Lab #5 (Building a planaria)

In this lab, we will build a planaria (a type of flatworm). Well, it won't really have all the various worm body parts – but it will have a head-to-tail axis with coordinates, that the worm can hopefully use to decide where to put its body parts.

The worm uses the function *setup_lab_worm*(). In the interest of making schedules reasonable, we've actually provided the entire function for you. All you need to do is understand it, run it (modifying parameters when needed), and – most importantly – make sense of the results. The reason for doing it this way is to leave more time for final projects.

- The worm is an array of 5 cells, connected as a straight line of cells. I.e., each cell is connected by a gap junction to its two neighbors (one ahead of it and one behind). The head and tail cells only have one neighbor. None of the GJs should have any gating function; all should have scale=0.1.
- Getting these worms to work (i.e., to generate a substantial ΔV from head to tail rather than collapsing to all cells having the same V_{mem}) is surprisingly difficult. We have thus taken a set of parameters (initial ion concentrations, diffusion constants, etc.) from Alexis that are known to work.
- Initial ion concentrations are thus a bit different than before:
    - The initial [Na], [K] and [Cl] in both the ICF and ECF are both specifically set
    - There is also a negatively-charged protein *P* that does not move through ion channels or GJs; this is what the slides call a negatively-charged fixed macromolecule.
    - The code also sets up a "mystery" ion *M* that establishes a gradient. There is initially more *M* in the head than the tail (since a higher V_{mem} in the head will attract more *M*). *This is what should kick off the positive-feedback process*. The code also sets up more Na in the tail than the head, so as to preserve charge neutrality.
- The head and tail cells have ligand-gated K channels that provide positive feedback:
    - They are based on a Hill inverter: a lower [*M*] in the cell (the buffer input) drives a higher G_K (the buffer output). The higher G_K drives the cell's V_{mem} more negative (since $V_{Nernst,K}$ is negative), which in turn further lowers [*M*] and so on.
    - You will vary the Hill-inverter parameters to see how that affects the worm.
- In this simple worm, the body cells do not have any ion channels at all. A real worm would likely be more complex – it would have the usual ion channels everywhere.

When your worm is set up, run the simulation for 50K seconds and watch how it evolves. Plot [*M*] and V_{mem} for the worm cells. What happens? Does the worm develop a substantial voltage gradient along its body? Does it similarly develop a substantial gradient of [*M*]?

Next, experiment with different parameter values for a total of three runs:

- Lower Hill-model gain: change *N* from 10 to 2 (while keeping *scale*=.1 and k_M=1)
- Finally, change to k_M=0.2 and *N*=5 (again keeping *scale*=.1).

For each one, perform the same simulation and plot the same results as above.

To turn in:

- Your main.py
- Graphs of [*M*] and V_{mem} vs. time for all five cells and all of the three parameter sets.

Also answer the following questions:

- Reducing the value of *N* tended to make the worm less likely to establish a gradient, and instead make it more likely for the [*M*] and V_{mem} to collapse to constant values all along the worm. Why might that be?
- What results do you see for the third set of parameters? The graph will likely only show three traces, because some of the traces will overlap each other. It might thus help to look at the V_m printed by *edb.dump*() as well. Have we succeeded at building a two-headed worm? If you have some computer time to burn, you might try running the simulation out to *t*=750K or so, to see if the unusual behavior persists. Do you believe that a true two-headed worm is feasible with a worm that has feedback only in its head and tail?
- Intuitively, do you think that increasing *GJ_scale* would make it more or less likely for the worm to develop a gradient? Why? Feel free to run a simulation or two to check your theory. You might change our first run to *scale*=1, or to *scale*=.01 and see what effect that has.

This simulation is your final lab on bioelectricity. However, there are several final-project choices that let you experiment further with planaria. We'll talk about them more in class.