The Influence of Potassium- and Sodium-Free Solutions on Sodium Efflux from Squid Giant Axons

R. A. SJODIN and L. A. BEAUGE

From the Department of Biophysics, University of Maryland School of Medicine, Baltimore, Maryland 21201, and the Marine Biological Laboratory, Woods Hole, Massachusetts 02543. Dr. Beaugé's present address is Instituto de Investigacion Medica, Mercedes y Martin Ferreyra, Cordoba, Argentina.

ABSTRACT The sensitivity of sodium efflux to the removal of potassium ions from the external solution and the change in sodium efflux occurring when sodium ions are also removed were observed to be related. When Tris was used to replace external sodium ions, increases in sodium efflux were always observed whether the sensitivity of sodium efflux to external potassium ions was weak or strong. Greater percentage increases in sodium efflux occurred, however, the greater the sensitivity of sodium efflux to external potassium ions. When lithium ions were used to replace external sodium ions, increases in sodium efflux occurred if the sensitivity of efflux to external potassium ions was strong whereas decreases in sodium efflux took place if the sensitivity of efflux to external potassium ions was weak. Intermediate sensitivities of efflux to external potassium resulted in no change in efflux upon substitution of lithium ions for external sodium ions. In the presence of 10^{-5} M ouabain, substitution of Tris for external sodium ions always resulted in a small decrease in sodium efflux. The data can be described in terms of a model which assumes the presence of efflux stimulation sites that are about 98% selective to potassium ions and about 2% selective to sodium or lithium ions.

INTRODUCTION

The ratio of the magnitude of sodium efflux in K-free seawater to that in 10 mM K seawater, the "K-free effect," varies in squid giant axons between the extremes of 0.2 and 0.8 (Hodgkin and Keynes, 1955; Caldwell et al., 1960; Sjodin and Beaugé, 1967, 1968 *a*; Mullins and Brinley, 1967). The response of sodium efflux to the removal of external sodium ions also varies in squid giant axons (Hodgkin and Keynes, 1955; Frumento and Mullins, 1964; Keynes, 1965; Mullins and Brinley, 1967; Sjodin and Beaugé, 1967, 1968; Baker, 1968). The purpose of this investigation was to see whether these variations are in any way correlated.

TABLE I

THE EFFECTS OF SUBSTITUTING LITHIUM IONS FOR EXTERNAL SODIUM IONS ON THE RATE CONSTANT FOR LOSS OF ^{24}Na

Axon diameter	Rate constant for ^{24}Na loss			Change in rate constant from Na to Li	Ratio $\left(\frac{0\ K}{10\ K}\right)_{Na}$
	10 mM K Na S.W.	K-free Na S.W.	K-free Li S.W.		
μ	$min^{-1} \times 10^{-3}$				
460	5.24	3.67	3.60	−0.07	0.70
500	5.40	4.00	2.40	−1.60	0.74
460	5.10	2.40	3.22	+0.82	0.47
440	4.57	3.15	3.13	−0.02	0.69
410	5.55	5.00	4.35	−0.65	0.90
500	4.16	2.91	2.91	0.00	0.70
510	3.98	2.79	1.17	−1.62	0.70
510	5.01	3.36	2.97	−0.39	0.67
513	3.33	2.73	2.22	−0.51	0.82
510	4.14	1.57	2.57	+1.00	0.38
510	5.42	3.47	3.40	−0.07	0.64
540	5.76	2.13	3.30	+1.17	0.37
460	5.87	3.35	2.68	−0.67	0.57
460	5.50	3.69	4.13	+0.44	0.67
410	2.19	1.07	1.47	+0.40	0.49
420	4.05	1.74	1.93	+0.19	0.43
400	3.38	1.52	2.64	+1.12	0.45
400	5.03	3.17	3.04	−0.13	0.63
410	3.37	1.99	2.13	+0.14	0.59
410	2.87	2.35	2.54	+0.19	0.82
460	3.23	1.91	2.14	+0.23	0.59
460	4.40	1.45	2.07	+0.62	0.33
440	2.70	1.38	1.50	+0.12	0.51

METHODS

Giant axons from the squid, *Loligo pealei*, were cleaned of surrounding small nerve fibers and microinjected with ^{24}Na. The method of microinjection and determination of sodium efflux was the standard method described previously (Hodgkin and Keynes, 1956; Caldwell et al., 1960; Brinley and Mullins, 1965; Sjodin and Beaugé, 1967, 1968). The external perfusion solutions used have been described by Sjodin and Beaugé (1967, 1968 *a*). The seawater in which Tris was substituted for NaCl contained 70% neutralized Tris base osmotically matched to 423 mM NaCl with a resultant pH of 7.9. The flow of external perfusion medium was controlled at a rate of 1.9 cc per min using a Harvard Apparatus infusion pump (Harvard Apparatus Co., Inc., Dover, Mass.). Experiments were performed at a temperature of 15°C. All axons studied had resting membrane potentials of at least −60 mv. All axons were excitable and gave propagated action potentials throughout the experiments.

TABLE II

THE EFFECTS OF SUBSTITUTING TRIS FOR EXTERNAL SODIUM IONS ON THE RATE CONSTANT FOR LOSS OF ^{24}Na

	Rate constant for ^{24}Na loss					
Axon diameter	10 mM K Na S.W.	K-free Na S.W.	K-free Tris S.W.	10 mM K Tris S.W.	K-free Na S.W. 10^{-5} M ouabain	K-free Tris S.W. 10^{-5} M ouabain
μ			$min^{-1} \times 10^{-3}$			
410	2.87	2.38	4.51			
460	3.23	1.95	4.84			
460	2.50	1.91			1.69	0.88
410	2.70	1.44	3.85		1.22	0.83
490	1.81	1.14	2.64		1.10	0.87
400	3.47	0.65	3.21	5.05		
400	3.23	2.47	4.84	5.86		
440	2.93	1.45			1.40	1.09
Mean	2.84	1.67	3.98	5.46	1.35	0.92

RESULTS

The effect of removing K ions from normal seawater was compared with the effect of removing Na ions under K-free conditions for each axon studied. The rate constants for loss of ^{24}Na measured in each solution using lithium and Tris as sodium substitutes are presented in Tables I and II. In the cases in which Tris was used as a sodium substitute, the influence of 10^{-5} M ouabain on the results was also determined. A typical experiment is illustrated in Fig. 1.

The results presented in Table I indicate that both increases and decreases in sodium efflux were observed when lithium ions were used to replace sodium ions. Furthermore, the data show that all decreases in sodium efflux occurred in axons in which the K-free effect was less than a 50% reduction in efflux. All increases in efflux with an increment in rate constant of $+1.00 \times 10^{-3}$ min^{-1} or greater, on the other hand, occurred in axons showing a K-free reduction of 55% or greater. All decreases in efflux having a decrement in rate constant of -1.00×10^{-3} min^{-1} or greater occurred in axons showing a K-free reduction of 30% or less. The Na-free effect in lithium seawater appears to be correlated with the potassium sensitivity of sodium efflux.

The data obtained using Tris as a sodium replacement indicate that only increases in sodium efflux occur in the Na-free medium over a wide range in the potassium sensitivity of sodium efflux. The absolute values of the increments in rate constant observed are rather uniform. The percentage increases in efflux, however, vary and are larger for the cases in which the percentage reductions in efflux occurring in the K-free effect are larger.

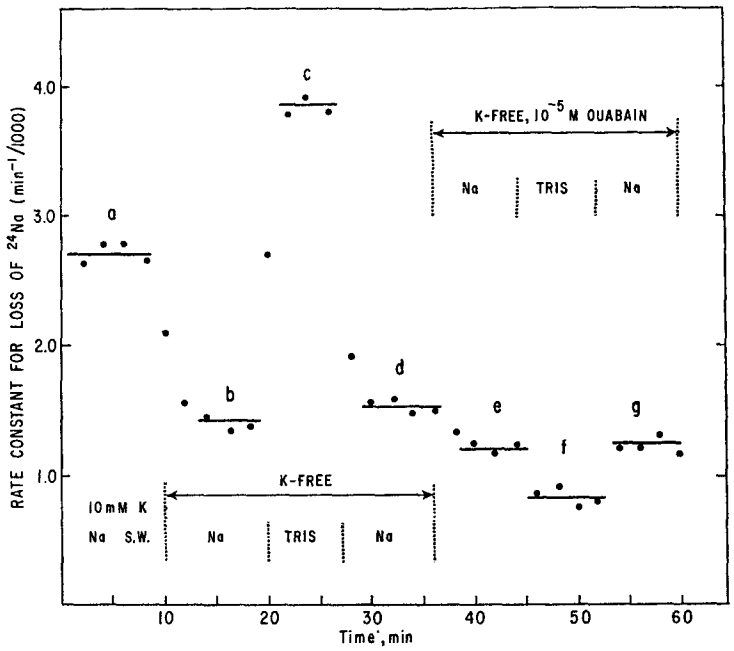

FIGURE 1. The results of a typical experiment in which Tris was substituted for external sodium ions are illustrated. The rate constant for ^{24}Na loss is plotted vs. time in each experimental solution: (*a*) 10 mM K, Na S.W.; (*b*) 0 K, Na S.W.; (*c*) 0 K, Tris S.W.; (*d*) 0 K, Na S.W.; (*e*) 0 K, Na S.W. + 10^{-5} M ouabain; (*f*) 0 K, Tris S.W. + 10^{-5} M ouabain; (*g*) 0 K, Na S.W. + 10^{-5} M ouabain.

The rate constant for loss of ^{24}Na to normal 10 mM K seawater is subject to normal variation. The Tris substitution experiments were performed on axons from a single batch of squid. The average rate constant is close to 3 units while the average for 23 axons in the lithium experiments is close to 4 units. It is of interest to normalize the data by plotting fractional changes in rate constant. In Fig. 2, the Na-free effect is plotted vs. the K-free effect for both sets of data. The linear relation shown by the least squares fit to the lithium data has a correlation coefficient of −0.8.

DISCUSSION

The main feature of the results obtained is the relative variability of the magnitude of sodium efflux in K-free, sodium seawater compared with the relative constancy of sodium efflux observed in the other solutions. When sodium efflux is expressed on a fractional basis, these facts are sufficient to account for the form of the curves in Fig. 2.

The variation in the potassium sensitivity of sodium efflux could arise in various ways. It seems likely that, in K-free media, potassium ions leak into

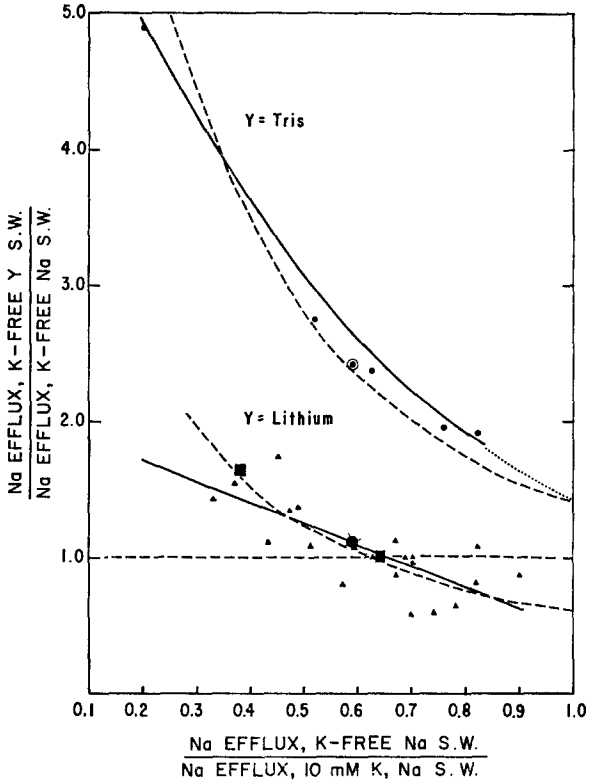

FIGURE 2. The Na-free effect is plotted vs. the K-free effect for each axon studied. The solid line through the points determined in lithium seawater is a least squares linear fit to the data having a correlation coefficient of -0.8 ($y = 2.02 - 1.53\ x$). The solid line through the upper set of points obtained in Tris-substituted seawater represents a least squares fit to a second-order polynomial, the equation for which is: $y = 3.01\ x^2 - 4.44\ x$. The broken line through the upper set of points is a plot of the equation $xy = 1.4$. The broken line through the lower set of points is a plot of the equation $xy = 0.62$. The latter two hyperbolic relations are discussed in the Appendix. ◉ and ◙ are points obtained for the same axon. Also, ■ denotes points obtained for the same axon.

the mesaxon and Schwann cell spaces from the interior of the axon (Baker et al., 1969 *b*) causing some K^+ to accumulate in these regions. If the effective external potassium ion concentration contributed by this source varied much from axon to axon, variable K-free effects would, of course, be expected. Though this mechanism cannot be definitely ruled out, final analytical values for axoplasmic potassium contents obtained by flame photometry did not indicate large differences in the rate of K leakage from the cells. Another possible reason for the variable K-free effects may lie in variations in the metabolic states of the axons which are undetectable by the methods applied.

An attractive hypothesis is that the observed results are due to variations in

the affinity of membrane sites for sodium ions. It is well-known that external sodium ions exert an inhibitory action at the membrane sites where K^+ stimulates outward sodium transport (Baker and Connelly, 1966; Baker, 1968). If the degree of inhibition varied due to a variation in the affinity of the sites for sodium ions, some of the observed results would be expected. The analysis to follow is made in order to determine within what range the affinity for sodium ions would have to vary to account for the observed variability.

The inhibitory action of external sodium ions on sodium efflux may be visualized in terms of a model in which sodium and potassium ions compete for occupancy of sites at the outer membrane surface. It is supposed that stimulation of sodium transport normally occurs when potassium ions occupy the sites. A mathematical basis for such a model is considered in the Appendix. Under normal conditions, it is supposed that relatively little stimulation of sodium efflux occurs when the sites are occupied by sodium ions and that the sensitivity of sodium efflux to external potassium ions is high. Even though the affinity of the sites for potassium ions is apparently about 35 times greater than that for sodium ions, a considerable increase in sodium efflux upon removal of external sodium ions is predicted by the model because the concentration of external sodium ions is about 40 times greater than that of external potassium ions. If, because of normal variation or other factors, the relative affinity of the sites for sodium ions is higher than stated, the sensitivity of sodium efflux to external potassium ions declines. The differences between results obtained with Tris and with lithium substitution are attributed to finite affinity of the sites for lithium ions while a negligible affinity for Tris ions is assumed. The direction of the change in sodium efflux occurring when lithium ions are substituted for external sodium ions depends on whether the action of lithium ions at the sites is more or less K^+-like than the action of sodium ions. A low sensitivity of sodium efflux to the presence of external potassium ions could come about as a consequence of an elevated affinity of the sites for sodium ions and an increased stimulating effect of sodium ions when occupying the sites. In this case, the model under consideration yields a higher affinity for sodium ions than for lithium ions and predicts a decrease in sodium efflux when lithium ions are substituted for external sodium ions, as observed.

When 10^{-5} M ouabain was present in the bathing medium, substitution of Tris for external sodium ions always resulted in a decrease in sodium efflux. In absolute magnitude, this decrease in efflux was much less than the increase in efflux observed under the same conditions in the absence of ouabain. If one regards the action of ouabain as one of abolishing the operation of a K^+- (and Na^+-) stimulated exchange pump, one might then regard the decrease in sodium efflux occurring in Tris-substituted seawater in the presence of ouabain as an "exchange-diffusion" effect of the type observed in skeletal muscle cells (Keynes and Swan, 1959; Sjodin and Beaugé, 1968 *b*; Beaugé and

Sjodin, 1968; Keynes and Steinhardt, 1968). The effect on sodium efflux of replacing external sodium ions with lithium ions in the presence of ouabain was not studied. Baker (1968), however, has observed "ouabain-insensitive" increases in sodium efflux under these conditions. The ouabain-insensitive sodium efflux that occurs in lithium seawater requires the presence of external calcium ions and is accompanied by an increased calcium influx (Baker et al., 1969 *a*). Part of the increased sodium efflux occurring in lithium seawater may, therefore, be due to a $Na^+:Ca^{++}$ interchange. Quantitatively, however, the amount of calcium influx becomes appreciable only at elevated internal sodium ion concentrations ($[Na]_i > 100$ mM). At the internal sodium ion concentrations determined by flame analysis of axoplasm samples in this work (average $[Na]_i = 75$ mM), the magnitude of calcium influx in lithium seawater would be much smaller than the magnitude of sodium efflux. Much of the lithium-induced sodium efflux observed in the present cases of high potassium sensitivity must be due to another type of interchange, possibly a $Na^+:Li^+$ exchange. This type of interchange could give rise to either increases or decreases in sodium efflux in lithium seawater depending upon the relative rates of $Na^+:Na^+$ and $Na^+:Li^+$ exchange.

There appears to be some resemblance between the present results and those obtained by Beaugé and Sjodin (1968) on sodium-enriched muscle cells. Here a large glycoside-sensitive component of sodium efflux was revealed and a small component due to glycoside-insensitive exchange diffusion. Another similarity is that, in the absence of glycosides, sodium-enriched muscle cells show an increase in sodium efflux when external sodium ions are replaced with lithium ions. Squid giant axons with a high sensitivity of sodium efflux to external potassium ions thus tend to resemble sodium-enriched muscle cells in these respects. On the other hand, squid giant axons with a rather low sensitivity of sodium efflux to external potassium ions tend to resemble muscle cells with a low internal sodium concentration (Sjodin and Beaugé, 1968 *b*). In this case replacing external sodium ions with lithium ions brings about a decline in sodium efflux. Also, squid giant axons with a low potassium sensitivity of sodium efflux show similarities to red blood cells (Garrahan and Glynn, 1967). Cardiac glycosides inhibited sodium efflux from red cells much more than removal of external potassium as observed by Sjodin and Beaugé (1969) in squid giant axons with a reduced sensitivity of sodium efflux to external potassium ions. Relevant to this discussion is the fact that De Weer[1] has been able to reduce the sensitivity of sodium efflux to external potassium ions in squid giant axons by decreasing the internal [ATP] to [ADP] ratio. Also, Caldwell and Schirmer (1965) have presented evidence that the potassium sensitivity of sodium efflux from squid giant axons is related to the free energy available to the sodium pump from ATP splitting. A carrier model with

[1] De Weer, P. 1969. Unpublished thesis results.

varying ionic affinities is not inconsistent with such findings as the membrane carrier sites may alter ionic affinities in accordance with the free energy supply.

Even though some similarities exist among the mechanisms transporting sodium ions in the various tissues mentioned, many significant differences remain as yet unexplained. Also, it is clear that a wide spectrum of modes exists in squid giant axons in which a sodium-potassium–coupled exchange pump may operate. The coupling may apparently vary from about three sodium ions transported outwardly per one potassium ion transported inwardly (Sjodin and Beaugé, 1968 *a*; Mullins and Brinley, 1969) to the situation described in this work where, in K-free Tris seawater, about 30 pmole/cm^2 sec of ouabain-inhibitable sodium efflux occurs when inward potassium transport must be very much reduced.

APPENDIX

Theoretical Considerations

The following assumptions are made. It should be stated that they are reasonable, based on experimental facts, and arbitrary. The aim is a first-order approximation rather than a complete description. It should also be stated that, in applying the model to the results, a separate experiment is used to evaluate each affinity and rate term.

1. A set of sites exists at the outer cell membrane surface that controls the efflux of sodium ions.
2. In the present study, the only cations capable of occupying the sites are K^+, Na^+, and Li^+. The sites have zero affinity for $Tris^+$.
3. Outward transport of sodium ions is stimulated and occurs at different rates when different cations occupy the sites.
4. The sites have discrete affinities for the three cations mentioned. All sites are assumed to have the same affinity for a particular cation. If a distribution of affinities should exist or a small fraction of the sites should have a much different affinity than the rest, an average uniform affinity is still assigned to all the sites.
5. Cooperative effects are regarded as second-order and are ignored as there is no way that they can be assessed from the present data.

The following general equation for sodium efflux, under these conditions, can readily be derived from a previous treatment in which ionic flux was assumed to be proportional to the fraction of sites occupied by a particular cation (Sjodin, 1961).

$$m_{Na} = \frac{k_K A_K([K]_o + \alpha) + k_{Na} A_{Na}[Na]_o}{A_K([K]_o + \alpha) + A_{Na}[Na]_o + 1} \quad (1)$$

Sodium efflux is denoted by m_{Na}, site affinities by A, and external concentrations by bracketed quantities. The quantity k_K represents the magnitude of sodium efflux when all the sites are occupied by potassium ions. This is taken to be the maximum rate of sodium transport and is arbitrarily scaled to unity so that $k_K = 1$. The quantity k_{Na} then represents, on the same scale, the rate at which sodium transport would

TABLE III
RELATIVE AFFINITIES AND RATES
PREDICTED BY MODEL

m_{Na} (0 K, Na S.W.) / m_{Na} (10 K, Na S.W.)	Affinities			Relative rates		
	A_K	A_{Na}	A_{Li}	k_K	k_{Na}	k_{Li}
	$\left(\frac{mM}{l}\right)^{-1}$					
0.30	5.7	0.16	0.27	1.00	0.11	0.28
0.50	5.7	0.22	0.33	1.00	0.24	0.32
0.80	5.7	0.60	0.33	1.00	0.42	0.32

occur if all the sites were occupied by sodium ions. In the absence of the quantity α in the equation, zero sodium efflux would be predicted in K-free Tris seawater. The stimulation of sodium efflux occurring in a K^+- and Na^+-free medium is likely to be due to potassium ions leaking out of the cell and accumulating in a region just outside the membrane. The quantity α represents the effective potassium concentration produced by this means. There is no method to accurately determine this quantity but certainly it must be less than 1.0 mM. It is arbitrarily taken to be 0.5 mM.

Values of the other parameters that fit the data were obtained as follows. The experimentally measured value for sodium efflux occurring in 10 mM K, Tris seawater was taken to be maximal sodium efflux and was scaled to equal 1. All other values for m_{Na} were obtained by scaling appropriate measured values of efflux. The average value of sodium efflux occurring in K-free Tris seawater was used to solve equation (1) for A_K. This quantity was assumed to remain constant in all additional calculations. In each experiment equation (1) gives one equation for the 10 mM K, Na seawater efflux and one equation for the efflux occurring in K-free, Na seawater. The resulting two equations can then be solved simultaneously for A_{Na} and k_{Na}. For each level of potassium sensitivity, a set of parameters consistent with the data can thus be obtained. The same procedure can be applied to the data obtained in lithium-substituted seawater with the additional fact that sodium efflux in 10 mM K, Li seawater does not differ from sodium efflux in 10 mM K, Na seawater (Sjodin and Beaugé, 1967, 1968 *a*). Parameters calculated from data for three values of potassium sensitivity are presented in Table III.

If equation (1) is plotted as a function of $[K]_o$ using constants holding for high potassium sensitivity, curves are obtained which give a satisfactory fit to data reported by Baker (1968) for the cases in which external Na is both present and absent. By postulating a similar transport activation mechanism involving two binding sites, Baker et al. (1969 *b*) obtained a potassium affinity of 4.0, expressed in the units of Table III. It was necessary to postulate that two sites must be occupied by potassium ions for activation to occur because of a slightly sigmoid character of the K-activation curve in the presence of high concentrations of sodium ions. In the present treatment, this region is approximated with simple rectangular hyperbolae. The results of Baker and Connelly (1966) on crab nerve and of Rang and Ritchie (1968) on mammalian nonmyelinated nerve do not appear to deviate from simple hyperbolic

relationships. In frog muscle, the K-activation curve is sigmoid in the presence of external sodium ions (Sjodin and Beaugé, 1968 *b*). However, in the absence of external sodium ions, the K-activation curve in frog muscle is nonsigmoidal.[2] It thus seems possible that a sigmoidal curve is a result of a degree of interaction between potassium and sodium ions in some cases rather than a consequence of two or more binding sites.

There is nothing particularly fundamental about the detailed shapes of the curves in Fig. 2. They are merely a consequence of adopting a very convenient way to plot the data and demonstrate correlation. Nevertheless, the mathematical form of the curves can be predicted. Let the K-free effect given by the coordinates of the abscissa in Fig. 2 be designated x and the Na-free effect plotted as ordinate be designated y. The product xy is found to be the ratio of sodium efflux in K-free Tris seawater to that in 10 mM K normal Na seawater. This ratio was observed experimentally to be rather constant (Table II) and to have an average value of 1.38. The relation $xy = 1.38$ is a hyperbola and the upper broken line in Fig. 2 is a plot of this equation. A similar procedure can be applied to the lithium substitution data to obtain the relation $xy = 0.62$ which is plotted as the lower broken line in Fig. 2.

This work was supported by a grant from the National Institute of Neurological Diseases and Stroke, United States Public Health Service (NB-07626).

Received for publication 7 March 1969.

REFERENCES

BAKER, P. F. 1968. Recent experiments on the properties of the Na efflux from squid axons. *J. Gen. Physiol.* **51**(5, Pt. 2): 172 s.

BAKER, P. F., M. P. BLAUSTEIN, A. L. HODGKIN, and R. A. STEINHARDT. 1969 *a*. The influence of calcium on sodium efflux in squid axons. *J. Physiol.* (*London*). **200**:431.

BAKER, P. F., M. P. BLAUSTEIN, R. D. KEYNES, J. MANIL, T. I. SHAW, and R. A. STEINHARDT. 1969 *b*. The ouabain-sensitive fluxes of sodium and potassium in squid giant axons. *J. Physiol.* (*London*). **200**:459.

BAKER, P. F., and C. M. CONNELLY. 1966. Some properties of the external activation site of the sodium pump in crab nerve. *J. Physiol.* (*London*). **185**:270.

BEAUGÉ, L. A., and R. A. SJODIN. 1968. The dual effect of lithium ions on sodium efflux in skeletal muscle. *J. Gen. Physiol.* **52**:408.

BRINLEY, F. J., JR., and L. J. MULLINS. 1965. Ion fluxes and transference numbers in squid axons. *J. Neurophysiol.* **28**:526.

CALDWELL, P. C., A. L. HODGKIN, R. D. KEYNES, and T. I. SHAW. 1960. The effects of injecting "energy rich" phosphate compounds on the active transport of ions in the giant axons of *Loligo*. *J. Physiol.* (*London*). **152**:561.

CALDWELL, P. C., and H. SCHIRMER. 1965. The free energy available to the sodium pump of squid giant axons and changes in the sodium efflux on removal of the extracellular potassium. *J. Physiol.* (*London*). **181**:25P.

FRUMENTO, A. S., and L. J. MULLINS. 1964. Potassium-free effect in squid axons. *Nature.* (*London*). **204**:1312.

GARRAHAN, P. J., and I. M. GLYNN. 1967. The behaviour of the sodium pump in red cells in the absence of external potassium. *J. Physiol.* (*London*). **192**:159.

HODGKIN, A. L., and R. D. KEYNES. 1955. Active transport of cations in giant axons from *Sepia* and *Loligo*. *J. Physiol.* (*London*). **128**:28.

[2] Sjodin, R. A. 1969. Unpublished observations.

HODGKIN, A. L., and R. D. KEYNES. 1956. Experiments on the injection of substances into squid giant axons by means of a microsyringe. *J. Physiol.* (*London*). **131**:592.

KEYNES, R. D. 1965. Some further observations on the sodium efflux in frog muscle. *J. Physiol* (*London*). **178**:305.

KEYNES, R. D., and R. A. STEINHARDT. 1968. The components of the sodium efflux in frog muscle. *J. Physiol.* (*London*). **198**:581.

KEYNES, R. D., and R. C. SWAN. 1959. The effect of external sodium concentration on the sodium fluxes in frog skeletal muscle. *J. Physiol.* (*London*). **147**:591.

MULLINS, L. J., and F. J. BRINLEY, JR. 1967. Some factors influencing sodium extrusion by internally dialyzed squid axons. *J. Gen. Physiol.* **50**:2333.

MULLINS, L. J., and F. J. BRINLEY, JR. 1969. Potassium fluxes in dialyzed squid axons. *J. Gen. Physiol.* **53**:704.

RANG, H. P., and J. M. RITCHIE. 1968. On the electrogenic sodium pump in mammalian non-myelinated nerve fibres and its activation by various external cations. *J. Physiol.* (*London*). **196**:183.

SJODIN, R. A. 1961. Some cation interactions in muscle. *J. Gen. Physiol.* **44**:929.

SJODIN, R. A., and L. A. BEAUGÉ. 1967. The ion selectivity and concentration dependence of cation coupled active sodium transport in squid giant axons. *Curr. Mod. Biol.* (*Amsterdam*). **1**:105.

SJODIN, R. A., and L. A. BEAUGÉ. 1968*a*. Coupling and selectivity of sodium and potassium transport in squid giant axons. *J. Gen. Physiol.* **51**(5, Pt. 2):152 s.

SJODIN, R. A., and L. A, BEAUGÉ. 1968*b*. Strophanthidin-sensitive components of potassium and sodium movements in skeletal muscle as influenced by the internal sodium concentration. *J. Gen. Physiol.* **52**:389.

SJODIN, R. A., and L. A. BEAUGÉ. 1969. Ouabain sensitivity of sodium efflux from squid giant axons in K- and Na-free solutions. Abstracts of the Biophysical Society 13th Annual Meeting. Los Angeles, California. A-162.