Supporting Information for

Controlling ionic conductivity through transprotein electropores in human aquaporin 4: a non-equilibrium molecular-dynamics study

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Mean residence-time data

Data to be inserted in eq. 3 (main text) for $\Delta t_i \; and \; \sigma_i$ have been extracted from the Cfg#2 simulation, where six conduction events take place. These data are presented below.

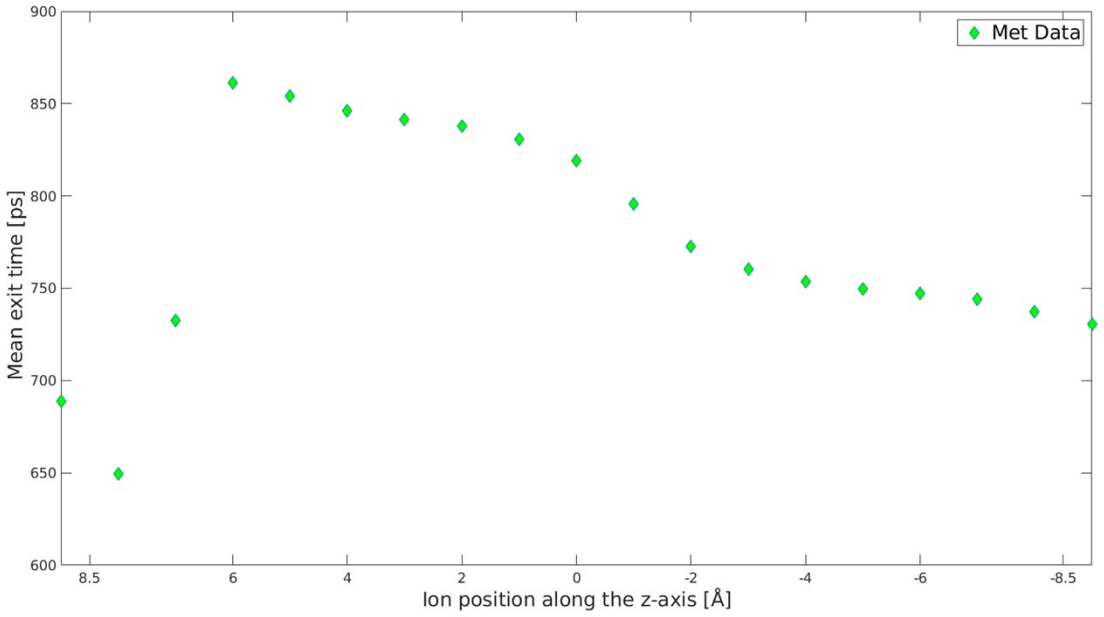
# event	Ion residence time within the channel [ps]	Single event ionic conductivity [S/m]
#1	215	23.72
#2	193	36.26
#3	572	10.63
#4	142	32.07
#5	405	12.25
#6	189	24.10

Table S1: Mean residence-time data for use in eqn. 3 of the main manuscript

Mean first-passage time technique

The analysis based on a first-passage approach is well suited to characterise the dynamics of the ions in the channel from the results of molecular-dynamics simulations. As suggested in [48], a meaningful way to apply MFPT theory to our simulations is the analysis of ionic dynamics in the channel via the Mean Exit-Time (MET) approach. It is defined as the average time taken for a particle to reach for the first time any of the boundaries given that its initial position within the channel is z_0.

To calculate the MET from the MD simulations, we divided the system into 30 layers of width d_i and at each timestep identify the chloride ions within the layer centred at z_0. Those particles are tracked until they reach either boundary and the time elapsed is recorded. From the collection of residence times of the particles starting at z_0 one can compute the average time to reach either boundary. This is repeated for all z_0 in the interval to obtain the MET from MD simulations. The algorithm, *ad-hoc* written in Fortran code, revealed the MET profile shown in Figure S1.



These results provide the characteristic residence times for chloride ions as a function of their position within the channel. From those values we can obtain the average time of residence in the channel for the six chloride ions, which results $673.89\ ps$.

Ionic-conductivity estimation from Casciola et al. [45] paper.

Authors studied the characteristics of pores formed in lipid bilayers maintained at a constant surface tension and subject to constant charge imbalance. This allowed the evaluation of structural (size) and electrical (conductance) properties of the pores formed. If we take into account data presented in figures 3 and 4, related to the electropore radius and ionic current, respectively, we can evaluate the current density value $J = \sigma E$ from which the conductivity value can be extracted. If one focus on the 20q charge imbalance condition (black curves, the smallest available electropore radius), for which a transmembrane (TM) value of 420 mV is furnished, the Electric field value across the membrane (≈30 Å thick, see text) results 0.014 V/ Å. The current value corresponding to the 10 Å electropore radius is 3 nA. With these values one can easily evaluate the current density from the known relationship $J = I/S$, being S the electropore section and eventually the conductivity value via $\sigma = J/E$, which results 6.86 S/m.

Ionic conductivity estimation from Wilson et al. [46] paper.

In this case, a constant electric field drives the ions passage through an endogenous protein channel. The electric field value is not explicitly furnished, but it can be easily evaluated from the applied voltage (100 mV) along the simulation box z-axis (106 Å length). The resulting electric field (applied on all the atoms inside the simulation box) is about 0.001 V/ Å.

The ionic current (chloride ions) due to this electric field is 35 pA (see Table 1 of [46]), which combined with the protein channel section (6 Å, see Fig.2 of [46]) together with $\sigma = J/E$ gives a conductivity value of 3.18 S/m.