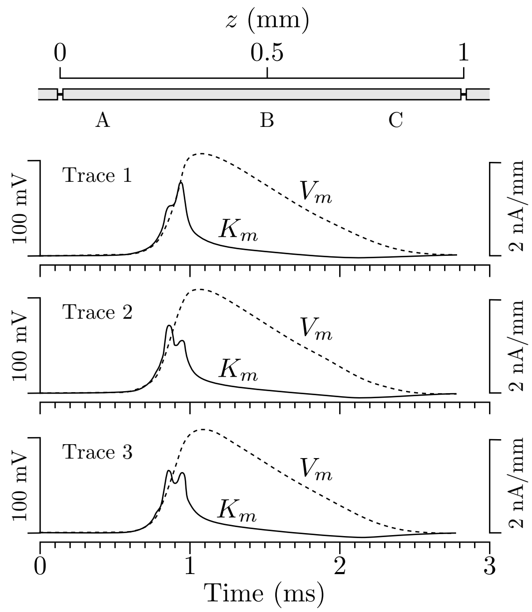
**Exercise 1.** Estimate the conduction velocity of the action potential from the measurements on a single myelinated nerve fiber shown in Figures 5.19-5.21 in volume 2 of the text..

**Exercise 2.** Define the *safety factor*.

**Exercise 3.** The membrane potential and membrane current per unit length at three sites in an internode of a myelinated fiber are shown in the following figure.



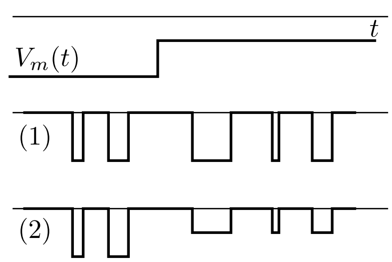

The measurement locations are A, B, and C. Traces 1, 2, and 3 are three pairs of traces obtained at different locations. The relations between the traces and the locations is unknown *a priori*.

a) If Trace 1 was recorded at location A, what is the direction of propagation of the action potential — i.e., in the $+z$-direction or the $-z$-direction?

b) If the action potential were propagated in the $+z$-direction, determine the correspondence between the traces and recording locations. Explain your choice.

c) Estimate the conduction velocity of the action potential of this fiber. Explain your method.

**Exercise 4.** The following figure shows two putative records of membrane currents recorded from two membrane patches, each of which contains a single channel, in response to a step of depolarizing membrane potential.




Each of these channels has a linear voltage-current characteristic when the channel is open.

a) Which, if any, of these records could be from a single, voltage-gated channel? Explain.

b) Which, if any, of these records could be from a single channel that is not voltage-gated? Explain.

**Problem 1.** A squid giant axon (which is an unmyelinated axon) has a diameter of 500 $\mu$m. The ionic currents during the passage of one action potential are shown in Figure 1. The normal internal

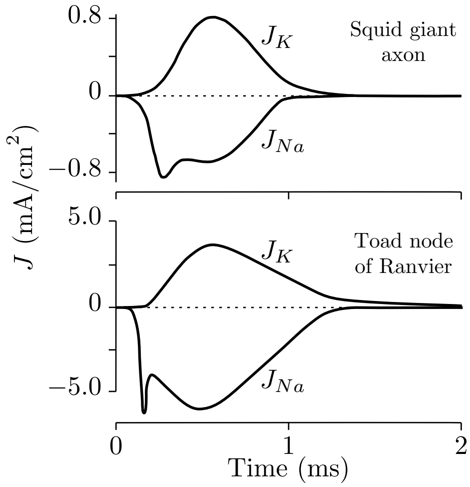



Figure 1: Comparison of ionic currents during an action potential for an unmyelinated squid giant axon and a myelinated toad node of Ranvier. These ionic currents are based on calculations of models of the squid giant axon (adapted from Cooley and Dodge, 1965, Figure 2.4) and toad node of Ranvier (adapted from Frankenhaeuser and Huxley, 1964, Figure 6).

concentration of sodium is 40 mmol/L. In contrast, consider a frog myelinated fiber for which the axon diameter (not including the myelin) is 10 $\mu$m, the fiber diameter (including the myelin) is 14 $\mu$m, the internodal length is 2 mm, the nodal length is 0.7 $\mu$m, and the nodal area is 22 $\mu$m$^2$. We shall assume that action potentials occur only at the nodes. The ionic currents at the node of Ranvier during the passage of an action potential are also shown in Figure 1. You may assume that the sodium current is negligible in the internodes. The normal internal concentration of sodium is 10 mmol/L in the frog fiber.

Both the squid unmyelinated fiber and the frog myelinated fiber conduct action potentials with about the same conduction velocity. This problem concerns the energetic efficiency of these two fibers.

a) Compute the number of moles of sodium entering each fiber per action potential per unit length of fiber.

b) Assume that the energy expended to pump the accumulated sodium out of the cell can be measured in terms of the number of ATP molecules hydrolyzed to ADP and assume that 3 moles of $Na^+$ are transported out of the axon for every mole of ATP hydrolyzed to ADP inside the axon by the ($Na^+$-$K^+$)ATPase pump. Find the ratio of energy expended per unit length per action potential in order to pump out the accumulated sodium for the squid unmyelinated fiber to that for the frog myelinated fiber.

c) Describe the advantages of the frog myelinated fiber over the squid unmyelinated fiber.

**Problem 2.** Figure 2 shows a detail of a propagating action potential calculated using a model of a myelinated nerve fiber (Figure 5.31 in volume 2 of the text).

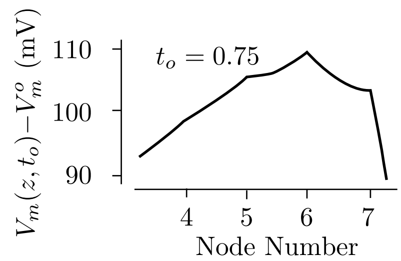
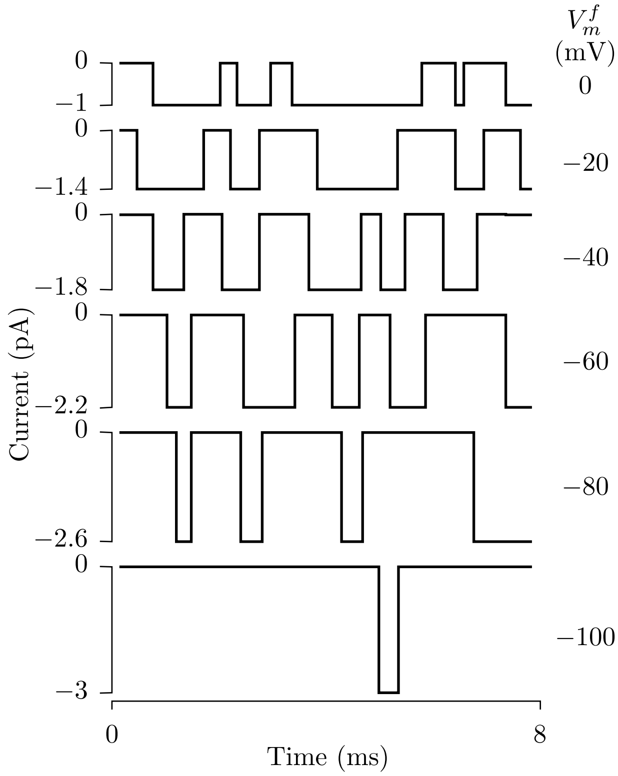



Figure 2: Membrane potential along a myelinated fiber computed from a model of electrical characteristics of the node and internode (Figure 5.31 in volume 2 of the text). The membrane potential is plotted as a function of distance along the fiber (expressed in units of internodal length where $L = 1.38$ mm).

a) Describe a method by which the data in Figure 2 could be analyzed to estimate the current $I_m$ flowing out of a node. Apply your method to calculate the current flowing out of node 6 at $t_0 = 0.75$ ms. Assume that $r_i = 140$ MΩ/cm$>> r_o$.

b) Describe a method by which the data in Figure 2 could be analyzed to estimate the current density $K_m$ flowing out of an internode. Apply your method to determine whether current is flowing into or out of the internode between nodes 5 and 6 at $t_0 = 0.75$ ms.

**Problem 3.** The voltage across a membrane patch is stepped from $V_m^o$ to $V_m^f$ at $t = 0$ and single-channel ionic currents are recorded as a function of time. Typical records at 6 different values of $V_m^f$ are shown in the following figure.




a) Is the open-channel voltage-current characteristic of this channel linear or nonlinear?

b) What is the conductance of the open channel?

c) What is the equilibrium (reversal) potential for this channel?

d) It is proposed that this channel is the voltage-gated sodium channel responsible for sodium-activated action potentials. Discuss this suggestion.

**Problem 4.** This problem deals with the relation of current to voltage for single ion channels. Assume that conduction through an open ion channel is governed by the equation

$$\mathcal{I} = \gamma(V_m - V_e),$$

where $\mathcal{I}$ is current through a single open channel, $\gamma$ is the conductance of a single open channel, $V_m$ is the membrane potential across the channel, and $V_e$ is the equilibrium (reversal) potential for the channel. For each of the channels in this problem, assume that $\gamma = 25$ pS and $V_e = 20$ mV.

a) The membrane potential $V_m$ and the *average* single-channel current $i$ obtained from three different single channels (A, B, and C) are shown in Figure 3. Both the membrane potential

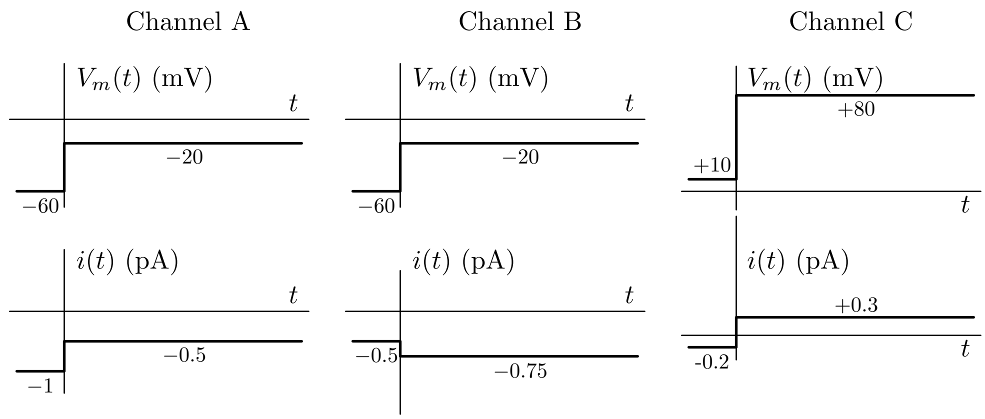



Figure 3: Average single-channel currents.

and current are plotted on a time scale such that the changes appear instantaneous and only the final values of these variables can be discerned in the plots; i.e., the kinetics are not shown. For each of these channels, answer the following questions and explain your answers:

i) Is this channel voltage-gated for the illustrated depolarization?

ii) Is the channel activated (opened) or inactivated (closed) by the illustrated depolarization?

b) Assume that each *voltage-gated* channel contains one two-state gate where $\tau$ is the time constant of transition between states. For each of the channels, sketch the time course of $i(t)$ on a normalized time scale $t/\tau$. Clearly show the current near $t = 0$.