PHYSIOLOGY

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New York
THE COLUMBIA UNIVERSITY PRESS
1908

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A LECTURE DELIVERED AT COLUMBIA UNIVERSITY
IN THE SERIES ON SCIENCE, PHILOSOPHY AND ART
NOVEMBER 27, 1907

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Set up, and published February, 1908.

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In the introductory lecture of the present course we were told that ours is the golden age of mathematics. As week after week has passed by since then, we have been led from one golden age to another, convinced, for the time, that the present brilliant achievements of each science outshine those of all the others. A few days ago I found on my desk an entomological monograph, the opening sentence of which reads, "The present age is the age of insects." I shall not attempt to harmonize the declarations of my Columbia colleagues with that of my entomological friend. But I feel that I would be derelict in my devotion to my own subject, if I did not state frankly at the outset of my lecture—what ought, however, to be a self-evident truth—that the present is preëminently the age of physiology. Nor, following again the example of my predecessors, need I be over-modest in my claims as to the place of physiology in the scientific hierarchy. For Fick speaks of it as "the highest and most fruitful generalization of the collective natural sciences," and Czermak calls it "the summit of all the sciences."

It need not be emphasized that no exact boundary line exists for any one of the biological sciences. The proper domain of each extends, at its borders, imperceptibly into the domains of all, and within the boundary zones it is difficult to say what belongs to one and what to another. With this in mind it is impossible sharply to delimit the science of physiology. Nevertheless its proper domain is easily surveyed. Physiology deals with the process of life, the living of living substance. It is a dynamic, not a static science. The form, structure and composition of living things do not properly come within its scope: they form the subject matter of morphological, static sciences. But the changes in form, structure and composition, which are manifestations of the life process, are proper subjects of physiological study. Its material exists wherever life exists. Whether it be the growth of a man or of a tree, the creeping of an amœba or the contraction of a muscle, the beating of a heart or the production of a disease by a bacterium, the mental activity of a brain or the response of an infusorian to light, the process of reproduction or of inheritance, the phenomena of nutrition or the behavior of an organism to changes in its environment—all of these and a thousand others are physiological phenomena and proper subjects of investigation in the physiological laboratory. It is true that many departments of learning, which essentially are branches of physiological science, have been so far specialized in the methods of their pursuit and their aims and augmented by non-physiological additions, as to entitle them to specific names. In such cases it often is not expedient for physiology to busy itself with the more remote results of the operations of its laws. The great biologist of the last century, Johannes Müller, was wont to say, "*Psychologus nemo nisi physiologus.*" But, although psychic phenomena are inextricably linked with neural processes, the right of psychology to be recognized as an entity, with the study of psychic phenomena as its prerogative, has been abundantly demonstrated by its achievements. So, too, the proceedings of human society are the resultants of the action in human beings of physiological principles. But the study of the resultants themselves falls within the special province of the sociologist. It is thus customary to recognize as largely independent sciences, such branches of knowledge as psychology, sociology, neurology, biological chemistry, experimental zoology, hygiene, bacteriology, pathology, and preventive medicine; but in all these there is a large element of pure physiology, and their adherents often deserve the name of physiologists. When I say that the present is preëminently the age of physiology I mean it seriously, since at no time has the physiological spirit, the spirit of examining vital phenomena by the aid of experimentation, so completely permeated and vitalized the biological sciences as now.

There exist many misconceptions regarding the subject matter and scope of physiology. In the popular mind physiology deals with the life processes of the human body. In reality human physiology is but one of its many interests. It has its anthropocentric aspect. Biocentric it is in reality. The popular conception of physiology as a science of the functions of gross anatomical organs expresses, too, but a small part of the truth. During the middle part of the last century a powerful school of investigators in Germany busied themselves largely with the functions of organs, and strongly impressed the science of their time and the popular mind. But one of the pronounced phases of physiological development in recent years has been a similar rich growth of the study of the life processes of the cell. Another popular misconception is that physiology deals only with the internal parts of organisms—a view that is confuted by the fact that there is now going on much investigation of the mutual relations of organisms and their environment, in other words, an expansion of what has been called external physiology, which might bear the newer title of œcology. But the widespread ignorance regarding the broad scope of physiology is in part explained by the fact that a large number of professed physiologists do busy themselves with, and most academic courses deal largely with, the vital phenomena of the internal parts of higher animals with the image of man ever in the background. The chief cause of this condition in turn is doubtless the rise of the science within medical schools and its continued close association with them, as a result of which the attention of investigators and teachers has been necessarily focused largely upon internal problems. This aspect of the science is mirrored in the text books, and is the chief aspect that is presented to the youth in his early studies. Unfortunately the university student has only a limited opportunity to correct his early false impressions, for the university has not yet accorded to physiology its rightful heritage as a pure science. Its freedom in research cannot be denied it, however, and popular misconceptions regarding its scope will disappear with its advance. The living of the living thing is the criterion by which the physiological phenomenon may be recognized.

The ways in which the vital process manifests itself seem at first sight numberless and incapable of mutual comparison. The contraction of a muscle, the secretion of a glandular product, the production of a sensation, the growth of an organism, the orientation of a motile body to rays of light, the passage of a nervous impulse, respiration, the circulation of blood, the transmission of a quality from parent to offspring, instinct, fatigue, a volitional act, the course of a germ disease, sleep, speech, laughter, thought, the digestion of food, the maintenance of bodily temperature, the hearing of sound, sight, the recognition by touch of a familiar object, memory, emotions, the inhibition of an existing action, hypnosis,—at first thought these phenomena appear to be of quite different kinds, each *sui generis* and incapable of comparison with the others. Have they common factors? Is it possible to unify them?

Through the ages various attempts have been made to do this. The appearance of the first of these attempts was nearly coincident with the culmination of Grecian culture. From that auspicious time down to the great Roman physician Galen, then across the long stretch of thirteen centuries, bridged by Galenic tradition, but barren of physiological discovery, to the rebirth of scientific, together with other, learning, and well into the seventeenth century, the doctrine of the *pneuma,* or spirits, reigned supreme. This doctrine was often expressed in vague, uncertain terms, and in the hands of the Stoic philosophers, the Pneumatic physicians, the scientific men of Alexandria, Galen and minor writers, it was variously portrayed. The *pneuma* was believed to be an extremely subtile material agent entering the body with the breath, and was spoken of as "very subtle air," "very lively and pure flame," "fluid," "of the nature of light," "vapor," "something analogous to the spirits of wine," and so on. Each vital action was a manifestation of its activity. In the heart dwelt the vital spirits; in the brain the animal spirits. They flowed and ebbed through the veins and arteries, they coursed along the nerves, they permeated the tissues, and they bubbled and effervesced. Through them the body felt and moved, was nourished and warmed, grew and reproduced. It was a genial, comforting belief, nothing was more plausible; in its light vital actions seemed simple enough; and so for two thousand years the spirits danced merrily along.

But there were hard-headed thinkers in the seventeenth century. We may even imagine that the skilful experimenter, Harvey, the discoverer of the circulation of the blood, had his doubts. It is true that Descartes made free use of the spirits in his clever portrayal of the working of the organic machine, but there were others, believers in the machine, who contended that its *Deus* was not the *pneuma*. The spirit of mechanism was in the air. With the beginning of a rational physics, stimulated largely by the discoveries of Galileo and Newton, and a rational chemistry, freed from alchemy, there arose those two curious groups of utopian theorizers, the iatro-physicists and the iatro-chemists, led respectively by Borelli and Sylvius. The one looked at the actions of the living being through the spectacles of the physicist, the other through those of the chemist; to the one vital actions were physical phenomena, to the other, chemical phenomena. Their gaze was in the right direction, and each believed that he saw a great light. But like the whole world of science of their time, they knew too little of the true physics and chemistry, and their interpretations of organic processes, while containing a considerable modicum of the truth, teemed with unwarranted hypothesis. It was not strange, therefore, that the iatro-movement was short-lived. Its influence, however, was not without value, for as the knowledge of physiological fact increased through experiment, and the world became accustomed to mechanical notions, the authority of the spirits became weakened, and gradually, very gradually, they ceased to be a factor in physiological reasoning. In popular speech, however, they persist even to our own day; for, as our moods change, we are in good spirits or bad spirits, full of spirit or lacking in spirit, high-spirited or low-spirited—phrases which stand as witnesses of a once powerful, but now discarded physiological doctrine.

As the spirits became deposed, scientific thinkers, dissatisfied with the mechanism of the time, still groped for something to take their place. There were spontaneous uprisings of such agencies as Van Helmont's *archeus*, Stahl's *anima*, Boerhaave's *principium nervosum*, and

Hoffmann's ether. None of these long survived, and soon after the middle of the eighteenth century they were definitely replaced and the widespread desire for a unifying principle was for the time set at rest, by the hypothesis of vital force. All physiologists had now come to realize that many of the chemical and physical phenomena of inorganic nature were to be observed also in living bodies. But they knew that the chemical composition of the latter differed from that of the former, and for the manufacture of the vital substance and for many of its actions they could find no parallel outside of living bodies. Most of them succumbed to the compelling power of their ignorance and acquiesced in the assumption that a peculiar principle resides in living things, a vital force (or energy, as we would call it to-day), differing in nature from the forces (or forms of energy) that exist in non-living things. Johannes Müller presented the vitalistic conception clearly as follows: "Organic bodies consist of matters which present a peculiar combination of their component elements, a combination of three, four, or more to form one compound, which is observed only in organic bodies, and in them only during life. Organized bodies, moreover, are constituted of organs, * * * each * * having a separate function; * * * and they not merely consist of these organs, but by virtue of an innate power, they form them within themselves. Life, therefore, is not simply the result of the harmony and reciprocal action of these parts; but is first manifested in a principle or imponderable matter, which is in action in the substance of the germ, enters into the composition of the matter of the germ, and imparts to organic combinations properties which cease at death." By the same author life is characterized as "the manifestation of the organic or vital force." Again, "Organic bodies participate in the general properties of ponderable matter. The laws of mechanics, statics, and hydraulics, are also applicable to them." The application of these laws to them is, however, "limited, from the circumstance that the causes of motion most engaged in them are essentially vital in their nature." A few bold spirits, like Reil in Germany and Magendie in France, argued against such a conception, but they formed a small minority, and the physiology of the time became essentially vitalistic.

This state of affairs prevailed for barely a century. Soon after its beginning oxygen was discovered, and the modern chemistry was begun. A few decades more and the new physics was founded on the doctrine of the conservation of energy. These two discoveries with their momentous consequences were epoch-making for physiology. The events of the inorganic world were at last conceived by the human mind in a rational manner, and the application of such conceptions to vital processes was not delayed. The assumption of a specific vital force was seen to be unnecessary. Men began to talk of vital phenomena in terms of the new sciences, and physiology began to be defined as the science of the physics and chemistry of living things. Such is the prevailing conception to-day.

Is the vital process more than physics and chemistry? Two facts stand out strongly in the physiology of the present day. One is the constant extension of physico-chemical principles into the explanations of hitherto mysterious functions; the other the seeming inadequacy of those principles to explain other functions. In their attitude toward this apparent inadequacy physiologists, while disavowing with almost entire unanimity their belief in the vital force of a century ago, may be said to be collected at present into two camps. By far the majority, while not denying the existence of puzzling problems, are yet possessed of an optimistic spirit and look forward with serenity to the unraveling of the mysteries of the organism, as the mysteries of the inorganic become more clear. They look at life, not as a distinct entity permeating and vitalizing a complex machine, but rather as the sum of the activities of that machine. In the opposite camp there are a few souls who, though they too have cast off the dross of the old conception, are rendered impatient and despondent by the occasional failure of present knowledge to explain, and they fly for refuge to a refined and essentially inexplicable vital residuum. They have succumbed to the inevitable reaction that follows rapid progress. But they are not vitalists, they say, at least not palæo-vitalists: they are neo-vitalists. Into the intricacies of neo-vitalistic views and into the shades of difference existing between them it is not opportune here to go, for they exert practically no influence on the physiology of the time. The hopeful investigator continues his endeavors, and with success, to interpret vital processes in accordance with physico-chemical laws. It seems to me that this is the most promising method. For less than one hundred years has it avowedly been in vogue, and these have been the years of most rapid advance. In this time many mysteries seemingly inexplicable have been clarified. It is futile to deny future rapid progress along the same lines, and the solving of problems that now defy the ingenuity of the experimenter. We confess our ignorance and our frequent failures, but we believe that we are on the right track. Physics and chemistry are not completed sciences. Their youth indeed is hardly passed. Their greatest achievements are probably yet to come. If what we know of physical mechanism to-day is not sufficient to insure us an understanding of the physiological machine, then let us look to what we shall learn to-morrow. Whatever the ultimate outcome, the solace of the vitalistic conception, it seems to me, should be resisted until we are prepared with full knowledge to maintain the final inefficacy of the physico-chemical mode of interpretation. If such a time ever arrives, it must necessarily be far in the future.

If the vital process be capable of a physico-chemical interpretation, it is at once understood that the methods of the physiologist must be the methods of physics and chemistry. And this is the case. In the physiological laboratory we employ the same methods that are used in the physical and the chemical laboratories, modified only in so far as is necessary to adapt them to the material employed for study and the specific problems to be solved. Specific physiological apparatus of precision in great variety has been devised, and specific methods of using it. But the apparatus and methods are physical and chemical in essence. The physiologist's material for study must necessarily be living material, except in so far as it is possible to deduce the vital phenomenon from the phenomena of non-vital substances—a procedure which, though often necessary, as is especially the case in much of the work of the chemical physiologist, is a procedure of limited value. In external and in much of internal physiology the living organism is used intact. With many problems of internal physiology, however, the method of vivisection must be employed—a method, which, notwithstanding the occasional charges of the uninformed, does not in either its theory or its practice imply cruelty or inhumanity.

Physiology has long since passed the stage where unaided observation alone is of value, and has become preeminently an experimental science. It is the task of the experimenter to alter one or more of the conditions under which the phenomenon occurs, to observe its change, if such appears, and thus to throw light upon the nature of the phenomenon itself, its relation to both its original and its changed conditions, and its causes. Herein lies the enormous difficulty of physiological work. The vital process is of a complexity unapproached, much less equaled, in the inorganic world. Living substance is never exactly the same at two successive periods. It is ever in unstable equilibrium, the seat of constant change, of augmentations and depressions, of physical and chemical mutations, and of what we in our ignorance call spontaneous activities; and the conditions of its activities are manifold and often obscure and unsuspected. To maintain the majority of these conditions intact, while altering one or more, is a superhuman task, one that is approached, but probably never realized in its entirety. The physiologist is thus constantly baffled in his pursuit of the desired object, and must needs exercise unwonted patience in the face of not infrequent failure. His progress is slow and his results can only approximate the mathematical exactness of the experimenter who deals with stable non-living matter.

Since the time when physiology assumed its physico-chemical aspect and entered upon its modern phase, what has been the trend of its research? Its energies were first directed chiefly to the study of the mechanical and other physical problems of the organs of vertebrate animals. The electrical method of stimulating living substance was devised, by which the latter can be made to act at the will of the experimenter,—a method the importance of which can scarcely be overestimated. The graphic method was early introduced and has been developed to the greatest refinement. By its use organic movements can be recorded graphically, and can then be easily analyzed into their space and time components and be studied at leisure. The working of the organs of the mammalian body, considered as physical machines, is now fairly well understood, although specific problems within this field are still being actively investigated. Very exact computations have been made of the amount of energy given off by the body in the form of heat and of muscular work, and it has been found to correspond very closely with the income of energy derived from the food and whatever bodily material may be consumed during the experiment. The principle of the conservation of energy applies as well to the living as to the non-living machine.

Chemical physiology, or, as it is now often called, biochemistry, developed gradually during the last century but did not become prominent until the last decade. It occupies now a foremost place among the branches of biological science. Much biochemical work is morphological; the determination of the chemical constituents and structure of substance once living, from which inferences may be drawn as to the chemical nature of living substance. Unfortunately living substance cannot be chemically analyzed directly, since all known methods at once kill it, and there is left only the non-living proteins, carbohydrates, fats, and other organic and inorganic compounds, the individual bricks, or, better, cleavage products of the complex unity. In determining these and their relationships great progress has been made, but we of the present are far removed from that state of smug satisfaction of some of the earlier investigators, to whom a living body represented only so many molecules of carbon, oxygen, nitrogen, hydrogen, sulphur and phosphorus. The problems of the chemical physiologist, as distinguished from the chemical morphologist, are in general the problems of metabolism,—which the Germans have aptly styled *"Stoffwechsel,"*—the chemical changes undergone by matter in the process of living, its building up and its breaking down, its anabolism and its katabolism. The intricacies of metabolism can scarcely be conceived by one not familiar with the attempts to follow them, and the biochemists deserve much credit for the ingenuity of their methods. They have been most successful in determining and isolating the multitudinous katabolic products of vital activity, both the intermediate and the final products, and in discovering clues to the individual steps in the katabolic process. They have even succeeded in making synthetically many of these vital products, an achievement which was inaugurated by Wöhler in 1828 in the manufacture of urea. The laboratory synthesis of vital products has become, indeed, almost a daily occurrence and has hence lost its former miraculous appearance. It is not, however, certain that the laboratory methods and the physiological methods employed in such synthesis are identical. The steps of the anabolic process are still obscure, and until they are better known, we can hardly look forward with confident satisfaction to the artificial manufacture of living substance. Yet physiological alchemists do exist, and the successful making of "life" has been heralded more than once to a sensation-loving world. Such an achievement is for the present only an idle dream, serving to gently and pleasurably titillate the cerebral cells of the dreamers.

Of recent years physiological physics and physiological chemistry have come to meet on common ground within the realm of the new science of physical chemistry. It has come to be clearly recognized that living substance consists of organic colloidal, or jelly-like, material, permeated by inorganic matter. The colloidal matter seems to consist of enormous complex molecules and aggregates of molecules; the inorganic matter partly of smaller, simpler molecules, and partly of ions, which are atoms or groups of atoms charged electrically. As the life process goes on, the living substance being now in a state of activity, now in a state of rest, there is a constant chemical and physical interplay between the two material constituents, and a constant interchange between them and the surrounding medium, in which the laws of osmosis play a prominent part. The careful investigation of the nature of these internal and external exchanges seems to be illuminating many time-honored physiological enigmas, such as absorption, secretion, excretion, and other instances of the passage of substances through membranes, the electrical phenomena of tissues, the nature of the nerve impulse, the fertilization of the ovum and the general nature of chemical changes within protoplasm—enigmas which have been constantly quoted in support of the vitalistic conception. But we should not be tempted by success along these lines to claim, as is sometimes done, that the life process is merely ionic or electrical or osmotic in nature. In investigating physiological problems by the aid of modern physical chemistry, we seem to be brought at times perilously near the electron theory of matter, and we are tempted to hazard the guess that the establishment of that theory would place the physiologist under renewed obligations to the physicist.

The study of ferments, too, is assisting—strange, innumerable, intangible bodies of uncertain nature, which, present in minute, almost imperceptible quantities, seem to facilitate vital chemical actions without entering directly into them. In the early years ferments were recognized as mediating the processes of digestion, and but few of them were known. Of late their number has been enormously increased, and a corresponding number of intracellular or extracellular chemical processes has been ascribed to their action. Each has its own specific chemical reaction to facilitate, and in many cases, at least, their action is reversible, *i.e.* one and the same ferment can aid both the decomposition of a complex substance into its constituents and the synthesis of those constituents into the complex substance. The ferments that function in vital processes are products of living matter, but recent research makes it increasingly clear that they act merely like catalytic agents of inorganic origin. The study of ferments has its dangerous aspect, for more than one investigator, with an eye single to their universality and efficacy, has in his cyclopean enthusiasm come to suspect that all the chemical processes of living organisms are mediated by them, and has even been led to make the narrow and unwarranted assertion that life itself is merely ferment action.

The discovery of protoplasm and the establishment of the cell theory have exercised a profound influence on the science of function. Until nearly the middle of the last century physiologists were in a sense groping in the dark, for the reason that although they were endeavoring to unravel the mystery of living substance, they had no conception of the real nature of that substance. When the times were ripe they were quick to recognize the value and significance of the new discoveries, and, indeed, played valuable parts in formulating and establishing the new doctrines. With the clear recognition of a definite substance as the physical basis of life, their energies were more definitely directed than before. One result of this has been the increasing and powerful growth, during the latter part of the last century and the early years of this, of general physiology. The rise of general physiology represents a movement away from the earlier study of the mechanics of organs, toward that of the vital phenomena of living substance itself, irrespective of its special position within the organism. General physiology is preeminently the physiology of to-day, whether its point of view and methods be physical or chemical.

The principle of organic evolution is in its essence a physiological principle. It represents a great physiological experiment which nature has been making since the beginning of living things, and is continuing to make. But the discovery of the facts and principles of organic evolution and the establishment of its theory have been accomplished only in small part by professed physiologists. Not even has the evolution of function—a field of great possibilities—been explored, except in a few small and isolated spots. The necessity of properly controlled experimentation in settling the vexed problems of evolution is, however, at last being recognized, and the next few decades promise to witness great advances in the discovery of the ways in which nature has made her great experiment.

It is not strange that with its intricacies and peculiar difficulties the solving of the problems of nervous function has proceeded slowly. The facts that nervous function is a property of the nerves, and that the brain is the seat of the mind, were probably first capable of scientific proof by the Alexandrians in the fourth century before Christ. The two great functions of sensation and motion were also recognized by the ancients, but that they were mediated by different nerves was first demonstrated by Sir Charles Bell, so late as 1811. The idea of the specific energy of nerves,—a phrase which means specific activity, —or the general principle that each nerve has specific functions with which it always responds, no matter how stimulated, was definitely proposed by Johannes Müller in 1826 for the nerves of special sense, and later was generalized for other nerves and other tissues. Since then great progress has been made in discovering by experiment the specific functions of individual nerves and in formulating therefrom theories of the general functions of nervous tissues. That different nervous activities are associated with different portions of the brain was early surmised, and before the middle of the past century such important nervous centers as those controlling respiration and the beat of the heart became located. Since then the nervous mechanism of a host of unconscious organic processes has been discovered. That the psychic portion of the brain does not function as a unit, but consists rather of a complex group of nervous organs, each with its specific functions—a fact that is of great moment in elucidating the relations of brain and mind—has been known for only a little more than thirty-five years. For it was in 1871 that Fritsch and Hitzig, by stimulating specific small areas of the surface of the cerebrum and obtaining in response specific muscular movements, first demonstrated a specific cerebral localization of functions. Since then the task of mapping out the outer layer, or cortex, of the cerebrum of a few mammals and man into centers, joined by nerve fibers with specific organs of the body and employed for the control of separate groups of muscles and for the work of the special senses, has proceeded to a considerable degree. Thus, we are now able to point to a certain portion of one of the convolutions of the cerebrum and say that its nerve-cells, or neurones, mediate the volitional act of contracting one's biceps muscle; we can say that the neurones in other localities mediate the separate acts involved in locomotion; in others, the changes of facial expression; and in still others, the enunciation of thoughts in the form of spoken words. We know with considerable exactness the positions of the separate centers for sight and hearing; less exactly those of the other special senses. Besides the sensory and motor centers, evidence points strongly toward the existence also of cortical regions which are elaborately joined to one another and to the sensory and motor regions by means of innumerable nerve fibers, and the function of which is to correlate, harmonize, or associate the work of the sensory and motor centers. Such association centers thus help to mediate the more complex psychical phenomena, such as memory and the association of ideas. We can even formulate helpful hypotheses of the neural accompaniments of various psychoses. According to James' theory of the emotions, for example, the perception of the automobile about to run us down leads to the feeling of fear only through the mediation of various organic processes, such as a quickening of the heart beat, pallor and trembling. The accompanying series of neural processes would consist in the activity, in turn, of visual sense organs, neurones conveying the visual impressions to the brain, cerebral neurones mediating the sensation and perception of the terrifying car, motor neurones controlling the peripheral muscular actions that are involved in the organic processes, neurones conveying to the brain the impressions of altered heart beat, constricted arteries, and trembling muscles, and lastly cerebral neurones mediating the feeling of fear. Because of its difficulty, much of the work of geographical exploration within the central nervous system is at present necessarily inexact, and moreover there is still much *terra incognita.* And even though we have thus come to know the gross functions of specific parts of the higher mammalian and human brains, we still know all too little of the processes by which the different parts are coördinated and made to subserve the many complex needs of the organism. The recent work of Professor Sherrington on the integrative action of the nervous system, is an admirable example of the kind of investigation that is needed in this field, and by its very excellence helps to emphasize the lack of our knowledge. The laboratories of physiological psychology, now numerous, are making many valuable contributions, especially to our knowledge of the mechanism of the special senses. But when I make a summary of what we now know of the physiology of the nervous system, I come to realize anew its paucity, compared with what we ought to know and will know, I am confident, in the long future. Here, it seems to me, is a field sadly needing tillage, and one where, though tillage be extremely difficult, the yield is certain to be rich.

All investigation here will lead up, in a sense, to the solving of that problem of problems, which has been for ages the focus of discussion and speculation, the problem of consciousness—"at once the oldest problem of philosophy and one of the youngest problems of science." For centuries it has been thought about, talked about, written about, and with what result? The elaboration of hypothesis after hypothesis, which smell of the lamp—fabrications of the philosopher's cell rather than of the physiologist's laboratory. Almost without exception they are elaborate exercises in dialectics, rather than real portrayals of the nature of that most striking of physiological phenomena. To the physiologist they are almost without exception arid and unsatisfying. "Words, words, words," replies Hamlet to the question of Polonius. At first thought, the theories of dualism and interaction seem best adapted to the obvious facts of human experience: the brain and mind are two distinct entities usually intimately associated, and each capable of inducing phenomena in the other. But deeper brooding, and especially a recognition of the mode of action of the non-psychic portions of the nervous system and the close dependence of psychic on cerebral phenomena, of "how at the mercy of bodily happenings our spirit is," make us seek a more genuinely physiological explanation.

The physiologist recognizes as the morphological basis of nervous actions the neurone or nerve cell, consisting of a compact cell body, from which radiate outward filaments, the nerve fibers. He finds in the nervous system of the higher animal or man millions of such neurones and many more millions of nerve fibers. These constitute seemingly a confused and inextricable mass, but by careful study he has been able to discover an exact and definite, though excessively intricate, nervous architecture. He finds that the bodies of neurones act as central stations, to which and from which flow the nervous impulses along the nerve fibers: the incoming impulses constituting the centripetal, or afferent, or sometimes sensory, impulses; the outgoing constituting the centrifugal, or efferent, or sometimes motor impulses. He recognizes as the physiological basis of nervous action, the reflex action, consisting of an afferent impulse, a central process, and an efferent impulse. He sees reflex acts combined in innumerable ways, and augmented and depressed by other reflex acts. He sees many of the most complicated actions of the individual performed with the aid of this reflex mechanism and without the aid of consciousness. He recognizes that a large proportion, if not the majority, of the individual's actions are reflex and unconscious actions. Lastly, he finds in reflex mechanisms no mysterious principle, but an ensemble of the same physico-chemical phenomena, which in one form or another he finds in other than nervous tissues, and in which the principle of the conservation of energy holds good. Turning now to conscious actions, he sees how indispensable to them, at least in the higher animal species and man, is a certain part of the cerebrum, especially the outer layer or cortex; and how the degree of intellectual development varies with the extent and complexity of this material structure. He sees how injury or disease of this part, or anything interfering with its proper activity, changes the individual from a sentient being into a non-thinking reflex machine. He sees acts, once consciously performed, now relegated to the unconscious reflex sphere. He sees how consciousness disappears in sleep, and how its manifestations vary under the influence of drugs. The cerebral cortex is composed of numberless neurones and is connected by afferent and efferent paths with the other portions of the nervous system. With these facts in mind, and though recognizing the intricacies of mental phenomena, the physiologist gets into the way of thinking that after all the mechanism of cortical actions is really the same as that of other nervous phenomena. He sees no objective, *a priori* reason why an entirely new causative principle should be introduced to explain the action of this small fraction of the nervous system. Whatever its nature, consciousness appears to him, not as a distinct entity grafted on to certain nerve structures, but as merely one of the modes of manifestation of the activity of those structures, just as chemical, thermal, and electrical phenomena are other modes. Being thus one of the signs of nervous activity, the physiologist finds it difficult to see how consciousness can act as a cause of nervous activity, any more than can the heat given off in such activity react to produce itself. The physiologist sees that nervous systems, with all their functions, have undergone an evolution; he recognizes orders of consciousness,—a low, simple, gradual beginning, he knows not where, a progressive increase in complexity as nervous systems complicate, and the final culmination in self-conscious man. The relations of consciousness in its simplest form to the nervous system seem to be the same in kind as in the human being. For the physiologist, looking at the matter in this light, Huxley has probably formulated the best working hypothesis in his famous essay, "On the hypothesis that animals are automata." After a lucid analysis of the actions of animals lower than man, he says: "The consciousness of brutes would appear to be related to the mechanism of their body simply as a collateral product of its working, and to be as completely without any power of modifying that working as the steam whistle which accompanies the work of a locomotive engine is without influence upon its machinery. Their volition, if they have any, is an emotion indicative of physical changes, not a cause of such changes." And later: "It is quite true that, to the best of my judgment, the argumentation which applies to brutes holds equally good of men; and therefore that all states of consciousness in us, as in them, are immediately caused by molecular changes of the brain substance. It seems to me that in men, as in brutes, there is no proof that any state of consciousness is the cause of change in the motion of the matter of the organism. If these positions are well based, it follows that our mental conditions are simply the symbols in consciousness of the changes which take place automatically in the organism; and that, to take an extreme illustration, the feeling we call volition is not the cause of a voluntary act, but the symbol of that state of the brain which is the immediate cause of that act. We are conscious automata." Objection after objection has been raised to the automaton hypothesis. It has been dialectically disproved many times. Its upholders have been charged with all the sins against logic, common sense, lucubration, spirituality and orthodoxy. And yet it will not down, for of all hypotheses it seems to accord most closely with the facts of neural physiology, as we know them to-day. It may perhaps prove to be not a finality; but whether in the distant future it be found correct or incorrect, it is from its general standpoint, it seems to me, that the physiologist of the present epoch can do his most helpful experimental work. The problem of consciousness should be taken into the physiological laboratory, and the conditions of the manifestation of psychic phenomena should be investigated by laboratory methods. All mental processes, even to the last degree, are dependent on and have their basis in brain processes. The physiologist should study in minute detail the cerebral process of each mental act. He can thus inform the psychologist as to the conditions under which psychic phenomena occur. "An individual fact is said to be explained," says John Stuart Mill, "by pointing out its cause." And again, "The cause of a phenomenon is the assemblage of its conditions." In this sense the explanation of consciousness, it would appear, ought to come, sooner or later, from the physiologists.

I have spoken of the physiological aspect of other sciences. Pathology, the science of disease, or, in other words, perturbed function, is peculiarly close to physiology, for there is no sharp line of demarcation between the normal and the abnormal. We may assume the successive chemical substances involved in a certain progressive physiological act to be represented by the series A, B, C, D, in which A is the substance from which the chain proceeds. By analytic and synthetic processes A gives rise to B, B to C, and C to D, which is the final end-product of the metabolism. Even with the same quantity of A and the same strength of stimulus, the quantities of B, C, and D produced in successive repetitions of the act may vary considerably, owing to unknown factors. It is only when the intermediate or final products become markedly increased or diminished in quantity in comparison with their usual amounts, that we speak of the function as pathological. The excitability of cells may be greatly augmented or diminished and still be within the limits of the normal. A tissue may grow excessively, as in tumors, or may waste away, and yet normal function be not seriously interfered with until remote limits are passed. Bacteria may live physiologically within an animal body. They produce and cast off toxins, which intrinsically are poisonous to the cells of their host. These, however, cause a physiological production of antitoxins in the body cells. So long as the antitoxins are sufficient in quantity and strength, they neutralize the poisonous toxins. If the latter get the upper hand they augment or depress the physiological activities of the cells of the host, and we speak of the result as a perturbation of function. The power of the organism to adapt itself to changed conditions and to maintain its physiological status is little short of marvelous. When, in spite of all endeavors, the physiological status is overwhelmed, then is the time for the pathologist to investigate and the physician or the surgeon to attempt to cure.

As in the biological sciences, so in the medical art, there exists a distinction between the morphologist and the physiologist, between the surgeon and the physician. The surgeon is the medical morphologist. His task is to remove diseased or injured tissue, to reunite separated structures, to restore structure or stimulate to its restoration, in short, to make structure normal, so that normal function may follow. The physician, on the other hand, is the medical physiologist. It is his endeavor to restore normal function. His life-long labor is an exercise in physiology. He should know his physiology as the surgeon should know his anatomy, minutely and to the last degree. He should know what health is before he tries to restore it. We all realize how rarely this ideal is reached, and we all have experienced the dire results of medical empiricism. Huxley likens nature and disease to two men fighting, the doctor to a blind man with a club who jumps into the mêlée, and strikes out right and left, sometimes hitting disease and sometimes hitting nature. Would not his blows be more telling if he were quite sure which of the combatants was nature and which disease? Wherein he fails to avail himself of present knowledge he is culpable. And yet he is not to be charged with the whole burden of his failure to cure. Some of this should be shared, I regret to confess, by the physiologists, for they still know too little of the normal action of the vital mechanism. So far is this true, that I am convinced that one of the surest and quickest means of inaugurating a rational and effective art of medicine is through the advancement of physiological discovery. All physicians must be in part empirics until the physiological millennium is ushered in.

If I have been understood aright, my hearers will have perceived that with a mighty subject matter which is pre-eminently its own, physiology extends a leavening influence into a host of other sciences and medicine as well. It is an unusually good example of the typical pure science, with its outlying affiliations and applications. Like many another natural science, its rise, growth, and early nurture were under the protecting wing of medicine. The physiologists of the early years, when their science was crystallizing out of the common mass of scientific knowledge, the men who first formulated its principles, and they who in later years developed it, were, with few exceptions, men of medical training who were under the influence of medical traditions and were guided by the medical spirit. In recent years the ties of the old traditions have been loosened, and the science is passing out from the parental shelter into the illimitable atmosphere of scientific freedom. Its aspirations in research are unhampered. Its achievements in research, in so far as it constitutes an academic theme, are limited by the fact that, except in a few isolated cases, physiology is still regarded by the university as primarily a medical science and its laboratories are housed in medical schools. This is a relic of early history. In consequence physiology must constantly breathe the medical atmosphere and must be influenced, whether it will or no, by medical ideals. This is not to be deprecated from the standpoint of physiological medicine, and the reciprocal advantage to physiology itself in this one aspect is also great. But this now anomalous state of affairs leads directly to two consequences: namely, first, that the broader biological aspects of the science are less dwelt upon than otherwise would be possible; and secondly, that where such aspects have been investigated the work has been done largely by men not professed physiologists and usually lacking the latter's exact training as experimentalists. The customary academic position of the science thus imposes a certain restraint upon physiological progress, and delays its full fruition.

It is idle to try to predict the ultimate fate of the science that is attempting to make clear the vital process. To some minds it is attractive to speculate, and even to dogmatize, concerning the limits of natural knowledge. The present task of the physiologist is to investigate, and continue to investigate, ceaselessly and fearlessly, with a spirit ever fresh and hopeful, seeking only the elusive truth, unmindful of the limits of natural knowledge and undeterred by the fear that the mystery of life will ever remain a mystery. He must be content to spend his energies in patient laboratory research, accumulating facts, unifying facts, and deducing laws for limited spheres of vital activity, and thus to lay the foundations for the broader generalizations that will come after his labor has ceased. By his constant association with the material substratum of the life process and the continual discovery of new and undreamed-of possibilities in its action, he gains a respect and even reverence for living matter which only he can possess. None but he can realize and understand its supreme beauty and harmony and sublimity. He cannot sympathize with, much less share, the feeling that the material is base and only the spirit is uplifting, for to him the material makes its uplifting nobility manifest. He likes to believe, and to act on the belief, that no physiological problem is forever insoluble, and though ignorance may be long-lived, he sees no necessary reason for an ultimate, eternal *ignorabimus*.