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Models of Neural Systems, WS 2020/21
Computer Practical 7
Assignment due: January 18th, 2021, 10 am

1. **Hodgkin-Huxley model of action potential generation.** Action potentials are a key feature of the nervous system and play a crucial role for neural computation. For the squid giant axon, the ionic mechanisms of action-potential generation were described by Hodgkin and Huxley. The complete model they proposed is as follows:

$$C_m \frac{\mathrm{d}V}{\mathrm{d}t} = -I_{\mathrm{Na}} - I_{\mathrm{K}} - I_{\mathrm{leak}} + I_e$$

where I_{Na} and I_{K} are the sodium and potassium currents that we already discussed in the previous sheet:

$$I_{\mathrm{Na}} = \bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}}),$$
$$I_{\mathrm{K}} = \bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}}),$$

with the reversal potentials $E_{\mathrm{Na}} = 50\,\mathrm{mV}$ and $E_{\mathrm{K}} = -77\,\mathrm{mV}$ and the maximal conductances $\bar{g}_{\mathrm{Na}} = 120\,\mathrm{nS}$ and $\bar{g}_{\mathrm{K}} = 36\,\mathrm{nS}$. The gating variables follow first-order kinetics:

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \alpha_x(V)(1-x) - \beta_x(V)x,$$

with $x \in \{n, m, h\}$ and the voltage-dependent transition rates α and β with voltage V in units of millivolts:

$$\alpha_n(V) = \frac{0.01(V+55)}{1-\exp(-0.1(V+55))}, \qquad \beta_n(V) = 0.125\exp(-0.0125(V+65)),$$
$$\alpha_m(V) = 0.1\frac{V+40}{1-\exp(-0.1(V+40))}, \qquad \beta_m(V) = 4\exp(-0.0556(V+65)),$$
$$\alpha_h(V) = 0.07\exp(-0.05(V+65)), \qquad \beta_h(V) = \frac{1}{1+\exp(-0.1(V+35))}.$$

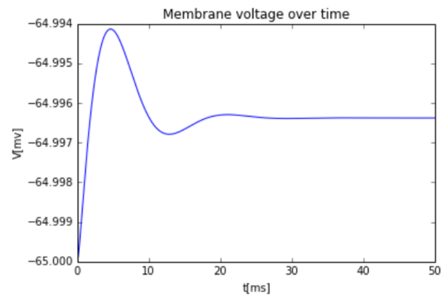
Please feel free to reuse code from the previous sheet!

Moreover, I_{leak} is a passive leakage current:

$$I_{\mathrm{leak}} = \bar{g}_{\mathrm{leak}}(V - E_{\mathrm{leak}})$$

with $\bar{g}_{\mathrm{leak}} = 0.3\,\mathrm{nS}$ and $E_{\mathrm{leak}} = -54.387\,\mathrm{mV}$. Lastly, I_e describes the experimentally applied current.

(a) Simulate the Hodgkin-Huxley model by numerically integrating the equations for V, n, m and h (4-dimensional system of ODEs). Use $I_e = 0$ A, $C_m = 1\,\mathrm{pF}$ and as initial values use $V(t=0) = -65\,\mathrm{mV}$, $m = 0.0529$, $h = 0.5961$, and $n = 0.3177$. Make sure that the integration time step is short enough to obtain a stable and accurate solution, but not so small that the integration takes too long (if you use the Euler method, a good choice might be $\Delta t = 10^{-2}$ ms). To see if you are on the right track, you should observe a damped oscillation with a very small amplitude as shown in the figure. If your y-axis uses a strange offset, you may want to try:




```
ax = plt.gca()
ax.ticklabel_format(useOffset=False)
```

(b) Apply now a constant external current $I_e = 20\,\mathrm{pA}$ and plot V, I_K, I_Na, and all gating variables as functions of time. To get a better impression of the currents tracking each other you might consider plotting both currents in the same plot and using the negative sodium current, $-I_\mathrm{Na}$. Plot the three gating variables in a single plot as well. To get a better resolution consider changing the size of the plot, eg. using

```
plt.figure(figsize=(15,5))
```

before plotting. Discuss the influence of the different currents at different phases of the action potential, and how these are related to the dynamics of the gating variables. Furthermore, plot the potassium gating variable n as a function of the voltage over the full time course. Repeat this analysis for potassium current I_K and voltage. This gives you two phase plane trajectories, i.e. two plots with, first, $n(t)$ on y-axis vs. $V(t)$ on x-axis and, secondly, $I_\mathrm{K}(t)$ vs. $V(t)$). Please interpret your results.

(c) Plot the firing rate of the model as a function of I_e over the range from 0 to 20 pA. Show that the firing rate jumps discontinuously from zero to a finite value when the current exceeds a certain value ('rheobase'). What is the approximate value of the rheobase? What is the difference to the firing rate curve you obtained for the leaky integrate-and-fire model in the fifth sheet? *Hints:* use a reasonable voltage threshold criterion for spike detections. Remind yourself of how to calculate the firing rate from a spike train (sheet 5).

(d) Apply a negative current pulse of $I_e = -5\,\mathrm{pA}$ for 5 ms followed by $I_e = 0\,\mathrm{pA}$ and see what happens. Plot voltage, sodium and potassium currents and gating variables as in part (b). Explain the obtained result.

(e) (**bonus**) Drive your Hodgkin-Huxley neuron with an external sinusoidal current $I_e = I_0 \sin(2\pi\nu t)$ with $I_0 = 2$ pA. Be careful: you need a conversion factor if you measure time in ms and frequency in Hz! Determine the neuron's firing rate as a function of the input frequency ν in Hz (think about the appropriate simulation time you need to measure a given firing rate). What do you observe? Why? To explain the phenomena you observe, you can provide plots of the time course of quantities you deem appropriate (e.g. voltage, currents, gating variables) for some representative frequencies (the number of bonus points depends on how thoroughly you discuss the different behaviors you see).

Please label all plots and axes. Please also interpret and comment on all results and plots. Upload your solution to Moodle (see also submission checklist in the general information section).

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