Lab #2 (Changing cell voltage *quickly*)

How to work as a group

This lab involves three parts – coding/simulating, thinking about the questions, and writing a report. You only need to turn in one report per group.

The goal of having only one written report per group is to save you time in writing and save me time in reading. However, my expectation is that everyone in the group runs the simulations and discusses the questions together. The goal is *not* to have only one person learn the material 😊.

Overview

In this lab, we'll use BITSEY to run more simulations of single cells. This time, our goal will be to understand the short-term effects of how cell voltages change quickly in QSS.

You can use the same BITSEY files as last week. This time, we'll be using the main file main_vlab2_QSS.py, and modifying the *setup_lab2*() and *setup_lab2b*() functions. You will notice that *setup_lab2*() is quite similar to *setup_lab1*(). How, then, is lab #2 different from lab #1?

In lab #1, we let the simulations run for many hours of simulated time. You probably saw that the V_{mem} waveforms started at roughly 0 volts, then quickly "settled" to a value in less than a second of simulated time, and then moved slowly (over tens of hours of simulated time) to their final values. In lab #2, we only care about those quickly-"settled" values – i.e., quasi steady state. Thus, all of our simulations will be just two seconds of simulated time. The nice thing about simulating in quasi steady state is that the simulations are all short 😊. This type of computation is how our neurons (and hence our brains) work.

Instructions

There are two changes for lab #2 vs. lab #1. First, we will run the simulations for only 2 seconds rather than the 100K seconds we used for lab #1 – so *python3 main_vlab2_QSS.py lab2 2*. Second, *setup_lab2*() uses more stable (but much slower) numerical-integration algorithms (*p.adaptive_timestep = False*). Don't worry – the runs will still be fast.

You will run two simulations for this lab. The first simulation run is to simply run *setup_lab2*() and save the graph of per-cell V_{mem}. This simulation has 4 cells, each with its own set of ion-channel conductivity values. Each cell should quickly move to its own QSS V_{mem} value. This shows how a neuron will work; changes in G_{Na} or G_K quickly move V_{mem} in QSS.

After you do that, you have one more simulation to run. *Setup_lab2b*() has four cells, all with the same ion-channel conductivity values as *setup_lab2*'s cell #2. However, each cell has a slightly different initial $[Na]_{int}$, resulting in a slightly different initial V_{mem}. We would like to see if negative feedback makes QSS behavior resilient to small changes in a cell's initial ion concentrations. *Setup_lab2b*() is partially written, and you will fill it in:

- Create 4 cells as usual, just as in *setup_lab2*().
- All four cells should have the ion-channel diffusion constants from cell #2 of the first simulation – so a potassium diffusion constant of 10.0e-18 (i.e., *Dm_array*[*K*,:]= 10.0e-

18), with the other ions remaining at their defaults. In *setup_lab2*(), this should have resulted in quasi-steady-state V_{mem}≈-57mV.

- Perturb the cells' initial [Na] *very slightly* as follows. Cell #0 gets its [Na] reduced by .025 moles/m^3, #1 by .020, #2 by .015 and #3 by .010 moles/m^3. This should be just enough so that each cell has its time=0 V_{mem} about 15mV higher than the previous cell (unlike lab #1, you will not compensate by changing another ion to restore charge neutrality). If you accidentally change the initial [Na] too much (and thus change the initial V_{mem} by more than about 0.5V), the simulator will not allow the simulation to run!

What happens as a result? The cells now have a different initial charge, and in fact no longer start out charge neutral. Their V_{mem} at time=0 will, therefore, now be nonzero (and in fact different in each cell). But does this affect the results at t=2 seconds? Turn in the graph of V_{mem} for both *setup_lab2*() and *setup_lab2b*().

Questions

Please answer the following questions:

1. Just as with lab #1, you can look at the data printed by *dump*() at the end of the simulation. In lab #1, we saw that for each individual ion, its flow through the pumps was equal and opposite to its flow through the ion channels. Is that still true for *setup_2*()? If not (and in fact it should not be), what claim can we make instead – that shows the system has reached quasi steady state? Back up this claim with simulation data.
2. Try to compute how quickly V_{mem} changes in theory and see how well it matches the simulation. Look at cell #0 at t=0.05 seconds for *setup_2*(). The simulation should have printed out the net ion flux into the cell in moles/(m^3·s). Based on this flux, compute the current into the cell. Then, using the cell-membrane capacitance and Q=CV, compute dV_{mem}/dt. Read the value of dV_{mem}/dt from the V_{mem} graph for cell #0 at t=0.05 seconds and see how closely it matches your computation. Hopefully you got a nice fast number! You will need to know the cell radius, the cell "patch capacitance" (i.e., the membrane capacitance in Farads/m^2) and the Faraday constant (which is the number of Coulombs per mole of a valence-1 ion). All of these constants are in **sim.py**.
3. In order to change V_{mem} by 100mV by moving, say, Na into the cell, how many moles of Na must move? More importantly, what fraction of the total Na in the cell is that? Does this help to explain why QSS voltage changes can happen so fast?
4. In the modified run, hopefully all four cells quickly moved to the same QSS V_{mem} – i.e., they were completely resilient to small changes in initial charge (and hence changes in initial V_{mem}). Can you explain why? Use our equivalent-circuit model (which predicts the QSS V_{mem}), and talk about which of the circuit parameters in the model (if any) were substantially changed by our small additions of charge.

What to turn in:

You should turn in two files: your main_vlab2_QSS.py and a report with the two V_{mem} graphs and the answers to the questions.

Summary of what we learned from this lab

Hopefully a few lessons come from this lab:

- QSS occurs when the *net* charge flux into a cell is zero (even though *individual* ions may still be entering or exiting the cell).
- QSS happens *fast*.
- QSS is quite robust to small random changes in ion concentrations.