Massachusetts Institute of Technology
Department of Electrical Engineering and Computer Science,
Department of Mechanical Engineering, Department of Biological Engineering,
Harvard-MIT Division of Health Sciences and Technology

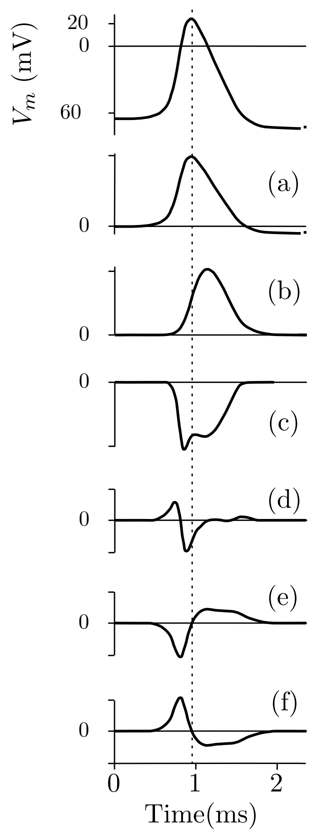
2.791J/2.794J/6.021J/6.521J/20.370J/20.470J/HST.541J

Quantitative Physiology: Cells and Tissues

Homework Assignment #7 — Issued: November 2, 2006
Due: November 9, 2006

Part of this week's homework assignment is to write a proposal for your Hodgkin-Huxley project.

Exercise 1. The top left plot in the following figure illustrates $V_m(z_o, t)$, which represents the transmembrane potential for a propagated action potential at a point z_o along an axon as computed according to the Hodgkin-Huxley model. The action potential is propagating in the $+z$-direction. The other six waveforms represent various components of current associated with this action potential. Outward current through the membrane is defined as positive and is plotted upward, current in the positive z-direction is defined as positive and is plotted upward. Identify each of the waveforms (a) through (f) with one of the choices (i) through (xii) in the right column. Briefly state your reason(s) for each choice.



(i) The total ionic current.

(ii) The internal longitudinal current.

(iii) The sodium current.

(iv) The potassium current.

(v) The calcium current.

(vi) The leakage (other) current.

(vii) The capacitance current.

(viii) The inductive current.

(ix) The total membrane current.

(x) The sodium pump current.

(xi) The potassium pump current.

(xii) The external longitudinal current.

Exercise 2. 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 $t = 0$.

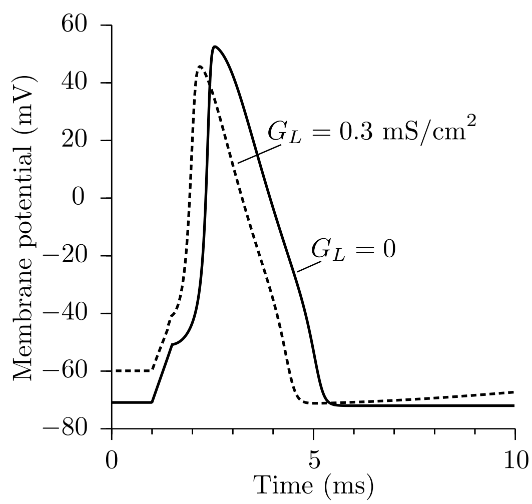
f) The potassium current is discontinuous at $t = 0$.

g) The factors $n(t)$, $m(t)$, and $h(t)$ are discontinuous at $t = 0$.

h) The time constants τ_n, τ_m, and τ_h are discontinuous at $t = 0$.

i) The steady-state values n_∞, m_∞, and h_∞ are discontinuous at $t = 0$.

Exercise 3. The following figure shows the response of the Hodgkin-Huxley space-clamped model model to a pulse of membrane current that has an amplitude of 40 μA/cm^2 and a duration of 0.5 ms. Results are shown for both the default parameters of the model, for which $G_L = 0.3$ mS/cm^2, and for $G_L = 0$.

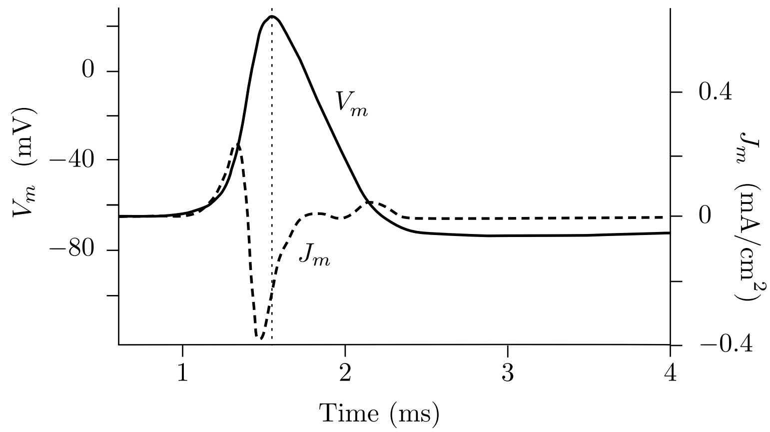


a) In 100 words or fewer explain why the resting potential is decreased by the decrease in leakage conductance.

b) In 100 words or fewer explain why the peak of the action potential is increased by the decrease in leakage conductance.

c) In 100 words or fewer explain why the undershoot of the action potential is eliminated by the decrease in leakage conductance.

Exercise 4. The following figure 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. The dotted vertical line marks the time of occurrence of the peak of the action potential.

a) The initial outward current is due primarily to which of the following:

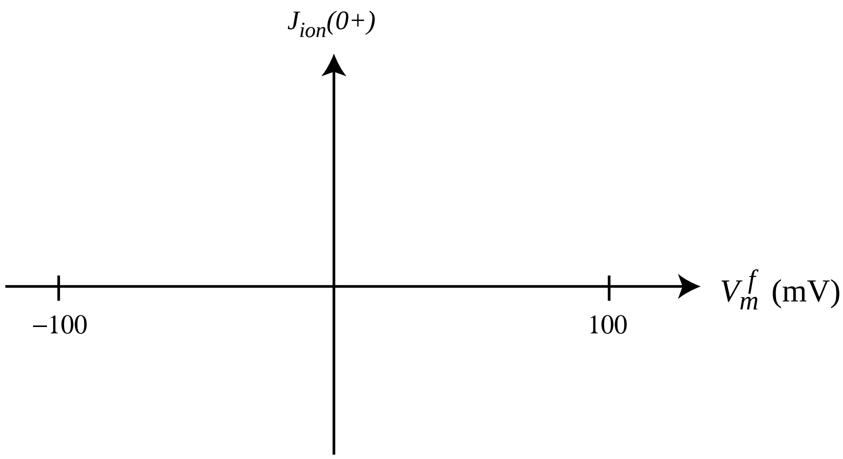
  i) an ionic current carried by sodium ions.
  ii) an ionic current carried by potassium ions.
  iii) an ionic current carried by chloride ions.
  iv) an ionic current carried by calcium ions.
  v) a capacitance current.

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.

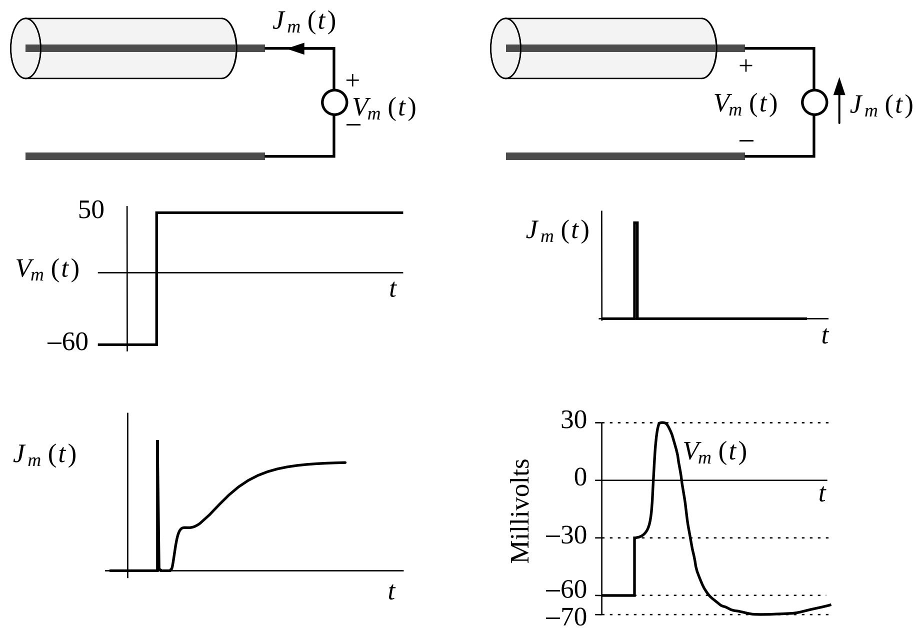
c) Before the peak of the action potential, the membrane potential increases from its resting value whereas the membrane current density is first outward (increasing and then decreasing) and then reverses polarity to become inward (decreasing and then increasing again). Discuss this complex relation 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 5. The ionic current density J_{ion} is calculated for default parameter values of the Hodgkin-Huxley model under voltage clamp conditions. The initial voltage V_m^i is held at 0 mV for a long time so that the currents are at steady state at $t = 0$. Then at $t = 0$, the voltage is stepped to V_m^f. On the axis below, sketch the value of the ionic current density that results at $t = 0^+$, $J_{ion}(0^+)$, as a function of V_m^f.



Put numerical labels on the axes. Explain the important features of your plot and why those features result from the Hodgkin-Huxley model.

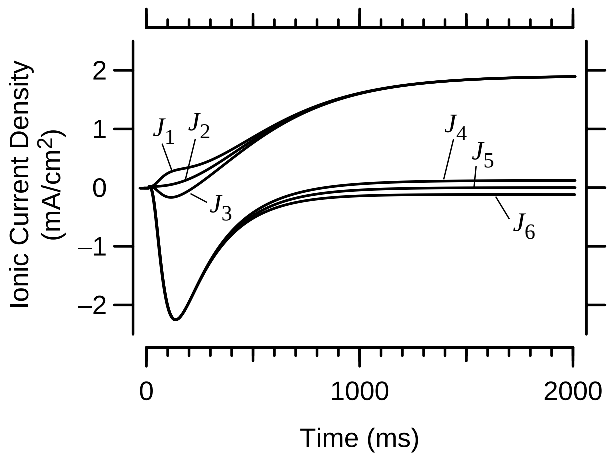
Problem 1. A squid giant axon is immersed in sea water that has a concentration of potassium and sodium of 10 and 400 mmol/L, respectively. Two measurements are made on this axon: the membrane current density in response to a step of membrane potential (left panel of following figure); the membrane potential in response to a brief pulse of membrane current density (right panel).



Part a. Find the smallest range of values of internal sodium concentration that is consistent with these measurements. Explain!

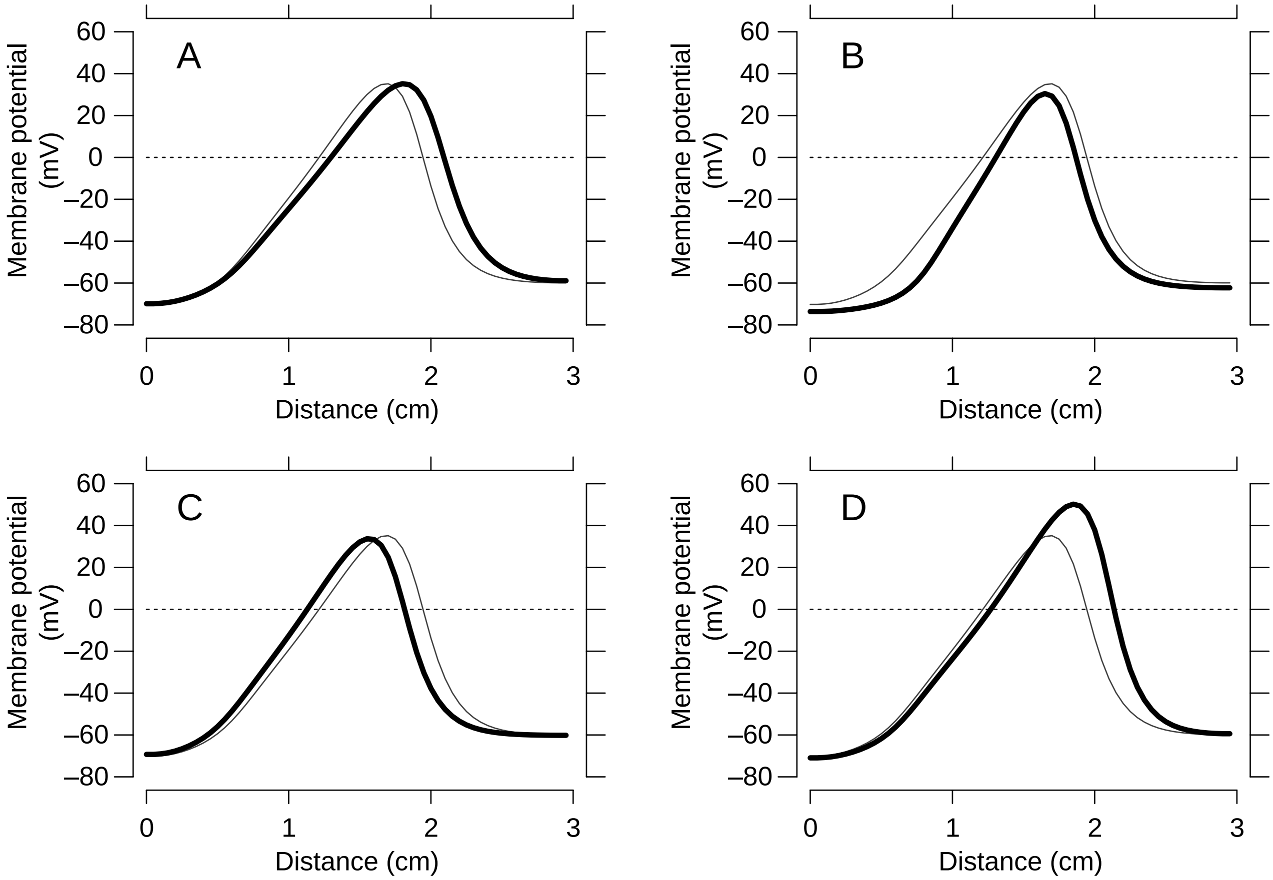
Part a. Find the smallest range of values of internal potassium concentration that is consistent with these measurements. Explain!

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 $c^o_{Na} = 50$ mmol/L? Explain.
Part b. Which curve represents the ionic current that results when all parameters have default values except $c^o_K = 400$ mmol/L? Explain.
Part c. Which curve represents the ionic current that results when all parameters have default values except $\overline{G}_{Na} = 0$? Explain.
Part d. Which curve represents the ionic current that results when all parameters have default values except $\overline{G}_K = 0$? Explain.

Problem 3. 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 $z = 0$.



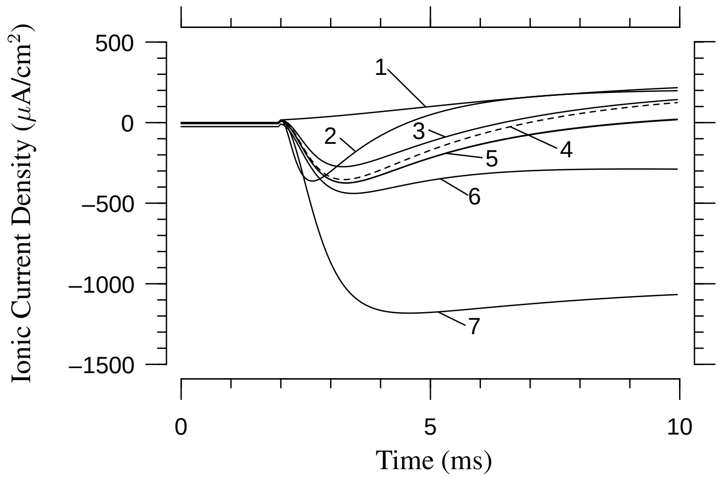
Each of A–D shows a plot with two curves: the thin gray curve was obtained for default parameters and the thick black curve was obtained for one of the tests cases. In each test case, a single parameter was changed from its default value. Default values of the axon characteristics are as follows — length: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

a. Which of A–D shows results when intracellular sodium concentration was reduced from $c^i_{Na} = 50$ 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 Ω·cm? Explain.

Problem 4. Ionic current densities are calculated for a space-clamped squid giant axon using the Hodgkin-Huxley model. For times $t < 2$ ms, the membrane potential is held at -60 mV. At time $t = 2$ ms, the membrane potential is stepped and held at -35 mV. Results are obtained using default values of all parameters, and for a series of experiments designed to model experimental manipulations of the axon. For each experiment, default values were used for all parameters except one. The resulting current densities are shown in the following figure.



The results correspond to the following experiments:

A. external sodium concentration decreased by factor of 2.
B. sodium conductance completely blocked using TTX.
C. half of the potassium conductance blocked using TEA.
D. external potassium concentration doubled.
E. membrane capacitance halved.
F. temperature increased $6°$C.
G. inactivation of sodium conductance removed using pronase.
H. others.

The dashed curve represents results for default values of all parameters. It may also represent results for one or more of the experiments listed above.

Part a. Which curve shows results when the external sodium concentration was decreased by factor of 2. Briefly explain.
Part b. Which curve shows results when the sodium conductance was completely blocked using TTX. Briefly explain.
Part c. Which curve shows results when half of the potassium conductance was blocked using TEA. Briefly explain.
Part d. Which curve shows results when the external potassium concentration was doubled. Briefly explain.
Part e. Which curve shows results when the membrane capacitance was halved. Briefly explain.
Part f. Which curve shows results when temperature was increased $6°$C. Briefly explain.
Part g. Which curve shows results when the inactivation of the sodium conductance was removed using pronase. Briefly explain.