

The Ionic Currents in the Myelinated Nerve Fiber

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I have been asked to lead the discussion off from the main track to the side line of the ionic currents in the myelinated nerve fiber. The voltage clamp analysis on the *Xenopus* nerve fiber is sufficiently complete to allow numerical solutions of the action potential and the excitability properties. The nerve model described by the equations obtained from the quantitative analysis shows many similarities with the squid fiber model, but there are also striking differences between the two nerves. Here will follow a short summary of the major voltage clamp findings on the nodal membrane obtained in my laboratory (see References). Then attention will be drawn to some points which deviate from the present quantitative description.

Step changes in the membrane potential are associated with changes in membrane permeability to sodium and potassium ions. Both the sodium and the potassium permeability changes are smooth continuous functions of membrane potential and time.

Changes in sodium and potassium currents are consequences of the permeability changes. These currents behave like passive ionic currents, *i.e.* they depend on potential and concentration as ions moving by diffusion in an electric field; the constant field equation describes satisfactorily the voltage and concentration dependence of these currents.

The potential and time dependence of the permeability changes has been described quantitatively in terms of variables m , h , n , and p and rate constants (α 's and β 's) which depend on potential but not on time.

The equations, obtained from the analysis of the voltage clamp experiments, describe the currents at step changes in membrane potential. These equations were then solved for the situation that the membrane currents can change the membrane potential. Such solutions show that the equations predict an action potential of nearly the same shape and amplitude as the action potential which is recorded from a single nerve fiber from *Xenopus laevis*. The equations also predict satisfactorily many other properties of the nerve fiber. Threshold, strength duration curve, subthreshold responses, and even slow

excitability changes such as those occurring during accommodation are predicted by the equations.

It is striking how the major lines in this analysis of the *Xenopus* nerve are closely related to those of the squid nerve. The regenerative activity is in both cases due to the sodium currents. Both fibers also undergo a change in potassium permeability. The details, however, in many cases are different. The potential and concentration dependence of the ionic currents is different in the two structures. The peak sodium current and the peak sodium permeability are clearly larger in the *Xenopus* fiber. The calcium ion seems to play about the same role for the two membranes.

The potassium-carrying mechanism shows, at very large cathodal steps, a rectification which does not seem to appear in the squid fiber. The mechanism of this rectification is at present entirely unknown, and it has been neglected in the equation system. The rectification appears at extreme potentials, outside the range for the action potential.

Some of the rate constants (β_n and β_h) are without doubt affected by the history of the fiber. This is in disagreement with the formal assumptions that the rate constants are independent of time.

A model made to describe the permeability changes in the nerve ought to account for the voltage clamp data, and at present it seems likely that such a model, before it can be accepted, must be checked with some new voltage clamp experiments.

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