

## Effect of size-asymmetric electrolyte on single-file osmosis

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Single-file osmosis through a 0.9 nm diameter semipermeable carbon membrane using various size-asymmetric electrolyte solutions is investigated using molecular dynamics simulations. In an uncharged pore, the osmotic flux with a KCl solution is found to be higher than that of in a NaCl solution, i.e.,  $J_{\text{KCl}} > J_{\text{NaCl}}$ , for the same concentration gradient of solute. Mean force and hydration analysis indicate that distinct ion-water and ion-pore molecular interactions cause a differential cation and anion affinity to the pore, leading to the observed size-asymmetric electrolyte dependence on osmotic flux. The water orientation in the pore during osmosis is also related to the ion affinity and exhibits a size-asymmetric electrolyte dependence. © 2006 American Institute of Physics. [DOI: 10.1063/1.2335969]

Osmosis is defined as the phenomenon in which a solvent is driven by its free energy gradient through a semipermeable membrane towards a solute-rich reservoir. Osmosis is critical to living organisms, as it is the primary mechanism for water transport in and out of cells and membranes. Osmosis is widely encountered in a variety of fields including metal ion separation applications and osmoregulation in biological cells.<sup>1</sup> A molecular description of osmosis is of fundamental importance to understand and mimic biological functions as well as to design better filtration membranes. Recent studies on osmosis using molecular dynamics (MD) include the understanding of the mechanism of solvent transport through small pores using hard-sphere atoms (see, e.g., Ref. 2). Studies were also performed to understand the effect of electrolyte on osmosis, but these were performed in leaky membranes where both water and ions go through the pore.<sup>3</sup> In this letter, using detailed MD simulations, we investigate the effect of size-asymmetric electrolytes on osmosis through an uncharged semipermeable membrane (only water is transported through the membrane pore). For an uncharged pore, the osmotic flux when the chambers are filled with a KCl solution is found to be higher compared to that of when the chambers are filled with a NaCl solution ( $J_{\text{KCl}} > J_{\text{NaCl}}$ ). Similar observations were made with salt solutions of KF and LiCl, i.e.,  $J_{\text{KF}} > J_{\text{LiCl}}$ . The differential affinity of the cation and the anion of the size-asymmetric electrolyte towards the pore effects the osmotic flux through the pore as well as the water orientation in the pore.

The MD simulation system (see Fig. 1 for a snapshot) consists of two square membranes (3.3 nm long in the  $x$  and  $y$  directions and 1.5 nm thick) connected back-to-back separating two electrolytes of different concentrations, with periodic boundary conditions applied in all the three directions. Each membrane consists of a semipermeable pore with a diameter of 0.9 nm. The membrane and the pore atoms are modeled as Lennard-Jones (LJ) atoms with parameters for carbon<sup>4</sup> and are frozen to their lattice positions. An extended simple point charge model<sup>5</sup> is used for water, while ions are modeled as charged LJ atoms.

MD simulations were performed using GROMACS 3.1.4 (Ref. 6) in the  $NVT$  ensemble, with the temperature of the fluid maintained at 300 K using a Berendsen thermostat. The electrostatic interactions were computed using the particle mesh Ewald method.<sup>7</sup> The LJ cutoff and the real space cutoff for electrostatic calculations were 1 nm. The low and high solute chambers were initially filled with the electrolyte of concentrations of 0.3M and 1.85M, respectively. Water was allowed to enter the pore during a 1 ns equilibration run. Thereafter, the simulation was run for 200 ps to ensure that the hydrostatic pressure in both chambers is the same ( $\approx 40$  bars). Two different equilibrated configurations were simulated in MD for 4 ns, keeping the initial number of water and solute molecules the same in both simulations. The trajectory was saved every 0.1 ps and the calculation of the potential of mean force (PMF) for postprocessing analysis was carried out on the fly during the simulation.

With the MD setup described above, simulations were performed for four different size-asymmetric electrolytes (KCl, KF, NaCl, and LiCl, having different bare and hydrated radii). The osmotic flux variation in all the simulations was calculated from the MD simulation by tracking the number of water molecules in the chambers every 0.1 ps. At the start of the simulation, osmosis is dominant leading to the accumulation of water molecules in the high solute chamber ( $\text{CH}_h$ ) and decrease in the number of water molecules in the low solute chamber ( $\text{CH}_l$ ). However, the increase in the number of water molecules in  $\text{CH}_h$  leads to an increase in the hydrostatic pressure developed that tends to drive the water molecules in the direction opposite to that of osmosis. At

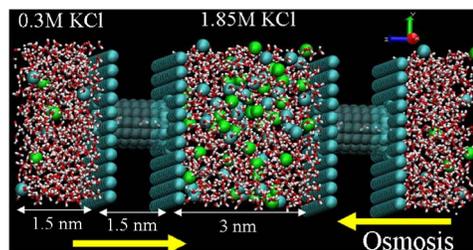


FIG. 1. Snapshot of the MD setup for osmosis. The middle chamber is  $\text{CH}_h$  (high solute concentration chamber) and the two outer chambers are  $\text{CH}_l$  (low solute concentration chambers).

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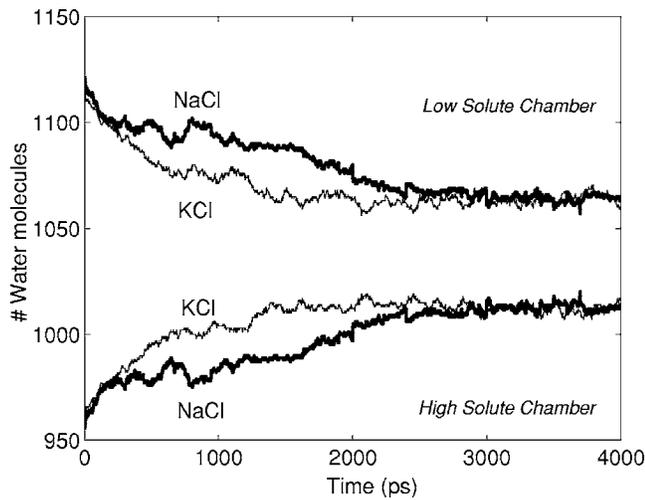


FIG. 2. Variation of the water occupancy in the two chambers during osmosis for NaCl and KCl electrolytes.

steady state, the hydrostatic pressure developed between ( $CH_h$ ) and ( $CH_l$ ) ( $\approx 74$  bars) balances the osmosis through the pore.

Figure 2 shows the variation of the number of water molecules with time in  $CH_l$  and  $CH_h$  chambers for KCl and NaCl solutions. We observe that the osmotic flux is higher when a KCl solution is used instead of a NaCl solution. In addition, the osmotic equilibrium is reached faster (in about 2 ns) when a KCl solution is used compared to the time required (close to 3 ns) with a NaCl solution. This dependence of the osmotic flux on the type of the salt can be explained by understanding the affinity of an ion (cation/anion) to a nanopore. The affinity of an ion to the nanopore mouth is defined as the closest approach of an ion to the pore mouth. For example, if a cation is closer to the pore mouth compared to an anion, this is referred to as cation affinity and vice versa. In the case of a KCl salt, we observed cation affinity (i.e.,  $K^+$  ions are closer to the pore mouth compared to the  $Cl^-$  ions) which led to a higher osmotic flux compared to an anion affinity in the case of a NaCl salt (the  $Cl^-$  ion was found to be closer to the pore mouth compared to the  $Na^+$  ion) which led to a lower osmotic flux. These observations and the inferences obtained from them are explained in more detail below.

The affinity of an ion towards a nanopore is primarily determined by two molecular interactions, namely, the ion-water interactions and the ion-nanopore interactions. Ion-water interactions determine the hydrated radius of an ion and are computed by accounting for the LJ and electrostatic interactions between the ion and the water molecules. Ion-nanopore interactions are computed by accounting for the LJ interaction between the ion and the carbon atoms of the nanopore. In a KCl solution, the LJ parameter,  $\sigma_{K^+-C} = 0.311$  nm, is smaller than the LJ parameter,  $\sigma_{Cl^- - C} = 0.365$  nm, implying that the  $K^+$  ion can go closer to the pore mouth compared to the  $Cl^-$  ion. In addition, the hydrated radius of a  $K^+$  ion (0.36 nm) is smaller than that of the  $Cl^-$  ion (0.39 nm), implying again that the  $K^+$  ion can go closer to the pore mouth region without significantly affecting its hydration shell as compared to a  $Cl^-$  ion. These observations are confirmed from PMF analysis shown in Fig. 3(a). In the low solute chamber ( $CH_l$ ), the PMF valley [see Fig. 3(a)] for the  $K^+$  ion in the centerline region is closer to

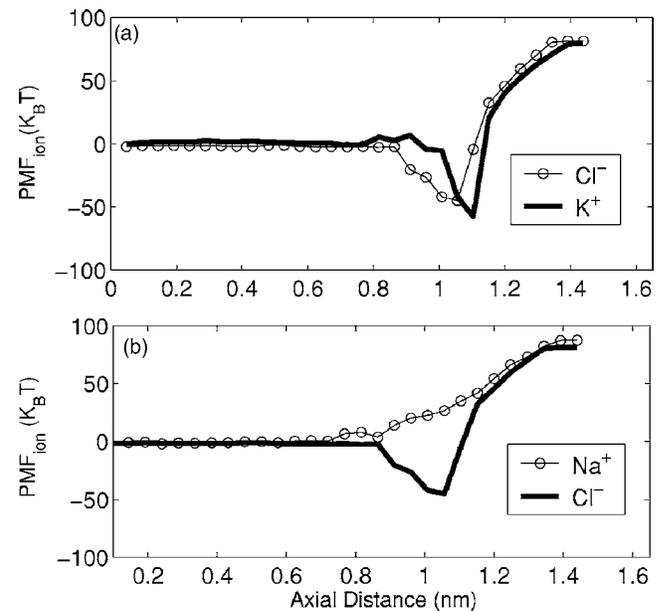


FIG. 3. Variation in the PMF of ions in the (a) KCl and (b) NaCl solutions along the centerline of  $CH_l$  chamber. The  $CH_l$ -nanopore interface is at an axial distance of 1.5 nm.

the pore mouth compared to that of the  $Cl^-$  ion. We also observed that near the pore mouth, the hydration number for the  $K^+$  ion is higher than that of the  $Cl^-$  ion. All the above observations imply a higher affinity of the  $K^+$  ion towards the pore mouth. We also observed that the water molecules close to the pore mouth orient with their oxygen atoms pointing towards the  $K^+$  ion and hydrogen atoms pointing towards the pore mouth. In fact, water molecules enter the pore with the same orientation i.e., with their dipole vector oriented in the direction from  $CH_l$  to  $CH_h$ . In the case of a NaCl solution, the LJ parameter,  $\sigma_{Na^+-C} = 0.3645$  nm, is similar to the LJ parameter,  $\sigma_{Cl^- - C} = 0.365$  nm, and thus the  $Na^+$  and  $Cl^-$  interactions with the carbon pore are similar. However, a smaller hydrated radius of the  $Cl^-$  ion (0.39 nm) as compared to the  $Na^+$  ion (0.42 nm) implies that the  $Cl^-$  ion can go closer to the pore mouth region without breaking its hydration shell as compared to the  $Na^+$  ion. This is also evident from the PMF valley observed for  $Cl^-$  ion close to the pore mouth in  $CH_l$ , as shown in Fig. 3(b). The water dipole orientation in the pore is in a direction opposite to that observed in the KCl solution case, i.e., from  $CH_h$  to  $CH_l$ . It was also observed that in the case of a KF solution (see Table I), the  $K^+$  ion is closer to the pore mouth and the water flux and water orientation were comparable to that of in a KCl solution. In a LiCl solution, the  $Cl^-$  ion is closer to the pore mouth as compared to the  $Li^+$  ion (which has higher hydration radius and strength of hydration shell as observed from

TABLE I. Hydration No. at the pore- $CH_h$  interface region for different salt solutions in the chamber during osmosis. Also listed are the LJ carbon-ion parameters and the ion with a higher affinity to the pore.

Salt	Ion	Hydration No.	$\sigma_{ion-C}$ (nm)	Affinity to pore
KCl	$K^+, Cl^-$	7, 5.75	0.311, 0.365	$K^+$
NaCl	$Na^+, Cl^-$	5.85, 6.5	0.3645, 0.365	$Cl^-$
KF	$K^+, F^-$	7.25, 5.95	0.311, 0.37	$K^+$
LiCl	$Li^+, Cl^-$	5.9, 6.5	0.41, 0.365	$Cl^-$

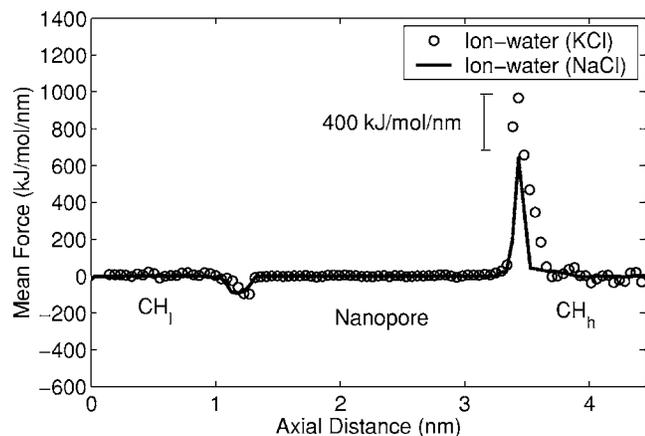


FIG. 4. Comparison of the ion-water mean force ( $\text{kJ mol}^{-1} \text{nm}^{-1}$ ) when the chambers contain either KCl or NaCl solutions.

the parameters given in Table I). In this case, the osmotic flux and the water orientation are similar to those observed in the case of a NaCl solution.

The above observations can be understood from a mean force analysis of the various ions and water molecules across the pore. Our earlier studies on osmosis<sup>8</sup> through semipermeable membranes have shown that in an uncharged pore, the asymmetry in the ion-water interaction across the axis of the pore initiates osmosis, while the water-water and wall-water interactions are symmetric and do not contribute much to osmosis. When the chambers were filled with a KCl solution, the ion-water mean force asymmetry across the pore (“pulling” water from the pore to  $\text{CH}_h$ ) is found to be higher than that of when the chambers were filled with a NaCl solution (see Fig. 4). This salt dependence of osmotic flux can also be understood from the hydration number of the ion with a higher affinity to the pore in the high solute chamber. As shown in Table I, when the chambers are filled with a KCl solution, the ion with higher affinity to the pore ( $\text{K}^+$ ) has a hydration number of 7, while in the case of a NaCl solution,

the ion with higher affinity to the pore ( $\text{Cl}^-$ ) has a slightly lower hydration number of 6.5. Thus, a  $\text{K}^+$  ion “pulls” more water molecules from the pore in the case of a KCl solution as opposed to the  $\text{Cl}^-$  ion in the case of a NaCl solution, i.e.,  $J_{\text{KCl}} > J_{\text{NaCl}}$ . Similar conclusions can be drawn by investigating the ion-water mean force, hydration number, and osmotic flux when the chambers are filled with KF and LiCl solutions (see Table I).

To conclude, the size-asymmetric electrolyte dependence of osmosis through a semipermeable pore was studied using MD simulations. The osmotic flux through the pore is influenced by the differential cation and anion affinity to the pore. Simulation results indicate that the higher ion-water mean force asymmetry across the pore in the KCl or KF solutions (as compared to the NaCl or LiCl solution) gives rise to a higher osmotic flux through the pore. These results were also understood from the hydration numbers of the ions close to the pore mouth. The water orientation in the pore also exhibited a size-asymmetric electrolyte dependence, depending on the cation/anion affinity to the pore.

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