IONIC CONDUCTANCE OF THE SURFACE MEMBRANE OF FROG VENTRICULAR MYOCARDIAL CELLS

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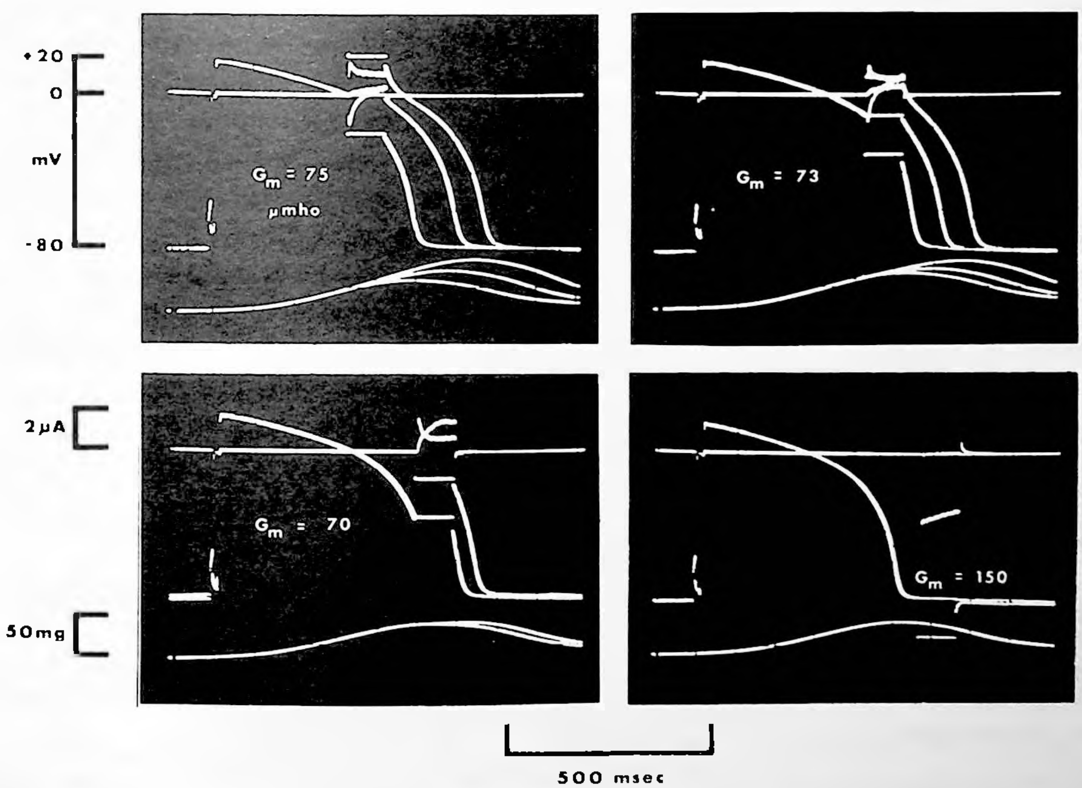
One of the major hypotheses of the ionic mechanism of the plateau of the cardiac action potential is based on the classic observation of Weidmann (1951) that the membrane conductance in Purkinje fibers is lower during the plateau of the action potential than at rest. This experiment has led to the conclusion that the potassium permeability is lower during activation than in the resting state. This is in contradiction to the case of the nerve membrane.

Conductance measurements in heart tissue are subject to a number of technical difficulties which may make interpretation of experimental results misleading. Since the perturbations in the membrane potential have been made by passage of electrical current pulses problems such as time dependent permeability changes during the pulse, voltage inhomogeneity, point application of current, extracellular resistance, capacitive coupling, and leakage current have always been present.



We have developed a new modification of the hybrid sucrose gap voltage clamp technique which eliminates or compensates for each of these difficulties. Essentially, a similar technique as that described by Morad and Orkand (J. Physiol. 219:167-189, 1971) was used with several new modifications: 1) a "guard gap" compartment which catches extracellular leakage current; 2) overshoot compensation technique for extracellular resistance; 3) electrostatic shielding between the current passing electrode and high impedance preamplifier input. This technique enables measurement of membrane current-voltage relations which are "instantaneous" within two msec. The membrane conductance at rest and during the plateau is measured as the slope of these current-voltage relations.

Our experimental results in the frog ventricle are in accord with the classical observation that the ionic conductance is higher at rest than during the plateau phase of the action potential. However an unexpected result from these experiments was that the conductance was constant during the entire plateau and rapid repolarization phases unlike Weidmann's experiment which seemed to show a decreasing conductance during the time course of the plateau. Figure 1 shows voltage clamp pulses applied at different times during the plateau and at rest and the calculated membrane conductances associated with each time.

It can be clearly seen that the conductance is constant during the plateau and then rises twofold at rest. These results were essentially unchanged in the presence of tetrodotoxin (10^{-6}M) which is known to block the primary sodium inward current. These results have important implications as to the nature of ionic transport in this excitable membrane. Since well-documented net Na^+, Ca^{+2}, and K^+ effluxes occur during the plateau large permeability changes must be occurring In other excitable systems (nerve and skeletal muscle) such permeability changes are accompanied by corresponding conductance changes since the movement of the various ionic species are independent of each other. The constant conductance observed during the plateau of the myocardial action potential must mean that as potassium permeability increases to repolarize the membrane the sodium and/or calcium permeability must be decreasing by exactly the correct amount to explain the constant total conductance. This relation between the changes in specific ionic permeabilities suggests that a cross-ionic interaction may occur in the membrane. A possible molecular mechanism for such an interaction might be a multi-ionic carrier which controls the ionic movements. For instance a counter transport of Ca^{++} and K^+ would be an attractive hypothesis to explain repolarization of the membrane. The counter-transport carrier concept, while well-known to "transport workers," is foreign to the electrophysiological community.

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EXCRETION RATES OF TRIMETHYLAMINE OXIDE IN ELASMOBRANCHS

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All elasmobranchs maintain relatively high concentrations of trimethylamine oxide (TMAO)