|  |  |
| --- | --- |
| Sanity check | 3 compartments – changing z in all. Variable ATPase   * Permanent change in Vm in all compartments * All dynamics act as expected |
| Sanity check | 3 compartments – changing z in all. Constant ATPase.   * Dynamics not playing out as expected. Sodium concentrations dropping too quickly. |
| Fix | Changed the way in which the constant ATPase rate is calculated. Now identical to the beginning of the simulation, rather than to a rate just before the drop. |
| Sanity check | 3 compartments – changing z in all. Constant ATPase.   * Dynamics corrected. * Model behaving similarly to Kira’s 6C |
| Sanity check | 3 compartments – changing z in middle. Dynamic ATPase   * Voltage higher in middle comp and lower in neighbours. * Dynamic not expected. |
|  |  |
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Report

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| --- | --- |
| Aim | Sanity check 1.  3 compartments, changing z in all. Jp variable. (Will repeat below with Jp Constant)  Expect it to behave as the single compartment (i.e. Kira 6A)  A picture containing chart  Description automatically generated |
| Setup | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3  Radius 5.000000e-05 5.000000e-05 5.000000e-05  Length 2.500000e-04 2.500000e-04 2.500000e-04  Volume 1.963495e-12 1.963495e-12 1.963495e-12  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 30.0  Timestep (ms): 1.0  ATPase Model type: J\_ATP = p \* (Na\_in/Na\_out)^3  Pump rate: 0.1  Area scale type: Constant  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  No change of intracellular impermeant anion concentration mid simulation  All compartments : change in intracellular impermeant anion charge - valence: -1.0, between: 400.0s and 1000.0s  No change of extracellular impermeant anion concentration mid simulation |
| Final values: | Graphical user interface, table  Description automatically generated  Cl driving force: 11.42mV |
|  | Chart  Description automatically generated |
|  | Graphical user interface  Description automatically generated with low confidence |
|  | A picture containing table  Description automatically generated |
|  | Chart, line chart  Description automatically generated |
| Boundary: | Timeline  Description automatically generated |
| Conclusion: | * Voltage in all compartments drop, as it does in Kira’s * Minimal, but certain change in driving force * Slight increase in sodium concentration * Change to concentration of impermeants follows the change of charge * All compartments at steady state * **Model behaving as expected. Next step to do the same but with constant ATPase** |
| Aim | Sanity check  Repeat the experiment above.  I found that my constant ATPase rate was possibly too fast and now I have changed it to be the ATPase rate at the beginning of the Sim (like Kira’s)  I expect to see the leak channel letting more sodium in +- 3mM when ATPase is constant.  3 comps.  Drop in z from -0.85 to -1.0 in all comps.  Constant ATPase. Constant Area scale.  A picture containing chart  Description automatically generated |
| Setup: | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3  Radius 5.000000e-05 5.000000e-05 5.000000e-05  Length 2.500000e-04 2.500000e-04 2.500000e-04  Volume 1.963495e-12 1.963495e-12 1.963495e-12  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 30.0  Timestep (ms): 1.0  ATPase Model type: Constant  Pump rate: 0.1  Area scale type: Constant  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  No change of intracellular impermeant anion concentration mid simulation  All compartments : change in intracellular impermeant anion charge - valence: -1.0, between: 600.0s and 1200.0s  No change of extracellular impermeant anion concentration mid simulation |
|  | Graphical user interface, application, table, Excel  Description automatically generated |
|  | Chart, line chart  Description automatically generated |
|  | A picture containing chart  Description automatically generateddriving force = 11.14mV |
|  | Chart, line chart  Description automatically generated |
| Na channel activation | A picture containing table  Description automatically generated |
|  | Chart, line chart  Description automatically generated |
| Boundary | Timeline  Description automatically generated with medium confidence |
| Conclusion: | * Sodium is increasing and therefore the Vm drops as expected when z is dropped. * This matches what is shown by Kira * Driving force changes are also observed * Very close to an equilibrium being reached |

|  |  |
| --- | --- |
| Aim: | With the constant ATPase rate now fixed I want to understand what would happen if I had 3 compartments and dropped impermeants in just the middle compartment.  I would expect that the variable ATPase rate is crucial in allowing a non-isopotential dendrite to develop.  By keeping the ATPase fixed I am not too sure what will happen. I am sceptical that the system will reach a steady state. |
| Setup: | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3  Radius 5.000000e-05 5.000000e-05 5.000000e-05  Length 2.500000e-04 2.500000e-04 2.500000e-04  Volume 1.963495e-12 1.963495e-12 1.963495e-12  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 40.0  Timestep (ms): 1.0  ATPase Model type: Constant  Pump rate: 0.1  Area scale type: Constant  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  No change of intracellular impermeant anion concentration mid simulation  Comp2 : change in intracellular impermeant anion charge - valence: -1.0, between: 800.0s and 1600.0s  No change of extracellular impermeant anion concentration mid simulation |
| Final vals: |  |
|  |  |
|  |  |
|  |  |
|  | Orange is compartment 2 |
|  | K+ flux in channel 1 and 3 |
|  | K+ flux in comp 2 |
|  |  |
| Conclusion | * With the ATPase being fixed, it seems that the set diffusion between compartments allows a non-isopotential neuron to exist. * Odd that the voltage in comp 2 increases when adding impermeants, while the other 2 compartments show a decreased voltage |

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| --- | --- |
| Aim | Repeat the experiment above and see if it behaves as Kira’s figure 8C |
|  | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3  Radius 5.000000e-05 5.000000e-05 5.000000e-05  Length 2.500000e-04 2.500000e-04 2.500000e-04  Volume 1.963495e-12 1.963495e-12 1.963495e-12  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 40.0  Timestep (ms): 1.0  ATPase Model type: J\_ATP = p \* (Na\_in/Na\_out)^3  Pump rate: 0.1  Area scale type: Constant  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  No change of intracellular impermeant anion concentration mid simulation  Comp2 : change in intracellular impermeant anion charge - valence: -1.0, between: 600.0s and 1800.0s  No change of extracellular impermeant anion concentration mid simulation |
|  | Cl driving force in comp1&3= 10.7727  Cl driving force in comp 2 = 12.4003 |
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| Conclusion | * Like the experiment above. Whether ATPase is fixed or dynamic, electrodiffusion allows non-isopotential dendrites to exist due to different impermeant anion charges in the various compartments. * The final voltage in this experiment is higher than expected… perhaps this is due to the constant area scale. * Next step would be to repeat this experiment with the dynamic area scale employed in Kira’s 8c * Perhaps the difference between mine and Kira’s is that there are more compartments so the voltage in comp2 is being dragged to the mean voltage of all 10 compartments which is lower |

|  |  |
| --- | --- |
| Aim | * Repeat the experiment above. * 3 compartments with a change to the middle compartment impermeants. |
| Setup | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3  Radius 5.000000e-05 5.000000e-05 5.000000e-05  Length 2.500000e-04 2.500000e-04 2.500000e-04  Volume 1.963495e-12 1.963495e-12 1.963495e-12  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 40.0  Timestep (ms): 1.0  ATPase Model type: J\_ATP = p \* (Na\_in/Na\_out)^3  Pump rate: 0.1  Area scale type: Am = Surface Area / volume  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  No change of intracellular impermeant anion concentration mid simulation  Comp2 : change in intracellular impermeant anion charge - valence: -1.0, between: 600.0s and 1800.0s  No change of extracellular impermeant anion concentration mid simulation |
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|  |  |
|  |  |
| Boundary |  |
| Conclusion: | * Even when the area constant is variable the voltage in the compartment increases slightly * Essentially the exact same result as previous experiment * Two possible next steps: a) make the radius and length the same as Kira’s multicompartment (was using the single compartment dimensions here). b) add more compartments to see if the voltage drops. |
|  |  |

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| Aim: | Same experiment as above just with different dimensions.  1um radius  10um length |
| Setup: | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3  Radius 1.000000e-05 1.000000e-05 1.000000e-05  Length 1.000000e-04 1.000000e-04 1.000000e-04  Volume 3.141593e-14 3.141593e-14 3.141593e-14  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 40.0  Timestep (ms): 1.0  ATPase Model type: J\_ATP = p \* (Na\_in/Na\_out)^3  Pump rate: 0.1  Area scale type: Am = Surface Area / volume  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  No change of intracellular impermeant anion concentration mid simulation  Comp2 : change in intracellular impermeant anion charge - valence: -1.0, between: 600.0s and 1200.0s  No change of extracellular impermeant anion concentration mid simulation |
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|  |  |
| Conclusion | * Vm gets more negative in 1 and 3. * Vm still drops in comp2 which is encouraging |

|  |  |
| --- | --- |
| Aim | Repeated experiment just with bigger drop in z |
|  | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3  Radius 5.000000e-05 5.000000e-05 5.000000e-05  Length 2.500000e-04 2.500000e-04 2.500000e-04  Volume 1.963495e-12 1.963495e-12 1.963495e-12  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 30.0  Timestep (ms): 1.0  ATPase Model type: J\_ATP = p \* (Na\_in/Na\_out)^3  Pump rate: 0.1  Area scale type: Am = Surface Area / volume  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  No change of intracellular impermeant anion concentration mid simulation  Comp2 : change in intracellular impermeant anion charge - valence: -1.4, between: 400.0s and 1200.0s  No change of extracellular impermeant anion concentration mid simulation |
| Final Vals |  |
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|  |  |
|  |  |
|  |  |
| Conclusion | * Same phenomena of increasing voltage occurring despite decreasing the impermeant charge even more. |

|  |  |
| --- | --- |
| Aim | Repeated experiment with drop in z in only 2 compartments but with 6 compartments |
| Setup | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3 Comp4 \  Radius 1.000000e-05 1.000000e-05 1.000000e-05 1.000000e-05  Length 1.000000e-04 1.000000e-04 1.000000e-04 1.000000e-04  Volume 3.141593e-14 3.141593e-14 3.141593e-14 3.141593e-14  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00  Comp5 Comp6  Radius 1.000000e-05 1.000000e-05  Length 1.000000e-04 1.000000e-04  Volume 3.141593e-14 3.141593e-14  Na\_i 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 40.0  Timestep (ms): 1.0  ATPase Model type: J\_ATP = p \* (Na\_in/Na\_out)^3  Pump rate: 0.1  Area scale type: Am = Surface Area / volume  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  No change of intracellular impermeant anion concentration mid simulation  Comp2 : change in intracellular impermeant anion charge - valence: -1.2, between: 600.0s and 1500.0s  No change of extracellular impermeant anion concentration mid simulation |
| Final vals |  |
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|  |  |
|  |  |
|  |  |
| Conclusion: | * Appears that the rise in impermeants is unrelated to the number of compartments |

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| --- | --- |
| Aim | In Kira’s 8C, she did not only drop the charge, she also added impermeant anions. In my previous experiments I was just changing the charge.  Here, I will be adding 5mM of impermeant anions at a charge of -1 to see what happens.  I expect similar results to Kira’s 8C. |
| Setup | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3  Radius 1.000000e-05 1.000000e-05 1.000000e-05  Length 1.000000e-04 1.000000e-04 1.000000e-04  Volume 3.141593e-14 3.141593e-14 3.141593e-14  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 40.0  Timestep (ms): 1.0  ATPase Model type: J\_ATP = p \* (Na\_in/Na\_out)^3  Pump rate: 0.1  Area scale type: Am = Surface Area / volume  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp2 : increase intracellular impermeant anion concentration - 5.0 mM, valence: -1.0, between: 600.0s and 1400.0s  No change of intracellular impermeant anion charge mid simulation  No change of extracellular impermeant anion concentration mid simulation |
| Final vals |  |
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|  |  |
|  |  |
|  |  |
| Conclusion: | Code to change impermeant anion concentration not working correctly. Charge of impermeants doesn’t seem to be changed |

|  |  |
| --- | --- |
| Aim: | Code fixed  Now repeating above |
|  | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3  Radius 1.000000e-05 1.000000e-05 1.000000e-05  Length 1.000000e-04 1.000000e-04 1.000000e-04  Volume 3.141593e-14 3.141593e-14 3.141593e-14  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 40.0  Timestep (ms): 1.0  ATPase Model type: J\_ATP = p \* (Na\_in/Na\_out)^3  Pump rate: 0.1  Area scale type: Am = Surface Area / volume  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp2 : increase intracellular impermeant anion concentration - 5.0 mM, valence: -1.0, between: 500.0s and 1500.0s  No change of intracellular impermeant anion charge mid simulation  No change of extracellular impermeant anion concentration mid simulation |
|  |  |
| Conc | Program crashed, chloride dropped too much |

|  |  |
| --- | --- |
| Aim | Repeated experiment as above, but with lower impermeant anion change.  Only increase by 2mM instead of 5mM.  Also found major error in the code for adding different species of impermeants which I have now corrected |
| Setup: | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3  Radius 1.000000e-05 1.000000e-05 1.000000e-05  Length 1.000000e-04 1.000000e-04 1.000000e-04  Volume 3.141593e-14 3.141593e-14 3.141593e-14  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 20.0  Timestep (ms): 1.0  ATPase Model type: J\_ATP = p \* (Na\_in/Na\_out)^3  Pump rate: 0.1  Area scale type: Am = Surface Area / volume  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp2 : increase intracellular impermeant anion concentration - 2.0 mM, valence: -1.0, between: 400.0s and 800.0s  No change of intracellular impermeant anion charge mid simulation  No change of extracellular impermeant anion concentration mid simulation |
| Final vals |  |
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| Conclusion | * Reaches steady state with new impermeant charge and concentration * My ECl drops very quickly relative to Kira’s and it ends up going back to normal almost. * Need to test with increasing impermeant anion concentrations |

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| Aim: | Repeat experiment above, just with increasing 5mM impermeants at valence of -1. |
|  | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3  Radius 1.000000e-05 1.000000e-05 1.000000e-05  Length 1.000000e-04 1.000000e-04 1.000000e-04  Volume 3.141593e-14 3.141593e-14 3.141593e-14  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 20.0  Timestep (ms): 1.0  ATPase Model type: J\_ATP = p \* (Na\_in/Na\_out)^3  Pump rate: 0.1  Area scale type: Am = Surface Area / volume  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp2 : increase intracellular impermeant anion concentration - 5.0 mM, valence: -1.0, between: 300.0s and 800.0s  No change of intracellular impermeant anion charge mid simulation  No change of extracellular impermeant anion concentration mid simulation |
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|  | * Vm still not dropping as expected * Ecl seems to drop but goes down much further than Kira’s * Similarly to the above, it seems that ATPase in adjacent comps need to work harder. * Next step is to make a static addition of impermeants and charge, more in line with Kira’s |

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| Aim | Testing the 3 compartments with static changes to impermeant anions during the simulation in all compartments. |
|  | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3  Radius 1.000000e-05 1.000000e-05 1.000000e-05  Length 1.000000e-04 1.000000e-04 1.000000e-04  Volume 3.141593e-14 3.141593e-14 3.141593e-14  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 40.0  Timestep (ms): 1.0  ATPase Model type: J\_ATP = p \* (Na\_in/Na\_out)^3  Pump rate: 0.1  Area scale type: Am = Surface Area / volume  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  ~~All compartments : increase intracellular impermeant anion concentration - 2.0 mM, valence: -1.0, between: 480.0s and 1200.0s~~  ~~No change of intracellular impermeant anion charge mid simulation~~  ~~No change of extracellular impermeant anion concentration mid simulation~~ |
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| boundary |  |
| Conclusion | * Implementation of static change appears to be working correctly * Not sure why there is a small upwards blip in the beginning of the drop * Next step to do the same experiment but change only the middle compartment |

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| Aim | Using static impermeant anion changes – change the concentration and charge of impermeants in only the middle compartment |
|  | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3  Radius 1.000000e-05 1.000000e-05 1.000000e-05  Length 1.000000e-04 1.000000e-04 1.000000e-04  Volume 3.141593e-14 3.141593e-14 3.141593e-14  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 30.0  Timestep (ms): 1.0  ATPase Model type: J\_ATP = p \* (Na\_in/Na\_out)^3  Pump rate: 0.1  Area scale type: Am = Surface Area / volume  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\* |
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| Conclusion | * Similar findings as with the dynamic xflux 🡪 voltage increasing in the compartment that the anions are added to, whilst voltage decreases in the neighbouring compartments * There is a slight uptick in the amount of anions added, and then a drop. Perhaps if I increase the rate of impermeant addition there will be a change to the dynamic |

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| Aim | Same experiment as above. Just increasing the rate of impermeant influx from 0.3mM per minute to 0.6 mM per minute |
|  | \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Compartment settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Comp1 Comp2 Comp3  Radius 1.000000e-05 1.000000e-05 1.000000e-05  Length 1.000000e-04 1.000000e-04 1.000000e-04  Volume 3.141593e-14 3.141593e-14 3.141593e-14  Na\_i 1.400000e-02 1.400000e-02 1.400000e-02  K\_i 1.226650e-01 1.226650e-01 1.226650e-01  Cl\_i 5.000000e-03 5.000000e-03 5.000000e-03  X\_i 1.549000e-01 1.549000e-01 1.549000e-01  z\_i -8.500000e-01 -8.500000e-01 -8.500000e-01  ATPase pump rate 1.036427e-06 1.036427e-06 1.036427e-06  KCC2 pump rate 2.072854e-08 2.072854e-08 2.072854e-08  Vm 0.000000e+00 0.000000e+00 0.000000e+00  Ek 0.000000e+00 0.000000e+00 0.000000e+00  ECl 0.000000e+00 0.000000e+00 0.000000e+00  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Extracellular anion concentrations:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Na: 145.0 mM  K: 3.5 mM  Cl: 119.0 mM  X: 29.5 mM  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Simulation settings:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Total time (mins): 20.0  Timestep (ms): 1.0  ATPase Model type: J\_ATP = p \* (Na\_in/Na\_out)^3  Pump rate: 0.1  Area scale type: Am = Surface Area / volume  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  Impermeant anion changes:  \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\* |
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|  | Doubling the rate of impermeant anion influx made the compartments voltages more similar to each other.  Still did not drop the voltage to pre-simulation levels |