MASSACHUSETTS INSTITUTE OF TECHNOLOGY
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Quantitative Physiology: Cells and Tissues
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Homework Assignment #8   Issued: November 18, 2004
Due: December 2, 2004

Reading
    Lecture 32 — Volume 2: 6.5-p407
    Lecture 33 — Volume 2: p407-416
    Lecture 34 — Volume 2: 6.3.2-6.3.6
   Lecture 35 — Volume 2: 6.6 6.7

Announcements

This homework assignment is due in 2 weeks, on December 2. Please note, however, that the final
HH oral presentations take place on December 1 and 3. Therefore, you might want to get started
early on this assignment.

HH Dry Runs are scheduled for November 23 (see schedule in the calendar section). Recitations on
that day are cancelled.

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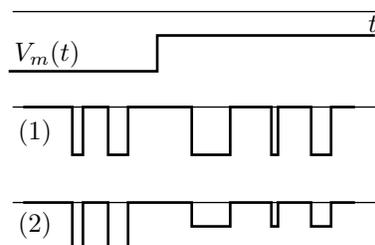
Each of these channels has a linear voltage-current characteristic when the channel is open.

  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 myelinated axon, shown schematically in Figure 5.8 of volume 2 of the text, has the dimensions $L = 2$ mm, $D = 14$ μm, $d = 10$ μm, $l = 0.7$ μm. The resistivity of the cytoplasm $\rho_i = 110$ $\Omega{\cdot}$cm, and the resistance of the extracellularly space can be assumed to be negligible. The membrane potential, V_m, and current per unit length, K_m, are shown in Figure 1 for a location at an internode as an action potential propagates down the fiber. Assume that the internode can be
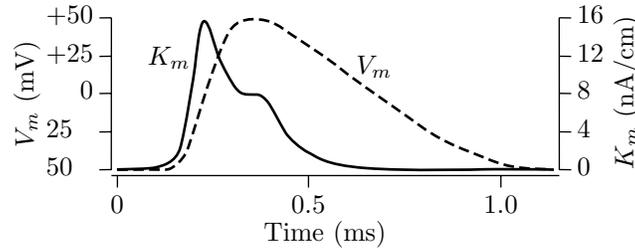

Figure 1: Membrane potential and current at an internode.

represented by a linear cable with the equivalent membrane model shown in Figure 2.
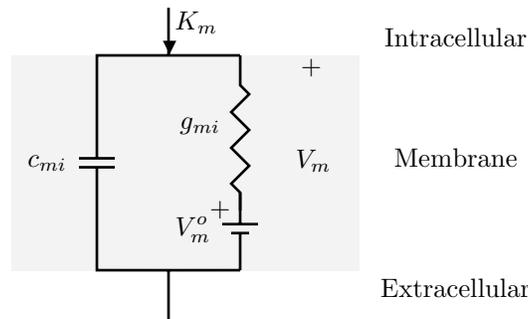

Figure 2: Model for voltage-current relation at an internode.

a) Estimate the conductance, g_{mi}, and capacitance, c_{mi}, per unit length of internode from the data given. [Hint - the capacitance current is zero when $dV_m/dt = 0$ and largest when dV_m/dt is large.]

b) Find the values of the membrane time constant, τ_{Mi}, and the axon space constant, λ_{Ci}, of the internode.

c) Find the specific conductance, G_{mi}, and capacitance, C_{mi}, per unit area of internodal myelin.

d) Given that the myelin is composed of 150 lamellae, find the specific conductance G_m, and capacitance, C_m, per unit area for a single layer of myelin membrane. How do these values compare to those of unmyelinated fibers?

e) Now consider an unmyelinated fiber whose diameter is 10 μm and whose membrane has a specific capacitance, C_m, and conductance, G_m, per unit area equal to that found in part d). What is the time constant, τ_M, and space constant, λ_C, of this fiber? Compare these results to those found in part b). What is the physiological significance of the difference?
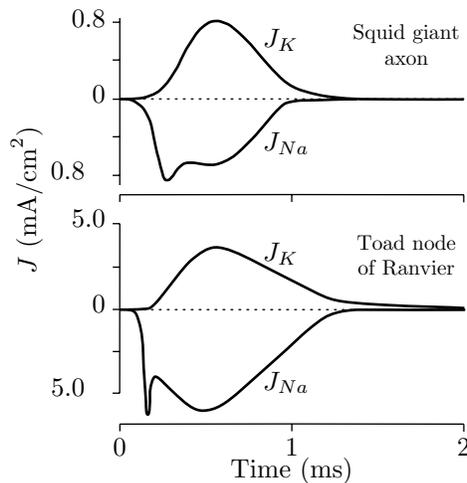
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Figure 3: Comparison of ionic currents during an action potential for an unmyelinated squid giant axon and a myelinated toad node of Ranvier. These ionic currents are based on calculations of models of the squid giant axon (adapted from Cooley and Dodge, 1965, Figure 2.4) and toad node of Ranvier (adapted from Frankenhaeuser and Huxley, 1964, Figure 6).

Problem 2. A squid giant axon (which is an unmyelinated axon) has a diameter of 500 μm. The ionic currents during the passage of one action potential are shown in Figure 3. The normal internal 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 μm, the fiber diameter (including the myelin) is 14 μm, the internodal length is 2 mm, the nodal length is 0.7 μm, and the nodal area is 22 μm^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 3. 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 3. Figure 4 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).

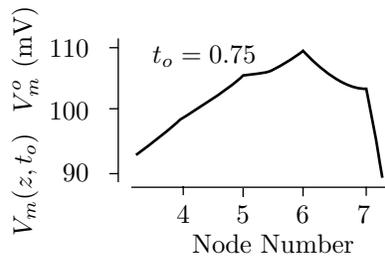a) Describe a method by which the data in Figure 4 could be analyzed to estimate the current

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Figure 4: 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).

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 4 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 4. Although there is considerable scatter, the ratio of the inner diameter d to outer diameter D of the layer of myelin that encircles a myelinated fiber tends to be about 0.74, as shown in the following figure, where every symbol represents measurements of d/D and d for a different fiber.
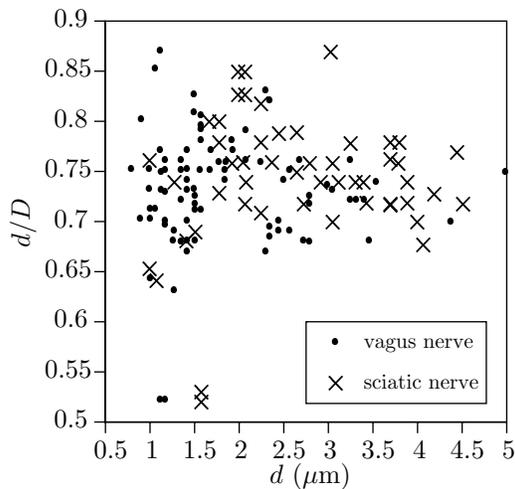

The point of this problem is to investigate the hypothesis that this relation between d and D results from an evolutionary optimization of the cable model.

Part a. Assume that the myelinated part (the internode) of a myelinated fiber can be represented by the cable model. Assume the myelin can be represented by a homogeneous electrical material with resistivity ρ_m and permittivity ϵ_m. Assume the intracellular conductor is a homogeneous conductor with resistivity ρ_w. Assume that the extracellular conductor has negligible resistance. Determine an expression for the space constant λ_C of this model in terms of the inner diameter d and the outer diameter D of the layer of myelin. Hint: The radial resistance of a cylindrical shell is given below.

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$$R = \frac{V}{I} = \frac{\rho_o}{2\pi L} \ln \frac{D}{d}$$
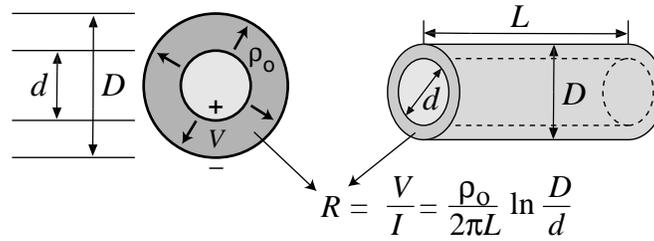
Part b. The expression derived in part a is plotted below
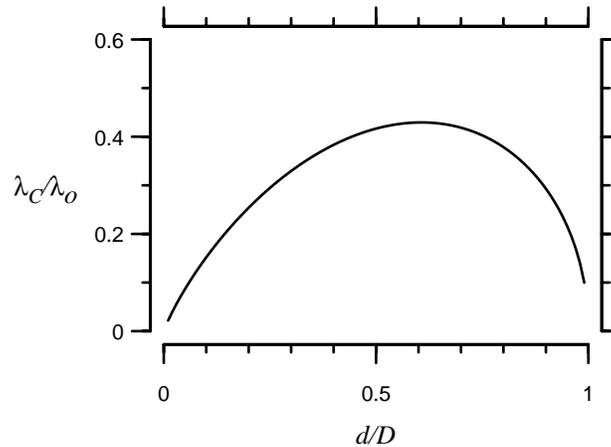
where $\lambda_o = D\sqrt{\rho_m/8\rho_w}$. Thus, if D is fixed (i.e., if the axon is constrained to fit into a constant volume), then λ_o is a constant, and λ_C is maximum when $d \approx 0.6D$.

b1) Explain in physical terms why the space constant gets smaller as the value of d decreases below $0.6D$.

b2) Explain in physical terms why the space constant gets smaller as the value of d increases above $0.6D$.

Part c. The value of d/D that maximizes the space constant of the cable model is remarkably close to the ratio of 0.74 seen experimentally. Nevertheless, it is smaller. One possible reason why it is smaller is that we ignored the resistance of the outer conductor r_o. How would the space constant's dependence on d/D change if the resistance of a thin layer of saline (thickness $= 0.1D$) were included in the calculation. Make a plot that contains both the old relation (shown in the previous plot) and the new relation. Briefly describe how the addition of the outer resistance changes the predicted space constant.

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