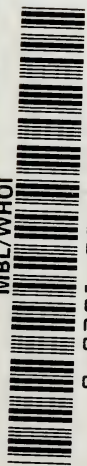


QH
367
S 43

MBL/WHOI



0 0301 0011323 9



LIFE : ITS NATURE,
ORIGIN AND MAINTENANCE

577
Sc 14

LIFE : ITS NATURE, ORIGIN AND
MAINTENANCE · AN ADDRESS
DELIVERED TO THE BRITISH ASSOCI-
ATION FOR THE ADVANCEMENT
OF SCIENCE, AT ITS MEETING AT
DUNDEE IN SEPTEMBER, 1912

BY

E. A. SCHÄFER, LL.D., D.Sc., M.D., F.R.S.

PROFESSOR OF PHYSIOLOGY IN EDINBURGH

LONGMANS, GREEN AND CO.
39 PATERNOSTER ROW, LONDON
NEW YORK, BOMBAY AND CALCUTTA

1912

10976

PREFACE

IN the following Essay, which formed the Presidential Address to the British Association at its meeting this year in Dundee, I have tried to indicate in clear language the general trend of modern bio-chemical inquiries regarding the nature and origin of living material and the manner in which the life of multicellular organisms, especially that of the higher animals and man, is maintained. I have also stated the conclusions which it appears to me may legitimately be drawn from the result of those inquiries, without ignoring or minimising such difficulties as these conclusions present.

There is, it may be admitted, nothing new in the idea that living matter must at some time or another have been formed from lifeless material, for in spite of the dictum *omne vivum e vivo*, there was certainly a period in the history of the earth when our planet could have supported no kind of life, as we understand the word; there can, therefore, exist no difference of opinion upon this point among scientific thinkers. Nor is it the first time that the possibility of the synthetic production of living substance in the laboratory has been suggested. But only those who are ignorant of the progress which bio-chemistry has made in recent years would be bold enough to affirm that the subject is not more advanced than in the days of Tyndall and of Huxley, who showed the true scientific instinct in affirming a belief in the original formation of life from lifeless material and in hinting at the possibility of its eventual synthesis, although there was then far less foundation upon which to base such an opinion than we of the present day possess. The investigations of Fischer, of Abderhalden, of Hopkins, and of others too numerous to mention, have thrown a flood of light upon the constitution of the materials of which living substance is composed; and, in particular, the epoch-making researches of Kossel into the chemical composition of nuclear substance—which in certain forms may be regarded as the simplest type of living matter, while it is certainly the *fons et origo* of all active chemical processes within most cells—have shown how much less complex in chemical nature this substance may be than physiologists were a few years ago accustomed to regard it. On this and other grounds it has lately been independently suggested by Professor Minchin that the first living material originally took the form, not of what is commonly

termed protoplasm, but of nuclear matter or chromatin : a suggestion which appears by no means improbable.

If the honoured names of Charles Darwin, Ernst Hæckel, and August Weismann are not found in the following pages, it is because exigencies of space and time rendered it necessary to deal mainly with the more modern developments of this chapter of evolutionary history. For other but not less cogent reasons all metaphysical speculations on the subjects dealt with have been avoided. The study of Natural Knowledge, as the Royal Society still quaintly describes in its title the investigation of the phenomena of Nature, is never properly advanced if mixed up with the 'supernatural' or if metaphysics is appealed to for the explanation of scientific problems which cannot at once be solved by ordinary scientific methods ; and it behoves us to eliminate all considerations involving the intervention of supernatural agencies just as much in connection with scientific inquiries into the nature and origin of life as with all other matters which are properly the subject of scientific investigation. This is not materialism, but common sense.

The first part of the subject of this Address is dealt with at considerable length and in a strictly scientific spirit by Le Dantec in 'The Nature and Origin of Life' ; as well as by Dastre in the book mentioned on the next page. To works such as these the reader is referred for the numerous details which it is impossible to include within the limits of a short Essay.

UNIVERSITY, EDINBURGH,
October, 1912.

LIFE: ITS NATURE, ORIGIN AND MAINTENANCE

EVERYBODY knows, or thinks he knows, what life is; at least, we are all acquainted with its ordinary, obvious manifestations. It would, therefore,

seem that it should not be difficult to find an exact definition. The quest has nevertheless baffled the most acute thinkers. Herbert Spencer devoted two chapters of his 'Principles of Biology' to the discussion of the attempts at definition which had up to that date been proposed, and himself suggested another. But at the end of it all he is constrained to admit that no expression had been found which would embrace all the known manifestations of animate, and at the same time exclude those of admittedly inanimate, objects.

The ordinary dictionary definition of life is 'the state of living.' Dastre, following Claude Bernard, defines it as 'the sum total of the phenomena common to all living beings.*' Both of these definitions are, however, of the same character as Sidney Smith's definition of an archdeacon as 'a person who performs archidiaconal functions.' I am not myself proposing to take up your time by attempting to grapple with a task which has proved too great for the intellectual giants of philosophy, and I have the less disposition to do so because recent advances in knowledge have suggested the probability that the dividing line between animate and inanimate matter is less sharp than it has hitherto been regarded, so that the difficulty of finding an inclusive definition is correspondingly increased.

As a mere word 'life' is interesting in the fact that it is one of those abstract terms which has no direct antithesis; although probably most persons would regard 'death' in that light. A little consideration will show that this is not the case. 'Death' implies the pre-existence of 'life'; there are physiological grounds for regarding death as a phenomenon of life—it is the completion, the last act of life. We cannot speak of a non-living object as *possessing* death in the sense that we speak of a living object as *possessing* life. The adjective 'dead' is, it is true, applied in a popular sense antithetically to objects which have never possessed life; as in the proverbial expression 'as dead as a door-nail.' But in the strict sense such application is not justifiable, since the use of the terms dead and living implies either in the past or in the present the possession of the recognised properties of living matter. On the other hand, the expressions *living* and *lifeless*, *animate* and *inanimate*, furnish terms which are un-

* *La vie et la mort*, English translation by W. J. Greenstreet, 1911, p. 54.

doubtedly antithetical. Strictly and literally, the words animate and inanimate express the presence or absence of 'soul'; and not infrequently we find the terms 'life' and 'soul' erroneously employed as if

Life not identical with soul.

identical. But it is hardly necessary for me to state that the remarks I have to make regarding 'life' must not be taken to apply to the conception to which the word

'soul' is attached. The fact that the formation of such a conception is only possible in connection with life, and that the growth and elaboration of the conception has only been possible as the result of the most complex processes of life in the most complex of living organisms, has doubtless led to a belief in the identity of life with soul. But unless the use of the expression 'soul' is extended to a degree which would deprive it of all special significance, the distinction between these terms must be strictly maintained. For the problems of life are

Problems of life are problems of matter.

essentially problems of matter; we cannot conceive of life in the scientific sense as existing apart from matter. The phenomena of life are investigated, and

can only be investigated, by the same methods as all other phenomena of matter, and the general results of such investigations tend to show that living beings are governed by laws identical with those which govern inanimate matter. The more we study the manifestations of life the more we become convinced of the truth of this statement and the less we are disposed to call in the aid of a special and unknown form of energy to explain those manifestations.

The most obvious manifestation of life is 'spontaneous' movement. We see a man, a dog, a bird move, and we know that they are alive. We

Phenomena indicative of life. Movement.

place a drop of pond water under the microscope, and see numberless particles rapidly moving within it; we affirm that it swarms with 'life.' We notice a small mass of clear slime changing its shape, throwing out

projections of its structureless substance, creeping from one part of the field of the microscope to another. We recognise that the slime is living; we give it a name—*Amœba limax*—the slug amœba. We observe similar movements in individual cells of our own body; in the white corpuscles of our blood, in connective tissue cells, in growing nerve cells, in young cells everywhere. We denote the similarity between these movements and those of the amœba by employing the descriptive term 'amœboid' for both. We regard such movements as indicative of the possession of 'life'; nothing seems more justifiable than such an inference.

But physicists* show us movements of a precisely similar character in substances which no one by any stretch of imagination can regard as living; movements of oil drops, of organic and inorganic mixtures, even of mercury globules, which are indistinguishable in their character from those of the living organisms we have been studying: movements which

* G. Quincke, *Annal. d. Physik u. Chem.*, 1870 and 1888.

can only be described by the same term amœboid, yet obviously produced as the result of purely physical and chemical reactions causing changes in surface tension of the fluids under examination.*

Similarity of movements in living and non-living matter.

It is therefore certain that such movements are not specifically 'vital,' that their presence does not necessarily denote 'life.' And when we investigate closely even such active movements as those of a vibratile cilium

or a phenomenon so intimately identified with life as the contraction of a muscle, we find that these present so many analogies with amœboid movements as to render it certain that they are fundamentally of the same character and produced in much the same manner.† Nor can we for a moment doubt that the complex actions which are characteristic of the more highly differentiated organisms have been developed in the course of evolution from the simple movements characterising the activity of undifferentiated protoplasm; movements which can themselves, as we have seen, be perfectly imitated by non-living material. The chain of evidence regarding this particular manifestation of life—movement—is complete. Whether exhibited as the amœboid movement of the proteus animalcule or of the white corpuscle of our blood; as the ciliary motion of the infusorian or of the ciliated cell; as the contraction of a muscle under the governance of the will, or as the throbbing of the human heart responsive to every emotion of the mind, we cannot but conclude that it is alike subject to and produced in conformity with the general laws of matter, by agencies resembling those which cause movements in lifeless material.‡

It will perhaps be contended that the resemblances between the movements of living and non-living matter may be only superficial,

Assimilation and disassimilation.

and that the conclusion regarding their identity to which we are led will be dissipated when we endeavour

to penetrate more deeply into the working of living substance. For can we not recognise along with the possession of movement the presence of other phenomena which are equally characteristic of life and with which non-living material is not endowed? Prominent

* The causation not only of movements but of various other manifestations of life by alterations in surface tension of living substance is ably dealt with by A. B. Macallum in a recent article in Asher and Spiro's *Ergebnisse der Physiologie*, 1911. Macallum has described an accumulation of potassium salts at the more active surfaces of the protoplasm of many cells, and correlates this with the production of cell-activity by the effect of such accumulation upon the surface tension. The literature of the subject will be found in this article.

† G. F. Fitzgerald (*Brit. Assoc. Reports*, 1898, and *Scient. Trans. Roy. Dublin Society*, 1898) arrived at this conclusion with regard to muscle from purely physical considerations.

‡ 'Vital spontaneity, so readily accepted by persons ignorant of biology, is disproved by the whole history of science. Every vital manifestation is a response to a stimulus, a provoked phenomenon. It is unnecessary to say this is also the case with brute bodies, since that is precisely the foundation of the great principle of the inertia of matter. It is plain that it is also as applicable to living as to inanimate matter.'—Dastre, *op. cit.*, p. 280.

among the characteristic phenomena of life are the processes of assimilation and disassimilation, the taking in of food and its elaboration.* These, surely, it may be thought, are not shared by matter which is not endowed with life. Unfortunately for this argument, similar processes occur characteristically in situations which no one would think of associating with the presence of life. A striking example of this is afforded by the osmotic phenomena presented by solutions separated from one another by semipermeable membranes or films, a condition which is precisely that which is constantly found in living matter.†

It is not so long ago that the chemistry of organic matter was thought to be entirely different from that of inorganic substances. But the line between inorganic and organic chemistry, which up to the middle of the last century appeared sharp, subsequently became misty and has now disappeared. Similarly the chemistry of living organisms, which is now a recognised branch of organic chemistry, but used to be considered as so much outside the domain of the chemist that it could only be dealt with by those whose special business it was to study 'vital' processes, is passing more and more out of the hands of the biologist and into those of the pure chemist.

Somewhat more than half a century ago Thomas Graham published his epoch-making observations relating to the properties of matter in the colloidal state: observations which are proving all-important in assisting our comprehension of the properties of living substance. For it is becoming every day more apparent that the chemistry and physics of the living organism are essentially the chemistry and physics of nitrogenous colloids. Living substance or protoplasm always, in fact, takes the form of a colloidal solution. In this solution the colloids are associated with crystalloids (electrolytes), which are either free in the solution or attached to the molecules of the colloids. Surrounding and enclosing the living substance thus constituted of both colloid and crystalloid material is a film, probably also formed of colloid, but which may have a lipid substratum associated with it (Overton). This film serves the purpose of an osmotic membrane, permitting of exchanges by diffusion

Chemical phenomena accompanying life.

The colloid constitution of living matter. Identity of physical and chemical processes in living and non-living matter.

* The terms 'assimilation' and 'disassimilation' express the physical and chemical changes which occur within protoplasm as the result of the intake of nutrient material from the circumambient medium and its ultimate transformation into waste products which are passed out again into that medium; the whole cycle of these changes being embraced under the term 'metabolism.'

† Leduc (*The Mechanism of Life*, English translation by W. Deane Butcher, 1911) has given many illustrations of this statement. In the Report of the meeting of 1867 in Dundee is a paper by Dr. J. D. Heaton (On Simulations of Vegetable Growths by Mineral Substances) dealing with the same class of phenomena. See also J. Hall-Edwards, Address to Birmingham and Midland Institute, Nov., 1911. The conditions of osmosis in cells have been especially studied by Hamburger (*Osmotischer Druck und Ionenlehre*, Wiesbaden, 1902-4).

between the colloidal solution constituting the protoplasm and the circumambient medium in which it lives. Other similar films or membranes occur in the interior of protoplasm. These films have in many cases specific characters, both physical and chemical, thus favouring the diffusion of special kinds of material into and out of the protoplasm and from one part of the protoplasm to another. It is the changes produced under these physical conditions, associated with those caused by active chemical agents formed within protoplasm and known as *enzymes*, that effect assimilation and disassimilation. Quite similar changes can be produced outside the body (*in vitro*) by the employment of methods of a purely physical and chemical nature. It is true that we are not yet familiar with all the intermediate stages of transformation of the materials which are taken in by a living body into the materials which are given out from it. But since the initial processes and the final results are the same as they would be on the assumption that the changes are brought about in conformity with the known laws of chemistry and physics, we may fairly conclude that all changes in living substance are brought about by ordinary chemical and physical forces.

Should it be contended that growth and reproduction are properties possessed only by living bodies and constitute a test by which we may differentiate between life and non-life, between the animate and inanimate creation, it must be replied that no contention can be more fallacious. Inorganic crystals grow and multiply and reproduce their like, given a supply of the requisite pabulum. In most cases for each kind of crystal there is, as with living organisms, a limit of growth which is not exceeded, and further increase of the crystalline matter results not in further increase in size but in multiplication of similar crystals. Leduc has shown that the growth and division of artificial colloids of an inorganic nature, when placed in an appropriate medium, present singular resemblances to the phenomena of the growth and division of living organisms. Even so complex a process as the division of a cell-nucleus by karyokinesis as a preliminary to the multiplication of the cell by division—a phenomenon which would *prima facie* have seemed and has been commonly regarded as a distinctive manifestation of the life of the cell—can be imitated with solutions of a simple inorganic salt, such as chloride of sodium, containing a suspension of carbon particles; which arrange and rearrange themselves under the influence of the movements of the electrolytes in a manner indistinguishable from that adopted by the particles of chromatin in a dividing nucleus. And in the process of sexual reproduction, the researches of J. Loeb and others upon the ova of the sea-urchin have proved that we can no longer consider such an apparently vital phenomenon as the fertilisation of the egg as being the result of living material brought to it by the spermatozoon, since it is possible to start the process of division of the ovum

Similarity of the processes of growth and reproduction in living and non-living matter.

and the resulting formation of cells, and ultimately of all the tissues and organs—in short, to bring about the development of the whole body—if

The question of vitalism and vital force.

a simple chemical reagent is substituted for the male element in the process of fertilisation. Indeed, even a mechanical or electrical stimulus may suffice to start development. *Kurz und gut*, as the Germans say,

vitalism as a working hypothesis has not only had its foundations undermined, but most of the superstructure has toppled over, and if any difficulties of explanation still persist, we are justified in assuming that the cause is to be found in our imperfect knowledge of the constitution and working of living material. At the best vitalism explains nothing, and the term 'vital force' is an expression of ignorance which can bring us no further along the path of knowledge. Nor is the problem in any way advanced by substituting for the term 'vitalism' 'neo-vitalism,' and for 'vital force' 'biotic energy.'* 'New presbyter is but old priest writ large.'

Further, in its chemical composition we are no longer compelled to consider living substance as possessing infinite complexity, as was thought

The possibility of the synthesis of living matter.

to be the case when chemists first began to break up the proteins of the body into their simpler constituents. The researches of Miescher, which have

been continued and elaborated by Kossel and his pupils, have acquainted us with the fact that a body so important for the nutritive and reproductive functions of the cell as the nucleus—which may be said indeed to represent the quintessence of cell-life—possesses a chemical constitution of no very great complexity; so that we may even hope some day to see the material which composes it prepared synthetically. And when we consider that the nucleus is not only itself formed of living substance, but is capable of causing other living substance to be built up; is, in fact, the directing agent in all the principal chemical changes which take place within the living cell, it must be admitted that we are a long step forward in our knowledge of the chemical basis of life. That it is the *form* of nuclear matter rather than its chemical and molecular structure which is the important factor in nuclear activity cannot be supposed. The form of nuclei, as every microscopist knows, varies infinitely, and there are numerous living organisms in which the nuclear matter is without form, appearing simply as granules distributed in the protoplasm. Not that the form assumed and the transformations undergone by the nucleus are without importance; but it is none the less true that even in an amorphous condition the material which in the ordinary cell takes the form of a 'nucleus' may, in simpler organisms which have not in the process of

* B. Moore, in *Recent Advances in Physiology*, 1906; Moore and Roaf, *ibid.*; and *Further Advances in Physiology*, 1909. Moore lays especial stress on the transformations of energy which occur in protoplasm. See on the question of vitalism Gley (*Revue Scientifique*, 1911) and D'Arcy Thompson (Address to Section D at Portsmouth, 1911).

evolution become complete cells, fulfil functions in many respects similar to those fulfilled by the nucleus of the more differentiated organism.

A similar anticipation regarding the probability of eventual synthetic production may be made for the proteins of the cell-substance. Considerable progress in this direction has indeed already been made by Emil Fischer, who has for many years been engaged in the task of building up the nitrogenous combinations which enter into the formation of the complex molecule of protein. It is satisfactory to know that the significance of the work both of Fischer and of Kossel in this field of biological chemistry has been recognised by the award to each of these distinguished chemists of a Nobel prize.

The elements composing living substance are few in number. Those which are constantly present are carbon, hydrogen, oxygen, and nitrogen.

With these, both in nuclear matter and also, but to a less degree, in the more diffuse living material which we know as protoplasm, phosphorus is always associated. 'Ohne Phosphor kein Gedanke' is an accepted aphorism; 'Ohne Phosphor kein Leben' is equally true. Moreover, a large proportion, rarely less than 70 per cent., of water appears essential for any manifestation of life, although not in all cases necessary for its continuance, since organisms are known which will bear the loss of the greater part if not the whole of the water they contain without permanent impairment of their vitality. The presence of certain inorganic salts is no less essential, chief amongst them being chloride of sodium and salts of calcium, magnesium, potassium, and iron. The combination of these elements into a colloidal compound represents the chemical basis of life; and when the chemist succeeds in building up this compound it will without doubt be found to exhibit the phenomena which we are in the habit of associating with the term 'life.'*

The above considerations seem to point to the conclusion that the possibility of the production of life—*i.e.*, of living material—is not so remote as has been generally assumed. Since the experiments of Pasteur, few have ventured to affirm a belief in the spontaneous generation of bacteria and monads and other micro-organisms, although before his time this was by many believed to be of universal occurrence. My esteemed friend Dr. Charlton Bastian is, so far as I am aware, the only scientific man of eminence who still adheres to the old creed, and Dr. Bastian, in spite of numerous experiments and the publication of many books and papers, has not hitherto succeeded in winning over many converts to his opinion. I am myself so entirely convinced of the accuracy of the results which Pasteur obtained—are they not within the

* The most recent account of the chemistry of protoplasm is that by Botazzi (*Das Cytoplasma u. die Körpersäfte*) in Winterstein's *Handb. d. vergl. Physiologie*, Bd. I., 1912. The literature is given in this article.

daily and hourly experience of everyone who deals with the sterilisation of organic solutions?—that I do not hesitate to believe, if living torulæ or mycelia are exhibited to me in flasks which had been subjected to prolonged boiling after being hermetically sealed, that there has been some fallacy either in the premisses or in the carrying out of the operation. The appearance of organisms in such flasks would not furnish to my mind proof that they were the result of spontaneous generation. Assuming no fault in manipulation or fallacy in observation, I should find it simpler to believe that the germs of such organisms have resisted the effects of prolonged heat than that they became generated spontaneously. If spontaneous generation is possible, we cannot expect it to take the form of living beings which show so marked a degree of differentiation, both structural and functional, as the organisms which are described as making their appearance in these experimental flasks.* Nor should we expect the spontaneous generation of living substance of any kind to occur in a fluid the organic constituents of which have been so altered by heat that they can retain no sort of chemical resemblance to the organic constituents of living matter. If the formation of life—of living substance—is possible at the present day—and for my own part I see no reason to doubt it—a boiled infusion of organic matter—and still less of inorganic matter—is the last place in which to look for it. Our mistrust of such evidence as has yet been brought forward need not, however, preclude us from admitting the possibility of the formation of living from non-living substance.†

Setting aside, as devoid of scientific foundation, the idea of immediate supernatural intervention in the first production of life, we are not only justified in believing, but compelled to believe, that living matter must have owed its origin to causes similar in character to those which have been instrumental in producing all other forms of matter in the universe; in other

**Life a product
of evolution.**

* It is fair to point out that Dr. Bastian suggests that the formation of ultra-microscopic living particles may precede the appearance of the microscopic organisms which he describes.—*The Origin of Life*, 1911, p. 65.

† The present position of the subject is succinctly stated by Dr. Chalmers Mitchell in his article on 'Abiogenesis' in the *Encyclopædia Britannica*. Dr. Mitchell adds: 'It may be that in the progress of science it may yet be possible to construct living protoplasm from non-living material. The refutation of abiogenesis has no further bearing on this possibility than to make it probable that if protoplasm ultimately be formed in the laboratory, it will be by a series of steps, the earlier steps being the formation of some substance, or substances, now unknown, which are not protoplasm. Such intermediate stages may have existed in the past.' And Huxley in his Presidential Address at Liverpool in 1870 says: 'But though I cannot express this conviction' (*i.e.*, of the impossibility of the occurrence of abiogenesis, as exemplified by the appearance of organisms in hermetically sealed and sterilised flasks) 'too strongly, I must carefully guard myself against the supposition that I intend to suggest that no such thing as abiogenesis ever has taken place in the past or ever will take place in the future. With organic chemistry, molecular physics, and physiology yet in their infancy and every day making prodigious strides, I think it would be the height of presumption for any man to say that the conditions under which matter assumes the properties we call "vital" may not, some day, be artificially brought together.'

words, to a process of gradual evolution.* But it has been customary of late amongst biologists to shelve the investigation of the mode of origin of life by evolution from non-living matter by relegating its solution to some former condition of the earth's history, when, it is assumed, opportunities were accidentally favourable for the passage of inanimate matter into animate; such opportunities, it is also assumed, having never since recurred and being never likely to recur.†

Various eminent scientific men have even supposed that life has not actually originated upon our globe, but has been brought to it from another planet or from another stellar system. Some of my audience may still remember the controversy that was excited when the theory of the origin of terrestrial life by the intermediation of a meteorite was propounded by Sir William Thomson in his Presidential Address at the meeting of this Association in Edinburgh in 1871. To this 'meteorite' theory ‡ the apparently fatal objection was raised that it would take some sixty million years for a meteorite to travel from the nearest stellar system to our earth, and it is inconceivable that any kind of life could be maintained during such a period. Even from the nearest planet 150 years would be necessary, and the heating of the meteorite in passing through our atmosphere and at its impact with the earth would, in all probability, destroy any life which might have existed within it. A cognate theory, that of *cosmic panspermia*, assumes that life may exist and may have existed indefinitely in cosmic dust in the interstellar spaces (Richter, 1865; Cohn, 1872), and may with this dust fall slowly to the earth without undergoing the heating which is experienced by a meteorite. Arrhenius,§ who adopts this theory, states that if living germs were carried through the ether by luminous and other radiations the time necessary for their transportation from our globe to the nearest stellar system would be only nine thousand years, and to Mars only twenty days!

But the acceptance of such theories of the arrival of life on the earth does not bring us any nearer to a conception of its actual mode of origin; on the contrary it merely serves to banish the investigation of the question to some conveniently inaccessible corner of the universe and leaves us in the unsatisfactory position of affirming not only that we have no know-

* The arguments in favour of this proposition have been arrayed by Meldola in his Herbert Spencer Lecture, 1910, pp. 16-24. Meldola leaves the question open whether such evolution has occurred only in past years or is also taking place now. He concludes that whereas certain carbon compounds have survived by reason of possessing extreme stability, others—the precursors of living matter—survived owing to the possession of extreme lability and adaptability to variable conditions of environment. A similar suggestion was previously made by Lockyer, *Inorganic Evolution*, 1900, pp. 169, 170.

† T. H. Huxley, Presidential Address, 1870; A. B. Macallum, 'On the Origin of Life on the Globe,' in *Trans. Canadian Institute*, VIII.

‡ First suggested, according to Dastre, by de Salles-Guyon (Dastre, *op. cit.*, p. 252). The theory received the support of Helmholtz.

§ *Worlds in the Making*, transl. by H. Borns, chap. viii., p. 221, 1908.

ledge as to the mode of origin of life—which is unfortunately true—but that we never can acquire such knowledge—which it is to be hoped is not true.* Knowing what we know, and believing what we believe, as to the part played by evolution in the development of terrestrial matter, we are, I think (without denying the possibility of the existence of life in other parts of the universe †), justified in regarding these cosmic theories as inherently improbable—at least in comparison with the solution of the problem which the evolutionary hypothesis offers. ‡

I assume that the majority of my audience have at least a general idea of the scope of this hypothesis, the general acceptance of which has within the last sixty years altered the whole aspect not only of biology, but of every other branch of natural science, including astronomy, geology, physics, and chemistry.§ To those who have not this knowledge I would recommend the perusal of a little book by Professor Judd, entitled 'The Coming of Evolution,' which has recently appeared as one of the Cambridge manuals. I know of no similar book in which the subject is as clearly and succinctly treated. Although the author nowhere expresses the opinion that the actual origin of life on the earth has arisen by evolution from non-living matter, it is impossible to read either this or any similar exposition in which the essential unity of the evolutionary process is insisted upon without concluding that the origin of life must have been due to the same process, this process being, without exception, continuous, and admitting of no gap at any part of its course. Looking therefore at the evolution of living matter by the light which is shed upon it from the study of the evolution of matter in general, we are led to regard it as having been produced, not by a sudden alteration, whether exerted by natural or supernatural agency, but by a gradual process of change from material which was lifeless, through material on the borderland between

* 'The history of science shows how dangerous it is to brush aside mysteries—i.e., unsolved problems—and to interpose the barrier placarded "eternal—no thoroughfare."'—R. Meldola, Herbert Spencer Lecture, 1910.

† Some authorities, such as Errera, contend, with much probability, that the conditions in interstellar space are such that life, as we understand it, could not possibly exist there.

‡ As Verworn points out, such theories would equally apply to the origin of any other chemical combination, whether inorganic or organic, which is met with on our globe, so that they lead directly to absurd conclusions.—*Allgemeine Physiologie*, 1911.

§ As Meldola insists, this general acceptance was in the first instance largely due to the writings of Herbert Spencer: 'We are now prepared for evolution in every domain. . . . As in the case of most great generalisations, thought had been moving in this direction for many years. . . . Lamarck and Buffon had suggested a definite mechanism of organic development, Kant and Laplace a principle of celestial evolution, while Lyell had placed geology upon an evolutionary basis. The principle of continuity was beginning to be recognised in physical science. . . . It was Spencer who brought these independent lines of thought to a focus, and who was the first to make any systematic attempt to show that the law of development expressed in its widest and most abstract form was universally followed throughout cosmical processes, inorganic, organic, and super-organic.'—*Op. cit.*, p. 14.

inanimate and animate, to material which has all the characteristics to which we attach the term 'life.' So far from expecting a sudden leap from an inorganic, or at least an unorganised, into an organic and organised condition, from an entirely inanimate substance to a completely animate state of being, should we not rather expect a gradual procession of changes from inorganic to organic matter, through stages of gradually increasing complexity until material which can be termed living is attained? And in place of looking for the production of fully formed living organisms in hermetically sealed flasks, should we not rather search Nature herself, under natural conditions, for evidence of the existence, either in the past or in the present, of transitional forms between living and non-living matter?

The difficulty, nay the impossibility, of obtaining evidence of such evolution from the past history of the globe is obvious. Both the hypothetical transitional material and the living material which was originally evolved from it may, as Macallum has suggested, have taken the form of diffused ultra-microscopic particles of living substance*; and even if they were not diffused but aggregated into masses, these masses could have been physically nothing more than colloidal watery slime which would leave no impress upon any geological formation. Myriads of years may have elapsed before some sort of skeleton in the shape of calcareous or siliceous spicules began to evolve itself, and thus enabled 'life,' which must already have possessed a prolonged existence, to make any sort of geological record. It follows that in attempting to pursue the evolution of living matter to its beginning in terrestrial history we can only expect to be confronted with a blank wall of nescience.

The problem would appear to be hopeless of ultimate solution, if we are rigidly confined to the supposition that the evolution of life has only occurred once in the past history of the globe. But are we justified in assuming that at one period only, and as it were by a fortunate and fortuitous concomitance of substance and circumstance, living matter became evolved out of non-living matter—life became established? Is there any valid reason to conclude that at some previous period of its history our earth was more favourably circumstanced for the production of life than it is now? † I have vainly sought for such reason, and if none be forthcoming the conclusion forces itself upon us that the evolution of non-living into living substance has happened more than once—and we can be by no means sure that it may not be happening still.

* There still exist in fact forms of life which the microscope cannot show us (E. A. Minchin, Presidential Address to Quekett Club, 1911), and germs which are capable of passing through the pores of a Chamberland filter.

† Chalmers Mitchell (Art. 'Life,' *Encycl. Brit.*, eleventh edition) writes as follows: 'It has been suggested from time to time that conditions very unlike those now existing were necessary for the first appearance of life, and must be repeated if living matter is to be reconstituted artificially. No support for such a view can be derived from observations of the existing conditions of life.' Cf. also J. Hall-Edwards, *op. cit.*

It is true that up to the present there is no evidence of such happening: no process of transition has hitherto been observed. But on the other hand, is it not equally true that the kind of evidence which would be of any real value in determining this question has not hitherto been looked for? We may be certain that if life is being produced from non-living substance it will be life of a far simpler character than any that has yet been observed—in material which we shall be uncertain whether to call animate or inanimate, even if we are able to detect it at all, and which we may not be able to visualise physically even after we have become convinced of its existence.* But we can look with the mind's eye and follow in imagination the transformation which non-living matter may have undergone and may still be undergoing to produce living substance. No principle of evolution is better founded than that insisted upon by Sir Charles Lyell, justly termed by Huxley 'the greatest geologist of his time,' that we must interpret the past history of our globe by the present; that we must seek for an explanation of what has happened by the study of what is happening; that, given similar circumstances, what has occurred at one time will probably occur at another. The process of evolution is universal. The inorganic materials of the globe are continually undergoing transition. New chemical combinations are constantly being formed and old ones broken up; new elements are making their appearance and old elements disappearing.† Well may we ask ourselves why the production of living matter alone should be subject to other laws than those which have produced, and are producing, the various forms of non-living matter; why what has happened may not happen. If living matter has been evolved from lifeless in the past, we are justified in accepting the conclusion that its evolution is possible in the present and in the future. Indeed, we are not only justified in accepting this conclusion, we are forced to accept it. When or where such change from non-living to living matter may first have occurred, when or where it may have continued, when or where it may still be occurring, are problems as difficult as they are interesting, but we have no right to assume that they are insoluble.

Since living matter always contains water as its most abundant constituent, and since the first living organisms recognisable as such in the geological series were aquatic, it has generally been assumed that life must first have made its appearance in the depths of the ocean.‡

* 'Spontaneous generation of life could only be perceptually demonstrated by filling in the long terms of a series between the complex forms of inorganic and the simplest forms of organic substance. Were this done, it is quite possible that we should be unable to say (especially considering the vagueness of our definitions of life) where life began or ended.'—K. Pearson, *Grammar of Science*, second edition, 1900, p. 350.

† See on the production of elements, W. Crookes, Address to Section B, Brit. Assoc., 1886; T. Preston, *Nature*, vol. 1x., p. 180; J. J. Thomson, *Phil. Mag.*, 1897, p. 311; Norman Lockyer, *op. cit.*, 1900; G. Darwin, Pres. Addr. Brit. Assoc., 1905.

‡ For arguments in favour of the first appearance of life having been in the sea,

Is it, however, certain that the assumption that life originated in the sea is correct? Is not the land-surface of our globe quite as likely to have been the nidus for the evolutionary transformation of non-living into living material as the waters which surround it? Within this soil almost any chemical transformation may occur; it is subjected much more than matters dissolved in sea-water to those fluctuations of moisture, temperature, electricity, and luminosity which are potent in producing chemical changes. But whether life, in the form of a simple slimy colloid, originated in the depths of the sea or on the surface of the land, it would be equally impossible for the geologist to trace its beginnings, and were it still becoming evolved in the same situations, it would be almost as impossible for the microscopist to follow its evolution. We are therefore not likely to obtain direct evidence regarding such a transformation of non-living into living matter in Nature, even if it is occurring under our eyes.

An obvious objection to the idea that the production of living matter from non-living has happened more than once is that, had this been the case, the geological record should reveal more than one palæontological series. This objection assumes that evolution would in every case take an exactly similar course and proceed to the same goal—an assumption which is, to say the least, improbable. If, as might well be the case, in any other palæontological series than the one with which we are acquainted the process of evolution of living beings did not proceed beyond Protista, there would be no obvious geological evidence regarding it; such evidence would only be discoverable by a carefully directed search made with that particular object in view.* I would not by any means minimise the difficulties which attend the suggestion that the evolution of life may have occurred more than once or may still be happening, but on the other hand, it must not be ignored that those which attend the assumption that the production of life has occurred once only are equally serious. Indeed, had the idea of the possibility of a multiple evolution of living substance been first in the field, I doubt if the prevalent belief regarding a single fortuitous production of life upon the globe would have become established among biologists—so much are we liable to be influenced by the impressions we receive in scientific childhood!

see A. B. Macallum, 'The Palæochemistry of the Ocean,' *Trans. Canad. Instit.*, 1903-4.

* Lankester (Art. 'Protozoa,' *Encycl. Brit.*, tenth edition) conceives that the first protoplasm fed on the antecedent steps in its own evolution. F. J. Allen (*Brit. Assoc. Reports*, 1896) comes to the conclusion that living substance is probably constantly being produced, but that this fails to make itself evident owing to the substance being seized and assimilated by existing organisms. He believes that 'in accounting for the first origin of life on this earth it is not necessary that, as Pflüger assumed, the planet should have been at a former period a glowing fire-ball.' He 'prefers to believe that the circumstances which support life would also favour its origin.' And elsewhere: 'Life is not an extraordinary phenomenon, not even an importation from some other sphere, but rather the actual outcome of circumstances on this earth.'

Assuming the evolution of living matter to have occurred—whether once only or more frequently matters not for the moment—and in the form suggested, viz., as a mass of colloidal slime possessing the property of assimilation and therefore of growth, reproduction would follow as a matter of course. For all material of this physical nature—fluid or semi-fluid in character—has a tendency to undergo subdivision when its bulk exceeds a certain size. The subdivision may be into equal or nearly equal parts, or it may take the form of buds. In either case every separated part would resemble the parent in chemical and physical properties, and would equally possess the property of taking in and assimilating suitable material from its liquid environment, growing in bulk and reproducing its like by subdivision. *Omne vivum e vivo*. In this way from any beginning of living material a primitive form of life would spread, and would gradually people the globe. The establishment of life being once effected, all forms of organisation follow under the inevitable laws of evolution. *Ce n'est que le premier pas qui coûte !*

We can trace in imagination the segregation of a more highly phosphorised portion of the primitive living matter, which we may now consider to have become more akin to the protoplasm of organisms with which we are familiar. This more phosphorised portion might not for myriads of generations take the form of a definite nucleus, but it would be composed of material having a composition and qualities similar to those of the nucleus of a cell. Prominent among these qualities is that of catalysis—the function of effecting profound chemical changes in other material in contact with it without itself undergoing permanent change. This catalytic function may have been exercised directly by the living substance or may have been carried on through the agency of the enzymes already mentioned, which are also of a colloid nature but of simpler constitution than itself, and which differ from the catalytic agents employed by the chemist in the fact that they produce their effects at a relatively low temperature. In the course of evolution special enzymes would become developed for adaptation to special conditions of life, and with the appearance of these and other modifications, a process of differentiation of primitive living matter into individuals with definite specific characters gradually became established. We can conceive of the production in this way from originally undifferentiated living substance of simple differentiated organisms comparable to the lowest forms of Protista. But how long it may have taken to arrive at this stage we have no means of ascertaining. To judge from the evidence afforded by the evolution of higher organisms it would seem that a vast period of time would be necessary for even this amount of organisation to establish itself.

The next important phase in the process of evolution would be the segregation and moulding of the diffused or irregularly aggregated nuclear

matter into a definite nucleus around which all the chemical activity of the organism will in future be centred. Whether this change were

due to a slow and gradual process of segregation or of the nature of a jump, such as Nature does occasionally make, the result would be the advancement of the living organism to the condition of a complete nucleated cell: a material advance not only in organisation but—still more important—in potentiality for future development. Life is now embodied in the cell, and every living being evolved from this will itself be either a cell or a cell-aggregate. *Omnis cellula e cellulâ.*

After the appearance of a nucleus—but how long after it is impossible to conjecture—another phenomenon appeared upon the scene in the occasional exchange of nuclear substance between cells.

In this manner became established the process of sexual reproduction. Such exchange in the unicellular organism might and may occur between any two cells forming the species, but in the multicellular organism it became—like other functions—specialised in particular cells. The result of the exchange is rejuvenescence; associated with an increased tendency to subdivide and to produce new individuals. This is due to the introduction of a stimulating or catalytic chemical agent into the cell which is to be rejuvenated, as is proved by the experiments of Loeb already alluded to. It is true that the chemical material introduced into the germ-cell in the ordinary process of its fertilisation by the sperm-cell is usually accompanied by the introduction of definite morphological elements which blend with others already contained within the germ-cell, and it is believed that the transmission of such morphological elements of the parental nuclei is related to the transmission of parental qualities. But we must not be blind to the possibility that those transmitted qualities may be connected with specific chemical characters of the transmitted elements; in other words, that heredity also is one of the questions the eventual solution of which we must look to the chemist to provide.

So far we have been chiefly considering life as it is found in the simplest forms of living substance, organisms for the most part entirely micro-

scopic and neither distinctively animal nor vegetable, which have sometimes been grouped together as a separate kingdom of animated nature—that of Protista. But

persons unfamiliar with the microscope are not in the habit of associating the term 'life' with microscopic organisms, whether these take the form of cells or of minute portions of living substance which have not yet attained to that dignity. We most of us speak and think of life as it occurs in ourselves and other animals with which we are familiar; and as we find it in the plants around us. We recognise it in these by the possession of certain properties—movement, nutrition, growth, and reproduction. We are not aware by intuition, nor can we ascertain without the

employment of the microscope, that we and all the higher living beings, whether animal or vegetable, are entirely formed of aggregates of nucleated cells, each microscopic and each possessing its own life. Nor could we suspect by intuition that what we term our life is not a single indivisible property, capable of being blown out with a puff like the flame of a candle; but is the aggregate of the lives of many millions of living cells of which the body is composed. It is but a short while ago that this cell constitution was discovered: it occurred within the lifetime, even within the memory, of some who are still with us. What a marvellous distance we have travelled since then in the path of knowledge of living organisms! The strides which were made in the advance of the mechanical sciences during the nineteenth century, which is generally considered to mark that century as an age of unexampled progress, are as nothing in comparison with those made in the domain of biology, and their interest is entirely dwarfed by that which is aroused by the facts relating to the phenomena of life which have accumulated within the same period. And not the least remarkable of these facts is the discovery of the cell-structure of plants and animals.

Let us consider how cell-aggregates came to be evolved from organisms consisting of single cells. Two methods are possible—viz.: (1) The adhesion of a number of originally separate individuals; (2) the subdivision of a single individual without the products of its subdivision breaking loose from one another. No doubt this last is the manner whereby the cell-aggregate was originally formed, since it is that by which it is still produced, and we know that the life-history of the individual is an epitome of that of the species. Such aggregates were in the beginning solid; the cells in contact with one another and even in continuity: subsequently a space or cavity became formed in the interior of the mass, which was thus converted into a hollow sphere. All the cells of the aggregate were at first perfectly similar in structure and in function; there was no subdivision of labour. All would take part in effecting locomotion; all would receive stimuli from outside; all would take in and digest nutrient matter, which would then be passed into the cavity of the sphere to serve as a common store of nourishment. Such organisms are still found, and constitute the lowest types of Metazoa. Later one part of the hollow sphere became dimpled to form a cup; the cavity of the sphere became correspondingly altered in shape. With this change in structure differentiation of function between the cells covering the outside and those lining the inside of the cup made its appearance. Those on the outside subserved locomotor functions and received and transmitted from cell to cell stimuli, physical or chemical, received by the organism; while those on the inside, being freed from such functions, tended to specialise in the direction of the inception and digestion of nutrient material; which, passing from them into the cavity of the invaginated sphere, served for the nourish-

Evolution of the cell-aggregate.

ment of all the cells composing the organism. The further course of evolution produced many changes of form and ever-increasing complexity of the cavity thus produced by simple invagination. Some of the cell-aggregates settled down to a sedentary life, becoming plant-like in appearance and to some extent in habit. Such organisms, complex in form but simple in structure, are the Sponges. Their several parts are not, as in the higher Metazoa, closely interdependent: the destruction of any one part, however extensive, does not either immediately or ultimately involve death of the rest: all parts function separately, although doubtless mutually benefiting by their conjunction, if only by slow diffusion of nutrient fluid throughout the mass. There is already some differentiation in these organisms, but the absence of a nervous system prevents any general co-ordination, and the individual cells are largely independent of one another.

Our own life, like that of all the higher animals, is an *aggregate life*; the life of the whole is the life of the individual cells. The life of some of these cells can be put an end to, the rest may continue to live. This is, in fact, happening every moment of our lives. The cells which cover the surface of our body, which form the scarf-skin and the hair and nails, are constantly dying, and the dead cells are rubbed off or cut away, their place being taken by others supplied from living layers beneath. But the death of these cells does not affect the vitality of the body as a whole. They serve merely as a protection or an ornamental covering, but are otherwise not material to our existence. On the other hand, if a few cells, such as those nerve-cells under the influence of which respiration is carried on, are destroyed or injured, within a minute or two the whole living machine comes to a standstill, so that to the bystander the patient is dead; even the doctor will pronounce life to be extinct. But this pronouncement is correct only in a special sense. What has happened is that, owing to the cessation of respiration, the supply of oxygen to the tissues is cut off. And since the manifestations of life cease without this supply, the animal or patient appears to be dead. If, however, within a short period we supply the needed oxygen to the tissues requiring it, all the manifestations of life reappear.

It is only some cells which lose their vitality at the moment of so-called 'general death.' Many cells of the body retain their individual life under suitable circumstances long after the rest of the body is dead. Notable among these are muscle-cells. McWilliam showed that the muscle-cells of the blood-vessels give indications of life several days after an animal has been killed. The muscle-cells of the heart in mammals have been revived and caused to beat regularly and strongly many hours after apparent death. In man this result has been obtained as many as eighteen hours after life has been pronounced extinct (Kuliabko); in animals after days have elapsed. Waller has shown that indications of life can be elicited from various tissues many hours and even days after

general death. Sherrington observed the white corpuscles of the blood to be active when kept in a suitable nutrient fluid weeks after removal from the blood-vessels. A French histologist, Jolly, has found that the white corpuscles of the frog, if kept in a cool place and under suitable conditions, show at the end of a year all the ordinary manifestations of life. Carrell and Burrows have observed activity and growth to continue for long periods in the isolated cells of a number of tissues and organs kept under observation in a suitable medium. Carrell has succeeded in substituting entire organs obtained after death from one animal for those of another of the same species, and has thereby opened up a field of surgical treatment, the limits of which cannot yet be described. It is a well-established fact that any part of the body can be maintained alive for hours isolated from the rest if perfused with serum (Kronecker, frog-heart), or with an oxygenated solution of salts in certain proportions (Ringer). Such revival and prolongation of the life of separated organs is an ordinary procedure in laboratories of physiology. Like all the other instances enumerated, it is based on the fact that the individual cells of an organ have a life of their own which is largely independent, so that they will continue in suitable circumstances to live, although the rest of the body to which they belonged may be dead.

But some cells, and the organs which are formed of them, are more necessary to maintain the life of the aggregate than others, on account of the nature of the functions which have become specialised in them. This is the case with the nerve-cells of the respiratory centre, since they preside over the movements which are necessary to effect oxygenation of the blood. It is also true for the cells which compose the heart, since this serves to pump oxygenated blood to all other cells of the body: without such blood most cells soon cease to live. Hence we examine respiration and heart to determine if life is present: when one or both of these are at a standstill we know that life cannot be maintained. These are not the only organs necessary for the maintenance of life, but the loss of others can be borne longer, since the functions which they subserve, although useful or even essential to the organism, can be dispensed with for a time. The life of some cells is therefore more, of others less necessary for maintaining the life of the rest. On the other hand, the cells composing certain organs have in the course of evolution ceased to be necessary, and their continued existence may even be harmful. Wiedersheim has enumerated more than a hundred of these organs in the human body. Doubtless Nature is doing her best to get rid of them for us, and our descendants will some day have ceased to possess a vermiform appendix or a pharyngeal tonsil: until that epoch arrives we must rely for their removal on the more rapid methods of surgery!

We have seen that in the simplest multicellular organisms, where one cell of the aggregate differs but little from another, the conditions for the maintenance of the life of the whole are nearly as simple as those for

individual cells. But the life of a cell-aggregate such as composes the bodies of the higher animals is maintained not only by the conditions for the maintenance of the life of the individual cell being kept favourable, but also by the co-ordination of the varied activities of the cells which form the aggregate. Whereas in the lowest Metazoa all cells of the aggregate are alike in structure and function and perform and share everything in common, in higher animals (and for that matter in the higher plants also) the cells have become specialised, and each is only adapted for the performance of a particular function. Thus the cells of the gastric glands are only adapted for the secretion of gastric juice, the cells of the villi for the absorption of digested matters from the intestine, the cells of the kidney for the removal of waste products and superfluous water from the blood, those of the heart for pumping blood through the vessels. Each of these cells has its individual life and performs its individual functions. But unless there were some sort of co-operation and subordination to the needs of the body generally, there would be sometimes too little, sometimes too much gastric juice secreted; sometimes too tardy, sometimes too rapid an absorption from the intestine; sometimes too little, sometimes too much blood pumped into the arteries, and so on. As the result of such lack of co-operation the life of the whole would cease to be normal and would eventually cease to be maintained.

We have already seen what are the conditions which are favourable for the maintenance of life of the individual cell, no matter where situated. The principal condition is that it must be bathed by a nutrient fluid of suitable and constant composition. In higher animals this fluid is the lymph, which bathes the tissue elements and is itself constantly supplied with fresh nutriment and oxygen by the blood. Some tissue-cells are directly bathed by blood; and in invertebrates, in which there is no special system of lymph-vessels, all the tissues are thus nourished. All cells both take from and give to the blood, but not the same materials or to an equal extent. Some, such as the absorbing cells of the villi, almost exclusively give; others, such as the cells of the renal tubules, almost exclusively take. Nevertheless, the resultant of all the give and take throughout the body serves to maintain the composition of the blood constant under all circumstances. In this way the first condition of the maintenance of the life of the aggregate is fulfilled by insuring that the life of the individual cells composing it is kept normal.

The second essential condition for the maintenance of life of the cell-aggregate is the co-ordination of its parts and the due regulation of their activity, so that they may work together for the benefit of the whole. In the animal body this is effected in two ways: first, through the nervous system; and second, by the action of specific chemical substances which are formed in certain organs and carried by the blood to

other parts of the body, the cells of which they excite to activity. These substances have received the general designation of 'hormones' (*ὁρμῶν*, to stir up), a term introduced by Professor Starling. Their action, and indeed their very existence, has only been recognised of late years, although the part which they play in the physiology of animals appears to be only second in importance to that of the nervous system itself; indeed, maintenance of life may become impossible in the absence of certain of these hormones.

Before we consider the manner in which the nervous system serves to co-ordinate the life of the cell-aggregate, let us see how it has become evolved.

Part played by the nervous system in the maintenance of aggregate life.
Evolution of a nervous system.

The first step in the process was taken when certain of the cells of the external layer became specially sensitive to stimuli from outside, whether caused by mechanical impressions (tactile and auditory stimuli) or impressions of light and darkness (visual stimuli) or chemical impressions. The effects of such impressions were probably at first simply communicated to adjacent cells and spread from cell to cell throughout the mass. An advance was made when the more impressionable cells threw out branching feelers amongst the other cells of the organism. Such feelers would convey the effects of stimuli with greater rapidity and directness to distant parts. They may at first have been retractile, in this respect resembling the long pseudopodia of certain Rhizopoda. When they became fixed they would be potential nerve-fibres and would represent the beginning of a nervous system. Even yet (as Ross Harrison has shown), in the course of development of nerve-fibres, each fibre makes its appearance as an amœboid cell-process which is at first retractile, but gradually grows into the position it is eventually to occupy and in which it will become fixed.

In the further course of evolution a certain number of these specialised cells of the external layer sank below the general surface, partly perhaps for protection, partly for better nutrition: they became nerve-cells. They remained connected with the surface by a prolongation which became an afferent or sensory nerve-fibre, and through its termination between the cells of the general surface continued to receive the effects of external impressions; on the other hand, they continued to transmit these impressions to other, more distant cells by their efferent prolongations. In the further course of evolution the nervous system thus laid down became differentiated into distinct *afferent*, *efferent*, and *intermediary* portions. Once established, such a nervous system, however simple, must dominate the organism, since it would furnish a mechanism whereby the individual cells would work together more effectually for the mutual benefit of the whole.

It is the development of the nervous system, although not proceeding in all classes along exactly the same line, which is the most prominent

feature of the evolution of the Metazoa. By and through it all impressions reaching the organism from the outside are translated into contraction or some other form of cell-activity. Its formation has been the means of causing the complete divergence of the world of animals from the world of plants, none of which possess any trace of a nervous system. Plants react, it is true, to external impressions, and these impressions produce profound changes and even comparatively rapid and energetic movements in parts distant from the point of application of the stimulus—as in the well-known instance of the sensitive plant. But the impressions are in all cases propagated directly from cell to cell—not through the agency of nerve-fibres; and in the absence of anything corresponding to a nervous system it is not possible to suppose that any plant can ever acquire the least glimmer of intelligence. In animals, on the other hand, from a slight original modification of certain cells has directly proceeded in the course of evolution the elaborate structure of the nervous system with all its varied and complex functions, which reach their culmination in the workings of the human intellect. ‘What a piece of work is a man! How noble in reason! How infinite in faculty! In form and moving how express and admirable! In action how like an angel! In apprehension how like a god!’ But lest he be elated with his psychological achievements, let him remember that they are but the result of the acquisition by a few cells in a remote ancestor of a slightly greater tendency to react to an external stimulus, so that these cells were brought into closer touch with the outer world; while on the other hand, by extending beyond the circumscribed area to which their neighbours remained restricted, they gradually acquired a dominating influence over the rest. These dominating cells became nerve-cells; and now not only furnish the means for transmission of impressions from one part of the organism to another, but in the progress of time have become the seat of perception and conscious sensation, of the formation and association of ideas, of memory, of volition, and all the manifestations of the mind.

The most conspicuous part played by the nervous system in the phenomena of life is that which produces and regulates the general movements of the body—movements brought about by the so-called voluntary muscles. These movements are actually the result of impressions imparted to sensory or afferent nerves at the periphery—*e.g.*, in the skin or in the several organs of special sense; the effect of these impressions may not be immediate, but can be stored for an indefinite time in certain cells of the nervous system. The regulation of movements—whether they occur instantly after reception of the peripheral impression or result after a certain lapse of time; whether they are accompanied by conscious sensation or are of a purely reflex and unconscious character—is an intricate process, and the conditions of their co-ordination are of a complex nature involving not merely the causation and contraction of certain muscles, but also the

Regulation of movements by the nervous system. Voluntary movements.

prevention of the contraction of others. For our present knowledge of these conditions we are largely indebted to the researches of Professor Sherrington.

A less conspicuous but no less important part played by the nervous system is that by which the contractions of involuntary muscles are regulated. Under normal circumstances these are always independent of consciousness, but their regulation is brought about in much the same way as is that

Involuntary movements.

of the contractions of voluntary muscles—viz., as the result of impressions received at the periphery. These are transmitted by afferent fibres to the central nervous system, and from the latter other impulses are sent down, mostly along the nerves of the sympathetic or autonomic system of nerves, which either stimulate or prevent contraction of the involuntary muscles. Many involuntary muscles have a natural tendency to continuous or rhythmic contraction which is quite independent of the central nervous system; in this case the effect of impulses received from the latter is merely to increase or diminish the amount of such contraction. An example of this double effect is observed in connection with

Effects of emotions. the heart, which—although it can contract regularly and rhythmically when cut off from the nervous system and even if removed from the body—is normally stimulated to increased activity by impulses coming from the central nervous system through the sympathetic, or to diminished activity by others coming through the vagus. It is due to the readiness by which the action of the heart is influenced in these opposite ways by the spread of impulses generated during the nerve-storms which we term ‘emotions’ that in the language of poetry, and even of every day, the word ‘heart’ has become synonymous with the emotions themselves.

The involuntary muscle of the arteries has its action similarly balanced. When its contraction is increased, the size of the vessels is lessened and they deliver less blood; the parts they supply accordingly become pale in colour. On the other hand, when the contraction is diminished the vessels enlarge and deliver more blood; the parts which they supply become correspondingly ruddy. These changes in the arteries, like the effects upon the heart, may also be produced under the influence of emotions. Thus ‘blushing’ is a purely physiological phenomenon due to diminished action of the muscular tissue of the arteries, whilst the pallor produced by fright is caused by an increased contraction of that tissue. Apart, however, from these conspicuous effects, there is constantly proceeding a less apparent but not less important balancing action between the two sets of nerve-fibres distributed to heart and blood-vessels; which are influenced in one direction or another by every sensation which we experience and even by impressions of which we may be wholly unconscious, such as those which occur during sleep or anæsthesia, or which affect our otherwise insensitive internal organs.

A further instance of nerve-regulation is seen in secreting glands. Not all glands are thus regulated, at least not directly; but in those which are, the effects are striking. Their regulation is of the same general nature as that exercised upon involuntary muscle, but it influences the chemical activities of the gland-cells and the outpouring of secretion from them.

Regulation of secretion by the nervous system.

By means of this regulation a secretion can be produced or arrested, increased or diminished. As with muscle, a suitable balance is in this way maintained, and the activity of the glands is adapted to the requirements of the organism. Most of the digestive glands are thus influenced, as are the skin-glands which secrete sweat. And by the action of the nervous system upon the skin-glands, together with its effect in increasing or diminishing the blood-supply to the cutaneous blood-vessels, the temperature of our blood is regulated and is kept at the point best suited for maintenance of the life and activity of the tissues.

Regulation of body temperature.

The action of the nervous system upon the secretion of glands is strikingly exemplified, as in the case of its action upon the heart and blood-vessels by the effects of the emotions. Thus an emotion of one kind—such as the anticipation of food—will cause saliva to flow—‘the mouth to water’; whereas an emotion of another kind—such as fear or anxiety—will stop the secretion, causing the ‘tongue to cleave unto the roof of the mouth,’ and rendering speech difficult or impossible. Such arrest of the salivary secretion also makes the swallowing of dry food difficult: advantage of this fact is taken in the ‘ordeal by rice’ which used to be employed in the East for the detection of criminals.

Effects of emotions on secretion.

The activities of the cells constituting our bodies are controlled, as already mentioned, in another way than through the nervous system, viz., by chemical agents (hormones) circulating in the blood. Many of these are produced by special glandular organs, known as internally secreting glands. The ordinary secreting glands pour their secretions on the exterior of the body or on a surface communicating with the exterior; the internally secreting glands pass the materials which they produce directly into the blood. In this fluid the hormones are carried to distant organs. Their influence upon an organ may be essential to the proper performance of its functions or may be merely ancillary to it. In the former case removal of the internally secreting gland which produces the hormone, or its destruction by disease, may prove fatal to the organism. This is the case with the suprarenal capsules: small glands which are adjacent to the kidneys, although having no physiological connection with these organs. A Guy’s physician, Dr. Addison, in the middle of the last century showed that a certain affection, almost always fatal, since known by his name, is associated with disease

Regulation by chemical agents: hormones. Internal secretions.

Suprarenals.

of the suprarenal capsules. A short time after this observation a French physiologist, Brown-Séguard, found that animals from which the suprarenal capsules are removed rarely survive the operation for more than a few days. In the concluding decade of the last century interest in these bodies was revived by the discovery that they are constantly yielding to the blood a chemical agent (or hormone) which stimulates the contractions of the heart and arteries and assists in the promotion of every action which is brought about through the sympathetic nervous system (Langley). In this manner the importance of their integrity has been explained, although we have still much to learn regarding their functions.

Another instance of an internally secreting gland which is essential to life, or at least to its maintenance in a normal condition, is the thyroid.

Thyroid.

The association of imperfect development or disease of the thyroid with disorders of nutrition and inactivity of the nervous system is well ascertained. The form of idiocy known as cretinism and the affection termed myxœdema are both associated with deficiency of its secretion: somewhat similar conditions to these are produced by the surgical removal of the gland. The symptoms are alleviated or cured by the administration of its juice. On the other hand, enlargement of the thyroid, accompanied by increase of its secretion, produces symptoms of nervous excitation, and similar symptoms are caused by excessive administration of the glandular substance by the mouth. From these observations it is inferred that the juice contains hormones which help to regulate the nutrition of the body and serve to stimulate the nervous system, for the higher functions of which they appear to be essential. To quote M. Gley, to whose researches we owe much of our knowledge regarding the functions of this organ: 'La genèse et l'exercice des plus hautes facultés de l'homme sont conditionnés par l'action purement chimique d'un produit de sécrétion. Que les psychologues méditent ces faits!'

The case of the parathyroid glandules is still more remarkable. These organs were discovered by Sandström in 1880. They are four

Parathyroids.

minute bodies, each no larger than a pin's head, imbedded in the thyroid. Small as they are, their internal secretion possesses hormones which exert a powerful influence upon the nervous system. If they are completely removed, a complex of symptoms, technically known as 'tetany,' is liable to occur, which is always serious and may be fatal. Like the hormones of the thyroid itself, therefore, those of the parathyroids produce effects upon the nervous system, to which they are carried by the blood; although the effects are of a different kind.

Another internally secreting gland which has evoked considerable interest during the last few years is the pituitary body. This is a small structure no larger than a cob-nut attached to the base of the brain. It is mainly composed of glandular cells. Its removal has been found (by

most observers) to be fatal—often within two or three days. Its hypertrophy, when occurring during the general growth of the body, is attended

by an undue development of the skeleton, so that the stature tends to assume gigantic proportions.

Pituitary. When the hypertrophy occurs after growth is completed, the extremities—viz., the hands and feet and the bones of the face—are mainly affected; hence the condition has been termed ‘acromegaly’ (enlargement of extremities). The association of this condition with affections of the pituitary was pointed out in 1885 by a distinguished French physician, Dr. Pierre Marie. Both ‘giants’ and ‘acromegalists’ are almost invariably found to have an enlarged pituitary. The enlargement is generally confined to one part—the anterior lobe—and we conclude that this produces hormones which stimulate the growth of the body generally and of the skeleton in particular. The remainder of the pituitary is different in structure from the anterior lobe and has a different function. From it hormones can be extracted which, like those of the suprarenal capsule, although not exactly in the same manner, influence the contraction of the heart and arteries. Its extracts are also instrumental in promoting the secretion of certain glands. When injected into the blood they cause a free secretion of water from the kidneys and of milk from the mammary glands, neither of which organs are directly influenced (as most other glands are) through the nervous system. Doubtless under natural conditions these organs are stimulated to activity by hormones which are produced in the pituitary and which pass from this into the blood.

The internally secreting glands which have been mentioned (thyroid, parathyroid, suprarenal, pituitary) have, so far as is known, no other function than that of producing chemical substances of this character for the influencing of other organs, to which they are conveyed by the blood. It is interesting to observe that these glands are all of very small size, none being larger than a walnut, and some—the parathyroids—almost microscopic. In spite of this, they are essential to the proper maintenance of the life of the body, and the total removal of any of them by disease or operation is in most cases speedily fatal.

There are, however, organs in the body yielding internal secretions to the blood in the shape of hormones, but exercising at the same time other functions. A striking instance is furnished by

Pancreas. the pancreas, the secretion of which is the most important of the digestive juices. This—the pancreatic juice—forms the external secretion of the gland, and is poured into the intestine, where its action upon the food as it passes out from the stomach has long been recognised. It was, however, discovered in 1889 by von Mering and Minkowski that the pancreas also furnishes an internal secretion, containing a hormone which is passed from the pancreas into the blood, by which it is carried first to the liver and afterwards to the body generally. This

hormone is essential to the proper utilisation of carbohydrates in the organism. It is well known that the carbohydrates of the food are converted into grape sugar and circulate in this form in the blood, which always contains a certain amount; the blood conveys it to all the cells of the body, and they utilise it as fuel. If, owing to disease of the pancreas or as the result of its removal by surgical procedure, its internal secretion is not available, sugar is no longer properly utilised by the cells of the body and tends to accumulate in the blood; from the blood the excess passes off by the kidneys, producing diabetes.

Another instance of an internal secretion furnished by an organ which is devoted largely to other functions is the 'pro-secretin' found in the cells lining the duodenum. When the acid gastric juice comes into contact with these cells it converts their pro-secretin into 'secretin.' This is a hormone which is passed into the blood and circulates with that fluid. It has a specific effect on the externally secreting cells of the pancreas, and causes the rapid outpouring of pancreatic juice into the intestine. This effect is similar to that of the hormones of the pituitary body upon the cells of the kidney and mammary gland. It was discovered by Bayliss and Starling.

The reproductive glands furnish in many respects the most interesting example of organs which—besides their ordinary products, the germ- and sperm-cells (ova and spermatozoa)—form hormones which circulate in the blood and effect changes in cells of distant parts of the body. It is through these hormones that the secondary sexual characters, such as the comb and tail of the cock, the mane of the lion, the horns of the stag, the beard and enlarged larynx of a man, are produced, as well as the many differences in form and structure of the body which are characteristic of the sexes. The dependence of these so-called secondary sexual characters upon the state of development of the reproductive organs has been recognised from time immemorial, but has usually been ascribed to influences produced through the nervous system, and it is only in recent years that the changes have been shown to be brought about by the agency of internal secretions and hormones, passed from the reproductive glands into the circulating blood.*

It has been possible in only one or two instances to prepare and isolate the hormones of the internal secretions in a sufficient condition of purity to subject them to analysis, but enough is known about them to indicate that they are organic bodies of a not very complex nature, far simpler than proteins and even than enzymes. Those which have been studied are all dialysable, are readily soluble in water but insoluble in alcohol, and are not destroyed by boiling. One at least—that of the medulla of the suprarenal capsule—

* The evidence is to be found in F. H. A. Marshall, *The Physiology of Reproduction*, 1911.

has been prepared synthetically, and when their exact chemical nature has been somewhat better elucidated it will probably not be difficult to obtain others in the same way.

From the above it is clear that not only is a co-ordination through the nervous system necessary in order that life shall be maintained in a normal condition, but a chemical co-ordination is no less essential. These may be independent of one another; but on the other hand they may react upon one another. For it can be shown that the production of some at least of the hormones is under the influence of the nervous system (Biedl, Asher, Elliott); whilst, as we have seen, some of the functions of the nervous system are dependent upon hormones.

Time will not permit me to refer in any but the briefest manner to the protective mechanisms which the cell-aggregate has evolved for its defence against disease, especially disease produced by parasitic micro-organisms. These, which with few exceptions are unicellular, are without doubt the most formidable enemies which the multicellular Metazoa, to which all the higher animal organisms belong, have to contend against. To such micro-organisms are due *inter alia* all diseases which are liable to become epidemic, such as anthrax and rinderpest in cattle, distemper in dogs and cats, small-pox, scarlet fever, measles, and sleeping sickness in man. The advances of modern medicine have shown that the symptoms of these diseases—the disturbances of nutrition, the temperature, the lassitude or excitement, and other nervous disturbances—are the effects of chemical poisons (*toxins*) produced by the micro-organisms and acting deleteriously upon the tissues of the body. The tissues, on the other hand, endeavour to counteract these effects by producing other chemical substances destructive to the micro-organisms or antagonistic to their action: these are known as *anti-bodies*. Sometimes the protection takes the form of a subtle alteration in the living substance of the cells which renders them for a long time, or even permanently, insusceptible (immune) to the action of the poison. Sometimes certain cells of the body, such as the white corpuscles of the blood, eat the invading micro-organisms and destroy them bodily by the action of chemical agents within their protoplasm. The result of an illness thus depends upon the result of the struggle between these opposing forces—the micro-organisms on the one hand and the cells of the body on the other—both of which fight with chemical weapons. If the cells of the body do not succeed in destroying the invading organisms it is certain that the invaders will in the long run destroy them, for in this combat no quarter is given. Fortunately we have been able, by the aid of animal experimentation, to acquire some knowledge of the manner in which we are attacked by micro-organisms and of the methods which the cells of our body adopt to repel the attack, and the knowledge is now extensively utilised to assist our defence. For this purpose protective serums or anti-

toxins, which have been formed in the blood of other animals, are employed to supplement the action of those which our own cells produce. It is not too much to assert that the knowledge of the parasitic origin of so many diseases and of the chemical agents which

Parasitic nature of diseases.

on the one hand cause, and on the other combat, their symptoms, has transformed medicine from a mere art practised empirically into a real science based upon experiment. The transformation has opened out an illimitable vista of possibilities in the direction not only of cure, but, more important still, of prevention. It has taken place within the memory of most of us who are here present. And only last February the world was mourning the death of one of the greatest of its benefactors—a former President of this Association*—who, by applying this knowledge to the practice of surgery, was instrumental, even in his own lifetime, in saving more lives than were destroyed in all the bloody wars of the nineteenth century!

The question has been debated whether, if all accidental modes of destruction of the life of the cells could be eliminated, there would remain a possibility of individual cell-life, and even of

Senescence and death.

aggregate cell-life, continuing indefinitely; in other words, Are the phenomena of senescence and death a natural and necessary sequence to the existence of life? To most of my audience it will appear that the subject is not open to debate. But some physiologists (*e.g.*, Metchnikoff) hold that the condition of senescence is itself abnormal; that old age is a form of disease or is due to disease, and, theoretically at least, is capable of being eliminated. We have already seen that individual cell-life, such as that of the white blood-corpuses and of the cells of many tissues, can under suitable conditions be prolonged for days or weeks or months after general death. Unicellular organisms kept under suitable conditions of nutrition have been observed to carry on their functions normally for prolonged periods and to show no degeneration such as would accompany senescence. They give rise by division to others of the same kind, which also, under favourable conditions, continue to live, to all appearance indefinitely. But these instances, although they indicate that in the simplest forms of organisation existence may be greatly extended without signs of decay, do not furnish conclusive evidence of indefinite prolongation of life. Most of the cells which constitute the body, after a period of growth and activity, sometimes more, sometimes less prolonged, eventually undergo atrophy and cease to perform satisfactorily the functions which are allotted to them. And when we consider the body as a whole, we find that in every case the life of the aggregate consists of a definite cycle of changes which, after passing through the stages of growth and maturity, always leads to senescence, and finally

* Lord Lister was President at Liverpool in 1896.

terminates in death. The only exception is in the reproductive cells, in which the processes of maturation and fertilisation result in rejuvenescence, so that instead of the usual downward change towards senescence, the fertilised ovum obtains a new lease of life, which is carried on into the new-formed organism. The latter again itself ultimately forms reproductive cells, and thus the life of the species is continued. It is only in the sense of its propagation in this way from one generation to another that we can speak of the indefinite continuance of life: we can only be immortal through our descendants!

The individuals of every species of animal appear to have an average duration of existence.* Some species are known the individuals of which live only for a few hours, whilst others survive for a hundred years.† In man himself the average length of life would probably be greater than the three-score and ten years allotted to him by the

Average duration of life and possibility of its prolongation.

Psalmist if we could eliminate the results of disease and accident; when these results are included it falls far short of that period. If the terms of life given in the purely mythological part of the Old Testament were credible, man would in the early stages of his history have possessed a remarkable power of resisting age and disease. But, although many here present were brought up to believe in their literal veracity, such records are no longer accepted even by the most orthodox of theologians, and the nine hundred odd years with which Adam and his immediate descendants are credited, culminating in the nine hundred and sixty-nine of Methuselah, have been relegated, with the account of Creation and the Deluge, to their proper position in literature. When we come to the Hebrew Patriarchs, we notice a considerable diminution to have taken place in what the insurance offices term the 'expectation of life.' Abraham is described as having lived only to 175 years, Joseph and Joshua to 110, Moses to 120; even at that age 'his eye was not dim nor his natural force abated.' We cannot say that under ideal conditions all these terms are impossible; indeed, Metchnikoff is disposed to regard them as probable; for great ages are still occasionally recorded, although it is doubtful if any as considerable as these are ever substantiated. That the expectation of life was better then than now would be inferred from the apologetic tone adopted by Jacob when questioned by Pharaoh as to his age: 'The days of the years of my pilgrimage are an hundred and thirty years; few and evil have the days of the years of my life been, and have not attained unto the days of the years of the life of my fathers in the days of their

* This was regarded by Buffon as related to the period of growth, but the ratio is certainly not constant. The subject is discussed by Ray Lankester in an early work: *On Comparative Longevity in Man and Animals*, 1870.

† The approximately regular periods of longevity of different species of animals furnishes a strong argument against the theory that the decay of old age is an accidental phenomenon, comparable with disease.

pilgrimage.' David, to whom, before the advent of the modern statistician, we owe the idea that seventy years is to be regarded as the normal period of life,* is himself merely stated to have 'died in a good old age.' The periods recorded for the Kings show a considerable falling-off as compared with the Patriarchs; but not a few were cut off by violent deaths, and many lived lives which were not ideal. Amongst eminent Greeks and Romans few very long lives are recorded, and the same is true of historical persons in mediæval and modern history. It is a long life that lasts much beyond eighty; three such linked together carry us far back into history. Mankind is in this respect more favoured than most mammals, although a few of these surpass the period of man's existence.† Strange that the brevity of human life should be a favourite theme of preacher and poet when the actual term of his 'erring pilgrimage' is greater than that of most of his fellow-creatures!

The modern applications of the principles of preventive medicine and hygiene are no doubt operating to lengthen the average life. But even if the ravages of disease could be altogether eliminated, it is certain that at any rate the fixed cells of our body must eventually grow old and ultimately cease to function; when this happens to cells which are essential to the life of the organism, general death must result. This will always remain the universal law, from which there is no escape. 'All that lives must die, passing through nature to eternity!'

Such natural death unaccelerated by disease—is not death by disease as unnatural as death by accident?—should be a quiet, painless phenomenon, unattended by violent change. As Dastre expresses it, 'The need of death should appear at the end of life, just as the need of sleep appears at the end of the day.' The change has been led gradually up to by an orderly succession of phases, and is itself the last manifestation of life. Were we all certain of a quiet passing—were we sure that there would be 'no moaning of the bar when we go out to sea'—we could anticipate the coming of death after a ripe old age without apprehension. And if ever the time shall arrive when man will have learned to regard this change as a simple physiological process, as natural as the oncoming of sleep, the approach of the fatal shears will be as generally welcomed as it is now abhorred. Such a day is still distant; we can hardly say that its dawning is visible. Let us at least hope that, in the manner depicted by Dürer in his well-known etching, the sunshine which science irradiates may eventually put to flight the melancholy which hovers, bat-like, over the termination of our lives, and which even the anticipation of a future happier existence has not hitherto succeeded in dispersing.

* The expectation of life of a healthy man of fifty is still reckoned at about twenty years.

† 'Hominis ævum cæterorum animalium omnium superat præter admodum paucorum.'—Francis Bacon, *Historia vitæ et mortis*, 1637. ✓

