
Introductory Remarks

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Introductory remarks

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When in December 1970 I organized a Discussion Meeting at the Royal Society concerned with the active transport of salts and water in living tissues, the focus of our deliberations was principally on the transport of the dominant biological cations: sodium in vertebrates, and potassium in insects. The anions chloride and bicarbonate were not totally neglected, and Jean Maetz, whose tragic death in a car accident a few years ago so saddened us all, gave us a masterly review (Maetz 1971) of their role in the transfer of salts in fish gills. But on looking through the published proceedings, one gets the impression that all the time it was sodium that was in the limelight with the thick black arrows, while chloride was relegated to the indignity of being passively transported, and was shuffled off with dashed lines in an obscure corner of the diagram. One of the reasons for this emphasis was, of course, the accident of the way in which the subject had happened to develop historically. As Hans Ussing pointed out in his introductory remarks (Ussing 1971), the existence of a multiplicity of ion pumps had been commonly accepted in the 1950s, but the discovery of Na,K-ATPase by Skou (1960), not unassisted by the availability of admirably specific blocking agents for sodium transport (Schatzmann 1953; Glynn 1957), quickly brought the sodium pump to the fore, and it has monopolized the centre of the stage ever since. During the next two days I hope that we can do something to redress the balance.

We ought, I suppose, to give some thought to the relative roles of anions and cations in living cells. Why is it that every cell, at least in the animal kingdom, has a sodium pump, and only a few can afford the luxury of a chloride pump? I do not propose to get into the business of making oracular pronouncements about the origin of life, even though the question of how membranes originated seems to me to be one of the key problems that is apt to be skated over too quickly by some of the prophets, but I offer you the speculation that the dominance of the sodium pump results from the fact that most large biological molecules are negatively rather than positively charged. I am not enough of a chemist to know whether that fact itself can properly be described as accidental, but I suggest that it had the consequence that once cells enclosed in semipermeable membranes had evolved, and the problem of volume regulation had arisen, Nature found it easiest to design a system in which an osmotic balance was maintained by an outwardly directed cation pump, and the anions were left to look after themselves with the aid of a Donnan equilibrium. Hence the first type of ion pump to develop was one for the active transport of sodium, and the low internal concentration of penetrating anions in the primitive animal cell could be regarded as secondary to the presence of substantial numbers of non-penetrating anions retained inside by virtue of their size, and the setting-up of a negative internal potential by the operation of the sodium pump to keep out chloride and bicarbonate.

Although it is not necessary to invoke a primary mechanism for the active transport of anions in order to account for their asymmetrical distribution in many types of cell, this does not mean that such an asymmetry is physiologically unimportant. One example of a situation where it comes into play is in the role of the red blood cell in transporting carbon dioxide from

the tissues to the lungs. In order to use the carrying capacity of the blood to the full, it is necessary for the equilibration of chloride and bicarbonate between cells and plasma to be complete within the period of less than a second that the blood spends in the capillaries at either end of its journey. The exchange of anions across the membrane of the red blood cell has therefore to be extremely rapid, and several of our speakers will be concerned with the molecular mechanism involved.

In certain excitable tissues there are ion-conducting channels selective for chloride in the membrane. Thus in striated and cardiac muscle fibres the relatively high chloride permeability of the membrane is functionally important in relation to the mechanisms of excitation-contraction coupling and repetitive firing, while the operation of inhibitory synapses in both vertebrates and invertebrates depends on the activation by chemical transmitters of chloride channels located in the postsynaptic membrane. Examples of the functioning of various types of chloride channel will be discussed later in the meeting.

Turning to the active transport of chloride, it appears that in plant cells the primary transport process may well involve anions rather than cations, the situation possibly differing from that in animal cells because of their tough cell walls. This afternoon we shall therefore give the floor to the plant physiologists to tell us about chloride movements in giant algal cells and elsewhere in the plant kingdom.

Tomorrow morning we shall consider some of the important new findings on the role of cotransport of anions and cations as an electrically neutral complex in isolated mammalian cells and in epithelial cells. Finally, we shall try to see how the several different mechanisms for the transfer of anions across individual cell membranes are put together in the functioning of various types of secretory epithelium.

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