Published in final edited form as:

J Comput Theor Nanosci. 2009 August 1; 6(8): 1948–1955. doi:10.1166/jctn.2009.1250.

Ion Rejection by Nanoporous Membranes in Pressure-Driven Molecular Dynamics Simulations

Kevin Leung^{*} and Susan B. Rempe^{*}

Sandia National Laboratories, MS 1415 and 0895, Albuquerque, NM 87185, USA

Abstract

We perform pressure-driven non-equilibrium molecular dynamics (MD) simulations to drive a 1.0 M NaCl electrolyte through a dipole-lined smooth nanopore of diameter 12 Å penetrating a model membrane. We show that partial, about 70–80%, Cl[−] rejection is achieved at a ~68 atmosphere pressure. At the high water flux achieved in these model nanopores, which are particularly pertinent to atomistically smooth carbon nanotube membranes that permit fast water transport, the ion rejection ratio decreases with increasing water flux. The computed potential of mean force of Cl[−] frozen inside the nanopore reveals a barrier of 6.4 kcal/mol in 1.0 M NaCl solution. The Cl[−] permeation occurs despite the barrier, and this is identified as a dynamical effect, with ions carried along by the water flux. Na⁺-Cl[−] ion-pairing or aggregation near the pore entrance and inside the pore, where the dielectric screening is weaker than in bulk water, is critical to Cl[−] permeation. We also consider negative charges decorating the rim and the interior of the pore instead of dipoles, and find that, with sufficient pressure, Cl[−] from a 1.0 M NaCl solution readily passes through such nanopores.

Keywords

Nanopores; Electrolytes; Ion Channels; Non-Equilibrium Molecular Dynamics; Pressure-Driven; Potential of Mean Force

1. INTRODUCTION

The ability of solid state nanoporous membranes to selectively transmit and reject ions has potential applications to nanofluidics, transport in electrode material and separator membranes in batteries, desalination, and nanotechnology.^{1, 2} Biological cell membranes also contain nanopores, composed of proteins, that selectively transmit and reject ions, a function critical to cells and many higher physiological processes.³ Ion rejection in nanopores, and the closely-related cation/anion rectification phenomenon,^{4–7} are broadly understood to arise from a combination of equilibrium effects,^{8–12} including pore diameter, which limits ion-hydrating water molecules and sometimes even larger ions; electrostatic and dielectric penalties; and the possible existence of binding sites and barriers. See Ref. [13] for a comprehensive review of additional modeling work of confined water and electrolyte.

Practical desalination applications are inherently non-equilibrium processes.¹⁴ They involve either using electric fields to remove ions of both charges by driving them in opposite directions, or more commonly pressure-driven motion of nearly pure water against the osmotic/chemical potential gradient from high salt concentration media to low salt regions. The pressure

gradient, inhomogeneous ion-pairing effects as the local salt concentration varies with time and space, and potential space charge due to local excess of cations or anions (especially near the channel entrance and exit regions) may complicate equilibrium analysis of ion blockage. Ion-pairing also occurs at equilibrium, particularly inside nanopores where the effective dielectric constant can drop to ~ 10 (see Refs. [15, 16]); but this effect may be further accentuated by an external driving force.

Figure 1 illustrates the pressure gradient as

$$V_p(z) = -Bz \quad (1)$$

applied to the H₂O oxygen site and salt ions alike.¹⁷ This potential overlies the anion rejection barrier at the entrance of the dipolar nanopore, which spans an otherwise impermeable membrane. The barrier is assumed to coincide with that calculated for the reservoir salt concentrations fixed at both ends of the pore. Salt rejection under $V_p(z)$ is obviously a non-equilibrium, metastable effect, as Na⁺ and Cl⁻ will eventually gain substantial favorable free energy if transported far across the membrane to the right-hand side. For reverse osmosis and most other real-world applications, however, the applied pressure P on aqueous systems is small. Using $P = F/a^2$ where F is the force, and approximating the water surface area a^2 as $a = V_w^{1/3}$ Å where $V_w = 29.9$ Å³ is the reciprocal water density under room conditions,¹⁷ an applied pressure of 68 atm. corresponds to $B = 0.0096$ kcal/mol/Å. Thus $V_p(z) = -Bz$ is clearly too small to modify significantly a barrier that exists over, at most, a 30 Å range (Fig. 1(a)).

In principle, pressure-driven effects can readily be investigated with non-equilibrium molecular dynamics (MD) simulations and atomistic models. The use of popular and cost-efficient water models like SPC/E¹⁸ inside narrow nanopores obviates the need to specify in advance the dielectric response of water in these regions. There are some practical obstacles, however. Water dynamics may already be slowed by the nanoscale confinement effects; ionic motion, usually slower than that of water, may be further limited, especially if there are charged trapping sites on the surface, leading to the need for long MD trajectories. MD simulations typically can achieve a description of system dynamics occurring on the order of nanoseconds or at most a microsecond. If ions are not observed to penetrate a membrane in a particular trajectory, it may mean either that the applied pressure is consistent with total ion rejection, or merely that longer runs are needed. To shorten the simulation times, unphysically large (up to 3000 atm.) pressures have often been used to drive liquid through model membranes to accelerate ion transport, particularly those inside narrow single-file water nanopores.^{19–21} However, this would yield B as large as 0.5 kcal/mol/Å, which can now substantially modify the shape and magnitude of ion permeation barriers. Thus, even though a simulation may contain a realistic atomistic membrane model, the limitations on available time scale may mandate a pressure that makes the simulation *unrealistic*. Given these difficulties, as mentioned in Ref. [22], most MD simulations of ion transport/blocking through nanopores utilize applied electric fields rather than applied pressure.

In this work, we apply pressure no greater than $B = 0.05$ kcal/mol (340 atm.) and investigate how the magnitude of B affects the Cl⁻ rejection ratio. We use a simplified, dipolar pore model with a 12 Å pore diameter, first reported in Ref. [16], to explore, qualitatively, electrolyte transport through nanoporous membranes. As the pore interior surface exhibits no roughness, transport of electrolyte will be fast²³ despite the modest applied pressure, thus permitting the investigation of pressure-driven phenomenon on nanosecond time scales. In this sense, our predictions should be particularly pertinent to pressure-driven flow through smooth nanotube membranes that permit inherent extremely fast water transport rates.^{22, 24, 25} We perform both equilibrium potential of mean force ($W(z)$) estimates and non-equilibrium MD simulations

of anion passage under external forces. We also explore the correlation between the two, and highlight the dynamical effects associated with pressure-driven electrolyte rejection through nanopores, where there is an electrostatic barrier associated with the anion but not the cation.

We further investigate the effect of decorating the rim of our nanopore with negative charges instead of a dipole layer. By varying solution pH and salt concentration, Holt et al.²⁵ determined that the “Donnan” ion exclusion mechanisms applies in carbon nanotubes. In other words, anions are repelled from the negatively charged rim region, and this substantially reduces the amount of salt (including the counter cation) that can pass through the nanotube. Hinds et al.²⁴ indeed found that there are approximately 4 COOH groups on the rims of ~2 nm diameter single-walled carbon nanotube while Fornasiero et al.²² report 7 such groups. Another mechanism of ion exclusion by a nanopore concerns the Debye screening length, λ . λ is proportional to the inverse square root of the salt concentration. If 2λ exceeds the pore diameter, ion rejection due to surface charge effects is proposed to be operative.²⁶ While our simulation conditions are set to yield λ on the order of a water diameter, the narrow pore diameter (~12 Å) in our model suggests that an unexpected ion transport mechanism may operate. Thus, we decorate the interior of the nanopore with negative charges and perform non-equilibrium simulations as well. Our simulations will clarify the mechanism of ion transport and rejection in these nanopores.

Our work differs from most simulations performed in the literature in the following ways:

1. The nanopores are hydrophilic;
2. They are wider than most previous modeling studies, and thus more similar to the carbon nanotube membranes studied in recent experimental work^{22, 25};
3. Due to the decorated rims (if present), local excess of cations or anions may build up near the entrance and exit regions, causing excess space charge to appear;
4. In contrast to the previous dipolar pore simulations,¹⁶ we do not use an electric field, but instead a pressure gradient.

This work is organized as follows. Section 2 documents the computation method and model used. The results are described in Sections 3 and 4 concludes this work with further discussions.

2. METHOD

MD simulations utilize the LAMMPS code,²⁷ the SPC/E water model,¹⁸ Na⁺ and Cl⁻ forces fields devised by Rajamani et al.,²⁸ and a coarse-grained “membrane geometry” nanopore model,¹⁶ (see Fig. 2). The dimension of the simulation cell is $40 \times 40 \times 120$ Å³. The two identical reservoirs are 26 Å deep and the membranes are each 34 Å thick. This dual-reservoir geometry was also used in Ref. [29], but osmotic pressure, not an Eq. 1-like pressure gradient, was responsible for the water flux therein. This configuration allows a space charge to build up over time in the middle reservoir, which initially contains no ions, and permits the simulation of non-equilibrium effects associated with preferential cation permeation.

Interactions between the ~12 Å diameter smooth nanopore surface with water and ions is hydrophilic and is fitted to mimic a tube of Lennard-Jones spheres. In addition, there is a uniform dipole layer with surface density times dipole magnitude $\sigma_d|d|$ such that a potential of -71.7 kcal/mol/ $|e|$ would be exerted inside the pore if it were infinitely long. This electrostatic potential attracts cations and repels anions in the leftmost pore, only. The magnitude of this dipole layer is about three times that found in a charge-neutral atomistic silica nanopore model,¹¹ but is less than that inside some biological trans-membrane channels.¹² The membrane surface also exhibits Lennard-Jones-like interactions with the electrolyte similar to that inside the nanopore, but it does not contain dipoles; otherwise, the electrostatic bias will vanish.¹⁶

The total number of water molecules is determined by setting the water density to be 1.0 g/cc at the middle of the 26 Å reservoirs. Then the appropriate number of H₂O molecules are randomly replaced by a Na⁺Cl⁻ contact ion pair to achieve a 1.0 M salt concentration in the entire system without further adjustment of the water content.

An equilibration run is conducted for 0.5 ns, after which all the Na⁺ and Cl⁻ in one of the reservoirs and most of the ions inside the nanopores are removed, and another 0.5 ns equilibration run is conducted. To satisfy electroneutrality, occasionally the starting configuration has one or two Na⁺ or Cl⁻ residing in one of the nanopores. This initialization procedure is also used for systems decorated with charges at the pore entrance, except that the total number of Cl⁻ ions in the system is decreased by the same amount of fixed charges introduced. Thus, when there are 8 fixed negative charges present, the Cl⁻ concentration is 0.7 M rather than 1.0 M.

As will be discussed in the next section, the pressure-driven water flux in this system is much higher than in single-file narrow nanotube simulations, and a 0.5 ns MD trajectory is more than sufficient to equilibrate the osmotic pressure. We have also varied the initial configurations and found that the Cl⁻ rejection ratio does not strongly depend on how the systems are prepared (see the next section).

To apply external pressure, we add a constant force to Na⁺, Cl⁻, and the oxygen site of H₂O along the *z* direction (from left to right in Fig. 2).¹⁷ We focus on *B* = 0.024 and 0.0096 kcal/mol (see Eq. 1), but consider other *B* values as test cases. Assuming a (29.9)^{2/3} Å water molecule surface area, the two *B* values exert 170 and 68 atm. pressures on pure H₂O, respectively. Since Na⁺ and Cl⁻ have radii different from that of H₂O, applying *V_p*(*z*) may seem to yield a different local “pressure” on these ions. However, ions are buffeted by water, constantly exchanging momenta with their hydration shells. Indeed, even if *V*(*z*) is applied only to water and not the ions, the MD results remain qualitatively the same (again, see the next section).

A Nose thermostat is applied to maintain the temperature at 300 K. This is crucial because energy is being added to the system via *V_p*(*z*). It also means that the dynamics are not strictly Newtonian. In this study, however, we are more concerned with qualitative features and do not consider the subtlety involved with NVE versus NPT ensemble dynamics. The net flux of water inside the nanopore in the *z*-direction is less than 10 m/s even at *B* = 0.024 kcal/mol. This is much smaller than the thermal velocity of water at *T* = 300 K; hence we have not subtracted the net flux when computing the temperature. H₂O molecules in the reservoir regions exhibit far smaller net drifts than those in the pore. Due to the periodic boundary conditions used, in the presence of a large cationic space charge in the middle reservoir, Cl⁻ can potentially back-flow through the rightmost nanopore. To prevent this, a Cl⁻ is placed at the exit of that nanopore to block anion passage (Fig. 2).

For this study of electrolyte pressure-driven flow across a simplified membrane/nanopore model, investigating water transport is not the main goal. Nevertheless, computing the water flux is crucial to quantifying the ion rejection ratio. This is estimated by breaking the trajectory into 100 ps or shorter segments, counting the net number of H₂O that have crossed the midpoint of the leftmost nanopore in each segment, and accumulating the results. The segment length is chosen for each *B* so that no water molecules traverse more than half the unit cell size in the *z* direction in that duration to avoid periodic boundary condition ambiguities. This criterion is also used to count the number of Cl⁻ passing through the nanopore. The ion rejection ratio over a trajectory is then one minus the number of permeant Cl⁻ divided by the number of permeant water molecules multiplied by 1/55.6, which is roughly the initial concentration of Cl⁻ in the leftmost reservoir in dipolar pore systems. The number of permeant Na⁺ is found to track that of Cl⁻. This is a qualitative estimate; the leftmost reservoir becomes depleted of

NaCl at long times, and the ion rejection ratio is underestimated when a few Cl^- have exited the leftmost reservoir. We end each simulation either when 7 Cl^- have crossed the mid-point of the leftmost nanopore, or in a few cases at $t = 6$ or 14 ns. As discussed earlier, initial NaCl concentrations in the rim-decorated nanopore simulations are slightly lower.

Equilibrium potential of mean force calculations apply the 2-point thermodynamic integration (TI) or “charging” procedure for ions frozen along the pore center at various z positions as described in Refs. [11–16], and [30]. A simulation cell half as large in the z direction (60 Å), with only a single reservoir, suffices to yield converged ion hydration free energy.¹⁶ A 2.0 ns MD trajectory is used for each TI sampling window. A more accurate 6-point integration formula is found to yield $W(z)$ values within 1.0 kcal/mol of the 2-point predictions at two select values of z .

3. RESULTS

3.1. Equilibrium Considerations

First we consider $W(z)$ for a Cl^- frozen at different positions inside a dipolar nanopore in the salt solution. Similar $W(z)$ calculations have been performed for Na^+ in pure water and in 1.0 M electrolyte.¹⁶ The larger Cl^- ion is, however, more susceptible to a pure confinement free energy penalty,¹⁰ in addition to electrostatic interactions screened by water and the counter ions present. Along the pore axis, a free energy difference of 6.4 kcal/mol emerges between the center of the reservoir and the middle of the dipolar nanopore.³¹ Although the dipole layer-induced repulsion of Cl^- rapidly falls off radially from the pore axis inside the reservoirs,¹⁶ this free energy profile is pertinent. For example, a Cl^- that approaches the nanopore entrance radially, say at $z = 12$ Å, will still experience an activation free energy of $W(z = 12 \text{ Å})$ when it approaches the pore axis at that value of z before it can enter the nanopore. We have not considered radial motion of Cl^- in $W(z)$ calculations because previous simulation inside silica model pores has shown that the effect on $W(z)$ is small.¹¹

Adding $V_p(z)$ to the equilibrium $W(z)$ modifies the barrier height by only a small fraction of 1 kcal for both values of B used. Given the barrier height of ~6 kcal/mol and the diffusion rate of Cl^- (which is related to the frequency factor for attempting barrier crossing in our case), we expect this B is sufficient to block Cl^- diffusion through the nanopore in nanosecond time scales under equilibrium conditions. Conversely, the dipolar layer attracts Na^+ , and the cation is sucked into the leftmost pore at the entrance region, but experiences a barrier when it attempts to *exit* the nanopore. (The unscreened Na^+ electrostatic energy profile is the inverse of Fig. 1 (a).)

3.2. Ion Rejection in Pressure-Driven Flow in Dipolar Pores

The non-equilibrium MD results are listed in Table I. Here we highlight two cases: $B = 0.024$ and 0.0096 kcal/Å. Figure 2 depicts snapshots in non-equilibrium dynamical simulations at different applied pressure gradients. At $t=0$, the “pure water” reservoir in the center is devoid of ions, and two Na^+ first become embedded in the dipole-lined leftmost nanopore. With $B = 0.024$ kcal/Å, 2 Na^+ and 2 Cl^- are observed either passing through or have exited the dipolar nanopore after just 0.7 ns (Fig. 2(b)) in addition to the Na^+ present at $t = 0$ ns. Another 2.15 ns later, 7 Cl^- have traversed to the middle reservoir, and the Na^+ -only occupancy of the dipole-lined leftmost nanopore—a stable configuration similar to that seen at $t = 0$ ns—is restored (Fig. 2(c)). 593 H_2O molecules have traversed the membrane in these 2.85 ns. The water flux is dynamically heterogeneous, and fluctuates between 7 and 32 H_2O in each 100 ps window. Counting only Cl^- , the salt solution that emerges through the left-most nanopore has a concentration of 0.66 M, which implies a rejection ratio of 34% compared to the 1.0 M concentration in the initial salt solution reservoir. We also conduct a second simulation with a

different initial configuration. The atomic positions here are generated by first performing a 0.5 ns MD run with a small $B = 0.0048$ kcal/mol/Å on the $t=0$ configuration of the first simulation; this B value and the short trajectory length allow water but no salt transport. The alternate run yields a 29% ion rejection ratio over a 2.3 ns trajectory. The results are thus consistent with the first run (Table I). Despite the 6.4 kcal/mol equilibrium barrier, applying this 170 atm. pressure leads to substantial Cl^- transmission.

The mechanism of Cl^- translocation is illustrated in the snapshots of Figures 2(b) and (d). It occurs in stochastic bursts, apparently enabled by Na^+/Cl^- contact ion pairing or larger aggregate formation that lowers the local, instantaneous Cl^- free energy near the barrier region. The leftmost nanopore entrance is indeed a bottleneck; once Cl^- moves past this region, it generally proceeds to the middle reservoir without recrossing. If $V_p(z)$ is only applied to H_2O but not Na^+ or Cl^+ at $B = 0.024$ kcal/mol/Å, the snapshot obtained at $t=1$ ns is qualitatively similar to that when the ions also experience $V_p(z)$; within this time, 3 Cl^- are observed to have passed through the nanopore. Conversely, when $V_p(z)$ is applied only to Cl^- and Na^+ , no ion translocation is observed in 1 ns MD trajectories—even when a Cl^- starts at the pore entrance and B is increased to 0.05 kcal/mol/Å. The tests confirm that the ion translocation is induced by the water flux and not the external forces acting directly on the ions. This feature is one major difference between electro-osmotic and pressure-driven ion flow through nanopores. In the former case, water is polarized by the electric field and screens its magnitude, but does not flow along the field directions or transport ions through its driven, collective motion. A second difference is, obviously, that cations and anions are being driven in opposite directions when an electric field is present.

For $B = 0.0096$ kcal/mol/Å, only 1 Na^+/Cl^- pair has passed through the leftmost nanopore within 3 ns (Fig. 2(e)). After 22.4 ns, 7 Cl^- have entered the middle reservoir. This translates into a Cl^- rejection ratio of 78%. The two B values and their corresponding water fluxes are roughly proportional to each other. A simulation initiated using the alternate configurations described for $B = 0.024$ kcal/mol/Å yields a similar 85% rejection rate (Table I). The two $B = 0.0096$ kcal/mol/Å runs consistently yield ion rejection ratios that are much higher than those for $B = 0.024$ kcal/mol/Å. Over the duration of the simulation, at least two or three cations persist in the nanopore, despite the fact that the average H_2O flux is found to be 85 molecules/ns. Na^+ transport occurs mainly as Na^+/Cl^- ion pairs or as larger ionic aggregates.

Other results for the dual reservoir, $L = 120$ Å simulation cell, tabulated in Table I, are consistent with these trends. The highest $B = 0.048$ kcal/mol/Å value yields the highest water flux and the lowest average ion rejection ratio. Note that when the ion flux through the membrane approaches the starting concentration of 1.0 M, the rejection ratio is small and exhibits large statistical noise. Statistics for the lowest $B = 0.0048$ kcal/mol/Å are also poor due to the slow electrolyte motion and the infrequency of ion permeation events, but the Cl^- rejection ratio is similar to those for $B = 0.0096$ kcal/mol/Å. The water flux scales linearly with B except for the highest B , suggesting $B \leq 0.0096$ kcal/mol/Å simulations are in the linear-response regime.

We also consider the effect of system size by increasing the thickness of reservoirs and membranes by a factor of 2 (i.e., $L = 240$ Å). At $B = 0.0096$ kcal/mol/Å, the water flux is significantly faster in the longer pore than that in the $L = 120$ Å system. It approaches that of $B = 0.024$ kcal/mol/Å for the $L = 120$ Å system. This result contrasts with water flux in carbon nanotube membranes reported earlier.²⁹ In our study, this higher water flux (not the main object of this work) can be attributed to less “roughness,” in the form of the reservoir-membrane interface, per unit length in the larger simulation cell, the wider pore diameter, and perhaps also to the Cl^- which “stoppers” the rightmost pore exit. For the longer pore, the ion rejection ratio also strongly depends on the water flux. We caution that shorter trajectories are used for these larger, more computationally costly systems.

Interestingly, a theoretical study with a water flux several orders of magnitude smaller than ours predicts opposite trends, namely, that higher water fluxes yield higher salt rejection (or “retention”) ratios, until a plateau is reached.²⁶ (See Fig. 6 in that work.) The mechanism depicted in that work is substantially different from ours. It appears to operate at low salt concentrations, and leads to almost no ion rejection at 0.1 M or higher concentrations (Fig. 5 of Ref. [26]). Our water and ion fluxes at $B = 0.0096$ kcal/mol/Å are comparable with those recently predicted in membranes made up of (8,8) or even more narrow carbon nanotubes.²¹ However, a much higher applied pressure is needed to achieve such water fluxes in that work, and the high polarizability of these metallic (8,8) tubes³² is not taken into account.

3.3. Pressure-Driven Flow in Charge-Decorated Pores

This section considers pressure-driven electrolyte flux through the membrane when the leftmost nanopore is decorated with fixed $-|e|$ charges along the rims or inside the leftmost nanopore instead of a dipolar layer. The added negative charges have Lennard-Jones parameters identical to those of the Cl^- force field.

Charges on the rims qualitatively mimic deprotonated COOH groups on the edges of carbon nanotube membranes.^{24, 25} The negatively charged spheres are placed 7.5 Å from the pore axis and 1 Å within the membrane.³³ While we have not performed potential of mean force calculations, the barrier induced by the rim charges should hinder Cl^- entry under equilibrium conditions. Instead, with $B = 0.024$ kcal/mol/Å, both Na^+ and Cl^- readily pass through the membrane. Unlike the dipolar pore case, a higher concentration of Na^+ is seen at the entrance region to compensate for the negative rim charges. Cl^- again enters the nanopore while forming contact ion pairs or even larger aggregates with the high local concentration of Na^+ there (see Fig. 3(a)). The initial NaCl concentration in the leftmost reservoir is a 0.70 M in this simulation. The output solution contains 0.51 M Cl^- . This yields a rejection ratio of only 37%. The water flux is similar to that in the dipolar nanopores. The ion rejection ratio is also fortuitously similar to the dipolar nanopore case at the same applied pressure. At a lower $B = 0.0096$ kcal/mol/Å, the rejection ratio increases. These MD simulations suggest that, even when the Donnan mechanism⁸ of ion rejection is observed in experiments with charged sites at the entrances, ²² a sufficiently high pressure should permit unhindered salt passage. Note that the experiments on the carbon nanotube membranes have been performed at less than 1 atm. excess applied pressure.²²

Figure 3(c) depicts a snapshot of a simulation where 8 $-|e|$ charges are arranged in a spiral at a radius of 6.5 Å inside the leftmost nanopore. They are meant to qualitatively mimic deprotonated SiO^- groups inside silica nanopores. At equilibrium, a layer of 8 Na^+ counter ions reside immediately next to the fixed negative charges. No free Na^+ and Cl^- are observed inside the nanopore. At $B = 0.024$ kcal/mol/Å, the water flux is slower than in dipolar pores, only averaging 80 $\text{H}_2\text{O}/\text{ns}$. After a 2.0 ns simulation, we observe 4 Cl^- penetrating and passing through this nanopore, buffeted the Na^+ counter ions already present and other Na^+ which enter as ion pairs (Fig. 3(c)). Cl^- exit the channel accompanied by Na^+ . 7 Cl^- have traversed the nanopore in 3.9 ns (Table I). No ion rejection can be inferred from this simulation. Nanoslits with fixed negative charges have been shown to yield anomalously high cation flux at low salt concentration.⁴ Here we demonstrate that narrow, 1.2 nm diameter nanopores lined with negative charges can yield high pressure-driven *anion* and cation transmission through ion pairing as well. Given the small lengthscales present, it is unclear whether the Debye model of ion exclusion applies. While the Debye length in 1.0 M salt solution is on the order of $\lambda \sim 3$ Å, the absence of free Na^+/Cl^- inside the pore at $t = 0$ seems to imply larger Debye screening length.

4. DISCUSSIONS

In non-equilibrium molecular dynamics (MD) simulations of pressure-driven electrolyte flow through nanoporous membranes, the applied pressure is typically inflated to accelerate the electrolyte motion so that significant salt and water motion can be observed within MD time scales. In this work, we investigate the effect of varying pressure on salt passage through a nanopore embedded in a solid membrane, with no need to apply extremely high pressures due to a simplified model free from features that would slow ion and water passage. This model may be particularly relevant to carbon nanotube membranes, which exhibit fast water transport rates.^{22, 24, 25} Cl^- repulsion is achieved at equilibrium due to a combination of nanoconfinement and electrostatic effects, while Na^+ exhibits attraction inside the pore.

We apply pressure to drive a 1.0 M NaCl electrolyte into the dipolar nanopore through a membrane. The pressure can be represented as a static potential $V_p(z) \sim -Bz$, which is superimposed on the dipolar repulsion of Cl^- screened to some extent by the nanoconfined water at finite membrane thickness.¹⁶ We compute the potential of mean force of Cl^- inside a dipole-lined nanopore penetrating a model membrane in the presence of a 1.0 M NaCl solution. A 6.4 kcal/mol barrier associated with Cl^- entry is predicted. For the pressures applied herein, in the range 34 to 340 atmospheres, $V_p(z)$ modifies the electrostatics-derived barrier height at the nanopore entrance by only a small fraction of a kcal/mol. If we only apply $V_p(z)$ to Na^+ and Cl^- , no ion transmission through the nanopore is observed in nanosecond time scales. In other words, the ion rejection ratio is unity. This is consistent with a barrier of magnitude significantly higher than $1 k_B T \approx 0.6$ kcal/mol. In published MD simulations where a large O (1000) atmosphere pressure is applied to drive water through more constricted nanopores, the pressure *may* modify the ion entry potential of mean force by several kcal/mol. To our knowledge, this effect has not been sufficiently investigated.

When $V_p(z)$ is also applied to water molecules, the resulting water flux leads to substantial salt translocation. Cl^- enters and passes through the nanopore in stochastic bursts after forming contact ion pairs or even larger ionic aggregates with Na^+ near the pore entrance. The ion rejection ratio decreases monotonically with water flux, falling from $\sim 75\%$ to $\sim 33\%$ between $B = 0.0096$ kcal/mol/Å and 0.024 kcal/mol/Å. Therefore equilibrium considerations, e.g., free energy calculations, do not completely determine ion rejection behavior, at least under these high water flux conditions.

This decrease with increasing water flux was not predicted at low flux rates that are orders of magnitude lower.²⁶ The mechanism responsible for the decrease is at present not precisely known. While Cl^- entry into nanopores is aided by ion-pairing due to the lower dielectric screening inside the confined nanopore, such aggregation is already present under equilibrium, the same zero water-flux conditions used in computing the potential of mean force. The rate of activated processes is usually described as $k \sim \kappa \exp(-\Delta G^\ddagger/k_B T)$, where $\Delta G^\ddagger$ is the free energy barrier and κ is a frequency factor. If κ , related to the probability that NaCl exists at the nanopore entrance region, scales as the water flux, it should be proportional to B and should not affect the ion rejection ratio. Here we conjecture that the electrostatic barrier at the pore entrance channels the local Na^+ and Cl^- fluxes into disparate spatial regions. Since ion pairing is observed to be critical for Cl^- passage into the narrow nanopore and this requires a Na^+ flux, κ may in fact scales as the square of the water flux at the highest water transport rates. (Recall that Na^+ does not aggregate at the entrance of dipolar nanopores, but actually favors the pore interior.)

An alternate explanation is that the larger water fluxes observed in our simulations of smooth nanopores reduce $\Delta G^\ddagger$. If so, it may be consistent with the fact that Cl^- is strongly bound to its hydration shell water molecules and the entire shell moves in unison over picosecond

timescales, resulting in a much larger pressure-induced effective force than an isolated Cl^- under the influence of $V_p(z)$ would experience. These rationales will be investigated in the future using longer runs and by varying the shape of the nanopore entrance barrier, or even by changing the temperature.

We also consider negative charges decorating the rim and the interior of the pore instead of dipoles. Experimentally, these systems have been known to reject anions.²² However, at a high enough pressure, Cl^- from a 1.0 M NaCl solution can still readily pass through such nanopores. This illustrates the importance of applying realistic pressures when conducting molecular dynamics simulations of salt rejection.

These preliminary model studies of pressure-driven transport of electrolyte through electrostatic barriers are meant to spark interest and future work in this important area. Further studies that vary the salt concentration and nanopore diameter, and apply more realistic atomistic pore models, will be conducted in the future.

Acknowledgments

We thank Tom Mayer for useful suggestions, and Chris Lorenz and Sameer Varma for discussions about applying pressure in molecular dynamics settings. This work was supported, in part, by Sandia's LDRD program, and, in part, by the National Institutes of Health through the NIH Roadmap for Medical Research. Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company, for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AL8500.

References

1. Gijs MAM. *Nat. Nanotech* 2007;2:268.
2. Cygan RT, Brinker CJ, Nyman MD, Leung K, Rempe SB. *MRS Bull* 2008;33:42.
3. Hille, B. *Ionic Channels of Excitable Membranes*. Sinauer Associates; Sunderland, MA: 2001.
4. Stein D, Kruithof M, Dekker C. *Phys. Rev. Lett* 2004;93:035901. [PubMed: 15323836]
5. Daiguji H, Yang PD, Majumdar A. *Nano Lett* 2004;4:137.
6. Gracheva ME, Vidal J, Leburton J-P. *Nano Lett* 2007;7:1717. [PubMed: 17516680]
7. Karnik R, Duan CH, Castelino K, Daiguji H, Majumdar A. *Nano Lett* 2007;7:547. [PubMed: 17311461]
8. Donnan FG. *J. Membr. Sci* 1995;100:45.
9. Beckstein O, Tai K-H, Sansom MSP. *J. Am. Chem. Soc* 2004;126:14694. [PubMed: 15535674]
10. Peter C, Hummer G. *Biophys. J* 2005;89:2222.
11. Leung K, Rempe SB, Lorenz CD. *Phys. Rev. Lett* 2006;96:095504. [PubMed: 16606277]
12. Varma S, Rempe SB. *Biophys. J* 2007;93:1093. [PubMed: 17513348]
13. Rasaiah JC, Garde S, Hummer G. *Annu. Rev. Phys. Chem* 2008;59:713. [PubMed: 18092942]
14. Mulder, M. *Basic Principles of Membrane Technology*. Kluwer; Dordrecht: 1997.
15. Marti J, Nagy G, Guardia E, Gordillo MC. *J. Phys. Chem. B* 2006;47:23987. [PubMed: 17125368]
16. Leung K. *J. Am. Chem. Soc* 2008;130:1808. [PubMed: 18201086]
17. Lorenz CD, Crozier PS, Anderson JA, Travesset A. *J. Phys. Chem. C* 2008;112:10222.
18. Berendsens HJC, Gridera JR, Straatsma TP. *J. Phys. Chem* 1987;91:6269.
19. Zhu FQ, Tajkhorshid E, Schulten K. *Biophys. J* 2002;83:154. [PubMed: 12080108]
20. Suk ME, Raghunathan AV, Aluru NR. *Appl. Phys. Lett* 2008;92:133120.
21. Corry B. *J. Phys. Chem. B* 2008;112:1427. [PubMed: 18163610]
22. Fornasiero F, Park HG, Holt JK, Stadermann M, Grigoropoulos CP, Noy A, Bakajin O. *Proc. Am. Acad. Sci.* (in press).
23. Joseph S, Aluru NR. *Nano Lett* 2008;8:452. [PubMed: 18189436]
24. Hinds BJ, Chopra N, Rantell T, Andrews R, Gavalas V, Bachas LG. *Science* 2004;303:62. private communications. [PubMed: 14645855]

25. Holt JK, Park HG, Wang YM, Stadermann M, Artyukhin AB, Grigoropoulos CP, Noy A, Bakajin O. Science 2006;312:1034. [PubMed: 16709781]
26. de Lint WBS, Benes NE. J. Membr. Sci 2004;243:365.
27. Plimpton, SJ. J. Comp. Phys. 1995. p. 1<http://lammmps.sandia.gov>
28. Rajamani S, Ghosh T, Garde S. J. Chem. Phys 2004;120:4457. [PubMed: 15268613]
29. Kalra A, Garde S, Hummer G. Proc. Natl. Acad. Sci 2003;100:10175. [PubMed: 12878724]
30. Asthagiri D, Pratt LR, Ashbaugh HS. J. Chem. Phys 2003;119:2702.
- 31.
32. Leung K, Marsman M. J. Chem. Phys 2007;127:154722. [PubMed: 17949206]
- 33.

Fig. 1.

(a) Black line: electrostatic energy experienced by Cl^- along the pore center in vacuum. Red and green: pressure induced potential $V_p(z) = -Bz$ for Cl^- , with $B = 0.0096$ and 0.024 kcal/mol/Å, respectively. (b) Equilibrium potential of mean force $W(z)$ for Cl^- frozen along the pore center in a 1.00 M NaCl electrolyte. (c) $W(z)$ added to $V_p(z)$ for the two values of B listed above.

Fig. 2.

Snapshots of electrolyte configuration with a dipolar layer present inside the leftmost nanopore. (a) $t = 0$ ns; (b) $t = 0.7$ ns $B = 0.024$ kcal/mol/Å; (c) $t = 2.85$ ns $B = 0.024$ kcal/mol/Å; (d) $t = 1.75$ ns $B = 0.024$ kcal/mol/Å (alternate initial configuration); (e) $t = 3.0$ ns $B = 0.0096$ kcal/mol/Å. Red, white, blue, and green spheres represent O, H, Na^+ , and Cl^- respectively. Periodic boundary conditions are applied in all three dimensions. The brown sphere at the right-side exit of the rightmost nanopore is a Cl^- fixed in space to prevent other Cl^- reaching the middle reservoir through the rightmost nanopore. Only one randomly chosen H_2O out of ten is depicted for clarity purposes. External pressure is applied by adding a constant force to all ions and water oxygens along the z direction (from left to right).

Fig. 3.

(a) 4 fixed negative charges (yellow spheres) on each rim of the leftmost nanopore, arranged symmetrically at a radius $R = 7.5 \text{ \AA}$ from the pore center, and at $z = 14$ and $46 \text{ \AA}$, respectively. The snapshot is taken 2 ns into the trajectory starting from a configuration with no Na^+ or Cl^- inside the channel. (b) and (c) 8 fixed negative charges inside the leftmost nanopore arranged in a spiral at $R = 6.5 \text{ \AA}$. (b) $t = 0 \text{ ns}$; (c) 2.0 ns . $B = 0.024 \text{ kcal/mol/\AA}$, in all cases, and no surface dipole is present.

Table I

Water flux (F_w in molecules/ns), numbers of permeant H_2O (N_w) and Cl^- flux (N_{Cl}), and ion rejection ratio (R) as a function of the applied pressure gradient B (in units of kcal/mol/Å), length of the double-reservoir simulation cell L (Å), run time t (ns), and type of electrostatic barrier that renders Cl^- entrance unfavorable in the leftmost pore: dipolar, charges on rim, or charges arranged in a spiral in the pore interior. In some cases multiple runs with different configurations are made. The dipolar pore cases start with 1.0 M NaCl in the leftmost reservoir, charge-decorated pores with a lower concentration (see text).

B	L	Type	t	F_w	N_w	N_{Cl}	R
0.048	120	Dipole	0.85	571	498	7	0.21
0.048	120	Dipole	0.65	618	402	7	0.03
0.048	120	Dipole	1.00	569	569	7	0.32
0.024	120	Dipole	2.75	216	593	7	0.34
0.024	120	Dipole	2.30	237	545	7	0.29
0.0096	120	Dipole	22.40	78	1754	7	0.78
0.0096	120	Dipole	14.20	85	1201	4	0.81
0.0048	120	Dipole	22.80	45	1024	6	0.68
0.0096	240	Dipole	1.50	270	405	7	0.04
0.0048	240	Dipole	6.00	99	596	4	0.63
0.024	120	Rim	3.70	239	882	7	0.37
0.0096	120	Rim	11.20	82	1265	7	0.56
0.024	120	Spiral	3.90	87	340	7	~0