Problem Set 2: The Hodgkin–Huxley Model
Vijay Balasubramanian

1 Introduction

In this exercise we want to simulate the dynamics of an action potential generated by the Hodgkin-Huxley model (Nobel Prize, 1963). As in problem set 1, we are going to numerically integrate the equations which govern the dynamics of the system. (You can read about in detail in the book of Dayan and Abbott, pp.166-p.175.)

2 The Principal Equations

Basic equation for all single-compartment models:

$$c_m \frac{dV}{dt} = -i_m + \frac{I_e}{A} \tag{5.6}$$

Specific membrane current of the Hodgkin-Huxley Model:

$$i_m = \bar{g}_{\mathrm{L}}(V - E_{\mathrm{L}}) + \bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}}) + \bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}}) \tag{5.25}$$

$$\begin{array}{lll} \bar{g}_{\mathrm{L}} = 0.003\mathrm{mS/mm}^2 & \bar{g}_{\mathrm{K}} = 0.36\mathrm{mS/mm}^2 & \bar{g}_{\mathrm{Na}} = 1.2\mathrm{mS/mm}^2 \\ E_{\mathrm{L}} = -54.387\mathrm{mV} & E_{\mathrm{K}} = -77\mathrm{mV} & E_{\mathrm{Na}} = 50\mathrm{mV} \end{array}$$

The activation and de-inactivation probabilities $n(t)$, $m(t)$ and $h(t)$ follow the same equation (here shown for $n(t)$):

$$\frac{dn}{dt} = \alpha_n(V)(1 - n) - \beta_n(V)n \tag{5.16}$$

Opening and closing rate function:

$$\alpha_n = \frac{0.01(V + 55)}{1 - \exp(-0.1(V + 55))} \qquad \beta_n = 0.125 \exp(-0.0125(V + 65)) \tag{5.22}$$

$$\alpha_m = \frac{0.1(V + 40)}{1 - \exp(-0.1(V + 40))} \qquad \beta_m = 4 \exp(-0.0556(V + 65)) \tag{5.24}$$

$$\alpha_h = 0.07 \exp(-0.05(V + 65)) \qquad \beta_h = 1/(1 + \exp(-0.1(V + 35)))$$

The time constants $\tau_n(V)$, $\tau_m(V)$ and $\tau_h(V)$ follow the same equation (here shown for $\tau_n(V)$):

$$\tau_n(V) = \frac{1}{\alpha_n(V) + \beta_n(V)} \tag{5.18}$$

Steady-state activation and de-inactivation rates n_∞, m_∞ and h_∞ follow the same equation (here shown for n_∞):

$$n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)} \tag{5.19}$$

3 Numerical Simulation

To calculate the time evolution governed by the equations of the Hodgkin-Huxley model, we have to set initial values for four quantities: the voltage, $V(t)$, and the three activation/deinactivation probabilities, $n(t)$, $m(t)$ and $h(t)$. The resting potential can be used as $V(t=0)$. Good values for $n(t=0)$, $m(t=0)$ and $h(t=0)$ are the voltage-dependent equilibrium values $n_\infty(V(t=0))$, $m_\infty(V(t=0))$ and $h_\infty(V(t=0))$, given by formula (5.19). This allows us now to calculate the specific membrane current $i_m(t=0)$ (eq. (5.25)).

Having all these initial values set up we can use eq. (5.6) to calculate the change in the membrane voltage $dV(t)$ for a small time step dt (assuming $I_e(t)$ is given). With this new value $V(t+dt)$, we update the time dependent activation and deinactivation probabilities $n(t+dt)$, $m(t+dt)$ and $h(t+dt)$ (eq. (5.16)). In the last step we update $i_m(t+dt)$ by using eq. (5.25).

This procedure is repeated until time t_{final} is reached.

4 Questions

0: Refresh your knowledge about the Hodgkin-Huxley model.

1: Give a short description of equation (5.25) including a description of the variables. Why do we use the form n^4 and m^3h?

2: Reproduce figure 5.9 (only the dashed lines for α_n, n_∞ and τ_n) for the voltage-dependent functions α_n, β_n, n_∞ and τ_n using eq. (5.22), eq. (5.19) and eq. (5.18).

3: Reproduce the left plot of figure 5.10 showing the voltage-dependent functions n_∞, m_∞ and h_∞ (eq. (5.19)). The rate functions are given in eqs. (5.22) and eqs. (5.24).

4: Reproduce the right plot of figure 5.10 showing the voltage-dependent time constants τ_n, τ_m and τ_h (eq. (5.18) and equivalent ones).

5: Now simulate the Hodgkin-Huxley model numerically. Use the following parameters: $\bar{g}_L = 0.003\, mS/mm^2$, $\bar{g}_K = 0.36\, mS/mm^2$, $\bar{g}_{Na} = 1.2\, mS/mm^2$, $E_L = -54.387\, mV$, $E_K = -77\, mV$, $E_{Na} = 50\, mV$, $c_m = 10nF/mm^2$, $A = 0.1mm^2$). Set the initial voltage $V(t=0)$ to the resting potential $V(t=0) = -65mV$. Initialize $n(t)$, $m(t)$ and $h(t)$ to their equilibrium values $n_\infty(V(t=0))$, $m_\infty(V(t=0))$ and $h_\infty(V(t=0))$. Reproduce the graphs in figure 5.11 of Dayan and Abbott (attached) qualitatively by simulating the injection of a suitable short (try some values!) external current $I_e(t)$ starting at $t = 5$ms. The action potential will not not look completely realistic, in part because we have left out some channels that real neurons have.

6: Simulate the blocking of the sodium channels by a toxin. To do this, set $\bar{g}_{\text{Na,new}} := \frac{1}{10}\bar{g}_{\text{Na}}$. Plot again the time courses as shown in figure 5.11. Now block (only) the potassium channels in the same way: set $\bar{g}_{\text{K,new}} := \frac{1}{10}\bar{g}_{\text{K}}$. Now see what would happen if the sodium channels were persistent. To do this substitute $m^3h \to m^4$. Do not change $\bar{g}_{\text{Na}}$ or $\bar{g}_{\text{K}}$ this time.