

Linkage of Physico-Chemical Processes in Biological Systems

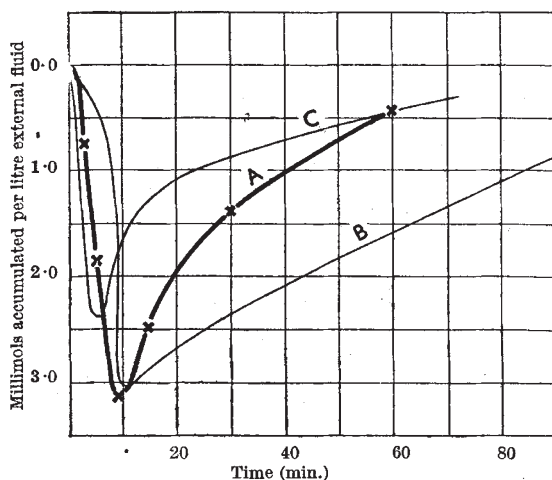
IN a recent communication in *NATURE*¹, it was pointed out that the shift of equilibrium between extracellular and intracellular potassium during fermentation of sugar either by yeast or bacteria^{2,3} was a striking example of the general application of certain principles underlying the accumulation of potassium in cells^{4,5,6,7}. If our views as to the nature of such in and out movement during fermentation are correct, it should occur with other cations besides the potassium ion, provided they can diffuse across the cell membrane, or in other words, it should not be *specific* for potassium.

Such another cation is ammonium, and we have recently found that a shift of the ammonium ion occurs in 'ammonia' yeast just as it occurs in 'potassium' yeast.

The 'ammonia' yeast was formed by replacing all the potassium in ordinary baker's yeast in the manner previously described⁸, the concentration of the external ammonium being $N/5$ and the process hastened by maintaining at 37° C. The concentration of potassium in such 'ammonia' yeast was much less than 1 mgm. K/100 gm. Yeast so treated was then washed a few times with 0.3 per cent sodium chloride, and left for some hours suspended in this solution, when the external ammonium ion concentration was about 20 mgm./100 ml. To a measured volume of this yeast suspension (1 in 3) was added a small amount of a concentrated solution of glucose and sodium acid phosphate to produce 1.4 per cent glucose in the mixture and $M/140$ phosphate, and to an equal volume of the yeast suspension the same addition was made but without the glucose. The ammonia content of the external solution was examined after varying times, and the values for the mixture containing glucose subtracted from the control figures, giving in one typical example curve *A* in the accompanying graph, which is compared with the curves of K accumulation, *B* and *C*, of Pulver and Verzar² with yeast (second experiment in their paper), and of Leibowitz and Kupermintz³ for bacteria (*E. coli*). Similar curves for 'ammonia' yeast were also obtained in repeat experiments on the same yeast where glucose in saline was added to the mixture from which glucose had disappeared by fermentation, and saline to the control mixture.

This movement of potassium and ammonium ions is in itself to be differentiated from possible specific effects of the ions on yeast activity or that of yeast extracts. For this there is an extensive literature. A short review is given, for example, by Stavely *et al.* in their first paper on zymine⁹. From a recent communication in *NATURE*⁹, Farmer and Jones appear to have obtained some new evidence in this field.

The explanation previously given of the potassium shift during fermentation, which now extends to a similar ammonium shift, would appear quite satisfactory, and relates to those principles which are fundamental to the accumulation of potassium in cells⁴⁻⁷. The ion movement would appear to be controlled by the effective product of the free phosphate and potassium (or ammonium) ion concentrations (free phosphate being present mainly as the univalent ion at the pH obtaining within and without the cells). When glucose diffuses into the cells, there is a very rapid formation of glycogen, according to Willstätter and Rohdewald¹⁰. In the first two minutes, 90-100 per



cent of glucose which has diffused in is present as glycogen. This stage is rapidly followed by a marked increase of phosphate esters formed from the glycogen. In the present explanation it is then supposed that the product of the potassium (or ammonium) and phosphate ion concentrations falls steeply and phosphate ions enter with K (or NH_4), the diffusible cations being held within by the electrostatic attraction of the newly formed non-diffusible ions. When these are broken down again the process is reversed, and K (or NH_4) leaves the cells.

This explanation does not imply that there is a simple equality of concentration products within and without the cell, as would be considered for a Donnan equilibrium of the simplified kind for very dilute solutions, for, apart from the effect of the total ionic concentration, the yeast cell membrane is practically non-distensible and the internal pressures are likely to be very much different from those without, with corresponding alteration of the ion activities; but it does imply that an equilibrium will occur with a definite ratio of the products of the ion concentrations (probably not far from unity) and that a change in this ratio will influence the movements of the ions in the direction of its restoration.

Further work on this question is in progress, being assisted by a grant to one of us from the Irish Medical Research Council.

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- ¹ Conway, E. J., *NATURE*, **150**, 461 (1942).
- ² Pulver, R., and Verzar, F., *Helvetica chim. Acta.*, **23**, 1087 (1940).
- ³ Leibowitz, J., and Kupermintz, N., *NATURE*, **150**, 233 (1942).
- ⁴ Conway, E. J., and Boyle, P., *NATURE*, **144**, 709 (1939).
- ⁵ Boyle, P., and Conway, E. J., *J. Physiol.*, **100**, 1 (1941).
- ⁶ Conway, E. J., *NATURE*, **147**, 574 (1941).
- ⁷ Donnan, F. G., and Conway, E. J., *NATURE*, **149**, 383 (1942).
- ⁸ Stavely, H. E., Christensen, L. M., and Fulmer, E. I., *J. Biol. Chem.*, **111**, 771 (1935).
- ⁹ Farmer, S. N., and Jones, D. A., *NATURE*, **150**, 769 (1942).
- ¹⁰ Willstätter, R., and Rohdewald, M., *Z. physiol. Chem.*, **247**, 269 (1937).

Mechanism of Lysis of Red Blood Cells

STUDY of the etiology of blackwater fever has led us to examine the wider problem of the mechanism of red cell destruction in the body. A summary of the preliminary work and the conclusions reached is given below.

We have observed that certain tissues (lung, liver, kidney, spleen, bone marrow and muscle) will lyse