Potassium Inactivation
in Single Myelinated Nerve Fibres of Xenopus laevis*

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Summary. 1. Voltage clamp measurements were performed on single myelinated nerve fibres of the frog Xenopus laevis.
2. During long-lasting depolarizations the potassium current decayed in a fast phase with a time constant of about 0.6 sec and a following slow phase with a time constant between 3.6 (V = 0) and 20 sec (V = 100 mV).
3. The decay of the potassium current was the result of an inactivation of the potassium permeability and not of a shift of the potassium equilibrium potential as shown by experiments in isotonic KCl solution.
4. At a hyperpolarization of −20 mV the potassium inactivation was fully removed. It remained incomplete even at large depolarizations. The steady-state inactivation curve was S-shaped but not symmetrical.
5. The experimental results could be described by extending the Hodgkin-Huxley equations introducing two terms of potassium inactivation.

Key-Words: Potassium Inactivation — Voltage Clamp — Ranvier Node.

In various preparations the potassium current slowly decays if the excitable membrane is kept depolarized. This decay has been ascribed to a slow inactivation of the potassium permeability which was found in squid axons (Ehrenstein and Gilbert, 1966; Armstrong, 1969), in nerve cells of snails (Hagiwara et al., 1961; Alving, 1969; Leicht et al., 1971; Neher and Lux, 1971) and in supramedullary cells of the puffer fish (Nakajima and Kusano, 1966). Similar results have been obtained in experiments on electroplaques (Nakamura et al., 1965; Bennett and Grundfest, 1966), Purkinje fibres of dog and sheep (Hall et al., 1963; Hecht et al., 1964) and striated muscle fibres of the frog (Adrian et al., 1970a, b; Kao and Stanfield, 1968, 1970; Stanfield, 1970).

In frog nerve fibres Frankenhaeuser and Waltman (1959) have shown that the membrane resistance increases during long-lasting depolarizations. These authors mentioned that in voltage clamp experiments the potassium current decreased and they interpreted their findings as an inactivation of the potassium permeability. Lüttgau (1960) has drawn

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the same conclusion from current clamp experiments on isolated frog nerve fibres. For the same preparation Moore (1967) reported a clear dependence of the maximum K current on the holding potential suggestive of a slow K inactivation process.

Frankenhaeuser (1963) introduced the variable $k$ for the potassium inactivation but did not present a detailed analysis. Therefore it seemed worthwhile to do voltage clamp experiments on frog nerve fibres to study the kinetics of this inactivation and its voltage-dependence as well as to obtain unequivocal proof that the observed phenomena were indeed caused by changes of the K permeability.

Preliminary reports on this work have appeared (Schwarz and Vogel, 1970, 1971).

**Methods**

The clawed frogs, Xenopus laevis, were kept at constant conditions (20°C, 14 hour-day and weekly feeding). Single fibres (mean diameter 19 μm) were isolated from the tibial nerve. The fibre was mounted in a perspex chamber. The investigated node of Ranvier was constantly superfused, the nodes on either side were kept in isotonic KCl solution and cut. The membrane currents were recorded with the voltage clamp technique of Dodge and Frankenhaeuser (1958) in a setup described by Koppenhöfer (1967). The current density was calculated from the recorded output voltage of the clamp amplifier by multiplication with $1/(14 \Omega \text{cm}^2)$ in accordance with Frankenhaeuser (1962a). At the beginning of each experiment the holding potential was determined at which $I_h = 0.7$. This potential was defined as the resting potential and the membrane potential, $V$, is given as displacement from this value. Depolarizations and outward currents are positive. The leakage current was calculated from anodal impulses assuming that this current was a linear function of membrane potential and did not change with time. The temperature in the experiments was kept at 21°C if not noted otherwise.

The solutions had the following composition (in mM): a) Ringer solution: 110.5 NaCl, 2.5 KCl, 2.4 NaHCO₃, 1.8 CaCl₂, pH = 7.1 to 8.0; b) isotonic KCl solution: 115.2 KCl, 1.8 CaCl₂, pH = 7.5.

**Results**

*The Effect and After-Effect of Sustained Depolarizations*

The membrane behaviour during and after long-lasting depolarizations was studied with the impulse program of Fig. 1 (upper row). After a 5-sec hyperpolarization to $-20 \text{mV} (V_1)$ cathodal pulses of 37 to 50 sec duration $(V_2)$ were applied yielding the membrane currents that are shown in the lefthand part of this figure. The common feature of records A to D is that during a sustained depolarization the delayed outward current declined from a peak value to a stationary value within 10 to 30 sec depending on $V_2$. With large depolarizations as in A and B ($V_2 = 80 \text{mV}$) this decay proceeded in two distinct phases while with weaker cathodal pulses as in D the first relatively rapid phase was nearly missing. This rapid phase appeared to be more vulnerable than the slow compo-