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Models of Neural Systems I, WS 2009/10
Computer Practical 7
Solutions to hand in on: December, 14th, 2009

1. **Sodium ion channel**

The sodium channel according to Hodgkin-Huxley model is given by:

$$I_{\mathrm{Na}}(V,t) = \bar{g}_{\mathrm{Na}} m(V,t)^3 h(V,t)(V - E_{\mathrm{Na}}) \tag{1}$$

where $E_{\mathrm{Na}} = 50\,\mathrm{mV}$ is the reversal potential of sodium and $\bar{g}_{\mathrm{Na}} = 120\,\mathrm{mS/cm^2}$ is its maximal conductance.

The gating variables m, h follow first-order kinetics (see Equation (3) in Exercise Sheet 6) with the following rate functions:

$$\alpha_m = 0.1\frac{V+40}{1-\exp(-0.1(V+40))} \qquad \beta_m = 4\exp(-0.0556(V+65)) \tag{2}$$

$$\alpha_h = 0.07\exp(-0.05(V+65)) \qquad \beta_h = \frac{1}{1+\exp(-0.1(V+35))} \tag{3}$$

(a) Plot the steady-state activation and time constant of m and h as a function of the membrane potential. Compare the results to the dynamics of the n variable. Which variable is activated and which deactivated by depolarisation? Which variable is fast/slow?

(b) Note that in contrast to the model of the persistent potassium current the sodium channels are described by a system of ordinary differential equations. In order to solve it, you need to modify your Euler method! First, define a function which takes as arguments the instantaneous values for m, h and returns their derivatives. Next, modify your Euler method so that it accepts a function returning any number of variables together with a vector of initial conditions and solves the corresponding system of differential equations. Calculate and plot the sodium current for $V = -20$ mV, $m(t=0) = 0.0529$, $h(t=0) = 0.5961$.

(c) Simulate the voltage clamp experiment for the sodium current using voltage steps from -65 mV to various command voltages V_c. Plot the sodium current as a function of time. Repeat for several values of V_c. Compare the results with respective plots of the potassium current. What are the mechanisms responsible for the sodium current rise and decay?

(d) Plot the instantaneous and stead-state I-V curves for sodium channels. Compare and discuss the results.

2. **Hodgkin-Huxley model of action potential generation**

Action potentials (aka spikes) are a dominant feature of nervous system and play crucial role in the computations performed by cortex, thalamus, cerebellum and associated structures. The ionic mechanisms of action potential generation were described on giant squid axon by Hodgkin and Huxley. The complete model they proposed is as following:

$$c_m \frac{\mathrm{d}V(t)}{\mathrm{d}t} = -I_{\mathrm{Na}}(V(t),t) - I_{\mathrm{K}}(V(t),t) - I_{\mathrm{leak}}(V(t),t) \tag{4}$$

where $I_{\mathrm{Na}}(V,t)$, $I_{\mathrm{K}}(V,t)$ are the sodium and potassium currents which we already discussed. $I_{\mathrm{leak}}(V,t)$ is a leakage current due to chloride and other ios and can be well described by a passive ion flow:

$$I_{\mathrm{leak}}(V,t) = \bar{g}_{\mathrm{leak}}(V - E_{\mathrm{leak}}) \tag{5}$$

with $\bar{g}_{\mathrm{leak}} = 0.3\,\mathrm{mS/cm^2}$ and $E_{\mathrm{leak}} = -54.387\,\mathrm{mV}$.

(a) Simulate a Hodgkin-Huxley model by numerically integrating equations for V, n, m, h (4-dimensional system of ODEs!). Take $c_m = 1\,\mu\mathrm{F/cm^2}$ and as initial values take: $V = -65\,\mathrm{mV}$, $m = 0.0529$, $h = 0.5961$, and $n = 0.3177$. Make sure that the integration time step is short enough to obtain a stable and accurate solution (test several values).

(b) Use an external current with density $i_e = 20\,\mu\mathrm{A/cm^2}$ and plot V, I_{K}, I_{Na} as functions of time. Which currents are responsible for different phases of action potential generation?

(c) Plot the firing rate of the model as a function of i_e over the range from 0 to 200 $\mu\mathrm{A/cm^2}$. Show that the firing rate jumps discontinuously from zero to a finite value when the current passes through the minimum value to produce a sustained firing. (*Hint:* to detect spikes test when the membrane potential crosses a predefined threshold).

(d) Apply a pulse of a negative current with $i_e = -5\,\mu\mathrm{A/cm^2}$ for 5 ms followed by $i_e = 0$ and show what happens. Can you explain the results?

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