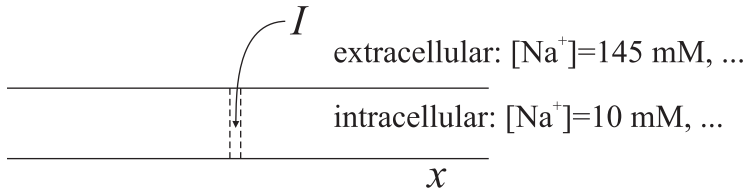
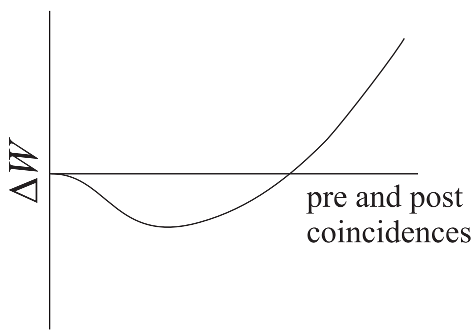
Short questions, biophysics.

1. If you double the radius of a neuron without changing the thickness of its cell membrane (or any channel densities), what happens to it's membrane time constant? Justify your answer.

2. Current is injected into a very narrow region of an infinitely long, constant diameter segment of a passive dendrite that is sitting in the standard extracellular medium (see figure below). Sketch the axial current (the current in the x-direction) and the transmembrane voltage (the voltage across the membrane, in case you don't know what "trans" means) versus x. Be careful with signs!!!



3. Consider the BCM rule in which the change in synaptic strength, W, first decreases with the number of coincident pre and postsynaptic spikes, and then increases. Explain why this rule is unstable if the threshold (the point where $\Delta W = 0$) is fixed.



4. Consider a linear differential equation of the form

$$\tau \frac{dx}{dt} = x - 2y$$
$$\tau \frac{dy}{dt} = -2x + y\,.$$

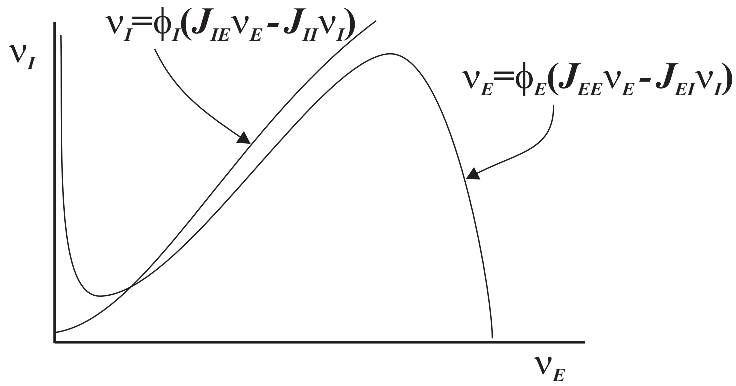
   (a) Sketch the trajectory whose initial conditions are $(x(0), y(0)) = (1, 1)$.
   (b) Sketch the trajectory whose initial conditions are $(x(0), y(0)) = (1, 0.9)$.

Short questions, networks.

1. A randomly connected network of spiking neurons is operating in the balanced and time-reversed regime, meaning it obeys the equations

$$\tau \frac{d\nu_E}{dt} = \nu_E - \phi_E(J_{EE}\nu_E - J_{EI}\nu_I)$$
$$\tau \frac{d\nu_I}{dt} = \nu_I - \phi_I(J_{IE}\nu_E - J_{II}\nu_I)\,.$$

where all the Js are positive and both ϕ_E and ϕ_I are monotonic increasing functions of their arguments. The nullclines look like:



   (a) Can the fixed point be stable?
   (b) If it can, sketch trajectories that converge to it. If it can't, sketch trajectories that wander off to ∞.

2. In a classical Hopfield network, the number of memories that can be stored in a network with N neurons is (choose one):
   (a) independent of N.
   (b) linear in N.
   (c) quadratic in N.
   (d) none of the above.

3. In the standard model of a neuron, the resting membrane potential is about 15 mV below threshold, and it takes 10s of EPSPs for the neuron to fire. Why would it be a bad idea to design a brain that contained only standard model neurons?

Long questions.

1. **Biophysics.** Consider a simplified version of the Hodgkin Huxley equations,

$$\begin{aligned} C\frac{dV}{dt} &= -g_L(V-\mathcal{E}_L) - g_0 x^n y^m (V-\mathcal{E}_{Na}) \\ \tau_x\frac{dx}{dt} &= -[x - x_\infty(V)] \\ \tau_y\frac{dy}{dt} &= -[y - y_\infty(V)]\,. \end{aligned}$$

Here C, g_L, g_0, τ_x and τ_y are constant, n and m are integers, and $\mathcal{E}_L$ and $\mathcal{E}_{Na}$ take on their usual values, -65 and 0 mV, respectively. The difference between x and y is that the former is activating ($x_\infty(V)$ is an increasing function of V) and the latter is inactivating ($y_\infty(V)$ is a decreasing function of V). As usual, both are sigmoidal. All parameters are in a biophysically reasonable range; details will be supplied below as needed.

The steady-state I-V (current-voltage) curve is found by fixing the voltage at some value and measuring the current. Given the above equations, the steady-state current, I, is given by

$$I = g(V-\mathcal{E}_L) + g_0 x_\infty^n(V) y_\infty^m(V)(V-\mathcal{E}_{Na})\,.$$

(a) Is the current in the above equation inward or outward? (3 marks)

(b) Sketch reasonable activation and inactivation curves ($x_\infty(V)$ and $y_\infty(V)$ versus V). "Reasonable" = "capable of producing an action potential." (3 marks)

(c) Plot, qualitatively, the steady-state current, I, versus V for following four cases. (12 marks)

i. $n = m = 0$

ii. $n = 0, m \neq 0$

iii. $n \neq 0, m = 0$

iv. $n \neq 0, m \neq 0$

(d) Which of these cases allow spiking, and why? (5 marks)

(e) Let $x_\infty(V)$ and $y_\infty(V)$ be very steep sigmoids versus V (e.g., $x_\infty(V) = [1 + \exp(-(V-V_0)/0.1)]^{-1}$). Assume that $x_\infty(V)$ has its sigmoid centered around -50 mV (for the above example that would mean $V_0 = -50$ mV), $y_\infty(V)$ around -40 mV, and $m = n = 1$. The voltage is raised instantaneously from rest (around -65 mV, where it has been for a long time) to -45 mV. Define $\tau = C/g_L$ (= membrane time constant). In the following conditions tell us whether or not the neuron is likely to spike, and why. (12 marks)

i. $\tau_y \ll \tau_x \sim \tau$.

ii. $\tau_x \ll \tau_y \sim \tau$.

iii. $\tau_y \ll \tau_x \ll \tau$.

iv. $\tau_x \ll \tau_y \ll \tau$.

(f) Assume you are in a regime that allows spiking. If g_0 becomes too large, the neuron can become stuck at high voltage (this is known as depolarization block). Explain how this can happen by showing that the steady-state I-V curve can have three fixed points. (5 marks)

2. **Network dynamics.** A very simplified discrete-time network evolves according to

$$x_i(t+1) = \Theta\left(\sum_{j=1}^{N} w_{ij} x_j(t) - \theta\right)$$

where w_{ij} is a random matrix whose elements are drawn *i.i.d.* from a distribution with mean zero and variance σ^2/N, θ is a constant (for now), and Θ is the Heaviside step function: $\Theta(x) = 0$ if $x \leq 0$ and 1 if $x > 0$. As usual, N is large.

(a) Let $x(t)$ be the mean firing rate of the neurons at time t: $x(t) \equiv N^{-1} \sum_i x_i(t)$. Show that $x(t)$ evolves according to

$$x(t+1) = 1 - \Phi\left(\frac{\theta}{\sigma x(t)^{1/2}}\right)$$

where Φ is of the cumulative normal function,

$$\Phi(z) \equiv \int_{-\infty}^{z} dx \, \frac{e^{-x^2/2}}{(2\pi)^{1/2}} \, .$$

Hint: The fact that x_i is only 0 or 1 should be very helpful. (10 marks)

To simplify equations, for the remainder of this question use σ=1.

(b) Solve graphically for the equilibrium value of x by plotting the right hand side of the update versus x and looking for intersection(s) with the 45° line. Show that if $\theta > 0$ there can be one, two or three equilibria while for $\theta < 0$ there is always one. (10 marks)

(c) Plot the equilibrium value(s) of x versus θ. Put θ on the y-axis and the equilibrium value(s) on the x axis. Make the range of θ large enough to capture the interesting behavior (i.e., regions in which there are one, two and three equilibria, and θ both negative and positive). Tell us which branches are stable and which are unstable. (10 marks)

(d) Let θ evolve according to

$$\theta(t+1) = \theta(t) + \epsilon(\theta_\infty(x(t)) - \theta(t)) \, .$$

Consider the regime $\epsilon \ll 1$, so that $\theta(t)$ changes very slowly. Choose the function $\theta_\infty(x)$ so that the system exhibits bursting; that is, so that x makes sudden, periodic, transitions between zero and a finite value. Indicate your choice by sketching $\theta_\infty(x)$ on the graph you made in part (c). Sketch also the trajectories on this graph. (10 marks)