Homework Assignment #7

Issued: November 8, 2004
Due: November 18, 2004

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Lecture 27 — Preparing an oral presentation
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Announcements
There is no homework assignment due this week, because of Veteran’s day. This assignment is due on the Thursday after Veteran’s day (November 18).

First Drafts of your HH project is due on November 19 (one day after this homework is due!). The first draft should consist of hardcopies of 3-5 technical slides of the type you plan to show during your final oral presentation. Each slide should be accompanied by a separate sheet of paper that lists approximately three bullet points that you will discuss in your presentation of this slide. The first draft should also contain a 1 page extended abstract for your HH project. The abstract should summarize your findings and explain why they are interesting.

Please take advantage of THIS week to work on your project plus the HH portion of this homework assignment!

Exercise 1. The following assertions apply to responses calculated according to the Hodgkin-Huxley model in response to a step of membrane potential applied at $t = 0$. For each assertion, state if it is true or false and explain your answer.

a) The leakage conductance is constant.
b) The sodium conductance is discontinuous at $t = 0$.
c) The potassium conductance is discontinuous at $t = 0$.
d) The leakage current is constant.
e) The sodium current is discontinuous at $t = 0$.
f) The potassium current is discontinuous at $t = 0$.
g) The factors $n(t)$, $m(t)$, and $h(t)$ are discontinuous at $t = 0$. 
h) The time constants $\tau_n$, $\tau_m$, and $\tau_h$ are discontinuous at $t = 0$.
i) The steady-state values $n_\infty$, $m_\infty$, and $h_\infty$ are discontinuous at $t = 0$.

**Exercise 2.** Figure 1 shows the relation between the membrane potential and the membrane current density during a propagated action potential as computed from the Hodgkin-Huxley model. The membrane current density consists of an initial outward current followed by an early inward current whose peak occurs before the peak in the action potential.

a) The initial outward current is due primarily to which of the following:
   i) an ionic current carried by sodium ions.
   ii) an ionic current carried by potassium ions.
   iii) an ionic current carried by chloride ions.
   iv) an ionic current carried by calcium ions.
   v) a capacitance current.

b) The early inward current is due primarily to which of the following:
   i) an ionic current carried by sodium ions.
   ii) an ionic current carried by potassium ions.
   iii) an ionic current carried by chloride ions.
   iv) an ionic current carried by calcium ions.
   v) a capacitance current.

c) Before the peak of the action potential, the membrane potential increases from its resting value whereas the membrane current density is first outward (increasing and then decreasing) and then reverses polarity to become inward (decreasing and then increasing again). Discuss this complex relation between membrane potential and current. In particular, explain how the Hodgkin-Huxley model accounts for the fact that the current can be both inward and outward during an interval of time when the membrane potential is depolarizing.
**Exercise 3.** Does the time constant of a cylindrical cell depend on its dimensions? Does the space constant of a cylindrical cell depend on its dimensions?

**Exercise 4.** For each of the following statements, assume that the electrical properties of a patch of the membrane of the cell can be represented as a parallel resistance and capacitance. Assume that the cell has a cylindrical shape with a radius that is small compared to the length of the cell. Determine if each assertion is true or false and give a reason for your choice.

a) For an electrically small cell, the membrane potential in response to a step of current through the membrane is an exponential function of time.

b) If a step of current is applied through one part of the membrane of an electrically small cell, the resulting changes in membrane potential will be constant along the length of the cell for all times after the step.

c) For an electrically large cell, the steady-state value of the membrane potential in response to a step of current applied through the membrane at one position along the cell is an exponential function of longitudinal position along the cell.

d) For an electrically large cell, the steady-state value of the membrane potential in response to a step of current applied through the membrane at one position along the cell is a Gaussian function of position along the cell.
**Problem 1.** The Hodgkin-Huxley model was used to compute **propagated** action potentials for default values of the parameters and for 4 test cases. The following plots show the spatial dependence of membrane potential that results 1 ms after the stimulus current was applied at \( z = 0 \).

Each of A–D shows a plot with two curves: the thin gray curve was obtained for default parameters and the thick black curve was obtained for one of the tests cases. In each test case, a single parameter was changed from its default value. Default values of the axon characteristics are as follows — length: 3 cm, radius: 0.0238 cm, cytoplasm resistivity: 35.4 \( \Omega \cdot \text{cm} \), extracellular specific resistance: 0 \( \Omega/\text{cm} \).

**a.** Which of A–D shows results when intracellular sodium concentration was reduced from \( c_{Na}^i = 50 \) to 25 mmol/L. Explain.

**b.** Which of A–D shows results when the maximum potassium conductance \( \overline{G}_K \) was increased from 36 to 72 mS/cm\(^2\)? Explain.

**c.** Which of A–D shows results when cytoplasmic resistivity was decreased from 35.4 to 30 \( \Omega \cdot \text{cm} \)? Explain.
Problem 2. Ionic currents are calculated for a space-clamped squid giant axon using the Hodgkin-Huxley model, with all parameters set to their default values (as listed on page 191 of volume 2 of the text) except for one parameter. For times $t < 0$, the membrane potential is held at $-75$ mV and the model is at steady state. At $t = 0$, the membrane potential is stepped to $+5$ mV and the resulting ionic current density is computed. Results for six calculations are shown in the following figure.

Part a. Which curve represents the ionic current that results when all parameters have default values except $c_{Na}^o = 50$ mmol/L? Explain.

Part b. Which curve represents the ionic current that results when all parameters have default values except $c_K^o = 400$ mmol/L? Explain.

Part c. Which curve represents the ionic current that results when all parameters have default values except $G_{Na} = 0$? Explain.

Part d. Which curve represents the ionic current that results when all parameters have default values except $G_K = 0$? Explain.

Problem 3. Space-clamped responses of the Hodgkin-Huxley model were calculated with the leakage conductance set to zero, $G_L = 0$, and with all other parameters set to their default values. The model was stimulated with a pulse of membrane current density of duration 0.5 ms; the amplitude was varied. The following figure shows the response for an amplitude of $40 \, \mu A/cm^2$.
For each amplitude of the pulse of membrane current density, the ionic current density \( J_{\text{ion}} \) and the membrane potential \( V_m \) were determined at \( t = 0.7 \) ms, where \( t = 0 \) marks the onset of the current pulse. The relation between \( J_{\text{ion}} \) at \( t = 0.7 \) ms and \( V_m \) at \( t = 0.7 \) ms that results when the pulse amplitude is varied is shown in the following figures. The left panel shows results for a broad range of membrane potential, from \(-80\) to \(+60\) mV. The right panel shows results for the narrower range from \(-76\) to \(-62\) mV.

![Graphs showing ionic current density and membrane potential](image)

**Part a.** Determine the value of the resting potential to within 1 mV. Explain your choice.

**Part b.** If the current stimulus is such that \( V_m(t) = -66 \) mV at \( t = 0.7 \) ms, does the membrane potential increase with time or decrease with time? Explain.

**Part c.** Determine the value of the threshold potential to within 1 mV. Explain your choice.

**Part d.** Between the resting potential and this threshold potential, determine whether \( |J_{Na}| > |J_K| \), \( |J_{Na}| = |J_K| \), or \( |J_{Na}| < |J_K| \). Explain.

**Part e.** Just above the threshold potential, determine whether \( |J_{Na}| > |J_K| \), \( |J_{Na}| = |J_K| \), or \( |J_{Na}| < |J_K| \). Explain.

**Problem 4.** The Hodgkin-Huxley model of a space-clamped squid giant axon stimulated by a pulse of membrane current of amplitude \( 20 \mu A/cm^2 \) and of duration \( 0.5 \) ms produces a membrane action potential. You can demonstrate this to yourself by running the space-clamped version of the Hodgkin-Huxley simulation software provided with this subject. Start by using the default parameters. If you change the membrane capacitance from \( 1 \mu F/cm^2 \) to \( 20 \mu F/cm^2 \), no action potential occurs.

**Part a.** Explain why no action potential occurs for the larger value of membrane capacitance. You may base your explanation on comparison of the membrane currents, conductances, and activation variables for the default parameters and for the increased capacitance condition. Alternatively, you may wish to perform additional computations with other values of membrane capacitance.

**Part b.** With membrane capacitance fixed at \( 20 \mu F/cm^2 \), determine a set of parameters that produce an action potential with a waveform that is identical to the action potential obtained with the default parameters. To determine whether or not the action potential is identical to that obtained with the default parameters, you can superimpose plots and/or look at the parameters computed from the responses. You should use the computer as a tool to check your ideas and not as a substitute for thinking. You should avoid a strictly trial-and-error approach. There are simply too many parameters in the Hodgkin-Huxley model for you to explore them all randomly. When you have arrived at a satisfactory solution, explain why your parameter change produces the desired result.
Problem 5. Constant currents $I_1$ and $I_2$ are applied to the exteriors of Axons 1 and 2, respectively, and the resulting time-independent changes in membrane potential are $v_{m1}(z)$ and $v_{m2}(z)$, respectively. $I_1$ and $I_2$ are adjusted so that $v_{m1}(0) = v_{m2}(0) = 10 \text{ mV}$. This change in potential is sufficiently small so that the membrane voltage-current characteristic may be assumed to be linear. You may also assume that $r_o \ll r_i$ for both axons and that $r_o$ is the same for both axons. The geometries and parameters for Axons 1 and 2 are given below, where $a$ is the axon radius, $\rho_i$ is the cytoplasmic resistivity, and $G_m$ is the specific membrane conductance.

<table>
<thead>
<tr>
<th>Axon #</th>
<th>$a$ (µm)</th>
<th>$\rho_i$ (Ω·cm)</th>
<th>$G_m$ (S/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>100</td>
<td>100</td>
<td>$5 \times 10^{-3}$</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>100</td>
<td>$(1/8) \times 10^{-3}$</td>
</tr>
</tbody>
</table>

a) Let $v_{m1}(-0.1)$ and $v_{m2}(-0.1)$ be the membrane potential changes at $z = -0.1 \text{ cm}$ for the two axons. Determine the value of the ratio $A = v_{m1}(-0.1)/v_{m2}(-0.1)$.

b) Determine the value of the ratio $B = I_1/I_2$.

Problem 6. A large unmyelinated axon is immersed in oil, and five different arrangements of electrodes for delivering current stimuli and for measuring potential responses are attached to the axon as shown below.
The stimulus current, a brief positive pulse at $t = 0$, is the same for each arrangement of electrodes. The pulse has a duration that is much shorter than the membrane time constant of the cell, and a strength that is low enough that the cell’s voltage response remains in its linear range of operation. The space constant of the cell is $\lambda_C$. In arrangement d, the potential is recorded and the current is delivered at the same longitudinal position. In part e, the electrodes are much longer than $\lambda_C$.

For each of the different arrangements (parts a-e in the figure) determine which of the following waveforms for $v(t)$ represents the deviation of the measured potential from its resting value. For each waveform, the horizontal axis corresponds to $v(t) = 0$, and the vertical axis to $t = 0$. If no waveform applies, answer None. Explain the basis of your choice in each case.