Neuroprothetics Exercise 4
Hodgkin & Huxley Model

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1 Hodgkin–Huxley model

The Hodgkin–Huxley (HH) model is a mathematical model that describes the action potential in neurons, which consists of multiple non-linear differential equations. In this task, the model is implemented with a Python script, which makes use of a forward and an exponential Euler OED solver to display the timely propagation of some quantities of the modelled neuron, like membrane potential ion current flow or opening probability of the involved ion channels.

1.1 Derivation of time constant τ_x and steady state value x_∞

The dynamics of different ion channels in the neuronal membrane determine how an action potential is generated. The subunits m, h (sodium channel) and n (potassium channel) determine the opening and closing rates of the ion channels, which determine the current that can flow across the membrane, eventually leading to a change in the membrane potential. The behaviour of each kind of subunit can be described by the characteristic time constant τ_x and the steady state value x_∞ for $x \in \{m, n, h\}$ in the following differential equation:

$$\frac{dx}{dt} = \frac{1}{\tau_x}(x_\infty - x)\,. \tag{1}$$

To derivate τ_x and x_∞, first, the rate equations which describe the dynamics of the subunits need to be considered:

$$\begin{aligned}
\alpha_m &= 1000 \cdot \frac{2.5 - 100 \cdot V}{e^{(2.5-100\cdot V)} - 1} & \beta_m &= 4000 e^{-500\cdot V/9} \\
\alpha_n &= 1000 \cdot \frac{0.1 - 10 \cdot V}{e^{(1-100\cdot V)} - 1} & \beta_n &= 125 e^{-25\cdot V/2} \\
\alpha_h &= 70 e^{-50\cdot V} & \beta_h &= \frac{1000}{e^{(3-100\cdot V)} + 1}\,.
\end{aligned} \tag{2}$$

Rearranging the rate equations to the form

$$\frac{dx}{dt} = \frac{1}{\tau_x}(x_\infty - x) = (\alpha + \beta)\left(\frac{\alpha}{\alpha + \beta} - x\right) \tag{3}$$

ensures that τ_x and x_∞ can be directly determined by comparing the coefficients. For $x = h$ for example:

$$\tau_h = \frac{1}{\alpha_h + \beta_h} = \frac{1}{70e^{-50\cdot V} + \frac{1000}{e^{(3-100\cdot V)}+1}} = \left(70e^{-50\cdot V} + \frac{1000}{e^{(3-100\cdot V)} + 1}\right)^{-1}$$

$$h_\infty = \frac{\alpha_h}{\alpha_h + \beta_h} = \frac{70e^{-50\cdot V}}{70e^{-50\cdot V} + \frac{1000}{e^{(3-100\cdot V)}+1}} = \left(1 + \frac{100}{7}\left(e^{3-150\cdot V} + e^{-50\cdot V}\right)^{-1}\right)^{-1}$$

for $x = m$ and $x = n$ this can be done correspondingly.

1.2 Gating parameters

In Figure 1, the characteristic time constants τ_x and steady-state values x_∞ of the different sodium and potassium ion channel subunits are displayed to visualize their dependency on voltage and temperature.

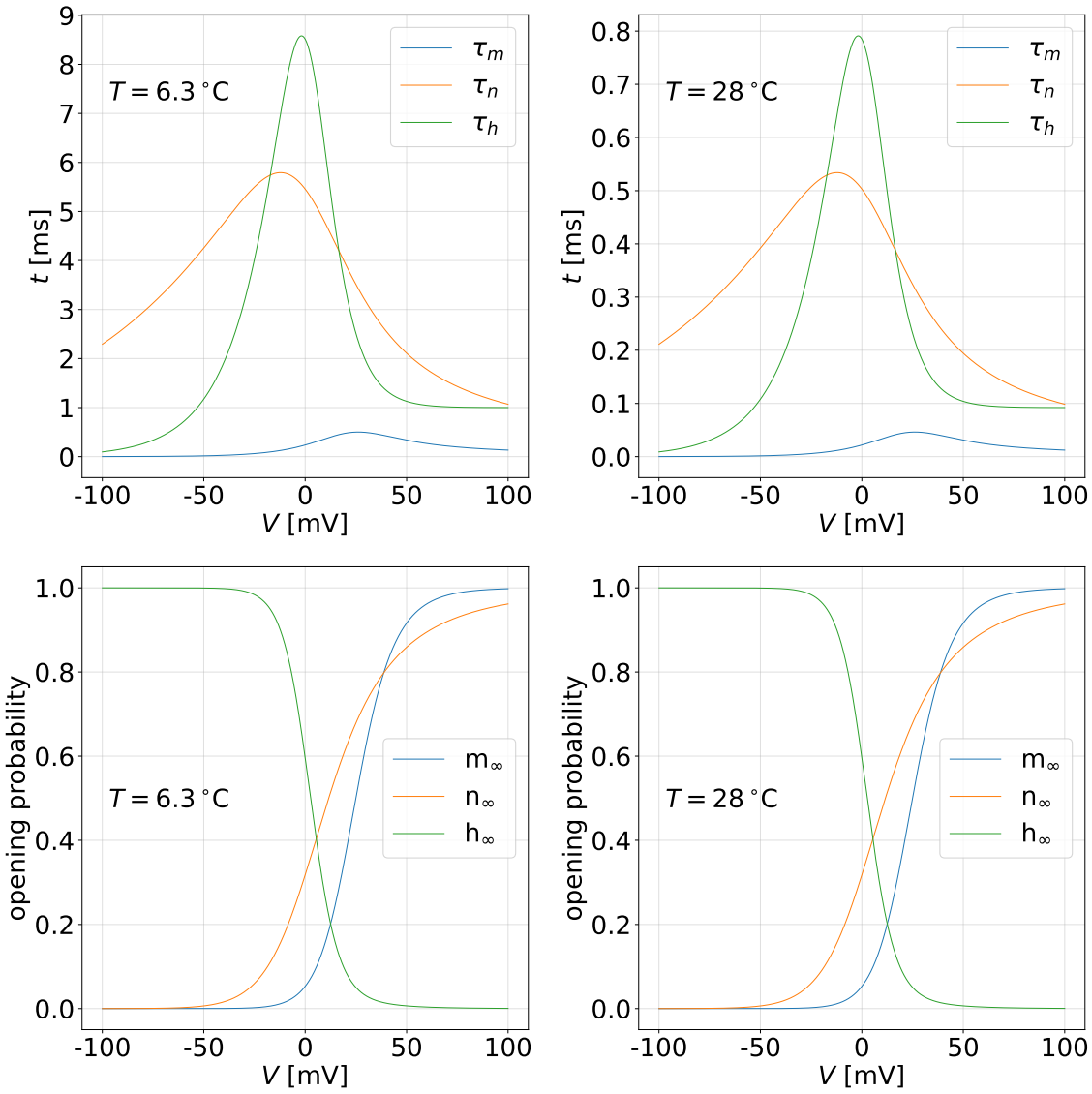

Figure 1: Visualiziation of the dependency of time constant τ_x (top plots) and steady-state value x_∞ (bottom plots) for the different subunits of the sodium (m and h) and potassium (n) ion channels on the membrane potential for different temperatures.

The gating variables shown in 1 do not change noticeably with respect to each other with a change in temperature. However, the time constants τ_x are smaller by a factor of more than 10 for the $T = 28\,^{\circ}\mathrm{C}$ case. This leads to the system approaching steady-state much quicker than in the low-temperature case. The opening probability, however, stays the same and is therefore independent of temperature.

The opening probability of the gating variables shows their functionality in producing an action potential. The n and m gates, which are responsible for opening the sodium and potassium channels, have a higher probability of being open when the voltage rises. Because of the higher time constant of n, it is slower, and therefore, the effects of the gating variable m, which is responsible for the opening of the sodium channels, will be dominant at first. This leads to a spike in the membrane potential. Eventually, the slower h and n gating variables will reach a steady state, resulting in a stop of sodium current (h gate inactivates the sodium channel) and a current of potassium ions (n gate activated) in the opposite direction, resulting in the membrane potential going back to zero. (More on that in section 3).

1.3 Input current and initial conditions

The model will be evaluated at two different temperatures since the temperature has a significant influence on the dynamics of the gating parameter τ_∞ as already seen in Figure 1. For that, the two input currents shown in Figure 2 will be fed to the model.

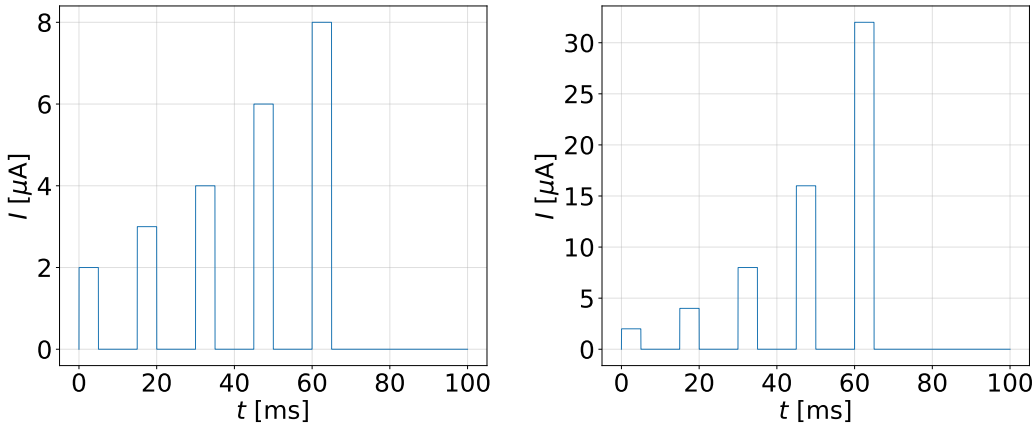

Figure 2: Input currents for the simulation at 6.3 °C (left) and 28 °C (right).

To run the model, we consider the constants in Table 1

Table 1: Constants

Conductances in mS			
$\bar{g}_{Na} = 120$	$\bar{g}_K = 36$	$\bar{g}_L = 0.3$	
Nernst/Resting potentials in mV			
$V_{Na} = 115$	$V_K = -12$	$V_L = 10.6$	$V_{\text{rest}} = 0$
Other constants			
$C_m = 1\mu\text{F}$	$T_1 = 6.3\,°\text{C}$	$T_2 = 28\,°\text{C}$	

and a temperature correction factor k depending on the temperature T of

$$k = 3^{0.1(T-6.3)}\,. \tag{4}$$

The model will then be run for a time span of $t = 100\,\text{ms}$ and in time steps of $\Delta t = 0.01\,\text{ms}$ for the two temperatures $T_1 = 6.3\,°\text{C}$ and $T_2 = 28\,°\text{C}$.

2 Results

The following Figures show the properties of the modelled neuron over the time span of $t = 100\,\text{ms}$. Figure 3 shows the membrane's potential of the neuron.

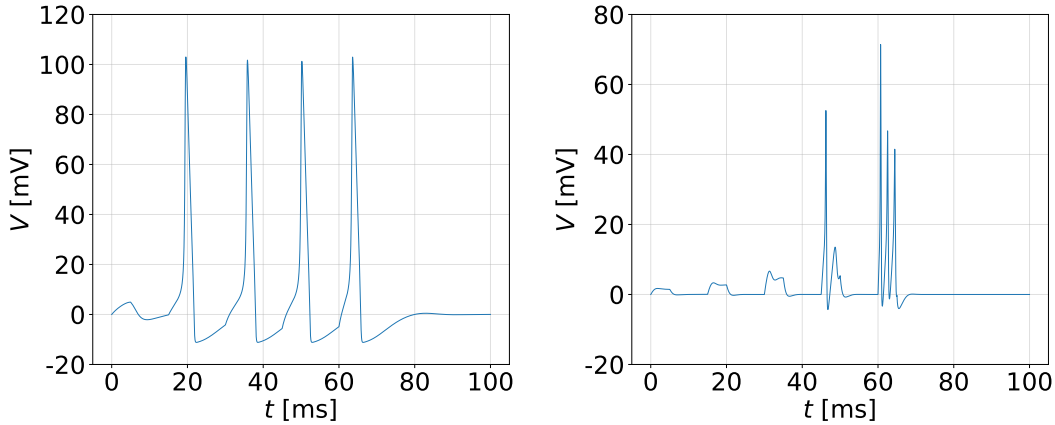

Figure 3: Membrane potential of neuron for $T_1 = 6.3\,°\text{C}$ (left) and $T_2 = 28\,°\text{C}$ (right).

The opening probability of the channel subunits m, n and h is shown in Figure 4.

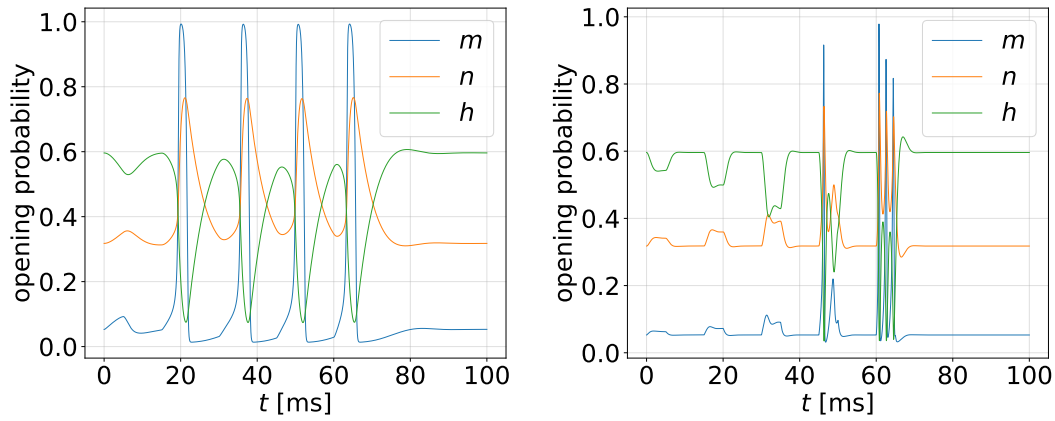

Figure 4: opening probability of the channel subunits m, n and h for $T_1 = 6.3\,°\text{C}$ (left) and $T_2 = 28\,°\text{C}$ (right).

Finally, Figure 5 shows the current flowing through the ion channels.

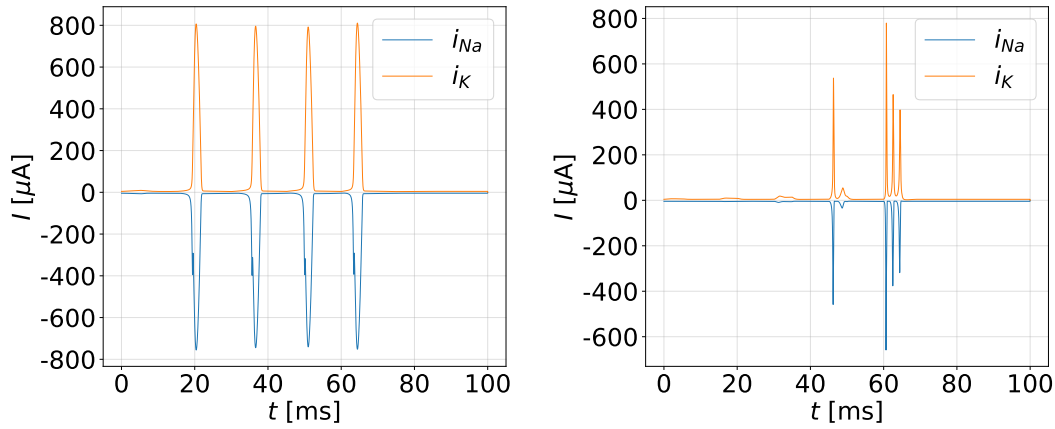

Figure 5: Current flow through ion channels for $T_1 = 6.3\,°\text{C}$ (left) and $T_2 = 28\,°\text{C}$ (right).

3 Analysis of the Results

For a better understanding of the behaviour of the model, a few characteristics will now be discussed.

3.1 Impact of different temperatures on membrane potential

There are three different aspects that are distinguishable between the model's response to different temperatures. The first difference visible in Figure 3 is that the model at $T_1 = 6.3\,°\text{C}$ produces four single, very similar, sharp peaks with an amplitude around $V_m = 105\,\text{mV}$, even though the input current increases each pulse, as shown in 2. After each peak, the potential drops down to $\approx 10\,\text{mV}$. The first input current pulse only triggers a small response in the membrane voltage.
The model at $T = 28\,°\text{C}$, however, starts with a very small rise in membrane potential. The first three input pulses are responsible for only slightly increasing membrane potential increases. At the fourth pulse, the membrane potential spikes to $\approx 55\,\text{mV}$ and seems to be followed up by a minor mini-spike. The fourth input pulse triggers a spike up to $\approx 70\,\text{mV}$ followed by two more spikes that are becoming smaller. Considering the much lower input current needed for an action potential in the model at $T = 6.3\,°\text{C}$, this also indicates a lower threshold. At this point, the input current is significantly higher than for the high-temperature case, which could lead to multiple spikes, as already discussed in Exercise 3. The Voltage, however, never drops much below zero in the case where $T = 28\,°\text{C}$.

The three main differences are summarized in table 2:

Table 2: Main differences in membrane potential

	$T = 6.3\,°\mathrm{C}$, $I_{in,max} = 8\,\mu\mathrm{A}$	$T = 28\,°\mathrm{C}$, $I_{in,max} = 35\,\mu\mathrm{A}$
max. potential amplitude	constantly high	increasing
peaks per input pulse	one	multiple but decreasing
negative overshoot	pronounced	barely

3.2 Role of the gating variables

The gating variables determine the opening probability of the subunits of the sodium ion channel (m and h) and the potassium ion channel (n). Therefore, the values of the gating variables directly determine the conductivity of the corresponding channels. When a potential difference is present (as is usually the case in neurons; the original Hodgkin-Huxley model defined the intracellular potential as the reference potential $V_{rest} = 0$), sodium and potassium ions will flow depending on the amount of the respective opened ion channels. This flow of charge carriers, of course, changes the membrane potential as the number of intracellular and extracellular ions changes.

While the gating variable m defines the three subunits of the sodium channels that allow ions to flow, the inactivation subunit h disables ion flow as long as it is active. When the subunits n are activated, the potassium channel becomes conductive to potassium ions. In the production of an action potential, firstly, the sodium channels are activated very rapidly. When the firing threshold is surpassed, the potassium channels self-amplify their activation, leading to a high current of sodium ions from outside to inside the cell (at rest, the concentration of sodium is much higher outside the cell than inside). Since sodium ions are positively charged, the intracellular potential will increase in a spike-like manner shortly after the inactivation subunit h comes into play and deactivates the sodium channels.
Additionally, the potassium channels are now being activated, allowing a current of negatively charged potassium ions along the concentration difference to the outside of the cell. This leads to a repolarization of the membrane potential, and since the sodium channel is still deactivated, it also leads to a time span where a new input current won't result in a new action potential (refractory period). Since the inactivation of the sodium channel and the activation of the potassium channel take some time to recover to a steady-state condition, the membrane potential drops below the resting potential after an action potential.

3.3 Consecutive action potentials at $T = 28\,°\mathrm{C}$

As already described in 3.1, there are multiple action potentials per input peak in the model at $T = 28\,°\mathrm{C}$. The amplitude of these action potentials, however, decreases over the time of an input pulse. The reason for this can be found in the gating variables.

In figure 6, the gating variables with the most pronounced action potentials are shown over a small time window. After the first peak, all three gating variables do not have enough time to return to their steady-state value. Especially the inactivation subunit h of the sodium channel constricts the sodium flow and, therefore, the self-amplification mentioned in 3.2.

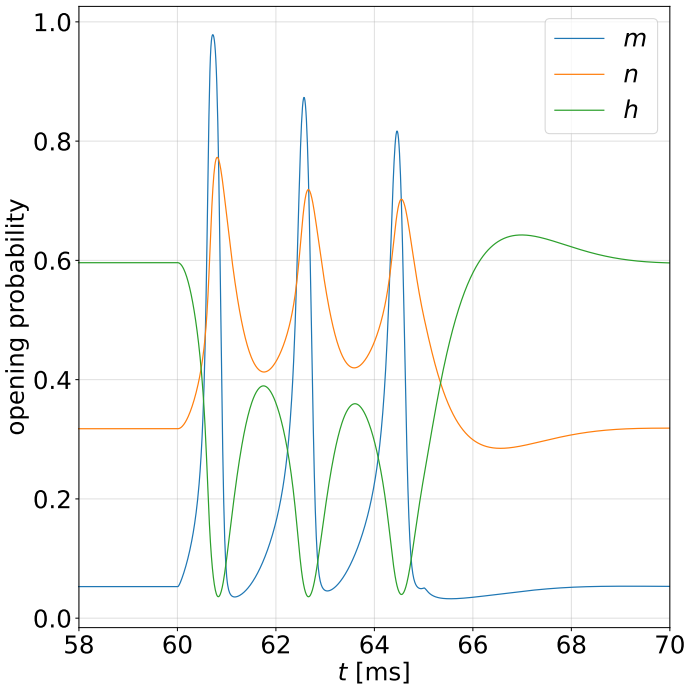

Figure 6: Zoom on gating variables behaviour at T_2.