Problem Set I

Due Wednesday, Oct 13, 2021

Note on the Homework

Please read how to submit a homework in our github page. Please choose to solve 3 out of the following 5 problems. People who work out extra problems will have extra credits that will be weighted in the final score of the course.

How Granule Cells Sample Inputs

We have discussed about the synaptic organization of the cerebellum. Mossy fibers, which are long range projections from various brain regions, make connections with granule cells, the most numerous ($\sim 10^{11}$) neurons in the whole brain. These granule cells have a very small convergence: each of which only receives inputs from a handful mossy fibers. The outputs of granule cells, called parallel fibers, travel along the cerebellar cortex for a few millimeters and synapse onto Purkinje dendrites. Purkinje cells have the highest convergence in the brain, each of which receives inputs from more than 10^5 synapses from parallel fibers. The granule-to-Purkinje projections are what we called in the class "Connecting dense array to sparse array with extreme convergence and divergence".

Why do we need so many granule cells? What can we say about the number of granule cells N, the number of mossy fiber inputs M, and the convergence of a granule cell K? Perhaps each granule cell is sampling a different combination of mossy fiber inputs. The higher the functional diversity, the more powerful computation downstream circuits (e.g., Purkinje dendrites) could perform, such as classification.

Assume each granule cell can choose K inputs out of all M mossy fibers, the number of possibilities is simply a binomial coefficient $\binom{M}{K}$. Now we ask the following questions.

- What is the probability p that granule cells all receive different combinations of inputs?
- For given N and M, plot p as a function of K, and show when p reaches its maximum.

- Using $N = 21000$, $M = 7000$, compute K when p approaches 95 percent of its maximum.
- Discuss whether it is beneficial to have small K when M is very large.

Quantitative Analysis of Dendritic Morphology

Attached you will find morphology data txt files (.swc) of one pyramidal dendrite, one Purkinjie dendrite, and one arbor from larval zebrafish. Use MATLAB or Python to write a simple program:

- Load the data file.
- Plot and visualize the neuronal 3D arbor shape.
- write a function to compute the mean path length form a dendritic segment to the soma
- Compute the spine reach zone area of the Purkinje dendrite, namely the gray area that can be reached by growing a spine on a dendrite (slide 46), assuming the spine length $s = 2\ \mu m$. And compare the total spine reach zone area with the arbor area, which may be defined as the convex hull area that embed the 2D arbor. For 3D pyramidal dendrites, choose a random 2D projection of the 3D morphology. Perform the same analysis.

In the swc file, each column has the following meaning (from left to right): segment index, segment type (cell body =1, dendrite = 3), x coordinate (μm), y coordinate (μm), z coordinate (μm), segment diameter (μm), father segment index (root index = -1).

Derivation of the Goldman-Hodgkin-Katz formula for membrane potential

The reversal potential we discussed in the class only take into account one type of ion. However, some channels are not quite selective, and we need to combine the current flow from multiple ions, and the result is the Goldman-Hodgkin-Katz formula for membrane potential. I will write down the equation here, and it is your homework to provide the derivation of this formula.

$$V_m = \frac{k_B T}{e} \ln \left(\frac{\sum_{i=1}^{N} P_{M_i^+} [M_i^+]_{out} + \sum_{j=1}^{N} P_{A_j^-} [A_j^-]_{in}}{\sum_{i=1}^{N} P_{M_i^+} [M_i^+]_{in} + \sum_{j=1}^{N} P_{A_j^-} [A_j^-]_{out}} \right). \qquad (1)$$

Here P denotes the permeability of a given ion.

Motif Analysis of C. elegans Connectome

Attached you will find the Adjacency Matrix of the *C. elegans* connectome, namely the the connectivity patterns of ~ 277 neurons in the worm can be represented by a matrix, in which $A[i, j]$ represents the number of connections from neuron i to neuron j (or from neuron j to i, depending on the convention). This matrix is asymmetric for a directed graph. Now use the software mfinder, also attached in the folder, to find 2 node and 3 node motifs. Present your results just like what we did in the lecture (slide 19), and show which motifs are overrepresented as compared to a random graph. There are detailed instruction on how to use the mfinder software, and make sure you understand what your are doing.

Integrate and Fire Neuron

An integrate and fire neuron has a subthreshold membrane potential that obeys the equation

$$C\frac{dV}{dt} = -\frac{V}{R} + I(t) \tag{2}$$

Once the voltage crosses threshold, the neuron fires a spike and V is reset to 0, as discussed in the class.

Consider the input current

$$I(t) = Q \sum_{k=-\infty}^{\infty} \delta(t - kT) \tag{3}$$

where a charge Q crosses the membrane periodically, and $\delta(x)$ is the Dirac delta function.

- Derive the subthreshold membrane potential as a function of time for this input current. Describe the transient and steady state behavior of the potential. Illustrate the result by qualitative or (even better) numerically quantitative graphs.
- Under what conditions will the neuron fire spikes? Compute the firing frequency of the neuron when the conditions for firing are met. Plot the firing frequency as a function of the interesting variables and explain.