

RESEARCH ARTICLE | DECEMBER 01 2023

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Daniel J. Rankin  ; David M. Huang  

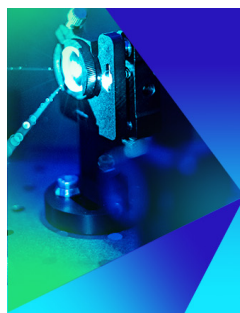


J. Chem. Phys. 159, 214705 (2023)

<https://doi.org/10.1063/5.0178576>



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Cite as: J. Chem. Phys. 159, 214705 (2023); doi: 10.1063/5.0178576

Submitted: 27 September 2023 • Accepted: 9 November 2023 •

Published Online: 1 December 2023



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Daniel J. Rankin  and David M. Huang^{a)} 

AFFILIATIONS

Department of Chemistry, School of Physics, Chemistry and Earth Sciences, The University of Adelaide, Adelaide, SA 5005, Australia

^{a)} Author to whom correspondence should be addressed: david.huang@adelaide.edu.au

ABSTRACT

We use a novel non-equilibrium algorithm to simulate steady-state fluid transport through a two-dimensional (2D) membrane due to a concentration gradient by molecular dynamics (MD) for the first time. We confirm that, as required by the Onsager reciprocal relations in the linear-response regime, the solution flux obtained using this algorithm agrees with the excess solute flux obtained from an established non-equilibrium MD algorithm for pressure-driven flow. In addition, we show that the concentration-gradient-driven solution flux in this regime is quantified far more efficiently by explicitly applying a transmembrane concentration difference using our algorithm than by applying Onsager reciprocity to pressure-driven flow. The simulated fluid fluxes are captured with reasonable quantitative accuracy by our previously derived continuum theory of concentration-gradient-driven fluid transport through a 2D membrane [D. J. Rankin, L. Bocquet, and D. M. Huang, J. Chem. Phys. 151, 044705 (2019)] for a wide range of solution and membrane parameters, even though the simulated pore sizes are only several times the size of the fluid particles. The simulations deviate from the theory for strong solute–membrane interactions relative to thermal energy, for which the theoretical approximations breakdown. Our findings will be beneficial for a molecular-level understanding of fluid transport driven by concentration gradients through membranes made from 2D materials, which have diverse applications in energy harvesting, molecular separations, and biosensing.

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I. INTRODUCTION

Transport of liquid mixtures and solutions through porous membranes is pivotal to many applications, including water desalination and purification,¹ chemical separations, energy generation² and storage,³ and biological and chemical sensing.⁴ However, the inadequate performance of current membranes limits the widespread adoption of these technologies.⁵ Membranes made from two-dimensional (2D) materials, such as graphene, molybdenum disulfide (MoS₂), or hexagonal boron nitride (hBN), hold great promise for tackling these challenges.^{6–9} However, gaps in knowledge of fundamental aspects of transport processes in 2D membranes, particularly those driven by the concentration gradients¹⁰ that are central to many applications, hinder the predictive design of 2D membranes.

The atomic-scale thickness of 2D membranes confers fundamentally different properties compared with conventional membranes, that are highly beneficial. For example, 2D membranes can circumvent the permeability–selectivity trade-off that often plagues conventional desalination or filtration membranes,⁶ whereby selectivity against transport of an unwanted component of a mixture is generally associated with reduced permeability to a desired component, with computer simulations of 2D graphene membranes achieving almost complete salt rejection along with water fluxes orders of magnitude larger than those of current desalination membranes.¹¹ The extreme thinness of 2D membranes also means that transmembrane gradients of, e.g., pressure, concentration, or electric potential can be enormous, resulting in huge driving forces for fluid transport. The orders-of-magnitude higher power densities for osmotic power generation of single-layer MoS₂ membranes

compared with conventional membranes were attributed partly to the massive salt gradient.¹² In nanopore-based sensing or sequencing of macromolecules, which provides a cheap, fast, and portable method of chemical or biological sensing, the single-atom thickness of 2D membranes offers the possibility of discriminating single monomers in biopolymers due to the membrane thickness being comparable to the inter-monomer spacing.^{6,9} Achieving this goal, however, requires precise quantification of ion fluxes both in the absence and presence of the biomolecule.

Although numerical simulations of fluid transport across 2D membranes have been carried out in the presence of concentration gradients using both continuum^{13,14} and molecular^{11,12,15–19} models, until our recent work,²⁰ no analytical theory existed to quantify the relationship between the solution and solute flow through a 2D membrane driven by a solute concentration gradient and basic parameters such as the membrane pore size and the strength and range of solute–membrane interactions. This theory was derived from a continuum hydrodynamic model of the fluid, and its quantitative accuracy was verified by comparison with computational fluid dynamics simulations.²⁰ However, the continuum fluid approximation can break down when the dimensions of the confining pores become comparable to the size of the fluid molecules,²¹ which could be an issue for 2D membranes even with large pores due to their atomic-scale thickness. Furthermore, continuum models cannot easily account for the effects of mechanical flexibility of the membrane, which can be significant for 2D membranes.^{16,22,23} They also do not readily predict from first principles some phenomena that can strongly impact nano-scale fluid transport, such as finite solid–fluid friction, inhomogeneous fluid properties, non-electrostatic ion-specific interactions, and non-ideal solutions.

However, modeling fluid transport due to a concentration difference across a porous membrane using molecular simulations is not straightforward. This is because the periodic boundary conditions that are generally used in such simulations creates an artificial concentration jump across the periodic boundary when a concentration difference is applied across the membrane. Without constraints, mixing of the solution would occur across the periodic boundary instead of across the membrane. Until recently, a generally suitable molecular algorithm for simulating steady-state transport of liquid mixtures driven by concentration gradients had not existed. To the best of our knowledge, all molecular simulations of concentration-gradient-driven transport through a 2D membrane until now have used a non-equilibrium molecular dynamics (NEMD) method in which the solute concentrations on either side of the membrane are set to be initially different and the resulting transient fluxes measured over time.^{11,12,15–19} Such simulations generally do not enable the solution and solute fluxes for a given transmembrane concentration difference to be accurately quantified since the concentrations change measurably over time in the relatively small systems that can be practically simulated. This can be especially problematic for electrolyte solutions since electrostatic screening depends on concentration, which could have a significant impact on fluid transport as a result of the large concentration gradients that occur across 2D membranes.

Methods for calculating concentration-gradient-driven transport from equilibrium simulations in the absence of a concentration gradient²⁴ also have deficiencies, particularly in the case of

electrolytes, since they do not account for the effects of spatial variations of concentration-dependent properties such as electrostatic screening. On the other hand, stochastic algorithms that combine molecular dynamics (MD) with a grand canonical Monte Carlo (GCMC) method for maintaining constant reservoir concentrations by inserting, deleting, or exchanging particles in the reservoirs^{25–28} suffer from low acceptance rates of stochastic particle moves at the high densities in liquids, and unphysical particle insertions can perturb the flow.²⁹ Deterministic MD algorithms have also been developed to simulate steady-state flow in a periodic system due to a concentration gradient by applying a supplementary force to solute and/or solvent molecules to mimic a chemical potential gradient,^{30–34} either throughout the system³³ or in small transition regions far from the membrane.^{30–32,34} Significant advantages of these methods over stochastic algorithms are that they are efficient even at liquid densities and that they do not involve unphysical particle insertion or deletion steps. However, most of these algorithms have significant deficiencies that limit their utility, such as not being applicable to complex geometries such as 2D membranes,³³ not explicitly modeling the concentration difference (and thus not accounting for spatial variations in concentration-dependent properties),³³ or not enabling independent control of differences in solute concentration and pressure across the membrane,^{30–32} which can lead to spurious effects, particularly at high solute concentrations, as discussed later on. One recent algorithm³⁴ has been developed that does not suffer from these issues, but it controls the solute chemical potential difference across the membrane, whereas the solute concentration difference is a more useful control parameter for direct comparison with experiments.

In this work, we have modified a previous deterministic NEMD algorithm³¹ for constraining the solute concentration difference across a porous membrane in a periodic system to enable independent control of the transmembrane pressure difference. As a proof-of-principle of its ability to simulate and accurately quantify steady-state concentration-gradient-driven fluid transport through 2D membranes, we have applied this algorithm to a model system comprising a binary Lennard-Jones (LJ) liquid mixture and a 2D LJ membrane. Using this model system, we have systematically investigated the effects of key parameters such as the membrane pore size, average solute mole fraction, and the strength and range of the solute–membrane interactions on the solution and solute fluxes. We have used these molecular simulation results to evaluate the accuracy of our previously developed continuum theory for predicting concentration-gradient-driven fluid transport through these atomically thin membranes.

II. COMPUTATIONAL METHODS

A. System details

All MD simulations were performed using the Large-scale Atomic/Molecular Massively Parallel Simulator (LAMMPS) [3 March 2020 graphics processing unit (GPU)-accelerated version],^{35,36} with initial simulation configurations constructed using Moltemplate (version 2.16.1)³⁷ and visualization of simulation trajectories carried out using OVITO (version 3.0.0).³⁸ The system comprised a binary liquid mixture (solute and solvent) and a single-layer planar solid membrane parallel to the x, y planes, containing an approximately circular hole centered at the origin [Fig. 1(a)].

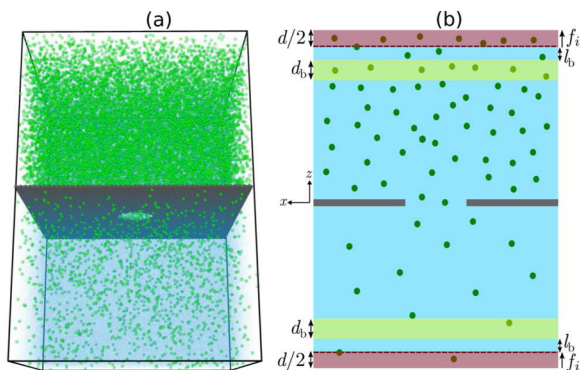


FIG. 1. (a) Snapshot of a typical MD simulation system, consisting of a binary LJ liquid mixture (solvent particles are translucent) and a single-layer planar fcc (111) lattice membrane with a circular pore. (b) Schematic of constrained concentration- and pressure-difference algorithm: a force f_i is applied perpendicular to the membrane to each particle of type i (solute or solvent) within a transition region (red) of width d ; the concentration ratio and pressure difference are measured between control regions (yellow) of width d_b on either side of the membrane a distance l_b from the transition region; the applied forces are dynamically adjusted to converge the concentration ratio and pressure difference to target values.

The solid particles were placed in a single layer of the (111) surface of a close-packed face-centered cubic (fcc) lattice (lattice constant $\sqrt{2}\sigma$), and their positions were fixed throughout the simulations. The Lennard-Jones (LJ) potential

$$u_{ij}(r_{ij}) = 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right], \quad (1)$$

was used for the interactions between particles, where r_{ij} is the distance between particles i and j , and ϵ_{ij} and σ_{ij} are parameters quantifying the strength and range, respectively, of their interactions. The solute–solute, solvent–solvent, and solute–solvent interaction parameters, ϵ_{ij} , and σ_{ij} , were set to the same values, ϵ and σ , respectively, in all simulations, while the parameters for the interactions between solute and solid (wall) particles, ϵ_{uw} and σ_{uw} , respectively, were varied for different simulations. (Throughout this paper, we use subscripts “u,” “v,” and “w” to denote solute, solvent, and wall particles, respectively.) Therefore, the solute and solvent particles were identical in all respects except for their interactions with the membrane. The potential was cutoff at a distance of 4σ , and all particles had mass m . LJ units are used throughout this work, with masses, distances, energies, temperatures, pressures, and times in units of m , σ , ϵ , ϵ/k_B , ϵ/σ^3 , and $\tau = \sqrt{m\sigma^2/\epsilon}$, respectively, where k_B is the Boltzmann constant. In all simulations, time integration was performed with the velocity-Verlet integrator with a time step of 0.005τ , and periodic boundary conditions were applied in all dimensions. Unless otherwise stated, simulations were carried out in the canonical (NVT) ensemble at a temperature of ϵ/k_B using a Nosé–Hoover^{39,40} style thermostat,⁴¹ with only the velocity components perpendicular to the flow (z) direction thermostatted in NEMD simulations.

B. Constrained concentration- and pressure-difference algorithm

To carry out NEMD simulations of steady-state flow due to concentration and/or pressure gradients, we adapted an algorithm by Khalili-Araghi *et al.*³¹ designed to maintain unequal solute concentrations across a membrane in a system with periodic boundary conditions. Specifically, we modified it to enable independent control of concentration and pressure differences. Here, we use the convention that the membrane lies in the x, y -plane at $z = 0$ in the primary simulation box.

The algorithm in Ref. 31 applies a supplementary constant force f_i in the direction perpendicular to the membrane to particles of type i in a small transition region of width d far from the membrane, as illustrated in Fig. 1(b). The algorithm was called the nonperiodic energy step method since the addition of this force is equivalent to applying a nonperiodic energy step or ramp of size $\Delta\epsilon_i = -f_i d$ across the transition region to the particles, which induces a concentration difference between the two sides of the membrane. The energy step $\Delta\epsilon_i$ needed to achieve a target ratio of the concentrations c_{i0}^+ and c_{i0}^- of species i in the upper and lower fluid reservoirs, respectively, can be estimated from the relationship for a system of non-interacting (ideal) particles at infinite dilution, $c_{i0}^+/c_{i0}^- = \exp(\Delta\epsilon_i/(k_B T))$. The applied force required to maintain this concentration ratio in this case is

$$f_i^{\text{ideal}} = -\frac{k_B T}{d} \ln \left(\frac{c_{i0}^+}{c_{i0}^-} \right), \quad (2)$$

which is used as the initial value of the applied force in the algorithm, i.e., $f_i(t=0) = f_i^{\text{ideal}}$. In general, an analytical relationship between the force and concentration difference or ratio does not exist for interacting particles. To account for the effect of particle–particle interactions, the forces are adjusted dynamically to converge to the target concentration ratio according to

$$f_i^{\text{KA}}(t + \Delta t) = f_i^{\text{KA}}(t) + \frac{\Delta t}{\alpha\tau_c} \Delta f_i^{\text{KA}}(t), \quad (3)$$

with

$$\Delta f_i^{\text{KA}}(t) = \frac{k_B T}{d} \left[\left\langle \ln \left(\frac{c_i^+}{c_i^-} \right) \right\rangle - \ln \left(\frac{c_{i0}^+}{c_{i0}^-} \right) \right], \quad (4)$$

where Δt is the simulation time step, α and τ_c are tunable parameters, c_i^+ and c_i^- are the instantaneous concentrations in the upper and lower reservoirs, respectively, and $\langle \dots \rangle$ denotes a time average over the interval $(t - \tau_c, t]$, i.e., over a duration τ_c immediately preceding the current time step. (We use the superscript “KA” to distinguish the equations in Ref. 31 from those in our modified algorithm, which are described below.) The instantaneous concentrations are measured in control regions each of width d_b on either side of the membrane and far from it [shown in yellow in Fig. 1(b)] that is sufficiently wide to calculate the average in Eq. (4) accurately. From Eq. (3), the concentration ratio is expected to converge to the target ratio c_{i0}^+/c_{i0}^- over a duration on the order of $\alpha\tau_c$.

To avoid calculating the average in Eq. (3) every time step and to reduce the chance of $\Delta f_i(t)$ becoming undefined due to c_i^+ or c_i^- being zero, we have modified the force update algorithm from that in Ref. 31 such that the applied force is updated every τ_c time

steps instead of every time step and the instantaneous concentrations are averaged over time before taking the logarithm. Therefore, we replace Eqs. (3) and (4) by

$$f_i(t + \tau_c) = f_i(t) + \frac{\Delta f_i(t)}{\alpha}, \quad (5)$$

and

$$\Delta f_i(t) = \frac{k_B T}{d} \left[\ln \left(\frac{\langle c_i^+ \rangle}{\langle c_i^- \rangle} \right) - \ln \left(\frac{c_{i0}^+}{c_{i0}^-} \right) \right], \quad (6)$$

respectively, where the time average $\langle \dots \rangle$ is taken over the interval $[n\tau_c, (n+1)\tau_c)$ for $n \leq t/\tau_c < n+1$ and $n \in \mathbb{Z}$. As in Ref. 31, Eq. (2) is used to initialize the applied force, and convergence to the target concentration ratio is expected to occur over a duration on the order of $\alpha\tau_c$. τ_c should be chosen sufficiently large to accurately estimate the time averages in the control regions and thus avoid large fluctuations in the applied forces calculated from these averages; α (and thus $\alpha\tau_c$) should be chosen small enough that convergence to the target occurs on a reasonable time scale, but too small a value can lead to large fluctuations in the applied forces that hinder convergence. The optimal choice of these parameters is expected to depend on the particular system as well as the size of the system.

In principle, the force update scheme specified by Eqs. (3) and (4) from Ref. 31 or our modified version specified by Eqs. (5) and (6) can be used to constrain the concentration difference across the membrane of any or all species in a multicomponent mixture. In Ref. 31, the external force was only applied to solute species (electrolyte ions in that case), whereas no external force was applied to the solvent (water). However, in general, applying an external force to solutes in the transition region without doing the same to the solvent will induce a hydrostatic pressure difference across the membrane that will affect the fluid fluxes, as we show below. Therefore, an external force must also be applied to the solvent particles to achieve the desired pressure difference. Instead of constraining the solvent concentration using Eq. (6) to achieve this goal, we use a force update scheme for the solvent that directly controls the pressure difference, which more closely mimics how applied fields would be controlled experimentally. Therefore, while we use Eqs. (5) and (6) to update the applied force on the solute particles, for the solvent particles (type $i = v$), we replace Eq. (6) by

$$\Delta f_v(t) = \frac{A}{N_v(t + \tau_c)} (\langle \Delta P \rangle - \Delta P_0), \quad (7)$$

where A is the cross-sectional area of the simulation box, ΔP_0 is the target pressure difference, $N_v(t + \tau_c)$ is the instantaneous number of solvent particles in the transition region at time $t + \tau_c$, $\Delta P = P^+ - P^-$ is the instantaneous pressure difference between the control regions on either side of the membrane, and the time average $\langle \dots \rangle$ is computed identically to that in Eq. (6). [Note that $\langle N_v \rangle$ may be a better choice than $N_v(t + \tau_c)$ in Eq. (7), as its use would reduce the fluctuations in the applied force.] P^\pm is calculated from the diagonal components of the per-atom stress tensor summed over atoms in the control regions using the `stress/atom` compute in LAMMPS.⁴² We note that this method is known to be inaccurate for computing the local pressure in inhomogeneous systems,^{43,44} for which more accurate but more computationally expensive and less widely

implemented alternatives^{43–45} exist. However, by keeping the control regions away from strong inhomogeneities in the fluid, this problem can be mitigated. For the initial applied force on the solvent particles, $f_v(t = 0) = 0$ is used in this work. However, a better choice given the initial solute force $f_u(t = 0)$ specified by Eq. (2) would be the value that makes $\Delta P = \Delta P_0$ according to the force balance in Eq. (11) below.

Note that this algorithm can be straightforwardly extended to electric-field-driven fluid transport. As demonstrated for a similar recent NEMD algorithm,³⁴ for a transmembrane voltage difference ΔV (which is minus the voltage drop across the transition region), an additional constant force $f_{e,i} = q_i \Delta V / d$ would be applied to each charged particle in the transition region that is proportional to the particle's charge q_i .

C. Simulation details

Two system sizes were simulated. Unless otherwise stated, a 50×50 unit-cell membrane and a total of 396 000 fluid particles were used. In addition, some non-equilibrium simulations were carried out with a larger 80×80 unit-cell membrane and a total of 1 622 016 fluid particles to verify that the simulations of the smaller system did not suffer from finite-size effects.

For each system size, fluid particles were placed on two cubic lattices of equal size on either side of the solid surface, which initially contained no pore, with the z dimension of the box sufficiently large that the particles did not overlap. All fluid particles were initially set to be solvent particles. The system was initially equilibrated in the isothermal–isobaric (NPT) ensemble for 10^6 time steps at a temperature of ϵ/k_B and pressure of ϵ/σ^3 using a Nosé–Hoover^{39,40} style thermostat and barostat⁴¹ with only the z dimension barostat for the fluid particles. The average box length in the z dimension measured over the last 10^5 time steps, by which time the instantaneous box length had plateaued, was used as the box length in all subsequent constant-volume simulations, which were at a temperature of ϵ/k_B . To reach this box length from the final system configuration in the NPT simulation, the z dimension of the box was deformed at constant velocity over 10^3 time steps while integrating the equations of motion with a Nosé–Hoover style thermostat. All solid atoms within a distance a of the origin were then deleted to create an approximately circular pore of radius a in the membrane, as illustrated in Fig. S1 of the supplementary material.

Equilibrium MD and NEMD simulations were carried out for various combinations of the solute–membrane interaction parameters ϵ_{uw} and σ_{uw} , pore radius a , and average solute mole fraction $\bar{\chi}$, with $\epsilon_{uw}/\epsilon = 0.5, 0.8, 1.2$ or 1.5 , $\sigma_{uw}/\sigma = 0.8, 1.2$ or 1.5 , $a/\sigma = 0$ (equilibrium simulations only), 3, 4, 6, or 8, and $\bar{\chi} = 0.05$ or 0.2 . In addition to NEMD simulations of concentration-gradient-driven flow, simulations of pressure-driven-flow without a concentration gradient were also carried out for selected systems using the algorithm in Ref. 46, which is similar in some respects to our constrained concentration- and pressure-difference algorithm but in which a constant and equal force ($f_u = f_v$) is applied to solute and solvent molecules in the transition region. Most simulations with a constrained concentration difference used a target transmembrane solute concentration ratio of $c_{u0}^+/c_{u0}^- = 20$, but ratios of 2, 3, and 5 were also used for selected systems to verify the linear response of the fluid fluxes to the applied driving force. Unless otherwise stated,

the transition region width d , control region width d_b , and distance l_b between the transition and control regions in the NEMD simulations were all 2σ (see Fig. 1), and the target pressure difference ΔP_0 was zero. Details of the simulated systems and their properties are given in Tables S1–S5 of the supplementary material.

Starting from the final simulation configuration from the previous NPT equilibration step, fluid particles were randomly converted into solute particles to give the desired average solute mole fraction. Additionally, for the NEMD simulations, the fluid particles were converted to achieve the maximum target solute concentration ratio of 20. Then, for each system geometry, a NEMD simulation was carried out using the constrained concentration- and pressure-difference algorithm with $\epsilon_{uw} = \epsilon$ and $\sigma_{uw} = \sigma$, reducing the target solute concentration ratio at intervals of $\sim 8 \times 10^6$ time steps to obtain steady-state simulation configurations at each of the desired concentration ratios. Figure 2 shows the variation of the solute concentration and pressure in the control regions with time from one of these simulations, which illustrates the ability of the algorithm to converge and maintain the concentration and pressure difference at the target values. The final configuration at each target concentration ratio was used as the starting configuration for simulations with other values of ϵ_{uw} and σ_{uw} at that target ratio. All these simulations used $\alpha = 50$ and $\tau_c = 50\tau$, which reliably resulted in stable

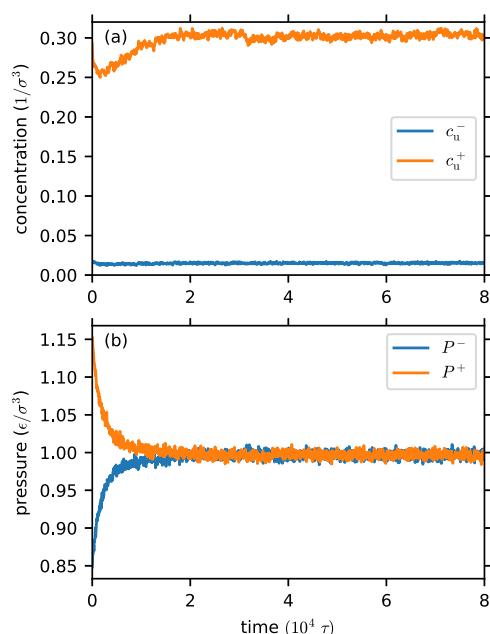


FIG. 2. (a) Solute concentration c_u and (b) pressure P in the upper (+) and lower (–) control regions vs time when applying the constrained concentration- and pressure-difference algorithm for a target concentration ratio $c_{u0}^+/c_{u0}^- = 20$ and target pressure difference $\Delta P_0 = 0$, starting from a configuration in which solutes were uniformly distributed on either side of the membrane at the target concentration ratio ($a = 6\sigma$, $\epsilon_{uw} = \epsilon$, $\sigma_{uw} = \sigma$, $\bar{\chi} = 0.2$). The initial unequal pressures in the two control regions are due to the initial applied force on solvent particles being set to zero, while the initial applied force on solute particles is specified by Eq. (2), which results in a non-zero transmembrane pressure difference for $c_{u0}^+/c_{u0}^- \neq 1$ [see Eq. (11) below].

convergence of the concentration ratio and pressure difference on a reasonable time scale.

For the NEMD simulations, an automated equilibration detection method⁴⁷ was used to determine when each system had reached a non-equilibrium steady state and to estimate the effective number of uncorrelated samples in order to calculate steady-state averages and statistical uncertainties (at the 95% confidence level) of fluctuating variables. Distribution functions such as solute concentration profiles, fluid density profiles, and pressure profiles were calculated only using data after the first 8×10^6 time steps of each simulation, which ensured the system was at equilibrium or in a non-equilibrium steady state.

It should be noted that changing solvent particles into solute particles with different solute-membrane interaction parameters resulted in deviations of the bulk pressure in the fluid reservoirs from the target pressure of ϵ/σ^3 in the NPT equilibration simulations, particularly at high concentrations, with average pressures in the equilibrium simulations varying from 0.93 to $1.00\epsilon/\sigma^3$ across the range of systems studied (Table S3 of the supplementary material). However, the bulk solution density remained approximately constant, varying from 0.782 to $0.787\sigma^{-3}$ across the range of solute-membrane interactions. Note that the creation of the membrane pore had a negligible effect on the bulk pressure and solution density.

III. RESULTS AND DISCUSSION

A. Application of constrained concentration- and pressure-difference algorithm

Figure 3 depicts the solute concentration, centerline solute concentration (calculated for solute particles within a distance σ of the axis passing through the pore center), and total (solute + solvent) fluid density profiles perpendicular to the membrane for a system to which our constrained concentration- and pressure-difference algorithm was applied, either with or without enforcing the pressure constraint $\Delta P_0 = 0$ using Eq. (7). (Results for the highest concentration ratio without the pressure constraint are not shown because the concentration ratio never converged to a steady state.) The method without the pressure constraint is equivalent to the original constrained concentration-difference algorithm of Khalili-Araghi *et al.*³¹ The system in Fig. 3 had a pore radius $a = 6\sigma$, solute mole fraction $\bar{\chi} = 0.2$, and overall repulsive solute-membrane interactions, as indicated by the solute depletion near the membrane in Fig. 3(a). Qualitatively similar results were obtained for other systems, as illustrated in the supplementary material for a system with the same solute-membrane interactions but a lower ($\bar{\chi} = 0.05$) solute mole fraction in Fig. S2 and for a system with the same solute mole fraction but attractive effective solute-membrane interactions in Fig. S3.

The solute concentration profiles with and without the pressure constraint in Figs. 3(a) and 3(b) are dramatically different. At first glance, the total fluid density profiles in Fig. 3(c) are similar. However, closer inspection, as shown in the inset, reveals a transmembrane density difference without the pressure constraint, which is induced by the net force exerted on the solution by the applied force on the solute particles used to constrain the concentration difference. The net force is manifested in a transmembrane pressure difference, as shown in the pressure profiles for the same system in Fig. 4 when the pressure difference is not constrained.

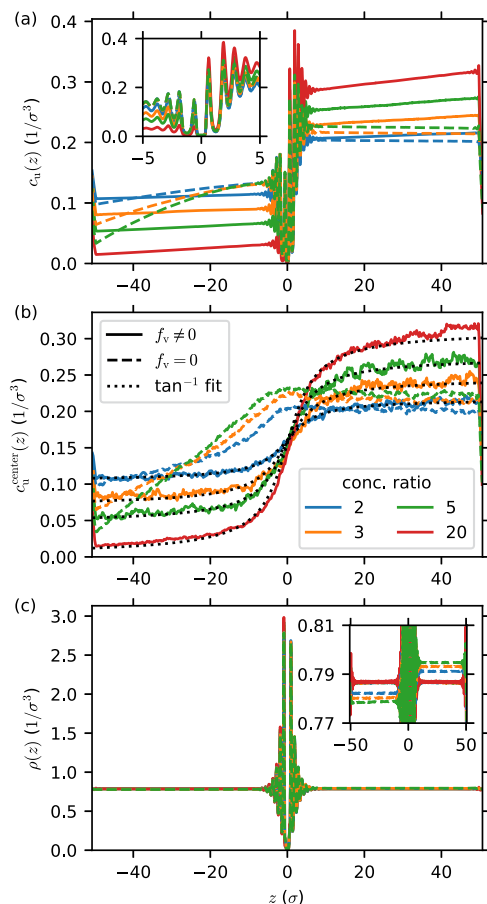


FIG. 3. (a) Solute concentration, (b) centerline solute concentration, and (c) total fluid density vs z coordinate in non-equilibrium simulations with ($f_v \neq 0$, solid lines) and without ($f_v = 0$, dashed lines) the transmembrane pressure difference constrained to be zero for $a = 6\sigma$, $\epsilon_{uw} = 0.5\epsilon$, $\sigma_{uw} = 0.8\sigma$, $\bar{\chi} = 0.2$, and various target solute concentration ratios c_{u0}^+/c_{u0}^- . The inset in (a) zooms in on z values near the membrane, whereas the inset in (c) zooms in on density values around the bulk density. The dotted black lines in (b) are the least-squares fit of the solid line to a function of the form $b_0 + b_1 \tan^{-1}(z/b_2)$ with fit parameters b_0 , b_1 , and b_2 .

On the other hand, constraining the pressure difference to $\Delta P_0 = 0$ results in equal pressures and total fluid densities on either side of the membrane. Fluid flow driven by the pressure difference polarizes the solute concentration near the membrane, resulting in the differing solute concentration profiles in Figs. 3(a) and 3(b) with and without the pressure constraint. As shown by the fitted curves in Fig. 3(b), the centerline solute concentration when both the concentration and pressure difference are constrained is consistent with theoretical predictions under conditions in which there is a concentration difference but no pressure difference and the solute–membrane interaction range is small compared with the pore radius, in which the concentration profile is expected to be an inverse tangent function of the axial coordinate.²⁰

Fluid fluxes were determined by counting the number of solute and solvent particles crossing the membrane as a function of time, as illustrated in Fig. 5 for two systems to which the constrained

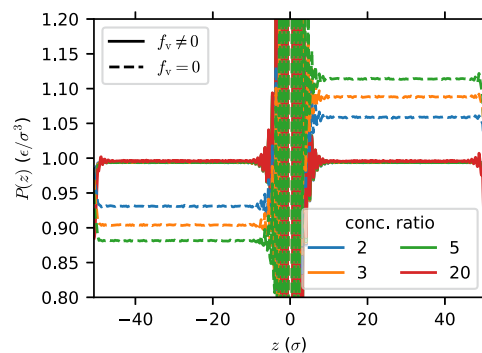


FIG. 4. Pressure profile in non-equilibrium simulations with ($f_v \neq 0$, solid lines) and without ($f_v = 0$, dashed lines) the transmembrane pressure difference constrained to be zero for the same conditions in Fig. 3.

concentration- and pressure-difference algorithm was applied with zero pressure difference. [In practice, we measured fluxes at the boundary of the simulation box, which was in the center of the transition region (see Fig. 1), which gives the same result as any plane parallel to the membrane in a steady state due to particle conservation.] The effective solute–membrane interactions in Figs. 5(a) and 5(b) are repulsive and attractive, respectively, i.e., the solute is depleted and enhanced near the membrane relative to the bulk, respectively. The linearity of the curves vs time shows both systems are in a steady state with constant fluid fluxes for most of the simulation. (Similar behavior was observed for all systems

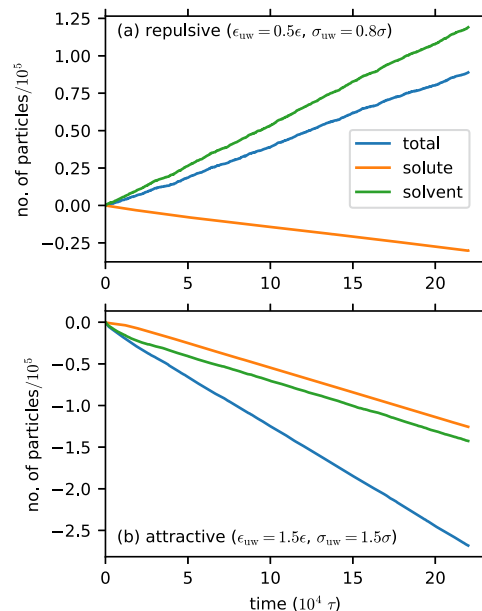


FIG. 5. Cumulative number of fluid (total, solute, or solvent) particles crossing the membrane vs time in simulations with $c_{u0}^+/c_{u0}^- = 20$ and $\Delta P_0 = 0$ for $a = 6\sigma$, $\bar{\chi} = 0.2$, and (a) repulsive ($\epsilon_{uw} = 0.5\epsilon$, $\sigma_{uw} = 0.8\sigma$) or (b) attractive ($\epsilon_{uw} = 1.5\epsilon$, $\sigma_{uw} = 1.5\sigma$) effective solute–membrane interactions. (Each point is an average over a time interval of τ_c .)

studied.) Consistent with expectations for systems with a transmembrane concentration difference but no pressure difference and for which solute diffusion dominates advection (Péclet number $Pe < 1$), the solute flux is in the direction of decreasing concentration, while the total solution flux due to concentration-gradient-driven diffusioosmosis is opposite in direction for membranes that repel and attract the solute, with flow towards increasing and decreasing concentration, respectively.¹⁰

The flux of particles of type i was calculated as a numerical derivative, $\dot{N}_i = \Delta N_i / \Delta t$, of the cumulative particle number N_i crossing the membrane vs time t in the steady state. The simulation trajectory was divided into intervals of 2×10^5 timesteps = $10^3 \tau$ for which the flux was calculated, from which the average flux with statistical uncertainties was obtained using the method described in Sec. II C. (We verified that the calculated uncertainties were insensitive to halving or doubling this time interval.) Figure 6 shows the total ($\dot{N} = \dot{N}_u + \dot{N}_v$) and solute (\dot{N}_u) fluxes vs the target concentration ratio for a system with repulsive effective solute-membrane interactions for low ($\bar{\chi} = 0.05$) and high ($\bar{\chi} = 0.2$) solute mole fractions with or without the $\Delta P_0 = 0$ pressure constraint. Consistent with expectations for this system, when no transmembrane pressure difference is applied, the total flux is towards increasing concentration, whereas the solute flux is towards decreasing concentration when the pressure constraint is enforced. On the other hand, both the total and solute flux are toward decreasing concentration without the pressure constraint due to pressure-driven flow as a result of the non-zero transmembrane pressure difference. The relative discrepancy between the total solution fluxes with and without the pressure constraint is similar for both solute mole fractions and different

concentration ratios, highlighting the general importance of applying the pressure constraint to obtain accurate fluxes in constrained concentration-difference simulations. The solute flux is significantly different with and without the pressure constraint, but the relative discrepancy is much smaller at the lower solute mole fraction due to the greater importance of solute diffusion over advection (lower Péclet number) at the lower mole fraction, suggesting that there may be circumstances in which the pressure constraint may not greatly affect the solute flux.

The pressure difference was not constrained in the original constrained concentration-difference algorithm in Ref. 31. The study for which the algorithm was developed focused on measuring the ionic current through biological membrane channels due to a concentration difference for a relatively dilute aqueous KCl electrolyte. A concentration ratio of 0.1:1 mol l⁻¹, pore radius $a \approx 0.55$ nm, and pore length $L \approx 6$ nm were considered for the OmpF porin that was studied. To maintain the concentration ratio across the pore, an external force $f = 0.557$ kcal mol⁻¹ Å⁻¹ was applied to the ions within a $d = 2.5$ Å transition region. As explained in Sec. III B, this force would create a pressure difference of magnitude $|\Delta P| = N_u f / A$ across the membrane, where N_u is the number of ions in the transition region and A is its cross-sectional area. Using $A = 123.5 \times 123.5$ Å² and the average ion concentration of $\bar{c}_u = 1.1$ mol l⁻¹ in these simulations gives $N_u \approx 25$, and thus $|\Delta P| \approx 6.3 \times 10^3$ kPa. Ignoring the hydraulic resistance of the pore ends for simplicity, which would reduce the flux further, the total solution flux due to this pressure difference can be estimated from the Hagen-Poiseuille equation,⁴⁸ $Q = \pi a^4 \Delta P / (8 \eta L)$, where η is the solution shear viscosity, which we have taken to be that of pure water, $\eta = 8.94 \times 10^{-4}$ Pa s.⁴⁹ Using the parameters above gives an estimate of the convective ion flux of $\bar{c}_u Q \approx 3 \times 10^7$ s⁻¹. The lowest total ionic current that was measured in Ref. 31 was ≈ 10 pA, which gives a lower bound (corresponding to a perfectly ion-selective channel) on the total ion flux of $\approx 6 \times 10^7$ s⁻¹. Therefore, the convective ion flux due to the induced pressure difference may have been non-negligible compared with that due to the applied concentration difference in this study.

B. Transport coefficients: Verification of linear response and Onsager reciprocity

From now on, we focus on NEMD simulations using our constrained concentration- and pressure-difference algorithm in which the pressure difference has been constrained to be zero. To quantify the concentration-gradient-driven fluid fluxes for all of the systems studied, we define two transport coefficients—the diffusioosmotic mobility

$$\kappa_{DO} \equiv -\frac{Q}{\Delta \Pi / (k_B T)}, \quad (8)$$

and the solute permeance

$$\mathcal{P}_s \equiv -\frac{J_u}{\Delta \Pi / (k_B T)}, \quad (9)$$

which characterize the total volumetric solution flux Q and solute flux $J_u = \dot{N}_u$, respectively, for a given transmembrane osmotic pressure difference $\Delta \Pi$ at temperature T . These definitions follow the

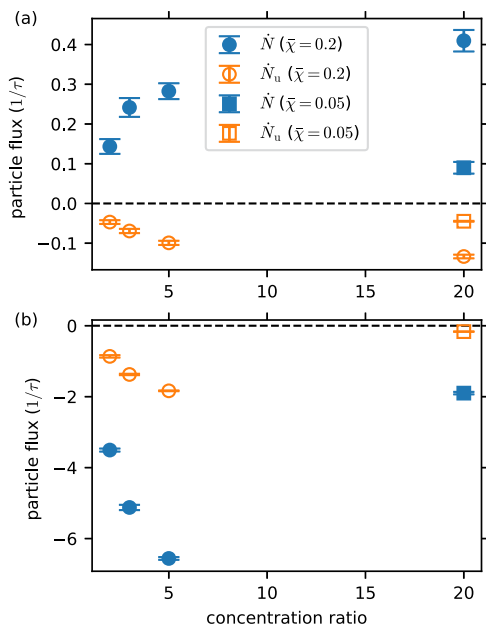


FIG. 6. Total (\dot{N} , filled symbols) and solute (\dot{N}_u , empty symbols) flux vs target concentration ratio c_{u0}^+ / c_{u0}^- for systems with $a = 6\sigma$, $\epsilon_{uw} = 0.5\epsilon$, $\sigma_{uw} = 0.8\sigma$, and $\bar{\chi} = 0.2$ (circles) or 0.05 (squares) in simulations with (a) $\Delta P_0 = 0$ pressure constraint and (b) no pressure constraint.

notation in our previous work,²⁰ in which we derived a theory of concentration-gradient-driven flow through 2D membranes for dilute solutions, but the equations above generalize them to arbitrary solute concentrations.^{33,50} Equations (8) and (9) reduce to the corresponding equations [Eqs. (33) and (34)] in Ref. 20 in the dilute solution limit, where $\Delta\Pi = k_B T \Delta c_u$.⁵⁰ The solution flux can be determined from the simulations as $Q = \frac{\dot{N}}{\bar{\rho}}$, where $\bar{\rho}$ is the bulk total fluid density, which we calculated as the average of the total fluid density in the upper and lower control regions, i.e., $\bar{\rho} = (\rho^+ + \rho^-)/2$.

As described recently for a similar NEMD simulation algorithm,³⁴ the transmembrane osmotic pressure difference $\Delta\Pi$ and hydrostatic pressure difference ΔP can be calculated by considering the balance of applied forces of the fluid particles in the transition region. Decomposing the applied force on each solute particle and each solvent particle as $f_u = f + \delta f_u$ and $f_v = f + \delta f_v$, respectively, such that $N_u \delta f_u + N_v \delta f_v = 0$, the force due to the osmotic pressure difference is $-A \Delta\Pi = N_u \delta f_u = -N_v \delta f_v$ (i.e., the net force on the fluid in the transition region due to $\Delta\Pi$ is zero), while the force due to the hydrostatic pressure difference is $-A \Delta P = (N_u + N_v) f = N f$, where N_u and N_v are the number of solute and solvent particles, respectively, in the transition region, N is the total number of fluid particles in the transition region, and A is its cross-sectional area.³⁴ (Note that, following the convention in Sec. II B, we have defined $\Delta\Pi$ and ΔP as differences across the membrane rather than across the transition region, as was performed in Ref. 34, so the sign in the previous equations is opposite that in the equivalent equations in Ref. 34.) From these equations, $\Delta\Pi$ and ΔP can be calculated in terms of the number of particles and the applied force on particles of each type in the transition region as

$$\Delta\Pi = -\frac{1}{A} \left(\frac{N_u N_v}{N_u + N_v} \right) (f_u - f_v), \quad (10)$$

and

$$\Delta P = -\frac{1}{A} (N_u f_u + N_v f_v). \quad (11)$$

Alternatively, $\Delta\Pi$ and ΔP can be calculated from the solute concentration and pressure, respectively, in the control regions. In this case, $\Delta P = P^+ - P^-$, i.e., the pressure difference evaluated in the constrained concentration- and pressure-difference algorithm. On the other hand, $\Delta\Pi$ can be estimated using the osmotic pressure of an incompressible ideal binary mixture, which can be derived from the entropy of mixing at any solute concentration (assuming the same solute and solvent molecular volume v) to be^{33,51,52}

$$\Pi = -\frac{k_B T}{v} \ln(1 - \chi) = -\rho k_B T \ln(1 - \chi), \quad (12)$$

where χ is the solute mole fraction and $\rho = 1/v$ is the total fluid density (which is assumed to be independent of χ). This equation reduces to the standard van't Hoff equation, $\Pi = c_u k_B T$, for $\chi \ll 1$. We have evaluated $\Delta\Pi = \Pi^+ - \Pi^-$ from Eq. (12) using the solute mole fraction, χ^+ and χ^- , and bulk fluid density, ρ^+ and ρ^- , in the upper and lower control regions, respectively. We have compared $\Delta\Pi$ and ΔP calculated from the applied force balance in the transition region and from the concentration/density or pressure in the control regions in Figs. S6 and S7, respectively, in the

supplementary material for all our non-equilibrium simulations. This includes simulations in which the osmotic pressure difference was non-zero and the pressure difference was constrained to be zero, simulations in which the osmotic pressure difference was non-zero and the pressure difference was unconstrained and thus non-zero, and simulations in which the osmotic pressure difference was zero and the pressure difference was non-zero. This comparison shows perfect agreement between ΔP calculated using either method, but $\Delta\Pi$ calculated from the control regions using Eq. (12) overestimates (by up to $\approx 15\%$) the value obtained from the transition region force balance using Eq. (10) for larger $\Delta\Pi$. The origin of this discrepancy is likely the absence of a well-defined “bulk” solute concentration in the upper or lower fluid reservoirs to unambiguously define the osmotic pressure in Eq. (12) in simulations with a non-zero concentration difference since the concentration varies throughout the system (see, e.g., Fig. 3). By contrast, even with a transmembrane pressure difference, the pressure profile is essentially flat in either reservoir except in the immediate vicinity of the transition region or membrane (see, e.g., Fig. 4), so the ΔP between the control regions is representative of the transmembrane pressure difference.

Using $\Delta\Pi$ from the force balance in the transition region, we have verified that the transport coefficients in Eqs. (8) and (9) were independent of the system size and transition region width for selected systems in Fig. S8. We have also verified that the transport coefficients were independent of $\Delta\Pi$, i.e., the systems were in the regime of linear response of the fluid fluxes to the applied osmotic driving force for selected systems, as shown in Fig. 7 for κ_{DO} and in Fig. S9 of the supplementary material for \mathcal{P}_s . The three selected systems encompassed those most likely to deviate from the linear response, namely those with the three highest solution flux magnitudes (which include those with the two highest solute flux magnitudes) at the highest target concentration ratio $c_{u0}^+/c_{u0}^- = 20$

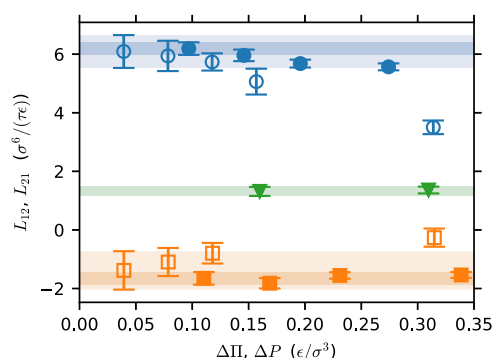


FIG. 7. $L_{12} = \kappa_{DO}/(k_B T)$ (filled symbols) and L_{21} (empty symbols) transport coefficients vs transmembrane osmotic pressure difference $\Delta\Pi$ and pressure difference ΔP , respectively, for flow driven exclusively by a concentration or a pressure difference for systems with $\bar{\chi} = 0.2$, $a = 6\sigma$, and various solute–membrane interaction parameters: $\epsilon_{uw} = 1.5\epsilon$, $\sigma_{uw} = 1.5\sigma$ (circles); $\epsilon_{uw} = 0.5\epsilon$, $\sigma_{uw} = 0.8\sigma$ (squares); $\epsilon_{uw} = 0.5\epsilon$, $\sigma_{uw} = 1.5\sigma$ (triangles). The dark and light translucent bands are 95% confidence intervals for L_{12} and L_{21} , respectively, for the lowest value of $\Delta\Pi$ and ΔP , respectively, for each set of solute–membrane interaction parameters. At least for the smaller values of $\Delta\Pi$ or ΔP , L_{12} and L_{21} are approximately constant and equal, verifying linear response and Onsager reciprocity.

for the pore radius $a = 6\sigma$ that was used in most of the simulations. As indicated by solid symbols in these figures, κ_{DO} and \mathcal{P}_s are independent of $\Delta\Pi$ up to the highest $\Delta\Pi$, except for the system with the largest fluxes ($\epsilon_{\text{uw}} = 1.5\epsilon$, $\sigma_{\text{uw}} = 1.5\sigma$, $\chi = 0.2$), for which linear response appears to hold up to $\Delta\Pi \approx 0.15\epsilon/\sigma^3$ ($c_{\text{u}0}^+/c_{\text{u}0}^- = 3$). Although a few simulations were carried out for systems with a larger pore radius of $a = 8\sigma$, for which the fluid fluxes were greater than those with $a = 6\sigma$ for the same solution and membrane properties, the fluxes were well within the range in which the system with the largest fluxes was still in the linear-response regime. Therefore, we can be confident that all systems besides that one were in the linear-response regime for the conditions simulated.

In the linear response regime, the fluid fluxes due to transmembrane differences in the hydrostatic pressure ΔP and osmotic pressure $\Delta\Pi$ (or, equivalently, chemical potential, $\Delta\mu$) are given by⁵³

$$\begin{bmatrix} Q \\ J_{\text{u}} - \bar{c}_{\text{u}}Q_{\text{v}} \end{bmatrix} = \begin{bmatrix} \Lambda_{11} & \Lambda_{12} \\ \Lambda_{21} & \Lambda_{22} \end{bmatrix} \begin{bmatrix} -\Delta P \\ -\Delta\mu \end{bmatrix}, \quad (13)$$

or using $\Delta\Pi = \bar{c}_{\text{u}}\Delta\mu$,³⁴ with $L_{11} = \Lambda_{11}$, $L_{12} = \Lambda_{12}/\bar{c}_{\text{u}}$, $L_{21} = \Lambda_{21}/\bar{c}_{\text{u}}$, and $L_{22} = \Lambda_{22}/\bar{c}_{\text{u}}^2$,

$$\begin{bmatrix} Q \\ J_{\text{u}}/\bar{c}_{\text{u}} - Q_{\text{v}} \end{bmatrix} = \begin{bmatrix} L_{11} & L_{12} \\ L_{21} & L_{22} \end{bmatrix} \begin{bmatrix} -\Delta P \\ -\Delta\Pi \end{bmatrix}, \quad (14)$$

where $\Lambda_{12} = \Lambda_{21}$ and $L_{12} = L_{21}$ by the Onsager reciprocal relations,^{53,54} $Q_{\text{v}} = J_{\text{v}}/\bar{c}_{\text{v}} = \dot{N}_{\text{v}}/\bar{c}_{\text{v}}$ is the volumetric solvent flux, and \bar{c}_{u} and \bar{c}_{v} are the average bulk solute and solvent concentrations, respectively, which we have calculated as the average of the concentrations in the upper and lower control regions, i.e., $\bar{c}_i = (c_i^+ + c_i^-)/2$. Note that a number of previous studies on concentration-gradient-driven transport^{33,34,50,55–58} have not distinguished between the total volumetric solution flux Q and the volumetric solvent flux Q_{v} in Eqs. (13) or (14), although this distinction is clear in the derivation by de Groot and Mazur⁵³ and in equations used in other studies.^{59,60} For the dilute solutions investigated in most of these studies, this distinction is not important since $Q \approx Q_{\text{v}}$ in this regime, but Q and Q_{v} can differ significantly at high solute concentrations such as those studied here, especially when the solute and solvent fluxes are in opposite directions.

From the definitions of the transport coefficients in Eqs. (8) and (14), $L_{12} = \kappa_{\text{DO}}/(k_{\text{B}}T)$, and given that $T = \epsilon/k_{\text{B}}$ in all our simulations, this means that L_{12} and κ_{DO} have the same numerical value in reduced LJ units in this study. For two of the systems for which L_{12} was measured in Fig. 7, we also measured L_{21} using the definition in Eq. (14) in simulations of pressure-driven flow in the absence of a transmembrane concentration difference for several pressure differences using the NEMD algorithm in Ref. 46. These results are presented in Fig. 7 and show that the $L_{12} = L_{21}$ reciprocal relation is verified, at least for the lowest applied pressures, with the consistency between our algorithm and the previously established and widely applied method in Ref. 46 demonstrating the validity of our method for quantifying non-equilibrium concentration-gradient-driven transport.

Figure 7 also shows that the pressure-driven flow simulations deviate from linear response at much lower values of ΔP than the

$\Delta\Pi$ values at which deviations occur in the concentration-gradient-driven flow simulations. This occurs because the solution flux for the pressure-driven flow is up to an order-of-magnitude higher than that for the concentration-gradient-driven flow in Fig. 7 for equivalent magnitudes of ΔP and $\Delta\Pi$, respectively, even if the excess solute volumetric flux, $J_{\text{u}}/\bar{c}_{\text{u}} - Q_{\text{v}}$, from which L_{21} is calculated is similar to the total solution flux Q from which L_{12} is calculated. As a result of the higher solution flux, the polarization of the solute concentration distribution around the pore and, therefore, deviations from the linear response, occur at lower ΔP for the pressure-driven flow than $\Delta\Pi$ for the concentration-gradient-driven flow. This means that much longer simulations were required to obtain roughly comparable statistical uncertainties in the linear-response regime for the pressure-driven flow simulations compared with the concentration-gradient-driven flow simulations, highlighting the computational benefits of directly measuring the diffusioosmotic mobility in NEMD simulations with an applied concentration gradient, at least for 2D membrane systems.

C. Comparison of simulation vs theory

We have previously derived a theory of fluid transport through a circular pore in an infinitesimally thin planar membrane due to a transmembrane concentration difference²⁰ by solving the continuum hydrodynamic (Stokes, advection–diffusion, and continuity) equations for low-Reynolds-number steady-state flow of a dilute solution of an incompressible Newtonian fluid under the assumptions that solute diffusion dominates solute advection (Péclet number $\text{Pe} \ll 1$) and that the effective solute–membrane interaction potential U is small compared with the thermal energy $k_{\text{B}}T$. This theory is straightforwardly generalized to arbitrary solute concentrations by analogy with a related theory derived for concentration-gradient-driven fluid transport parallel to a planar surface at high solute concentration.^{33,50} The equations derived in Ref. 20 for the transport coefficients quantifying the fluid fluxes at low concentration apply at high concentration, while the distinction between low and high solute concentrations is manifested in the concentration dependence of the osmotic pressure driving force in Eqs. (8) and (9). Therefore, the diffusioosmotic mobility κ_{DO} quantifying the total solution flux is²⁰

$$\kappa_{\text{DO}} = \frac{2k_{\text{B}}Ta^3}{\pi\eta} \int_0^1 d\zeta \zeta^2 \int_0^\infty dv \left(\frac{e^{-U/(k_{\text{B}}T)} - 1}{1 + v^2} \right), \quad (15)$$

and the solute permeance \mathcal{P}_s quantifying the solute flux (evaluated at the pore mouth at $z = 0$) is²⁰

$$\mathcal{P}_s = 2D \int_0^a dr \frac{re^{-U/(k_{\text{B}}T)}}{\sqrt{a^2 - r^2}}, \quad (16)$$

where a is the pore radius, η is the solution shear viscosity, D is the solute diffusivity, and the oblate–spheroidal coordinates ζ and v are defined in terms of the radial and axial coordinates by $r = a\sqrt{(1 + v^2)(1 - \zeta^2)}$ and $z = av\zeta$, respectively. The effective solute–membrane interaction potential U , which includes contributions both from direct solute–membrane interactions and indirect solvent-mediated interactions, is defined by²⁰

$$c(\zeta, v) \equiv c_{\text{u}\infty}(\zeta, v)e^{-U(\zeta, v)/(k_{\text{B}}T)}, \quad (17)$$

where $c(\zeta, \nu)$ is the solute concentration distribution and $c_{u\infty}(\zeta, \nu)$ is a hypothetical solute concentration distribution for the same boundary conditions but with $U = 0$.

The theory yields simple scaling relationships for the transport coefficients as a function of the pore radius a and strength ϵ and range λ of U in the limits of weak interactions ($\epsilon \ll k_B T$) and a small ($\lambda \ll a$) or large ($\lambda \gg a$) interaction range relative to the pore size.²⁰ Although none of our simulations correspond strictly to the $\lambda \ll a$ or $\lambda \gg a$ limits, λ is significantly smaller than a for all, but the smallest pore studied. Our simulation results are consistent with the predicted scaling in the $\lambda \ll a$ limit, in which κ_{DO} and \mathcal{P}_s are both expected to be proportional to the pore radius a^{20} as shown in Fig. 8. Figure 8 also shows that κ_{DO} is approximately independent of the average solute mole fraction for the simulated conditions, whereas \mathcal{P}_s depends significantly on the average solute mole fraction. The behavior of \mathcal{P}_s appears to be due to a subtle interplay of the opposing diffusive and advective solute fluxes for the systems in Fig. 8, which is not captured by the theory as it assumes that solute advection is negligible.

The dependence of κ_{DO} and \mathcal{P}_s on the solute–membrane interaction strength and range parameters, ϵ_{uw} and σ_{uw} , are given in the supplementary material in Figs. S10 and S11, respectively. It should be noted that the strength and range of U are not simply proportional to these parameters due to the complex many-body contributions to the effective interactions. Interestingly, Fig. S10 shows a linear dependence of κ_{DO} and \mathcal{P}_s on ϵ_{uw} for fixed σ_{uw} , which is consistent with the predicted scaling with the effective solute–membrane interaction strength ϵ for $\epsilon \ll k_B T$, even though the direct solute–membrane interactions are certainly not weak in

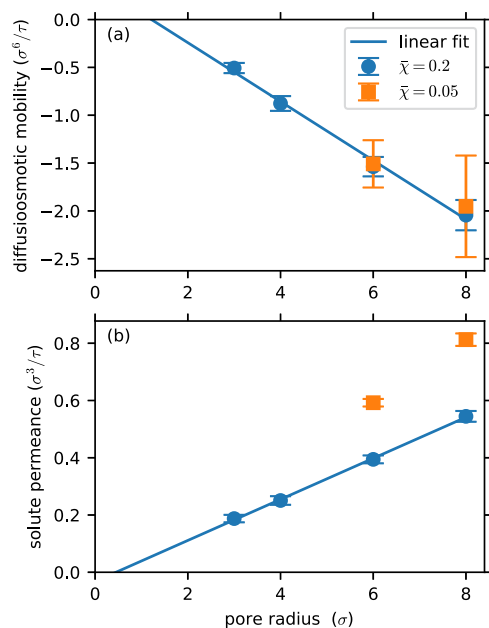


FIG. 8. (a) Diffusioosmotic mobility and (b) solute permeance vs pore radius for simulations with $c_{u0}^+/c_{u0}^- = 20$ and $\Delta P_0 = 0$ for systems with $\epsilon_{uw} = 0.5\epsilon$, $\sigma_{uw} = 0.8\sigma$, $a = 6\sigma$, and $\tilde{\chi} = 0.2$ (circles) or 0.5 (squares). The solid lines are linear fits to the data for $\tilde{\chi} = 0.2$.

all cases. The dependence of κ_{DO} and \mathcal{P}_s on σ_{uw} for fixed ϵ_{uw} shown in Fig. S11 is more complex, in part because σ_{uw} controls not only the range but also the strength of the direct solute–membrane interactions since a given solute particle interacts with more membrane particles as σ_{uw} increases; thus, \mathcal{P}_s varies non-monotonically while κ_{DO} even changes sign with increasing σ_{uw} .

We have used Eqs. (15)–(17) to predict κ_{DO} and \mathcal{P}_s for all the simulated systems without using any information from the NEMD simulations. We used analytical equations fitted to equilibrium MD simulation data for the diffusivity and shear viscosity of the LJ fluid over a wide range of density and temperature for the same interaction cutoff distance in our simulations⁶¹ to obtain $D = 0.0697\sigma^2/\tau$ and $\eta = 1.84\epsilon\tau/\sigma^3$ for the temperature $T = \epsilon/k_B$ and total bulk density $\rho_\infty \approx 0.787\sigma^{-3}$ in all the simulations. To obtain U from Eq. (17), we used the solute concentration profile from an equilibrium MD simulation with the same solute–membrane interaction parameters, pore radius, and average solute mole fraction as the NEMD simulation for which the transport coefficients were being predicted. In this case, $c_{u\infty}(\zeta, \nu)$ in Eq. (17) is a constant and equal to the bulk solute concentration in the equilibrium simulation. Distributions of the solute concentration and total fluid density in all the equilibrium simulations, in one dimension (1D) as a function of the axial (z) or radial (r) coordinate and in two dimensions (2D) as a function of both r and z , are given in Figs. S29–S38 of the supplementary material. The integrals in Eqs. (15) and (16) were computed using the quad and nquad functions, respectively, in the SciPy Python package, and 2D solute concentration distributions were interpolated using a bivariate spline with the RectBivariateSpline SciPy function.

The pore radius a in Eqs. (15) and (16) corresponds to where the hydrodynamic boundary conditions are applied in the continuum theory and does not necessarily correspond to the definition of the pore radius used up to this point, which was the distance from the pore center within which the centers of solid atoms were absent. The Gibbs dividing surface from equilibrium MD simulations has previously been shown to describe the hydrodynamic boundary position in NEMD simulations of fluid flow accurately,⁶² and so we have used this prescription to define an effective pore radius a_h to replace the actual pore radius a in Eqs. (15) and (16), given by

$$\int_0^{a_h} r[\rho_\infty - \rho(r, z = 0)] dr = \int_{a_h}^\infty r\rho(r, z = 0) dr, \quad (18)$$

where the total fluid density $\rho(r, z = 0)$ in the plane of the membrane pore at $z = 0$ was obtained from the 2D equilibrium distribution $\rho(r, z)$ by the same bivariate spline interpolation described earlier for the solute concentration distribution. [In practice, the second integral was calculated up to a finite value of r beyond which the total fluid density $\rho(r, z = 0)$ was zero.] As shown in Fig. S39 of the supplementary material, a_h is within a few percent of a , so either a or a_h could be used in Eqs. (15) and (16) with little difference. (The dependence of a_h on the solute–membrane interaction strength and range parameters, ϵ_{uw} and σ_{uw} , for fixed a are also given in the supplementary material in Figs. S40 and S41.)

Figure 9 compares the diffusioosmotic mobility κ_{DO} from the simulations with that calculated from the theory for all the simulated systems (which includes variations in pore radii,

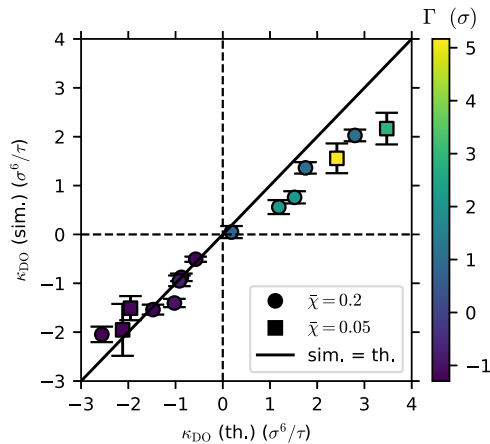


FIG. 9. Diffusioosmotic mobility from simulations vs theory for all systems except for those with the strongest attractive solute–membrane interactions ($\epsilon_{uw} = 1.5\epsilon$, $\sigma_{uw} = 1.5\sigma$) for $c_{u0}^+/c_{u0}^- = 20$. Symbols are colored by the surface solute excess Γ (units: σ), and different symbol shapes distinguish high ($\bar{\chi} = 0.2$, circles) and low ($\bar{\chi} = 0.05$, squares) average solute mole fractions. The simulation and theory values are equal along the solid line.

average solute mole fraction, and the strength and range of solute–membrane interactions) except for those with the strongest attractive solute–membrane interactions ($\epsilon_{uw} = 1.5\epsilon$, $\sigma_{uw} = 1.5\sigma$). The latter data are not included because they occur on a very different scale from the rest of the data, making visualization on the same figure difficult, and because the assumption in the theory of weak solute–membrane interactions certainly breaks down for these systems. A comparison of all the simulated systems in the linear-response regime is given in Fig. S12 of the supplementary material. The simulations and theory are also compared in Fig. S13 of the supplementary material for calculations using the actual pore radius a instead of the effective pore radius a_h in the theory, showing that this choice makes little quantitative difference.

There is good quantitative agreement between the theory and simulations for most of the data in Fig. 9, although deviations are evident for larger magnitudes of κ_{DO} , especially for positive κ_{DO} . Discrepancies between the theory and simulations are not entirely surprising, given the number of approximations made in the theory, namely weak effective solute–membrane interactions, a small Péclet number, and an infinitesimally thin planar membrane. The discrepancies appear to be largely due to the breakdown of the assumption of weak effective solute–membrane interactions, as indicated by the correlation between the deviation of the theory from the simulation results and the surface solute excess Γ used to color the data points in Fig. 9, which quantifies the degree of adsorption ($\Gamma > 0$) or depletion ($\Gamma < 0$) of the solute at the membrane surface relative to the bulk. Γ in Fig. 9 was calculated from the solute concentration profile $c_u(z)$ perpendicular to a membrane containing no pore in an equilibrium MD simulation of a system with otherwise identical fluid and membrane properties to the NEMD simulation using

$$\Gamma = \int_0^\infty \left(\frac{c_u(z)}{c_{u\infty}} - 1 \right) dz, \quad (19)$$

where, in practice, the upper integration limit in Eq. (19) was taken to be the maximum value of z in the simulation box [this choice was not crucial as $c_u(z) \rightarrow c_{u\infty}$ within the simulation box].

On the other hand, there does not appear to be a clear correlation between the discrepancies between the theory and simulation for κ_{DO} and other potentially relevant parameters such as the Péclet number Pe , pore radius a , or solute–membrane interaction strength and range parameters, ϵ_{uw} and σ_{uw} , as shown in Figs. S14–S17 of the supplementary material, in which the data points have been colored by the value of these parameters. We estimated Pe , which measures the relative magnitude of solute advection to solute diffusion, by

$$Pe = \left| \frac{\bar{c}_u Q_v}{J_u - \bar{c}_u Q_v} \right|, \quad (20)$$

where we have used the solvent volumetric flux Q_v instead of the total volumetric flux Q to quantify the advective solute flux because the total flux Q includes the diffusive component.

Figure 10 shows a similar comparison between theory and simulation to Fig. 9 but for solute permeance \mathcal{P}_s . Since solute advection is assumed to be negligible ($Pe \ll 1$) in the theory but is clearly significant in many of the simulations, for which $0.02 \lesssim Pe \lesssim 0.5$, in Fig. 11, we have also compared \mathcal{P}_s from the theory with the solute permeance from the simulations calculated from the diffusive flux only, which we define as

$$\mathcal{P}_{s,diff} \equiv - \frac{(J_u - \bar{c}_u Q_v)}{\Delta\Pi / (k_B T)}. \quad (21)$$

As with Fig. 9, we have excluded data for the strongest attractive solute–membrane interactions ($\epsilon_{uw} = 1.5\epsilon$, $\sigma_{uw} = 1.5\sigma$) simulated from Figs. 10 and 11, but the corresponding plots containing all the simulation data can be found in Figs. S18 and S19, respectively, in the supplementary material. As for κ_{DO} , the use of the actual pore radius a or effective pore radius a_h in the theory makes little difference, as shown in Fig. S20 in the supplementary material.

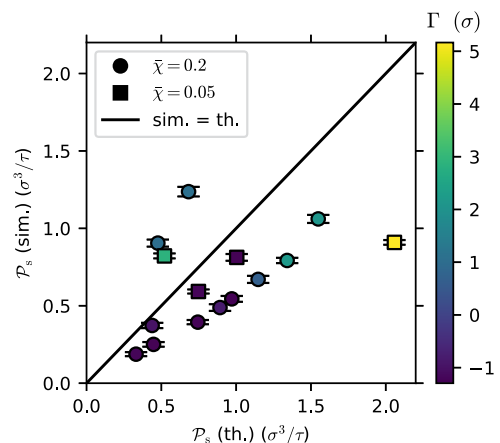


FIG. 10. Solute permeance from simulations vs theory for all systems for $c_{u0}^+/c_{u0}^- = 20$ except for those with the strongest attractive solute–membrane interactions ($\epsilon_{uw} = 1.5\epsilon$, $\sigma_{uw} = 1.5\sigma$). Symbols are colored by the surface solute excess Γ (units: σ), and different symbol shapes distinguish high ($\bar{\chi} = 0.2$, circles) and low ($\bar{\chi} = 0.05$, squares) average solute mole fractions. The simulation and theory values are equal along the solid line.

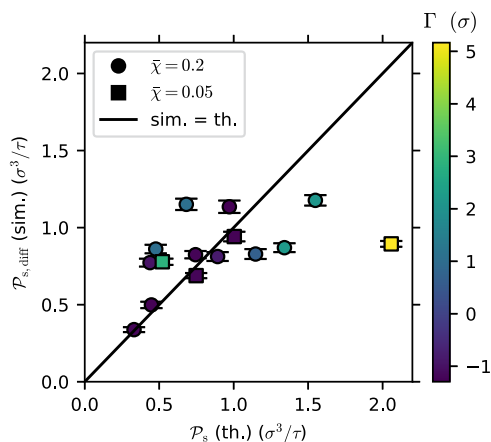


FIG. 11. Solute permeance from simulations (calculated from diffusive flux only) vs theory for all systems for $c_{u0}^+/c_{u0}^- = 20$ except for those with the strongest attractive solute–membrane interactions ($\epsilon_{uw} = 1.5\epsilon$, $\sigma_{uw} = 1.5\sigma$). Symbols are colored by the surface solute excess Γ (units: σ), and different symbol shapes distinguish high ($\bar{\chi} = 0.2$, circles) and low ($\bar{\chi} = 0.05$, squares) average solute mole fractions. The simulation and theory values are equal along the solid line.

The agreement between the theory and simulations is not as good for the solute permeance as for κ_{DO} , but the agreement appears to improve by excluding the advective flux from the simulation definition of the solute permeance. As for κ_{DO} , the discrepancies between the theory and simulation appear to be most strongly correlated with the strength of the effective solute–membrane interactions as quantified by the surface solute excess used to color the symbols in Figs. 10 and 11 (similar plots for all the simulated systems colored by the Péclet number Pe , pore radius a , or solute–membrane interaction strength and range parameters, ϵ_{uw} and σ_{uw} , are given in Figs. S21–S28 in the supplementary material). The stronger deviation of the theory from the simulations for the solute permeance than for the diffusioosmotic mobility as the solute–membrane interaction strength is increased, even when the advective solute flux is excluded, is consistent with our previous comparison of the theoretical predictions of these transport coefficients with the numerical solution of the full unapproximated continuum hydrodynamic model from which the theory was derived.²⁰ This comparison showed the solute permeance to be more sensitive than the diffusioosmotic mobility to the breakdown of the assumption of weak solute–membrane interactions in the theory, even at low Péclet numbers for which the advective solute flux was negligible.

IV. CONCLUSION

We have developed a constrained concentration- and pressure-difference algorithm for non-equilibrium molecular dynamics simulations of steady-state fluid transport driven by concentration and/or pressure differences across a porous membrane in a system with periodic boundary conditions. Our algorithm adapts a previous algorithm by Khalili-Araghi *et al.*,³¹ which controls the transmembrane concentration difference by applying an external force to solute particles in a transition region far from the membrane, by also applying an external force to solvent particles in

the transition region to control the transmembrane pressure difference. Applying this algorithm to a model system comprising a binary Lennard-Jones liquid mixture and a 2D Lennard-Jones membrane containing a circular pore, we have simulated steady-state concentration-gradient-driven fluid transport across a 2D membrane with molecular resolution for the first time, enabling accurate quantification of the solution and solute fluxes due to a given applied concentration difference. We have shown that the application of the pressure-difference constraint has a significant effect on the solute concentration distribution across the membrane and the steady-state solution flux due to a transmembrane concentration difference for both low and high average solute concentrations, although the solute flux is less affected by the pressure-difference constraint at low solute concentrations. We have also shown that the solution flux due to an applied concentration difference generated by our algorithm is consistent with Onsager reciprocity in the linear-response regime by comparison with fluid fluxes due to an applied pressure difference. Furthermore, we have shown that directly simulating a transmembrane concentration difference is far more efficient for quantifying the concentration-gradient-driven solution flux in the 2D membrane systems studied than the indirect approach of applying the Onsager reciprocal relations to pressure-driven flow simulations. This is because only very small pressure differences can be applied before the pressure-driven fluid fluxes deviate from linear behavior. Finally, we have shown that our recently developed theory of concentration-gradient-driven flow across a 2D membrane,²⁰ although derived for a continuum fluid model, gives reasonably good quantitative agreement with the molecular simulations, especially for the total fluid flux, demonstrating its utility for quantifying fluid transport driven by a solute concentration gradient even in molecular systems. Nevertheless, deviations from the simulation results are evident, particularly for strong solute–membrane interactions, for which the assumptions of the theory breakdown.

SUPPLEMENTARY MATERIAL

The supplementary material contains details of the parameters and properties of all the simulated systems, additional non-equilibrium simulation results (concentration, density, and pressure distributions; comparison of transmembrane osmotic pressure and hydrostatic pressure differences calculated by different methods; verification of linear response for the solute permeance; verification of the independence of measured transport coefficients of system size and transition region width; additional plots of transport coefficients vs system parameters; additional comparisons of transport coefficients obtained from simulation and theory), and solute concentration and total density distributions from equilibrium simulations.

ACKNOWLEDGMENTS

This work was supported by the Australian Research Council under the Discovery Projects funding scheme (Grant No. DP210102155). This research was undertaken with the assistance of resources and services from the National Computational Infrastructure (NCI), which is supported by the Australian Government,

and from the University of Adelaide's Phoenix High-Performance Computing service.

AUTHOR DECLARATIONS

Conflict of Interest

The authors have no conflicts to disclose.

Author Contributions

Daniel J. Rankin: Formal analysis (supporting); Investigation (supporting); Methodology (equal); Writing – original draft (equal); Writing – review & editing (supporting). **David M. Huang:** Conceptualization (lead); Data curation (lead); Formal analysis (lead); Funding acquisition (lead); Investigation (lead); Methodology (equal); Project administration (lead); Supervision (lead); Writing – original draft (equal); Writing – review & editing (lead).

DATA AVAILABILITY

Moltemplate³⁷ input scripts for creating the initial simulation configurations and sample LAMMPS^{35,36} input scripts for running each type of MD simulation in this study can be found at <https://doi.org/10.25909/17139593>. Other data that support the findings of this study are available from the corresponding author upon reasonable request.

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