leg in response to exteroceptive stimulation on the leg and on the skin of the trunk behind and near the leg make their appearance at about the same time. These reflexes begin at about the same time that antigravity action of the legs can first be detected. This is before there is rotation of the leg or passive bending of the knee under antigravity pressure.

The leg begins to rotate passively under antigravity pressure at about the time that antigravity action of the leg can first be detected and this is before there is flexion of the knee; but antigravity action of the leg has been observed in specimens in which there was no passive rotation of the leg.

The plantar reflex begins as an action of the leg as a whole, and only later is restricted to action of the distal segments of the leg. At about the time that active flexion of the knee appears in walking there is the first reflex flexion of the knee, foot and digits in response to plantar stimulation, and active extension of the knee in walking appears at about the same time. Stepping backward first appears after the plantar reflex stage of the digits, and in the earliest observed case of the backward step there was active extension of the toes as the animal lifted the foot from the substratum in the extreme position of abduction.

Active rotation of the leg in walking makes its appearance distinctly after there is passive rotation of the leg under antigravity pressure and it first occurs in the extreme phase of abduction.

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Accumulation of Potassium in Living Cells—a Non-equilibrium Condition.

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Previous workers[1,2] have suggested that the relative excess of potassium observed in divers living cells and tissues might be accounted for by assuming that ionic equilibrium is not attained during the life of such systems but is most nearly approached by the most mobile ions. But no completely satisfactory theory has yet been proposed, nor has any experimental proof been adduced. This

[1] André, G., and Demoussy, E., *Bull. Soc. Chim. Biol.*, 1925, vii, 806.

[2] Osterhout, W. J. V., PROC. SOC. EXP. BIOL. AND MED., 1926, xxiv, 234.

paper gives experimental proof that a non-equilibrium state exists, and explains the mechanism of accumulation.

If in its normal state a living cell were in ionic equilibrium with the surrounding medium any increase in the concentration, or, more properly, in the activity of an ion in the surrounding medium should, if it leads to any change, result in an increase in the activity of the same ion within the cell. Conversely, decrease outside should lead to decrease inside. If decrease outside should be found to produce increase inside or vice versa, it appears impossible to account for the observed facts except by assuming the existence of a non-equilibrium state.

Experiments were made on the unicellular coenocytic marine alga *Valonia macrophysa* Kütz. from which large amounts of intracellular sap may be obtained for analysis. Under normal conditions this sap has a pH of about 6.2 and potassium and sodium ion concentrations of roughly 0.5 M and 0.1 M, as compared with a pH of 8.2, and potassium and sodium ion concentrations of roughly 0.01 M and 0.5 M, respectively, in sea water. Since both this sap and sea water are dilute aqueous solutions containing little or no organic material, no sensible error will be introduced by considering ion concentrations rather than activities.

Sufficient isotonic sodium chloride solution was added to different samples of sea water to reduce the potassium ion concentration to 90, 75 or 50% of that in normal sea water. Comparable lots of about 60 *Valonia* plants were placed in these solutions for different periods varying from 9 hours to 8 days, with control lots in normal sea water. After exposure, the sap was collected, and the concentration of sodium, potassium and chloride determined in each. These analyses show that reduction in the potassium content of the sea water leads to a slight but distinct increase in its concentration in the sap. This can only be accounted for by assuming that the cells are not normally in ionic equilibrium with the surrounding sea water.

The way in which this non-equilibrium state is maintained may be pictured as a result of a mosaic constitution of the protoplasmic surface. Areas permeable to cations only alternate with areas permeable to anions only, the size of the areas being somewhat greater than the effective diameter of the electrical fields surrounding the ions present.[3, 4] In the normal state carbonic acid produced by protoplasmic metabolism will dissociate yielding hydrogen and bicarbo-

[3] Michaelis, L., *J. Gen. Physiol.*, 1925, viii, 33.

[4] Höber, R., and Höber, J., *Arch. ges. Physiol.*, 1928, ccxix, 260.

nate ions. The hydrogen ions thus produced inside the cell reach a concentration of about 100 times that in the surrounding sea water, as can be shown by direct measurements, and will therefore pass out through the cation permeable areas, other cations entering the cell through the same areas to maintain local electrical neutrality. In this process the available cations will enter at rates determined by the combined effects of their activity gradients and their penetrabilities through the protoplasmic surface. By analogy with the cation permeable "dried" celloidin membrane we may expect these penetrabilities to follow the same sequence as the mobilities of the different ions in free diffusion, but to differ much more widely from ion to ion. Under these conditions penetrability will outweigh activity gradient and therefore more potassium will enter the cell than sodium. The divalent cations (Ca and Mg) will also penetrate slowly. The bicarbonate ion like the H ion will be present in the sap in a concentration many times exceeding that in the surrounding sea water, and will pass out through the anion permeable areas, its place being taken by chloride in order to maintain local electrical neutrality. Since these processes lead to a continued increase in the amount of osmotically active material in the cell, the cell must take in water and grow.[2] In this way attainment of equilibrium is prevented so long as CO_2 is being produced by the cells, and potassium accumulates in the cell.

Exposure of *Valonia* cells to sea water mixed with isotonic sodium chloride may be supposed to increase the disparity between the penetrabilities of potassium and sodium and hence lead to the observed increase in the proportion of potassium. Presumably any slight increase in permeability, no matter how caused, would lead to the same result. We may picture the protoplasmic surface as being of a porous nature, the pores being capable of variation in diameter, and owing their restricted ion permeability to charges resident in the walls of the pores. Hence these ions with the smallest effective diameters (as judged by their mobility in dilute aqueous solution) will penetrate most readily, and for each ion there will be a characteristic relation between pore diameter and penetrability. We may suppose this to take the form shown in Fig. 1 for different cations. In the case of *Valonia* the normal state of the cell would be characterized by the relative penetrabilities shown at A; in our experiments the state would be like that shown at B, the penetrability of $K^{\cdot}$ being increased relative to $H^{\cdot}$ and $Na^{\cdot}$. Serious injury or death would lead toward the condition shown at C. It is assumed that HCO_3' and Cl' pass through their appropriate type of area

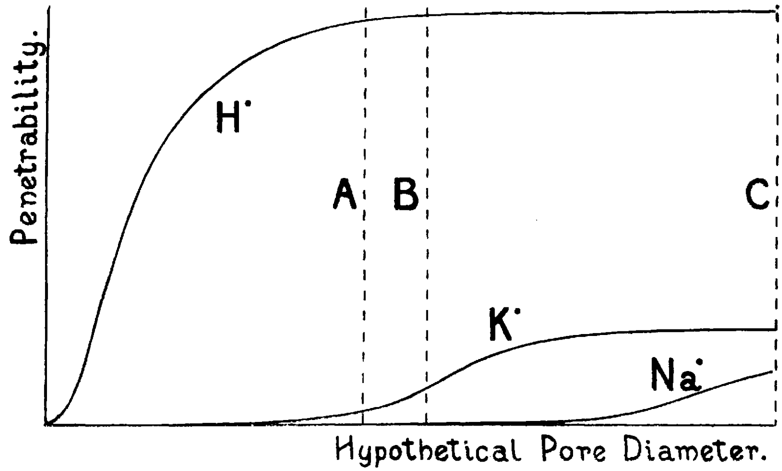

FIG. 1.

with relative ease. The intake of many substances, especially organic compounds, may be complicated by factors other than those here considered.

Thus we may account for such diverse phenomena as the intake of ions by vascular plants, the accumulation of vanadium in the blood of *Ascidia*, the different ratios of potassium to sodium in mammalian erythrocytes, and so forth. Physiological alterations in the end products of oxidation, (*e. g.*, lactic acid production) or in protoplasmic permeability should lead to corresponding alterations in the ion content of cells and tissues such as are known to characterize plant galls and malignant tumors in animals.