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| Experiment | Setup | Conclusion |
| A | **Small scale Non-isopotential neuron** | |
| Experiment-A1 | 3 compartments – fluxing impermeants **(z=-1)** at a rate of **0.2mM/min**   * Observed slight non-isopotential effect, final z =-0.8506 | Achieved non-isopotential middle compartment but with slow rate and in dynamic fashion |
| Experiment-A2 | 3 compartments – fluxing impermeants **(z=-1)** at a rate of **0.5 mM/min**   * Increased effect, final z = -0.8515 | Achieved non-isopotential middle compartment but with slow rate and in dynamic fashion |
| Experiment-A3 | 3 compartments – fluxing impermeants **(z=-1)** at a rate of **4 mM/min**   * Increased effect, final z= -0.866 | Achieved non-isopotential middle compartment but with slow rate and in dynamic fashion |
| Experiment-A4 | 3 compartments – fluxing impermeants **(z=-2)** at a rate of **10 mM/min**   * Dramatically increased effect, final z =-1.2 | Achieved non-isopotential middle compartment but with slow rate and in dynamic fashion |
| Experiment-A5 | 3 compartments – fluxing impermeants **(z=-2)** at a rate of **10 mM/min** with **ATPase constant**   * Similar effect with constant ATPase and constant Area Scale, perhaps just getting to a steady state quicker. | Achieved non-isopotential middle compartment but with slow rate and in dynamic fashion |
| Experiment-A4-2 | Same as A4 just with longer time frame to try get an equilibrium | Achieved non-isopotential middle compartment but with slow rate and in dynamic fashion |
| Experiment-A5-2 | Same as A5 just with variable Area Scale | Achieved non-isopotential middle compartment but with slow rate and in dynamic fashion |
| B | **10 compartment non-isopotential neuron** | |
| Experiment-B1 | 9 Comp + Soma model, fluxing impermeants in comp 3 and 7  Useful in that I found several errors which were corrected. | Poor experiment, too many changes to know what was going on. |
| Experiment-B2 | 10 Comp model, fluxing impermeants in comp 2 | Unexpected changes occurring in final compartment  Possibly due to an error in the electrodiffusion calculations as I was using concentrations rather than moles to transfer ion |
| Experiment-B3 | Made changes to the electrodiffusion order and made use of moles as opposed to concentrations. | Success in replicating figure 8C, but with only 4 compartments |
| Experiment-B4 | Confirming the results of experiment B3 just with 8 compartments instead of 4 | Successfully extrapolated to 8 compartments.  Not quite at steady state, but clearly show the non-isopotential multicompartmental model with constant Cl driving force |
| C | **Testing synapse code** |  |
| Experiment-C1 | * Sanity check for inhibitory input – ensure spike occurs appropriately. * Correct spike dynamics   Ions not yet at steady state by end of Sim | Happy with the dynamic of the synapse.  My chloride driving force ends up at -11.22 mV, Kira’s is -11.25 mV.  Encouraged that the ions converge but not quite at a steady state by the end of the sim |
| Experiment-C2 | * Same setup as Experiment C1 just for a longer run time. * Correct spike dynamics | Still not perfectly at steady state, will need to run the Sim significantly longer.  Because the actual values of the ions converge in every compartment, I’m confident it will function as the previous multicompartment simulation with identical compartments |
| D | **Formal multicompartment non-isopotential neuron** |  |
| Experiment-D1 | Multicompartment model with multiple anion fluxes 🡪 proving that the model can be non-isopotential with a fixed chloride driving force | Fluxing impermeant anions (**ATPase constant**) results in a non-isopotential neuron with a fixed cl driving force |
| Experiment-D2 | add [X] to compartment 4 and 8, with no z changes | Changing just impermeant anion concentration does not result in a non-isopotential neuron.  Not at a steady state |
| Experiment-D3 | Same as D1 just with ATPase static | ATPase being on or off does not change the dynamic. |
| Experiment-D4 | Same as D1 just longer experiment and static ATPase | Successful but complicated to understand because of the multiple fluxes |
| Experiment-D5 | Same as D4 just with z flux in compartment 8 only and allowed to run for a long time | Successful! Likely Figure 2A |
| Experiment-D6 | Same as D5 just with no x flux, only z decreases and increased effect.  Z: -0.85 🡪 -1.2 | Success, managed to get a voltage drop of +- 4mv in affected compartment |
| Experiment-D7 | Same as D5 just with no x flux, only z increase and increased effect.  Z: -0.85 🡪 -0.5 | Strange result. STORM crashed at 87% completion but still good enough to understand effect.  Voltage increase by 8mV and there is a small chloride driving force difference of 0.08mV |
| Experiment-D8 | Same as D7 just with no x flux, only z increase and increased effect.  Z: -0.85 🡪 -0.1 | Running on beast. There is a significant exponential effect to this.  Final voltage increase by +- 27mV and decrease in driving force by 3.5mV.  Still not too sure what is the mechanism here. |
| Experiment-D9 | Same as D7 just with no x flux, only z decreases and increased effect.  Z: -0.85 🡪 -1.6 | Complete |
| Experiment-D10 | Same as D7 just with no x flux, only z increase and increased effect.  Z: -0.85 🡪 -1.25 | Complete but electrodiffusion was not correct so need to re-do |
| Experiment-D11-V2 | Same as D10 but with Area Scale off | Complete but electrodiffusion was not setup correctly so need to rerun |
| Experiment – D10-V2 | Same as D10 with z=-1.25 but with no soma (just 9 compartments), area scale on, for 420s | Complete |
| Experiment-D11-V3 | Same as D10-V2 but with Area Scale off | Complete 🡪 FIGURE 2 |
| Experiment-D12 | Same as D10 but with z = -0.65 | Complete 🡪 FIGURE 3 |
| Experiment-D13 | Same as D12 but with z = -0.45 | Complete 🡪 FIGURE 3 |
| Experiment-D14 | Same as D12 but with z = -1.05 | Complete 🡪 FIGURE 3 |
| Experiment-D15 | Same as D10 but with Area Scale AND ED OFF | Complete |
| Experiment -D16 | Just a default run with z = -0.85 to get a baseline experiment with 9 comps | Complete 🡪 FIGURE 3 |
| E | **Optimal simulation settings for synapse experiments** |  |
| E1-2 | Assess the basic synapse functionality, and experiment design. | Need to start the synapse a bit later (more time to get to steady state)  Possibly start at 2 seconds  More time at the end to assess steady state.  Possibly run for 10 seconds instead of 5.  Could consider fewer compartments for faster runtime  Achieved a -0.6mV drop here with a NT conc of 1mMol  Consider multiplying NT concentration by 4 to increase the effect |
| E1-3 | Assessing the changes to the inhibitory synapse from E1-2 | Need to delay synapse and start the simulation at values that are closer to the steady state values, especially in the soma.  Increasing the NT concentration made the spike smaller. Only a 0.22mV drop  It might be possible that the interval timing is not capturing the peak of the synapse because the synapse only lasts for 2 ms.  Definitely need to increase the simulation time to get to a steady state.. possibly to 30 seconds. |
| E1-4 | Apply changes from E1-3 🡪Get default inhibitory synapse parameters and setup | Increasing the NT concentration made the spike smaller (only 0.001 mM change) in the chloride concentration  Still not starting the experiment at the ideal steady state |
| F | **Baseline experiments for first figures** |  |
| Experiment-F1 | Increasing impermeant concentration only in compartment 4 | Change to cell volume. No change in Vm. No changes to driving force |
| Experiment-F2 | Decreasing impermeant concentration only in compartment 4 | In progress on STORM 🡪 crashed.  No changes to driving force |
| Experiment-F4 | Completely default Sim with impermeants at -0.85 and all default concentrations | Complete |
| Experiment-F5 | Increasing X at rate of 30mM/min with Ar off. | Complete |
| Experiment-F6v4 | Same as F5 but just an increase of 100mM/min. | Complete 🡪 FIGURE 1 |
| G | **Inhibitory synapses on various z values** |  |
| Experiment-G1 | Synapse onto Comp8, z = -1.2 (ExpD6) | Time and length constants calculated |
| Experiment-G2 | Synapse onto Comp8, z = -0.1 (ExpD8) | Time and length constants calculated |
| Experiment-G3 | Synapse onto Comp8, z = -1.2 (ExpD6) | Time and length constants calculated |
| Experiment-G4 | Synapse onto Comp8, z = -0.1 (ExpD8) | Time and length constants calculated |
| H | **Inhibitory current injection on various z values** |  |
| Experiment-H1 | 5mA current onto Comp8 for 1s, z = -1.25 (ExpD10-V2) | Running on Laptop |
| Experiment-H2 | 5mA current onto Comp8 in experiment D16 (z=-0.85) |  |
| I | **Single dendrite with multiple impermeant anions** |  |
| Experiment-I1 | Comp 2 with z=-1.25 and comp 8 with z=-0.45 and all other compartments with normal z = 0.85. Ar Off. ED On. ATPase constant. dt = 10-6 . Total time 420 s (7mins), fluxing between 120-180s | For figure 3C |
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