York University BPHS 3090 (Winter 2014) - HW 7

Due Date: Apr. 4, 2014 9:30 AM

Questions

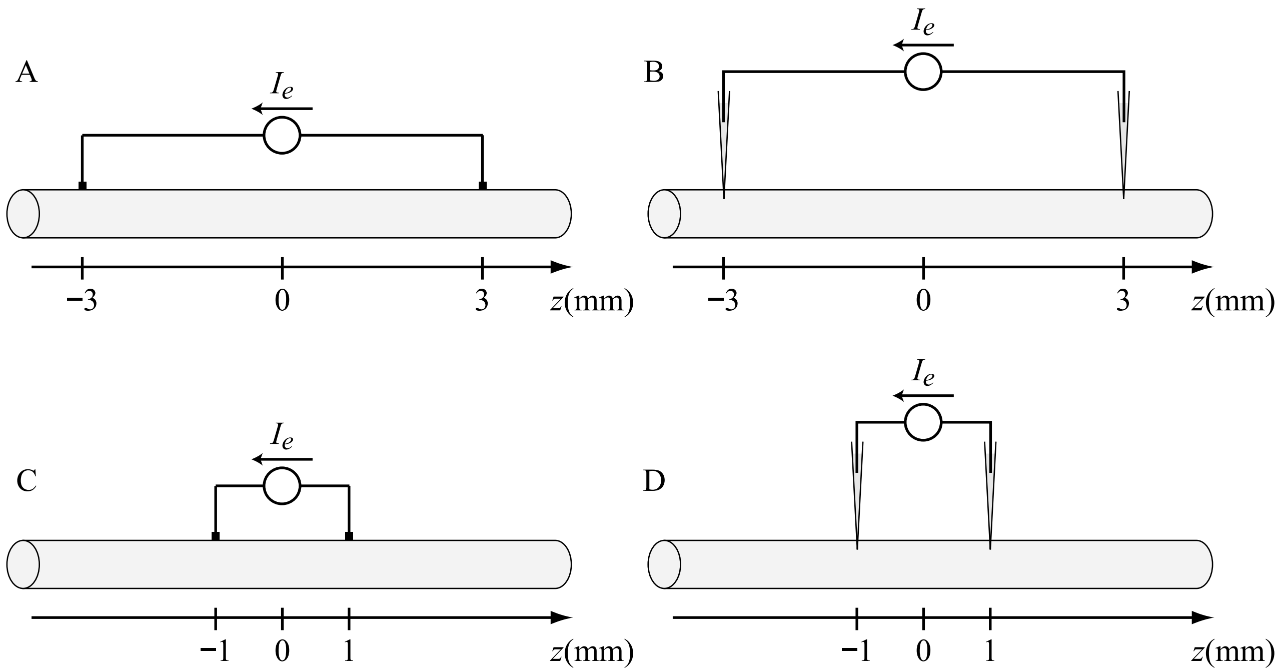
1. The table below shows the measured channel density obtained using one of two methods. In one, the macroscopic conductance of a whole cell was measured and then divided by the surface area of the cell and by the single-channel conductance; the result is the number of channels per unit area (μm^2. If a channel behaves ohmically, its conductance γ is expected to be a constant, which is why an estimation of the channel conductance can be obtained based on macroscopic ohmic ideas

Preparation	γ (pS)	Channels number/μm^2
Sodium		
Squid giant axon	4	330
Frog node	68	400-2000
Rat node	14.5	700
Bovine chromaffin	17	1.5-10
Potassium		
Squid giant axon	12	30
Frog node	2.7-4.6	570-960
Frog skeletal	15	30
Mammalian BK	130-240	

a. Before the upstroke of an action potential in the frog skeletal muscle, the probability of both the sodium and potassium channel being open changes. Assume the membrane of frog skeletal muscle is at rest, and that, at rest, only potassium channels are open, with probability 0.06. What is the resistance of $0.5\ \mathrm{cm}^2$ of this membrane?

b. It is also known that, during the upstroke of an action potential in squid giant axon, the probability of a sodium channel being open changes; at rest, the probability of an open channel is 0.01, while at the peak of an action potential it is 0.2. Consider $0.6\ \mathrm{mm}^2$ of cell membrane. On the average, how many channels change from closed to open as the membrane moves from rest to peak (i.e., during the upstroke of the action potential) ?

2. A large invertebrate axon is immersed in oil and stimulated with a constant current $I_e > 0$. The current is delivered using a pair of electrodes that are in one of four configurations, as illustrated in the following figure.



The current I_e is sufficiently small that the cell behaves as a linear cable. The specific resistances of the internal and external conductors are 100 kΩ/cm and 10 kΩ/cm, respectively. The specific conductance and capacitance of the membrane are 1 mS/cm and 0.1 μF/cm, respectively. The membrane potential is allowed to come to steady state. [Remember: V_m is positive when the inside of the cell is positive with respect to the outside of the cell. Also, the reference direction for the longitudinal currents is in the $+z$ direction.]

a) For which configuration is the intracellular longitudinal current at $z = 0$, $I_i(0)$, most positive? Explain briefly.

b) For which configuration is the transmembrane potential $V_m(z)$ at $z = 1$ mm most positive? Explain briefly.

c) For each configuration, let V_{max} represent the maximum value of the membrane potential $V_m(z)$ along the axon, i.e.,

$$V_{max} = \max_z(V_m(z))$$

For which configuration is V_{max} most positive? Explain briefly.

3. For the following remarks, state whether each of the following are true or false, and give sufficient reason to support your claim.

a. Tetrodotoxin (TTX) blocks the flow of potassium through the sodium channel.

b. The macroscopic sodium current recorded by an electrode in a cell is a sum of the signle-channel sodium currents that flow through single sodium channels.

c. For a channel with one two-state gate, there is no distinction between the single open-channel current, and the average single-channel current.

d. Ionic and gating currents give identical information about the kinetic properties of a channel

4. Myelinated axons are ensheathed along their entire length, and between two adjacent myelin segments, there are approximately 1 μm long gaps called nodes of Ranvier; at the nodes, the axon is exposed to the extracellular space - this can be seen in the figure below. For this given myelinated axon, $L = 2$ mm, $D = 14$ μm, $d = 10$ μm, and $l = 0.7$ μm.

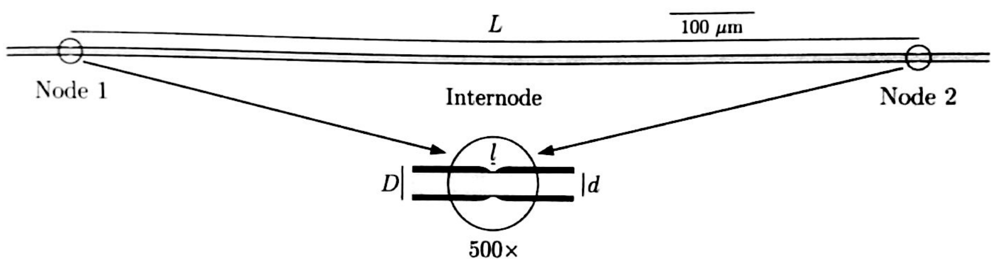


Figure 1:

The resistivity of the cytoplasm $\rho_i = 110\Omega \cdot \text{cm}$, and the resistance of the extracellular space can be assumed to be negligible. The membrane potential, V_m, and the current per unit length, K_m, are shown below for a location at an internode as an action potential propagates down the fiber. Assume that the internode can be represented by a linear cable with the equivalent membrane model shown in the figure below, which depicts the intracellular, membrane, and extracellular space respectively.

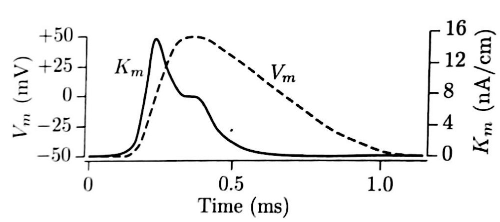


Figure 2: Graph depicting the relationship between membrane potential and current at an internode as functions of time

a. Estimate the conductance, g_m, and the capacitance, c_m, per unit length of internode from the data given. Remember that the capacitance current is approximately zero when $\frac{dV_m}{dt} = 0$ and largest when $\frac{dV_m}{dt} = 0$ is large.

b. Find the values of the membrane time constant, τ_{Mi}, and the axon space constant, λ_{Ci} of the internode - what do these values imply regarding the myelinated axon?

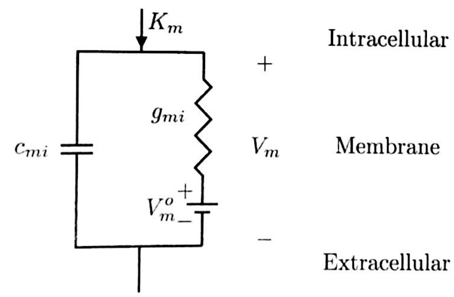


Figure 3:

c. Find the specific conductance, G_{mi}, and the capacitance, C_{mi}, per unit area of internodal myelin. What does this value for the specific conductance tell you about the myelin and its effects?

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

e. Consider an unmyelinated fiber whose diameter is 10 μm and whose membrane has a specific capacitance, C_m, and a 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, and explain the physiological significance of the difference?

5. The figure below shows a detail of a propagating action potential calculated using a model of a myelinated nerve fiber (Weiss vol.2, Fig.5.31).

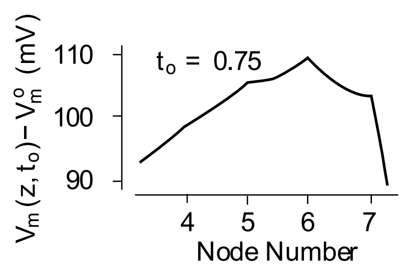


Figure 4: Membrane potential along a myelinated fiber computed from a model of electrical characteristics of the node and internode (vol.2, Fig.5.31). The membrane potential is plotted as a function of distance along the fiber (expressed in units of internodal length where $L = 1.38$ mm).

a) Describe a method by which the data in the figure 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 $\gg r_o$.

b) Describe a method by which the data in the figure 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.