials are liberated from injured cells which promote cell-division. If, now (somewhat in the sense of Goldschmidt's theory), we imagine a differential distribution of such cell-division hormones, this might explain the directed growth in the organism. Naturally nothing is known about the stimulation of *directed* growth by means of hormones.

Somewhat similar remarks apply to the *third* growth factor, the discovery of which must be regarded as one of the most important in modern biology—the 'mitogenetic rays' revealed by Gurwitsch (among numerous papers see especially Gurwitsch, 1926, and Reiter and Gabor, 1926). From the growing-point, e.g. of an onion root, rays of short wave-length proceed which excite cell-division when they encounter tissues capable of proliferation (e.g. another onion root, or a yeast culture). The radiation corresponds to a short-wave ultra-violet and accordingly penetrates plates of quartz. Various animal tissues have been shown to generate the radiation. But very little is known at present regarding the excitation of directed growth by mitogenetic rays. Blacher (1930) comes to the conclusion that in the regeneration of the tail in Axolotls and newts mitogenetic rays issue from the disintegrating dead tissues. The form of the regenerating organ, which is at first cone-shaped, is interpreted as resulting from the action of mitogenetic rays issuing at an earlier period from the central part of the body rather than from the peripheral parts.

Finally, a *fourth* element in the production of directed growth has been suggested: the production or restoration of a biodynamic equilibrium. Such a point of view has been applied especially to the problem of regeneration, but may also be referred to in this connexion. Przibram (1922) has attempted to work out an energetic theory of development. If we ascribe a 'potential' to every formative force, on the analogy of electrical potential, &c., we can understand by this the capacity to develop a definite form, but without necessarily having a concrete idea of the nature of the process. Every organism which possesses definite axes is to be regarded as a system in which the magnitude of the formative forces is different in different directions. With increasing magnitude the resistance to the formative potential becomes greater (analogously to the introduction of conductors into an electrical circuit). The loss of parts represents a raising of the formative potential. If we denote the potential of development at the end of an axis by p, then, with the removal of a piece from this axis a rise to the value of P will occur, and the potential difference $P—p$ will give an acceleration of growth representing 'regeneration', until the dynamic equilibrium characteristic of the organism is restored. Equilibrating processes proceed with greater velocity the farther the system is removed from the state in which equilibrium occurs, so that the restoration proceeds at first quickly and then more slowly the nearer it approaches to its final equilibrium. This actually holds for regeneration-curves based on numerous quantitative experiments. The velocity of regeneration is directly proportional to the length cut off, and indirectly to the time which has elapsed since the injury occurred. This theoretical foundation has been applied by Przibram to numerous problems of regeneration, especially to the phenomena of compensation. It also leads to the interpretation of 'form quality' as a velocity-relation, i.e. the assumption that in every organ different growth processes occur which are normally so graded that some definite one 'gains the upper hand', whilst in cases of injury from amputation and consequent regeneration one of the concurrent processes may take the lead instead. In this way Przibram explains 'homoiosis', e.g. the regeneration of an antenna instead of an eye in crustaceans. In this way he approaches the ideas of Goldschmidt reached by quite a different route.

Growth shows itself to be to a large extent independent of the remaining component processes, especially differentiation (e.g. proliferation may continue in tissue culture for years with little differentiation); there seems, indeed, to be an antagonism between proliferation and differentiation.

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In the foregoing account we have confined ourselves exclusively to the primary processes of development. It is beyond the scope of this book to enter into further details of the manner in which the general framework thus laid down is modelled and altered by the influence of hormones, of the nervous system, and of function.

E. **Polarity and Symmetry**

The most general directions of development are marked out by the axes of polarity and symmetry. A polar axis appears to be present in every organism that is capable of development. The 'classical' example of this is the layering of the sea-urchin egg with its three zones, of which the unpigmented vegetative layer yields the primary mesenchyme, the orange pigmented layer yields the primitive gut, and the unpigmented animal layer the ectoderm. The layering stands in connexion with the attachment of the oocytes in the maternal organism. A similar polar arrangement of egg substance is widely distributed among animal eggs.

It was, however, reserved for the investigations of Child and his pupils to deepen our knowledge of the nature of polarity to an important degree (see his Summaries, 1926 and 1929 *a*, with complete references). The most general characteristic of the physiological axes is their different susceptibility to chemical and physical agents, shown by the course of cytolysis, death, and other signs of the action of poisons, and often also by acclimatization to low concentrations and intensities, in which cases the regions which are most susceptible to lethal concentrations and intensities most speedily become acclimatized to low concentrations of many reagents. Axial differences of sensitivity were discovered in all forms that have been investigated from this point of view (200 species of all the larger animal groups, with the exception of Arthropods, and 50 species of Algae), and with the most diverse chemical and physical agents. The fact that the axial susceptibility differences are the same for different agents indicates that a general quantitative physiological differential is the primary factor. The general parallelism between differences in sensitivity and intensity of metabolism shows that quantitative differences in metabolism form an essential factor in such cases; hence the axial gradients represent metabolic gradients. With the differences of susceptibility are connected axial differences with respect to permeability, respiration (as shown by expenditure of oxygen and production of carbon dioxide), reduction of potassium permanganate, and of electrical potential. Similarly, gradients manifest themselves in the graduation of differentiations (e.g. different frequency of one, two, or many polar forms, in the hydropolyp, *Corymorpha*; graduation of head-frequency in the regeneration of planarians, according to the level of section). By means of conditions which influence the physiological activity, the polarity and symmetry can be influenced, suppressed, or determined. Thus, e.g., according to Gilchrist (1929), new axes of polarity can be established in Amphibians by a temperature gradient, at the hot end of which a secondary axial system arises; in Hydroids by means of the enhanced intensity of metabolism as a result of injury, so that, for example, in *Corymorpha*, by means of a star-shaped wound a new head perpendicular to the existing one arises with stolons opposite to it. This possibility of experimental influence, for example, the fact that a piece of hydroid, when it grows freely in the water, produces hydranths, when attached to the bottom and its metabolism is in consequence inhibited, it produces a hinder end, shows that the physiological axes are determined by quantitative and not by qualitative differences. Conditions which suppress the physiological axes are such as to abolish the quantitative differences in various regions. New axes are indicated by new gradients. If the unity of the gradient is disturbed, a unitary individual is no longer obtained. Different organs grow on different levels of the gradient. Since, however, polarity and symmetry are in the first instance quantitative differences, it seems that differences of the concentration of substances at different levels constitute the first step to qualitative differences. In this way the gradients appear as the adequate physiological basis for polarity and symmetry.

Since physiologically more active regions govern the less active they ensure the harmony of the organism. If the dominance of these regions disappears, 'physiological isolation' of the parts no longer governed by them takes place (cf. 1929 *b*). In many organisms the original gradients disappear during development, and new ones appear. Thus in Child's sense, Spemann's centre of organization appears as a secondary region of dominance, which is distinguished not qualitatively but quantitatively by its stronger activity from the rest of the embryo, and—like Gilchrist's high temperature—raises the activity of the surrounding tissue to that level in which medullary plate develops. Organizers are not peculiar to the development of Amphibia: the growing-point of a plant, the head of a piece of a Planarian, the local injury which determines a new axis in Hydroids, are all organizers. Many facts suggest that the influence of a region of dominance has a transmissive rather than a transportative character, i.e. that it consists in a form of transmission of energy through the protoplasm or along a boundary surface rather than a transportation of material.

Some objections have recently been brought forward against the theory of gradients (cf. Weiss, 1928 *c*, p. 91 f.). First, against the assumption that the gradients signify a decline in activity of the total metabolism. In opposition to this Parker (1929) has recently been unable to show a 'metabolic gradient' by measuring the regional production of carbon dioxide in worms. Secondly, against the assumption that the activity gradient in the germ possesses a regular relation to its polar organization. In opposition to which Ranzi, on the basis of his investigations of the susceptibility of the embryonic stages of cephalopods, comes to the conclusion that this sensitivity is determined solely through the degree of complication of the organ concerned, and not in any sense by an axial gradient. Similarly, Portsmann (1927), in investigating the de-differentiation of sea-anemones, has found that this does not proceed schematically from above downwards, but organs of different degrees of differentiation react quite differently to potassium cyanide (e.g. the most resistant part, the oesophagus, lies close by the tentacular region which is the most damaged). Finally, Parker (among other authors) believes that the metabolic gradients only represent a measure of activity, but cannot be regarded as causes of morphogenesis.

With regard to the two former objections, the gradient theory must not be conceived too schematically. It seems to be proved that germ regions in which vigorous developmental processes are going on are distinguished by a higher susceptibility; but it is not a general rule, especially in higher organisms, that the regions of different activity are always ordered in a simple axial sequence. According to Weiss, it is not demonstrated that the axial gradients, which, however, are *indicators* for regional differences of the physiological activity, represent too, in Child's sense, veritable *factors* of development, locally raised metabolic activity being the cause for local developmental processes. He points out especially that the gradients only express quantitative differences of activity and therefore do not yield an explanation for the qualitative differences of the developmental processes (1930, pp. 92 ff.). This objection, however, does not seem to be decisive; for it is not at all difficult to imagine how differences which are only quantitative at first may lead later to qualitative differences. The chemical changes, which are perpetually going on in the developmental system, will follow most rapidly in those parts which are the richest in reacting materials; these processes continuing a longer time, the phase difference between the processes on the 'high' and on the 'low' end of the gradient will always increase. Finally, there will be a point where at the one pole reactions are already performed which are not yet attained on the other: the difference which was first only gradual and quantitative becomes now a qualitative one. Of course, the axial gradients represent no more a complete explanation of development than any other chemical representation; although certain metabolic intensities may favour the development of this or that organ, it is, however, not at all explained how the organism can develop organs which are characterized by material, form, and arrangement.

Apart from this problem, many results favour Child's view that the organizer action rests, at bottom, on the quantitative basis of a metabolic gradient.

Penners and Schleip (1928, cf. also Schleip and Penners, 1926) have repeated, with the aid of modern technique, a classical experiment of experimental embryology. Frogs' eggs compressed between glass plates and turned upside down yield the so-called double monsters of Schultze. It was here shown that a blastoporic lip can also develop outside the region of the grey crescent, i.e. outside the sphere of the organizer. Thus every part of the embryonic surface can form a cleavage cavity, whence it results that the centre of organization is distinguished not qualitatively but quantitatively from the remainder of the surface of the egg. Similarly, Runnström (1926 *a*), by treatment with hypotonic sea-water, obtained supernumerary archenteric primordia in the sea-urchin egg, so that the gut-forming potentialities extend up to the animal pole, although to a decreasing extent. Hörstadius (1928) found, in cases of longitudinal section and formation of a whole embryo in the sea-urchin egg, that the invagination always appears at the most vegetative point. The latter forms a centre of organization on which the development of organs in general depends, and the arrangement of any given material (in cases of fusion) is thus guaranteed. Ubisch (1929) observed gastrulation even in the animal half of the egg after treatment with lithium. Goetsch (1926) has compared the buds of *Hydra* with Spemann's organizers, since they are able in cases of injury to the mother's body, or when implanted, to use other parts as material for their development. The same holds for the 'complantation' experiments of Issajew (1926) and for the results of Rand, Bovard, and Minnich (1926), who implanted a second head under the crown of tentacles in *Hydra*, and then cut off the original one. In these cases no new head formed, but the implanted head took possession of the whole of the rest of the organism. After removal of the differentiated parts of a hydroid the middle piece is not polarized; only through introduction of an intact end-piece is the polarity established for the formation of a crown of tentacles or a basal disk. Thus the polarity in less organized parts is determined by more differentiated ones, in a manner analogous to that in which a piece of iron becomes magnetized by contact with a magnet (Goetsch, 1927).

Goetsch has recently reviewed a great number of interesting experiments which point in the same direction (1929). If, for example, foot-ends (lowest potential) are attached to both ends of a piece from the middle of *Hydra*, there appears a head at the place which is now the most active, namely, in the middle region. Or, if a *Cordylophora* (Hydroid) is placed in a glass tube, a head arises wherever there is an opening in the tube.

In the 'frustulae' of *Microhydra*, which drop off and attach themselves to the bottom of the container, heads always develop at a point opposite to the place of attachment, quite irrespectively of the part of the body at which attachment has occurred.

In many eggs (e.g. Ascidians) the bilateral symmetry is already visibly marked out in the fertilized egg. In others it must be predetermined, either in the form of an invisible structure, or of a gradient which is graduated not only in a polar axis, but also in the plane of symmetry. For, parthenogenetically developing eggs, e.g. of the frog, also show bilateral symmetry, in which case—if the parthenogenesis is excited by pricking (Brachet)—the median plane shows no relation to the place of puncture. Already Roux, however, had demonstrated that the meridian of the place of entrance of the sperm coincides with the first cleavage furrow; the original bipolarity seems, therefore, to be changed by the outer influence. The coincidence between the place of entrance of the sperm and the first furrow is, however, not at all absolute (Weigmann, 1927; Bánki, 1927).

Between the plane of the first cleavage and the future median plane there is also, in Amphibians (Smith, Vogt, Bánki) and Echinoderms (v. Ubisch), no binding connexion. In the amphibian egg, the median plane coincides almost with the symmetry plane of the 'grey crescent'.

Finally, as regards the third axis, and thus bilateral asymmetry, each half in a later bilaterally asymmetrical system may at first possess the ability to produce 'right' or 'left' structures, and the normal bilateral asymmetry comes about in consequence of the possession, by processes in one half, of a developmental lead or advantage; so that it only remains to the other half to carry out the opposite processes. Various experiments (cf. e.g. above, p. 152, Goerttler) show that the left side normally possesses a developmental lead over the right, and this leads to the normal *situs viscerum*. If, on the other hand, this advantage is overcome—in the simplest case by separation of the left side—

then in sea-urchin eggs (Hörstadius) and in *Triton* eggs (Spemann and Falkenberg) the developmental processes in the right half of the germ, which are otherwise dominated by the left, are able to manifest themselves and we obtain *situs inversus viscerum* (for a detailed analysis, cf. Weiss, 1930, pp. 90 ff.). The determination of the axes in amphibian extremities is already reviewed above.

F. **Regeneration**

After accomplishment of development, the 'organizing potencies' of the different regions, at first considerable, are extinguished, and remain only at certain points of the body which are said to be capable of 'regeneration'. We shall restrict our remarks on regeneration to a few words (cf. Korschelt, 1927).

The first problem to be treated is the question of the material for regeneration. The old principle, 'like produces like', holds good for some tissues—nerves, epidermis—these being regenerated by simple 'sprouting' of the tissues of the stump. But it does not hold for every case. This is demonstrated, for example, by an experiment of Weiss: he removed the whole skeleton from a newt's extremity, and amputated the extremity thus freed from bone; though the skeleton within the old stump was not regenerated, the removed distal parts of the extremity were regenerated with their complete skeleton. The greatest portion of the regenerate is produced by the indifferent blastema which undergoes differentiation. Hence the question of the origin of this blastema arises. It has been demonstrated for very different animals, that regeneration in quite a unitary manner proceeds from relatively undifferentiated cells which often wander to the place of regeneration from places far removed from it. This has been established, for example, for *Hydra* ('interstitial cells', Schultze), for *Triclads* (Lus), *Rhabdocoeles* (Hein), *Polychaetes* (Pflugfelder), *Lumbricids* (Weizmann), *Lumbriculids* (Sayles, Weizmann). In this way the old controversy (Driesch, Schaxel) whether the re-differentiation of

Clavellina resulted from a real de-differentiation and new formation, or a new production of the organism from reserve-cells which have remained embryonic, has been decided approximately in Schaxel's sense. Whilst Huxley (1926) was not able to settle the question whether the new formation proceeds from embryonal reserve cells or from the de-differentiated cells themselves, Spek (1927), by means of vital staining, has now demonstrated the presence of amoeboid, omnipotent 'drop-cells' which alone are responsible for new development in budding and regeneration, and in cases of new development following reduction and de-differentiation. In the regeneration of vertebrates, however, such a wandering of regeneration cells does not take place: if a haploid arm is implanted to a diploid triton larva, the regenerated arm after amputation is haploid like the stump and not diploid like the body. In the regeneration of the leg in amphibians, primitive undifferentiated mesenchyme cells are probably the most important material of regeneration (Hellmich, 1930).

Thus we come to the important question of 'metaplasia'. Metaplasia is the name given to the process in which a differentiated cell-material loses its differentiation, becomes embryonic, and undergoes new differentiation. How far there is 'metaplasia' in this sense requires new investigation. The well-known example is the lens of *Triton* (derived normally from epidermis) which is regenerated from the iris (derived from the brain). The iris yields material for the regeneration of the lens as well as of the *retina* (Wachs, 1920); the *tapetum nigrum* also yields material for the regeneration of the *retina*. It seems, however, that the *tapetum* is to be considered as 'relatively indifferent'. A veritable transformation of a cell of one sort into one of another is demonstrated, as regards related tissue forms (e.g. blood and connective tissue cells, Maximow), by means of culture *in vitro*; but it seems not to be proved definitively that after a regression of its differentiations the cell actually recovers an enlarged 'differentiation potency'. This possibility should remain open for certain botanical examples, as the regeneration of a whole *Begonia* from a leaf fragment, and especially for the formation of galls. Thus Küster (1926), after a study of the Cynipid galls, comes to the conclusion that every kind of cells of the plant can produce every other, and no kind of specificity is peculiar to the tissue-layers and kinds of tissues in the organs of the plant.

The study of regeneration shows that ontogenesis and regeneration are essentially of the same kind. It follows from the essence of the segregation of the developmental system into independent part-systems that the organization of the regenerated part depends always upon the remaining stump, and not upon the whole organism. This can be proved in many ways. If a foreleg is transplanted, in a salamander larva, in the place of a hind leg and amputated within the transplanted part, a foreleg is regenerated; hind legs, transplanted in the shoulder region, behave in a reverse manner. Guyénot's doctrine of 'regeneration territories' teaches us just the same: the animal (amphibian, reptile) is supposed to be divided into a mosaic of different regions, which possess specific capacities for regeneration (see the Summary, 1927). The existence of such territories is shown in three ways: (1) by the absence of any kind of regeneration after total destruction of the region concerned; (2) by the specific regenerative functions of these regions as shown after the mere releasing stimulus of an arbitrarily connected nerve (in this consists the arrangement of Locatelli); and (3) by the specific regenerative functions of a fragment of the region concerned after transplantation into other places in the body. Thus Valette (1929) found that after complete transverse separation of the point of the snout of the newt regeneration does not occur, and by a special arrangement of the experiment it is shown that the result does not depend on the presence or absence of nerves. Similarly the paw only regenerates when basal parts of it remain (Guyénot and Schotté, 1926), and the tail does not regenerate after total extirpation (Schotté, 1926).

The rules of determination hold good also for regenerative processes. Before a certain stage, the blastema is not yet determined; thus, in Weiss's experiment, tail blastema may yield a leg. After a certain time, the blastema is already determined to develop certain organs and develops *herkunftsgemäss* on transplantation. This not only holds for the regeneration of amphibian legs and tails, but also for the regenerative buds of planarians (Goetsch, 1926). The organizing influence starts from the stump, and the determination is not realized 'part for part' but as a whole, as is proved by the formation of bones in a leg deprived of skeleton, and especially by Weiss's 'whole regenerates from the cross-section of a half-extremity'.

Further, the regeneration-blastema is an 'equipotential system'. A unitary extremity, for example, arises from divided and fused blastema (if the axes are parallel). A lower organism represents a single 'reaction-system', comparable with a regulative egg or an ontogenetic or regenerative organ-rudiment, which may yield a whole after any division, splitting, and fusion. The last-mentioned fact is illustrated by the curious 'reintegration', the tendency to form a unitary individual, as is manifested by experimentally produced double monsters in planarians (Steinmann) and *Hydra* (Goetsch, Issajew). It is a characteristic feature peculiar to regeneration that the 'organization potency' of the stump only includes the faculty to restore the distal parts, but not the proximal ones. If, for example, a fragment of an organ, a piece of extremity, is implanted so that the proximal end is directed outwards, a mirror image of the implanted part is regenerated. Thus the distal end is not able to produce the more proximal parts, but only a repetition of itself.

In the excitation of growth, as a component process of regeneration, necro-hormones resulting from the injury may play an important part. The proliferation thus stimulated, being a centre of strongest activity, may attract the 'organizing' influences of the surroundings in a way similar to that in the hetero-genetic limb induction.

Ontogenesis and regeneration being essentially uniform, the theoretical considerations concerning the component processes of the former hold good, *mutatis mutandis*, also for regeneration. In any case, we may regard regeneration as a primary property of the organism, not as a secondary mechanism produced by selection as Weismann thought. This is in accordance with the fact that the capacity of regeneration diminishes in the phylogenetic as well as in the ontogenetic scale.

Regeneration suggests in a special manner the application of dynamic conceptions, which may be expressed in the concept of the organic 'field'; for we do not have here, as in the case of ontogeny, a material organized from the beginning, but at first we have an unorganized aggregate of cell-material, into which order only comes gradually, as though it were organized by a field of force governing cell-motion and growth.

XI

THE HISTORICAL CHARACTER OF THE ORGANISM

THERE still remains one great problem of development which we have left completely out of account in all the preceding: namely, its historical character. On the basis of a multitude of facts we are compelled to assume that organisms have developed from 'simpler' to 'higher' forms. For ontogeny this problem takes the form of Haeckel's 'biogenetic law', according to which ontogeny is the 'recapitulation' of phylogeny, and, secondly, phylogeny is the 'mechanical cause' of ontogeny. There is no doubt that this formulation of Haeckel's is exposed to important objections. We need not enter upon a detailed critique of the 'biogenetic law' since de Beer (1930) has recently provided an admirable criticism dealing with all the modern data. We need only pick out one or two especially striking points. It is clear that Haeckel's parallelizing is not right even for the beginning of the process. For the egg, for example, of man, this system of innumerable developmental potencies, which realize themselves in the progress of development, can in no way be compared with the hypothetical unicellular organism from which phylogeny took its starting-point. The first stage already shows that we cannot speak of a 'recapitulation' of phylogeny by ontogeny. Secondly, the distinction between caenogenesis and palingenesis is extremely doubtful. If it is agreed that the recapitulation of phylogeny is only realized with innumerable modifications, displacements, &c., then it is clear that the door is open to the arbitrary whim of the interpreter. Moreover, as de Beer has shown in a most ingenious way, the ontogenetic stages of the ancestor can be mixed up in the ontogeny of the descendants in the most varied manner, far beyond the limits of caenogenesis of Haeckel, which merely represents one among many possibilities. De Beer derives this from Goldschmidt's law of the independence of the reaction velocities of different genes, whence, in a striking way, phylogenetic developments appear to be traceable to the principle of heterochrony—at least in so far as the origin of new genes is not involved. We cannot, then, speak of a 'recapitulation', i.e. a successive repetition of the adult states of the ancestors in the ontogeny of the descendants; the 'repetition' of ontogenetic stages of the ancestors in the ontogeny of the descendants (mixed up with one another by heterochrony), manifested in ontogenetic resemblances, is therefore only a proof for the relation of such forms, but not a demonstration of the adult structure of the ancestors. Finally, the concepts of phylogeny and ontogeny lie on different planes, so that this parallelizing is not possible without further difficulty. For phylogeny itself is only a collective name for a long series of individual ontogenies. Thus, ontogenetic development cannot, in principle, repeat the 'history of the phyla', which itself is only an abstraction, but merely the past ontogenies. In somewhat different words, we can say that ontogeny cannot, in principle, run through an ancestral series, because the embryo of the higher animal form is never identical with another lower animal form. The members of the phylogenetic series are independent living forms, whilst embryonal stages are mere transition stages.

That feature which received a rather unfortunate formulation in Haeckel's 'law' nevertheless remains: namely, that the developmental system out of which a higher organism arises at the present day must have been summed up gradually over a very long period of time in the course of its racial history, and that in ontogeny the *Anlagen* collected in phylogeny are progressively unfolded. *Anlagen* not indeed in the sense of 'determinants' for individual organs, but *Anlagen* for the whole organism, which act in such a way that from a sea-urchin egg a sea-urchin always arises, and from a human egg always a human being, and which general *Anlagen* are, in the course of ontogeny, progressively determined to the bringing forth of individual organs. Since the lower levels of development are, in both phylogeny and ontogeny, the presuppositions for the higher, so it results that a general parallelism between them occurs, although this is naturally far from a 'recapitulation'. The logical foundation of the comparison of ontogeny and phylogeny has been investigated by Woodger (1931) with the help of his conceptual system.

After we have fully dealt with its 'totality' or 'organismic' aspects, a formulation is thus still to be sought for the historical side of the problem of the germ. It must be admitted that we are far removed from a satisfactory solution. We seem to have here a clear contrast to the physico-chemical occurrences. For the latter exhibit no historical enhancement; a physico-chemical system assimilates itself to the outer relations, but it is never able to enhance itself and pass over to a higher level of complication, as we must assume has happened in the course of phylogeny. Attempts have been made to deprive this fundamental character of the organism of its special position: hysteresis, as, for example, it is exhibited in residual magnetism, the behaviour of colloids, e.g. the dependence of the precipitation of a colloid on the treatment it has previously received, signifies the dependence of the state of a system on its history, and thus its 'historical' character. (The most important recent discussions of this topic from the standpoint of theoretical physics are those of Raschevsky, 1929 *a*, *c*.) But it should be noted that these physical analogies do not touch the essential features of the historical character of the organic: the double process of phylogenetic accumulation of *Anlagen* and their ontogenetic evolution (cf. also pp. 70 ff). Here is the point of attack of the 'mnemonic' theories which compare organic historicity to psychological memory, and which lead from Hering to Semon, Rignano, and Bleuler's (1925) interesting doctrine of the 'psychoide'. From the empirical side, however, the problem is scarcely touched.

We know very little about the way in which already existing genes change in the course of phylogeny, and we know nothing whatever about how new genes arise. These questions naturally carry us far beyond experimental embryology into the spheres of genetics and evolution, and therefore we may leave them.

XII

THE SYSTEM THEORY

WE have now completed our journey through the forest of investigations, thoughts, and theories which crowd upon us in the branch of biological science which we have been considering. Many fruitful ideas, a wonderful variety of striking facts have been noted; also a quantity of theoretical undergrowth to which we have had to apply the critical axe. After having indicated, in the foregoing chapters, how far experimental and theoretical investigation is advanced in the explanation of development, it now remains to summarize the theoretical results of our essay from the point of view of the problem of life in general.

The examination of the developmental theories leads us to just the same result as was gained, in Part I, by means of general considerations. In fact the general tendencies of the newer developments in biology are reflected with special clearness in relation to the problem of development. The fundamental error of 'classical' mechanism lay in its application of the additive point of view to the interpretation of living organisms. It attempted to analyse the vital process into particular occurrences proceeding in single parts or mechanisms independently of one another. In Weismann's machine theory of development we encounter the classical example of this point of view. Vitalism, on the other hand, while being at one with the machine theory in analysing the vital processes into occurrences running along their separate lines, believed these to be co-ordinated by an immaterial, transcendent entelechy. Neither of these views is justified by the facts. We believe now that the solution of this antithesis in biology is to be sought in an *organismic* or *system theory* of the organism which, on the one hand, in opposition to machine theory, sees the essence of the organism in the harmony and co-ordination of the processes among one another, but, on the other hand, does not interpret this co-ordination as Vitalism does, by means of a mystical entelechy, but through the forces immanent in the living system itself.

All the more recent theories of development, however much they may differ in detail, show this same common tendency. Goldschmidt's theory of genetics is strictly mechanistic, but is not a machine theory; it is one which regards the germ as a whole as a polyphasic chemical system. From the more vitalistic side we find the view which emphasizes the wholeness of the organism in the demand of Heidenhain for the rejection of the view of development which regards it as a sum of separate processes, and its replacement by one which sets the whole of the organic germ with its in-dwelling 'syntony' in the forefront. Gurwitsch has endeavoured, in his Field theory, to make the factor of the whole, which Driesch regards as ultimate, amenable to geometrical analysis. Spemann's definitive conclusion is that we must keep the germ as a whole in view, if we are to solve the problem of determination, and that a theory which treats development as a process involving preformed separate parts which are independent of one another is untenable. The final result to which we come, as the general tendency of modern movements in embryology, is therefore as follows: we must view the germ as a whole, as a unitary system, which accomplishes the developmental process on the basis of the conditions which are present in it and depend on the organization of its material parts.

In this way we obtain a simple solution of the two most troublesome problems of development, namely, that of the 'whole' and of 'teleology'. Driesch originally founded his Vitalism on the proposition that the fate of a part of the germ depends on its place in the whole. The newer experimental embryology, especially the work of Spemann, has established this proposition in a manner surpassing all expectations. But it is important to remember that this concept of the 'whole' has two different meanings. For Driesch it meant the typical end-result which was only to be reached in the future, and since the germ strives towards this an entelechy is required to guide the developmental processes. But the 'whole' upon which, according to Spemann, the fate of the parts of the germ is dependent (e.g. transplanted presumptive epidermis which becomes brain) means something quite different; for Spemann it means the momentary total state of the living system, not the typical end-state to be reached in the future. This 'whole' is thus a spatially and temporally well-defined material and energetic state which leaves no place for the action of a non-material entelechy.

The aspect which the problem of teleology assumes in organismic biology has already been referred to in the foregoing parts (pp. 8, 103). Dysteleological developmental processes, such as the formation of monsters, super-regenerates, and the like, may be interpreted by supposing that a process, which in a subordinated partial system is teleological (in the sense of whole-making), may be accidental or dysteleological as regards the total system. The dysteleological formations are thus related to the 'encaptic' character of the organic system. That we are still to-day far removed from being able to show how the multitude of single 'teleologies' in development result from the system-principle is evident. Nevertheless we must be glad to possess a starting-point from which the problem, which has been removed from scientific investigation by the vitalistic interpretation it has been given, can be progressively solved.

By saying that the developing germ is to be conceived as a unitary system, it is emphasized, at the same time, that development in its essential features is not to be interpreted in the sense of the 'cell theory'. The organism is not a secondary unit in which the single cells play the most important role, but the primary unity and wholeness of the individual prevails in all stages of its life (cf. especially Dürken, 1929 *b*). We have investigated first the formative movements and have found them essentially movements of the whole germ, the single cells passively following these motions. The same holds good for the analysis of segregation. Experience shows that the cell-divisions of cleavage are irrelevant for the limitation of the presumptive organ regions, the arrangement of the latter not being changed by the divisions. We find, in regulative eggs, segregation to be caused by organizers which arise not by means of cell-divisions, but by means of a specialization of plasmatic areas, without regard to whether the egg is already divided into blastomeres or not. The inductive action is quite independent of cleavage. In mosaic eggs, cell-division is a means neither of segregation nor of differentiation, since these take place, with respect to the total germ, before cleavage occurs. Regulation shows with particular clearness that development is not an action of the single cells but of the whole germ; it is only to be understood if we conceive the whole germ as a unitary system. The determination of regeneration does not occur by part-for-part actions, but the regenerate is determined as a whole, as shown, e.g., by the production of bones by skeleton-free extremities. Development is, at last, epigenesis, i.e. neo-formation of manifoldness. The germ is a primary unity and wholeness; development is a function of the whole and not a sum of cell-actions. Development teaches us, with perfect clearness, that 'inadequacy of the cell theory' which Whitman emphasized long ago.

That the theory of development and of life in general must be a 'system theory'—that is no more to be doubted or disputed. The question only remains what relation there is between this 'system theory' and physics. We may ask ourselves, *first*, whether a physico-chemical explanation of development is possible *at present*, or whether specific biological notions are required for it. There can be no doubt how this question is to be answered. In its present state, developmental physiology cannot avoid the use of specific biological concepts. We have also seen that the chemical and physico-chemical theories, Goldschmidt's theory, crystal analogy, Gestalt theory, cannot yield a complete explanation of development. There remains, therefore, for the present state of investigation at least, only one possibility: that of an 'organismic' theory, using specific biological concepts. For the explanation of development we are driven to assume a specifically biological type of organization in systems capable of development—a type of organization (not a soul or entelechy which governs and controls the material merely as its 'means') dependent upon and exhibited in the organized material (the injury of which involves a disturbance of the *Gestalt*) in the same way in which the crystalline type is exhibited in the crystal; a type of organization moreover which is not identical with, nor at present reducible to, any known form of physico-chemical *Gestalt*, nor to chemical equilibrium, crystalline form, or any other known sort of physical or chemical configuration.

But, however we may conceive the organic configuration as regards its nature and mode of action—we have noted a number of possibilities of this sort in the chapter on organismic theories—we can say one thing about a theory of development to be reached in the future, namely, that it must give equal weight to three points. First, to the physico-chemical aspect of the problem; the organic germ is a polyphasic colloidal system and for that reason development exhibits certain characteristic features, e.g. the separation of organ-forming regions, the distinction between mosaic and regulative eggs, &c., perhaps also Spemann's organizer action. But beyond this the germ exhibits yet other properties. It is, in its organization, causing effects which have nothing analogous in inorganic systems, a configuration unique in the world. Every theory of development must take into account these 'organismic' relations. The organic germ is a unique structure also in regard to the third feature which must be taken into account in a future theory of development: if the fundamentals of our contemporary biology have even a grain of truth we must assume that the germ as we see it before us is a structure which in its faculties has been collected in geological times. Moreover, this historical accumulation, and the progressive evolution of these collected faculties in the course of individual development, is not comparable with any other process in the world. These are three features of which a future theory of development must take account. But the student of knowledge may also point out that what a logical investigation reveals as the necessary points of view of organic nature, exhibit themselves to a factual investigation as the real fundamental problems of the organism for which a theory is to be sought, namely physico-chemical system, organization, and history.

One more point may be referred to. Vitalism in its 'proofs' proceeds from the facts of experimentally disturbed development. The 'organismic' biology in our sense regards *normal* development as the proper proof of the autonomy of the organism. It is much more remarkable that from the undifferentiated or almost undifferentiated egg there should arise an enormously differentiated organism, a sea-urchin, or a human infant, than that a half-sea-urchin germ can still become a whole sea-urchin. The facts of regulation which vitalism brings forward as proof of the autonomy of the organism provide no such thing; for they are by no means insusceptible of a physico-chemical explanation or at least of analogy—if, namely, development itself only had some analogue in the inorganic world. But this great wonder, the raising of the level of organization, the accumulation and evolution of faculties, &c., is given by no crystal or chemical system. It is not that there is 'wholeness' in the organic realm in general which is decisive, for such is also exhibited by inorganic systems—but the *kind* of totality—the *developing* totality. That gives us the deepest insight into organic nature which belongs to its natural unfolding—but not that which we elicit from it by 'lever and screw'.

Be that as it may. Nevertheless we believe we have pointed out the way along which biology must progress in the future towards a theory of development. The critical work which was afforded—not by the author of this study, who is conscious enough that the latter has the character merely of a summary, but by a series of distinguished investigators and thinkers—has once and for all shown the inaccessibility of a series of ways along which the solution of the problem of development has been sought. We have composed this critique in order to make clear the path for a future development. The discussion can be closed—the enduring results of investigation are established, but along the one remaining possible way new investigations can begin with fresh courage.

Thus, we must not abstract—in the manner of the previous physico-chemical theories—from the specific vital peculiarities, we must put them in the centre of the theory of development. Only when a theory of vital organization has been elaborated will the *second* question be treatable, namely, the question whether this theory is in principle reducible to physics. We have seen in the first part how difficult it is to answer this question in any decisive manner. There are many more possibilities than the silly alternative mechanism or vitalism suggests. At bottom, however, this conflict does not seem to us to be decisive. What is essential is to regard living things as unitary systems, and the vital phenomena as phenomena of such, the characteristic organization of which is grasped neither through the physico-chemical interpretation of the particular processes, nor yet by supposing it guided by a non-spatial factor in the vitalistic sense. If, however, this view is correct, it will then be the fundamental task of biology to discover the laws which govern the organic event as a whole. We can only proceed 'organismically' in order to formulate the laws which govern the organic system. Whether biological laws are in the end resolvable into those of physics—that is a question which can be allowed to rest at the present day. Our goal must be to develop biological law as a system complete in itself and to leave to the future whether or in what way it is to be derived from the ultimate assumptions of physics, as has happened with chemistry which at first also developed as an independent science (and could only develop in this way).

We may, perhaps, go one step further. We may ask: What are to be the most general assumptions we must make for the deduction of the empirically established detailed laws? In other words: What will be the fundamental principles of a system of 'organismic biology'?

Naturally, the answer to this question can only be given in an entirely provisional and tentative form. It seems clear, however, that the following two principles are fundamental.

The first must be a law of 'biological maintenance', somewhat in the form: 'the organic system tends to preserve itself.' It needs no emphasizing that every theory of life hitherto proposed must have admitted as fundamental the characteristic of organisms expressed in this principle. Roux recognized it in his 'self-regulation'. But he made the mistake of regarding it from the standpoint of the machine theory, which necessitated the assumption of subsidiary machines for regeneration—an assumption which has proved to be untenable. It is this, too, which the vitalists call the 'directedness' (*Gerichtetheit*) or the 'purposefulness' of the organic. The 'directing agents' of the vitalists reduce at bottom to the forces which condition the maintenance of the organic system. The necessity of some such principle as we have indicated is explicitly recognized in the Gestalt theory. We believe, of course, that a 'law of organic equilibrium' must, at least provisionally, be regarded as specifically biological.

As already mentioned (p. 107), it may be possible in certain cases to interpret this physico-chemically, e.g. in the regulative eggs, as a restoration of a chemical equilibrium, but this is not possible as a *general* solution. This holds, in the first place, for the adult organism, existing as it does in a 'dynamic equilibrium' (better 'pseudo-equilibrium') which is far removed from such a type of equilibrium as the chemical and is therefore capable of doing work. Similarly, we may regard the processes of regulation of organ rudiments, of regeneration, of reintegration and so on, as cases of restoration of the 'biodynamic equilibrium', but we cannot connect concrete physico-chemical ideas with this. Moreover, in the developing embryo the validity of our principle in the form given above is limited by a second one, that of the 'tendency towards maximal organization'. Consequently the first can only hold in a general form, which may be formulated as follows: 'The developmental system possesses in each of its temporal slices an exceptional condition (*ausgezeichnete Zustandsbedingung*) towards which the system tends, and towards which it tends to return after disturbance.' This assumption gives the general premise from which follow the detailed laws of normal and regulative development. Segregation as 'chemo-differentiation' and 'layering' represents a special case of the production of such an exceptional state, since after every reaction initiated by the genes a production of a definite 'segregation' must occur. Restoration of the state of the system after injury will always be possible so long as new and diverse system-conditions have not been established in the separate parts of the system. This proposition gives the limits of regulation. For this does not occur in cases of mechanical disturbance (pressure, centrifuge) if segregates already formed are brought into abnormal relations; in cases of division if segregates already formed and constituting fixed system-conditions are totally removed; in cases of fusion if segregates already formed are prevented from uniting (on account of a divergent arrangement of their axes), or if such segregates are brought into atypical relations in the system (multiple development in embryos united cross-wise). The same holds for the regulation of organ rudiments and in those cases of regeneration in which a chemical or physical interpretation of the biological principle of maintenance obviously seems to be hopeless.

As a second principle of 'organismic biology' we have that of 'hierarchical order' both in a static and a dynamical sense. In the static sense hierarchical order is certainly fundamental for the organic. The same also holds of course for the inorganic, with its hierarchy of electron, atom, molecule, mycella, and crystal. But physics has no occasion to concern itself with this, because the laws of the higher levels of organization are deducible from the fundamental physical axioms. If, however, our view of the 'biological statistic of higher order' is justified, we can see why the spatial hierarchical order must have a far greater significance in the organic realm. As we saw in Part I, the mere fact that the organic exhibits a level of organization above that of the inorganic in no wise proves that its laws are not derivable from those adopted by physics as its fundamental postulates—the laws of the physical 'organisms' of various orders are still derivable from these. But their underivability is given if our theory of the 'biological uncertainty principle' is right. If, in consequence of the complication and individuality of living organisms, it were only possible to obtain laws expressing statistical averages of 'higher order', then of course the irreducibility of the laws of these organisms of 'higher order' to the fundamental assumptions of physics would also be given. For then the building up of higher levels of organization from the lower will always involve new laws which are not deducible from the laws of the lower levels. It will then be clear that the hierarchical mode of organization must have a far deeper significance for the living organism than for inorganic things, and must therefore be a fundamental principle of biological law.

The same holds for hierarchical order in the dynamical sense. We can call the principle of the division hierarchy in metazoa the principle of the 'tendency towards maximal organization', and then formulate it somewhat as follows: 'So long as an organic system has not yet reached the maximum organization possible to it, it tends towards it.' We have seen that a physico-chemical theory of the elevation of the level of organization and of the degree of multiplicity of developing systems, which is accomplished through the component processes of formation, segregation, differentiation, and growth, is not possible, at all events at the present day. We are therefore justified in approaching this problem by means of a specifically biological theory. We are seeking for methods of formulation which take account of entities of the biological order, quite apart from the particular physico-chemical processes which lead, say, to cell-division here or there, or to particular formative processes or particular differentiations.

We can then substitute for the general expression 'organization' in our formula the series of expressions signifying the special sides of this organization, and say: the developing system tends towards a maximum formation (*Gestaltung*), &c., which is characteristic of it. And if, further, we summarize (they cannot be surveyed in detail) the modes of action which condition formative movements, organ-formations, differentiations, directed growth, &c., under 'biological fields', we can then attempt to fill in the general formula with concrete content for particular cases, as Gurwitsch and his pupils have done so successfully, and thus draw up the geometrical laws according to which the 'passage to increasing organization' (formation, segregation, differentiation, growth) is accomplished.

It goes without saying that the present sketch is far removed from attempting to give in any way a conclusive result. It must here suffice to point out that such a deductive procedure not merely permits a derivation of the empirically established laws, but those general principles also have the character of working hypotheses, since consequences drawn from them have proved to be capable of an empirical test, and have occasionally been of heuristic value. We need only recall Przibram's explanations of concrete regenerative phenomena which were obtained purely deductively from the assumption of the maintenance of the organism in its 'bio-dynamic equilibrium' (another expression for what is asserted in our first principle).

XIII

CONCLUSION

We have employed the data and theories of development as a paradigm for the various explanations of life in general. Had we begun with some other aspect of biological phenomena—metabolism, stimulus and movement, or phylogeny—we should reach problems and consequences which are in principle the same. The conflict between 'mechanism' and 'vitalism' can thus be decided in a manner which does not unconditionally justify either view, but which takes over the valuable features of both theories, e.g. the knowledge that the characteristic properties of life are based on material systems from mechanism, the recognition of the 'wholeness' of the vital phenomena from vitalism. Beyond mechanism and vitalism is the possibility of an 'organismic biology'. This view sees the essential feature of life in its character as a system, and the chief task for biology in the future is the establishment of the laws of biological systems. Whereas the older mechanism neither saw nor wished to see this fundamental characteristic of life, and whereas vitalism put a philosophical construction in the place of natural scientific investigation, the value of the view here developed by us lies in the fact that it places the character of wholeness, which vitalism rightly emphasizes, in the focus of attention, but regards it as a concrete object of scientific investigation, not one for philosophical speculation.

We all know how much remains to be done in this region of scientific endeavour. We all feel dissatisfied with contemporary biology and its problematic state. The mechanistic prejudices on the one side and vitalism on the other have together prevented the development of a specifically biological theory from the beginning. If biologists were convinced from the first that life was a collection of physico-chemical processes, or that it was a metaphysical problem, it is not surprising that original ideas, genuine biological laws and theories, have so seldom been set up. But if these prejudices which stand in the way of the recognition of biology as an independent science are put aside the progress which will lead it to the control of life in thought and practice need no longer be delayed—a task which without doubt will not be accomplished in a day, but one which must be accomplished if an eternal hiatus is not to remain in the structure of our science.

On the other hand the voluntary submission of biology to the supremacy of mechanics has not benefited it greatly. If we compare the multiplicity of discoveries, the beauty and elegance of theories, and the technical achievements which belong to physics with the results of biology we cannot suppress a feeling of frustration. Biology is certainly a younger and more difficult science; that cannot be denied. But at its very birth physics appeared on the scene as a wonderfully clear and profound system of ideas. The whole development from Copernicus to the Relativity theory, from Lavoisier to Niels Bohr, certainly constitutes an enormous enrichment of the picture of nature, but it can hardly be said that the latter did not already possess for its creators that wonderful clarity which we so much admire in it to-day. In contrast to this we are still far from possessing a theoretical system in biology, in spite of the fact that it has a development of two hundred years behind it. To us it seems that this backwardness is due to the fact that we have not *wished* to grant the status of an independent science to biology. Had it developed freely, unperturbed by neighbouring sciences, as physics did, it would be better developed at the present day. Growing up under the shadow of physics it has languished like a plant deprived of light. If this inhibition is removed the originality and precision which it could not attain under so powerful an influence will present themselves in due course.

If it is permissible to conclude a scientific investigation with a personal opinion, it may be said that it seems to us that the necessity for a new orientation of biology is not only a purely technical scientific matter but also a general cultural one. We believe that the numerous attempts appearing to-day to find a foundation for theoretical biology point to a fundamental change in the world picture which is taking place now that the view based on the classical physics has reached its limits; that is its deeper, general cultural meaning. The colossal development of physics, the age of technology with its triumphs and disillusionments in respect to the real progress of humanity, the mechanism of biology and the disregard of the individual life in modern society—these are all different expressions of the same spirit of the age. We know how in modern physics a fundamental transformation has occurred in the classical ideas. From the practical standpoint the World War has shown us to what lengths we can go with the means that the inorganic sciences have placed in our hands. It may be that that will prove to have been the climax of the age of mechanics. The new movement in biology which gives a special place to the organic realm may perhaps also be a symptom of a general change of spirit, in which we believe and for which we hope. The recognition of the worth of the living being, which now no longer seems an indifferent mechanical artifact, a new valuation of human life also, which formerly has seemed an indifferent means to an end—that would be nothing else but a different expression for one and the same thing. The machine, which we have learnt so wonderfully to govern, has brought man down to its own level. Our control of organic nature is still in its infancy because it is so difficult for us to accustom ourselves to regarding it as anything but a mechanical artifact. But if we can acknowledge its specificity and value it will not exclude itself from either our knowledge or our will. Then the knowledge and conquest of organic nature will make good the injuries created by one-sided devotion to the inorganic in our world and in ourselves. The age of technology is becoming weary of itself—let us hope that an organismic one will follow it to offer new prospects to the future of humanity.

LIST OF LITERATURE

ABBREVIATIONS

A.E.M. = *Zeitschrift für wissenschaftliche Biologie*, Abteilung D: Roux's *Archiv für Entwicklungsmechanik der Organismen.*
B.Z. = *Biologisches Zentralblatt.*
Natwiss. = *Die Naturwissenschaften.*

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