Exercise 3: Hodgkin-Huxley model

In the lecture, the Hodgkin-Huxley model was defined by the following set of differential equations:

$$C\frac{dV}{dt} = I - \bar{g}_{K^+}n^4(V - E_{K^+}) - \bar{g}_{Na^+}m^3h(V - E_{Na^+}) - g_L(V - E_L) \quad (1)$$
$$\frac{dn}{dt} = \frac{n_\infty(V) - n}{\tau_n(V)} \quad (2)$$
$$\frac{dm}{dt} = \frac{m_\infty(V) - m}{\tau_m(V)} \quad (3)$$
$$\frac{dh}{dt} = \frac{h_\infty(V) - h}{\tau_h(V)} \quad (4)$$

It is convenient to rewrite the last three equations in the form

$$\frac{dx}{dt} = \alpha_x(V)(1 - x) - \beta_x(V)x \qquad \text{where } x \in \{n, m, h\}. \quad (5)$$

The coefficients $\alpha_x(V)$ and $\beta_x(V)$ represent the (voltage-dependent) activation and inactivation rates, respectively, for the gate x. With these coefficients, the steady-state activation variables $x_\infty(V)$ and the time constants $\tau_x(V)$ in equations (2)–(4) are given by

$$x_\infty(V) = \frac{\alpha_x(V)}{\alpha_x(V) + \beta_x(V)} \qquad \text{and} \qquad \tau_x(V) = \frac{1}{\alpha_x(V) + \beta_x(V)}. \quad (6)$$

In this exercise the task is to make and test a computer program that solves the Hodgkin-Huxley model (1)–(4) for a rectangular input-current pulse

$$I(t) = \begin{cases} I_{\text{max}} & t_{\text{stim,on}} \leq t \leq t_{\text{stim,off}} \\ 0 & \text{else} \end{cases} \quad (7)$$

and with the initial condition

$$V(0) = V_{\text{rest}} \quad (8)$$
$$n(0) = n_\infty(V_{\text{rest}}) \quad (9)$$
$$m(0) = m_\infty(V_{\text{rest}}) \quad (10)$$
$$h(0) = h_\infty(V_{\text{rest}}) \,. \quad (11)$$

Here, V_{rest} denotes the resting potential of the neuron, i.e. the stationary membrane potential in the absence of any input I.

Many numerical schemes exist for solving ('evaluating') sets of differential equations. Here you can use the simplest one, that is the *forward Euler* method. In this scheme the differential dynamics $dy/dt = f(y,t)$ is approximated by

$$\frac{y(t) - y(t-\Delta t)}{\Delta t} = f(y(t-\Delta t), t-\Delta t)$$
$$\Rightarrow y(t) = y(t-\Delta t) + \Delta t \cdot f(y(t-\Delta t), t-\Delta t).$$

(i) Evaluate the HH-equations (1)–(4) at the times $t \in \{0,\ \Delta t,\ 2\Delta t,\ \ldots,\ T-\Delta t,\ T\}$ assuming a constant input current $I_{\text{max}} = 10\ \mu A/cm^2$ by using the numerical forward Euler method. To this end, use the Python-script skeleton provided in `exercise_3.py`. Complete the following functions (search for ## `TO BE IMPLEMENTED`):

- `stimulus()`
- `update()`
- `simulate()`

A detailed description of each of these functions, i.e. what it is *supposed* to do, is found in the documentation (see docstring of the respective function). Default parameter values and parameter functions are provided in Table 1 below. Note that these parameters are already implemented in `set_parameters()`. Plot the input current $I(t)$ and the resulting membrane potential $V(t)$ (the code for plotting is already implemented in the script skeleton). A correct implementation should lead to a figure as shown in Figure 1.

(ii) Set the stimulus amplitude to a negative value, that is, $I_{\text{max}} = -10\ \mu A/cm^2$, and plot the resulting membrane potential (when as in (i) $t_{\text{stim,on}} = 5$ ms and $t_{\text{stim,off}} = 30$ ms). Can you explain the result?

(iii) Use the code you have as a starting point for finding the $f - I$ curve of the HH neuron. Note that for some 'subthreshold' currents, the HH-model responds by firing spikes for a while before becoming silent. This corresponds to zero firing rate here. What is the threshold current for sustained firing for the present version of the HH-model?

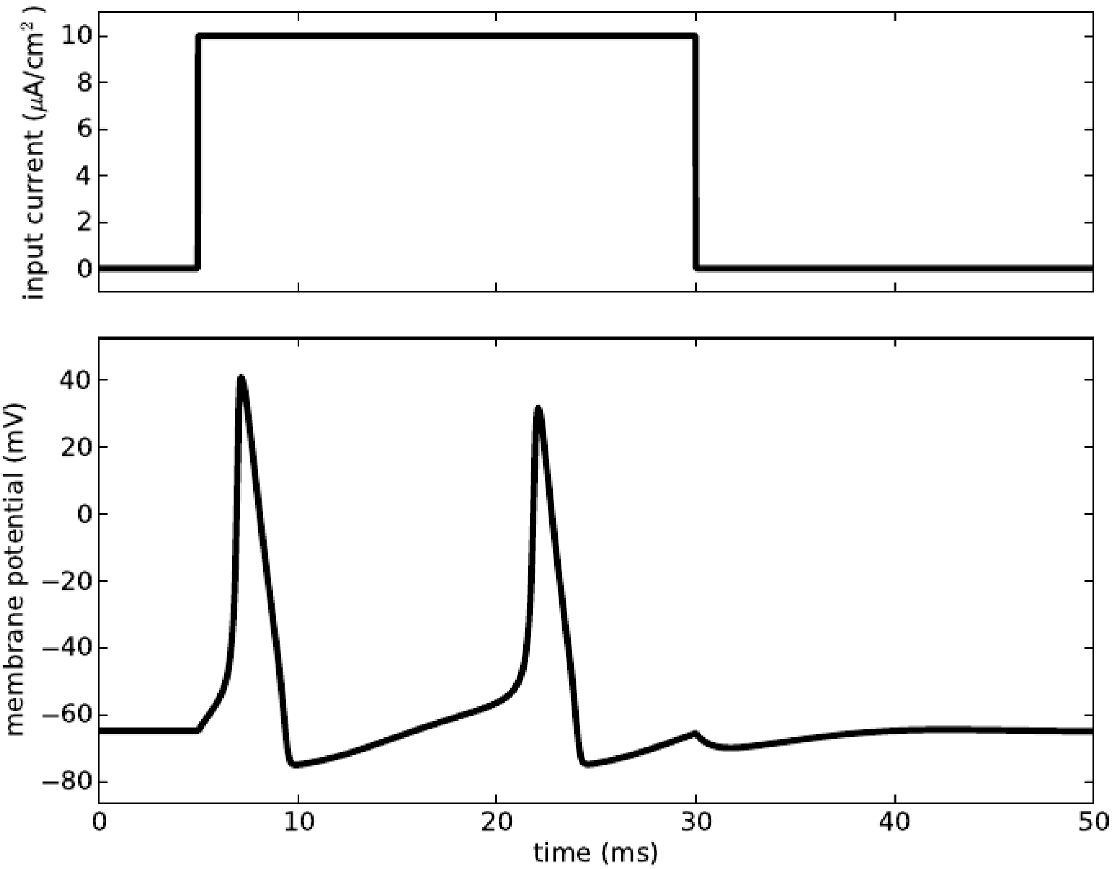

Figure 1: Result of (i). Input current (top panel) and resulting membrane potential (bottom panel) for the default parameters given in Table 1

$$
\begin{aligned}
\Delta t &= 0.025 \text{ ms} \\
T &= 50 \text{ ms} \\
\alpha_n(V) &= \tfrac{0.01 \text{ ms}^{-1}(V+55 \text{ mV})}{1-\exp(-[V+55 \text{ mV}]/10 \text{ mV})} \\
\beta_n(V) &= 0.125 \text{ ms}^{-1}\exp(-[V+65\text{mV}]/80\text{mV}) \\
\alpha_m(V) &= \tfrac{0.1 \text{ ms}^{-1}(V+40 \text{ mV})}{1-\exp(-[V+40 \text{ mV}]/10 \text{ mV})} \\
\beta_m(V) &= 4 \text{ ms}^{-1}\exp(-[V+65 \text{ mV}]/18 \text{ mV}) \\
\alpha_h(V) &= 0.07 \text{ ms}^{-1}\exp(-[V+65 \text{ mV}]/20 \text{ mV}) \\
\beta_h(V) &= \tfrac{1 \text{ ms}^{-1}}{1+\exp(-[V+35 \text{ mV}]/10 \text{ mV})} \\
V_{\text{rest}} &= \text{-65 mV} \\
C &= 1 \ \mu\text{F/cm}^2 \\
E_{\text{Na}^+} &= 50 \text{ mV} \\
E_{\text{K}^+} &= \text{-77 mV} \\
E_{\text{L}} &= \text{-54.387 mV} \\
\bar{g}_{\text{Na}^+} &= 120 \text{ mS/cm}^2 \\
\bar{g}_{\text{K}^+} &= 36 \text{ mS/cm}^2 \\
\bar{g}_{\text{L}} &= 0.3 \text{ mS/cm}^2 \\
I_{\text{max}} &= 10 \ \mu\text{A/cm}^2 \\
t_{\text{stim,on}} &= 5 \text{ ms} \\
t_{\text{stim,off}} &= 30 \text{ ms}
\end{aligned}
$$

Table 1: Default parameter values and parameter functions.