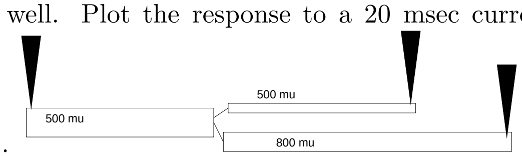
Homework

In this set of exercises, you will build and simulate a number of different types of neural models.

1. (a) Build a cable which is 1000 microns long and 2 microns in diameter by breaking it into 20 50 micron pieces. Assume that the axial resistance is 100 $\Omega - cm$, the transmembrane resistance is 10000 $\Omega - cm^2$ and the capacitance is $1\mu F/cm^2$. The resting potential is -65 mv. Assume that the boundary conditions at either end are sealed so there is no leak. Inject the first compartment with $1\mu A/cm^2$ current for 10 msec. If this was just a single isolated compartment, the voltage would rise by 10 mV. However, the rest of the cable shunts the current. What is the peak potential in the first compartment. What is the peak potential at the other end of the cable? What times do the peaks in the first and last compartments occur? How big must the current be to raise the potential in the last compartment by 5 mV? What is the peak voltage at the site of injection when the voltage in the last compartment has been raised by 5 mV? Apply the same current for 100 msec. This should be long enough to reach steady state. Given $V(0)$, the voltage of the first compartment, cable theory tells us that the voltage in the last compartment is roughly $V(0)\exp(-L/\lambda)$ where L is the length of the cable and λ is the space constant. Compute λ. Does this ballpark estimate agree with your numerical calculation - that is, is the steady state in the last compartment what you'd expect it to be? Appendix B in chapter 6 of Dayan and Abbot could be helpful in guiding your work.

   (b) Using this same cable, inject sinusoidal current into the first compartment, $I(t) = I_0 \sin(2\pi\omega t)$ where $I_0 = 10\mu A/cm^2$. Choose 5, 10 , 20, 40, and 100 Hz currents. For each of these, measure the peak deviation from rest for compartments 1 and 20, and the phase-difference between the peaks in these compartments. The phase difference is the time difference between peaks divided by the period and multiplied by 2π.

2. Construct a cable model with passive parameter as in the previous problem which consists of a 4 micron diameter cable of length 500 microns broken into 10 pieces. This branches into two cables, one has a diameter of 1 micron, length 500 microns, and the other has diameter 2 microns and length 800 microns. Break the shorter into 10 piences and the longer into 15 pieces. (Each piece will be 50 microns long.) Stimulate the cable at each of the three ends indicates in the picture below and record at these ends as well. Plot the response to a 20 msec current pulse that is 10 μA/cm^2.



3. Solve the single compartment Hodgkin Huxley equations using the parameters for the potassium gate given on page 171 equation 5.22, the sodium kinetics from equation 5.24, and the conductances and reversal potentials in equation 5.25. Note that Dayan & Abbott use conductance of mS/mm^2, so you should multiply them by 100 to get to our standard units. Use $C_m = 1\mu\text{F/cm}^2$ for the capacitance. Start with initial conditions of $V = -65$ mV,$m = .05$, $n = .32$, $h = .596$. Now inject a constant current of 4 $\mu A/cm^2$. Inject a current of 8 $\mu A/cm^2$. You should see repetitive firing. Now, a really cool experiment which was done by Guttman and Rinzel (J. Physiol. 1980 Aug;305:377-95). On top of the constant applied current of 8 $\mu A/cm^2$ inject a 5 msec pulse of 5 $\mu A/cm^2$. If you time this correctly (I started the model at the above initial conditions with the constant bias current of 8 and apply the impulse 104 msec later), you can kill the repetive firing and bring the system to rest. This illustrates an important phenomena – bistability, in which there is both a stable repetitive firing mode and a stable equilibrium. If you increase the bias current to say 15 $\mu A/cm^2$then bistability is lost and all that there is are repetitive action potentials. Compute the FI-curve for this model by incrementing the current in steps of 5 $\mu A/cm^2$from 0 to 100 and determining the period. Show that if the current is too high you also lose repetitive firing. Figure out the maximum current you can apply and still get periodic behavior. (Note, if you use my software, XPP, and you learn to use AUTO, you can compute the FI curve rather easily!)

4. The Connor-Stevens model contains an additional current called the A-current. Equations for this are given in appendix A in chapter 6 of Dayan & Abbott. Simulate this model and compute the FI curve over a range of currents from 0 to 20 $\mu A/cm^2$ in steps of 2. The CS model can fire at arbitrarily low rates. Use the conductances and reversal potentials on page 197 with equations 6.33-6.37 for the gating functions given on page 224.

5. The T-type calcium current is crucial for producing bursts in the thalamus and in other areas of the brain. We will look at the behavior of this current using equations 6.38-6.41 in Dayan and Abbott for the currents. The equations are:

$$\begin{aligned} C\frac{dV}{dt} &= -g_L(V - E_L) - g_T M_\infty^2(V)h(V - E_{Ca}) + I(t) \\ \frac{dh}{dt} &= (H_\infty(V) - h)/\tau_H(V) \end{aligned}$$

Note that we have set m to it's steady state because m is quite fast compared to h. Use $g_L = 0.05mS/cm^2$, $C = 1\mu F/cm^2$, $g_T = 1mS/cm^2$, and $E_{Ca} = 150mV$, $E_L = -75mV$. The rest state for these values is $V = -72mV$ and $h = 0.1$ so that the T-current is only partially inactivated. Inject a hyperpolarizing pulse of $-1\mu A/cm^2$ for 100 msec and simulate the reaponse for 1000 msec. You should see a rebound spike. Change the length of the hyperpolarization to 20 msec and you will see a smaller rebound. Inject a constant depolarizing current of $1 \mu A/cm^2$ for 200 msec. You should see a small spike since the T-current is not completely inactivated. Many neuromodulators act to alter the resting potential of neurons. Set the applied current to zero and change the leak to -60 mV. The resting potential of the cell goes up to -57 mV and h is nearly zero. Try to evoke a spike with a depolarizing input. All you will get is the passive response. You should be able to get a very big rebound response when you inject a hyperpolarizing current.