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SODIUM CURRENTS IN THE MYELINATED NERVE FIBRE OF *XENOPUS LAEVIS* INVESTIGATED WITH THE VOLTAGE CLAMP TECHNIQUE

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It has previously been shown (Dodge & Frankenhaeuser, 1958) that the nodal membrane of frog nerve fibres responds to stepwise changes of membrane potential with a flow of current strikingly similar to that which occurs in the squid giant axon (Hodgkin & Huxley, 1952*a*, *b*, *c*, *d*; Hodgkin, Huxley & Katz, 1952). A cathodal step is associated with an initial transient current followed by a delayed lasting outward current. The variation of the amplitude of the initial current with membrane potential, the definite potential at which the initial current changes direction, the dependence of this potential on the external sodium ion concentration, and the variation of the nodal action potential with sodium concentration (Huxley & Stämpfli, 1951), suggest that the initial current of the nodal membrane is indeed a sodium current, as it is in the squid giant axon (Hodgkin & Huxley, 1952*a*).

In the present investigation it will be shown that the effect of changing the external sodium ion concentration is quantitatively consistent with the idea that the nodal membrane, when depolarized, undergoes a transient large increase in its sodium permeability, that this permeability depends on the membrane potential, but not on the sodium concentration, and that the initial current is a flow of sodium ions moving passively down the electrochemical gradient for sodium. Further quantitative analysis of the voltage clamp data will be published later.

METHODS

Preparation. The experiments were made on large (25–30 μ) single myelinated fibres dissected from the sciatic nerve of the clawed toad (*Xenopus laevis*), and were carried out at room temperature (19–22° C).

Solutions with two different sodium concentrations were used. Sodium was replaced by either choline chloride or sucrose in the solutions with low sodium concentration. The compositions of

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the solutions were: (mM) '100% Na'—NaCl 112·0, KCl 2·5, $CaCl_2$ 2·0, $NaHCO_3$ 2·5; '37% Na'—NaCl 39·9, KCl 2·5, $CaCl_2$ 2·0, $NaHCO_3$ 2·5, choline chloride 72·1; '37% Na'—NaCl 39·9, KCl 2·5, $CaCl_2$ 2·0, $NaHCO_3$ 2·5, sucrose 144·2.

Voltage clamp. The isolated fibre was mounted in a Perspex chamber which had four pools of Ringer's solution separated by three transverse partitions, and the fibre was sealed with petroleum jelly at the partitions. Changes in the membrane potential of the node under investigation were measured with external electrodes by an amplifier system using negative feedback through the fibre. The membrane was clamped to rectangular step potential changes by a second amplifier system, as previously described in detail (Dodge & Frankenhaeuser, 1958). Fibres from *Xenopus laevis* were used for these experiments because the lower series impedance of the internode, due to the large fibre diameter, diminished the time of 'ringing' in the voltage clamp system. The resolution of the time course of the membrane currents was therefore increased compared to that attained with the fibres from *Rana esculenta.* In addition, it was much easier to maintain the *Xenopus* in uniformly good condition in the laboratory throughout the year. One artifact, not previously discussed, needs to be mentioned. When the fibre was enclosed in very tight petroleum jelly seals, the apparent membrane capacitance of the node was observed to increase slowly during a long experiment to as much as ten times its value at the beginning of the experiment. Examination of such fibres with a microscope revealed signs of constriction at the site of the seals, which were easier to observe on the larger *Xenopus* fibres than on the *Rana esculenta* fibres, but which were present on both. These effects were diminished or absent when the seals fitted less tightly. Surface tension forces in the capillary, formed in the petroleum jelly around the fibre, may have distorted the myelin so as to increase the capacitance of the internode. A number of fats and waxes were tested without success in attempts to avoid this difficulty. The artifact did not have an appreciable effect on the ionic currents of a voltage-clamped node, but resolution of rapid changes in the ionic current at short times after a change in the membrane potential was lost in the large capacitative surge. Although the artifact was greatly reduced with looser seals, the resulting drift and noise in the potential measuring system, which vary inversely with seal resistance (Frankenhaeuser, 1957), were then disturbing. We therefore chose to use tight seals and to do the experiments quickly before the artifact became appreciable.

Current calibration. The scale for the current measurements was calculated according to eqn. (1) in Dodge & Frankenhaeuser (1958): $I_m = V_{ED}/A_N Z_{ED}$. V_{ED} was measured as the output of the feedback amplifier. $A_N Z_{ED}$ was taken as 32 $\Omega.cm^2$ when the solution in pool E was cocaine Ringer's solution, or as 22·5 $\Omega.cm^2$ when isotonic KCl was used. (These figures were obtained in the following way: the relation between axis cylinder diameter and outside diameter was assumed to be 0·6 (Rushton, 1951); the specific resistance of the axis cylinder was assumed to be 110 Ω.cm (Stämpfli, 1952); the nodal gap width was taken as $2{\cdot}5 \times 10^{-4}$ cm, since gap width was found to be independent of fibre diameter and this figure is the mean of measurements on 63 fibres; internodal length was taken as 0·23 cm, 0·30 and 0·15 being the extreme values observed; the ratio of the resting nodal membrane resistance to the internodal resistance was measured as about 3:1; the ratio of the nodal resistance when the node was in KCl to the internodal resistance was measured as about 0·75:1.)

Nomenclature. Potentials are given as inside potential minus outside potential, and outward current as positive. E is used for absolute values of potentials. V is used for potentials relative to the resting potential, thus $V = E - E_r$.

RESULTS

The first aim of this investigation was to find out whether or not the equilibrium potential for the initial current could be identified with the sodium equilibrium potential. The sodium equilibrium potential (V_{Na}) should shift when external sodium concentration $[Na]_o$ is altered, with a value predicted

by the well-known Nernst equation, provided that the measurements are made so rapidly that the internal sodium concentration remains unchanged during the measurement.

The equilibrium potential for the initial current is here defined as the potential at which the current record, after corrections for capacity current, starts with zero slope showing a hump neither of inward nor of outward current (cf. Hodgkin & Huxley, 1952*a*). It was first determined by interpolation between records taken close to the potential where the initial current reversed in direction, as in Fig. 1 for pulses between 114 and 171 mV. This method was

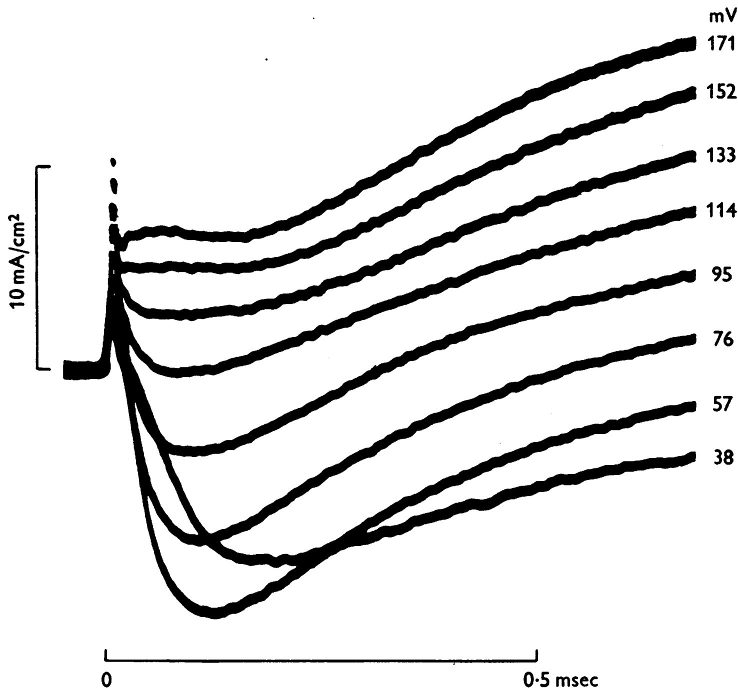

Fig. 1. Records of membrane currents associated with cathodal step voltage changes. Traces superimposed during experiment. Potentials during step marked. Potential kept at V = 0 for about 1·5 sec between steps; time and current calibration marked; outward current positive (upward); temp. 22° C. Axon 3 in Table 1.

tedious and in later experiments another method was as a rule adopted: the peak initial currents were plotted against the membrane potential during the step (see Fig. 2), and the steady-state currents for anodal pulses were also plotted. It was found that the equilibrium potential measured with the first method agreed to within 2 or 3 mV with the value obtained by noting where the straight line through the anodal points (interrupted line in Fig. 2) intersected the curve of the initial peak currents. This second method was

based on the assumption that the non-specific leak current through the membrane was linearly proportional to the size of the potential step. Although this may not be strictly true, the agreement between the two methods showed that the second one was sufficiently accurate for practical measurements of the equilibrium potential.

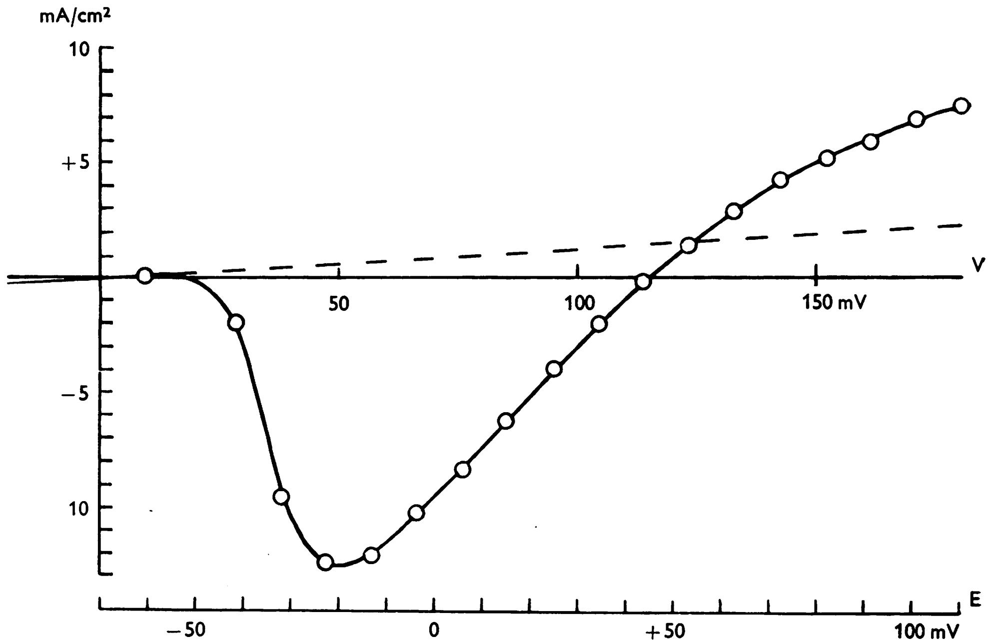

Fig. 2. Peak initial currents plotted against the membrane potential during the step. From records of Fig. 1 and others taken at intermediate steps. A smooth curve is drawn through the plotted points. The interrupted line is extrapolated from records with anodal polarizations.

The equilibrium potential (for simplicity called V_{Na}) was determined from voltage clamp runs with the appropriate solution surrounding the node under investigation. The solution was changed between the runs, and mean values were obtained in each experiment for V_{Na} and for the shift (ΔV_{Na}) of V_{Na} (i.e. V_{Na} in solution with 100% Na minus V_{Na} in solution with 37% Na). In Table 1 these measurements are presented as obtained in six experiments. The theoretical value calculated from the Nernst equation for ΔV_{Na} is 25 mV for the change 100% $[Na]_o$ to 37% $[Na]_o$. The mean experimental value of 20·9 mV was lower than the theoretical value, but there were two systematic errors, both of which had the effect of giving a measured value that was less than the true value. The first error was that caused by the attenuation in the voltage recording system (see Dodge & Frankenhaeuser, 1958, p. 81). This error certainly varied from experiment to experiment and was judged to be 5–20%, i.e. 1–4 mV. The second error was introduced because the amplifier

had to be rebalanced between the runs, except in Expt. 1, and the small hyperpolarization of about 3 mV caused by the low sodium solution was neglected in this procedure. The conditions in Expt. 1 were exceptionally stable, because of particularly tight seals, allowing solution changes and clamp runs without any adjustment of amplifier balance; attenuation was judged to be negligible, and the clamp amplifier compensated automatically for the hyperpolarization in the low sodium solution. The ΔV_{Na} of 24·4 mV obtained in this experiment therefore required no significant correction, while the other measured values were estimated to be 3–7 mV too low on account of the errors.

TABLE 1

Axon	Na substitute	100% Na V_{Na} (mV)	37% Na V_{Na} (mV)	ΔV_{Na} (mV)	S.D. for ΔV_{Na} (mV)
1	Choline	116·8	92·4	24·4	1·50
2	Choline	130·6	109·5	21·4	0·95
3	Choline	125·8	105·7	20·0	0·82
4	Sucrose	130·5	112·5	18·0	2·25
5	Sucrose	128·5	107·4	21·1	2·32
6	Sucrose	125·4	105·0	20·4	0·75
	Mean	126·3	105·4	20·9	

The experimental shift of V_{Na} thus seemed almost to have the theoretical value of 25 mV. This indicated that the total membrane current at the time of the peak of the initial current was, almost exclusively, sodium current and a non-specific leak current that was proportional to the voltage step and was independent of sodium concentration.

It was previously pointed out that a plot of the peak initial currents (in *Rana esculenta* fibres) against the potential during the step is essentially similar to a corresponding plot of the sodium currents in the squid fibre (Dodge & Frankenhaeuser, 1958). The most striking difference is that, for large pulses with a normal external sodium concentration, the current in the squid fibre is linearly proportional to the membrane potential (Hodgkin & Huxley, 1952*a*), whereas the current plot is clearly curved in this region in the *R. esculenta* fibres (Dodge & Frankenhaeuser, 1958, Fig. 5). The *Xenopus* fibres showed a current–voltage relation (Figs. 2 and 5) very similar to that of the *R. esculenta* fibres.

If the peak sodium conductance (g_{Na}), defined as the sodium current divided by the driving potential for sodium, ($g_{Na} = I_{Na}/V - V_{Na}$), is calculated from the current–voltage relation, it is clear that g_{Na} for a pulse of 180 mV would only be about 40–50% of g_{Na} for a pulse of 65 mV. The sodium conductance–membrane potential curve thus had a maximum at about 65 mV and decreased appreciably at higher pulse amplitudes. An effect of this kind could appear if the ratio between the time constant with which sodium conductance is turned on, and the time constant with which the sodium conductance is inactivated, greatly decreases for large pulses, or, in other words, if inactivation for large

pulses were so rapid that the sodium conductance was largely inactivated before it was fully turned on. But g_{Na} could also be derived in another way, by measuring the instantaneous conductance when the cathodal pulse was interrupted at the peak of the sodium current (see Hodgkin & Huxley, 1952*b*; Dodge & Frankenhaeuser, 1958, Fig. 9). Such measurements suggested that sodium conductance did decrease for 180 mV pulses to about 80% of its maximum value, but showed clearly that it was well above the 40–50% value.

In the latter case the calculation of g_{Na} was based on the measurement of inward current only, whereas in the former case it was based on the measurement of inward currents at pulses smaller than V_{Na}, and outward currents at pulses larger than V_{Na}. It is well known that simple semipermeable membranes show a kind of rectification such that the currents are larger at corresponding driving potentials $(V-V_{Na})$ when the ions passing through the membrane move from a solution of high ionic concentration to a solution of low concentration, than when the ions move in the reverse direction. The ion concentration in the membrane itself is larger, and the membrane conductance higher, in the first situation, and the rectification is explained by the different membrane concentrations (Goldman, 1943; Hodgkin & Katz, 1949; Teorell, 1949). The next step was, therefore, to check whether the 'rectification' at large pulses could be accounted for by some simple treatment that would take into consideration the concentration within the membrane. The 'constant field equation' as described by Goldman (1943) and by Hodgkin & Katz (1949) was applied to the data. The equation that was used is:

$$I_{Na} = P_{Na}\frac{F^2E}{RT}[Na]_o\frac{\exp\{(E-E_{Na})F/RT\}-1}{\exp\{EF/RT\}-1}, \qquad (1)$$

where I_{Na} is sodium current, E is absolute value of membrane potential at the time of measurement of current, E_{Na} is sodium equilibrium potential, $[Na]_o$ is external sodium concentration, R is the gas constant, T the absolute temperature, F is the Faraday and P_{Na} is the sodium permeability constant of the membrane. This equation is the same as eqn. 2·4 of Hodgkin & Katz (1949), rearranged for differences in nomenclature (V in their version equals $-E$ in ours, and they defined positive current as inward whereas we took it as outward), and with the term for internal sodium concentration replaced according to the Nernst equation, i.e. $[Na]_i = [Na]_o \exp\{-E_{Na}F/RT\}$.

Equation (1) was inverted to give

$$P_{Na} = I_{Na}\frac{RT}{F^2E}\frac{1}{[Na]_o}\frac{\exp\{EF/RT\}-1}{\exp\{(E-E_{Na})F/RT\}-1}. \qquad (2)$$

The sodium permeability could then be calculated from the experimental data. I_{Na} and V_{Na} were measured, V was known for the applied pulses. E $(=V+E_r)$ was required, but E_r was unfortunately not always measured. Earlier measure-

ments on *R. esculenta* fibres (Frankenhaeuser, 1957) and occasional measurements on *Xenopus* fibres during this investigation indicated that the resting potential was about -70 mV. This value was therefore used for the calculations.

The sodium permeability (P_{Na}) was calculated by eqn. 2 for the peak currents of the voltage clamp records in Figs. 1 and 2, and the permeability was plotted against pulse amplitude V in Fig. 3. The P_{Na}, as calculated in this way, reached a ceiling value and then decreased slightly at applied potentials exceeding about $+130$ mV; at pulse amplitude 180 mV it was as a rule about 80–90 % of the maximum. A very satisfactory point was that measurements of the instantaneous currents gave a value of the permeability that was independent of the potential at which the instantaneous current was

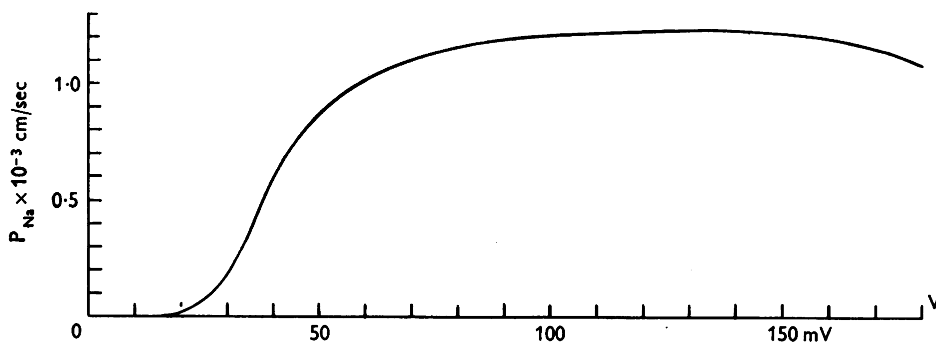

Fig. 3. Sodium permeability as calculated from the continuous line in Fig. 2 with eqn. 2, plotted against pulse amplitude V.

measured. This was not the case when the state of the membrane was defined by the sodium conductance (g_{Na}).

The next step in the analysis was to compare the peak initial currents in normal (100 % Na) Ringer's solution with those in low $[Na]_o$. This is illustrated by Figs. 4, 5 and 6. In Fig. 4 are shown the membrane currents of three successive voltage clamp runs, *A* with 100 % Na-Ringer's solution, *B* with 37 % Na, and *C* again with 100 %. Inspection of the traces shows immediately that the inward currents are much smaller in low $[Na]_o$ and that the traces at 104 and 114 mV in *A* and *C* have a clear hump of inward current, whereas in *B* they have a hump of outward current. The value of V_{Na} was thus clearly shifted. In Fig. 5 the peak currents are plotted against V and E. A smooth curve was drawn through the experimental points of the two runs in 100 % Na (Fig. 5*A*), and the sodium permeability was calculated from it with eqn. 2, by using an assumed value for the resting potential of -70 mV. The calculated values for the sodium permeability are plotted against V in Fig. 6. These values of P_{Na}, computed from the peak initial currents in the 100 % Na solution, may then be used according to eqn. 1 to compute the $I_{Na}-V$ curve in low $[Na]_o$. The only additional assumptions required are: (1) that the

inside sodium concentration does not change, and (2) that P_{Na} undergoes the same variation with time and membrane potential in the two solutions, i.e. that P_{Na} is independent of sodium concentration and of sodium current. The continuous line in Fig. 5*B* was calculated in this way from the currents in Fig. 5*A*. The agreement between the experimental measurements and the

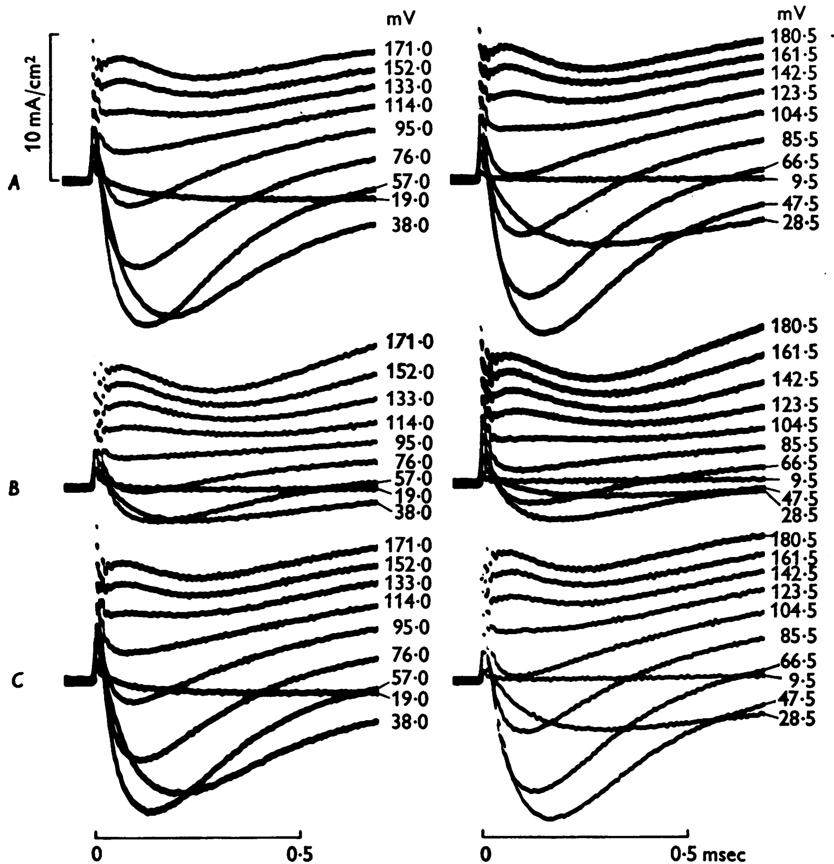

Fig. 4. Membrane currents associated with cathodal step voltage changes of values as marked. *A* with node N_0 in 100% Na. *B*, 37% Na. *C*, 100% Na. Clamp runs taken in order *A*, *B*, *C*. Choline chloride used as Na substitute. Experiment on axon 1 in Table 1. Temperature 23° C.

continuous line was striking. Such comparisons of the observed and calculated currents were made for the other experiments reported in Table 1, and yielded similar results, which, however, were complicated by the facts that the observed shift in V_{Na} was some mV less than the theoretical shift, and that the resting membrane potential changed a few mV between the two solutions. Discrepancies in the current–membrane potential relation were then no greater than could be accounted for by the systematic errors discussed above. In Expt. 1, which was chosen for illustration, these errors were judged

Fig. 5. Peak initial currents of Fig. 4 plotted against V and E. *A*; + from Fig. 4*A*, ○ from Fig. 4*C*; continuous line drawn smoothly through experimental points; interrupted line from anodal polarizations. *B*; ○ from Fig. 4*B*; continuous line calculated from eqn. 1 for 37% Na, and P_{Na} as given by Fig. 6.

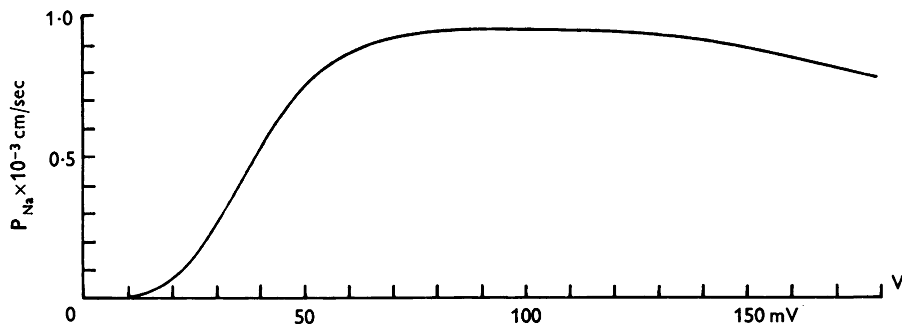

Fig. 6. Sodium permeability as calculated from eqn. 1 for currents given by continuous line in Fig. 5*A*, plotted against voltage change during step.

to be negligible, probably as a result of the increased stability obtained by very tight seals.

DISCUSSION

A voltage clamp system for myelinated nerve fibres, which has a response stable and fast enough to control accurately the potential across a node of Ranvier, has made possible the measurement of the ionic currents that flow as a result of a change in the nodal membrane potential (Dodge & Frankenhaeuser, 1958). These currents are seen to be similar to those of the squid giant axon membrane, which have been thoroughly analysed (Hodgkin & Huxley, 1952*a*, *b*, *c*, *d*; Hodgkin *et al.* 1952).

The ionic currents in response to a cathodal step consisted in general of a small step current proportional to the membrane potential change and to the resting nodal conductance, and of an initial transient current followed by a lasting outward current. The net membrane current at short times was inward over the range of voltage changes from 20 to 100 mV, and of sufficient magnitude to discharge the membrane capacitance at the observed rate during the rising phase of an action potential. When corrected for the step current the initial transient inward current was maximum for an applied pulse of about 65 mV, declining with larger pulses to be zero at about 120 mV. For still larger pulses the initial current was outward. Analysis of the similar phenomenon in the squid membrane revealed the initial current to be carried by sodium ions. The first step in the present analysis was then to identify the ionic species carrying the initial transient current.

It was shown that the potential at which the initial voltage clamp current reversed its direction from inward to outward, was changed by 18·0–24·4 mV when the external sodium concentration was changed from that in the 'normal' Ringer's solution (100% Na) to 37% Na. Nernst's equation predicts a change of 25 mV for the sodium equilibrium potential with this change in concentration. The systematic errors involved in the measurements were estimated as described earlier (see Dodge & Frankenhaeuser, 1958) to be 1–7 mV. After the measured values for ΔV_{Na} had been corrected for these errors, it was clear that the agreement between the theoretical ΔV_{Na} and the experimental ΔV_{Na} was sufficiently good to permit the conclusion that the initial permeability change was a reasonably specific increase in sodium permeability, at times not exceeding that of the peak of the initial current.

Judging from earlier investigations (reviewed by Hodgkin, 1958) this finding was rather to be expected, since the membrane of the frog nerve fibre behaves like a sodium electrode at the time of the peak of the action potential (Huxley & Stämpfli, 1951; Stämpfli, 1956).

The next step in the analysis was to try to find an expression for the sodium permeability that could be applied to the currents on the assumption that the permeability changed with a finite speed when the membrane potential was

changed. The first expression that was tried was the sodium conductance, defined as $g_{Na} = I_{Na}/V - V_{Na}$, since this expression has been so successfully applied to the squid fibre voltage clamp data. It was soon realized that this treatment gave one $g_{Na} - V$ curve when g_{Na} was calculated from the peak currents during cathodal pulses (i.e. from plots like Figs. 2 and 5), but a different curve when calculated from the instantaneous inward currents when the membrane was repolarized at the time of the peak of the sodium current. The former method gave lower values for g_{Na} with large pulses than the latter. In the first case inward currents were measured for pulses smaller than V_{Na} and outward currents at pulses larger than V_{Na}, whereas in the second case only inward currents were measured throughout. It therefore seemed profitable to try to fit the data to an expression for permeability that takes into account the rectification shown by a simple membrane separating a solution of high ionic concentration from one of low ionic concentration.

The 'constant field equation' (see Goldman, 1943 and Hodgkin & Katz, 1949) is based on simple assumptions and accounts for the rectification that is caused by the difference in ionic concentrations. The derivation of the constant field equation has been described by these authors and need not be repeated here. The assumptions on which the derivation is based will be given for the convenience of the reader: '(1) that ions in the membrane move under the influence of diffusion and the electric field in a manner which is essentially similar to that in free solution; (2) that the electric field may be regarded as constant throughout the membrane; (3) that the concentrations of ions at the edges of the membrane are directly proportional to those in the aqueous solutions bounding the membrane; and (4) that the membrane is homogeneous' (cited from Hodgkin & Katz, 1949). Equation 1, p. 193, was derived directly from eqn. 2·4 in the paper by Hodgkin & Katz by the modifications already described.

It has been shown (p. 195) that eqn. 1 accounts rather well for both the rectification and the relative current amplitudes in the two solutions, and furthermore it was found that the measured permeability was independent of the instantaneous potential at which it was measured. It was therefore clear that the state of the membrane could be rather well described in terms of the sodium permeability P_{Na} as obtained from the constant field equation.

It may further be pointed out that no additional assumptions were required to obtain the relation I'_{Na}/I_{Na} in two solutions with the concentrations $[Na]'_o$ and $[Na]_o$ since this relation is:

$$\frac{I'_{Na}}{I_{Na}} = \frac{[Na]'_o/[Na]_o \exp\{(E_{Na} - E)F/RT\} - 1}{\exp\{(E_{Na} - E)F/RT\} - 1}$$

from eqn. 1 and is identical (if allowance is made for a difference in convention as to the polarity of the potentials) with eqn. 12 of Hodgkin &

Huxley (1952*a*), which they used for comparing the currents in different solutions.

The sodium currents may be separated from the total membrane current by a procedure similar to that used by Hodgkin & Huxley (1952*a*). Comparison between two current records taken in two different $[Na]_0$'s showed some 'crossing over' of the traces, especially for large pulse amplitudes, indicating an apparent reversal of direction of I_{Na} at a fixed potential. The crossing over was of about the same magnitude as that shown in Fig. 5 of Hodgkin & Huxley (1952*a*). Since the time course of the sodium currents could also be measured from records of the instantaneous currents at repolarizations, this method was preferred for the experiments that will be reported subsequently.

In summary, it may be said that the observed change in the sodium equilibrium potential was, within the range of experimental errors, predicted by theory, and that the constant field equation could be used to define the sodium permeability (P_{Na}) without ambiguity. Sodium conductance (g_{Na}) could not be used.

SUMMARY

1. Experiments with a voltage clamp technique were made on single nodes of Ranvier in myelinated fibres from *Xenopus laevis*.

2. The initial membrane currents associated with step cathodal changes of the potential across the nodal membrane were measured and analysed.

3. The equilibrium potential for the initial membrane current (V_{Na}) was shifted by 18·0–24·4 mV when the external sodium concentration was changed from the normal level to 37 % of normal.

4. The measured ΔV_{Na} of 18·0–24·4 mV was close to the theoretical value of 25 mV, when the systematic errors (1–7 mV) involved in the measurements were taken into account.

5. Peak initial current plotted against membrane potential showed a curved line at large potentials, in contrast to the squid fibre currents where a straight-line relation has been found. This indicates a rectification in the membrane.

6. The state of the membrane could not without ambiguity be defined by sodium conductance (g_{Na}).

7. Sodium permeability (P_{Na}), as described by the constant field equation, accounted rather well for the rectification and gave the same $P_{Na} - V$ curve for measurements at various instantaneous potentials.

8. P_{Na} was found to be independent of external sodium concentration and sodium current.

9. It is concluded that the initial voltage clamp current was due to sodium ions moving passively in the electro-chemical gradient for sodium, as in the squid giant axon.

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REFERENCES

DODGE, F. & FRANKENHAEUSER, B. (1958). Membrane currents in isolated frog nerve fibre under voltage clamp conditions. *J. Physiol.* **143**, 76–90.

FRANKENHAEUSER, B. (1957). A method for recording resting and action potentials in the isolated myelinated frog nerve fibre. *J. Physiol.* **135**, 550–559.

GOLDMAN, D. E. (1943). Potential, impedance, and rectification in membranes. *J. gen. Physiol.* **27**, 37–60.

HODGKIN, A. L. (1958). Ionic movements and electrical activity in giant nerve fibres. *Proc. Roy. Soc.* B, **148**, 1–37.

HODGKIN, A. L. & HUXLEY, A. F. (1952*a*). Currents carried by sodium and potassium ions through the membrane of the giant axon of *Loligo*. *J. Physiol.* **116**, 449–472.

HODGKIN, A. L. & HUXLEY, A. F. (1952*b*). The components of membrane conductance in the giant axon of *Loligo*. *J. Physiol.* **116**, 473–496.

HODGKIN, A. L. & HUXLEY, A. F. (1952*c*). The dual effect of membrane potential on sodium conductance in the giant axon of *Loligo*. *J. Physiol.* **116**, 497–506.

HODGKIN, A. L. & HUXLEY, A. F. (1952*d*). A quantitative description of membrane current and its application to conduction and excitation in nerve. *J. Physiol.* **117**, 500–544.

HODGKIN, A. L., HUXLEY, A. F. & KATZ, B. (1952). Measurements of current–voltage relations in the membrane of the giant axon of *Loligo*. *J. Physiol.* **116**, 424–448.

HODGKIN, A. L. & KATZ, B. (1949). The effect of sodium ions on the electrical activity of the giant axon of the squid. *J. Physiol.* **108**, 37–77.

HUXLEY, A. F. & STÄMPFLI, R. (1951). Effect of potassium and sodium on resting and action potentials of single myelinated nerve fibres. *J. Physiol.* **112**, 496–508.

RUSHTON, W. A. H. (1951). A theory of the effects of fibre size in medullated nerve. *J. Physiol.* **115**, 101–122.

STÄMPFLI, R. (1952). Bau und Funktion isolierter markhaltiger Nervenfasern. *Ergebn. Physiol.* **47**, 69–165.

STÄMPFLI, R. (1956). Nouvelle méthode pour enrégistrer le potentiel d'action d'un seul étranglement de Ranvier et sa modification par un brusque changement de la concentration du milieu extérieur. *J. Physiol. Path. gén.* **48**, 710–714.

TEORELL, T. (1949). Membrane electrophoresis in relation to bio-electrical polarization effects. *Arch. Sci. physiol.* **3**, 205–219.