Theoretical Neuroscience I

Exercise 4: Hodgkin-Huxley Model

Due: Wednesday, 27 November, 2019

The Hodgkin-Huxley model explains the action potential of the squid giant axon. The present version is taken from Dayan&Abbott, Sections 5.5, 5.6, and 5.11.

1 State variables and parameters

The HH-model uses a single-compartment model with a leak ("passive") conductance and, in addition, two further voltage-dependent ("active") conductances (Na^+ and K^+). The dynamic equation of the membrane potential therefore takes into account three membrane currents and an electrode current:

$$c_m \frac{dV}{dt} = -i_L - i_{Na} - i_K + i_e, \qquad i_L = \bar{g}_L (V - E_L) \tag{1}$$

The membrane capacity, maximal conductances, and associated reversal potentials are:

$$\begin{array}{ccc} & c_m = 10\, nF/mm^2 & \\ \bar{g}_L = 3\, \mu S/mm^2 & \bar{g}_{Na} = 1200\, \mu S/mm^2 & \bar{g}_K = 360\, \mu S/mm^2 \\ E_L = -54.402\, mV & E_{Na} = 50\, mV & E_K = -77\, mV \end{array}$$

The sodium and potassium currents additionally depend on "activation variables" $n(V,t)$, $m(V,t)$, and $h(V,t)$

$$i_{Na} = \bar{g}_{Na}\, m^3\, h\, (V - E_{Na}) \qquad i_K = \bar{g}_K\, n^4\, (V - E_K) \tag{2}$$

which describe the voltage-dependence of the collective opening and closing of channels. The activation variables are goveassociated dynamic equations are

$$\frac{dn}{dt} = \frac{1}{\tau_n} [n_\infty - n], \qquad \frac{dm}{dt} = \frac{1}{\tau_m} [m_\infty - m], \qquad \frac{dh}{dt} = \frac{1}{\tau_h} [h_\infty - h]$$

where $\tau_n(V)$, $\tau_m(V)$, $\tau_h(V)$ and $n_\infty(V)$, $n_\infty(V)$, $h_\infty(V)$ are six functions of voltage V provided in three Matlab files **HH_equi_tau_n.m**, **HH_equi_tau_m.m**, and **HH_equi_tau_h.m**.

Run Matlab-script **HH_visualise.m** to plot these functions.

2 Iterative integration

Rearranging the dynamic equation of the membrane potential, we obtain (see assignments)

$$\frac{dV}{dt} = \frac{1}{\tau_{eff}} \left[V_\infty^{eff} - V \right]$$

$$\tau_{eff}(t) = \frac{c_m}{\bar{g}_L + \bar{g}_{Na} m^3 h + \bar{g}_K n^4} \qquad V_\infty^{eff}(t) = \frac{\bar{g}_L E_L + \bar{g}_{Na} m^3 h E_{Na} + \bar{g}_K n^4 E_K + i_e}{\bar{g}_L + \bar{g}_{Na} m^3 h + \bar{g}_K n^4} \tag{3}$$

where τ_{eff} and V_∞^{eff} are the time-varying time-constant and equilibrium potential.
Given the state variables and input current at time t

$$V(t), n(t), m(t), h(t), i_e(t)$$

as well as the time-constants and equilibrium values at time t

$$\tau_{eff}(t), \tau_n(t), \tau_m(h), \tau_h(t), \qquad V_\infty^{eff}(t), n_\infty(t), m_\infty(t), h_\infty(t)$$

our task is to compute the state variables a time $t + \Delta t)$

$$V(t + \Delta t), n(t + \Delta t), m(t + \Delta t), h(t + \Delta t)$$

For a sufficiently small Δt, state variables and input current can be assumed to remain constant over Δt, permitting us to use the analytical solution of the relaxation equations:

$$\begin{aligned}
V(t + \Delta t) &= V_\infty^{eff}(t) + \left[V(t) - V_\infty^{eff}(t) \right] \exp\left(-\frac{\Delta t}{\tau_{eff}(t)} \right) \\
n(t + \Delta t) &= n_\infty(V) + \left[n(t) - n_\infty(V) \right] \exp\left(-\frac{\Delta t}{\tau_n(V)} \right) \\
m(t + \Delta t) &= m_\infty(V) + \left[m(t) - m_\infty(V) \right] \exp\left(-\frac{\Delta t}{\tau_m(V)} \right) \\
h(t + \Delta t) &= h_\infty(V) + \left[h(t) - h_\infty(V) \right] \exp\left(-\frac{\Delta t}{\tau_h(V)} \right)
\end{aligned}$$

3 Assignments

- Analytically derive Eqn. (3) from Eqns. (1) and (2) in order to verify the expressions for τ_{eff} and V_∞^{eff}!
- Iteratively simulate the state variables – $V(t)$,n(t), $m(t)$, $h(t)$ – over a period of $40\,ms$ in steps of $\Delta t = 0.1\,ms$ for different input currents (as specified below).
- First simulate with a zero input current $i_e(t) = 0\,nA/mm^2$ and observe the *resting values* approached by each state variable. For this simulation only, choose the initial conditions.

$$V_0 = -70\,mV, \qquad n_0 = 0.3, \qquad m_0 = h_0 = 0.0$$

Note the steady-state values (resting values) towards the end of the simulation:

$$V_{ss} \qquad n_{ss}, \qquad m_{ss}, \qquad h_{ss}$$

- Plot the time evolution of the membrane voltage and, separately, plot the time evolution of the gating variables.

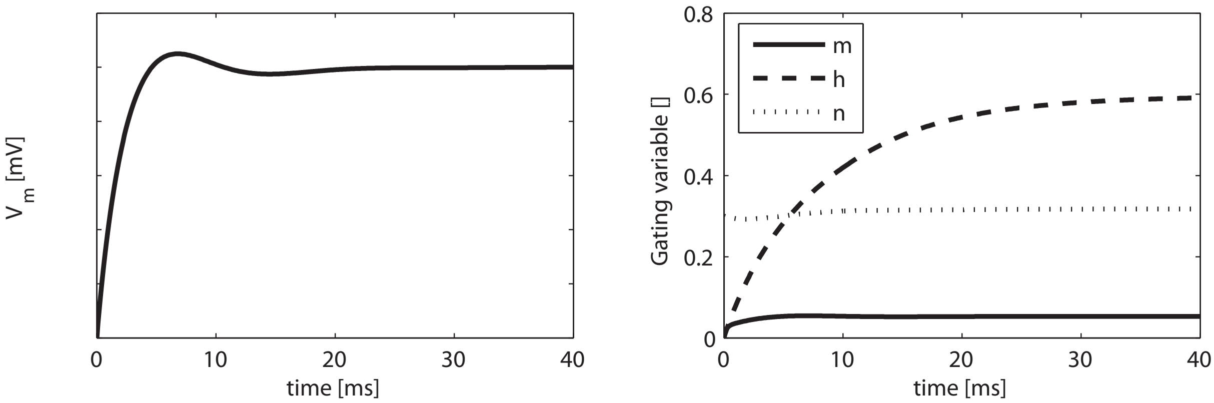

Figure 1: Your plots should look like this!

- Second simulate with an input current $i_e(t) = 100\, nA/mm^2$ to obtain action potentials. For this simulation, choses the previously determined *resting values* as initial conditions:

$$V_0 = V_{ss} \qquad n_0 = n_{ss}, \qquad m_0 = m_{ss}, \qquad h_0 = h_{ss}$$

  Your simulation should now show action potentials!

- Repeat the previous simulation, but with a 'blocked' sodium conductance, setting $\bar{g}_{Na} = 0$. This simulates the action of a pharmacological agent such as strychnine.

- Repeat the simulation once again, but with a 'blocked' potassium conductance, setting $\bar{g}_K = 0$. This simulates the action of pharmacological agent such Caesium or TTA.