AMATH 422/522
Problem set 5

Working together is absolutely encouraged. Please do not refer to previous years' solutions.

For each problem: together with any analysis or explanations, turn in both all code and all relevant plots, labeled and with all line styles, marker sizes etc. adjusted for readability.

Please note: E+G stands for our book, by Ellner and Guckenheimer.

I **Simulating Markov chains and neural spiking.** In electrically active cells, different ion channels correspond to different membrane currents. These currents can be "inward," tending to increase the intracellular potential (such as the Na current), or "outward," tending to decrease it (such as the K current). What actually happens to this potential therefore depends on the balance between inward and outward currents.

Here, we will consider an inward current carried by an ion channel with three states: one open state, O, and two closed states, C_1 and C_2. As in the above, state C_1 cannot make a transition to state O and vice-versa. We assume that state C_2 has shorter residence times than states C_1 or O. Here is the transition matrix of a Markov chain that we will use to simulate these conditions. The state $S_1 = 1$ corresponds to C_1, $S_2 = 2$ corresponds to C_2, and $S_3 = 3$ corresponds to O:

$$\begin{pmatrix} .98 & .1 & 0 \\ .02 & .7 & .05 \\ 0 & .2 & .95 \end{pmatrix}$$

When a single inward channel is open, a current of $+1$ units flows through the channel.

We will consider an outward current that is carried by an ion channel that also has one open state, O, and two closed states, C_1 and C_2. According to the same convention, the corresponding transition matrix is:

$$\begin{pmatrix} .9 & .1 & 0 \\ .1 & .6 & .1 \\ 0 & .3 & .9 \end{pmatrix}$$

When a single outward channel is open, a current of -1 units flows through the channel.

Assume there are a total of $N_{inward} = 100$ inward channels, each evolving independently under a realization of the Markov kinetics above. If n_{inward} of these channels are in the open configuration at timestep t, then the total inward current is $+n_{inward}$.

Assume there are a total of $N_{outward} = 50$ outward channels, each evolving independently under a realization of the Markov kinetics above. If $n_{outward}$ of these channels are in the open configuration at timestep t, then the total outward current is $-n_{outward}$ units.

Thus, the net current into the cell at timestep t is $n_{inward} - n_{outward}$: the number of open inward channels minus the number of open outward channels. In our model, the cell will produce an action potential (spike) in a given timestep if this net current is greater than a threshold value T.

Assume that the channels have settled into equilibrium (i.e., that a time has passed that is large enough since a simulation was initialized). Plot the probability that the cell will produce a spike in a given timestep, as a function of the spiking threshold T. (That is, T should be on horizontal axis, and a probability on the vertical axis.) There are at least two ways of doing this: (1) by computing the equilibrium state probabilities, and simulating many coin tossings, or (2) by computing the equilibrium state probabilities, and using the form of the binomial distribution.

Repeat this for $N_{inward} = 10$, $N_{outward} = 5$ and for $N_{inward} = 1000$, $N_{outward} = 500$, and for any other combinations of values you wish. Write a few sentences reporting on any qualitative changes that you observe, using the language and concepts of signal to noise ratio. For AMATH 522, also either (a) give a formula or set of formulas which gives a clear mathematical explanation of the trends that you see, including considerations and implications of both the mean and the variance of the underlying currents, or (b) discuss their implication for the ways that neurons might be built in order to be reliable, including one reference to the literature on "ion channel noise."