from equilibrium obviously does not disprove the validity of a theory explicitly restricted to "non-equilibrium" or perhaps better, "dynamic equilibrium" conditions. Similar arguments might equally well have been used to disprove Briggs's own theory, which also implies the absence of true equilibrium. It seems possible that Briggs was misled by my unfortunate use of the word "equilibrium" in the discussion of certain equations where the term "dynamic equilibrium" would have been more exact (l.c., pp. 403-4). These equations not only indicate the upper limits of ion accumulation during dynamic equilibrium, but also predict that if true equilibrium were actually attained, accumulation of ions would stop, just as Briggs showed by more elaborate reasoning. This true equilibrium would be attainable only in the absence of all metabolism, and it is this, rather than the dynamic equilibrium indicated by the title and context of my paper, which is discussed by Briggs. In addition to his theory there is therefore also my own theory which is physically sound and antedates and underlies his.

What is more important is the fact that, while my theory is, with minor modifications, competent to explain the observed conditions in the case of *Valonia*, Briggs's theory is not. According to Briggs's own calculations, his theory falls short of predicting the observed accumulation of potassium by more than one-half (l.c. p. 259). To put the matter in another way : his explanation would be adequate if sea-water had a pH of 6·3 instead of 8·0, a potassium content of $10^{-5} N$ instead of about $10^{-2} N$, and a chloride content of $10^{-5} N$ instead of about $0·5 N$. Since such assumptions would be fantastic, it is clear that Asprey is not justified in stating that the accumulation of solutes in *Valonia* can be explained by Briggs's theory. The same can probably be said in regard to the case of *Nitella*, which is not analysed by Briggs.

I see no good reason for denying the possibility of cyclic changes in permeability such as Briggs assumes. On the contrary, his constructive contribution to current thought in this field seems to me both opportune and valuable. Certainly no theory as yet advanced can be regarded as more than a working hypothesis. But Briggs's is only one of several such hypotheses, and will eventually have to be supplemented if not supplanted by other explanations which are better able to account for what we know to be true about the accumulation of solutes in living cells.

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May 11.

[1] Asprey, G. F., *Proc. Roy. Soc.*, B, **112**, 451-72 ; 1933.
[2] Briggs, G. E., *ibid.*, **107**, 248-69 ; 1930.
[3] Brooks, S. C., *Protoplasma*, **8**, 339-412 ; 1929.

After the remarks of Prof. Brooks in the final paragraph of his letter it would be ungracious as well as only part of the truth if I merely stated that I was not misled about the point of dynamic equilibrium and that I maintain that his theory is thermodynamically unsound. The rest of the truth is that it was a critical consideration of his theory that led me to suggest an alternative.

The theory suggested by Prof. Brooks assumes a membrane consisting of a mosaic of areas, some permeable to anions and some to cations, between the cell-sap and the external solution. An accumulation in the sap of ions, such as K and Cl, is explained by the anions of an electrolyte, such as H_2CO_3, passing through the anionic areas in exchange for Cl ions and the cations through the cationic areas in exchange for K ions.

Let us consider a simple system : in the sap, H and HCO_3 ions are maintained by the production of carbon dioxide at a concentration higher than that outside the enclosing membrane, the concentration of H equals that of HCO_3, the mobility of the two ions is assumed to be equal whether in the liquid or in the membrane ; the same applies to K and Cl ions except that their concentration is the same in the sap as outside. If K ions are to be driven into the sap against a concentration gradient then there must be a gradient of electric potential, the sap being negative to the outside : if Cl ions are to be driven in, the gradient must be in the opposite direction. It is obvious that the sap as a whole will be at the same potential as the external solution, since the H ions pass out of the sap as rapidly as the HCO_3 ions. Near to the anionic areas the sap will be positive and the external solution negative to the bulk solutions because the HCO_3 ions have a shorter path to the outside than have the H ions, and hence in the sap there will be a local excess of Cl ions and deficit of K ions, while outside the reverse will hold. Near the cationic areas it will be in the outside solution that there will be a local excess of Cl and deficit of K ions. There will be no accumulation of K and Cl ions in the sap from outside in such a system ; the H ions passing out will be balanced electrically by the HCO_3 ions passing out with equal facility. Anions could be accumulated if HCO_3 passed out more readily and the sap was positive to the external solution, or cations if the reverse held, but not both. Such were the objections raised to Brooks's theory.

The theory which I suggested resembled the above only in that it postulated the production of an electrolyte by the cell which was permeable to both ions. For the mosaic it substituted periods of greater permeability to anions alternating with periods of greater permeability to cations. Prof. Brooks says such a theory cannot explain the condition in *Valonia* without fantastic assumptions. The mechanism can account for accumulation to any extent ; it is only a question of the ratio, inside to outside, of the concentration of the ions of the produced electrolyte. The numerical example was based on the data of Osterhout and Dorcas[1] for carbon dioxide, which was assumed to be the electrolyte. To account for the known accumulation of potassium chloride, the not unreasonable assumption of a greater concentration of undissociated carbonic acid at an earlier stage in the history of the cell or the production of other electrolytes is required. On the basis of the former assumption the cell in question would be losing ions such as Cl under the conditions given. This would be a necessary consequence of any theory involving permeability of the membrane to anions, for the concentration of HCO_3 ions in the external solution is greater than that in the sap according to the data of Osterhout and Dorcas used in the calculation.

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May 29.

[1] Osterhout and Dorcas, *J. Gen. Physiol.*, **9**, 255 ; 1925.