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, or if you're using Python, scipy.solve_ivp. The equations are:

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

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

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

$$\beta_n(V) = 0.125\exp(-(V+65)/80) \quad (4)$$

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

$$\beta_m(V) = 4\exp(-(V+65)/18) \quad (6)$$

$$\alpha_h(V) = 0.07\exp(-(V+65)/20) \quad (7)$$

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

   Let $C = 10\,\text{nF/mm}^2, \bar{g}_L = .003\,\text{mS/mm}^2, \bar{g}_K = 0.36\,\text{mS/mm}^2, \bar{g}_{Na} = 1.2\,\text{mS/mm}^2, E_K = -77\,\text{mV}, E_L = -54.387$ mV, and $E_{Na} = 50$ 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 $I_{stim} = 200$ 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 $\bar{g}_K$?

   (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 to the plot of firing rate versus I_{stim} 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: 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).

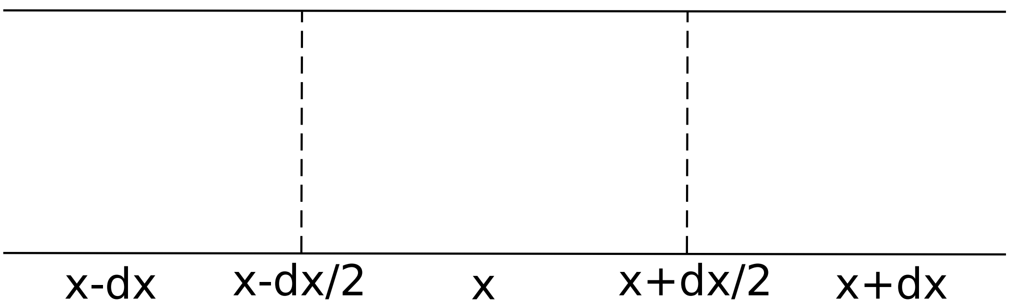
(a) Sketch the nullclines in V-h space for $V_h = -60, -50$ and -40 mV. Put voltage on the x-axis and h on the y-axis. For each equilibrium, tell us whether it is stable or unstable, or hard to tell without a detailed stability analysis.

(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 $h = 1$.

5. **The passive cable equations.**

Consider a passive cable with radius a, as shown here,



This is a bare-bones schematic; in addition to what's shown, there is an external current, $I_e(x,t)$, and a current associated with channels, $I_m(x,t)$.

We want to derive the cable equation, which we'll eventually restrict to the passive cable equation. We'll start with the equation for the membrane potential, $V(x,t)$,

$$C\,\frac{\partial V(x,t)}{\partial t} = I(x - dx/2) - I(x + dx/2) - I_m(x,t) + I_e(x,t) \tag{50j}$$

where C is the capacitance of the piece of dendrite between the dotted lines. Next is the equation for the current,

$$I(x - dx/2) = \frac{V(x - dx) - V(x)}{R} \tag{50k}$$

where R is the resistance along the dendrite, between $x - dx$ and x. A virtually identical expression holds for $I(x + dx)$. Inserting these into the equation for the voltage yields

$$C\,\frac{\partial V(x,t)}{\partial t} = \frac{V(x - dx) - 2V(x) + V(x + dx)}{R} - I_m(x,t) + I_e(x,t)\,. \tag{50l}$$

(a) Verify that when you Taylor expand the voltage terms on the right hand side to lowest non-vanishing order, this becomes

$$C\,\frac{\partial V(x,t)}{\partial t} = \frac{dx^2}{R}\,\frac{\partial^2 V(x)}{\partial x^2} - I_m(x,t) + I_e(x,t)\,. \tag{50m}$$

That's the cable equation! However, we want sensible answers in the limit $dx \to 0$. For that we need to know how C and R scale with dx.

(b) First, resistance. We may have learned in our physics class that resistance is proportional to length and inversely proportional to area – something that makes sense from $I = V/R$. It thus makes sense to define the resistitivy of a material, here denoted r_L, via $R = r_L \times \text{length/area}$. For our setup (remember that the cylinder has radius a), this means

$$R = r_L \frac{dx}{\pi a^2}\,. \tag{50n}$$

Next, the capacitance. That scales with area: the more area for a given voltage, the more the charge. Thus, it makes sense to define the specific capacitance via $C = c_m \times \text{area}$. For our setup, the relevant voltage is across the dendritic walls, so the relevant area is $2\pi a dx$. We thus have

$$C = c_m 2\pi a dx. \tag{50o}$$

Insert these into the equation for the membrane potential, and show that

$$c_m\,\frac{\partial V(x,t)}{\partial t} = \frac{a}{2r_L}\,\frac{\partial^2 V(x)}{\partial x^2} - \frac{I_m(x,t)}{2\pi a dx} + \frac{I_e(x,t)}{2\pi a dx}\,. \tag{50p}$$

(c) There's still a dependence on dx, but this time it makes sense, since we can define the current densities

$$i_m(x,t) \equiv \frac{I_m(x,t)}{2\pi a dx} \tag{50qa}$$

$$i_e(x,t) \equiv \frac{I_e(x,t)}{2\pi a dx}\,. \tag{50qb}$$

Inserting these into the above equation almost gives us the passive cable equation. The last thing we need to do is write down an expression for i_m in terms of the voltage. We could use Hodgkin-Huxley type equations, but here we'll stick to passive channels. For that we'll write, as usual,

$$I_m = \frac{V - \mathcal{E}}{R_m} \tag{50r}$$

where $\mathcal{E}$ is the reversal potential. Note that R_m is the resistance across the membrane. As usual, resitance is proportional to distance divided by area. However, we're mainly interested in the area dependence; distance is the thickness of the membrane, which is really small. We'll thus define

$$R_m = \frac{r_m}{2\pi a dx}\,. \tag{50s}$$

Here r_m depends on the membrane, but it's about the same for dendrites and neurons. Combining this with the equation for I_m, and taking into account the definition of i_m, we have

$$i_m = \frac{V - \mathcal{E}}{r_m}\,. \tag{50t}$$

Show that when you insert this into our current version of the cable equation, and multiply by r_m, you end up with the standard cable equation.