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9.01 Introduction to Neuroscience
Fall 2007

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9.01 Problem Set 1: Cellular neurophysiology

Fall 2007

Due Friday, Sept. 21 at 12 noon.

No late submissions will be accepted.

This problem set will develop your understanding of the action potential. Many of the exercises will make use of a computer program called `HHsim`, which is described in an accompanying handout. While collaboration is allowed, you are required to write up your solutions independently, as well as document the names of your collaborators. In your answers, please try to address all major points yet also be concise.

1. The Nernst potential

Suppose that astronauts discover life on Mars. They excitedly bring it into the lab on board their spaceship, and measure the following ionic concentrations (in mM).

	intracellular	extracellular
Li^+	130	60
Br^-	70	200
Mg^{2+}	0.001	10

The membranes of Martian cells are permeable to lithium, but not to bromide and magnesium.

Question A (6 pts): What are the Nernst potentials of the three types of ions, calculated at body temperature 37°C ? Give the value of the intracellular potential with the convention that the potential of the extracellular space is zero. Make sure to get the sign right, as it's even more important than the exact number!

Question B (3 pts): How do the Nernst potentials change if a typical Martian temperature of 10°C is used instead? Just indicate the direction of the change for each ion (no need to calculate exact numbers).

2. Activation and inactivation of the voltage-gated sodium channel

One of the most confusing aspects of the action potential is the presence of distinct “activation” and “inactivation” processes, which are both voltage-dependent, and both affect the conductance of the sodium channel. Activation and inactivation have opposite *effects* on the sodium conductance, and hence on voltage. However, inactivation is *not* the absence of activation! They are actually two independent processes. Indeed, it is possible for the sodium channel to be activated and inactivated at the same time.

In `HHsim`, activation and inactivation variables are plotted in the bottom graph of the main window. The m variable quantifies the amount of “activation” and the h variable

quantifies the amount of “inactivation.” Both variables take on values between 0 and 1. Here is how the words correspond to the numbers:

	0	1
m	deactivated	activated
h	inactivated	deinactivated

Question A (4pts): For sodium current to flow, the sodium channel must be _____ (activated/deactivated), and _____ (inactivated/deinactivated). In other words, m should not be ____ (0/1) and h should not be ____ (0/1).

Question B (4pts): What effect does depolarization (a shift in the membrane voltage to a less negative value) have on activation and inactivation? What is the effect in terms of m and h ?

The variables m and h are plotted as functions of time in yellow and green traces of the bottom graph of the HHSim main window. The simulator starts out with the neuron at its resting potential. Click on the yellow or green trace to display its value in the lower right hand corner.

Question C (4pts): What is the value of m at rest? Does that mean the sodium channels are activated or deactivated? What is the value of h at rest? Does that mean the sodium channels are inactivated or deinactivated?

3. Activation of the voltage-gated potassium channel

The potassium channel is simpler than the sodium channel, because it lacks inactivation. There is just a single activation variable n , taking on values between 0 (deactivated) and 1 (activated). The sodium current is said to be *transient*, because depolarization can only make it flow temporarily, before inactivation shuts it down. The potassium current is said to be *persistent*, because depolarization can make it flow indefinitely.

Question A (2pts): For potassium current to flow, the potassium channel must be _____ (activated/deactivated). In other words, n should not be ____ (0/1).

Question B (2pts): What effect does depolarization (a shift in the membrane voltage to a less negative value) have on activation? What is the effect in terms of n ?

The variable n is plotted as a function of time in the cyan trace of the bottom graph of the HHSim main window. The simulator starts out with the neuron at its resting potential. Click on the cyan trace to display the value of n .

Question C (2pts): What is the value of n at rest? Does that mean the potassium channels are activated or deactivated?

4. Action potential

Click on the purple Stim1 button at the bottom left of the main window. The button simulates the effect of injecting a current pulse into the cell through a microelectrode. In the upper graph of the main window, the stimulus current is plotted as a purplish line, while the membrane voltage is plotted as a red line. The stimulus current is positive, and is said to be *depolarizing*. You should see an action potential, or “spike” in the membrane voltage.

Question A (4pts): Based on observation of your simulation, make a drawing of what happens to the membrane voltage, m , h , and n . Two of the variables change more rapidly, and two of them change more slowly. Which are which?

Question B (8pts): Explain why it’s important for the slow variables to be slow, in the generation of an action potential.

Now click on the Stim2 button to apply a negative, or *hyperpolarizing* current pulse to the cell. Notice that this also results in a spike. This behavior may be a bit surprising at first. To understand it, you’ll have to think about the voltage-dependence of the channels.

Question C (8pts): Explain why a negative current pulse is able to cause an action potential.

5. Repolarization

Press the Channels button at the top of the main window. A Channels window will pop up. Press on the Delayed Rectifier (potassium) button. The button will change from colored to gray, meaning that the channel is disabled. Now press the yellow Nudge button at the bottom of the main window (you could also press the Run button if you like).

Question A (6pts): The membrane voltage jumps up rapidly, performing the upstroke of the action potential. Explain why this happens.

Question B (4pts): After the upstroke of the action potential, the membrane voltage does not repolarize, instead settling at a positive value. What is that value? (Click on the red trace to find out.) Explain why the membrane voltage does not repolarize.

If you would like to reenable the channel after you are done with this exercise, press on the Delayed Rectifier button again. The button will change from gray back to colored.