**Materials and methodology**

*Single compartment model.* The single compartment dendrite model consisted of a cylindrical semi-permeable membrane separating the extracellular solution from the intracellular milieu with variable volume (Fig. 1A). The extracellular ionic concentrations were assumed constant (Table 1). Permeable ions in the model were K+, Na+ and Cl- with their usual charges, while impermeable anions A were assumed to be a heterogenous group of impermeant ions with average intracellular charge z and extracellular charge -1. The model included ionic leak currents for the permeable ions, Na-K ATPase transporters and K-Cl co-transporters (KCC2). Cell volume change was based on osmotic water flux and incorporated a membrane surface area scaling mechanism. An analytical solution to the model at steady state was derived (see supplementary material). The model was initialised assuming conditions close to electroneutrality and an osmotic equilibrium between the intracellular and extracellular compartments. A forward Euler approach was used to update variables at each time step, with a dt of 1 ms. Using a dt of smaller magnitude did not influence the results in Fig. 1-5. Code was written in Python 2.

*Membrane potential.* The membrane potential Vm was based on the “Charge Difference” approach of Fraser and Huang (2004) as follows:

where F is Faraday’s constant, ionic charge is summed, Cm is the membrane capacitance and Am the membrane scaling constant, which will be described later. This approach is favourable because the initial voltage can be calculated without assuming a steady state and then consistently updated using the same equation.

*Permeable ion concentrations.* Intracellular concentrations of the permeable ions Na+, K+ and Cl- were updated individually by summing trans-membrane fluxes. Leak currents were calculated using the standard equivalent circuit model formulation . Na+ and K+ were influenced by the Na-K ATPase with pump rate Jp, which was approximated by a cubic function dependent on the transmembrane sodium gradient, following Keener and Sneyd (2008):

where P is the default constant pump rate. Because it is a function of the sodium gradient, Jp decreases as [Na+]i depletes. This formulation has been shown to be similar to more accurate kinetic models reliant on ATP concentration (Keener and Sneyd, 2008). The ATPase pumps 2 K+ ions into the cell for every 3 Na+ ions out and these constants must be multiplied by Jp for each ion respectively. K+ and Cl- were influenced by flux through the type 2 K-Cl co-transporter (KCC2), JKCC2, which was based on the model proposed by Doyon et al (2016):

where gKCC2 is a fixed conductance constant and EK and ECl are the Nernst potentials for K+ and Cl- respectively. JKCC2 is 0 when EK=ECl. gKCC2 was increased by a fixed constant per time step in Fig. 3A and Fig. 6. Summating the flux mechanisms, each ion was updated as follows:

*Volume.* Change in compartment volume, W, was assumed to be instantaneous and calculated by changing the previous volume proportional to the ratio of intracellular to extracellular osmolarity, and respectively:

Intracellular ion concentrations were updated again after volume change in each time step. Volume changes were manifested in the cylindrical compartment as change in the length of the compartment such that membrane surface area scales with volume. Am, the constant scaling ratio as used in Fraser and Huang (2004), was derived based on this assumption, with r the compartment radius and h its height:

*Anion flux.* Impermeable anions were manipulated in the compartment in Fig. 4-6 and Fig. 8 through several mechanisms. Anions could be added to the compartment at a constant rate dependent on Am and have either the same average intracellular A charge z = -0.85 (Fig. 4C, 6B, 8), or a different one, usually -1 (Fig. 5C, D). In these cases, the absolute mols of A in the compartment increased. Alternatively, the charge of a species of intracellular A was slowly changed imitating a charge-carrying trans-membrane reaction (Fig. 5A, B, 6C). In this case, the absolute mols of intracellular A did not change and it was assumed charge imbalance was mopped up by the extracellular milieu. Finally, extracellular A- were manipulated in Fig. 4D by decreasing equivalent mols extracellular Cl- for the increase in extracellular A-, thus maintaining osmolarity and electroneutrality in the extracellular space.

*Multi-compartment model.* The single compartment dendrite model was incorporated in a multi-compartment model by allowing electrodiffusion to occur between individual compartments operating as described above. Compartments were initialised with a radius of 0.5 μm and length of 10 μm except in the case of the growth cone in Fig. 8 (length of 6 μm). Compartments were linked linearly without branching; a total length of 10 connected compartments was used in Fig. 6-7. The time step dt was decreased to 1e-3 ms for all simulations using multiple compartments. Code was written in Python 3.

*Electrodiffusion.* The Nernst-Planck equation (NPE) was used to model one-dimensional electrodiffusion, based on Qian and Sejnowski (1989). The NPE incorporates fluxes because of diffusion and drift, the latter being important for calculating the influence of changes in charge on ionic concentrations. It has been shown to be more accurate than using Jdiffusion alone in small structures like dendrites (Qian and Sejnowski, 1989). The NPE for J the flux density of ion C is calculated:

where D is the diffusion constant of ion C (Table 1), z is its charge, [C] is its concentration and x is the distance along the longitudinal axis over which electrodiffusion occurs. The NPE was implemented between compartments i and i+1, assuming the i🡪i+1 direction is positive, using a forward Euler approach. The midpoints of the compartments were used to calculate dx, i.e. , and the concentrations of C in each compartment were averaged to obtain Jdrift, ensuring that Ji🡪i+1 = Ji+1🡪i, where the fluxes are in units of mols/(s dm2):

The flux was multiplied by the surface area between compartments and then divided by compartment volume to determine the flux in terms of molar concentration (M/s), i.e. and finally implemented numerically with a forward Euler approach. The implementation mirrors that in Qian and Sejnowski (1989) for non-branching dendrites, but has been adjusted for compartments whose volumes can change:

*Systematic review of KCC2-Cl- literature.* \*\*\* Fig. 3C…

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|  | Value | Description |
| Constants | | |
| F | 96485.33 C/mol | Faraday’s constant |
| R | 8.31446 C/V | Universal gas constant |
| T | 298.15 K | Absolute temperature |
| Parameters | | |
| Cm | 2 10-4 F/dm2 | Membrane capacitance |
| gNa | 5 nS/dm2 | Na+ leak conductance |
| gK | 50 nS/dm2 | K+ leak conductance |
| gCl | 10 nS/dm2 | Cl- leak conductance |
| gKCC2 | 10 nS/dm2 | KCC2 conductance |
| r | 0.5 μm | Radius |
| Am | 4 μm-1 | Membrane scaling constant |
| P | 10-2.432631 / F | Default pump rate constant |
| [Na+]e | 145 mM | Extracellular Na+ concentration |
| [K+]e | 3.5 mM | Extracellular K+ concentration |
| [Cl-]e | 119 mM | Extracellular Cl- concentration |
| [A-]e | 28.5 mM | Extracellular A- concentration |
| DNa | 1.33 10-7 dm2/s | Na+ diffusion constant |
| DK | 1.96 10-7 dm2/s | K+ diffusion constant |
| DCl | 2.03 10-7 dm2/s | Cl- diffusion constant |
| Variables (default steady state) | | |
| Vm |  | Membrane potential |
| [Na+]i |  | Intracellular Na+ concentration |
| [K+]i |  | Intracellular K+ concentration |
| [Cl-]i |  | Intracellular Cl- concentration |
| [Az]i |  | Intracellular Az concentration |
| z | -0.85 | Average charge of intracellular A |
| W |  | Volume |
| h |  | Compartment height |