

MEMBRANE POTENTIALS IN THE DONNAN EQUILIBRIUM.

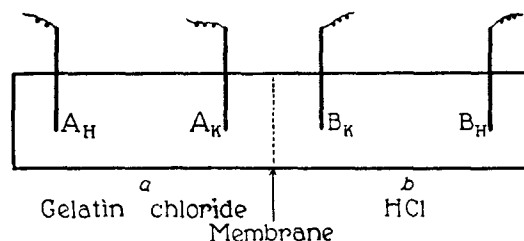
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The development of Loeb's theory of the colloidal behavior of the proteins has recently been criticized by A. V. Hill.¹ This criticism seems to be based on a misunderstanding, which it is hoped the following considerations may help to clear up.

The arrangement of the experiments in question is quite clearly indicated by the diagram given by Hill, which is reproduced herewith.



(The diagram gives, however, no indication of the hydrostatic pressure due to the liquid in the manometer tube, which is a necessary condition for equilibrium. For further details of the experiments Loeb's original papers and book² may be consulted.) A_H and B_H represent hydrogen electrodes; A_K and B_K , calomel electrodes connected to the solutions by saturated KCl.

Loeb measured the potential difference between A_K and B_K , which he termed the observed P.D., or membrane potential. He also meas-

¹ Hill, A. V., *Proc. Roy. Soc. London*, Series A, 1923, cii, 705.

² Loeb, J., *Proteins and the theory of colloidal behavior*, New York and London, 1922.

ured the pH of each solution separately; that is, he measured the P.D. between A_H and A_K and that between B_H and B_K . The difference between these values he termed, somewhat unfortunately, perhaps, the calculated P.D. This term is being replaced in his more recent writings by the term hydrogen electrode potential. The agreement between the membrane potential and the hydrogen electrode potential was interpreted by Loeb to indicate the applicability of Donnan's theory of membrane equilibria.

Donnan had predicted that when two solutions were separated by a membrane impermeable to one ion of one of the solutions, but permeable to other ions, then, at equilibrium, the product of the concentrations of the diffusible ions on one side of the membrane should be equal to the product of the corresponding concentrations on the other side. He further predicted that a potential difference should exist between the two solutions, and that its magnitude should be given by the relation

$$E = \frac{RT}{F} \ln \frac{x}{y}$$

where x and y represent the concentrations of any one of the diffusible ions in the two solutions, and the other symbols have their usual meaning. These relations were deduced by Donnan on the basis of the laws of thermodynamics, as applied to the equilibrium in a system of the type already defined.

Hill maintains that this agreement of the quantities which Loeb has termed membrane potential and hydrogen electrode potential "is a necessary consequence of *any* mechanism which does not offend the Second Law of Thermodynamics. . . ." This is quite true; but in this case it is just this particular mechanism of a membrane impermeable only to gelatin which has brought about the establishment of equilibrium. It had been shown repeatedly that the collodion membranes used in Loeb's experiments were impermeable to proteins but permeable to simple inorganic electrolytes. The existence of protein ions in these solutions was shown by the earlier experiments³

³ Hardy, W. B., *J. Physiol.*, 1905-06, xxxiii, 251.

Pauli, W., *Kolloidchemie der Eiweisskörper*, Dresden and Leipsic, 1920.

Michaelis, L., *Die Wasserstoffionenkonzentration*, Berlin, 1914 and 1922.

Sørensen, S. P. L., *Compt. rend. trav. Lab. Carlsberg*, 1917, xii.

Robertson, T. B., *The physical chemistry of the proteins*, New York and London, 1918.

of Hardy, Pauli, Michaelis, Sørensen, Robertson, Loeb,² and others, on electrical migration and electrometric titration of protein solutions. Hence the conditions necessary for the establishment of a Donnan equilibrium were known to be satisfied; Loeb's experiments tested and verified this idea.

Hill's criticism takes no account of the fact that Loeb's experimental demonstration of the existence of a potential difference was made in a system conforming to the requirements postulated by Donnan. Since Donnan's reasoning was based on the laws of thermodynamics, of course it may be said that the experimental verification of his equation, connecting membrane potentials with ion concentrations, is simply a consequence of the laws of thermodynamics. The same might be said of the experimental verification of Nernst's formula for the E.M.F. of a concentration cell, or of almost any other of the classical experiments of physical chemistry.

Hill's reasoning to the effect that the p.d. between A_H and B_H must be zero is correct, but he seems to forget that the very condition by which this equilibrium is rendered possible is the presence of a membrane impermeable to protein ion. One is not justified in imagining, as Hill does, "that for any physical reason whatever, not *necessarily* because of the existence of a Donnan Equilibrium involving an indiffusible ion, there is a difference of potential between two solutions in equilibrium with one another." In these experiments the difference of potential must depend on the fact that the protein cannot get through the membrane, since that is the only thing that prevents the solutions from being identical at equilibrium. We have the charged or ionic protein, and the membrane impermeable to it; these are the conditions necessary for the existence of a Donnan equilibrium.

The striking facts which Loeb has discovered are the existence of a measurable difference in ion concentrations and of a corresponding measurable difference in potential between the solutions on the two sides of the membrane. These facts can be satisfactorily explained by Donnan's theory, and Loeb has shown how they can be used to explain other properties of protein solutions, notably, the effect of electrolytes on osmotic pressure. Hill has offered no alternative explanation for these facts. Loeb has explained them quantitatively; unless some better quantitative explanation can be proposed, the applicability of Donnan's theory will stand.