

Exercise 3: Hodgkin-Huxley model

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

$$C \frac{dV}{dt} = I - \bar{g}_{K^+} n^4 (V - E_{K^+}) - \bar{g}_{Na^+} m^3 h (V - E_{Na^+}) - g_L (V - E_L) \quad (1)$$

$$\frac{dn}{dt} = \frac{n_\infty(V) - n}{\tau_n(V)} \quad (2)$$

$$\frac{dm}{dt} = \frac{m_\infty(V) - m}{\tau_m(V)} \quad (3)$$

$$\frac{dh}{dt} = \frac{h_\infty(V) - h}{\tau_h(V)} \quad (4)$$

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

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

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

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

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

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

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 $t \in \{0, \Delta t, 2\Delta t, \dots, T - \Delta t, T\}$ assuming a constant input current $I_{\max} = 10 \mu A/cm^2$ 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, $I_{\max} = -10 \mu A/cm^2$, 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?

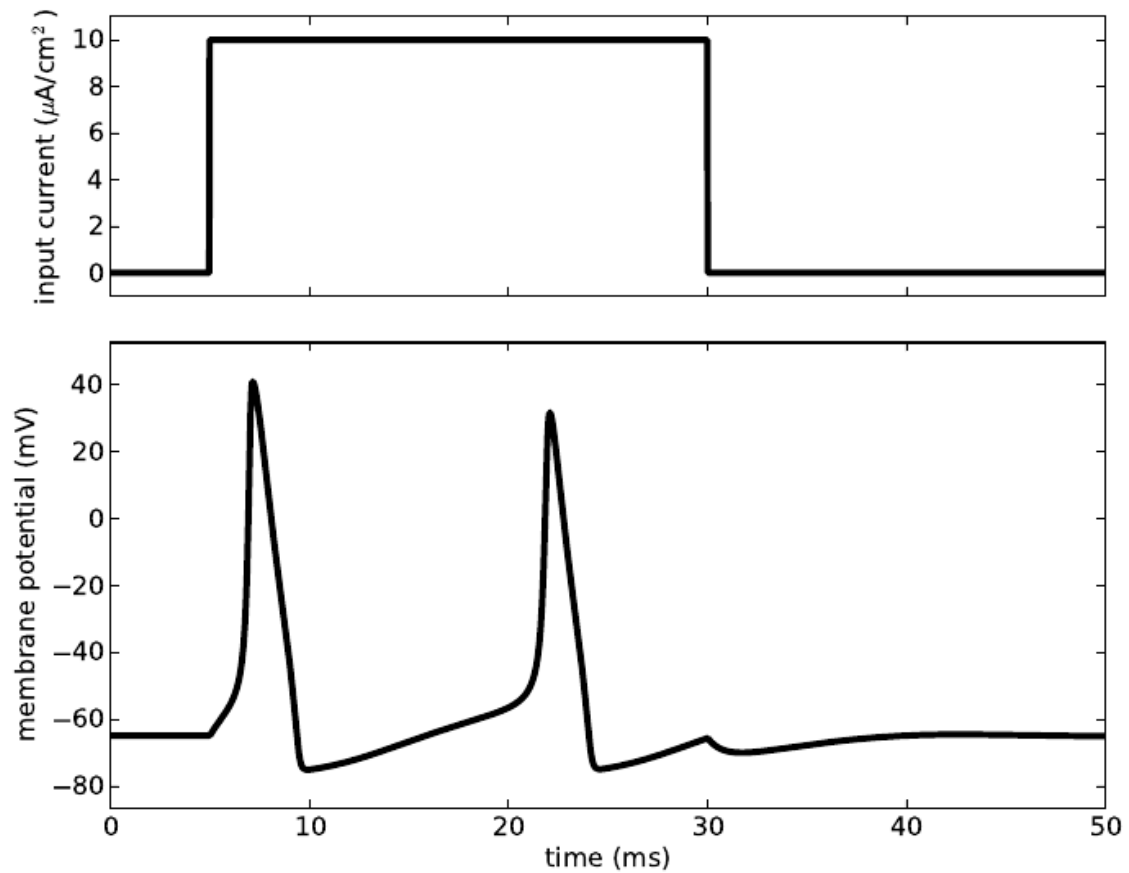


Figure 1: Result of (i). Input current (top panel) and resulting membrane potential (bottom panel) for the default parameters given in Table 1

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

Table 1: Default parameter values and parameter functions.