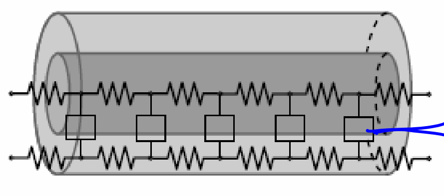
Core Conductor Model



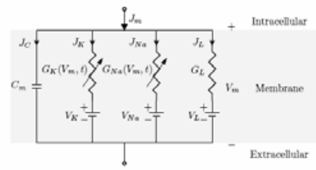
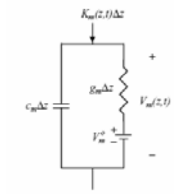


Figure 4.6

HH model
nonlinear
Electrically active cells
Action potential
Node of Ranvier



Cable model
linear
Electrically active / inactive cells
Sub-threshold behavior (graded potential)
Internode

Let $v_m(z,t) = V_m(z,t) - V_m^o$ and $|v_m(z,t)| << |V_m^o|$:

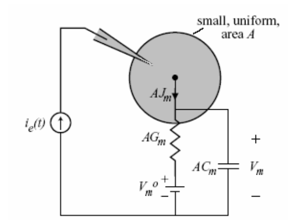
$$v_m(z,t) + \tau_M \frac{\partial v_m(z,t)}{\partial t} - \lambda_C^2 \frac{\partial^2 v_m(z,t)}{\partial z^2} = r_o \lambda_C^2 K_e(z,t)$$

where

$$\lambda_C^2 = \frac{1}{g_m(r_o + r_i)}$$ space constant

$$\tau_M = \frac{c_m}{g_m}$$ time constant

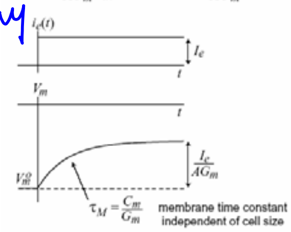
① electrically small cell



⇒ exponential decay in time with $\tau = \tau_M$

$$i_e(t) = AJ_m = AC_m \frac{dV_m}{dt} + AG_m(V_m - V_m^o)$$

$$\frac{AC_m}{AG_m}\frac{dV_m}{dt} + V_m = V_m^o + \frac{i_e(t)}{AG_m}$$



② electrically large, const current

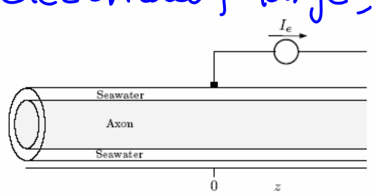


Figure 3.9

⇒ exponential decay (in space) with λ_C

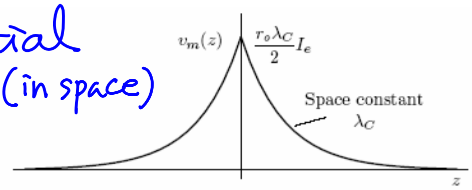


Figure 3.11

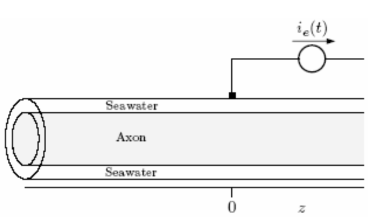


Figure 3.22

⇒ Fast decay in space/time

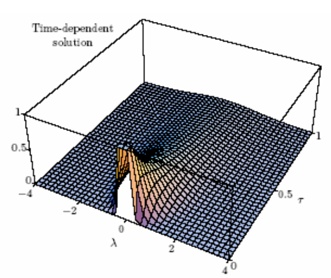


Figure 3.25

Problem 1. A 50 μm diameter unmyelinated fiber is placed in oil. A thin layer of sea water clings to the fiber, and the extracellular potential response to an external current $i_e(t)$ is measured as indicated schematically in Figure 1. The extracellular potential $\Delta v_o(z,t)$ is a function of time and

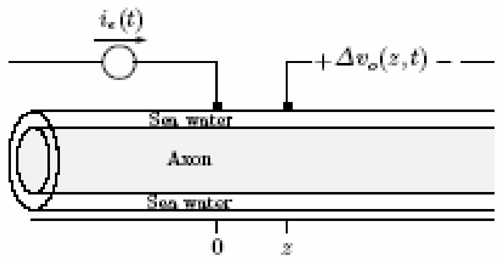


Figure 1: Schematic diagram for the measurement of extracellular potentials. $\Delta v_o(z,t)$ is the difference between the extracellular potential measured at z and that measured at a distant electrode (not shown).

position along the fiber. Two different types of measurements are obtained for this fiber.

Measurement #1

In response to a brief pulse of current, the monophasic extracellular action potential is measured and found to have a peak amplitude of 40 mV. The transmembrane action potential has a peak amplitude of 120 mV relative to the resting potential.

Measurement #2

The stimulus current is a step $i_e(t) = I_e u(t)$ where $u(t)$ is the unit step function. The amplitude of the current I_e is reduced until the relation between the current amplitude and amplitude of the voltage response is linear. It is found that for a current amplitude of $I_e = 0.5$ μA, the extracellular voltage response is related linearly to the current and all further measurements are obtained at this current level. The time dependence of the voltage response $\Delta v_o(z,t)$ at a location z is shown in Figure 2. The steady-state value of the extracellular potential is shown as a function of position in

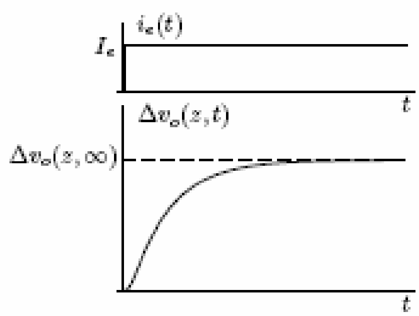


Figure 2: Response of a cell (lower panel) to a step of current (upper panel) as a function of time at a single location. The steady-state value of the step response is $\Delta v_o(z,\infty)$ is shown with a dotted line.

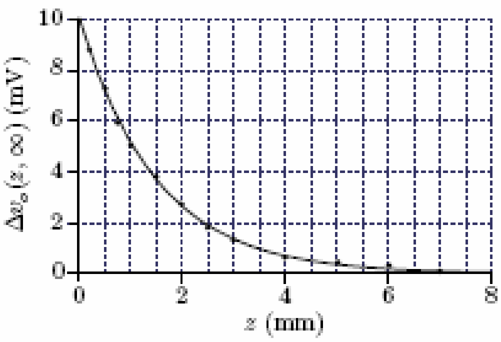


Figure 3: Measurement of steady-state value of the extracellular potential in response to a step of current.

a) Determine the value of the cell space constant, λ_C.

b) Determine the value of the extracellular longitudinal resistance per unit length, r_o.

c) Determine the value of the intracellular longitudinal resistance per unit length, r_i.

d) Determine the value of the membrane conductance per unit length, g_m.

e) Determine the value of the specific membrane conductance (the conductance per unit area of membrane), G_m.

f) Determine the resistivity of the cytoplasm, ρ_i.

Solution to Problem 1

Problem 1. Measurement 1 gives information about the longitudinal resistances,

$$\left|\frac{\Delta V_o(z,t)}{\Delta V_m(z,t)}\right| = \frac{r_o}{r_o + r_i}.$$

Measurement 2 gives information about other cable parameters since

$$\Delta v_o(z,\infty) = -\frac{r_o}{r_o+r_i}\Delta v_m(z,\infty) = \left(\frac{r_o}{r_o+r_i}\right)\left(\frac{r_o\lambda_C}{2}\right) I_e e^{-|z|/\lambda_C}.$$

a. The spatial dependence of the steady-state extracellular potential is exponential and the space constant can be obtained from the initial slope of the potential as shown in Figure 4. Therefore, $\lambda_C = 1.5$ mm.

b. From Measurement 1, $r_o/(r_o + r_i) = 40/120 = 1/3$ implies that $r_i/r_o = 2$. In addition, Measurement 2 shows that

$$\Delta v_o(0,\infty) = \left(\frac{r_o}{r_o+r_i}\right)\left(\frac{r_o\lambda_C}{2}\right) I_e = 10\,\text{mV},$$

which implies that

$$10^{-2} = \frac{1}{3}\left(\frac{r_o \cdot 0.15}{2}\right) 5\times 10^{-7}.$$

The solution for $r_o = 8\times 10^5\ \Omega$/cm.

c. The above results are combined to yield $r_i = 16\times 10^5\ \Omega$/cm.

d. The space constant is

$$\lambda_C = 0.15 = \frac{1}{\sqrt{g_m(r_o+r_i)}} = \frac{1}{\sqrt{g_m \cdot 24\times 10^5}},$$

which can be solved to yield $g_m = 1.85\times 10^{-5}$ S/cm.

e. The specific membrane conductance is

$$G_m = \frac{g_m}{2\pi a} = \frac{1.85\times 10^{-5}}{2\pi 25\times 10^{-4}} = 1.18\times 10^{-3}\ \text{S/cm}^2.$$

f. The longitudinal resistance per unit length of cytoplasm is $r_i = \rho_i/(\pi a^2)$ so that

$$\rho_i = r_i \pi a^2 = (16\times 10^5)\pi(50\times 10^{-4})^2 = 126\ \Omega\text{-cm}.$$

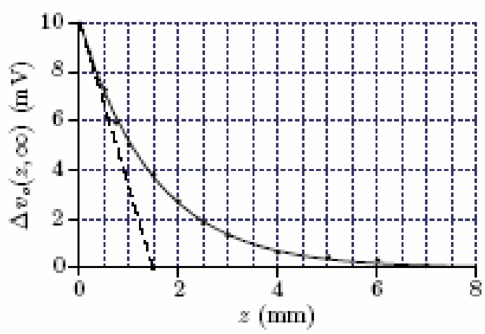
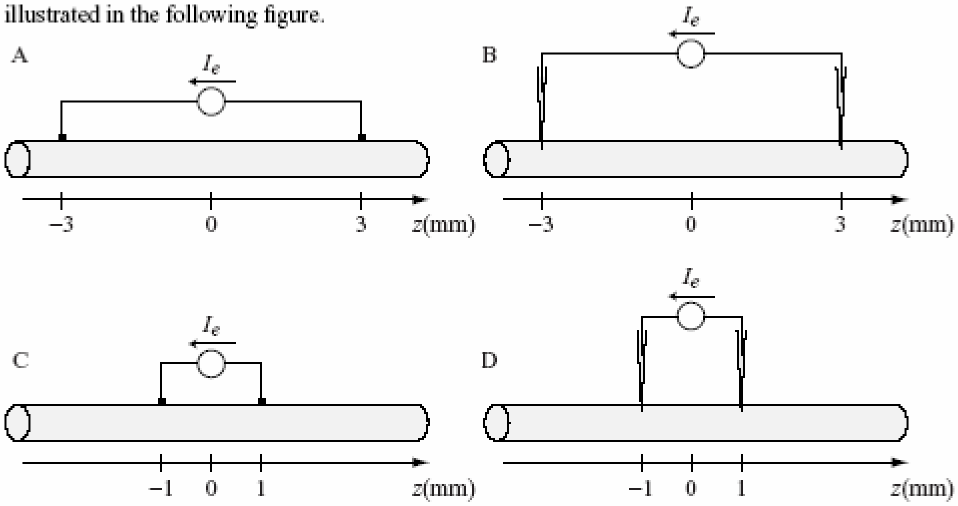


Figure 4: Estimation of space constant from measurements of steady-state value of the extracellular potential (Problem).

Problem 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.]

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

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

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

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

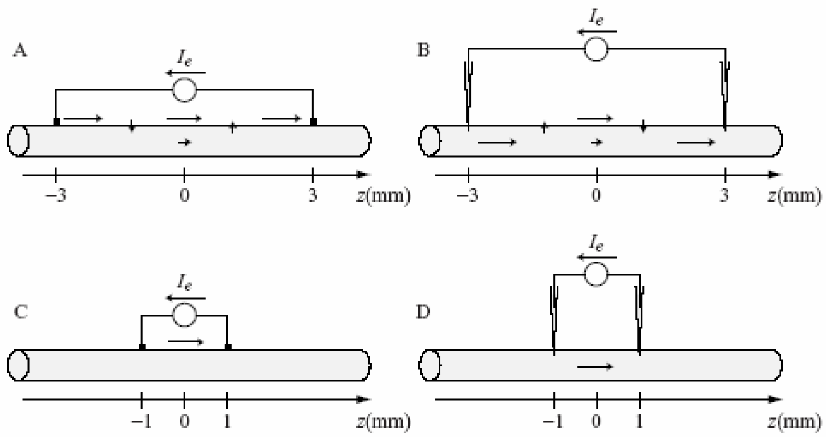
For which configuration is V_{max} most positive? Explain briefly.

Solution to Problem 2

Problem 2. The space constant is

$$\lambda_C = \sqrt{\frac{1}{1\ \text{mS/cm}^2 110\ \text{k}\Omega/\text{cm}}} \approx 1\ \text{mm}$$

Part a. When the electrodes are separated by many space constants, as in cases A and B, then the current partitions between the inside and outside according to the ratio of r_o to r_i. Since the outside resistance is 10 times less than the inside resistance, 10 times more current flows outside than inside in cases A and B. When the electrodes are closely spaced, little current passes through the membrane. The result is that most of the current passes through the external conductor for case C, and through the internal conductor in case D. These results are shown graphically below.



Thus, the internal longitudinal current at $z = 0$ is mose positive in case D.

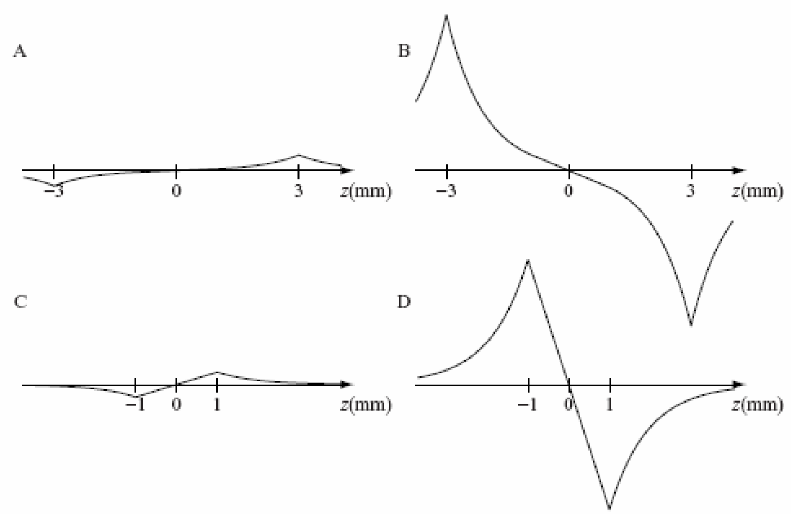
Part b. The transmembrane potentials are exponential functions of distance. All of the space constants are equal. However, the magnitudes are not. For extracellular electrodes, the peak membrane potential is

$$v_m(z) = \frac{r_o \lambda_c}{2}.$$

By symetry, for intracellular electrodes, the peak membrane potential is

$$v_m(z) = \frac{r_i \lambda_c}{2}.$$

Thus the peak membrane potential is 10 times as great for the intracellular electrodes. The following plot shows the membrane potential versus z for each of the four cases.



The potential is most positive at $z = 1$ mm in case C.

Part c. Since the positive and negative peaks are closer in case D than in case B, the positive peak in case B is approximately 20% bigger than the positive peak in case D. Thus, the maximum potential V_{max} is most positive in case B.