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Electromotive Phenomena and Membrane Permeability

Jacques Loeb

lege, Kalamazoo, Mich., toward a fund of $100,000.

THE trustees of the Joseph Bonnheim Memorial Fund, founded in 1897 by Albert Bonnheim and Fannie Bonnheim, of Sacramento, in memory of their son, have conveyed the entire property of the trust, now valued at approximately $100,000, to the University of California. The income of the endowment will be devoted to scholarships in the University of California for young men and young women.

CONSTRUCTION is about to begin on a laboratory building, to cost $100,000, to be erected by the University of California on the new 465-acre site just purchased by the University of California, at a cost of $55,000, for its citrus experiment station and graduate school of tropical agriculture at Riverside. The director of this work of agricultural research at Riverside is Dr. Herbert J. Webber, former professor of plant breeding in Cornell University.

WORK has begun on the foundation for the five-story building of the Hunterian Laboratory connected with Johns Hopkins Medical School. The new building is located at the corner of Wolfe and Madison Streets, will be 50 by 100 feet and will cost about $65,000.

NEW YORK UNIVERSITY has added to its graduate school courses in surgery by which it will be possible for graduate students to secure the advanced academic degrees of master and doctor of science. The course does not deal with the technique of surgical practise but with subjects such as the application of biological science to surgical diagnosis and therapy.

MR. JAMES COLE ROBERTS, of the United States Bureau of Mines, Denver, has been appointed to the Joseph Austin Holmes professorship of safety and efficiency engineering in the Colorado State School of Mines.

DR. ROBERT S. MORRIS, formerly of the Johns Hopkins University, has been appointed to the Frederick Forchheimer chair of medicine in the medical department of the University of Cincinnati.

DR. ROBERT H. MULLIN, director of the laboratories of the Minnesota State Board of Health and assistant professor of pathology and bacteriology at the University of Minnesota, has accepted an offer from the University of Nevada, at Reno, to take charge of the hygienic laboratories of that institution.

DR. H. G. EARLE has been appointed professor of physiology at the University of Hong Kong.

DR. HERMANN JORDAN, docent in Tübingen, has been called as associate professor of comparative physiology in Utrecht, as successor to the late Professor A. A. W. Hubrecht.

PROFESSOR BENECKE, of the Berlin Agricultural School, has been called to the chair of botany at Münster, as successor to Professor Correns.

DR. BORIS ZARNIK, associate professor at Würzburg, has accepted the professorship of zoology at the University of Constantinople.

DISCUSSION AND CORRESPONDENCE

ELECTROMOTIVE PHENOMENA AND MEMBRANE PERMEABILITY

IN his very interesting presidential address, printed in SCIENCE, Professor Bayliss[1] discusses among other things the origin of electromotive forces in living cells. In this discussion Professor Bayliss adopts the theory, originally suggested by Ostwald and elaborated by Bernstein, R. Lillie and Höber, that the E.M.F. observed in living tissue is due to a selective ion permeability in the sense that normally only cations are able to diffuse through the membrane, but that if the membrane is injured or if a cell is active its membrane becomes also permeable for anions. As a consequence of this increase in permeability the spot where this happens must become negative if compared with a spot of normal or resting tissue. To quote Professor Bayliss:

> I referred previously to the electrical change in excitable tissues and its relation to the cell membrane. It was, I believe, first pointed out by Ostwald and confirmed by many subsequent investigators, that in order that a membrane may be impermeable to a salt it is not a necessary condition

1 SCIENCE, 1915, N. S., XLII., No. 1085, p. 509.

that it shall be impermeable to both the ions into which this salt is electrolytically dissociated. If impermeable to one only of these ions, the other, diffusible, ion can not pass out beyond the point at which the osmotic pressure due to its kinetic energy balances the electrostatic attraction of the oppositely charged ion, which is imprisoned. There is a Helmholtz double layer formed at the membrane, the outside having a charge of the sign of the diffusible ions, the inside that of the other ions. Now, suppose that we lead off from two places on the surface of a cell having a membrane with such properties to some instrument capable of detecting differences of electrical potential. It will be clear that we shall obtain no indication of the presence of the electrical charge, because the two points are equipotential, and we can not get at the interior of the cell without destroying its structure. But if excitation means increased permeability, the double layer will disappear at an excited spot, owing to indiscriminate mixing of both kinds of ions, and we are then practically leading off from the interior of the cell, that is, from the internal component of the double layer, while the unexcited spot is still led off from the outer component. The two contacts are no longer equipotential. Since we find experimentally that a point at rest is electrically positive to an excited one, the outer component must be positive, or the membrane is permeable to certain cations, impermeable to the corresponding anions. Any action on the cell such as would make the membrane permeable, injury, certain chemical agents, and so on, would have the same effect as the state of excitation. If we may assume the possibility of degrees of permeability, the state of inhibition might be produced by *decrease* of permeability of the membrane of a cell, which was previously in a state of excitation owing to some influence inherent in the cell itself or coming from the outside. This manner of accounting for the electromotive changes in cells is practically the same as that given by Bernstein.

The suggestion of Ostwald was questioned by physical chemists, *e. g.*, Walden, Tammann and Nernst. Recent experiments carried on in the writer's laboratory have shown that the attempt to explain the E.M.F. in tissues by the idea of a selective ion permeability and its changes (which the writer had originally also adopted) is neither tenable nor necessary. Space permits to point out only a few of the reasons for this statement.

1. Loeb and Beutner found that if we lead off from two places on the surface of an intact plant leaf (*e. g.*, rubber plant) or fruit (*e. g.*, apple) with two solutions of the same electrolyte but of different concentration, the lower concentration is always positive to the higher; and the E.M.F. depends upon the ratio of the two concentrations as expressed by Nernst's well-known formula. In the most ideal objects for this purpose the E.M.F. corresponds quantitatively to Nernst's formula. In all cases a spot of tissue (no matter whether plant or animal) in contact with distilled water is positive if compared with a spot in contact with a physiological salt solution or a Ringer solution.[2]

According to the theory of Bernstein, which Bayliss adopts, a spot of muscle or leaf in contact with distilled water should be negative to a spot in contact with a physiological salt solution, since we know that distilled water causes an increase in permeability. This increase in permeability is shown not only by the facts of cytolysis, but also by direct observations on the eggs of *Fundulus* in the writer's floating experiments. Thus one of the most general phenomena in electrophysiology contradicts the theory of selective ion permeability.

The experiments of Beutner and of Loeb and Beutner have shown that the E.M.F. which appear at the surface of living tissues can be imitated if we bring a watery salt solution in contact with a substance immiscible in water, such as lecithin or oleic acid (which for experimental purposes was dissolved in guaiacol).[3] According to Beutner's theory[4] traces of the salts are soluble in the water immiscible phase and one ion combines here with an anion or cation (or both combine in the case of an amphoteric electrolyte). The common ion of the salt in the water and of the water immis-

[2] Loeb, J., and Beutner, R., *Biochem. Ztschr.*, 1912, XLI., p. 1.

[3] Loeb and Beutner, *Biochem. Ztschr.*, 1913, LI., p. 288; 1914, LIX., p. 195.

[4] Beutner, *Ztschr. f. physik. Chem.*, 1914, LXXXVII., p. 385; *Jour. Am. Chem. Soc.*, 1914, XXXVI., pp. 2,040 and 2,045.

cible salt determines the E.M.F. On the basis of this assumption Beutner has been able to explain the observed phenomena thermodynamically, and his theory accounts for all E.M.F. at phase boundaries.

It follows from this theory that a spot of tissue in contact with distilled water should be positive to one in contact with a physiological salt solution, which is actually the case.

It was known that if we lead off from two spots of a muscle with a KCl and NaCl solution of the same concentration, the spot in contact with KCl appears negative to that in contact with NaCl. Loeb and Beutner could show that this was also true for the boundary between oleic acid or lecithin and salt solutions, and it was explained by Beutner on the assumption (which could be verified) that KCl is more soluble in the water immiscible phase than NaCl, that the Cl combines with some constituent of the water immiscible phase, and that the Cl ion, being the common ion, determines the E.M.F.

2. It is well known that an injured spot of a tissue is negative to a non-injured spot (current of injury), and this is explained on the basis of Bernstein's or Bayliss's theory by assuming that the specific cation permeability of the membrane is abolished by the injury and that the anions will also reach the outer boundary of the injured spot. Loeb and Beutner have published experiments which show that the so-called current of injury has nothing to do with an alteration of permeability, but that it is in all probability due to the existence of an internal E.M.F. situated at the internal boundary of the membrane.[5] If it is true that the junction of the outer boundary of an organ, *e. g.*, an apple, with a salt solution must become the seat of an E.M.F., the same must be true for the boundary of the membrane with the internal liquids of the tissues containing electrolytes. If we could show that this internal E.M.F. is generally smaller than the E.M.F. at the outside surface when we lead off from the latter with a physiological salt solution, the so-called current of injury would find a simple explanation. As a matter of fact, acids, KCl, and other substances give rise to negative potentials if compared with that of a physiological salt solution of the same concentration, and it is quite possible that such a solution exists at the inner boundary of the membrane. When we lead off from two intact spots on the surface of an organ we do not notice the existence of the internal potentials, since they are opposite and equal; but if we destroy the membrane on one spot and lead off from this spot and from an intact spot of the skin the injured spot must be negative to the normal spot, since in reality we measure in this case the difference between the outer and the inner potentials of the membrane. The idea that such a layer exists at the internal surface has received support by a series of experiments by Loeb and Beutner, some of which may be mentioned. When we cut an apple in two and lead off with salt solutions of the same kind and concentration from the intact outer surface and from the cut, the cut is negative, as was to be expected. When we remove more and more of the flesh of the apple, while leaving the skin unaltered, the difference of potential between outside skin and cut surface at first remains unchanged; but if we remove so much that the salt solution (with which we lead off from the cut surface to the measuring instrument) reaches the internal surface of the rind, the E.M.F. between the intact and injured part of the apple becomes less and finally disappears. In this case the salt solution replaces, in our opinion, the natural layer of liquid on the inner surface of the skin.

When we press the skin of an apple on one spot with the soft part of our finger without causing an abrasion of the skin, that spot becomes negative to a non-pressed spot; and yet we can show that the permeability of the skin is intact. This can be shown by the fact that the concentration effects produced by applying solutions of different concentrations are still the same as in any intact part of the skin; while this is no longer the case if we cause an abrasion. The explanation which we ventured to give for the fact that the pressed spot be-

[5] Loeb and Beutner, *Biochem. Ztschr.*, 1912, XLIV., p. 304.

comes negative was that the pressure displaces the layer of acid or any other substance which may be responsible for the inner potential, and replaces this substance by the juice pressed out from some of the soft cells of the flesh of the apple, but without altering the permeability of the skin.

Under these conditions the fact that the active part of a tissue becomes negative to a part at rest finds its simple explanation on the assumption that in the active part of the tissue substances are formed which temporarily alter the potential at the inner surface in such a sense as to make the outside on that spot appear more negative. There is no necessity for assuming any increase in the permeability of the skin.

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WHAT IS HELLENISM?

IT would usually be both foolish and ungrateful to criticize the choice of illustrations used by a lecturer in an attempt to make clearer a worthy proposition. When, however, the illustration is in very common use, though more often in another manner, when it is sure to remain in common use, and when moreover it has great and positive value, its misuse is dangerous enough to merit attention. The address of Professor Harrison, published in SCIENCE of October 23, 1914, urges us to make science of practical value. We may all well do what we can to share and spread the motive and accomplish its aim. In this address, Professor Harrison contrasts Hellenism and Hebraism, apparently in the sense that Hellenism typifies clear thought, and Hebraism vigor in practise. We are all familiar with the contrast of Greek and Hebrew culture, in which the former represents reason, and the latter faith, as the guiding principle of conduct. Professor Harrison's contrast strikes me as both novel and unsound.

The Hellenic culture which has influenced subsequent civilization was essentially the culture of Athens. The usual idea of Athenian culture is that it was characterized by marvellous activity. As to the culture typical of Athens, we can go back to the greatest Greek historian, and as to Greek ideals, to the greatest Greek philosopher, both of them men whose works are still commonly regarded as preeminent in their fields. The opinion of Thucydides with regard to the Athenians is expressed over and over. In Chapter III. of Book I., he puts his views into the mouth of the envoy of Corinth, who is addressing an assembly in Sparta:

> The Athenians are addicted to innovation, and their designs are characterized by swiftness alike in conception and execution; you have a genius for keeping what you have got, accompanied by a total want of invention, and when forced to act you never go far enough. Again, they are adventurous beyond their judgment, and in danger they are sanguine; your wont is to attempt less than is justified by your power, to mistrust even what is sanctioned by your judgment, and to fancy that from danger there is no release. Further, there is promptitude on their side against procrastination on yours; they are never at home, you are never from it: for they hope by their absence to extend their acquisitions, you fear by your advance to endanger what you have left behind. They are swift to follow up a success, and slow to recoil from a reverse. Their bodies they spend ungrudgingly in their country's cause; their intellect they jealously husband to be employed in her service. A scheme unexecuted is with them a positive loss, a successful enterprise a comparative failure. The deficiency created by the miscarriage of an undertaking is soon filled up by fresh hopes; for they alone are enabled to call a thing hoped for a thing got, by the speed with which they act upon their resolutions. Thus they toil on in trouble and danger all the days of their life, with little opportunity for enjoying, being ever engaged in getting: their only idea of a holiday is to do what the occasion demands, and to them laborious occupation is less of a misfortune than the peace of a quiet life. To describe their character in word, one might truly say that they were born into the world to take no rest themselves and to give none to others.

The ethics of Aristotle represents happiness as the goal of human effort, and work as absolutely indispensable to happiness. No single quotation would give an adequate idea of the