HOMEWORK 2 Due Oct 5th

1. **Shunting inhibition**
Consider the passive membrane equation with a pair of exponential, conductance-based synapses:

$$\begin{aligned} C_m \frac{dV}{dt} &= -g_{CL}(V - V_{CL}) - \bar{g}_{syn,1} x_1 (V - V_{syn,1}) - \bar{g}_{syn,2} x_2 (V - V_{syn,2}), \\ \frac{dx_1}{dt} &= -\frac{x_1}{\tau_{syn}} + \delta(t - \hat{t_1}), \\ \frac{dx_2}{dt} &= -\frac{x_2}{\tau_{syn}} + \delta(t - \hat{t_2}), \end{aligned}$$

In what follows let $C_m = 1\mu F/cm^2$, $g_{CL} = 0.1 mS/cm^2$, $\tau_{syn} = 5ms$, $\bar{g}_{syn,1} = 0.005 mS/cm^2$, $\hat{t_1} = 10ms$, and $V_{CL} = -70mV$.

   (a) Ignore the second synapse by setting $\bar{g}_{syn,2} = 0 mS/cm^2$, and use the Euler code *passive.m* or the XPP code, *passive.ode* to simulate the system with initial conditions $V(0) = V_{CL}$ and $x_1(0) = 0$. Plot $V(t)$ and $x_1(t)$ for $t \in [0, 100ms]$ for the cases where 1) $V_{syn,1} = -85mV$, 2) $V_{syn,1} = 0mV$, and 3) $V_{syn,1} = -70mV$. When $V_{syn,1} = -70mV$ does the synaptic input impact the membrane potential dynamics?

   (b) Now modify the code to include include a second 'shunting' synapse with $V_{syn,2} = -70mV$, $\hat{t_2} = 10ms$, and $x_2(0) = 0$. Plot $V(t)$ for $g_{syn,2} = 0, 0.005, 0.1$, and $0.5 mS/cm^2$ (all on the same plot). Set $V_{syn,1} = 0mV$. Comment on how the activation of the shunting synapse impacts the membrane potential response to the depolarizing synapse.

   (c) Consider the limit $\tau_{syn} \to \infty$ and $t > \hat{t_1}, \hat{t_2}$. Find expressions for τ_{eff} and V_{eff} such that the membrane dynamics are represented by:

$$\tau_{eff} \frac{dV}{dt} + V - V_{eff} = 0.$$

   Let $V_{syn,1} = 0mV$. With $V_{syn,2} = -70mV$ (shunting synapse) plot $V_{eff} - V_{CL}$ for $g_{syn,1}$ ranging over $(0, 0.2)$ mS/cm^2 for fixed $g_{syn,2} = 0$ and $g_{syn,2} = 0.5$ (on the same plot). Do the same, except set $V_{syn,2} = -85mV$ (hyperpolarizing synapse). Briefly comment on the different effects of shunting vs. hyperpolarizing synapses on the rest state of the membrane potential.

2. Reproduce Figure 5.19 in Dayan & Abbott. That is simulate the effects of synaptic depression and changes in the frequency of a neuron. Do this by solving the differential equation

$$\frac{dP}{dt} = (1 - P)/\tau_D - aPr(t)$$

where $\tau_D = 500msec$, $a = 0.4$, and $r(t)$ is a series of step function changes in rates. (Note that in D&A the rates are in Hz which should be divided by 1000 to convert to rates per millisecond, the units here. Since the background rate is 25 Hz, you should use initial conditions as $P(0) = 1/(1 + 0.25\tau_D a)$. I modeled the rate as follows:

$$r(t) = r_0 + d_1 H(t - t_1) + d_2 H(t - t_2) + d_3 H(t - t_4)$$

where $H(t)$ is the Heaviside step function and d_1, d_2, d_3 are the changes in rates, e.g., $d_1 = 0.1 - 0.027$ (a change from 25 Hz to 100 Hz). In *XPP*, I wrote

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r(t)=r0+d1*heav(t-t1)+d2*heav(t-t2)+d3*heav(t-t3)
par r0=.025,d1=.075,d2=-.09,d3=.03
par t1=200,t2=500,t3=1000
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You should plot $1000r(t)P(t)$ which is the actual output of the neuron (in Hz). In *XPP*, just add the line

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aux out=1000*p*r(t)
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Since *XPP* allocates a fixed amount of storage, you should boost it and also up the bounds:

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@ maxstor=100000,bound=10000
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3. Binocular rivalry. As I mentioned in class, a standard model for binocular rivalry consists of two groups of neurons that mutually inhibit each other and which have synaptic depression. Here is a simple spiking model:

$$\begin{aligned} \tau_m \frac{dV_j}{dt} &= I - (V_j - E_L) - g s_{3-j}(V_j - E_{syn}) \\ \tau_s \frac{ds_j}{dt} &= -s_j \\ \frac{dP_j}{dt} &= (1 - P_j)/\tau_d \end{aligned}$$

where $j = 1, 2$ and we have the following reset conditions: when $V_j = V_T$, V_j is reset to E_L, $s_j = s_j + P_j$ and $P_j \to f_D P_j$ (in this order). Choose the following parameters: $E_L = -65mV$, $\tau_m = 20msec$, $\tau_s = 15msec$, $\tau_d = 500msec$, $f_D = 0.2$, $V_T = -50mV$, $E_{syn} = -85mV$. Start with unequal initial conditions, for example, $V_1 = V_2 = -65$, $s_1 = s_2 = 0$ and $P_1 = 1, P_2 = .5$ to break the obvious symmetry of the system. Apply $I = 20mV$ (not a current as we have already implicitly multiplied by R_m) and vary g_{syn} from 0 to 10 (dimensionless!). Describe what happens. In particular, you should find 3 regimes: (i) alternate single spikes for each cell; (ii) cell 1 fires a bunch of spikes, then cell 2 fires a bunch and so on; (iii) one cell shuts down and the other keeps firing. Run the simulation for 1500 msec and plot, say, s_1, s_2 If you are careful, you should be able to get, say cell 1 to fire 10 times and then cell 2 and so on.

4. Synaptically coupled integrate-and-fire neurons. Use the same equations as the previous question, but with the fiollowing changes. Instead of synaptic depression, use alpha function synapses as follows

$$\begin{aligned} \frac{ds_j}{dt} &= y_j \\ \frac{dy_j}{dt} &= -a^2 s_j - 2a y_j \end{aligned}$$

with the reset rule, that when V_j is reset, $y_j \to y_j + a\exp(1)$; here a is the reciprocal time constant for the synapse and $\exp(1) \approx 2.71828$ is the Euler constant. Choose $E_{syn} = -80, -50, 0$ mV and $g = 0.1$. Start with initial data that are not identical, e.g, $s_j = 0, y_j = 0$ and $V_1 = -60, V_2 = -65$ and choose $I = 20mV, \tau_m = 20ms, E_L = -70, V_{reset} = -80, V_{th} = -54$. Integrate the equations for 1000 msec and plot the last 100. Vary a between 1 and 0.02; look for synchrony and anti-phase behavior (offset by exactly a half cycle). In particular, show that for slow enough synapses, the neurons will synchrnonize with inhibition.

5. **HH and synaptic inputs.** There is a class of GABA-ergic neurons called the Chandelier cells that form axo-axonic synapses onto pyramidal cell neurons. The reversal potential of GABA receptors can be quite high at the axon of the pyramidal cell and much more negative on the soma and dendrites. Thus, some recent experiments have suggested that the Chandelier to pyramidal synapse might be effectively excitatory (Szabadics et al 2006, Science). They found a reversal potential of -73 mV at the dendrites and -48 mV at the axon hillock. Is this enough to elicit an action potential via stimulation? Explore this question by using the Hodgkin-Huxley equations for your axon and adding $-I_{GABA}$ to the equations where:

$$I_{GABA} = gs(V - E_{syn})$$

and

$$\frac{ds}{dt} = H(t - t_1)H(t_1 + t_d - t) - s/\tau_{syn}$$

where $H(t)$ is the Heaviside step function. Fix $\tau_{syn} = 5, 10, 15$ msec, t_d=1 msec, $t_1 = 50$ msec. Let g_{syn} vary between 0 and 1 mS/cm^2 and let V_{syn} vary between -48 and -73 mV in steps of 5 mV. For the 3 time constants and 6 values of V_{syn}, find the minimum value of g_{syn} such that the synapse will elicit an action potential sometime between 0 and 150 msec. If it never produces an action potential in that time period, say so. Plot the response of the voltage for $g_{syn} = 0.5mS/cm^2$, $\tau = 5msec$ and V_{syn} from the 6 values above. Given that the typical extracellular concentration of chloride is 110 mM in the mammalian brain, what is the intracellular concentration at 37 degrees Celsius needed to produce a -48 mV reversal potential and -73 mV reversal potential? (There seems to be a chloride gradient in pyramidal cells due to variations in the chloride pump.)