SCIENCE

VOL. LVII MARCH 9, 1923 No. 1471

The Physical Basis of Life: PROFESSOR EDMUND B. WILSON ... 277

Darwin and Pasteur—an Essay in Comparative Biography: THE LATE WILLIAM THOMPSON SEDGWICK ... 286

Edward Emerson Barnard: DR. OLIVER J. LEE ... 289

Scientific Events:
The Haber Process; International Scientific Cooperation; Research Service to the Industries of Michigan; Public Lectures of the Chicago Section of the American Chemical Society; Organization of Scientific Men in the Northwest; The Meeting of the American Chemical Society in New Haven 291

Scientific Notes and News ... 295

University and Educational Notes ... 299

Discussion and Correspondence:
The Feeding Power of Plants: DRS. A. R. DAVIS, D. R. HOAGLAND and C. B. LIPMAN. *The Personal Equation of the Astronomers:* PROFESSOR KNIGHT DUNLAP ... 299

Quotations:
Copernicus ... 302

Scientific Books:
Howarth on the British Association for the Advancement of Science: PROFESSOR BURTON E. LIVINGSTON ... 303

Safranin and Methyl Green: DR. H. J. CONN 304

Special Articles:
Furfural as a Biological Reagent: DR. C. E. THARALDSEN ... 305

SCIENCE: A Weekly Journal devoted to the Advancement of Science, publishing the official notices and proceedings of the American Association for the Advancement of Science, edited by J. McKeen Cattell and published every Friday by

THE SCIENCE PRESS

100 Liberty St., Utica, N. Y. Garrison, N. Y.
New York City: Grand Central Terminal

Annual Subscription, $6.00. Single Copies, 15 Cts.

Entered as second-class matter January 21, 1922, at the Post Office at Utica, N. Y., Under the Act of March 3, 1879.

THE PHYSICAL BASIS OF LIFE[1]

I HAVE been much honored by the invitation to speak on this occasion, but for me it has meant more; for the man in whose memory the Sedgwick Memorial Lectureship has been established was my life-long and cherished friend. My theme to-day is drawn from an infinitesimal but all-including world, bounded by the horizon of the compound microscope, a world that may seem far distant from Sedgwick's own broad domain of sanitary science and the public health. I am sure, however, that such would not have been his own view; for Sedgwick was one of the pioneer teachers of general biology in this country, and it was his life-long habit to think of the phenomena of life in terms of the activities of protoplasm.

I have a lively recollection of how he and I, in the days of our youth, when fellow students at Yale, fell under the spell of Huxley's Edinburgh address on the "Physical basis of life," at that time still a subject of widespread popular discussion. In this celebrated discourse, delivered in 1868, the eminent English biologist set forth certain general conclusions concerning protoplasm which had gradually taken shape through the work of such investigators as De Bary, Max Schultze, Kühne, Brücke and Lionel Beale. Huxley's presentation of the subject was a masterpiece, both of English style and of philosophical breadth of outlook. In part for this reason, still more because of its supposed materialistic implications, it aroused immediate and widespread public attention. Huxley himself warned that to accept his conclusions would be "to place one's foot on the first rung of a ladder which in most people's estimation is the reverse of Jacob's and leads to the antipodes of heaven"; nevertheless, he insisted that

[1] The first Sedgwick Memorial Lecture, delivered in Boston, December 29, 1922. It will hereafter be published in fuller form, with illustrations, under the auspices of the Department of Biology and Public Health, Massachusetts Institute of Technology.

he was individually no materialist but on the contrary believed materialism to involve grave philosophic error. Despite this disclaimer, his conclusions aroused a storm of criticism and protest which came to a climax a few years later when Tyndall, in the famous Belfast address, proclaimed his faith in non-living matter as offering the "promise and potency of every form of terrestrial life." Huxley's heresy of sixty years ago has become an orthodox platitude to-day; but the problems of protoplasm still hold us fast with a gripping interest that has lost nothing of its force with the flight of time. In what light do Huxley's conclusions appear after the biological progress of half a century?

It is necessary to bear in mind that those conclusions were formulated before modern cytology had been born, and long before the cell had been clearly thought of as a colloidal system. From our present point of view we employ the word protoplasm as a collective term to designate the substances that constitute the active or living materials of which cells are composed. I use the plural form, substances, advisedly; for it is here in the first place that Huxley's statements now require recasting in more modern terms. To many readers his discussion conveyed the impression that protoplasm is a single chemical substance or "living protein." In his opening words he speaks of the physical basis of life as "some one kind of matter common to all living beings." He pictures a union of lifeless substances, such as water, ammonia and carbon-dioxide, to form "the still more complex body, protoplasm"; and the properties of this substance, he affirmed, must result from the nature and disposition of its molecules. "The thoughts to which I am now giving utterance," said Huxley, "and your thoughts regarding them, are the expression of molecular changes in that matter of life which is the source of our other vital phenomena."

In one sense, no doubt, these words are true; but evidently they do not express the whole truth. Long ago it became perfectly plain that what we call protoplasm is not chemically a single, homogeneous substance. It is a mixture of many substances, a mixture in high degree complex, the seat of varied and incessant chemical transformations, yet one which somehow holds fast for countless generations to its own specific type. The evidence from every source demonstrates that the cell is a complex organism, a microcosm, a living *system*. With the microscope we distinguish in this system a clear ground-substance or *hyaloplasm* in which are suspended a great variety of formed bodies, widely diverse in form and function, each of which plays its own particular part in the activities of the system. Examples of these are the nucleus, the cytoplasmic chondriosomes and plastids; the Golgi-bodies and central bodies, and many kinds of granules and fibrillæ. Some of them seem to be permanent, others to be transitory formations that come and go in the kaleidoscopic operations of cell-life. Which of them are alive? Which, if any, constitute the physical basis of life? What, in other words, is protoplasm?

These are embarrassing questions. One of the most pleasing functions of the teacher of elementary biology is to demonstrate to the laboratory student the substance of a living cell and assure him cheerfully that he is beholding protoplasm; and by good luck it rarely occurs to the disciple to cross-examine his master on the subject. Were it otherwise, how many a bad quarter of an hour might we have to endure! For the truth is that the more critically we study the question the more evident does it become that we can not single out any one particular component of the cell as the living stuff, *par excellence*. Of this fact most experienced cytologists, including such eminent leaders as Flemming, Strasburger, Bütschli, Kölliker and Heidenhain, long since became convinced. "No man," said Flemming, "can definitely say what protoplasm is . . . In my view that which lives is the entire body of the cell." It is this view of the physical basis of life that has impressed us more and more as our knowledge of the cell has advanced; and this is as true of the physiologist and the chemist as of the cytologist. I quote a distinguished biochemist. "We can not," says Professor Hopkins, "without gross misuse of terms, speak of the cell life as being associated with any particular type of molecule. Its life is the expression of a particular dynamic equilibrium which obtains in a polyphasic system. Certain of the phases may be separated, but life is a property of the cell as a whole, because it depends upon the equilibrium displayed by the totality of coexisting phases." This conclusion is in substance precisely the same as that of the cytologist.

I repeat, therefore, that when we speak of protoplasm as the physical basis of life, we mean simply the sum total of all the substances that play any active part in the cell life; and we can not, I think, exclude from the list such substances as water and inorganic salts which we commonly think of as "lifeless." At first sight this may seem a rather barren conclusion; but the fact is quite otherwise. No conception of modern biology offers greater promise of future progress than that the cell regarded as a whole is a colloidal system, and that what we call life is, in the words of Czapek, a complex of innumerable chemical reactions in the substance of this system. Modern investigation has indeed already profited so much by the point of view thus offered as to suggest that the study of protoplasm and the cell may be destined to pass more and more into the hands of the physiologist, the physicist and the chemist. In any case the rising tide of cell-research in these directions is of good augury for the future experimental analysis of vital phenomena. There are, however, other aspects of the problem which still escape the precise quantitative methods of the physicist and chemist, or are only beginning to come within their range, but none the less are essential to our view of the general problem. I refer to those phenomena with which the cytologist, the embryologist and the geneticist must try to deal; and it is especially to this side of the question that I here ask attention.

The cytologist is first of all struck by the extraordinary pains that nature seems to take to ensure the perpetuation and accurate distribution of the components of the system in cell-division, and hence in heredity. Nothing is more impressive than the demonstration of this offered by the nucleus of the cell; but its obvious meaning has often been disregarded or treated with a blind scepticism which pretends that no meaning exists. To our limited intelligence, it would seem a simple task to divide a nucleus into equal parts. The cell, manifestly, entertains a very different opinion. Nothing could be more unlike our expectation than the astonishing sight that is step by step unfolded to our view by the actual performance. The nucleus is cut in two in such a manner that every portion of its net-like inner structure is divided with exact equality between the two daughter-nuclei; and the cell performs this spectacular feat with an air of complete and intelligent assurance. The nuclear substance is spun out into long threads or chromosomes; these are divided lengthwise into exactly similar halves; they shorten, thicken, separate and pass to opposite poles; and from the two groups formed are built up two daughter-nuclei, while the cell-body divides between them. In outward appearance such a process seems to contradict all physical principles, but its meaning has now become perfectly plain. In a general way it means, as Roux pointed out forty years ago, that the nucleus is not composed of a single homogeneous substance, but is made up of different "qualities" or components; and it means that these components are strung out in linear alignment in the threads so that they may be divided and distributed in a particular manner through the longitudinal doubling of the threads.

This conclusion led the way in a series of investigations that have brought forth some of the most notable discoveries of our time. The direct cytological evidence of a serial alignment of smaller bodies along the nuclear threads has thus far indicated the fact in only a somewhat rough and ready fashion, showing hardly more than the fact that the nuclear threads may often be seen to contain smaller bodies or "chromomeres" aligned in a single series, and sometimes showing definite size-differences. It seems certain, however, that this visible structure is no more than the rough expression of a finer one that lies beyond the reach of the microscope; and fortunately genetic experiment has here come to the rescue with indirect evidence on a grand scale, derived from experiments on the mechanism of Mendelian heredity. This evidence was brought forward mainly by Morgan, Sturtevant, Bridges and their coworkers in their widely known studies on heredity in the fruit-fly *Drosophila*, an object which offers unparalleled opportunities for extended and accurate experiment owing to the readiness with which it can be bred under standardized conditions, the remarkable speed of its development, and its frequent production of heritable mutations. I regret the necessity that limits my reference to this remarkable work to a bare indication of its most general results. It has brought a final demonstration of the fact, established in a more general way by earlier observers, that the nuclear threads or chromosomes seen during cell-division play an essential part in the process of hereditary transmission. It has removed every doubt that the Mendelian phenomena may be fully explained by the behavior of the chromosomes or their components (as was first indicated in a more general way by Sutton, Boveri and DeVries).

It has brought overwhelming confirmation of the correctness of Roux's conception of the nuclear threads as linear aggregates of specifically different smaller entities of some sort, we know not what. For all this we had in some degree been prepared by earlier researches; but what now follows seems at first sight, I confess, completely incredible. The evidence drives us on to the conclusion that even the smallest details of heredity depend upon the behavior of infinitesimal units or "genes," far more minute than the chromomeres, strung out in linear series in the nuclear threads, each of its own specific kind and self-perpetuating by growth and division. It has made clear the fact that in the conjugation and disjunction of these bodies lies the ultimate explanation of Mendel's fundamental law. And, finally, in the midst of our struggles to assimilate all this, we are dealt a final blow with the remorseless demonstration that these units must be of definite number, separated by fairly definite and constant intervals, and *arranged in a definite and invariable serial order!* When we try to reckon with this series of demands, we find ourselves fairly gasping for breath. Such results are indeed staggering—to a certain type of mind even harder to believe than those which physicists are now asking us to accept concerning the structure of atoms. Nevertheless, *they are probably true!*

It is necessary to emphasize the fact that these conclusions did not arise in the fertile imagination of a Bonnet, a Buffon, or a Weismann. They are the product of concrete and extended experiments under carefully controlled conditions; they have made possible precise and quantitative prediction; and the data can be confirmed by laboratory experiment almost as readily as those with which the physicist or the chemist has to deal. In these respects they are comparable in validity with many of the concepts of physical science. It is possible, I suppose, to consider such conclusions as nothing more than a convenient fiction or algebraic symbolism, a kind of ideal model by means of which the genetic facts may conveniently be grouped. Those, however, who prefer to take their point of departure in the observed cytological facts will be more likely to make use of the actual model which every dividing cell displays to us in visible reality—a model that is not less impressive because at present the cytologist sees it only in broad outline with no more than dim indications of the finer complications inferred from the results of genetic research. And in point of fact it was this actual model from which came the first suggestions for the foregoing conceptions, and thus made possible some of the most important experimental researches on heredity in our time. Even if considered only as working instruments, therefore, these conceptions have a practical value almost comparable to that of the atomic theory as employed in chemistry and physics.

Cytology and genetics have thus combined to make real to us the existence of an organization of the nuclear region of the cell-system that is as complex and wonderful as any pictured by the fantasy of the speculative nature-philosophers. But we can not rest content with this demonstration. Inevitably we are led on—perhaps I should say led back—to the question whether an organization of similar type, or in any degree approaching to such a type, may also exist in the cytosome or extra-nuclear region of the cell-system. Conservative cytological opinion has been extremely reluctant even to recognize such a possibility. We have been too prone to take the cytoplasmic region of the cell-system, so to speak, at its face value; too ready to think of it as a vague and formless mass devoid of definite organization, or organized only by the domination of the nucleus. We have long been accustomed to think of the history of the cytosome as a simple mass division in fundamental contrast to the complicated meristic process seen in nuclear division. Facts are, however, slowly accumulating which may compel a revision of this notion. Recent cytological studies bring prominently into view the fact that many of the formed bodies are directly transmitted either as such or in the form of pre-existing specific material from mother-cell to daughter-cell.

Vague indications of such a conclusion were long since given by the plastids of plant-cells, which are certainly in many cases, perhaps in all cases, self-perpetuating by growth and division without loss of their identity, though their distribution to the daughter-cells during division often seems to be an irregular or quite incidental process. At a later period it was demonstrated that the centrioles or central bodies, which form the foci of mitotic cell-division, are often self-perpetuating by a similar process, but in this case are handed on in a perfectly definite manner from cell to cell during division. More recent cytological studies raise the question whether still other formed bodies may not show a similar behavior. This question has not yet been definitely answered, but evidence has been coming in which places under suspicion the chondriosomes and the Golgi-bodies. Both these are in many cases handed on during division from mother-cell to daughter-cell, sometimes segregating with a precision that almost suggests that seen in case of the chromosomes. In many cases the chondriosomes take their place in separate groups about the equator of the karyolinetic spindle, draw apart into corresponding equal daughter-groups, move towards the poles and enter the respective daughter-cells. Whether these bodies individually considered have a permanent identity and are self-perpetuating by division is still a disputed question. Undoubtedly they are sometimes actually cut in two during cell-division; and in one well-determined case (spermatocytes of the scorpion *Centrurus*) all the chondriosomes become aggregated into a single ring-shaped body that is accurately divided in the course of the ensuing division. Often, it is true, the chondriosomes seem to be passively sorted out or segregated into two approximately equal groups; but in all these cases the possibility remains open that they may multiply by division at an earlier period. Were such the case their history in division would be comparable to that often seen in case of the plastids of plant-cells; and in point of fact an important group of observers, headed by Meves and by Guilliermond, have concluded from direct cytological observations that plastids may arise by the transformation of chondriosomes. If this should prove to be correct, substantial ground would be given for the conclusion that the chondriosomes may multiply by division since the plastids undoubtedly have this power. Still less is known of the Golgi-bodies in this regard; but recent studies have clearly shown that these bodies, too, group themselves in a definite manner about the mitotic spindle during cell-division and separate into two distinct groups which pass into the two respective daughter-cells.

Doubtful or disputed points aside, it already seems clear that in a large class of cases the specific substances of which the chondriosomes and Golgi-bodies are respectively composed are not formed *de novo* in the daughter-cells, but are somehow directly derived from corresponding components of the mother-cell. It is now certain, further, that in some cases their segregation in the daughter-cells can not be regarded as a merely passive or mechanical result of mitosis but is determined by a more definite and significant relation between these bodies and the centers of division; for as has recently been demonstrated by Bowen the chondriosomes are sometimes definitely oriented with respect to the centers in a manner that almost suggests that which characterizes the behavior of the chromosomes. In all this we see surface indications of a more deeply-lying process by which the complex cytoplasmic system may perpetuate itself intact from one generation to another or, by a modification of this process, may split up into secondary more limited systems according to a definite and predetermined plan. This will become clearer when we take a broader survey of the origin of the cytoplasmic formed bodies in general, a problem which now opens before us with a new significance.

It is possible that some, perhaps many, of the visible formed bodies are transmitted from mother-cell to daughter-cell in the form of chondriosomes, possibly also of Golgi-bodies, which are later transformed into bodies of more differentiated types. An important group of observers have in fact advocated such a conclusion; but its validity still remains in doubt. On the other hand it is a widely prevalent view that many of the formed bodies arise *de novo*, being built up anew in the hyaloplasm by localized processes of chemical and morphological synthesis; but in respect to this question we may readily fall into error. Permit me to illustrate this by reference to some old observations of mine on those classical objects for the study of protoplasm, the transparent eggs of certain sea-urchins and starfishes.

When mature these eggs show with great beauty a structure somewhat like that of an emulsion, consisting of innumerable spheroidal bodies suspended in a clear continuous basis or hyaloplasm. These bodies are of two general orders of magnitude, namely, larger spheres or *macrosomes* rather closely crowded and fairly uniform in size, and much smaller *microsomes* irregularly scattered between the macrosomes, and among these are still smaller granules that graduate in size down to the limit of vision with any power we may employ. It is probable that both macrosomes and microsomes may be of several, perhaps many, different kinds; but this may here be disregarded.

The important fact here to be emphasized is that this so-called "alveolar" structure is not a primary characteristic of this protoplasm. It is of secondary origin, arising by the appearance in the homogeneous ground-substance of extremely minute scattered bodies which by growth and crowding together finally produce the emulsion-like structure. In the middle stages of this process the protoplasm gives an interesting picture. When viewed under a relatively low magnification, *e. g.*, 300-500 diameters, only the larger bodies are seen; but as step by step we increase the magnification, step by step we see smaller and smaller bodies coming into view, at every stage graduating down to the limit of vision. This remains true even with the highest available powers. The microscopical picture offered by such protoplasm is thus somewhat like the telescopic picture of the sky. At each step in the improvement of the telescope new and fainter stars have come into view. At each step the astronomer has felt sure that still more powerful telescopes would bring into view stars hitherto unseen. The cytologist is equally sure that if the present limits of direct microscopical vision could be extended we should see disperse bodies still more minute; and the invention of the ultra-microscope has in fact made us directly aware of the existence of suspended protoplasmic particles too small to be seen directly by the ordinary microscope, but made evident by their halos when viewed by the ultra-microscope in powerful reflected light.

In these eggs the smallest dispersed visible particles give us the impression that they are formed *de novo* in the structureless ground-substance. But manifestly it is illogical to affirm an origin *de novo* of any formed body because it first becomes visible at a particular enlargement, even the greatest at our present command. Here, clearly, is an enormous gap in our knowledge. All the available data—I can not here review them—indicate that below the horizon of our present high power microscopes there exists an invisible realm, peopled by a multitude of dispersed particles, a realm that is quite as complex as the visible one with which the cytologist is directly occupied. And the evidence further indicates, apart from all controversies concerning the nature of the so-called colloidal solutions, that many of these bodies are of much greater dimensions than the molecules of even the most complex organic substances.

We have now arrived at a borderland where the cytologist and the colloidal chemist are almost within hailing distance of each other —a region, it must be added, where both are treading on dangerous ground. Some of our friends seem disposed to think that the cytologist should here call a halt and hand over his inquiry to the chemist and the physicist with a farewell greeting. The cytologist views the matter somewhat differently. Unless he is afflicted with total paralysis of his cerebral protoplasm he can not stop at the artificial boundary set by the existing limit of microscopical vision. He is rudely pushed forward by the impact of a series of stubborn facts with which he must somehow try to reckon. He can not get out of his head that microscopical picture of progressively diminishing magnitudes which, as if viewed through an inverted telescope, disappear at last in vanishing perspective in the sub-microscopical depths. At the nearer end of this vista are the plastids, larger or smaller, each of its own specific type, and self-perpetuating by growth and division. A step beyond are the central bodies, often of such minuteness as to lie almost on the horizon of microscopical vision, but still capable of self-perpetuation by growth and division, of enlargement to form much larger bodies, and of exerting far-reaching effects on the surrounding structures. One more step and the cytologist is beyond the help of the microscope, wandering blindly in an unseen but none the less real world. The pathologists tantalize him with visions of disease-germs which no eye has yet seen, so minute as to pass through a fine filter, yet beyond a doubt self-perpetuating and of specific type. The geneticists continually crowd upon him with fresh demonstrations of those unseen somethings aligned in orderly array in the nuclear threads, each preserving its own specific type amid all the shifting events of the nuclear life, without modification by its fellows, and somehow, generation after generation handing on its individual characteristics to its descendants.

With all this in mind the cytologist finds reason enough to exercise his wits upon the apparently structureless ground-substance or hyaloplasm that seems to constitute the fundamental basis of protoplasm and to be the source of many of its formed elements. He can not resist the evidence that the appearance of a simple, homogeneous colloidal substance offered by the hyaloplasm is deceptive; that it is in reality a complex, heterogeneous or polyphasic system. He finds it difficult to escape the conclusion, therefore, that the visible and the invisible components of the protoplasmic system differ only in their size and degree of dispersion; that they belong to a single, continuous series, and that the visible structure of protoplasm may give us something like a rough magnified picture of the invisible. The cytologist is led still further to the conclusion that the ultra-microscopical dispersed particles of the hyaloplasm may be as highly diversified chemically as are the visible formed bodies, and that they are of all orders of magnitude; further, that it is they which constitute the sources, or at least the formative foci, of those larger formed bodies that we have so often but erroneously assumed to arise *de novo*. For my part, I am disposed to accept the probability that many of these particles, as if they were submicroscopical plastids, may have a persistent identity, perpetuating themselves by growth and multiplication without loss of their specific individual type. And lastly, there are many facts made known especially by experimental embryology, which indicate that it is in the apparently structureless hyaloplasm that the real problem of the cytoplasmic organization lies; and the same facts drive us to the conclusion that the submicroscopical components of the hyaloplasm are segregated and distributed according to an ordered system.

I am tempted to a larger development of this subject with reference to the problem of development, but time forbids. Good biological society has of late looked decidedly askance upon all corpuscular or micromeristic conceptions of the cell. To consider them seriously at this day requires a certain amount of courage. By some singular process of casuistry such conceptions have been supposed to place the fundamental problems of biology beyond the reach of scientific investigation. An ingenious philosopher has said that corpuscular hypotheses in general would make of the world—or of the cell—a mere puzzle-picture which we cut up into small pieces only to put them together again to form the same picture. The reply to this gibe, evidently, is the pragmatic one. Modern physical science has cut the whole world up into very small pieces and has thus far seemed to manage fairly well with the pictures rebuilt from them. The fathers of the cell-theory engaged in a somewhat similar operation when they resolved the living body into its component cells. Some of the successors of these pioneers, even down to our own day, have seemed to find something very reprehensible in this conduct; nevertheless, the cell-theory has somehow managed to survive as an effective means of biological progress. Perhaps, therefore, the youthful sciences of cytology and genetics may hope for lenient treatment if they try to go somewhat further along the path marked out by their forefathers. Many earlier hypotheses of this type failed by reason of their too speculative character and because too much was claimed for them, either by their authors or by critics who wished to destroy them. Such was the case, for instance, with Weismann's speculations on the architecture of the germ-plasm, of DeVries on intracellular pangenesis, and of Altmann concerning the general significance of the protoplasmic granules. But we are not here concerned with merely theoretical constructions but with questions of fact that are directly and insistently forced on our attention by concrete microscopical and experimental studies on the cell. It is our business as students of cytology and genetics to answer these questions if we can. And lastly, I would remark that I am not here attempting to resuscitate the old conception of the cell as an assemblage or colony of elementary organisms or primary vital units —perhaps it is such, perhaps not—nor am I able to see how the possibilities here considered are in any manner out of harmony with the conception of the cell as a colloidal system.

We approach the final stage of our inquiry. We have, as it were (to return to Bergson's metaphor), taken the cell to pieces. How shall we put it together again? It is here that we first fairly face the real problem of the physical basis of life; and here lies the unsolved riddle. We try to disguise our ignorance concerning this problem with learned phrases. We are forever conjuring with the word "organization" as a name for the integrating and unifying principle in the vital processes; but which one of us is really able to translate this word into intelligible language? We say pedantically—and no doubt correctly—that the orderly operation of the cell results from a dynamic equilibrium in a polyphasic colloidal system. In our mechanistic treatment of the problem we commonly assume this operation to be somehow traceable to an original pattern or configuration of material particles in the system, as is the case with a machine. Most certainly conceptions of this type have given us an indispensable working method—it is the method which almost alone is responsible for the progress of modern biology—but the plain fact remains that there are still some of the most striking phenomena of life of which it has thus far failed to give us more than the most rudimentary understanding.

The nebulous state in which the whole concept of organization still remains is brought home to us when we attempt to deal with the fact that every organism either is, or at some time has been, a single cell. When it has come to full development the organism consists of coordinated parts, displaying a multitude of cunning devices—anatomical, physiological or chemical—that make provision for the harmonious cooperation of its activities and for its protection and maintenance. To this extent its organization is obvious and intelligible; and to the same extent the organism is clearly a piece of mechanism, a living machine. But let us review the building of this machine by following it backwards, step by step, to its starting point. Step by step we find the intricate machinery of life vanishing before our eyes until nothing remains but a single cell, the egg. In the egg-cell, complex though it may be in its own way, not a trace seems to remain of the coordinating and unifying devices of the adult; but who will maintain that the egg is not as specifically organized and as truly alive as the adult to which it gives rise?

It is an old notion to which modern research has given a certain semblance of support that the embryo is already present in the egg, blocked out, as it were, "in the rough" in the cytoplasm, so that development has only to impress upon it the finishing touches; but there is now conclusive evidence that the rough model, with the more than doubtful exception of one or two of its most general features, is itself the product of antecedent localizing operations of development. The main features of this process, often perfectly evident before the egg begins its cleavage into cells, may in some cases readily be followed by the eye. It is an impressive spectacle that is offered by the egg when busily engaged at its work of blocking out the embryo, without visible tools or model, but with an uncanny air of deliberate purpose and mastery of technique that any human artist might envy.

What then constitutes the organization of the egg? No one is yet able to answer. The embryologist, the cytologist, the physiologist and the biochemist—all of these alike have thus far only skirted the outermost rim of the problem. We can not predict how far the cytologist of the future may be able to penetrate within it; but it would seem that sooner or later his way will finally be blocked by inherent limitations of the microscope determined by the wave-length of light. If we are ever to find our way into the innermost arcanum of the cell other methods must be employed; and we must marshal all the resources of experimental embryology, genetics, biophysics and biochemistry. Experimental embryology has contributed many important discoveries towards elucidating the phenomena of development, but it has also emphasized our failure thus far to solve the central problem. From this source, indeed, came the facts on which Driesch, a distinguished pioneer in this field, based his famous argument against the machine-theory of development and in favor of a new philosophy of vitalism. The rock on which the whole mechanistic conception of organization and development splits, he insisted, is the fact that a *fragment* of an egg may undergo complete development and produce a perfect dwarf embryo. This argument may fail to convince us—it does fail—but no one has yet found an adequate reply to it. All, on the contrary, now points to the essential correctness of Driesch's contention that at the real beginning of development the cytoplasm of the egg is devoid of any structural pattern or machine-like configuration that foreshadows the plan of the future embryo. Not alone the structural details of the embryo but the very plan on which it is built is constructed anew in the course of development.

May we then seek a solution of the puzzle in the nucleus of the egg? Perhaps. It is no longer open to doubt that the development of particular characters somehow depends upon the presence in the nucleus of corresponding particular and separate units; and this conclusion loses nothing of its force by reason of the fact that the precise nature of the units is still unknown. We know from Boveri's celebrated experiments that normal development depends on the normal combination of these units. Genetic evidence is now opening far-reaching horizons of future discovery by the accumulating demonstration that no one of the nuclear units plays an exclusive rôle in the determination of any single character. It has been made clear that the individual unit may affect the production not merely of one character but of many. Conversely the probability is shaping itself that the production of any single character requires the cooperation of several or many units, possibly of all. I believe it is not a great overstatement when I say that every unit may affect the whole organism, and that all the units may affect each character. We begin to see more clearly that the whole cell-system may be involved in the production of every character. How then are hereditary traits woven together in a typical order of space and time? It is the same old puzzle made larger and more insistent but not yet, so far as I can see, brought nearer to its solution. We are ready with the time-honored replies: It is the "organism as a whole"; it is a "property of the system as such"; it is "organization." These words, like those of Goldsmith's country parson, are "of learned length and thundering sound." Once more, in the plain speech of everyday life, their meaning is: *We do not know.*

I do not in the least mean by this that our faith in mechanistic methods and conceptions is shaken. It is by following precisely these methods and conceptions that observation and experiment are every day enlarging our knowledge of colloidal systems, lifeless and living. Who will set a limit to their future progress? But I am not speaking of to-morrow but of to-day; and the mechanist should not deceive himself in regard to the magnitude of the task that still lies before him. Perhaps, indeed, a day may come (and here I use the words of Professor Troland) when we may be able "to show how in accordance with recognized principles of physics a complex of specific, autocatalytic, colloidal particles in the germ-cell can engineer the construction of a vertebrate organism"; but assuredly that day is not yet within sight of our most powerful telescopes. Shall we then join hands with the neo-vitalists in referring the unifying and regulatory principle to the operation of an unknown power, a directive force, an archæus, an entelechy or a soul? Yes, if we are ready to abandon the problem and have done with it once for all. No, a thousand times, if we hope really to advance our understanding of the living organism. To say *ignoramus* does not mean that we must also say *ignorabimus.* I do not believe that a confession of ignorance leaves us with no recourse save vitalism. To maintain that observation and experiment will not bring nearer to a solution of the puzzle would be to lapse into the dark ages. Perhaps Professor Henderson is right when he expresses his belief that organization has finally become a category that stands beside those of matter and of energy. Perhaps there is no problem or none that we can formulate without talking nonsense. Perhaps we should go no further than to record and analyze the existing order of phenomena in living systems without losing sleep over the imaginary problem of a unifying principle. Let us politely salute all these uncomfortable possibilities and go our way. For my part, I find it more amusing to look forward to a day when the great riddle may give up its secret.

EDMUND B. WILSON

DARWIN AND PASTEUR: AN ESSAY IN COMPARATIVE BIOGRAPHY[1]

PLUTARCH's "Parallel Lives," although read and admired throughout the ages, have found remarkably few imitators. Why this is so would be an interesting question. Perhaps the rise of Christianity, with quintessence of altruism and an instinctive recognition that comparisons, if not necessarily odious, are often unkind, has something to do with it. Perhaps the spirit embodied in that most charitable of pagan maxims—*de mortuis nil nisi bonum*—has also played its part. The modern neglect of Plutarch's method is the more remarkable because it is the basic method of modern science, and the tap root of modern thinking and working. Science owes an immense and growing debt to comparative anatomy, comparative geology, comparative physiology, and comparative pathology. More lately it has produced also the rich fruits of comparative philology, comparative philosophy, comparative politics, comparative psychology, comparative religion and comparative literature. Why not, then, back to Plutarch and the potential field of comparative biography?

Ruminating thus in the blessed quiet hours of a professorial holiday, and braced by the cool airs of an Alpine valley, I could not resist the temptation to revive Plutarch's method by a comparison of the two great master minds of the Victorian era whose labors have thrown upon the mysteries of the living world a clear and penetrating light, a blaze which time may dim but can never extinguish.

Charles Robert Darwin wrought upon the mind of his time a complete change in the point of view concerning the origin, the nature and the relationships of mankind and other living things. Louis Pasteur disclosed to the astonished gaze of the nineteenth century a new world of microscopic life dwelling upon us, within us, and about us, working sometimes for good and sometimes for evil. Darwin was a silent Savonarola, Pasteur a sedentary Columbus of Biology. Such masters invite study and comparison.

To Charles Darwin and Louis Pasteur belongs the rare distinction of having changed completely the point of view of their own and probably later generations.

Nothing had been more interesting or more puzzling throughout the ages than the origin and relationships of the various kinds or species of plants and animals. Dogs, cats and sheep; oaks, elms and willows—how did they come to be so alike, and yet so different? The ancients had their theories, but these were set aside or forgotten in the Christian world when the biblical account of creation came to be literally accepted. That account, like many that had preceded it, affirmed a strictly supernatural origin for plants and animals, and so overcame all difficulties. But by the middle of the nineteenth century the world was growing impatient of supernaturalism, especially in the exaggerated form this had taken on in the Middle Ages, and was ready for a change, so that when Darwin published his great work on the "Origin of Species" in 1859 it was com-

[1] The accompanying essay was left uncompleted by the late William Thompson Sedgwick of the Massachusetts Institute of Technology, when he died, as we all wish to, quickly and before his work was finished. Such an essay may be not only especially timely in this Pasteur anniversary, but may also be useful at a time when men of faith are attacked by men of ignorance and credulity.—G. J. P.