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Models of Neural Systems, WS 2020/21
Computer Practical 6
Assignment due: January 11th, 2021, 10 am

1. **Potassium channel.** The gate model was first introduced by Hodgkin and Huxley to describe the voltage and time dependence of ion conductances in the squid axon. Today it is still the standard model of the ion current flow through transmembrane channels. One of its main assumptions is that the probability of opening and closing of an ion gate is described by a first-order kinetic equation:

$$\frac{\mathrm{d}n}{\mathrm{d}t} = \alpha_n(V)(1-n) - \beta_n(V)n \tag{1}$$

where $\alpha_n(V)$ and $\beta_n(V)$ are voltage-dependent transition rates.

The potassium current in the Hodgkin-Huxley model is given by:

$$I_\mathrm{K} = \bar{g}_\mathrm{K} n^4 (V - E_\mathrm{K}) \tag{2}$$

where $E_\mathrm{K} = -77\,\mathrm{mV}$ is the reversal potential of potassium and $\bar{g}_\mathrm{K} = 36\,\mathrm{nS}$ is its maximum conductance. The rates $\alpha_n(V)$ and $\beta_n(V)$ are given by:

$$\alpha_n(V) = \frac{0.01(V+55)}{1-\exp(-0.1(V+55))}, \quad \beta_n(V) = 0.125\exp(-0.0125(V+65)), \tag{3}$$

where V is expressed in **mV**, and α_n and β_n are both expressed in units of $\mathbf{ms}^{-1}$. **Hint:** There's no need to rescale the units and the numbers can be taken as they are (i.e. operate in millivolts and milliseconds). But pay attention when determining the unit of the currents in your plots.

(a) Write Python functions defining $\alpha_n(V)$ and $\beta_n(V)$ (you may also write $\mathrm{d}n/\mathrm{d}t$ and I_K for later use).

(b) Plot the activation time constant $\tau_n(V) = 1/(\alpha_n(V) + \beta_n(V))$ and the steady-state activation $n_\infty(V) = \alpha_n(V)/(\alpha_n(V) + \beta_n(V))$ in a voltage range of -150 mV $\leq V \leq 150$ mV. Also verify the latter analytical expression by looking at the transient response, i.e. numerically integrate equation 1 using an Euler scheme for a particular voltage and initial condition of your choice. To see if you are on the right track, for a command voltage of $-40\,\mathrm{mV}$ the steady state is $n_\infty \approx 0.68$ and it should reach this value in $\approx 23\,\mathrm{ms}$ (difference to steady state smaller than 0.001) from $n(t=0) = 0.0$.

(c) *Voltage clamp.* Simulate the current responses I_K to voltage steps under voltage-clamp conditions:

$$V(t) = \begin{cases} V_c & \text{if } t \geq 2 \text{ ms}, \\ -65 \text{ mV} & \text{otherwise.} \end{cases} \tag{4}$$

with the initial condition $n(t=0) = 0.3177$. You can use the Euler integration method. Plot I_K as a function of time. Repeat the simulation for different values of command voltage V_c from the range $[-100\,\mathrm{mV}, -40\,\mathrm{mV}]$. Please note that the integrated function explicitly depends on time (because the command voltage changes after 2 ms). Do not rewrite your Euler method, but better extend your current solution so that it can handle both cases.

What can be learned from this experiment? What is the predicted effect of the potassium current on the membrane potential? Explain the obtained results by referring to the plots of n_∞ and τ_n.

(d) *Current-voltage relation.* Plot the I-V relation for the instantaneous (using $n(t=0)$ from c)) and the steady-state (n_∞) potassium current.

2. **Sodium ion channel.** According to the Hodgkin-Huxley model, the sodium channel is given by:

$$I_{\mathrm{Na}}(V,t) = \bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}}) \tag{5}$$

where $E_{\mathrm{Na}} = 50\,\mathrm{mV}$ is the reversal potential of sodium and $\bar{g}_{\mathrm{Na}} = 120\,\mathrm{nS}$ is its maximal conductance. The gating variables m, h follow first-order kinetics (see Equation 1) with the following rate functions:

$$\alpha_m = 0.1\frac{V+40}{1-\exp(-0.1(V+40))} \qquad \beta_m = 4\exp(-0.0556(V+65)) \tag{6}$$

$$\alpha_h = 0.07\exp(-0.05(V+65)) \qquad \beta_h = \frac{1}{1+\exp(-0.1(V+35))} \tag{7}$$

(a) Write all necessary functions and plot the steady-state activation (m_∞, h_∞, analogous to n_∞) and time constant (τ_m, τ_h, analogous to τ_n) of m and h as a function of the membrane potential. Compare the results to the dynamics of the n variable. Which variables are activated/deactivated by depolarisation? Which variables are fast/slow?

(b) The gating of the potassium current was described by a single ordinary differential equation. Please note that the sodium channels are described by a system of two ordinary differential equations. Simulate and plot the sodium current for $V = -20\,\mathrm{mV}$, $m(t=0) = 0.0529$, $h(t=0) = 0.5961$ over time. To see if you are on the right track, you should observe a minimum of $\approx -1240\,\mathrm{pA}$ (may vary due to your choice of timestep) followed by a relaxation to the steady state of $\approx -50\,\mathrm{pA}$ reached after $\approx 15\,\mathrm{ms}$ (difference to steady state smaller than 0.01).

(c) Simulate the voltage clamp experiment for the sodium current using voltage steps from -65 mV to various command voltages V_c, as given in equation 4. Use initial values from b). Plot the sodium current as a function of time for several values of the command voltage V_c. What mechanisms are responsible for the sodium current rise and decay?

(d) Plot the instantaneous and steady-state I-V curves for sodium channels. For the instantaneous case use the initial values of the gating variables as given in b). Compare with 1d) and discuss the results.

(e) (**bonus**) What happens if you repeat the voltage clamp experiments from before (initial conditions as before) but this time investigating the (negative) sum of both currents ($-I_{\mathrm{K}} - I_{\mathrm{Na}}$)? Plot the time course for varying command voltages (similar ranges as for the sodium experiment). Please speculate how this relates to neural activity.

Upload your solution to Moodle (see also submission checklist in the general information section). Please, comment your code and provide short answers to the questions in each task.

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