

modalities of the same molecular apparatus, this is not very likely since all efforts to select alternative translocation modes of the red cell Ca pump have so far failed.

Over the past few years however, evidence that ATP is involved in the extrusion of Ca in squid axons has been interpreted as indicating interaction between ATP and the Na:Ca countertransport mechanism. An interesting alternative is that Ca extrusion is in fact mediated by red-cell-type pumps in most if not all, cells, and that the Na:Ca countertransport, when present, operates in parallel with this pump, either as an extra Na or extra Ca 'pump' depending on the relative electrochemical gradients of these two ions. (Mullins in *Membrane Transport Processes* 2, 371 (eds Tosteson, Ovchinnikov & Latorre) (Raven Press, 1978)). Some support for this view has been provided by the elegant experiments of DiPolo (*Nature* 274, 390; 1978) who has shown that in the absence of Na gradients there is an ATP-dependent uphill extrusion of Ca across the squid-axon membrane, a convenient tissue for research on the Na:Ca countertransport.

But the real distribution of plasma-membrane Ca pumps has yet to be determined. However, recent findings concerning the red cell (Mg+Ca) ATPase can be applied to the reinvestigation of Ca pump distribution.

Although (Ca+Mg) - stimulated ATPase activity has been reported in microsomal preparations of many origins, what makes the widespread existence of red-cell-type Ca pumps so uncertain is the lack of specific Ca pump inhibitors; the highly compartmentalised distribution of Ca in nucleated cells which complicates the interpretation of Ca-flux data in intact cells; and the bewildering variability of kinetic parameters of the Ca-stimulated microsomal ATPases which contrasts with the invariance exhibited by other ATPases associated with ionic pumps like the Na pump or the sarcoplasmic reticulum Ca pump.

Similar variability is also exhibited by the red cell Ca pump. Minor differences in the treatment of intact cells and in the preparation of the resealed ghosts or membrane fragments, can produce changes in the apparent K_m for Ca of nearly three orders of magnitude (from, say, 1 μ M to 1 mM) as well as up to 40-fold differences in V_{max} . Similar inconsistency among enzymes of different origin is hardly proof of identity but if we understood the reasons for the variability of the red cell (Ca+Mg) ATPase we might learn how to obtain consistent behaviour and try the trick on the other

enzymes.

Recent experiments with the red cell (Ca+Mg)ATPase suggest two main reasons for the observed variability. In 'broken' membrane preparations, the ATPase activity is, at least in part, associated with vesicular membrane fragments. Although these vesicles must be substantially more permeable to Ca than the original membrane, the maximum rate of Ca extrusion through the pump is so high that it can easily exceed the rate at which Ca can be supplied to the pump from outside the vesicles. Under these conditions Ferreira (thesis, Cambridge University, 1977) has pointed out that the actual Ca concentration inside the population of vesicles with normal topology might be considerably lower than that in the bulk medium. The apparent Ca affinity would therefore look lower than the true Ca affinity of the pump and the kinetics of Ca activation might also be considerably distorted depending on the proportion of membrane area forming right-side out vesicles. The ionophore A23187 is known to incorporate readily into red cell membranes increasing their effective Ca permeability. When this ionophore was added to red cell (Ca+Mg)ATPase preparations having a low apparent Ca affinity, Scharff and Foder (*Biochim. biophys. Acta* 483, 416; 1977) found that the high Ca affinity believed to represent the true affinity of the undisturbed enzyme was often, but not always, fully recovered. Vesicle artefacts of this nature, therefore, seem to be able to account for at least part of the variability observed with the red cell enzyme.

An additional explanation is provided by recent findings from Gopinath

and Vincenzi (*Biochem. biophys. Res. Commun.* 77, 1203; 1977) which confirm the existence in the red cell cytoplasm of large amounts of a polypeptide, possibly identical to the phosphodiesterase activator purified from brain tissues, which can bind reversibly to the internal surface of the membrane and interact with the red cell Ca pump in such a way as to produce a marked increase in the Ca affinity (and the V_{max} ?) of low-affinity enzyme preparations. The conditions which control the formation or breakdown of the activator-pump complex, both in the intact cell under physiological or experimental conditions and in enzyme preparations, are still poorly understood; and so is the potential physiological role of the activator as a regulator of Ca transport. But what seems clear is that the association is weak and reversible and can easily be altered by minor differences in the treatment of intact cells or membrane fragments thus inducing variability.

One can now apply this knowledge and also that derived from the characterisation of a phosphorylated intermediate of the red cell Ca pump (Schatzman & Burgin, *Ann. N.Y. Acad. Sci.*, in the press) to re-investigate the properties of the (Mg+Ca)ATPase in microsomal preparations of different origins, this time by measuring the enzymic activity in the presence of ionophore and activator and by comparing the Ca phosphorylation product with that of red-cell membrane fragments. This should help establish whether failure of identification rather than genuine absence is the cause of the uncertainty surrounding Ca pump distribution. □



A hundred years ago

WE have received from Messrs. Eberstein, of Dresden, a specimen of an interesting "walking-stick for naturalists or tourists." The stick is a perfect *multum in parvo*, and contains quite a museum of scientific instruments. The handle alone contains a compass, a double magnifying glass, or pocket microscope, and a whistle. Below it there is a thermometer on one side of the stick and a sand-glass on the other. The body of the stick is partly hollow, and in its interior holds a small bottle, which is intended to contain chloroform or ether for killing insects. Along the outside of the body there is a half-metre measure, showing decimetres and centimetres. Near the end of the stick a knife-blade may be

opened, which serves for cutting off objects which cannot be reached by hand, such as aquatic plants, &c. At the extreme end a screw may hold in turn a spade (for botanists), a hammer (for geologists or mineralogists), a hatchet, or a strong spike, which would be of great use on glaciers. The whole is neatly finished in black polished wood.

DR. SCHLIEMANN is at Constantinople, and intends resuming his excavations in the Troad if he can obtain from the Porte fifty soldiers as a guard against robbers. From Berlin it is stated that a summary account of the German excavations at Olympia says that the number of marble objects found during the last three winters is 904; of bronzes, 3,734; of terra cottas, 904; of inscriptions, 429; and of coins, 1,270. All the more important ruins have been photographed, and the third volume of the official account is about to appear. An exhibition of all the casts taken will shortly be opened at Berlin.

From *Nature* 18, 1 August, 372; 1878.