Neuroprothetik Exercise 4
Hodgkin & Huxley Model

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1 Time constants and steady state values

Here, the differential equations for the gating variables m, n and h are investigated. The gating variables are described by equation 1 with α_x and β_x being the rate values for gate x. Equation 1 can be derived from the idea that each gate can only have to discrete states: open and closed. x then describes the probability, that the gate is open. Therefore, α_x and β_x describe the rate of opening and closing of the gate. When Hodgkin and Huxley tried to fit their data to analytical equations, they came up with 3, 4 and 5 for the transition-values. Only later it was discovered, that the transition-rate is mostly depending on the thermal energy in the cell and therefore Boltzmann-Distributed and the equations of Hodgkin and Huxley roughly describe such a distribution. The factor k thereby accounts for the influence of the cell-temperature T.

$$\frac{dx}{dt} = [\alpha_x(1-x) - \beta_x x]k, \quad x \in \{m, n, h\} \tag{1}$$

$$k = 3^{\frac{T-6.3\,^\circ\mathrm{C}}{10\,^\circ\mathrm{C}}} \tag{2}$$

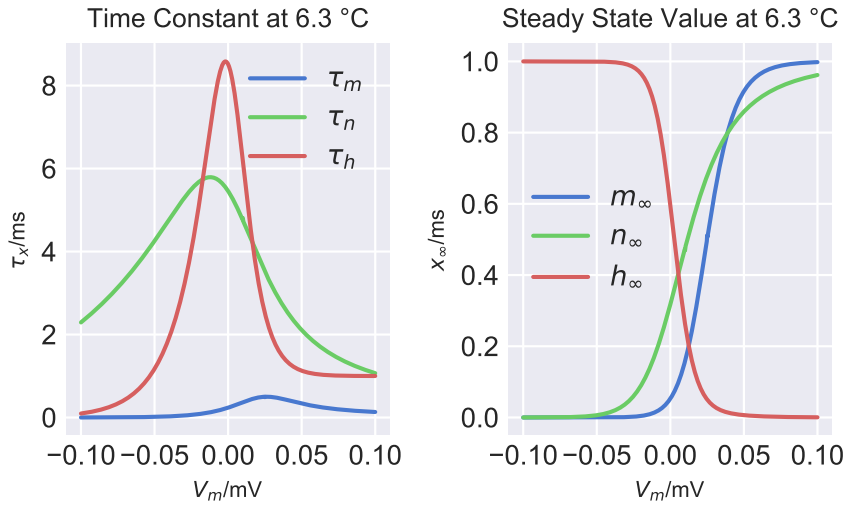
$$\alpha_m = \frac{25\,\mathrm{mV} - V_m}{10\,\mathrm{mV} \cdot (exp(\frac{25\,\mathrm{mV}-V_m}{10\,\mathrm{mV}}) - 1)} \qquad \beta_m = 4 \cdot exp(\frac{-V_m}{18\,\mathrm{mV}}) \tag{3}$$

$$\alpha_n = \frac{1\,\mathrm{mV} - 0.1 \cdot V_m}{10\,\mathrm{mV} \cdot (exp(\frac{10\,\mathrm{mV}-V_m}{10\,\mathrm{mV}}) - 1)} \qquad \beta_n = 0.125 \cdot exp(\frac{-V_m}{80\,\mathrm{mV}}) \tag{4}$$

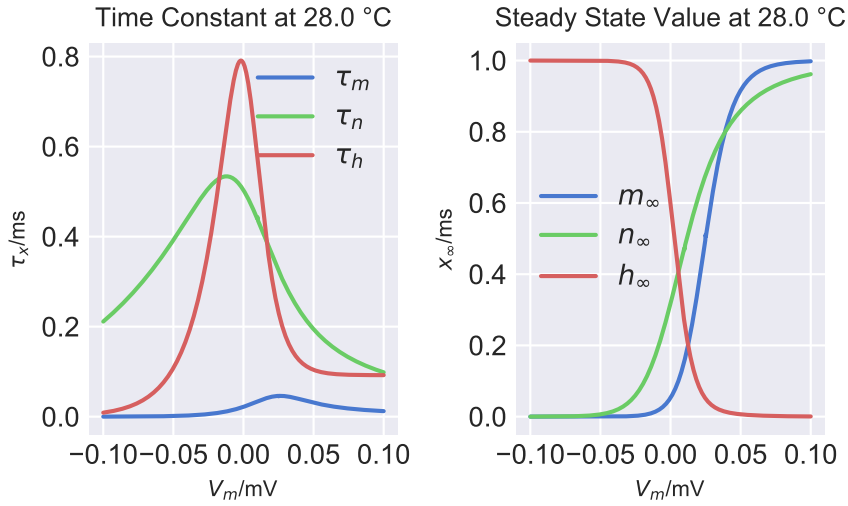
$$\alpha_h = 0.07 \cdot exp(\frac{-V_m}{20\,\mathrm{mV}}) \qquad \beta_h = \frac{1}{exp(\frac{30\,\mathrm{mV}-V_m}{10\,\mathrm{mV}}) + 1} \tag{5}$$

To derive the time constant τ_x and steady-state-values x_∞, the equation 1 can be written as followed as in 6. Because both α_x and β_x are depending on the membrane potential V_m, so does τ_x and x_∞. Figures 1a and 1b show the time constant τ_x and the steady-state-value x_∞ for a membrane potential between $V_m \in \{-100\,\mathrm{mV}, 100\,\mathrm{mV}\}$ for 6.3 °C and 28 °C.

$$\frac{dx}{dt} = \frac{1}{\tau_x}(x_\infty - x) = \frac{1}{\alpha_x + \beta_x}(\frac{\alpha_x}{\alpha_x + \beta_x} - x) \tag{6}$$



(a) The time constants and steady-state-values for a neuron at temperature 6.3 °C



(b) The time constants and steady-state-values for a neuron at temperature 28 °C

As one can see, the steady-state-value does not depend on the ambient-temperature, only τ_x does. An increased temperature thereby corresponds to a lower time constant. This only seems logical, when we remember that the energy required for the gating-process is thermal energy. A higher temperature (and therefore more thermal energy)

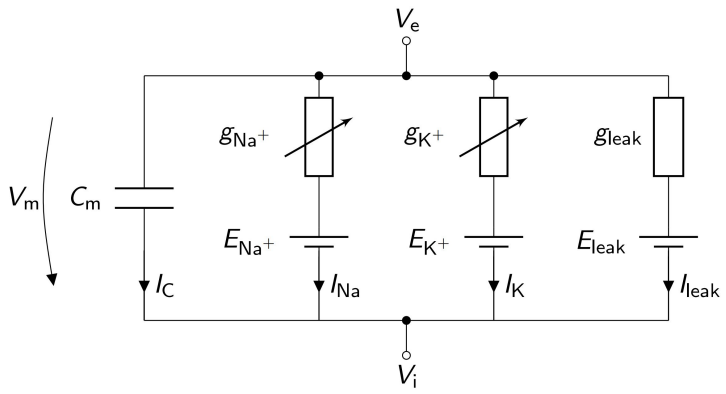


Figure 2: Simple equivalent circuit of a neuron

therefore translate into a faster switching between the two states.

2 Hodgkin & Huxley Neuron Model

In this secton, the whole Hodgkin and Huxley model is implemented and solved using an Exponential-Euler-Solver as well as an Explicit-Euler-Solver. Those solvers were implemented in Exercise 3. In addition to the gating-equations in section 1, the Hodgkin and Huxley Model also consists of three equations 7, 8 and 9 for the ion currents, i_{Na} for the sodium-current, i_K for the potassium-current and i_{leak} for the remaining currents (also called leak-current). Here, g_x describes the conductivity and E_x the resting potential for channel $x \in \{Na, K, leak\}$.

$$i_{Na} = g_{Na} m^3 h \cdot (V_m - E_{Na}) \tag{7}$$

$$i_K = g_K n^4 \cdot (V_m - E_K) \tag{8}$$

$$i_{leak} = g_{leak} \cdot (V_m - E_{leak}) \tag{9}$$

The membrane potential then can be calculated using the simple equation of the equivalent circuit of a neuron shown in Figure 2 and equation 10

$$\frac{dV_m}{dt} = \frac{1}{C_m}(i_{in} - i_{Na} - i_K - i_{leak}) \tag{10}$$

2.1 Experiments

Now, the model will be stimulated with two patterns at two different temperatures:

(A) At 6.3 °C, the stimulation will occure for 5 ms with a pause of 10 ms and the following amplitued: [1, 2, 3, 4, 5] µA cm^{-2}

(B) At 28 °C, the stimulation will occure for 5 ms with a pause of 10 ms and the following amplitued: [2, 4, 8, 16, 32] µA cm^{-2}

Figures 3 and 4 show the time-plot of the membrane potential, gating variables, current densities and the input pattern for both stimulations. The phase plot of both stimulations on the V/i-plane is shown in Figure 5

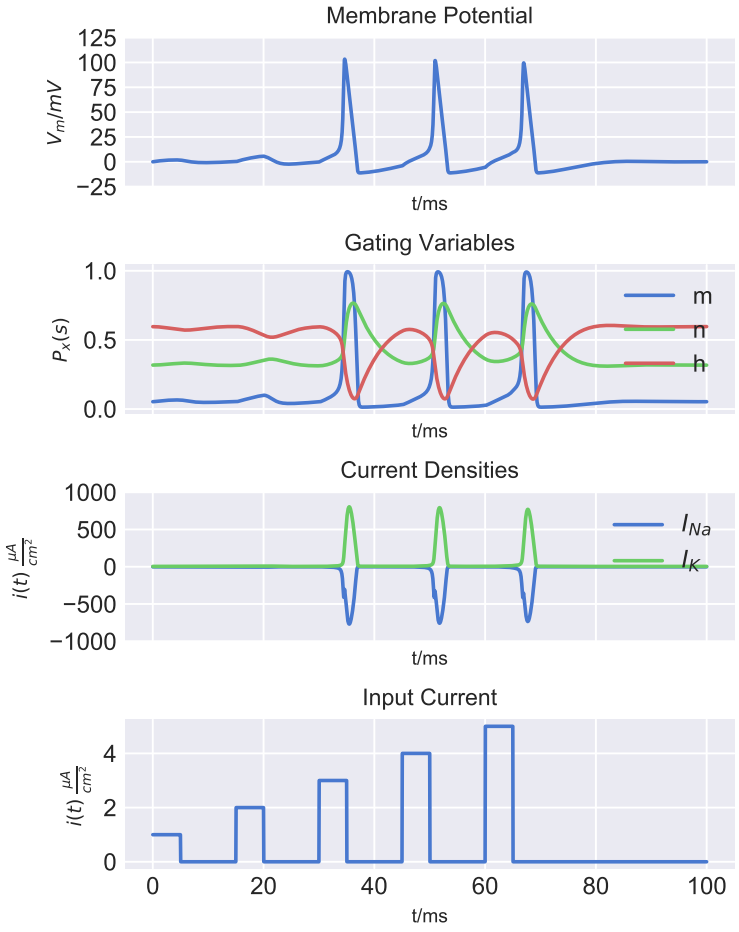


Figure 3: From top to bottom: The membrane potential, the gating variables, current densities and input pattern (A) at 6.3 °C

2.2 Analysis of the Results

When comparing the results for different cell-temperature, we should use the same stimulation-pattern for both temperatures. Therefore, Figure 6 and 7 show the sim-

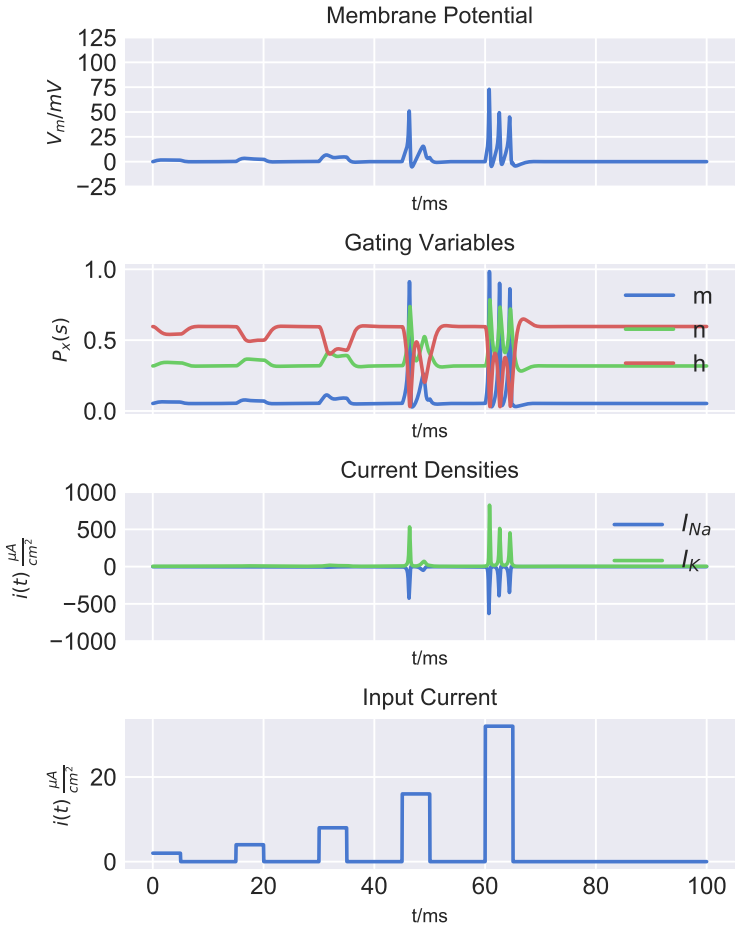


Figure 4: From top to bottom: The membrane potential, the gating variables, current densities and input pattern (B) at 28 °C

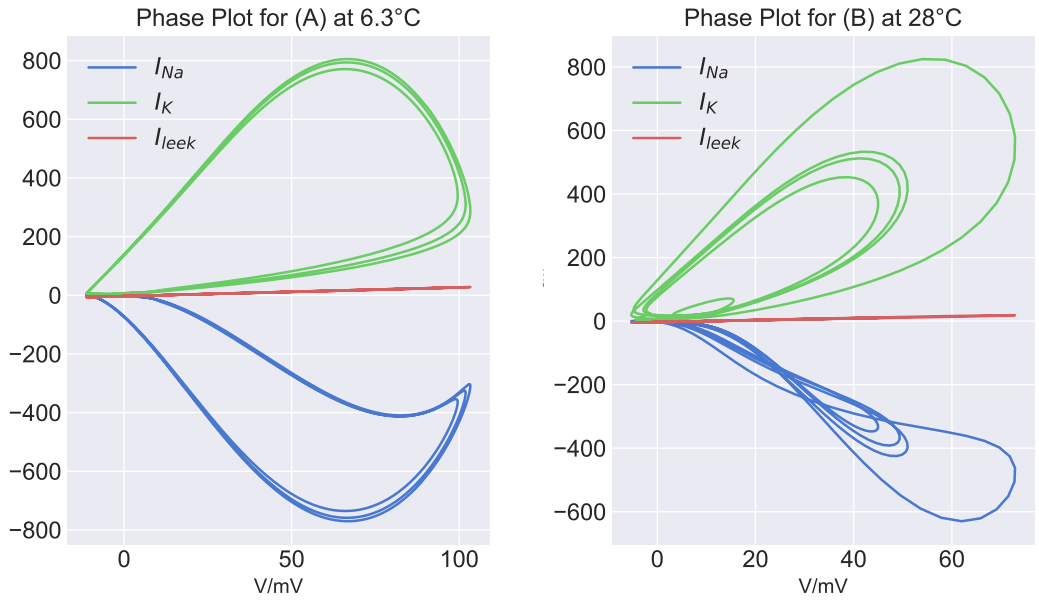


Figure 5: The phase plot for stimulation pattern (A) at 6.3 °C (left) and (B) at 28 °C (right)

ulations for pattern (B) at 6.3 °C and pattern (A) at 28 °C respectively. As one can see, the cell-temperature has a significant impact on the generation of action potentials. At 28 °C, the smaller stimulation (A) with maximal $5\,\mu A\,cm^{-2}$ is not powerful enough to polarize the membrane so far that it can generate an action potential. A higher temperature and therefore a smaller time constant increases the speed at which the gates open and close and therefore there is not enough time for a high strong membrane potential to build up to trigger an action potential (Comparing Figure 7 with 3). On the other side, a higher temperature allows for a higher action potential frequency, if the polarization is high enough (See Figure 6). Because of the smaller time constant, the relative refractory period is also shortened, and therefore multiple action potentials can occur where before only one was possible (See Figure 4).

A action potential is triggered when the membrane potential is above a certain threshold. This leads to an opening of both sodium an potassium-channels due to an increase of the gating-variables m and n. The sodium-channels open way before the potassium-channels due to a way smaller time constant (See Figure 1a). This leads to an increased sodium-current into the cell and therefore depolarizes the membrane even more, which creates an feedback loop. Now the slower potassium-gates start to open which allows for an outflow of potassium-ions out of the cell. This results, together with the increasing of the inactivation-gate h, in an decreasing of the depolarization until it falls slightly below the resting potential. From here, the potential slowly increases until it reaches

the resting potential again and a new action potential can be triggered.

Using the stimulation patter (B) at 28 °C (See Figure 4), we can observe multiple spikes i a short period of time, but with decreasing amplitude. This can easily be explained looking at the gating variables, especially the inactivation-variable h. As seen in Figure 1b, this variable still has a rather high time constant. Due to this it cannot return to its steady-state-value after each spike, but remains at an higher level. This leads to an decreasing influx of sodium-ions into the cell and therefore to an smaller peak of the action potential.

The phase plot 5 shows all possible voltage- and current-combinations. Starting at 0 mV and 0 µA cm^{-2}, I_K can only take the green route, while the only possible path for I_{Na} is the blue one. This plots shows the relation between the increased sodium-current and membrane depolarization as well as the delayed (in membrane-potential-domain, not time-domain) beginning of the potassium-current. On the right side of Figure 5 we can also observe the smaller action potentials. One benefit of the phase plot is, that the direct relation between current and membrane potential is more obvious. On the other hand, the missing time-dimension makes it difficult to see which loop is passed first (e.g. in the right plot, using only the phase plot we cannot see whether the smaller action potentials happend first or last).

In general one can say that the Hodgkin-Huxley-Model (HH) allows for a deeper understanding of the processes inside a neural cell and why certain properties exist. Therefore, for learning the fundamentals this model is definitely better suited than the much simpler Leaky-Integrate-and-Fire-Model (LIF) from Exercise 3. On the other hand, the LIF is able to perform rather similar than the HH, while only solving one differential equation instead of four. For a single neuron, this does not make much difference, but when simulation a whole network of such neurons, the computational performance of the used model becomes more and more important. Therefore, if I have no special reason to do other, I would prefer to implement the LIF-Model for a more general observation of many neurons and the HH-Model if I only have to oberserve a single or very few neurons.

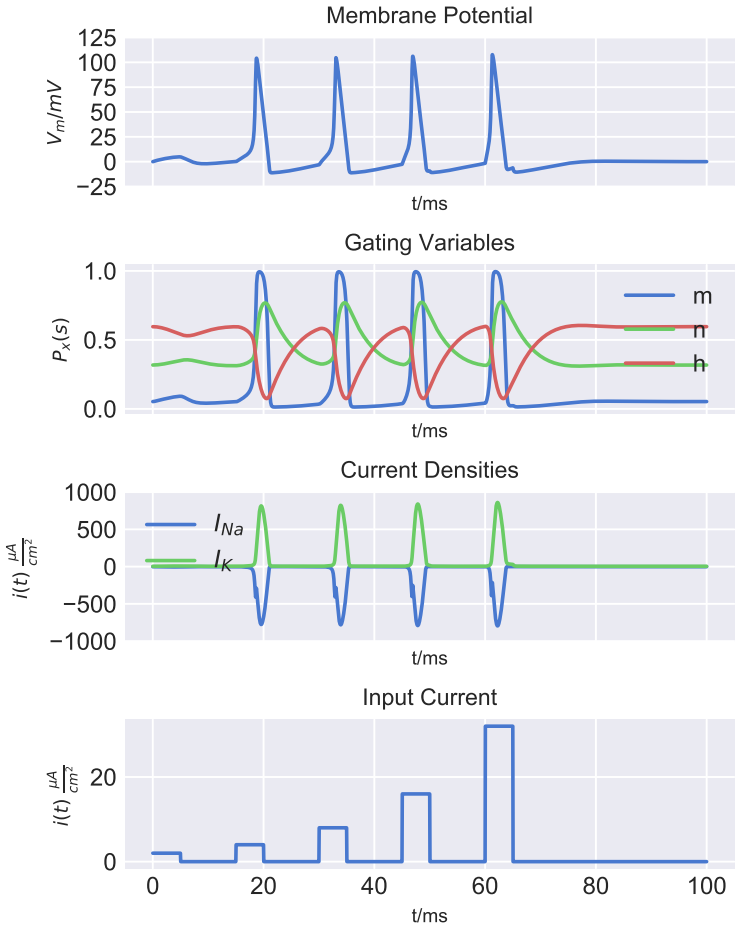


Figure 6: From top to bottom: The membrane potential, the gating variables, current densities and input pattern (B) at 6.3 °C

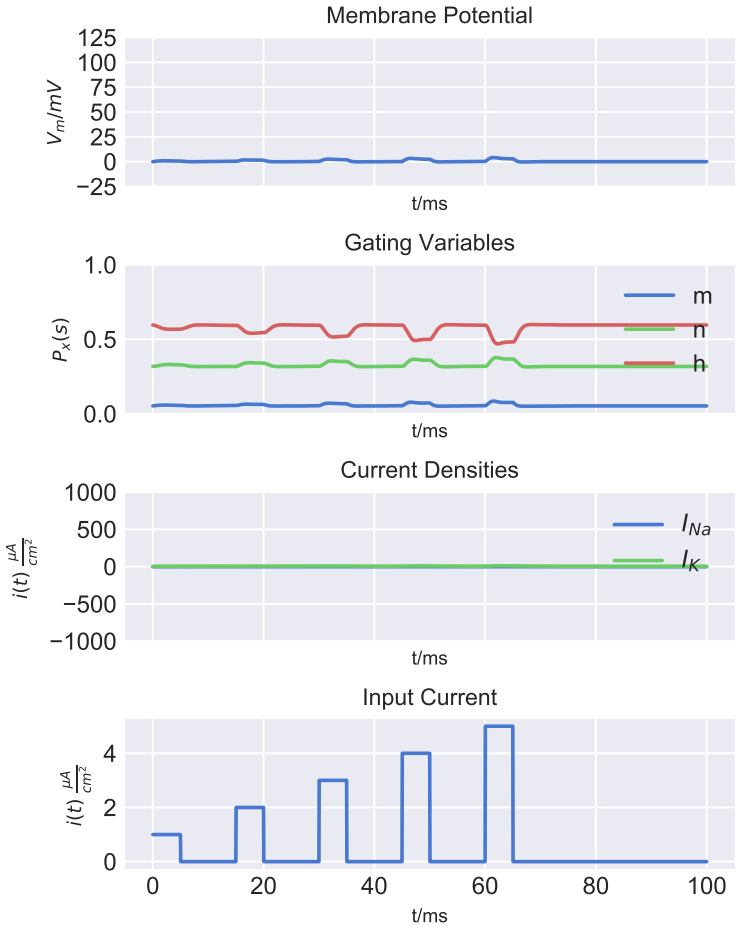


Figure 7: From top to bottom: The membrane potential, the gating variables, current densities and input pattern (A) at 28 °C