

Assignment 1

Theoretical Neuroscience [Gatsby]

TAs:

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1. Subthreshold neurons

As we saw in class, the membrane potential, V , of a totally passive neuron (with external input) obeys the equation

$$\tau \frac{dV}{dt} = -(V - \mathcal{E}_L) + V_{in}(t) \quad (1)$$

where $V_{in}(t)$ is the external input. Show that this has the solution

$$V(t) = \mathcal{E}_L + (V(t_0) - \mathcal{E}_L)e^{-(t-t_0)/\tau} + \int_{t_0}^t \frac{dt'}{\tau} e^{(t'-t)/\tau} V_{in}(t'). \quad (2)$$

Show that under the change of variables $t' = t - s$, this becomes

$$V(t) = \mathcal{E}_L + (V(t_0) - \mathcal{E}_L)e^{-(t-t_0)/\tau} + \int_0^{t-t_0} \frac{ds}{\tau} e^{-s/\tau} V_{in}(t-s). \quad (3)$$

This has an especially nice form in the limit $t_0 \rightarrow -\infty$,

$$V(t) = \mathcal{E}_L + \int_0^\infty \frac{ds}{\tau} e^{-s/\tau} V_{in}(t-s). \quad (4)$$

2. 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:

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

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

Remember to keep your units consistent. $F/S = \text{Farad/Siemens} = 1 \text{ second}$.

- Run the simulations with $I_{stim} = 200 \text{ nA/mm}^2$. Plot the membrane potential (V) and gating variables (m , h , and n) versus time.
- Write down expressions for the equilibrium values of the gating variables (m_∞ , h_∞ , and n_∞), and plot them versus voltage.
- 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 behavior. Type I behavior is when the firing rate begins at zero and increases continuously without any jumps.
- What happens to the plot of firing rate versus I_{stim} as you decrease \bar{g}_K ?
- 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} ?

3. 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).

- 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 $V_0 > (1 + \tau^2 \omega^2)^{1/2} \Delta V$.

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

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

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

- Draw the nullclines for an α and β of your choice.
- What are the conditions on α and β for there to be three fixed points?
- Assume α and β are such that there are three fixed points. Determine the stability of each of them. Draw trajectories starting near $x = y = 0$.
- Assume α and β are such that there is one fixed point. Determine its stability. Draw trajectories starting near $x = y = 0$.

5. **And more nullclines.** Assume that the x and y nullclines are given by

$$y = a_x x \quad x\text{-nullcline} \tag{7a}$$

$$y = a_y x \quad y\text{-nullcline}. \tag{7b}$$

The nullclines cross at $x = y = 0$, so that's a fixed point (the only one). Its stability depends on the dynamics. Define

$$s_x \equiv \left. \frac{dx}{dt} \right|_{x>0, y=0} \tag{8a}$$

$$s_y \equiv \left. \frac{dy}{dt} \right|_{x=0, y>0}. \tag{8b}$$

There are four main possibilities:

$$(s_x, s_y) = (\text{positive}, \text{positive}), (\text{positive}, \text{negative}), (\text{negative}, \text{positive}), (\text{negative}, \text{negative}). \tag{9}$$

For each of these, determine, if possible, the sign of the trace and determinant of the linear dynamics, and thus the number of positive and negative eigenvalues, for:

$$1. \quad a_x > 0 \quad \text{and} \quad a_y < 0 \tag{10a}$$

$$2. \quad a_x < a_y < 0 \tag{10b}$$

$$3. \quad a_y < a_x < 0. \tag{10c}$$

Note the “if possible” part – that’s because in some cases the trace and/or determinant can have either sign.

There are 12 possible cases, which seems like a lot, but you’ll quickly see patterns.

6. **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).

- 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.
- Find the condition on V_h that guarantees more than one equilibrium.
- 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 $h = 1$.

7. Green functions

Consider the equation

$$\tau \frac{\partial G(x, t)}{\partial t} = \lambda^2 \frac{\partial^2 G(x, t)}{\partial x^2} - G(x, t) + \delta(x)\delta(t) .$$

Assume $G(x, t)$ satisfies this equation. Now consider a second equation,

$$\tau \frac{\partial U(x, t)}{\partial t} = \lambda^2 \frac{\partial^2 U(x, t)}{\partial x^2} - U(x, t) + i_e(x, t)r_m .$$

Show that

$$U(x, t) = \int dx' dt' G(x - x', t - t') i_e(x', t') r_m .$$

$G(x, t)$ is known as the Green function, and it's occasionally very useful. As in the next problem.

8. Dendrites.

As you'll recall from lecture notes (see also <http://www.gatsby.ucl.ac.uk/~pel/tn/notes/biocables.pdf>), the passive cable equation is

$$\tau \frac{\partial u(x, t)}{\partial t} = \lambda^2 \frac{\partial^2 u(x, t)}{\partial x^2} - u(x, t) + i_e(x, t)r_m$$

where $u(x, t)$ is the membrane potential relative to rest, $i_e(x, t)$ is the injected current density, and r_m is the specific membrane resistance (it's proportional to actual resistance times area).

Let's assume that $i_e(x, t)$ is produced by a fast synapse – like AMPA. Because of the “fast” part, we'll approximate the current density by

$$i_e(x, t) = \alpha e^{-x^2/2d^2} \delta(t)$$

where $\delta(t)$ is the Dirac delta function. Write down an expression for $u(0, t)$.