Problem Set 3.1

Membrane Potential, Action Potential, and Nerve Conduction

1. Muscle cells are long, multinucleated cells that are shaped something like cylinders that taper near the ends. Consider a 10-cm length of a muscle cell that is 50 μm in diameter. Assume that the cell is a right circular cylinder and that the capacitance of the muscle cell membrane is $1\ \mu F\ cm^{-2}$. Neglect the ends of the cylinder and edge effects where the membrane bends at the edges.
   A. How many charges have to move across the membrane in order to produce a potential of −80 mV, negative inside?
   B. The total concentration of anions (negatively charged ions) in the cytosol is about 150×10^{-3} M, and the total concentration of cations (positively charged ions) is about the same. About how many cation charges are there in the cytosol of the muscle cell of 10 cm length and 50 μm diameter?
   C. Compare the calculations in part A and part B. The ions that move across the membrane to produce the membrane potential of −80 mV are what fraction of the cytosolic cations?

   Helpful hints: One mole of charge is 9.649×10^4 C. This is the **Faraday**.
2. The chord conductance equation for the membrane potential derived for you Chapter 3.1 is incomplete. This is because at the same time there is passive movement of ions there occurs electrogenic active movement of ions. The Na−K pump carries a current and so contributes to the membrane potential directly. The contribution of the pump to the resting membrane potential can be estimated by noting the effect on the potential after inhibiting the pump with a specific inhibitor, **ouabain**. When ouabain is added, the membrane potential depolarizes by about 2 mV. The pump current can be estimated as

$$I_p = \frac{\Delta V_p}{R_m} \qquad [3.PS1.1]$$

   where I_p is the pump current, ΔV_p is the drop in voltage when the pump is inhibited, and R_m is the membrane resistance.
   A. If $R_m = 1000\ \Omega\ cm^2$, what is the pump current per cm^2 of membrane?
   B. Convert this answer to a flux of univalent ions in units of $mol\ cm^{-2}\ s^{-1}$.
   C. The density of Na−K pump sites, estimated by ouabain binding studies, is usually about $1000\ \mu m^{-2}$. If the pump has a turnover of about $120\ s^{-1}$, which is the number of completed reactions per second, and it pumps 3 Na^+ ions out for each completed cycle, what is the Na^+ flux across the membrane? This answer should be given in units of $mol\ cm^{-2}\ s^{-1}$.
   D. Convert the flux of Na^+ in part C to a current in units of amps cm^{-2}.
   E. If the pump transports 2 K^+ in for each completed turnover, calculate the K^+ flux in units of $mol\ cm^{-2}\ s^{-1}$.
   F. Convert the K^+ flux to a current in units of amps cm^{-2}.
   G. What is the net current carried by the pump, calculated both as mol charge $cm^{-2}\ s^{-1}$ and as amps cm^{-2}?
   H. How does the current and flux carried by the pump, calculated on the basis of the pump density and postulated turnover number, compared to the current and flux calculated by the depolarization caused by inhibition of the pump?
3. Assume that a membrane is permeable only to Na^+ and K^+. The concentrations of ions are:

$$[Na^+]_o = 145\ mM [Na^+]_i = 12\ mM$$

$$[K^+]_o = 4\ mM \quad [K^+]_i = 155\ mM$$

   A. Calculate the equilibrium potential for Na, E_{Na}.
   B. Calculate the equilibrium potential for K, E_K.
   C. Given the following table for g_K and g_{Na}, calculate the membrane potential, E_m, using the chord conductance equation.

Time (ms)	g_K	g_{Na}
0	0.366751	0.010589
0.4	2.186175	37.48381
0.8	5.478086	31.23947
1.2	9.486194	21.33964
1.6	13.48798	14.36902
2	17.05401	9.674778

   D. Graph the membrane potential against time. Does this vaguely resemble an action potential?

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E. The membrane potential during an action potential cannot be calculated solely by the chord conductance equation. Why not? *Hint*: Think of the assumptions used in deriving the chord conductance equation.

4. The action potential on a motor neuron lasts about 1.5 ms. A large motor neuron conducts the action potential at about $100\ \mathrm{m\ s^{-1}}$.
   A. Calculate the distance between the beginning of the action potential and its end during its conduction down the fiber. (At any time, the action potential is located in a place on the neuron; because the action potential does not occur instantaneously, it must be spread out in space. This question asks how spread out is the action potential.)
   B. The nodes of Ranvier are interruptions in the myelin sheath in myelinated fibers, and typically they are located about 1 mm apart along the length of the axon. The action potential that you calculated in part A is spread out over how many nodes of Ranvier?
   C. In saltatory conduction, what "jumps" from node to node?
5. Pain information from the skin travels to the spinal cord over several different kinds of axons. The $A\delta$ fibers conduct action potentials at up to $30\ \mathrm{m\ s^{-1}}$ whereas the small unmyelinated C fibers conduct more slowly. This information is processed beginning in the spinal cord where interneurons are used to connect the pain information to a motor neuron, which conducts at up to $100\ \mathrm{m\ s^{-1}}$. Consider a sharp pain that occurs at the end of the fingers, about 1 m away from the spinal cord. Calculate the minimum reaction time based on these speeds of conduction, allowing for two synaptic delays in the cord of 1 ms each.
   Reactions involving higher order nervous function (things you have to think about—such as braking your car) take longer because of the additional numbers of neurons involved in the pathway.
6. Suppose the internal specific resistance of the axoplasm is $50\ \Omega\ \mathrm{cm}$. Calculate the internal resistance of an axon 10 mm long if it has a radius of $5\ \mu\mathrm{m}$. Repeat the calculation for an axon with an internal radius of $500\ \mu\mathrm{m}$.
7. Assume that the dielectric constant of myelin is 8 and the thickness of one layer is 7.5 nm. Assume a radius of $5\ \mu\mathrm{m}$.
   A. Calculate the specific capacitance (the capacitance per unit area) of a single layer assuming it is a flat sheet. Calculate the capacitance if the axon is 10 cm long.
   B. Calculate the specific capacitance if the myelin sheath is $2\ \mu\mathrm{m}$, assuming it is a flat sheet. Calculate the total capacitance if the axon is 10 cm long.
   C. How do these differences in the capacitances affect the space constant? The time constant?
   D. Recalculate the capacitances in A and B assuming they are a coaxial capacitance. How much difference does it make to assume that the membrane is planar?
8. A cell has the following conditions:

$$[\mathrm{Na}^+]_o = 145\ \mathrm{mM} \quad [\mathrm{Na}^+]_i = 10\ \mathrm{mM}$$
$$[\mathrm{K}^+]_o = 4\ \mathrm{mM} \quad [\mathrm{K}^+]_i = 150\ \mathrm{mM}$$
$$[\mathrm{Ca}^{+2}]_o = 1.2\ \mathrm{mM} \quad [\mathrm{Ca}^{+2}]_i = 0.3\ \mu M$$

   A. Calculate E_{Na}, E_{K}, and E_{Ca}.
   B. If $g_{\mathrm{K}} = 100\ g_{\mathrm{Na}}$ and $g_{\mathrm{Na}} = 5\ g_{\mathrm{Ca}}$, calculate E_{m} at rest.
   C. Calculate the net driving force for I_{Na}, I_{K}, and I_{Ca}.
   D. Calculate the relative values of I_{Na}, I_{K}, and I_{Ca}.
9. From the graph in Figure 3.2.9, estimate the average conductance for Na^+ during the action potential by approximating the conductance as a triangle. Estimate the average E_{m} the same way. Calculate the average flux of Na^+ using the E_{Na} in the figure. Estimate the cytosolic content of Na^+, assuming the cell is a sphere with a radius of $20\ \mu\mathrm{m}$. How much does a single action potential change E_{Na}?
10. From the graph in Figure 3.2.14, estimate the unitary *current* carried by the K^+ channels in squid axons (right panel). If E_{m} is -70 mV in these cells, estimate the unitary *conductance* under physiological conditions.
11. Assume an axon has an internal diameter of $1\ \mu\mathrm{m}$ and a myelin sheath $1\ \mu\mathrm{m}$ thick. The internal specific resistance is $100\ \Omega\ \mathrm{cm}$. For the myelin sheath, use a dielectric constant of 8 and a transmembrane resistance of $2 \times 10^5\ \Omega\ \mathrm{cm}^2$.
   A. Calculate the internal resistance per unit length.
   B. Calculate the capacitance per unit length.
   C. Calculate the transmembrane resistance per unit length.
   D. Calculate the time constant.
   E. Calculate the space constant.
12. Assume an unmyelinated axon has an internal diameter of $1\ \mu\mathrm{m}$ and an internal specific resistance of $100\ \Omega\ \mathrm{cm}$. Assume the single plasma membrane is 7.5 nm thick and has a dielectric constant of 8. The transmembrane resistance is $1000\ \Omega\ \mathrm{cm}^2$.
   A. Calculate the internal resistance per unit length.
   B. Calculate the capacitance per unit length.
   C. Calculate the transmembrane resistance per unit length.
   D. Calculate the time constant.
   E. Calculate the space constant.
13. Assume that the extracellular $[\mathrm{Ca}^{2+}] = 1.2\ \mathrm{mM}$ and the intracellular $[\mathrm{Ca}^{2+}] = 0.1\ \mu\mathrm{M}$.
   A. Calculate the equilibrium potential for Ca^{2+}.
   B. If a channel was to open when $E_{\mathrm{m}} = -50$ mV, which way would Ca^{2+} go?
   C. Is this a positive or a negative current?

14. Suppose you depolarize an axon to threshold midway between its initial segment and its terminus.
    A. In which direction would the action potential travel?
    B. What would happen if you simultaneously began an action potential at the initial segment and at a point midway between the initial segment and the terminus?
15. A myelinated nerve is treated with tetrodotoxin in the middle of the axon. What happens to action potentials conducted from the initial segment toward the axon treated with tetrodotoxin?
16. Ouabain is a naturally occurring substance that inhibits the Na,K-ATPase with high affinity. When added to a neuron, the membrane potential depolarizes by about 2 mV. Why does this happen?
17. An excitable cell has the following conditions:

$$[\mathrm{Na}^+]_o = 145\ \mathrm{mM} \quad [\mathrm{Na}^+]_i = 10\ \mathrm{mM}$$

$$[K^+]_o = 4\ \mathrm{mM} \quad [K^+]_i = 150\ \mathrm{mM}$$

After passing a number of action potentials in a short time, the following changes occurred:

$$[\mathrm{Na}^+]_o = 140\ \mathrm{mM} \quad [\mathrm{Na}^+]_i = 15\ \mathrm{mM}$$

$$[K^+]_o = 7\ \mathrm{mM} \quad [K^+]_i = 145\ \mathrm{mM}$$

Calculate E_{Na} and E_{K} for the two conditions. If at rest $g_{\mathrm{K}} = 10\, g_{\mathrm{Na}}$, calculate the resting membrane potential at rest for both sets of ionic composition. What effect would this have on action potentials?

18. In the plot of threshold current against stimulus time, the rheobase is difficult to determine because it is the extrapolation of threshold current at infinite time. Using the Weiss equation, suggest a different plot of the equation that would allow determination of I_{rh} by extrapolation of a linear curve, and calculation of τ_{SD} from the slope of the line.
19. Consider an excitable cell with a resting membrane potential of -60 mV and a uniform threshold potential of -40 mV. For the following questions, refer to Figure 3.2.15.
    A. If the membrane is hyperpolarized to -65 mV, what would the sign of the total current be? What would happen as a result of this current?
    B. If the membrane was depolarized to -50 mV, what would the sign of the total current be? What would happen as a result of this current?
    C. If the membrane was depolarized to -35 mV, what would the sign of the total current be? What would happen as a result of this current?
20. Dendrites are not right cylinders but taper as they extend away from the body, or soma, of the neuron. Neurotransmitters cause either a depolarization or hyperpolarization (postsynaptic potentials) that is conveyed electronically through the cytoplasm. Would these postsynaptic potentials decay away differently for thin versus wider dendrites?