Supporting Information

\mathbf{to}

Multiscale modeling of a rectifying bipolar nanopore: explicit-water versus implicit-water simulations DOI: 10.1039/C7CP01819C

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Introduction

This Supporting Information (SI) provides additional details to the main text that tells a story with a limited, but sufficient amount of data. The bipolar nanopore studied here serves as a case study for the general statement that reduced models are able to reproduce the device behavior in spite of the fact that they get the molecular-level physics wrong. This work provides a computational insight into how we can resolve this dichotomy.

Basically, the reduced model must include all the details (degrees of freedom) that are necessary to reproduce the appropriate output given by the system as a response to the input signal. We distinguish "important" and "unimportant" degrees of freedom from the point of view of the device function. In the particular case of the bipolar nanopore, it was important that the reduced model reproduced the axial behavior of the ionic concentration profiles right. To achieve this, the presence of explicit water molecules in the model seems less important.

We present figures with extra results more or less in the order they are mentioned in the main text and discuss them briefly in the captions. We show results for voltage dependence (Fig. SI 1), bulk concentration dependence (Figs. SI 5 and SI 6), σ -dependence (Figs. SI 2 and SI 4) concentration (Figs. SI 4, SI 6, SI 7, and SI 9) and potential profiles (Fig. SI 10) for

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cases missing from the main text, electrochemical potential profiles (Fig. SI 11) obtained from NP+LEMC, and technical details: error calculation (Fig. SI 3) and potential calculation (Fig. SI 8). The same diffusion coefficients were used in all figures as in the ones in the main text. At the end, we present a description of the computational methods in more detail compared to the Appendix of the main text.

Video

The SI also includes a video clip from an MD simulation showing Na⁺ and Cl⁻ ions moving in the nanopore in the ON and the OFF state ($c = 1 \text{ M}, \sigma = 1 e/\text{nm}^2$). The video has been prepared with VMD [1]. Below, we show a snapshot from the video. Red and blue spheres represent Cl⁻ and Na⁺ ions, respectively.

The video at a good resolution can be watched by clicking at the figure below or at this link: https://youtu.be/SBHBw7req98





Figure SI 1: Current vs. voltage curves for concentrations c = 0.5 and 1 M as computed from NP+LEMC (lines with small symbols) and MD (large symbols with error bars) for $\sigma = 1 e/\text{nm}^2$. The inset shows the rectification as a function of voltage (U > 0). Rectification is defined as |I(U)/I(-U)|, where U and -U are the corresponding voltages of the ON and OFF states, respectively.



Figure SI 2: Current vs. surface charge curves for concentration c = 0.5 M as computed from NP+LEMC (lines) and MD (symbols with error bars) for voltages -200 mV (OFF) and 200 mV (ON). Results for c = 1 M are seen in Fig. 2 of the main text.



Figure SI 3: One method to estimate statistical errors of the currents provided by MD simulations. Current is measured by counting the number of ion crossings through the pore (see the insets). The error is estimated by plotting the running average of the current: the number of ions that crossed the pore divided by time (converted to pA) as a function of time. Upper and lower limits (red lines) are drawn for the second half of the run. The distance between these lines defines the error [2]. This kind of estimation of error agreed (in order of magnitude) with that using block averages and computing the error from the mean deviation of the block averages from the total average. Problems arise with both methods when sampling is inadequate. A typical example is the OFF state current of Na⁺ in the figure where a drift is observed in the running average as a function of time. It is uncertain whether running longer simulations results in further increase (indicating larger error) or the current decreases and starts to fluctuate (indicating smaller error). We suggest treating the MD results with reservation, especially in the OFF states.



Figure SI 4: Concentration profiles of Na⁺ (A and B) and Cl⁻ (C and D) for different values of σ (see the numbers next to the curves) as obtained from MD (A and C) and NP+LEMC (B and D) for the ON (top panels) and OFF (bottom panels) sign of the voltage. Concentration profiles have been computed in the same way in the two models: the average number of ions in a slab has been divided by the effective volume available for the ions. Inside the pore, the same cross section was used (radius 1 nm) in both cases. The agreement is quite good in the ON state. In the OFF state, the MD profiles show a larger difference between the N and P zones compared to NP+LEMC profiles. A qualitative agreement, however, is present.



Figure SI 5: Total currents in the ON and OFF states as functions of NaCl concentration for $\sigma = 1 \ e/\text{nm}^2$. Black symbols connected with lines are NP+LEMC data, while blue symbols are MD data. Ionic currents decrease as concentration decreases, but they decrease faster in the OFF state. Depletion zones are more pronounced at low concentrations (see Fig. SI 6). Therefore, rectification increases with decreasing concentration (see inset). We show only NP+LEMC results for c < 0.5 M, because sampling with MD at low concentrations is problematic.



Figure SI 6: Normalized concentration profiles of Cl⁻ (panel A) and Na⁺ (panel B) for different concentrations for $\sigma = 1 \ e/\text{nm}^2$ as obtained from NP+LEMC simulations for the ON (top panels) and OFF (bottom panels) sign of the voltage. The profiles are normalized by the bulk values. Increase of concentration inside the pore is proportional to the increase of bulk concentration in the OFF state, while in the ON state this increase is not proportional due to saturation. Currents, therefore, decrease faster in the OFF state, as concentration decreases (see Fig. SI 5). This results in a rectification that increases with decreasing concentration.



Figure SI 7: Contour plots of concentrations of water molecules (turquoise), Na⁺ (blue), and Cl⁻ (red) ions as obtained from MD simulations in the ON state (panel A) and in the OFF state (panel B) for $\sigma = 1 \ e/\text{nm}^2$ and c = 1 M. Coloring is designed to overemphasize peaks in order to reveal structure. The scales of panels A and B are the same.

Figure SI 8: Comparison of potential profiles computed by two different methods. Solid lines are from solving Poisson's equation with zero Dirichlet boundary condition on the surface of the confining cylinder from charge profiles computed from the average density profiles for the charges of ions and water molecules provided by the MD simulations. Symbols have been obtained from sampling the potentials on the fly with test charges using 20,000 snapshots given by each MD simulation. The potential was sampled by computing it using periodic boundary conditions and excluding those charges that are within 0.05 nm distance from the test charge. Using other values did not influence the results considerably: 0.05 nm is a good compromise between noise from overlapping of test charges and system charges and errors from ignoring system charges close to the test charge. Averaging over the cross section have been done for the effective cross section (R = 1 nm in the pore) just as in the case of concentration profiles. The agreement justifies using zero Dirichlet boundary conditions in the Poisson calculations in Figs. 5 and 6 of the main text.

Figure SI 9: Illustration of the double layers formed on the two sides of the membrane in NP+LEMC. Concentration profiles are shown for different σ values for the ON (left panels) and the OFF (right panels) state. Red and blue curves refer to Cl⁻ and Na⁺, respectively. The curves inside the pore are not shown to emphasize the double layer and to make the effect of the surface charge and voltage more visible.

Figure SI 10: Components of the mean electrical potential as obtained from NP+LEMC. Free charges are the ionic charges plus the pore charges. They produce an electric potential (black solid curves) that counteracts the applied potential (red dot-dashed curves) so that the total potential (blue dashed curves) is vertical in the baths as it is supposed to be since the baths are low-resistance elements. The potentials of free charges have opposite slopes in the ON and OFF states and they are related to the double layers of opposite signs (see Fig. SI 9) in this model. On the right hand side, for example, positive slope indicates Cl⁻ excess in the double layer, while negative slope indicates Na⁺ excess (the situation on the left hand side is reversed). In the implicit solvent model, therefore, the formation of the double layers is a natural outcome of the calculations necessary to obtain a self-consistent system.

Figure SI 11: Electrochemical potential profiles and its chemical and electrical components for (A) Na⁺ and (B) Cl⁻. The electrical component is defined as the interaction with the mean electrical field (see Fig. SI 10). This definition is arbitrary, but reasonable. The electrochemical potential profile is the outcome of the calculations, while the chemical component is the difference of the electrochemical and electrical terms. The chemical term is $\mu_i^0 + kT \ln c_i(z) + \mu_i^{\text{EX}}(z)$, where $\mu_i^{\text{EX}}(z)$ is the part of the excess chemical potential excluding the interaction with the mean field. The chemical potential profiles more or less follow the variation of the concentration profiles. The electrochemical profile is monotonic as it should be because its gradient is the driving force of the transport. Note that the electrochemical potential profile in the OFF state has a large slope in the depletion zones and a small slope in the peak zones. This is necessary to compute a system satisfying the continuity equation, because concentration is low in the depletion zone and large in the peak zone.

Technical details

Explicit-water model studied with MD All-atom MD simulations were performed with the GROMACS (v.5.0.4) program suite [3, 4] using the leap-frog integrator with a 2 fs time step. Bonds involving H atoms were kept rigid. Our system was constructed from a model membrane and an aqueous solution containing Na⁺ and Cl⁻ ions. We constructed the model membrane with the help of the Nanotube Builder plugin in the VMD program suite [1]. This carbon nanosheet (CNS) is composed of two graphene-like sheets (with holes) and a CNT were constructed and joined together resulting in our toy model membrane (see Fig. 1 of the main text). In addition to Lennard-Jones (LJ) interactions (for LJ parameters, see Table SI 1), simple fractional point charges were assigned to the atoms of the channel to create a nearly homogeneous surface charge. The amplitude of the fractional charges were chosen to create a prescribed surface charge on the pore wall. The channel has been made bipolar by using 841 positive charges on the left hand side and 841 negative charges on the right hand side of the cylindrical pore wall (blue and red dots in Fig. 1). The CNS/CNT structure built from the C atoms was kept rigid in a way that their positions were not updated during the MD simulation (freeze option of GROMACS).

The system was filled with SPC water molecules ($\sim 11,000$ molecule) and LJ and point charge type ions (110-190 anions and the same number of cations depending on the designated concentration and charge density on the channel wall). Water molecules and ions are not present in the space bounded by the CNSs and the CNT. The CHARMM27 force field variant implemented in GROMACS [5] was used for the membrane (carbon-like interaction sites) and for the ionic species (see Table SI 1).

The dimensions of the simulation box were $6 \times 5.2 \times 16.8$ nm, with periodic boundary conditions (PBC) applied in all spatial directions. The pore was H = 6.035 nm long (the distance of C atoms in the two CNSs). The distance of the atomic centers of the channel atoms from the centerline of the channel was 1.136 nm (R_c in Fig. 1). To achieve ± 200 mV potential difference between the two ends of the simulation box a 0.012 V/nm external electric field was applied. The membrane was kept in the center of the box by harmonic position restraints. The systems were thermostated to 298.15 K by a modified version of the Berendsen (velocity rescaling) algorithm [6].

The concentrations were established in the bulk regions on the two sides of the membrane

	σ / nm	ϵ / kJmol^{-1}
С	0.36705	0.33472
Na^+	0.24299	0.19623
Cl^-	0.40447	0.6276

Table SI 1: LJ parameters of the carbon atoms of the membrane/nanotube (C), and the ions $(Na^+ \text{ and } Cl^-)$. The charges of Na^+ and Cl^- ions are e and -e, respectively. The partial charges of the nanopore wall are determined by the prescribed surface charge, the surface area, and the number of point charges (2×841). The parameters of the SPC water are found in the literature [7]. The parameters of the cross interactions are given by the Lorentz-Berthelot mixing rule.

with an iterative procedure. In the preliminary simulations we put in ions and performed a 100 ns long NVT simulation to achieve steady state, then we checked the ionic concentrations and corrected particle numbers (if needed) and did the same simulation again. Once we reached the target concentrations in the bulk phases, 200 ns long NVT production runs were started from the obtained configurations.

An ion was considered to cross the channel if it is initially at one side of the membrane and then ends at the opposite side of the membrane after propagating through the channel.

Implicit-water model studied with NP+LEMC In the reduced model designed for NP+LEMC calculations the membrane and pore penetrating it are defined by hard walls with which the ions cannot overlap. The cylindrical pore's radius and length were calculated to mimic the CNT model of the MD simulations as closely as possible on the basis of an estimated distance of closest approach of ions to the carbon atoms. We used the values R = 0.97 nm and H = 6.4 nm for the pore radius and length, respectively. The fractional point charges have been placed at the same positions as in the CNT model. Also, their magnitudes are the same. Therefore, the pore models are electrostatically identical in the MD and NP+LEMC systems.

The ions are charged hard spheres immersed in a dielectric continuum that models the solvent implicitly. The ionic diameters are 0.19 and 0.362 nm for Na⁺ and Cl⁻, respectively, while the dielectric constant is $\epsilon = 78.5$. The ions interact through the screened Coulomb potential electrostatically if the ions do not overlap (which is forbidden, see Eq. 2 of the main text). The diffusion coefficients of Na⁺ and Cl⁻ were $D_{\text{Na}^+}^{\text{bulk}} = 1.333 \times 10^{-9} \text{m}^2 \text{s}^{-1}$ and $D_{\text{Cl}^-}^{\text{bulk}} = 2.032 \times 10^{-9} \text{ m}^2 \text{s}^{-1}$, respectively, in the bulk. The diffusion coefficients in the pore

Figure SI 12: The computational cell for the NP+LEMC system. The NP equation is solved for the transport region confined by the blue line. This domain is divided into volume elements. The LEMC simulation is performed for the whole cell including the equilibrium bulk regions outside the transport region. Red and blue spheres represent Cl^- and Na^+ ions, respectively.

 (D_i^{pore}) are adjustable parameters in the calculations. They have been fitted to the results of the MD simulations as described in the main text.

The system is rotationally symmetric, therefore, we use a cylindrical simulation cell (see Fig. SI 12). Two cylindrical compartments on the two sides of the membrane represent the two regions between which the ion transport flows. These have equilibrium and non-equilibrium parts. The non-equilibrium part (the transport region) is the computational domain (defined by blue line in Fig. SI 12). This region is divided into volume elements. The boundary conditions are prescribed on the outer surfaces of the two half cylinders confining this region from left and right (the blue line). More details are found in our papers [8, 9, 10, 11].

The problem is solved on a discretized grid iteratively; the electrochemical potential is changed until the continuity equation, $\nabla \cdot \mathbf{j}_i(\mathbf{r}) = 0$, is satisfied. The iteration can be sum-

	MD	NP+LEMC
Ions	LJ + point charge	Hard sphere + point charge
Water	SPC	Continuum background: ϵ and $D_i(\mathbf{r})$
Pore	CNT + point charges	Hard cylinder + point charges
Membrane	CNS	Hard walls
Boundary conditions	PBC in all dimensions	Half-cylinders on both sides
\rightarrow concentration	\rightarrow same on the two sides	\rightarrow prescribed on the cylinders
\rightarrow electrical potential	\rightarrow constant E_z field	\rightarrow prescribed on the cylinders

Table SI 2: Summary of differences between the MD and NP+LEMC systems.

marized as

$$\mu_i[n] \xrightarrow{\text{LEMC}} c_i[n] \xrightarrow{\text{NP}} \mathbf{j}_i[n,m] = -\frac{1}{kT} D_i c_i[n] \nabla \mu_i[m] \xrightarrow{\nabla \cdot \mathbf{j}_i[n,n+1]=0} \mu_i[n+1], \quad (1)$$

namely, the electrochemical potential for the next iteration, $\mu_i[n+1]$, is chosen so that the flux computed from it and the concentration in the previous iteration, $c_i[n]$, satisfies conservation of mass for every elementary cell.

The concentration in the *n*th iteration, $c_i[n]$, is obtained from LEMC simulations. This simulation technique assumes that the system is in local equilibrium in every volume element. This local equilibrium is characterized by a local value of the electrochemical potential. In grand canonical particle insertions and deletions, this value is used in the acceptance probabilities of these insertions/deletions. The result of the LEMC simulation is the average number of ions in each volume element and thus, the concentration. Also, the mean electrical potential can be sampled on the fly by using the inserted ions as test charges (profiles of Fig. SI 10 were computed this way).

The resulting electrochemical potential profiles fluctuate around limiting distributions due to statistical uncertainties in the LEMC simulations. The final results are obtained as running averages.

Differences between MD and NP+LEMC Boundary conditions are treated differently in MD and NP+LEMC (see Table SI 2). In MD, the driving force of the transport is a homogeneous electric field along the z direction and ions leaving the cell at one end are fed back on the other end due to PBC applied in the z dimension. In NP+LEMC, the simulation cell is finite. Both concentrations and electrical potentials are prescribed on the half-cylinders (blue line in Fig. SI 12) on the two sides of the membrane.

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