# 3 – multiple impermeant anion valence changes

## 3.1 The effects of different impermeant anion valences

We next performed five simulations each with decreasing impermeant anion charge (z) in compartment 8 (-0.65;-0.75;-0.85;-0.95;-1.05) (schematic 3). Figure 3a shows near linear relationships between IA charge and IA concentration, compartment volume and membrane potential.

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**Schematic 3. Impermeant anion charge (valence) in Comp-8 manipulated in five separate simulations**

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Figure 3a**. Local impermeant anion(IA) charge sets local IA concentration, volume, and membrane potential.** Drops in concentration and membrane potential in the compartment with charge decreases **(left & right pane)**. Compartment volume increases linearly with decreasing IA valence **(middle pane)**

Figure 3b shows an inverse relationship between charge of impermeant anions and Cl- concentration; and an opposite, direct, correlation with Na+ and K+ concentration in Comp8. There were no changes to the transmembrane driving forces for any ion, however the boundary driving forces were impacted with equal but opposing voltages pulling ions from Comp8/Comp9 and Comp7/Comp8in a “tug-of war” scenario that establishes a steady state ion concentration gradient between compartments.

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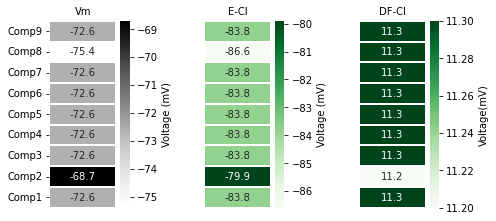
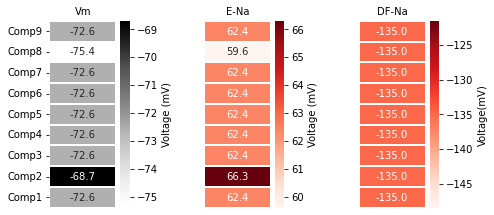
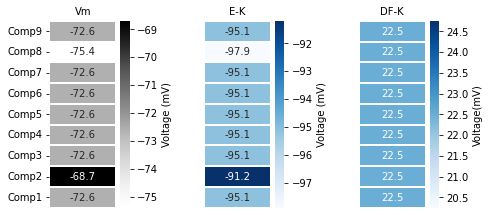
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Figure 3b. **Impermeant anion charge sets up non-uniform concentration gradients between compartments maintained by competing axial driving forces.** Five simulations were conducted where the impermeant anion charge in Comp 8 differed (z = -0.45; -0.65; -0.85;-1.05; -1.25). *Top row:* The steady state permeant ion concentrations varied linearly in relation to decreasing IA charge resulting in a concentration gradient between Comp8 and its neighbouring compartments. *Middle row:* There was no change to steady state transmembrane driving forces. *Bottom row:* Boundary(axial) driving forces increase in amplitude in relation to the absolute difference between the IA charge and the default charge of -0.85. The direction of the force is determined whether the IA charge is greater or lesser than -0.85.

## 3.2 Different impermeant anion valences within the same dendrite

We next simulated a multicompartmental model with opposing valence changes in compartment 8 (z=-0.45) and compartment (-1.25) (fig3c). The concentration of anion and volume either compartment changed in opposite directions to each other with none of the non-manipulated compartments being affects. We also showed that in this multicompartment model there can be microdomains of all anions relative to the valence of impermeants.

Graphical user interface

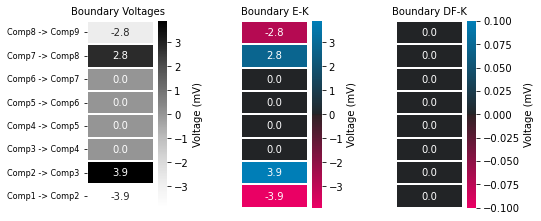
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Description automatically generatedIn the compartment 8 and compartment 2 there were opposing fluctuations in the membrane potential of the compartment (fig3d). Equal changes to the reversal potential for each ion created constant driving forces irrespective of the ion concentrations.

Figure 3c**. Multiple ion microdomains occur in compartments with varied impermeant anion charge (IA).** *Top row:*We altered impermeant anion average charge in Comp8 (z=-0.45) and Comp2 (z=-1.25) between 120 and 180s. This resulted in respective changes to IA concentration and compartment volume in Comp8 and Comp2. *Middle row:* No changes demonstrated in IA concentrations and cell volumes in non-manipulated compartments. *Bottom row:* Distinct microdomains of local ion concentration differences occurring due to the change in IA average charge, persisting beyond the manipulation period.

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Figure 3d**. Constant ion driving forces despite varied membrane potentials across the multicompartment dendrite with altered impermeant anion valences.** We altered impermeant anion average charge in Comp8 (z=-0.45) and Comp2 (z=-1.25) between 120 and 180s. *Top row:* Membrane potential increase in Comp8 and decrease in Comp2. *Middle row:* Ionic reversal potential increases and decreases in Comp8 and Comp2 respectively. *Bottom row:* No changes to steady state driving forces at the end of the simulation.