

Neuroprothetik Exercise 4

Hodgkin & Huxley Model

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1 Time constants and steady state values

Derive the relationship between the rate equations for α_x , β_x and the time constant τ_x and steady state value x_∞ with $x \in m, n, h$. To gain these two variables bring the gating ODEs found in the appendix A into the following form:

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

Answer:

By rewriting the gating ODEs from appendix A as

$$\begin{aligned} \frac{dx}{dt} &= [\alpha_x(1 - x) - \beta_x x]k \\ &= k(\alpha_x + \beta_x)\left(\frac{\alpha_x}{\alpha_x + \beta_x} - x\right) \end{aligned} \quad (2)$$

and comparing this to

$$\frac{dx}{dt} = \frac{1}{\tau_x}(x_\infty - x) \quad (3)$$

we find that

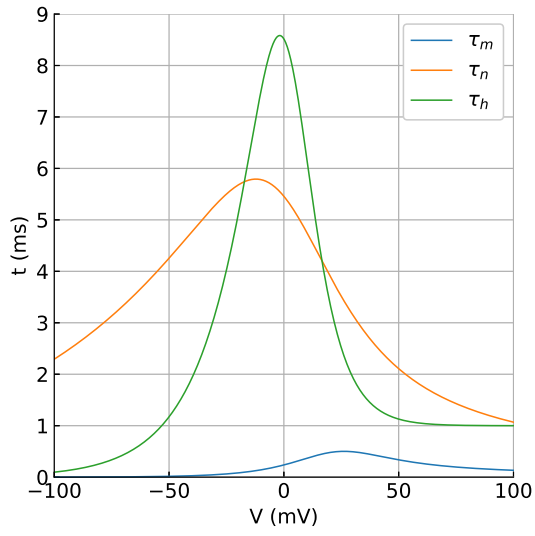
$$\tau_x = [k(\alpha_x + \beta_x)]^{-1} \quad (4)$$

and

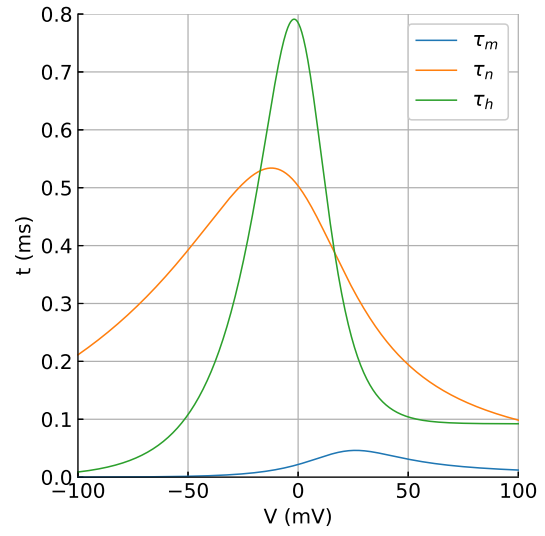
$$x_\infty = \frac{\alpha_x}{\alpha_x + \beta_x} \quad (5)$$

for $x \in m, n, h$ where $k = 3^{0.1(T-6.3)}$.

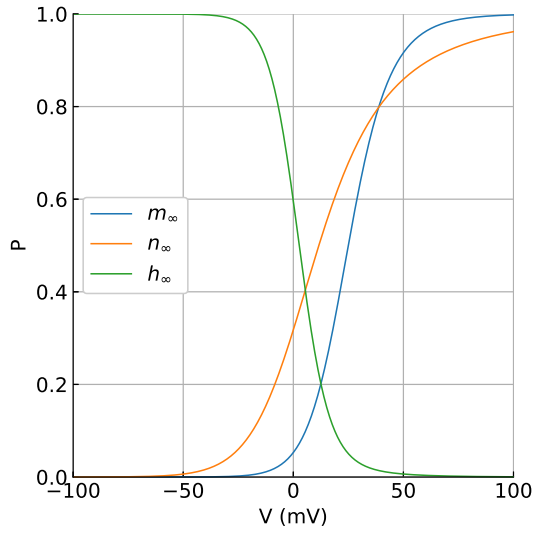
Figure 1 shows τ_x and x_∞ plotted against the voltage $V \in [-100mV, 100mV]$ at 6.3°C and 28°C using the parameters given in the appendix of the exercise sheet.



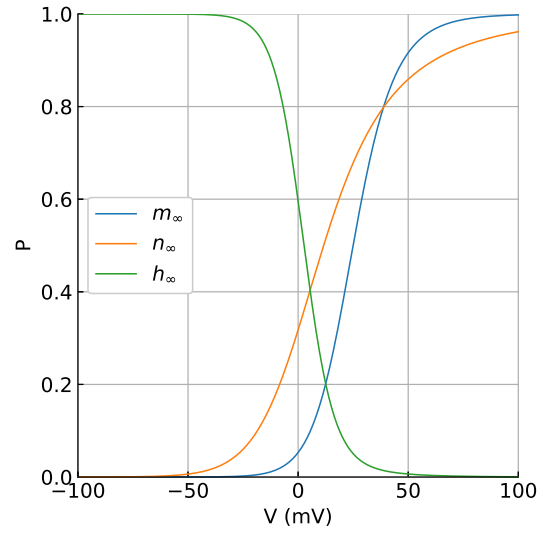
(a) Time constants τ_x at 6.3 °C.



(b) Time constants τ_x at 28 °C.



(c) x_∞ at 6.3 °C.



(d) x_∞ at 28 °C.

Figure 1: Parameters τ and x_∞ for the gating variables m , n and h for 6.3 °C and 28 °C.

Explanation and interpretation:

Both characteristic values are plotted for 6.3 °C and 28 °C respectively and over a membrane voltage range of $V \in [-100 \text{ mV}, 100 \text{ mV}]$. Looking at equation 5 as well as figures 1c and 1d, the steady state values show no temperature dependency. The gates timeconstants τ_x however, are coupled to the temperature by the factor k as can be seen in equation 4 and in figures 1a and 1b. While their general behaviour (comparing the shapes of the plots) remains the same, k is used to downscale the timeconstants as the underlying Boltzmann equations would lead to faster processes for higher temperatures. For the steady state gates depicted in figures 1c and 1d it can be seen that the open-probability for the activation gates m and n increases increasing membrane potential, while at the same time the open-probability of the inactivation gate h decreases. Also, the slope of the Na inactivation gates shows a steeper decline than that of the activation gates showing a higher sensibility to changes in the membrane potential.

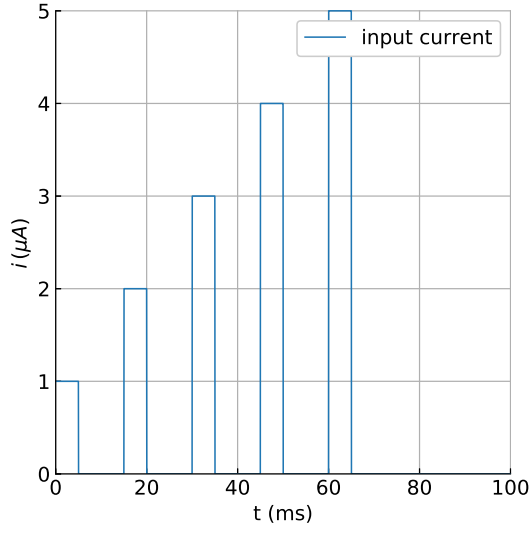
2 Hodgkin & Huxley Neuron Model

In contrast to the LIF Model from exercise 3 the Hodgkin & Huxley Neuron Model will spike on its own due to the nature of the underlying differential equations.

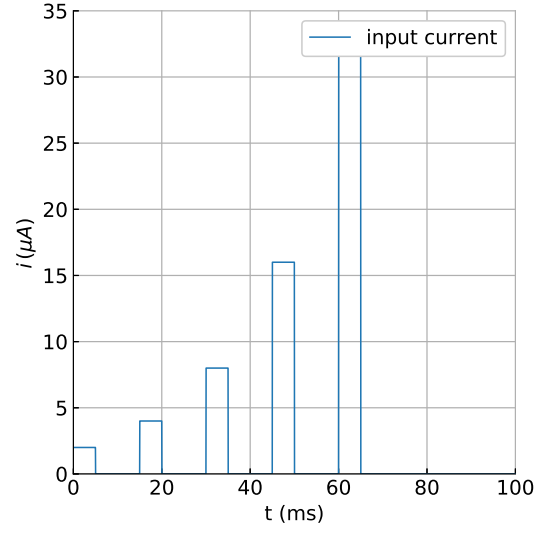
2.1 Implementation

See `hodgkinHuxley.py` for implementation details. The plots are generated by `plot_hh.py`.

2.2 Experiments

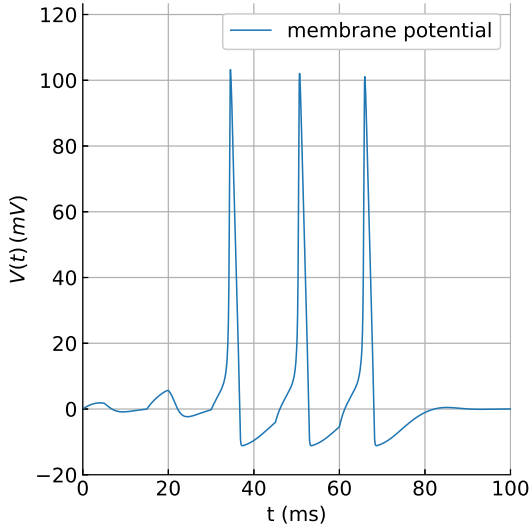


(a) Input current at 6.3°C .

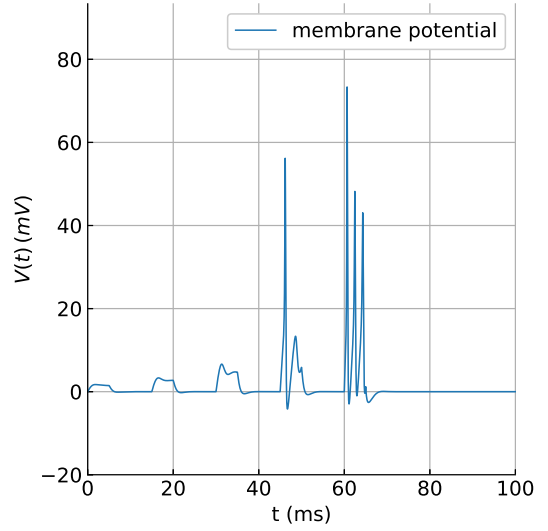


(b) Input current at 28°C .

Figure 2: Input currents for different temperatures.

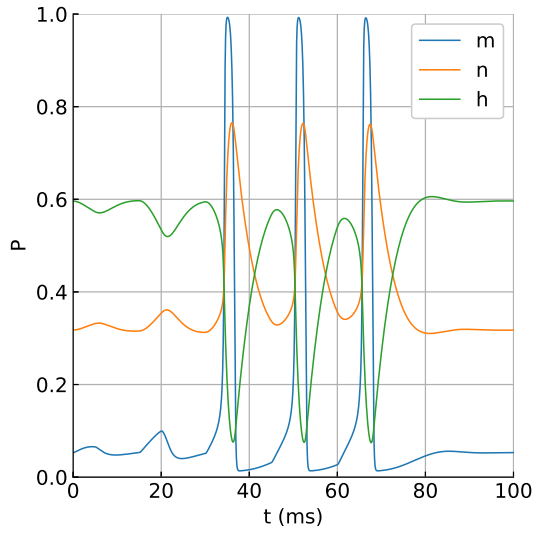


(a) Membrane potential for 6.3°C and the input visible in figure 2a.

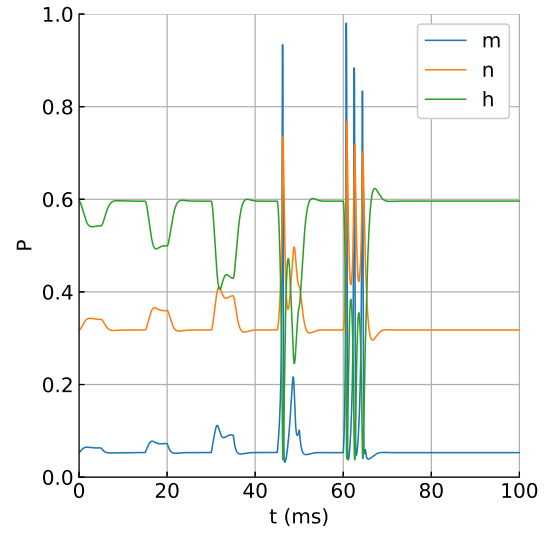


(b) Membrane potential for 28°C and the input visible in figure 2b.

Figure 3: Membrane potentials for different input current and temperature tuples.

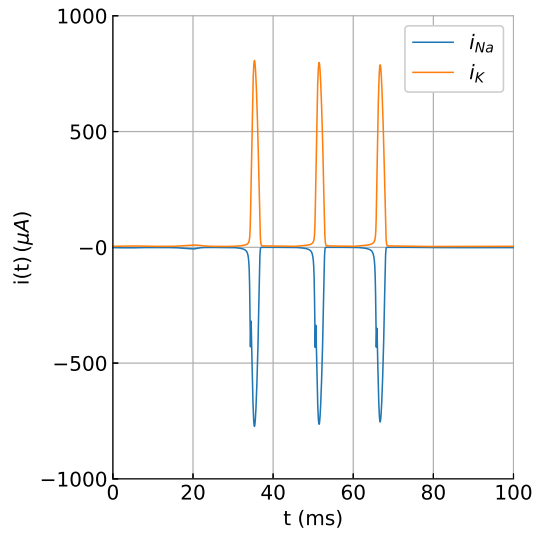


(a) Gate variables for 6.3°C and the input visible in figure 2a.

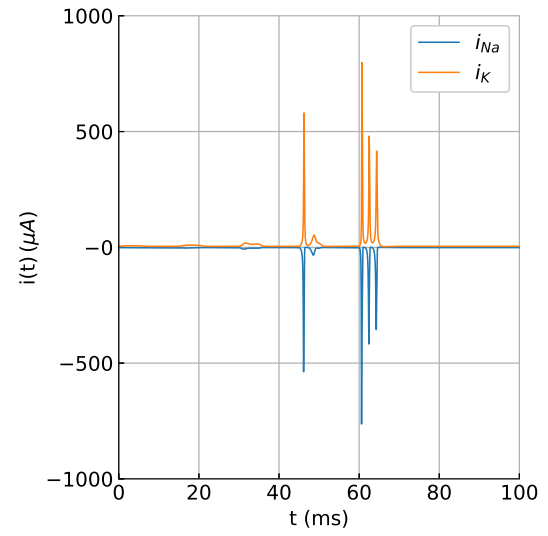


(b) Gate variables for 28°C and the input visible in figure 2b.

Figure 4: Gating variables m , n , h for different input current and temperature tuples.

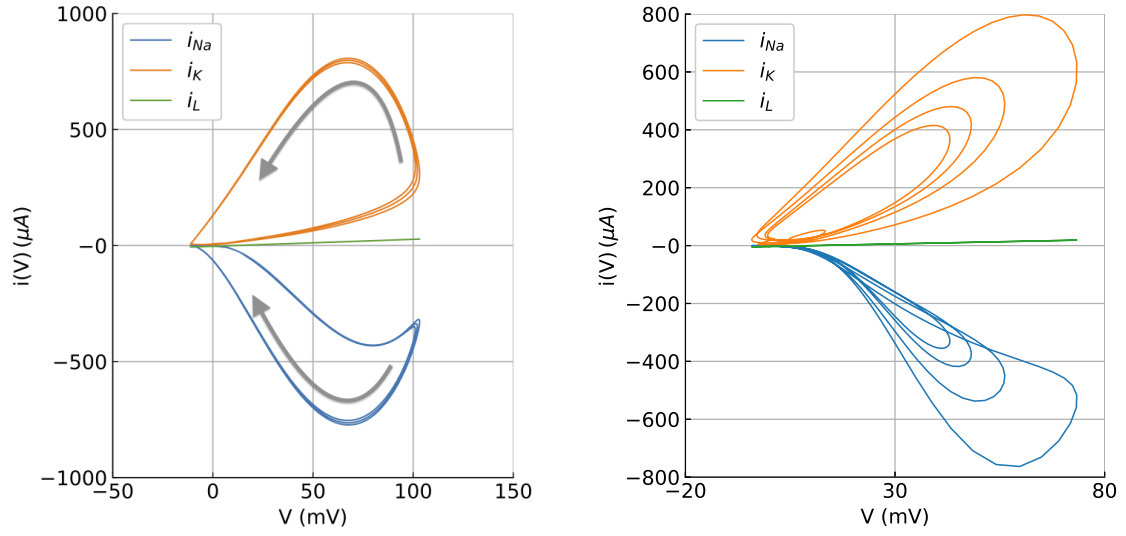


(a) Currents i_{Na} and i_K for 6.3°C and the input visible in figure 2a.



(b) Currents i_{Na} and i_K for 28°C and the input visible in figure 2b.

Figure 5: Currents i_{Na} and i_K for different input current and temperature tuples.



(a) Phase plot for $6.3^\circ C$ and the input visible in figure 2a. (b) Phase plot for $28^\circ C$ and the input visible in figure 2b.

Figure 6: Currents i_{Na} and i_K for different input current and temperature tuples.

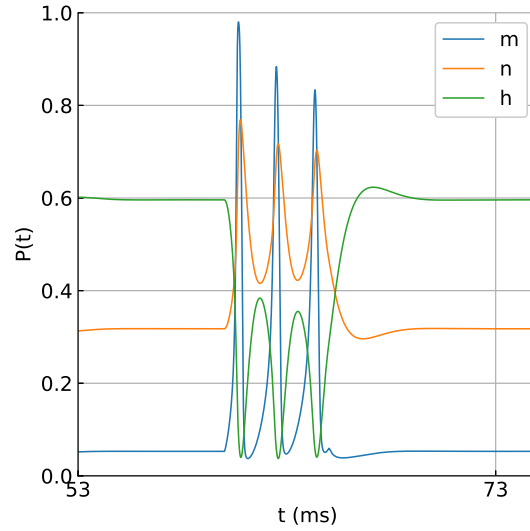


Figure 7: Close-up of gating variables at $28^\circ C$ from 4b.

2.3 Analysis of the results

In this exercise the HH-model is simulated at two different conditions. Temperatures as well as the stimulus current densities differ between the experiments. Which means that the different results are can not be allocated to one parameter alone.

1. Describe the difference between the results at 6.3 °C and 28 °C:

Due to the temperature dependance of the timeconstants given in equation 4, they are smaller at higher temperatures, which is why the gates react faster to input changes at 28 °C than at 6.3 °C. The gates dependancy on the timeconstants is also visible in equation 3.

The stiff behaviour can also be observe by comparing the two plots of the membrane potential in figure 3. The steps of the input current are filtered at 6.3 °C and the system converges slower than at higher temperatures, due to the low-pass behaviour of the system. The membrane potential at 6.3 °C on the other hand looks more spiky.

Furthermore, excitation with 32 μ A at 28 °C leads to a fast sequence of cell excitations with decreasing peak amplitude, due to missing refractory time between the excitations.

2. How is the action potential generated and what is the role of the different currents and gating variables:

There are three different gating variables considered in the HH-model. The sodium and potassium channel activation gates, m and n respectively, and the sodium channels inactivation gate h . Each sodium channel consists of three m gates responsible for opening the channel and one h gate which is supposer to inactivate the channel. The potassium channels on the other hand are build from four n gates.

The main currents involved in de- and repolarisation of the membrane potentials are i_{Na} and i_K .

For an action potential to be generated the cell membrane potential has to increase beyond a certain threshold value V_{thr} . Once V_{thr} is surpassed the m and n gates are activated and the fast sodiums channels open, enabling more sodium to flow into the cell. This opening od sodium channels in return further depolarises the cell membrane (positive feedback) opening up more and more sodium channels while V_m approaches the sodium Nerst potential. At the same time potassium channels start to open and the inactivation gates begin close some of the sodium channels (both are much slower than the sodium activation gates). The peek is reached when the potassium efflux i_K overtakes the sodium influx i_{Na} . Now the cell starts to repolarize. The inactivation gates close more and more sodium channels while the flow through the potassium channels pushes the membranepotential continuously towards the potassium Nernst potential. Since those channels are slow to close, the cell is hyperpolarised before reaching its resting potential at which all voltage dependent channels are back in their steady states.

3. Explain why consecutive action potentials decrease in amplitude (at 28 °C):

The membrane potential in Figure 3b shows a pattern of consecutive action potentials with decreasing amplitudes between $t = 60$ ms and $t = 65$ ms. This can be explained by having a closer look at the gating variables during that timespan, depicted in Figure 7. While in the first experiment at 6.3°C the neuron can passively recover from the action potential by restoring the membranes resting potential and steady state this is not possible in the second experiment at 28°C coupled with an input current of $32\ \mu\text{A}$. The closeup plot of the activation gates shows that the gates have not yet had the chance to get back to their steady values before the next cell depolarisation is started. It can be seen, that the open-probability for the sodium inactivation gate is only at $h = \frac{h_{rest}}{2}$ to $\frac{h_{rest}}{3}$, leaving more sodium channels inactivated and thus decreasing the possible sodium ion influx. This becomes clear also when looking at the reduce ionic currents in Figure 5b. Due to this circumstance the rise of membrane potential is in over all slower.

4. How can you interpret the phase plot:

The first observation, looking at both phase plots in Figure 6 is, that the leakage current i_{leak} appears to be a straight line, depending linearly on the membrane potential and barely changing on the intervall of 0 mV to 100 mV.

Figure 6a shows the phase plot for 6.3°C . The arrows show the direction of the i_{Na} and i_K phase diagrams over time: clockwise for sodium, counterclockwise for potassium.

It can be seen that in the beginning of the depolarisation up to 10 mV both sodium and potassium current are around 0. As the depolarisation increases, the voltage depend sodium and potassium channels are activated. Since the sodium channels timeconstant τ_m is much faster than the potassium channels, we observe a steep increase in sodium current while the potassium current increases almost only linearly. As the increased influx of sodium further depolarises the membrane towards the sodium equilibrium voltage, more and more voltage dependant sodium channels open, leading to a steady increase in sodium inflow (positive feedback).

At around 80 mV i_{Na} reaches a local maximum. Now the slower inactivation gate h starts inactivating parts of the sodium channels, and i_{Na} starts to decrease. When the membrane potential reaches about 100 mV the action potassium reaches it's peak.

Though both i_{Na} and i_K increase, the potassium efflux starts overtaking the inward sodium current, which leads to the decrease of the cells membrane potential. While V_m decreases the sodium and potassium gates close. Again, the sodium gates are faster. The continuing potassium efflux leads to a short hyperpolarisation. Once all voltage gated channels are back in their initial state the membrane potential goes back to $V_{rest} = 0$.

5. Explain the difference between the LIF and the HH model, why would you implement one or the other:

The leaky integrate and fire neuron model is a theoretical neuron model that can be seen as a functional approximation of the Hodgkin Huxley model which yields a passive description of the cell membrane potential based on a simplified circuit consisting of a resistor, a capacitor and a battery. It is commonly used in computational investigations of spiking neurons. However, action potentials need to be introduced by hand by defining a Voltage V_{spike} to be triggered when the membrane potential surpasses a predefined threshold V_{thr} and hyperpolarisation is neglected. Over all, the LIF model shows of the basic idea behind action potentials, but does not in fact model the actual behaviour observed in nature.

In contrast to that, the Hodgkin & Huxley model is based on actual experiments on the giant axon of the squid. The HH-model takes in to account not only the leakage conductivity, membrane voltage, capacity and battery but models the complete cell dynamics down to the single ion-channels and gating variables by using a single set of four differential equations. Those describe the cell dynamics in the resting as well as the action potential and repolarisation phase.