Assignment 6
Theoretical Neuroscience [Gatsby]

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1. **The Hodgkin-Huxley neuron**

Numerically integrate the Hodgkin-Huxley equations with matlab (or your favorite package). If you're using matlab, it's a good idea to use the Matlab `ode45` function. The equations are:

$$C\frac{dV}{dt} = -\overline{g}_{Na}m^3h(V-E_{Na}) - \overline{g}_K n^4(V-E_K) - \overline{g}_L(V-E_L) + I_{stim} \tag{1}$$

$$\frac{dx}{dt} = \alpha_x(1-x) - \beta_x x \qquad \text{where } x \text{ is } m, n \text{ or } h \tag{2}$$

$$\alpha_n(V) = 0.01(V+55)/\left[1-\exp(-(V+55)/10)\right] \tag{3}$$

$$\beta_n(V) = 0.125\exp(-(V+65)/80) \tag{4}$$

$$\alpha_m(V) = 0.1(V+40)/\left[1-\exp(-(V+40)/10)\right] \tag{5}$$

$$\beta_m(V) = 4\exp(-(V+65)/18) \tag{6}$$

$$\alpha_h(V) = 0.07\exp(-(V+65)/20) \tag{7}$$

$$\beta_h(V) = 1/\left[\exp(-(V+35)/10)+1\right] \tag{8}$$

Let $C = 10\,\mathrm{nF/mm^2}, \overline{g}_L = .003\,\mathrm{mS/mm^2}, \overline{g}_K = 0.36\,\mathrm{mS/mm^2}, \overline{g}_{Na} = 1.2\,\mathrm{mS/mm^2}, E_K = -77\,\mathrm{mV}, E_L = -54.387\,\mathrm{mV},$ and $E_{Na} = 50\,\mathrm{mV}$. Use an integration time step of 0.1 ms.

Remember to keep your units consistent. F/S = Farad/Siemens = 1 second.

(a) Run the simulations with $I_{stim} = 200\,\mathrm{nA/mm^2}$. Plot the membrane potential (V) and gating variables (m, h, and n) versus time.

(b) Write down expressions for the equilibrium values of the gating variables (m_∞, h_∞, and n_∞), and plot them versus voltage.

(c) Plot the firing rate versus I_{stim}, up to a firing rate of 50 Hz. The firing rate should jump suddenly from zero to a non-zero value. This is called a type II behaviour. Type I behaviour is when the firing rate begins at zero and increases continuously without any jumps.

(d) What happens to the plot of firing rate versus I_{stim} as you decrease $\overline{g}_K$?

(e) Spikes are initiated at the axon hillock, where the axon meets the soma. This is because $\overline{g}_{Na}$ is very high there. What happens to the plot of firing rate versus I_{stim} as you increase $\overline{g}_{Na}$?

2. **The linear integrate and fire neuron**

An approximate treatment of spiking neurons is to think of them as passively integrating input and, when the voltage crosses threshold, emitting a spike. This leads to the linear integrate and fire neuron (sometimes called the leaky integrate and fire neuron, and often abbreviated LIF), which obeys the equation

$$C\frac{dV}{dt} = -g_L(V - \mathcal{E}_L) + I_0 \,.$$

This is just the "linear integrate" part. To incorporate spikes, when the voltage gets to threshold (V_t), the neuron emits a spike and the voltage is reset to rest (V_r).

(a) Compute the firing rate of the neuron as a function of I_0. This firing rate will be parameterized by three numbers: $\mathcal{E}_L$, V_t, and V_r.
Hint #1: The firing rate is the inverse of the time it takes to go from V_r to V_t.
Hint # 2: Changing variables, and defining new quantities, almost always makes life easier. For example, you might let $v = V - \mathcal{E}_L$ and define $V_0 \equiv I_0/g_L$ and $\tau \equiv C/g_L$.

(b) Let $I(t) = g_L V_0 \sin(\omega t)$, $V_r = \mathcal{E}_L$, $V_t = \mathcal{E}_L + \Delta V$, and define $C/g_L \equiv \tau$. Start with $V_0 = 0$ and integrate for a long enough time that the neuron equilibrates. Then increase V_0 *very* slowly compared to the time constant, τ. Show that the neuron will start spiking repetitively when $V_0 > (1 + \tau^2\omega^2)^{1/2}\Delta V$.

3. **Warmup nullclines.** Consider a model that is bound to come up again, in one form or another,

$$\tau_x\frac{dx}{dt} = -x + \tanh\big(\beta(x - y)\big)$$
$$\tau_y\frac{dy}{dt} = -y + \alpha x.$$

For all questions, assume $\alpha > 0$ and $\beta > 1$.

(a) Draw the nullclines for an α and β of your choice.

(b) What are the conditions on α and β for there to be three fixed points?

(c) Assume α and β are such that there are three fixed points. Determine the stability of each of them. Draw trajectories starting near $x = y = 0$.

(d) Assume α and β are such that there is one fixed point. Determine its stability. Draw trajectories starting near $x = y = 0$.

4. **Hodgkin-Huxley nullclines.** Consider a simplified Hodgkin-Huxley type model,

$$\begin{aligned}
\tau\frac{dV}{dt} &= -(V - \mathcal{E}_L) - hm(V)V \\
\tau_h\frac{dh}{dt} &= h_\infty(V) - h \\
m(V) &= \frac{1}{1 + \exp(-(V - V_t)/\epsilon_m)} \\
h_\infty(V) &= \frac{1}{1 + \exp(+(V - V_h)/\epsilon_h)}
\end{aligned}$$

with parameters

$$\begin{aligned}
\mathcal{E}_L &= -65 \text{ mV} \\
V_t &= -50 \text{ mV} \\
\epsilon_h &= 10 \text{ mV} \\
\epsilon_m &\ll 1 \text{ mV}\,.
\end{aligned}$$

The remaining parameter, V_h, will be specified as needed (it will take on a range of values).

(a) Sketch the nullclines in V-h space for $V_h = -60, -50$ and -40 mV. Put voltage on the x-axis and h on the y-axis. For each equilibrium, tell us whether it is stable or unstable, or hard to tell without a detailed stability analysis.

(b) Find the condition on V_h that guarantees more than one equilibrium.

(c) For a value of V_h (which you choose) such that there is more than one equilibrium, sketch the trajectories starting at V slightly greater than V_t and $h = 1$.