Homework 4: The Hodgkin and Huxley model

2014-12-04

If you have not completed exercise 8, go through the problems given there before you continue with this homework assignment. In this assignment you will explore Hodgkin and Huxley's model of the action potential. In step 1-4 you will fill in the missing parts of the code-shell given to you on the course home page, file name hw4CodeShell.m. In step 5-8 you will use your code in order to simulate the behavior of the membrane potential as well as the gating variables of the neuron at different input currents. You will investigate the threshold potential as well as the refractory period of the specific neuron simulated.

The differential equation of the membrane potential is given by the following equation

$$C_m \frac{\mathrm{d}V}{\mathrm{d}t} = -I_{Na} - I_K - I_L + I_{ext}$$

where C_m is the membrane capacitance, I_i is the respective ion currents given by the functions below and I_{ext} is external (input) current.

$$\begin{aligned} I_{Na} &= g_{Na} m^3 h \left(V - E_{Na}\right) \\ I_K &= g_K n^4 \left(V - E_K\right) \\ I_L &= g_L \left(V - E_L\right) \end{aligned}$$

The dynamics of gating variables m, n and h are given by the following differential equations

$$\begin{aligned} \frac{\mathrm{d}m}{\mathrm{d}t} &= \alpha_m(V)(1-m) - \beta_m(V)\, m \\ \frac{\mathrm{d}h}{\mathrm{d}t} &= \alpha_h(V)(1-h) - \beta_h(V)\, h \\ \frac{\mathrm{d}n}{\mathrm{d}t} &= \alpha_n(V)(1-n) - \beta_n(V)\, n \end{aligned}$$

where the rate functions are, unit [1/ms]

$$\begin{aligned}\alpha_m(V) &= 0.1\,(V+45)\,/\,(1-\exp(-(V+45)/10))\\ \beta_m(V) &= 4\exp(-(V+70)/18)\\ \alpha_h(V) &= 0.07\exp(-(V+70)/20)\\ \beta_h(V) &= 1/\,(1+\exp(-(V+40)/10))\\ \alpha_n(V) &= 0.01\,(V+60)\,/\,(1-\exp(-(V+60)/10))\\ \beta_n(V) &= 0.125\exp(-(V+70)/80)\end{aligned}$$

This information was given to you during lecture 8 and it was somewhat treated during exercise 8.

1. In *Section 1 - Constants* of the code-shell, the constants of the model are declared. Fill in the values given below. Due to that the equilibrium potentials are given in mV, the membrane potential V will be given in mV. Time is given in ms due to the rate functions declared above.

$$\begin{aligned}&C_m = 1 \quad [\mu\text{F/cm}^2] & &\\ &E_{Na} = 45 \quad [\text{mV}] & g_{Na} &= 120 \quad [\text{mS/cm}^2]\\ &E_K = -82 \quad [\text{mV}] & g_K &= 36 \quad [\text{mS/cm}^2]\\ &E_L = -59.387 \quad [\text{mV}] & g_L &= 0.3 \quad [\text{mS/cm}^2]\end{aligned}$$

2. In *Section 2 - Channel gating kinetics, rate functions* of the code-shell the rate functions of the gating variables' dynamics are given as function handles. (This code was written in exercise 8.4.) You do not have to add code to this section. In *Section 3 - Membrane currents*, the functions of the ion currents are declared. Fill in the expressions according to the functions given above.

3. In *Section 4 - External current* you should state that the external current is 0 for every time t. We will use this setup for our initial simulations.

4. In *Section 5 - Defining the differential equation*, the differential equations of V, m, n and h are given as a function handle on matrix form, `dAlldt`, of the variable `X = [V m n h]` and time `t`. Make sure you understand why it looks like it does. (Hint: compare with the differential equations given above and use the fact that `V = X(1)`, `m = X(2)` and so on, as stated in the code.)

5. Run sections 1-5 (use evaluate cell). You have now defined the constants and the functions of the model and are ready to simulate its behavior. In *Section 6 - The Steady State*, you will determine appropriate initial values of the variables V, m, n and h to use in the following sections. As can be seen in the code, the initial values, `initial_values`, are all set to zero. The simulation time span is set to 500 ms, see `tspan`. Run the section. `ode45` will solve the differential equations and a figure will be created which includes three subplots. The subplot in the top shows the membrane potential V during the simulation period, the subplot in the middle presents the gating variables during the simulation period and the bottom subplot shows the external current. Determine the steady state values of the variables V, m, n and h from the figure (with one significant figure (värdesiffra)) and use them as the initial values in the following sections.

6. Now you have implemented the Hodgkin and Huxley model and hopefully you want to investigate some of the characteristics of the action potential. In *Section 7 - Find the threshold potential and specify the refractory period* you are supposed to use different values on the external current to find out the threshold potential of the neuron. For this investigation, it would be convenient to gradually increase the external current by some factor k. Example code is given in the code-shell. Run the section and it will create a corresponding plot as in Section 6 but with the new external current.

7. During an action potential, the gating variables are varying in a specific way. Describe what is happening physiologically during an action potential by the simulated behavior of the gating variables.

8. What is the refractory period? Can you explain it by the simulated behavior during an action potential? Optional: Use the external current to investigate the refractory period.