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THE PHYSICAL BASIS OF LIFE[1]

IT is frequently stated that the cell is the unit of life, and this is a convenient form of expression, but its exact truth depends upon the conception that one has of life. The cell may be regarded as the morphological unit of life, but form in and of itself, and as recognized by the eye, is not essential to the manifestations of life. We know no life apart from matter, and matter and energy are the only things that we do know. When matter becomes endowed with life, it does not cease to be matter; it does not lose its inherent properties; it is not released from the laws that determine its structure, its attractions and its motions. In studying the organized cell of living things, whether vegetable or animal, whether bone or brain, it should always be borne in mind that it is material in composition, subject to the fundamental laws that govern matter, and possessed of the properties essential to matter.

The only essential, characteristic and constant difference between living and non-living matter is that within the former there is constant and rhythmic metabolism, while in the latter no such process occurs. The living cell is made up of active, labile molecules and these molecules consist of numerous atoms, and each atom contains a large group of electrons; atoms and electrons are in ceaseless, rhythmic motion, while groups of atoms are being constantly cast out of the molecule and replaced by new groups split off from matter outside the molecule. Metabolism, the one char-

[1] Address of the president before the Association of American Physicians, Washington, May 11, 1909.

acteristic phenomenon of living matter, involves intramolecular change; consequently the molecule, and not the cell, is the unit of life. Matter is endowed with life when it becomes the seat of that form of energy which makes of it a metabolic mechanism. As soon as a molecule becomes the seat of assimilation and excretion it is no longer dead; it lives. As a result of assimilation, it acquires the property of building up its own substance; then polymerization follows and reproduction in its simplest form begins. The one phenomenon always manifested by living matter and never exhibited by non-living matter is metabolism. Verworn says:

Vital motion, metabolism, is a complex motion very strongly characterizing the living organism; it consists in the continued self-decomposition of living substance, the giving off to the outside of the decomposition products, and in return, the taking on from the outside of certain substances which give to the organism the material with which to regenerate itself and grow by the formation of similar groups of atoms, *i. e.*, by polymerization. This is characteristic of all living substance.

Aristotle apparently recognized that metabolism is the one characteristic of living matter, for he said:

Life is the assemblage of the operations of nutrition, growth and destruction.

The Greek philosopher and scientist did not know all that is now known about cells, molecules, atoms and electrons, but we must admit that he had a fairly clear conception of the most essential characteristic of living matter.

Du Bois Raymond said that the matter in crystals and non-living substances is in a condition of indifferent static equilibrium, while that in living bodies manifests a motile equilibrium. Bechterew says that we know of nothing in the inorganic world that contains or consists of motile compounds.

Matter is alive when it feeds and excretes. Crystals grow, and in a sense they multiply, but their growth is not intramolecular; it is by accretion. The living molecule not only absorbs; it assimilates. It chemically alters what it receives. The atomic groups taken into living molecules enter into new combination. The living molecule is not stable; it is highly labile. Its composition is never constant; it is never in a condition of equilibrium. There is a constant reaction between the living molecule and other molecules. This reaction consists in the absorption and assimilation of certain atomic groups and the casting out of others. Apart from other matter it could not exist.

What is accomplished by this constant interchange of atomic groups between the living molecule and outside matter? It is for the purpose of supplying the living molecule with energy. Allen expresses this fact as follows:

The most prominent and perhaps most fundamental phenomenon of life is what may be described as the energy *traffic*, or the *function of trading in energy*. The chief physical function of living matter seems to consist in absorbing energy, storing it in a higher potential state, and afterwards partially expending it in the kinetic or active form. We find in living matter a peculiar proneness to change its composition under the stimulus of slight changes in the energy-equilibrium between itself and its surroundings, energy being readily absorbed and readily dispersed. The absorption of energy coincides with deoxidation and the building up of large molecules. The building up of these large molecules is always accomplished by slow steps; but when formed, the said molecules are very unstable, irritable or, in modern phrase, *labile*. They may be broken down by degrees in some instances; in others their structure may be so precarious as to collapse on the slightest disturbance.

The lability of such a molecule may be compared to that of a house of cards, which can be taken to pieces card by card, or may collapse at once. But the word lability is applied not only to destructive, but also to constructive instability. The molecules of living substance are prone to constructive as well as destructive changes; but as in the house of cards the constructive changes are the most gradual; and as the structure grows more complex, construction becomes more difficult, and collapse is more imminent. It should be distinctly understood, however, that it is not the mere size of the molecules that makes them labile, but rather the manner in which they are linked together and the amount of potential energy which is included in the molecule.

It is probable that in the absorption of energy by the living molecule, oxygen is released from combination with carbon or hydrogen, and is attached to nitrogen, while in the liberation of energy the inverse takes place. Nitrogen and phosphorus, sometimes with iron and manganese, seem to be, as it were, the master elements within the living molecule. It is by virtue of their chemism that groups are detached from extracellular matter, taken into the living molecule, and assimilated by an atomic rearrangement; and, furthermore, it is on account of the lability of the compound thus formed that potential energy is converted into kinetic and all work is accomplished.

Life is function and not form, and moreover it is a molecular function. The cell is made up of many and possibly of diverse molecules, but it is the function of the intracellular molecules that determines the nature of its activities. The following quotation from Nussbaum, as given by Loeb, shows that the biologist recognizes that the cell is not the unit of life.

The cell is not the ultimate physiologic unit of life, even though it must remain such for the morphologist. We are, however, not able to tell how far the divisibility of a cell goes, and how we can determine the limit theoretically. Yet, for the present, it will be well not to apply to living matter the conceptions of atoms and molecules which are well defined in physical chemistry. The notion, Micella, introduced by Naegele, might also lead to difficulties, as the properties of living matter are based upon both nuclein and protoplasm. The cell consequently represents a multiple of individuals.

Pflüger has shown that the egg, which has been thought to be a biologic unit, can give rise to many individuals, and Loeb states that his own experiments, as well as those of Driesch, confirm this finding.

In his interesting monograph on the "Biogen Hypothesis," Verworn objects to saying that a molecule lives. He states that this is illogical.

A living thing is only that which demonstrates the phenomenon of life—something that changes itself. A molecule of a given compound, so long as it remains unchanged, can not be said to be living.

Then, in order not to speak of living molecules, he introduces the term "biogen molecule." Surely, this is a distinction without a difference. I agree with the distinguished German physiologist that a molecule of a cell, so long as it remains unchanged, can not be said to be living, but the point is that living molecules do not remain unchanged. When life is latent, as it is in spores, seeds and ova, the molecule can not be said to be alive, neither are the cells alive; but when placed under favorable conditions, the change between atomic groups in the molecule and the extracellular food substance begins, and life manifests itself. A seed contains the germinative cell, a specific ferment and the stored food. The seed is not alive; it possesses only latent life. So long as it remains merely a seed the ferment has no action on the stored food, but place it under suitable conditions of temperature and moisture and the ferment begins to break down the stored protein, and as a result of the chemical cleavage induced by the ferment, relatively simple nitrogenous bodies, such as the mono-amino acids, tyrosin and leucin, and the diamino bodies, arginin and lysin, are formed. These substances begin to react with the molecules within the germinative cell, and latent life is quickened into the active form; the mechanism begins to work and growth commences. Many of the lower forms of life can not feed upon the proteins. This is true of the yeast cell. These cells grow rapidly when placed in a solution of sugar and nitrates, but proteins must be broken up by putrefactive bacteria before yeast organisms can feed upon them. Indeed, many of the cells in the body of man can not feed upon the complex proteins, which must be split up into simpler groups by the digestive enzymes before the cell molecules can absorb and assimilate them. Even the carbohydrate starch must be hydrated and its elements rearranged as the constituents of a more labile molecule before it can become a source of energy in muscle. Solutions of proteins injected into the blood of man are poisonous, but the same substances, after being properly split up, are valuable sources of energy, and some are essential to the continuance of those functions that constitute life.

The atomic groups cast out from the living molecule are not altogether waste products, for among them are the specific secretions which act upon the extramolecular substance, and fit it for absorption and assimilation. Many of these substances have a reversible action. The colon bacillus will feed at one time on solutions of highly complex proteins, the secretion splitting up the large molecule into smaller groups, thus acting as an analytical agent. The same bacillus will grow in a medium that contains available nitrogen only in the form of amino-acids, its secretion acting as a synthetical agent and building up complex bodies out of simpler ones. It is by means of the specific secretion that the living cell, or the molecules of which it is composed, feeds, or, in other words, breaks up the pabulum placed within its reach into groups suitable for absorption or assimilation. In case of fixed cells the food stuff must be brought to the cell or within close range of it before it can be prepared for assimilation. Life in a cell molecule ceases when food is withdrawn, or when the secretion is wanting, or from any cause made inactive. No living molecule can continue to function when new material is wanting. Each living, acting molecule has a selective action in the assimilation of new material, and this is quite indicative of metabolism being a chemical or intramolecular process. It might be supposed that a living molecule is a highly complex body, possibly with many basic and many acid groups. In the process of metabolism an acid group is cast out and this enters into one of the molecules of the foodstuff, setting free another acid group which takes the place of the group cast out. In this way the living molecule feeds, regenerates itself, and supplies itself not only with new matter but with energy. These movements are rhythmical and continue in the same tempo so long as conditions remain the same. It may be that groups of different sizes are cast out and replaced from time to time, smaller groups being thrown off more, and larger ones less, frequently. We have reason for believing that in many living molecules there are at least two kinds of metabolism which occur simultaneously, but in different tempo. The more frequent consists in casting out from the living molecule relatively small groups consisting largely of oxidation forms of carbon and hydrogen. The less frequent is a nitrogenous metabolism in which urea or some antecedent of this substance is eliminated and is replaced by fresh material. It is possible that individual molecules are broken up beyond repair in the nitrogenous metabolism, the worn-out one having already reproduced its successor by polymerization. The tempo with which these processes of metabolism occur may be altered by changing the external conditions. When the speed is too great or when it is too slow continued metabolism, or life, may be endangered. The tempo is altered when it becomes necessary for the living matter to do work. More energy must be absorbed, the greater the work done, and this needed increase in energy can be secured only by increasing the speed with which the metabolic process takes place.

I wish to call attention to the fact that in even the simplest unicellular organism its normal processes are purposeful. The cell molecules attract substances that serve them best as foods. From these they select the parts that they can utilize, and reject the parts that can not serve them. This is true, however, only within certain limits, because often they do absorb substances that lead to their own destruction. Their selection seems to be guided by chemism, which on the whole leads them in the safe way, but may cause their destruction.

It is not my purpose to discuss at this time the question of the relation between the existence of a nervous system and conscious action or psychical activity, but I do wish to call attention to the fact that low forms of life in which there is no trace of nerve tissue behave in a purposeful manner. Many of the low forms of life in which there is no trace of the development of the sense of sight, or sound or feeling, are responsive to light, to sound and to stimulation. We see most convincing evidence of this in the phenomena of helio-, thermo-, chemio- and galvano-tropism. Under the influence of optical, thermic, chemic and electric stimuli these low forms of life, devoid of any trace of nervous system, manifest movements that serve them in self-protection, in securing food and in reproduction. These lower forms of life without nerve tissue apparently learn by experience to choose between what is good and what is bad for them. Metalnikov placed carmin in a fluid in which ciliated infusoria were swimming. At first they absorbed the carmin granules, but having done so once, they could not be induced to try this food again. This behavior, it must be admitted, is much the same as that of the dog which, having been struck with a stick once, runs away when he again meets the same man with a stick. Certain infusoria that feed upon bacteria select the species upon which they feed. The movements of infusoria in pursuit of their prey are certainly purposeful, if not conscious. The readiness with which low forms of life accommodate themselves to altered environment shows that they are capable of being trained or educated to a certain extent. Stahl has shown that a certain plasmodium flees when sprinkled with salt, but if the salt be added to the medium gradually the organism accommodates itself to the new medium. Purposeful action is manifested by plants as well as by animals, and by both unicellular and multicellular plants. This is in evidence in the movements of algæ and moulds. Leaves turn toward the sources of light and heat, and the roots seek nourishment in the earth. The capability of responding to certain stimuli is common to all cell life, whether it be vegetable or animal.

In multicellular animals, such as man, we have colonies, or groups of cells, or organs, bound together. Each kind of cell has its own peculiar molecular composition and through these living molecules the work of the organ is accomplished. A framework of bone, cartilage and connective tissue support and hold in position these organs. They are supplied with food material by a common system of blood and lymph vessels, and their harmonious action is secured through the nervous system. The digestive organs roughly prepare the food for all, but each has its own secretion which shapes the pabulum for intramolecular assimilation. This is accomplished in both instances by means of specific ferments that are formed within the cell molecules. These enzymes bring about changes in the pabulum at the relatively low temperature of the body which can be wrought by inorganic chemicals only at much higher temperature and after prolonged action.

The cell molecules in each organ of the higher animals have their own peculiar composition and manifest their own peculiar function. The chemical composition of the liver differs from that of every other organ in the body. The liver cell molecules cast out their own characteristic products and absorb and assimilate special atomic groups. Moreover, the tempo of metabolism probably differs in each organ, or at least the cell molecules of each organ have their own optimum tempo to which their metabolic processes conform. The more complicated the structure of the cell molecule, the more energy may be stored in it, the greater its lability and the greater is its susceptibility to altered conditions. In the nervous system the molecular structure is the most complex, the amount of stored energy is at the maximum, and the readiness with which this energy may be released is most manifest. In the active central nervous system, or the brain, we have the highest manifestation of the molecular functions that characterize life. The molecules that make up this structure are most susceptible to alteration in conditions. In their function they are influenced by slight disturbances in other organs. We have heard much of late concerning the influence of mind upon the body, and many who speak upon this subject seem to assume that there is some entity, called mind, that controls the body to which it is superior, and apart from which it may exist. This dualistic doctrine is as old as the philosophy of Plato; it always has been and remains to-day a dogma without scientific support, and as a hypothesis it has led to the discovery of no scientific fact. Every attempt to apply it to the treatment of disease has led to the development of conscious or unconscious charlatanism, and has resulted in more or less marked atavism. The term functional disease is now being used by those who know but little concerning the functions of the body in either normal or abnormal states. It seems to be inferred or assumed by those using this expression that a mysterious power has been given to some to set the mechanism of the disordered body aright, although those supposed to be possessed of this gift have no knowledge of, or but imperfect and superficial acquaintance with, the functions of the various organs and their interrelations. In truth we have no evidence of the existence of a functional disease as thus understood. In health the several organs of the body function harmoniously; in disease there is lack of perfect harmony, and we know of no disease in which this condition does not exist. We may not always be able to find where the basic fault lies, but shall we for this reason stop looking for it, shut our eyes, give over our search and ask some individual, quite ignorant of the body and its functions, to undertake the task of inducing harmonious activities? Of mind apart from the body we know nothing. Of the brain as one of the correlated organs we know something, and by continued and patient research we hope to learn much more. We do know that the cell molecules of the brain are the most complex, the most highly labile and the most susceptible to external influences of any of the structures that constitute that community of organs which makes up the individual. We know that the introduction of such poisons as alcohol, morphine and cannabis indica into the blood, leads to disorder of cerebral function; that failure to function properly on the part of the liver, kidney, spleen or other organ, modifies the activity of the brain; and that, on the other hand, altered function in the brain may disturb the functions of these other organs. The medical profession is fully aware of the fact that man thinks not only with his brain, but in a certain sense with every organ in his body. In other words, we know that the perfection of activity of the brain is modified and determined by the proper and healthy activity of other organs of the body, although we are ready to admit that our knowledge along this line is by no means complete. We have studied in myxedema the effect of disordered function in the thyroid upon the central activity. We have learned that in chronic malaria, the central activities, the ideals and the philosophy not only of the individual but of nations, may be debased; that in uncinariasis and other forms of parasitism like results may follow. In short, medical observation and study have shown that healthy cerebral function is to be found only when the activity of the brain is properly influenced by normal function of all the correlated organs. We know equally well the influence of the brain on the other organs of the body. We are fully aware of the fact that impulses may be started in the brain through any of the five senses that may favorably or unfavorably influence the activities of correlated organs, and for centuries the medical profession has employed this physiological principle in the treatment of disease. Savory dishes, pleasingly garnished, through the sense of sight and smell tempt the appetite and stimulate the flow of the digestive juices. Cheerful surroundings aid digestion. Cheering words improve the circulation, and hope is often the best tonic that the physician can administer. As I have stated, the medical profession has understood and has utilized these physiological facts for centuries, and there is nothing in them to justify the founding of any new cult. That the brain of one individual may be modified in its activity by the sounds that fall from the lips of another is as much of a physical fact as that of the contraction of a muscle by the passing of an electric current through its nerve. There is nothing in this to justify a dualistic doctrine involving the existence of mind apart from and superior to matter. Indeed, every step in the process is in accord with the laws of physics and chemistry. The vocal organs of the speaker set in motion the sound waves that strike upon the ear of the hearer, the auditory nerves carry the impulse to the brain center, and the brain molecules respond. There is nothing in it that the most materialistic of philosophers might not endorse. Sensibility, or the capability of responding to stimuli, is, as Claude Bernard said, to a certain extent the starting-point of life; it is a primary phenomenon and from it all others, physiological, intellectual and moral, develop. Bechterew holds that irritability or sensibility is due to a motile cohesion in the biomolecule, and that psychical activity is the result of a complex function of this molecule. Since nothing comes from nothing, the basis of psychical action must lie in the physico-chemical elements of the organism.

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ETHNOLOGICAL EVIDENCE THAT THE CALIFORNIA CAVE SKELETONS ARE NOT RECENT

SINCE the discovery of the celebrated Calaveras skull, many human skulls and skeletons have been found in caves along the west slope of the middle Sierra.[1] The presence of human

[1] See Sinclair, *Univ. Calif. Pubs.*, Am. Arch. and Eth., Vol. 7, No. 2, 1908.