Problem Set 5 – Extensions of the Hodgkin-Huxley model

Computational Neuroscience Summer Program

June, 2010

In this problem set you will be extending the standard Hodgkin-Huxley model you constructed in Problem Set 4. In this extended model we will be simulating the actions of individual voltage-dependent Sodium and Potassium channels. Feel free to re-use any code from Problem Set 4 that you think would be useful. Write up your results in a text editor of your choosing. Include any relevant figures. Include a printout of your Matlab code as well as any calculations that aren't in the code. You may work individually or in groups, but each student should hand in their own report.

Equations

|		
$\tau_x(V)\frac{dx}{dt} = x_\infty(V) - x$	$\tau_x(V) = \frac{1}{\alpha_x(V)+\beta_x(V)}$	$x_\infty(V) = \frac{\alpha_x(V)}{\alpha_x(V)+\beta_x(V)}$
$\alpha_n(V) = \frac{.01(V+55)}{1-exp(-.1(V+55))}$	$\alpha_m(V) = \frac{0.1(V+40)}{1-exp(-.1(V+40))}$	$\alpha_h(V) = 0.07 * exp(-.05(V + 65))$
$\beta_n(V) = 0.125 * exp(-.0125(V + 65))$	$\beta_m(V) = 4 * exp(-.0556(V + 65))$	$\beta_h(V) = \frac{1}{1+exp(-.1(V+35))}$
$P_K = n^4$	$P_{Na} = m^3 h$	
$g_K = \bar{g}_K P_K$	$g_{Na} = \bar{g}_{Na} P_{Na}$	

Problems

1. Construct and simulate the stochastic K^+ channel model as shown in the state diagram below. The diagram shows transitions between different states of a K^+ channel. The symbols α_n and β_n represent the opening and closing rates, respectively, of individual K^+ channels (these are the same variables you used in Problem Set 4). Set the rate constants equal to their value at 10 mV (i.e., use α_n(10mV) = 0.65/ms and β_n(10mV) = 0.05/ms). Transitions are made between states with each iteration of your program if a random number chosen uniformly between 0 and 1 is less than the corresponding rate for that transition time. For example, if a channel is in state 1, that channel will transition to state 2 during the current iteration of your program if the chosen random number is less than $4\alpha_n dt$. As the channel(s) make transitions between states, keep track of whether state 5 is occupied. If so, assume that each channel conducts 1 pA (10^{-12} A) of current; otherwise no current flows through the channel. Plot currents generated by this model for N =1, 10, and 100 channels over a 20 ms period (use dt = 0.01 ms).
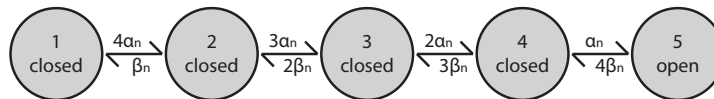
2. The Hodgkin-Huxley description of the K^+ channel predicts the current flowing in these simulations would be Nn^4 pA, where N is the number of K^+ channels and n is the K^+ activation variable (same as in Problem Set 4). On a single plot, show the amount of current predicted by the Hodgkin-Huxley prediction and the amount of current predicted with the stochastic model. (Use N = 1000.)

3. Construct an stochastic Na$^+$ channel model analogous to the K$^+$ model, using the state diagram below. The symbols α_m and β_m represent opening and closing rates of the three main subunits of the sodium channel. Activation and deinactivation rates of the sodium channel gate are represented by k_1, k_2, and k_3. Set the rate constants equal to their value at 10 mV (i.e., use α_m(10 mV) =5.034/ms, α_h(10 mV) =0.0016/ms, and β_m(10 mV) =0.0618/ms). Use k_1 = 0.24/ms, k_2 = 0.4/ms, and k_3 = 1.5/ms. As the channel(s) make transitions between states, keep track of whether state 4 is occupied. If so, assume that each channel conducts -1 pA (10^{-12} A) of current; otherwise no current flows through the channel. Plot currents generated by this model for M =1, 10, and 100 channels over a 20 ms period.
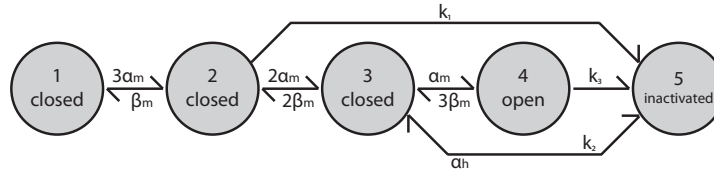
4. The Hodgkin-Huxley description of the Na$^+$ channel predicts the current flowing in these simulations would be Mm^3h pA, where M is the number of Sodium channels. On a single plot, show the amount of current predicted by the Hodgkin-Huxley prediction and the amount of current predicted with the stochastic model. (Use M = 1000.)

5. Challenge problem. Modify the Hodgkin-Huxley model from Problem Set 5 to explicitly simulate Sodium and Potassium channels using the stochastic models above (to start, use $N = M = 1000$). You will need to update the transition probabilities α_n, α_m, α_h, β_n, and β_m with each time step, since those transition probabilities are voltage-dependent. k_1, k_2, and k_3 are constants. Hint: P_X is equal to the total proportion of X channels currently open. Simulate a 20 ms interval. Apply an external current of I_{ext} = 5 nA/mm^2 from 5 to 8 ms. Plot V, P_K, and P_{Na} as a function of time.