Assignment 1
Theoretical Neuroscience

Mandan Ahmadi (mandana@gatsby.ucl.ac.uk)

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1. **The Hodgkin-Huxley neuron**

Numerically integrate the Hodgkin-Huxley equations with matlab. Best idea is to use the Matlab `ode45` function. The equations are:

$$
\begin{aligned}
C\frac{dV}{dt} &= -\bar{g}_{Na}m^3h(V-E_{Na}) - \bar{g}_K n^4(V-E_K) - \bar{g}_L(V-E_L) + I_{stim} && (1)\\
\frac{dx}{dt} &= \alpha_x(1-x) - \beta_x x \qquad \text{where } x \text{ is } m, n \text{ or } h && (2)\\
\alpha_n(V) &= 0.01(V+55)/\left[1-\exp(-(V+55)/10)\right] && (3)\\
\beta_n(V) &= 0.125\exp(-(V+65)/80) && (4)\\
\alpha_m(V) &= 0.1(V+40)/\left[1-\exp(-(V+40)/10)\right] && (5)\\
\beta_m(V) &= 4\exp(-(V+65)/18) && (6)\\
\alpha_h(V) &= 0.07\exp(-(V+65)/20) && (7)\\
\beta_h(V) &= 1/\left[\exp(-(V+35)/10)+1\right] && (8)
\end{aligned}
$$

Let $\mathrm{C} = 1\ \mu\mathrm{F/cm^2}, \bar{\mathrm{g}}_\mathrm{L} = .003\ \mathrm{mS/mm^2}, \bar{\mathrm{g}}_\mathrm{K} = 0.36\ \mathrm{mS/mm^2}, \bar{\mathrm{g}}_\mathrm{Na} = 1.2\ \mathrm{mS/mm^2}, \mathrm{E_K} = -77\mathrm{mV}, \mathrm{E_L} = -54.387\ \mathrm{mV}$ and $\mathrm{E_{Na}} = 50\ \mathrm{mV}$. Use an integration time step of 0.1 ms.

Hint: Choose a surface area for your membrane and make sure you get all the units right. Remember, $F/S = \mathrm{Farad/Siemens} = 1$ second. You won't see any spikes unless you apply some input current (try 200 nA/mm^2).

(a) Plot a spike (V versus time). Plot the gating variables as a function of time during a spike. What happens?

(b) Plot the equilibrium value of the gating variables (e.g., m_∞) as a function of voltage.

(c) Plot the firing rate versus I_{stim}. The firing rate should suddenly jump 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 as you decrease $\bar{g}_K$?

(e) Spikes are initiated at the axon hillock, where the axon meets the soma. This is because $\bar{g}_{Na}$ is very high there. What happens as you increase $\bar{g}_{Na}$?

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: Compute the time it takes the voltage to go from V_r to V_t. The inverse of this time is the firing rate.
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) Now consider a time-varying input current $I(t)$. Show that if the neuron doesn't spike (we raise the threshold to ∞) and $V(t=0) = \mathcal{E}_L$, then

$$g_L \int_0^\infty dt\,(V(t) - \mathcal{E}_L) = \int_0^\infty dt\, I(t)\,.$$

Note that $\int_0^\infty dt\, I_0(t)$ is the total injected charge.

3. **The quadratic integrate and fire neuron**

Another popular model, the quadratic integrate and fire (QIF) neuron, obeys the equation

$$C\frac{dV}{dt} = g_L\frac{(V - V_t)(V - V_r)}{V_t - V_r} + I(t)$$

where $V_t > V_r$. Here the spike mechanism is a little different than with the LIF: a spike is emitted when $V = +\infty$, at which point the voltage is rest to $-\infty$. (Yes, the voltage does go to infinity in finite time.)

(a) Show that when $I = 0$, the voltage has fixed points at V_r and V_t. (A fixed point is a voltage at which $dV/dt = 0$.) Which one is stable and which is unstable? Why?
Hint: Consider the equation $dx/dt = f(x)$. A fixed point occurs at values of x such that $f(x) = 0$. Let x_0 be one such fixed point. To find its stability, linearize by letting $x = x_0 + \delta x$ where δx is small, plug that into the ODE, Taylor expand, and keep only the linear term. The result is $d\delta x/dt = f'(x_0)\delta x$ where a prime denotes a derivative. The sign of $f'(x_0)$ tells you about stability. In other words, it tells you whether δx decays to zero (the fixed point is stable to small perturbations) or grows exponentially (the fixed point is unstable).

(b) Let $I(t) = I_0 =$ constant. Find the range of I_0 that allows fixed points. The value of I_0 at which the fixed points disappear is called the *threshold*.

(c) For a value of I_0 that allows fixed points, linearize around the stable one and compute the time constant. How does the time constant behave near threshold? What does this mean in terms of the neurons ability to integrate small fluctuations in the input (e.g., $I(t) = I_0 + \delta I(t)$ where $\delta I(t)$ is small).
Hint: In the previous hint we had the linearized equation $d\delta x/dt = f'(x_0)\delta x$. If $f'(x_0) < 0$, then the time constant, τ is $1/[-f'(x_0)]$, because the equation can be written $\tau d\delta x/dt = -\delta x$.

(d) (Optional) Compute the firing rate as a function of I_0.

Hint #1: As usual, it simplifies your life to make a change of variables. In this case a good one is $V = (V_t + V_r)/2 + v(V_t - V_r)/2$.

Hint #2: As in the previous problem, you will want to compute the time it takes the neuron to go from reset ($V = -\infty$) to threshold ($V = +\infty$); the inverse of this is the firing rate. A couple math things you will need to know. First, suppose you have the equation $dx/dt = f(x)$. Usually we solve this for x as a function of t. However, we can write the equation $dt/dx = 1/f(x)$, and solve it for t as a function of x. This is easy, since we have only x on the right hand side,

$$t(x_b) = t(x_a) + \int_{x_a}^{x_b} \frac{dx}{f(x)},$$

which we write

$$t(x_b) - t(x_a) = \int_{x_a}^{x_b} \frac{dx}{f(x)}.$$

The left hand side, $t(x_b) - t(x_a)$, is just the time it takes for x to go from x_a to x_b. This formalism can be used to compute the period of the QIF neuron (and the LIF).

Second,

$$\int_{-\infty}^{+\infty} \frac{dx}{1 + x^2} = \pi,$$

which is easily verified by making the change of variables $x = \tan(\theta)$.