MENG 21200 - Principles of Engineering Analysis II
Winter 2023

Molecular Engineering
University of Chicago

Project – Modeling Neuronal Dynamics

DATE: February 14, 2023

Guidelines:

1. You have **3 days (72 hours) to complete the project**. You may select the optimal 3 day window for your schedule between Wednesday, February 15 at midnight to Wednesday, February 22 at 11:59 pm to start and complete your project.
2. **This project should be completed independently**. You are not permitted to discuss the project with other students in the class or anyone else. The course instructor and TAs are the only people with whom you may discuss the project and seek assistance.
3. For this project, you are allowed to use the Chapra and Canale textbook, your notes from lecture, or your problem sets. In addition, you are allowed to use any code that you have written thus far for the purposes of the course.
4. You are allowed to use the materials posted on the course Canvas page.
5. You are allowed use the official Python resource pages:
   https://www.python.org/
   https://matplotlib.org/
   https://www.scipy.org/
   http://www.numpy.org/
6. **No other online resources are allowed.**
7. **Submit your solution to the project to Canvas**, **both** in the format of a single Jupyter notebook **and** PDF of that notebook.
8. The project will be graded with respect to (i) the accuracy of your solution, (ii) the methodology applied, (iii) your presentation of the results with a focus on clarity and professionalism, (iv) your creativity in developing your solution, and (v) your engineering interpretation of the results.
9. The project should be viewed as an open-ended engineering project, so you are encouraged to analyze the system more than is specifically prompted and to take the analysis and presentation of results in directions of interest to you.
10. **Any violation of these rules will be viewed as a breach of academic ethics** and subject to severe repercussions.

Score: ________________

Like any system, the brain can be analyzed on multiple levels. We can study the activity of individual neurons, the coordinated activity of neurons in a network, the activity of populations of neurons, the relations between different populations neurons, or even the relations between the activity of different brain regions.

Here, we will focus on the large-scale analysis of the activity of two populations of neurons. Neurons in the brain encode information in their firing of action potentials which are stereotyped signals consisting of a rapid (~1 ms) increase and decrease in the voltage of the neuron with an amplitude of about 100 mV. Since all action potentials are the same, most of the information is encoded in the timing and number of action potentials. A large amount of information can be obtained from the firing rate of the neurons. If we are looking at the activity of the overall population, this would be the fraction of neurons in this population that are firing at each timepoint. While averaging at this scale prevents us from looking at what single neurons are computing, this type of analysis can be useful to study the stability of neuronal dynamics, the propagation of the activity, the effect of external input, and noise-induced fluctuations -- all of which you will do here!

In 1972, UChicago math professor Jack Cowan and his postdoctoral student Hughes Wilson (who also did his Ph.D. at UChicago) developed a set of differential equations that can describe the change in the activity of connected populations of neurons which propelled a series of discoveries and developments in the field of computational and theoretical neuroscience. If we have a network consisting of two populations of neurons in which one is excitatory (makes the target more likely to fire action potential) and one is inhibitory (makes the target less likely to fire action potential), the model can be written as follows:

$$\begin{cases} \tau \dfrac{dE}{dt} = -E(t) + \big(1 - r \cdot E(t)\big) \cdot f_E[W_{E\leftarrow E} \cdot E - W_{E\leftarrow I} \cdot I + h_E(t) + n_E] & (1) \\ \tau \dfrac{dI}{dt} = -I(t) + \big(1 - r \cdot I(t)\big) \cdot f_I[W_{I\leftarrow E} \cdot E - W_{I\leftarrow I} \cdot I + h_I(t) + n_I] & (2) \end{cases}$$

where:

- $E(t)$ and $I(t)$ are the fractions of neurons active as a function of time in the excitatory and inhibitory populations, respectively.
- $W_{X\leftarrow Y}$ is the weight of the connections from neurons in population Y to neurons in population X.
- h_X is the external input to population X.
- n_X is noise to population X.
- f_Y is the "activation function" which is a sigmoidal function of the type: $f_Y[x] = \frac{1}{1+\exp[-a_Y(x-\theta_Y)]} - \frac{1}{1+\exp\,(a_Y\theta_Y)}$ with a_Y and θ_Y being parameters defining its shape.
- The first term accounts for the decay in the activity of the population in the absence of any input.

- The second term accounts for the effect of input to the neurons from neurons in the E population, I population, the external input, and the noise. It is multiplied by $(1 - rE)$ or $(1 - rI)$ to account for the time following their activity in which the neurons cannot fire.

Based on this model for neuronal dynamics, address the following questions:

(a) Determine the meaning of the parameters (a_Y and θ_Y) in the activation function. In addition, what is the purpose of the second term $\left(\frac{1}{1+\exp{(a_Y \theta_Y)}}\right)$ in the activation function?

(b) Model the evolution of $E(t)$ and $I(t)$ during 200 ms using:

(i) The parameters:

$$a_E = 1.2;\ \theta_E = 2.8;\ a_I = 1;\ \theta_I = 4;\ \tau = 3\text{ ms};\ r = 1$$
$$W_{E\leftarrow E} = 12\ W_{E\leftarrow I} = 4;\ W_{I\leftarrow E} = 13;\ W_{I\leftarrow I} = 11$$
$$h_E = 0;\ h_I = 0; n_E = 0; n_I = 0$$

With the initial conditions:

- $E(0) = 0.3$ and $I(0) = 0.2$
- $E(0) = 0.2$ and $I(0) = 0.2$

(ii) The parameters:

$$a_E = 1.3;\ \theta_E = 4;\ a_I = 2;\ \theta_I = 3.7;\ \tau = 8\text{ ms};\ r = 1$$
$$W_{E\leftarrow E} = 16;\ W_{E\leftarrow I} = 12;\ W_{I\leftarrow E} = 15;\ W_{I\leftarrow I} = 3$$
$$h_E = 1.25;\ h_I = 0;\ n_E = 0;\ n_I = 0$$

With the initial conditions: $E(0) = 0$ and $I(0) = 0$

How is the activity evolving in each of these cases, and what is your interpretation of the behavior of the neuronal networks? If it reaches steady-state, what is the value of E and I at steady-state?

(c) The evolution of the state of each neuronal population can be understood by examining the phase space which is a representation of all the possible states in the system. In this case, the phase space covers all the different combinations of E and I.

(i) The switch from one state to the next is determined by the system of ODEs provided. Using the set of parameters from part (b)(i), make a quiver plot to show the direction in which E and I change for each combination of E and I parameters.

(ii) You should be able to see the vectors converging to certain points in the phase space and diverging from others. At these points the magnitude of the vectors should be approaching zero which means that these are fixed points, *i.e.*, if the system is in one of these steady-states, it will stay in it in the absence of any fluctuations. Consequently, we can determine these fixed points by looking at when dE/dt and dI/dt are both zero. Plot the curves corresponding to each of these conditions on top of the quiver plot.

Note: For each equation, you will need to set the value of either E or I and calculate the corresponding value of the other neuron activity. When doing so, let the value that you set be less than or equal to 0.49.

Bonus: Determine the reason behind the maximum value we provided and add a step to your code that determines the maximum value that can be used for any set of parameters.

(iii) Overlay the trajectory the system follows starting from each of the initial conditions from part (b)(i) on the plot.

(iv) Determine the values of E and I at each of the fixed points. Which ones are stable, and which are unstable fixed points?

(v) **Bonus:** Create a colorized contour plot of the phase space of the <u>initial</u> E and I values that visualizes the fixed point to which the neuron activity will converge.

(d) Repeat parts (c)(i) through (c)(iv) for the parameters and initial conditions from part (b)(ii). Discuss and interpret your observations.

(e) All the prior simulations have been performed in the absence of any random noise, so the system evolves in a deterministic manner starting from any point in the phase space. However, the trajectory could vary significantly between trials if we add some noise.

(i) Model the evolution of $E(t)$ and $I(t)$ during 200 ms using the parameters from part (b)(i) but allowing n_E and n_I be values sampled from a standard normal distribution at each timepoint. Recall that a standard normal distribution is centered at 0 (*i.e.*, has a mean of 0) and has a standard deviation of 1. Start with $E(0) = 0$ and $I(0) = 0$.

In the absence of noise, how would you expect this model to behave? Why? How are the dynamics of the network different in this case? Does the behavior of the network vary between runs?

Note: You may find the `numpy.random` library to be valuable for sampling from a normal distribution.

(ii) Perform the same analysis as in part (e)(i) but using $E(0) = 0.1$ and $I(0) = 0.1$.

(iii) In the absence of noise, the initial condition in part (e)(ii) results in the system converging to the (0, 0) fixed point. However, you should be observing an initial decrease in activity as if it was converging to (0, 0) followed by a sudden increase to a different state. Is it converging to a specific state? If yes, which one?

We are interested in how the behavior of the network varies between simulations due to the stochasticity introduced by the random noise. There are two important points in the dynamics observed: first, when the network activity changes from a noisy decreasing trend to a noisy increasing behavior, and second, when the network activity increases at its highest rate.

By running many simulations using the same parameters and initial conditions, and using noise values at each time step sampled randomly from a standard normal distribution:

(iv) Estimate the distribution of the times at which each of the two critical points are reached. Comment on the shape of the distributions and how they relate to each other.

(v) Overlay on the phase space diagram the positions at which these critical points occur from all the simulations. Could you have predicted the positions of either set of points?

(vi) What do you expect would happen if the noise was sampled from a normal distribution with a smaller standard deviation (*e.g.*, 0.9)? Prove it and explain how your observations support your expectation.