Problem Set 6 (due Thurs Apr 22)
Extensions of the Hodgkin-Huxley model

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Download the MATLAB script: cc.m, (Available in the assignment section.)
which is for simulating the Hodgkin-Huxley model in current clamp. You can read Chapter 5 of Dayan and Abbott for an explanation of the model equations. Note that conductances, capacitances, and currents are given per unit area. More specifically, capacitances are in $\mu F/mm^2$, conductances in $mS/mm^2$, and current in $\mu A/mm^2$. Furthermore, time is in msec, and voltage in mV.

1. Firing frequency vs. applied current. Modify the code so that you can simulate the response of the HH model to a step change from zero applied current to positive current.

   (a) Simulate the behavior for applied currents of 0.01, 0.05, 0.1, and 5 $\mu A/mm^2$. Start from the initial conditions given in the code. For each case, graph the voltage vs. time, and describe in words the behaviors that you see.

   (b) You described four qualitatively different behaviors above. Find the three threshold values of the current that separate these four types of behavior. In other words, there is some value of the applied current below which behavior 1 holds, and above which behavior 2 holds. And so on for the other thresholds.

   (c) One of the four types of behavior you should have described above is convergence to repetitive firing of action potentials that continues indefinitely. What is the minimum frequency of such firing? What is the maximum frequency? Can you explain why repetitive firing is impossible above this maximum?

2. The MATLAB code is provided with initial conditions for $V$, $m$, $h$, and $n$, which are approximately the fixed point of the HH model at zero applied current. In this problem, you’ll explore the effects of varying the initial conditions.

   (a) Change the initial condition for $V$ so that it is 5 mV higher the value given in the code, and simulate for 100 msec. Graph the resulting $V$ as a function of time. You will see that the model settles back to the fixed point without much ado.

   (b) Now change the initial condition for $V$ so that it is 10 mV higher the value given in the code, and simulate for 100 msec. Graph the resulting $V$ as a function of time. Now you will see an action potential before the model settles back to the fixed point.

   (c) Approximately determine the threshold voltage above which an action potential is evoked, and below which one is not evoked.

3. Post-inhibitory rebound. Experiment with the following stimulation: start with zero applied current, step to a negative value, and then step back to zero. Find an amplitude and duration of the negative step such that the HH model fires an action potential afterwards, a phenomenon known as post-inhibitory rebound. Plot $V$, $m$, $h$, and $n$ as a function of time. Explain in words why this phenomenon happens.

4. Write MATLAB code to simulate the Connor-Stevens model and reproduce Figure 6.1 of Dayan and Abbott. You can use the above code for the Hodgkin-Huxley model as a starting point. To debug your code, use the fact that the model should converge to the steady state $V = -68$ mV, $m = 0.0101$, $h = 0.9659$, $n = 0.1559$, $a = 0.5404$, and $b = 0.2887$, if the applied current is zero.
5. Download B. Ermentrout, Linearization of F-I curves by adaptation, Neural Comput. 10:1721-9 (1998) Write MATLAB code to simulate the model described in Section 4.1, and reproduce Figure 2A. The paper gives certain parameters per cm², rather than per mm². This is a different convention than Dayan and Abbott—don’t get confused by it. Also graph $z$ versus time, and explain in words how its behavior is related to the spike frequency adaptation in Figure 2A.

Note: The basic model described in Section 4.1 has the same equations as the Hodgkin-Huxley model, but with different parameters. It is inspired by Traub’s model of hippocampal neurons. The adaptation current can be interpreted in a number of ways. Ermentrout calls it an M-current, after the muscarine-sensitive potassium current. It could also be interpreted as a slow inhibitory autapse with a time constant of 100 ms. An autapse is a synapse made by a neuron onto itself. Finally, it could be regarded as a simplified model of calcium-dependent potassium current. In that case, the variable $z$ would represent calcium concentration. An explicit model for the accumulation of calcium is given in Section 4.2 of the paper.

6. Change the reversal potential of the adaptation current to 0, and let $g = 0.01 \text{ mS/mm}^2$. Show that the resulting model is bistable with zero applied current. This means that there are two stable states, one quiescent and the other firing. More specifically, you can demonstrate bistability by showing that it is possible to toggle between the two states using transient current pulses. For example, you could start with the neuron at rest, and then apply a transient depolarizing current pulse that causes the neuron to fire repetitively even after the pulse is over. Then you could apply a transient hyperpolarizing current pulse that causes the neuron to stop firing and remain quiescent even after the pulse is over. Explain in words the reason for this bistability.

Note: Here the extra current can be interpreted more than one way. There is some resemblance to a persistent calcium current (though the reversal potential is too low). It is also like a slow excitatory autapse with a time constant of 100 ms.