Model of osmosis in a single-file pore

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Single-file transport of water and other small molecules through narrow pores in osmosis has drawn considerable attention in recent years due to its extensive application in biology and industry. In this work, we propose a discrete model to describe nonideal osmosis through single-file pores. Every site is assumed to be occupied by a molecule according to experiments and simulations. Hence, a dense chain can always be found, and collective hopping is the only movement method enabling the molecular chain to move. The roles of solute in osmosis are clarified in this model. Those molecules reflected at the pore entrance produce osmotic pressure, and those inside the pore contribute to the flow resistance of the molecular chain. The solute molecules that can enter the pore but cannot penetrate it may significantly reduce the osmotic flux, although they are all rejected by the pore. This conclusion can help to clarify the emerging debate about whether the reflection coefficient of the fully rejected solute can be less than 1. The design of highly efficient membrane pores may also benefit from this study.

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I. INTRODUCTION

Single-file transport has been observed in many natural and man-made nanopores, including ion channels [1], aquaporins (AQPs) [2], carbon nanotubes (CNTs) [3], and other synthetic materials [4]. A key feature of such transport is that molecules inside the pore cannot pass each other. As a pervasive transport phenomenon, osmotic flow plays an important role in many fields of biology [5,6] and industry [7]. Many important properties of osmotic flow through single-file pores are thought to be attributed to this feature, including the sieving effect [8]. Therefore, it is not surprising that the single-file transport of osmosis has been widely investigated [3]. However, the role of solutes in single-file osmosis and the coupled flow of solvent and solute have not been thoroughly elucidated to date [6,9].

A phenomenological model proposed by Kedem and Katchalsky (K-K equations) [10] has been widely used in various membrane systems, including cell membranes. In this model, the first reflection coefficient, which quantifies the achieved osmotic flux compared with the ideal flux, is assumed to be 1 for the completely rejected solute. However, several experiments involving single-file pores [11,12] suggest an inconsistency with this basic assumption. The reflection coefficients for several solutes were found to be less than 1 despite not being able to pass through the pore at all. The geometries of the solute and the pore entrance were suspected to be responsible for this abnormal phenomenon. Therefore, limitations may exist for the K-K equations in single-file osmosis. However, the phenomenon has not received much interest, and an improved and quantified explanation is still lacking [9], which may have influenced the understanding of other single-file transport processes.

To clarify the problem, the details of molecular movement should be considered in the single-file pore. Finkenstein [6] predicted the presence of single-file transport across protein pores on a cell membrane and expanded the awareness of such a transport process. Tom Chou [13–15] analyzed the osmosis through a single-file pore based on the exclusion process. In his analysis, the pore was divided into several discrete sites, with a particle able only to hop to a neighboring empty site. Osmotic flow was induced by different concentrations of solvent across the membrane. The influence of the particle-pore interaction on the flow was also discussed. His work opened a new field of transport through a single-file pore and has influenced many subsequent studies [3,16].

After the discovery of the atomic structures of aquaporin-1 (AQP1) [2] and other narrow pores [1], more details of single-file transport were discovered by simulation [17–19]. For example, an end-to-end chain of water with random hopping can always be found in a narrow CNT [20]. Berezhkovskii *et al.* [3] introduced the continuum time random walk (CTRW) model to describe this type of movement. A good correlation was found between the predicted diffusion coefficient and simulation results obtained from molecular dynamics (MD) [3]. Based on the CTRW model and nonequilibrium thermodynamics, the flux of solvent in ideal osmosis could be predicted using concise and elegant methods [17,21]. This model described the situation of a continuum limit for water molecules across single-file pores without considering the presence of solute molecules in the pores. The authors claimed that there was a complementary relationship between their model and Chou's [14]. Although the CTRW model fits well with ideal osmosis [17,21], it fails to consider the condition that solute molecules can enter the pore, which is very common in biological transport. Therefore, reliable treatment of the nonideal solute is important in the modeling of single-file osmosis. Such treatment may also enable one to understand the inconsistency between the K-K equations and the experiments for the single-file osmosis [11,12].

In this work, we adopt a discrete-sites method to analyze the osmotic flow across a single-file pore. It is assumed that

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every site in the pore is occupied by one molecule. Therefore, an end-to-end chain can always be found. Similar to the CTRW model, the collective hopping is the only movement behavior in the pore; this behavior is somewhat similar to the MD simulation results [20,21]. The mobility of solute between two neighboring sites is obtained according to the overall free energy change due to the presence of the solute in the pore. The roles of solute in osmosis are clarified based on the flux of the solvent and solute. This model may help to explain the inconsistency between experiments and the classical theory in the nonideal osmosis through single-file pores.

The paper is organized as follows. In Sec. II we list a classic description of the osmosis. Then we establish a simple model to explain the dynamics of particles inside the single-file pore in Sec. III. Their results are presented and compared to the theory in Sec. IV. Finally, we present our conclusions in Sec. V.

II. CLASSIC DESCRIPTION OF OSMOSIS

A. Osmotic permeability and diffusion permeability

If two reservoirs containing a dilute solution with different solute concentrations are separated by an ideal semipermeable membrane, then water flows from the lower concentration reservoir to the other reservoir. For a single pore, the water flux is proportional to the concentration difference of the solute ΔC_s:

$$j_w = p_f \Delta C_s, \tag{1}$$

where p_f (m^3/s) is called the osmotic permeability of the pore.

Water molecules can also diffuse across the membrane. To quantify the ability for water diffusion, a fraction of water can be labeled, i.e., isotope labeling, to ensure that they can be traced during experiments. These molecules are usually regarded as "tracers" and are believed to have almost the same properties as those of normal water molecules. Therefore, tracers can freely diffuse across the membrane, which is different from osmosis with volume flux. The diffusion rate of tracers across a single pore is also proportional to its concentration difference ΔC_{tr}:

$$j_{tr} = p_d \Delta C_{tr}, \tag{2}$$

where p_d (m^3/s) is called the diffusion permeability of the pore.

For a single-file pore with an average number of n solvent molecules inside, the CTRW model predicts that the two coefficients can be related by $p_f/p_d = n + 1$ [21].

B. General situations

For general situations, the osmotic pressure difference and the hydrostatic pressure difference across the membrane are coupled. Kedem and Katchalsky [10] proposed the following equations based on nonequilibrium thermodynamics:

$$J_v = L_{vv}\,\Delta P + L_{vD}\,\Delta\Pi, \tag{3}$$

$$J_D = L_{Dv}\,\Delta P + L_{DD}\,\Delta\Pi, \tag{4}$$

where J_v [$m^3/(m^2\,s)$] is the volume flux across the membrane, J_D [$m^3/(m^2\,s)$] is the relative flow of the solute versus water and is a measure of the exchange flow, L_p is the hydraulic conductivity, L_{pD} is the osmotic permeability of the membrane, L_{Dp} is called the ultrafiltration coefficient, and ΔP and $\Delta\Pi$ are the differences in the hydrostatic pressure and the osmotic pressure, respectively. J_v and J_D are defined as

$$J_v = J_w\,V_w + J_s\,V_s, \tag{5}$$

$$J_D = \frac{J_s}{\overline{C_s}} - J_w\,V_w, \tag{6}$$

where J_w [$mol/(m^2\,s)$] and J_s [$mol/(m^2\,s)$] are the molar fluxes of solvent and solute, respectively, V_w and V_s are the molar volumes of solvent and solute, respectively, and $\overline{C_s}$ is the average solute concentration in the membrane. To make Eqs. (3) and (4) more convenient to use, the model was simplified to

$$J_v = L_p(\Delta P - \sigma_o\,\Delta\Pi), \tag{7}$$

$$J_s = \overline{C_s}(1-\sigma_s)J_v + \omega\,\Delta\Pi, \tag{8}$$

where σ_o and σ_s are collectively known as the reflection coefficients, ω is the mobility of the solute, ΔC_s is the concentration difference of the solute. It is assumed that σ_o and σ_s have the same value via the Onsager relations [10]. It was this assumption that was found to be inconsistent with the experiments [11,12].

III. MODEL DESCRIPTION

In this study, we consider the transport process across a single-file pore connecting two reservoirs. The mole fractions of solvent and solute molecules in the left (right) reservoir are represented as $X_{L,0}$ and $X_{L,1}$ ($X_{R,0}$ and $X_{R,1}$, respectively). According to MD simulations, a dense chain of molecules can be found in many single-file pores, including the CNT [20,22] and AQP1 [21]. The CTRW model assumes that the pore can be divided into n discrete sites based on the average n molecules in the pore [3]. Numbers from 1 to n can be used to represent the corresponding sites. The movement of the molecular chain is achieved by collective hopping. This phenomenon means every site inside the pore is assumed to be occupied by one molecule. In a hopping event, all the molecules collectively hop to the left or the right. For example, a molecule on the site i may move to the site $i-1$ or $i+1$. The migration approach is an extreme situation without considering the influence of the molecule-pore interaction on the particle density. However, the model is able to reflect some characteristics of the single-file transport.

In this work, we also adopt a discrete model similar to CTRW with the difference that solute molecules can also enter the pore and interact with the solvent. If there are no solute molecules in the two reservoirs, the solvent chain collectively hops in both directions with the average rate k_0. In other words, $k_0\,dt$ is the probability for the solvent chain to hop in one direction per unit time dt. The collective hopping rate can be described by Kramers' theory [15,16,23]:

$$k_0 = \omega_0 \exp\left(-\frac{\Delta G_0}{k_B T}\right), \tag{9}$$

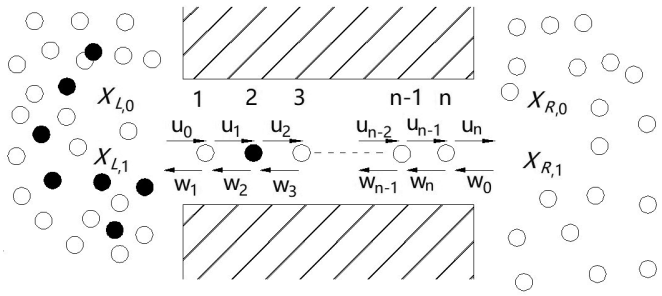

FIG. 1. Kinetic scheme of transport across the pore. Two reservoirs are separated by a membrane with several single-file pores. The collective hopping is assumed to be the only effective means to move inside the pore. Note the hopping rate u_i (w_i) represents the rate of the chain with only one solute from site i ($i+1$) to $i+1$ (i), with the other sites occupied by solvent particles in the process.

where ω_0 is the prefractor or the attempt rate in Kramers' theory, ΔG_0 is the overall free energy barrier of the chain during the hopping event, and k_BT is the thermal fluctuation.

If solute molecules are present in the reservoir and they can enter the pore, the collective hopping rates may be influenced. Here we use the following method to define the solute based on its migration properties. In general, the migration properties of solute and solvent are always different. Let us consider a situation where a solute molecule is located on site i (not the first or the last site), with the remaining sites all filled with solvent. Due to the presence of the solute particle, the free energy barrier for the chain to hop to the right has changed $\Delta G_{i\to i+1}$. Therefore, the collective hopping rate to the right becomes

$$\omega_0 \exp\left(-\frac{\Delta G_0 + \Delta G_{i\to i+1}}{k_BT}\right) = k_0 u_i, \tag{10}$$

where $u_i = \omega_0 \exp(-\Delta G_{i\to i+1}/k_BT)$ refers to the relative rate of solute to solvent. Accordingly, if there is only one solute molecule present inside the pore and it is located on site i, the collective hopping rate of the chain can be specified as $u_i k_0$ (hopping to right) or $w_i k_0$ (hopping to left), as shown in Fig. 1. In the model, the relationship $u_0\, u_1 \cdots u_n = w_0\, w_1 \cdots\ w_n$ should be satisfied because of the rule that no net flux of solute occurs without a concentration difference.

During the evolution of the chain's arrangement, the possibilities of molecules entering and leaving the pore are calculated as follows:

(1) A solute molecule enters the pore from the left (right), and a solvent molecule leaves from the right (left). The entrance rate of solute from a reservoir is proportional to its concentration or the mole fraction in the reservoir [15,16,23]:

$$k_{L,1} = X_{L,1}\omega_0 \exp\left(-\frac{\Delta G_0 + \Delta G_{0\to 1}}{k_BT}\right) = X_{L,1}u_0 k_0, \tag{11}$$

where $k_{L,1}$ is the hopping rate with a solute molecule entering the pore from the left reservoir, and $\Delta G_{0\to 1}$ refers to the additional free energy barrier between the left reservoir and site 1 due to the solute molecule. Meanwhile, in the subscript of the hopping rate, L or R indicates the original reservoir of the newly entered particle, and 0 or 1 indicates the species of the particle.

(2) A solvent molecule enters the pore from the left (right), and a solute molecule leaves from the right (left). Similarly, the hopping rate can be written as

$$k_{L,0} = X_{L,0}\omega_0 \exp\left(-\frac{\Delta G_0 + \Delta G_{n\to n+1}}{k_BT}\right) = X_{L,0}u_n k_0. \tag{12}$$

(3) A solute molecule enters the pore from the left (right), and a solute molecule leaves from the right (left). The collective rate will be influenced by their corresponding hopping rates. It is assumed that the overall free energy barrier is the sum of the barriers on the respective sites. Thus, the collective rate is

$$\begin{aligned} k_{L,1} &= X_{L,1}\omega_0 \exp\left(-\frac{\Delta G_0 + \Delta G_{0\to 1} + \Delta G_{n\to n+1}}{k_BT}\right) \\ &= X_{L,1}u_0 u_n k_0. \end{aligned} \tag{13}$$

Because the solute concentration is much lower than that of the solvent, the probability of finding a solute molecule in the pore is relatively small, with the probability of finding two solute molecules even smaller. Therefore, it is reliable that the assumption should not influence the system's evolution. We also use this rule to address other situations with multibarriers in a hopping event. We will show in Sec. IV B that this assumption can be used to explain the experimental data.

(4) A solvent molecule enters the pore from the left (right), and a solvent molecule leaves from the right (left). In this process, the number of solvent molecules in the left reservoir increases by 1, while the solvent number is reduced by one in the other side. Therefore, the free energy change is the chemical potential difference across the membrane. According to the principle of detailed balance [24], the rates in the two directions can be related by

$$\frac{k_{L,0}}{k_{R,0}} = \exp\left(-\frac{\Delta\mu_w}{k_BT}\right) = \frac{X_{L,0}}{X_{R,0}}, \tag{14}$$

where $\Delta\mu_w$ denotes the chemical potential difference of the solvent across the membrane.

To quantify $k_{L,0}$ and $k_{R,0}$, we must introduce the influence of the solute on the solvent. In the tracer diffusion experiment, the tracer can be treated as a special "solute" with the same properties as that of the solvent. The entrance rates of the solvent and the tracer from the left (right) reservoir can be written as $k_{L,0} = k_0 X_{L,0}$ and $k_{L,1} = k_0 X_{L,1}$, respectively ($k_{R,0} = k_0 X_{R,0}$ and $k_{R,1} = k_0 X_{R,1}$, respectively). The sum of the entrance rates of all the species is $k_{L,0} + k_{L,1} + k_{R,0} + k_{R,1} = 2k_0$. In ideal osmosis, the solutes cannot enter the pore, namely, $k_{L,1} = k_{R,1} = 0$. Zhu *et al.* [21] and Hummers *et al.* [17] assumed that the hopping rates of the solvent chain obeyed the relationship $k_{L,0} + k_{R,0} = 2k_0$. Therefore, the sum of the entrance rates of all the species is also $2k_0$. These two special situations suggest that an upper limit does exist for the sum of the entrance rates of all species. This phenomenon can be understood as follows. All molecules experience a random force exerted by neighboring molecules so that their movement is also random. The random motion is attributed to thermal fluctuations, and its strength is reflected by the temperature. If instantaneous fluctuations are sufficiently strong, a molecule may overcome the barrier and enter the pore because of the large force it experiences. In other words, a collective hopping

event occurs. If the temperature does not change, the thermal fluctuations will not change. Therefore, it is reasonable that there is an upper limit to the probability of the particles' collective hopping. To match the previous results, we adopt the hypothesis that the entrance rates of all species are related by the following equation:

$$\sum_{i=1}^{n}(k_{L,i}+k_{R,i})=2k_0, \tag{15}$$

where n refers to the number of the species in the two reservoirs. This formula introduces the influence of solute on the entrance of the solvent in a simple and straightforward method.

Based on the above descriptions, we can quantify all of the possibilities of the next hopping event based on the current arrangement of molecules in the pore. The analytical solution for osmosis through a one-site pore is provided in the following section, whereas it becomes too complicated to solve for a pore with more sites. Thus, we turn to computer simulation to study the evolution of the system from the random initial state with the Gillespie algorithm (kinetic Monte Carlo) [25]. With the stochastic method, we can simulate the arrangement evolution for a long procedure. The fluxes of all species are obtained by counting the molecules that translocate from one reservoir to the other. The standard error bars were averaged by nine independent simulations.

IV. RESULTS AND DISCUSSION

A. Two species in a one-site pore

For a two-species osmotic system connected by a single-file pore, two filled states exist: solute-filled (P_1) and solvent-filled (P_2), as shown in Fig. 2. We can write the following equations regarding the transition rates:

$$\begin{aligned}
k_1 &= k_0 X_{L,1} u_0 u_1,\\
k_2 &= k_0 X_{R,1} w_0 w_1,\\
k_3 &= k_0 X_{L,1} u_0,\\
k_4 &= k_0 X_{R,1} w_0,\\
k_5 &= k_0 X_{L,0} u_1,\\
k_6 &= k_0 X_{R,0} w_1.
\end{aligned}$$

Obviously, the filling situation only converts between two states: solvent occupied and solute occupied. Based on the principle of the Markov chain [24], the probabilities of the two states are related by

$$\frac{P_1}{P_2}=\frac{k_5+k_6}{k_3+k_4}. \tag{16}$$

The probabilities of the solvent and solute coming from the left are $(P_1k_5+P_2k_7)/(P_1k_5+P_2k_7+P_1k_6+P_2k_8)$ and $(P_1k_1+P_2k_3)/(P_1k_1+P_2k_3+P_1k_2+P_2k_4)$, respectively. For simplicity, we use x and y to represent the two intermediate variables. Thus, the fluxes of the solvent and solute can be expressed as

$$\begin{aligned}
J_1 &= P_1x(k_1+k_5)-P_1(1-x)(k_2+k_6)\\
&= \frac{k_3k_5-k_4k_6+(k_5+k_6)(k_7-k_8)}{k_3+k_4+k_5+k_6},
\end{aligned} \tag{17}$$

$$\begin{aligned}
J_2 &= P_2y(k_3+k_7)-P_2(1-y)(k_4+k_8)\\
&= \frac{(k_1-k_2)(k_3+k_4)+k_3k_5-k_4k_6}{k_3+k_4+k_5+k_6}.
\end{aligned} \tag{18}$$

Accordingly, the two reflection coefficients in Eqs. (7) and (8) can be obtained:

$$\sigma_o=\frac{J_1V_1+J_2V_2}{J_{1,\mathrm{ideal}}V_1}, \tag{19}$$

$$\sigma_s=\frac{J_1}{J_1V_1+J_2V_2}, \tag{20}$$

where V_1 and V_2 are the partial molar volumes, and $J_{1,\mathrm{ideal}}$ is the solvent flux for ideal osmosis. We can find a shared item in the numerator of the flux expressions in Eqs. (17) and (18). This indicates the mutual effects on flux of the two components after solute molecules entering the pore. This property can be elucidated by the reflection coefficients. On the other hand, the calculation of the reflection coefficients requires the molar volume of solute and solvent, unless the flux of one species is zero. Since the flux of solute is generally much smaller than that of solvent, the flux of the two species can also be used to approximately analyze the magnitude of σ_o and σ_s.

B. Comparison with previous works

Now we compare our model with the CTRW model for two situations: the tracer diffusion and ideal osmosis. Figure 3 shows the diffusion flux of the tracer and osmotic flux of the solvent when $X_{L,1}$ increases from 0 to 0.05, for pores with different lengths. The right reservoir contains pure solvent. All the fluxes in this work are expressed using k_0 as a unit.

Clearly, both the diffusive and osmotic flux increase linearly with the difference in solute concentration. This finding agrees well with the basic rules of diffusion and osmosis for the dilute solution. The number of sites in the pore has a different effect in the two situations. Shorter pores are favorable for tracer diffusion. The osmotic flux in ideal osmosis, in contrast, is independent of the site number because every hopping event indicates that a water molecule has been conducted. From this figure, it is clear that the current model can well represent the fundamental prediction of the CTRW model.

The single-file transport of the tracer has been investigated for a long time [26]. Previous studies [27,28] have found that the density of the particles inside the pore can greatly influence the tracer diffusion. For a lone particle in an infinitely long single-file pore with discrete sites, the particle can freely hop to neighboring empty sites. The particle's movement is "memoryless," and the diffusion is a "normal" diffusion with the mean square displacement in proportion to the observed time. However, if several particles coexist in the pore, the correlations between the vacancies cannot be ignored and may influence the particles' movement. When a particle hops in a certain direction, a vacancy is left at the initial site, and the next site in the same direction may become occupied by another particle. Therefore, the next hopping is more likely to occur in the reverse direction. The mean square displacement will be proportional to $\sqrt{t}$ instead of t, and subdiffusion of the particles can be observed [27]. For a single-file pore with a finite number of molecules, rapid exchange of molecules may occur between

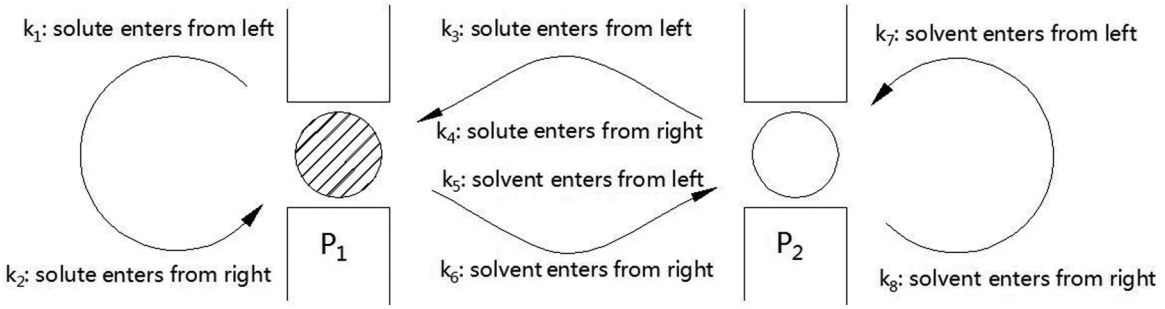

FIG. 2. Transition between two states (solute and solvent) in the one-site model. Every hopping event denotes another particle replacing the former.

the pore and the two reservoirs. The formation of vacancies inside the pore is unlikely to occur and can be neglected for relatively short chains considered. Accordingly, the main mechanism leading to the $\sqrt{t}$ dependence in the single-file diffusion is absent. And the collective hopping method is applicable for a short single-file pore, as shown in MD studies of AQPs [21] or CNTs [20]. In the following section, we will show that our model can complement previous models [3,15] in several aspects.

In MD simulations, it is observed that the solvent-pore interaction strength can affect the number of water molecules and their distribution for single-file transport [20,29–31]. As the interaction strength increased, the average number of water molecules inside the pore increased until the pore was filled. The diffusion rate also reached a maximum around this critical interaction. Further increasing the water-pore interaction could result in a decrease in the diffusion rate. For biological pores, the water-pore interaction is more complicated, whereas several clues have been identified. Horner *et al.* [32] summarized the diffusion permeability of a series of pores containing a single-file part. These researchers determined a logarithmic relationship between the diffusive mobility and the number of hydrogen bonds between water and the residues in the pore. Here we aim to discuss the diffusion of the chain of solvent based on this model. In the equilibrium state, the collective hopping rate can be expressed based on Eq. (9). If an end-to-end chain has formed inside the pore, then stronger attraction between the chain and the pore will reduce the chain's mobility. It is reliable to believe that the free energy barrier increases in this process. If there are m binding sites between the chain with the pore and the contribution of one binding site is ΔE, the energy barrier during hopping can be roughly expressed as $\Delta G_0 + m\,\Delta E$. Then the new hopping rate will change to $k_0 = \omega_0 \exp[-(\Delta G_0 + m\,\Delta E_0)/k_B T]$.

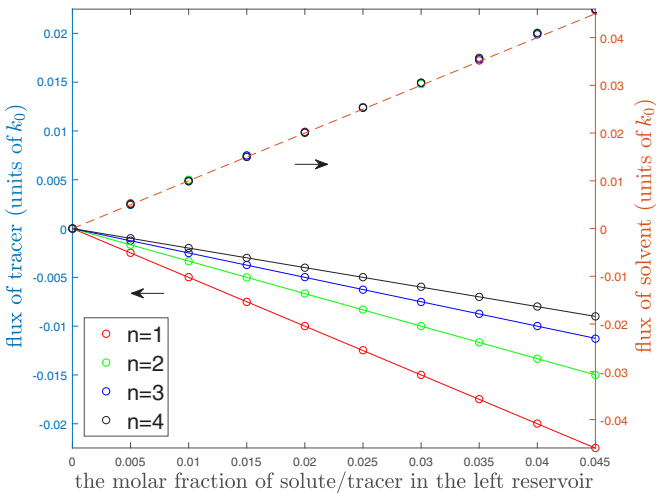

FIG. 3. The flux of the tracer in the simulation of diffusion and the flux of the solvent in ideal osmosis. The dashed and the solid lines represent the flux predicted by the CTRW model.

According to Zhu [21], there is a simple relationship between the diffusion permeability of a single-file pore p_f and the collective hopping rate, $p_f = v_w k_0$, where v_w is the volume of one water molecule. In a single-file pore, p_f can be roughly related to the diffusion coefficient of solvent across the pore D_w, $D_w = 3np_f/\pi r$ [6,33], where n and r refer to the average number of water molecules inside the pore and the pore radius, respectively. In experiments, D_w is relatively easy to obtain and is often used to characterize the mobility of water molecules.

With the above equations, we can obtain the dependence of the diffusion coefficient on the number of hydrogen bonds between the water chain and the pore:

$$\ln(D_w) = \ln\left(\frac{3nv_w}{\pi r}\right) - \frac{\Delta G_0}{k_B T} - \frac{m\Delta E_0}{k_B T}. \qquad (21)$$

For a series of protein pores with similar lengths and an average number of water molecules, a logarithmic relationship can be found between D_w and m, which is consistent with Horner's experiments [32]. Compared with Horner's work, we find the contribution of one binding site to the overall energy barrier is approximately $0.155\,k_B T$, which fits well with the conclusion that the binding energy is as low as a few $k_B T$ [34]. Although this value is small, multiple hydrogen bonds can reduce the diffusion coefficient by two orders of magnitude.

C. Influence of the entrance and exit rates of the solute

For a nonideal solute molecule, the penetration process across the pore involves entering, translocating, and leaving. Therefore, it is important to analyze the interaction between the solute molecules and the entrance or internal sites.

According to the principle of detailed balance [24], the hopping rates between two sites are related by their relative free energy. Therefore, the entrance and exit rates at one end of the pore are not independent of each other. If a strong

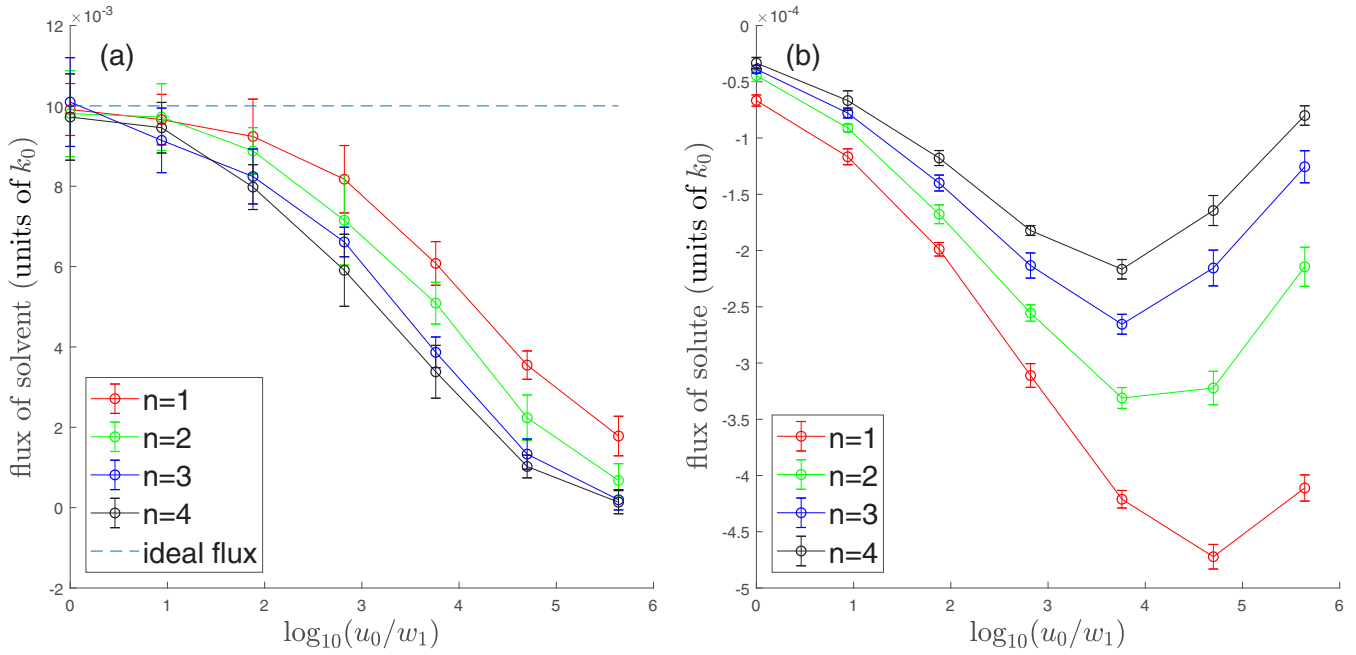

FIG. 4. The flux of solvent (a) and solute (b), as a function of the pore-solute interaction. The mole fractions of all the species in the two reservoirs are maintained as a constant: $X_{L,0} = 0.99$, $X_{L,1} = 0.01$, $X_{R,0} = 1.0$, $X_{R,1} = 0$. The dotted line in (a) refers to the flux of solvent in an ideal osmotic system.

attraction exists between the solute and the pore, then the solute molecules are more likely to stay inside the pore rather than leaving, i.e., the entrance rate is relatively larger, and the exit rate is smaller. Kolomeisky [23] assumed that the hopping rates between the two sites are related by

$$\frac{u_0}{w_1} = \frac{u_0(\epsilon = 0)}{w_1(\epsilon = 0)} \exp\left(\frac{\epsilon}{k_B T}\right) \tag{22}$$

if the interaction between the solute and latter site changes. In this equation, $u_0$and w_1 refer to the forward and backward hopping rates, respectively; ϵ is the change of the solute-site interaction. In this equation, we also adopt a similar strategy. Assuming the pore is uniform and symmetric, the original hopping rates are as follows: $u_0 = u_1 = \cdots = u_n = w_0 = w_1 = \cdots = w_n = 0.1$. The interaction between the solute and the ends of the pore varies so that u_0 and w_1 will change to $u_0 t$ and w_1/t (t is an intermediate variable). The mole fractions of solute in the two reservoirs remain 0.01 and 0, as used previously.

Figure 4 shows the influence of the entrance and exit rates on the fluxes of solvent and solute. It is observed that the higher entrance rate of solute simply reduces the flux of solvent, whereas the solute flux exhibits a nonmonotonic behavior during the increase of u_0/w_1. The trends of the solvent and solute flux can be understood as follows. According to Eq. (15), the sum of the entrance rates for all species is limited. Therefore, as the entrance rate of solute increases and the exit rate decreases, the overall entrance rate of solvent from the two reservoirs will be reduced. Because the respective mole fractions of solvent in the two reservoirs remain unchanged, the respective entrance rate of solvent from the two reservoirs both decrease. As a result, the difference of the migration probabilities of solvent in the left and right directions also decreases. In other words, the achieved flux of solvent decreases, as shown in Fig. 4(a). Because the volume flux is mainly contributed by solvent, the driving force in osmosis can be directly related to the entrance rate of solute (or the rejection probability). On the other hand, further increasing the attraction leads to an overly low probability for the exit rate of the solute. The excessively long residence time of the solute jeopardizes the flux of all the species and even causes the pore to be blocked. This phenomenon was also reported in MD simulations [35,36]. For example, urea molecules can fill the CNT and expel water molecules via the strong C-C interaction [37]. Therefore, there exists an optimized pore-solute interaction maximizing the solute flux.

D. Influence of the translocation rates of the solute

Figure 5 shows the fluxes of the solvent and the solute as a function of the translocation rate of the solute through a pore with two sites. The influence of the entrance rate of the solute is demonstrated by three situations. We can determine that the increase in the translocation rates of solute is beneficial to the flow of solute, whereas the effect on the solvent is reversed. For the situation $u_0 = 0.1$, as u_1 increases from 0 to $0.512\,k_0$, the flux of solvent is reduced by only 10% and appears to reach a saturation value. A similar increasing trend for the solute flux can also be observed. This trend means that the entrance and exit rates become the limiting factor for the penetration of solute and solvent.

If u_0 is relatively larger, then the decreasing trend of the solvent flux becomes more obvious. No saturation values for the solute flux are observed. Moreover, the flux of solute significantly increases as the translocation rates increase. For $u_0 = 0.5$ or 1.0, the solvent and solute flux can even reach the same order of magnitude with large translocation rates.

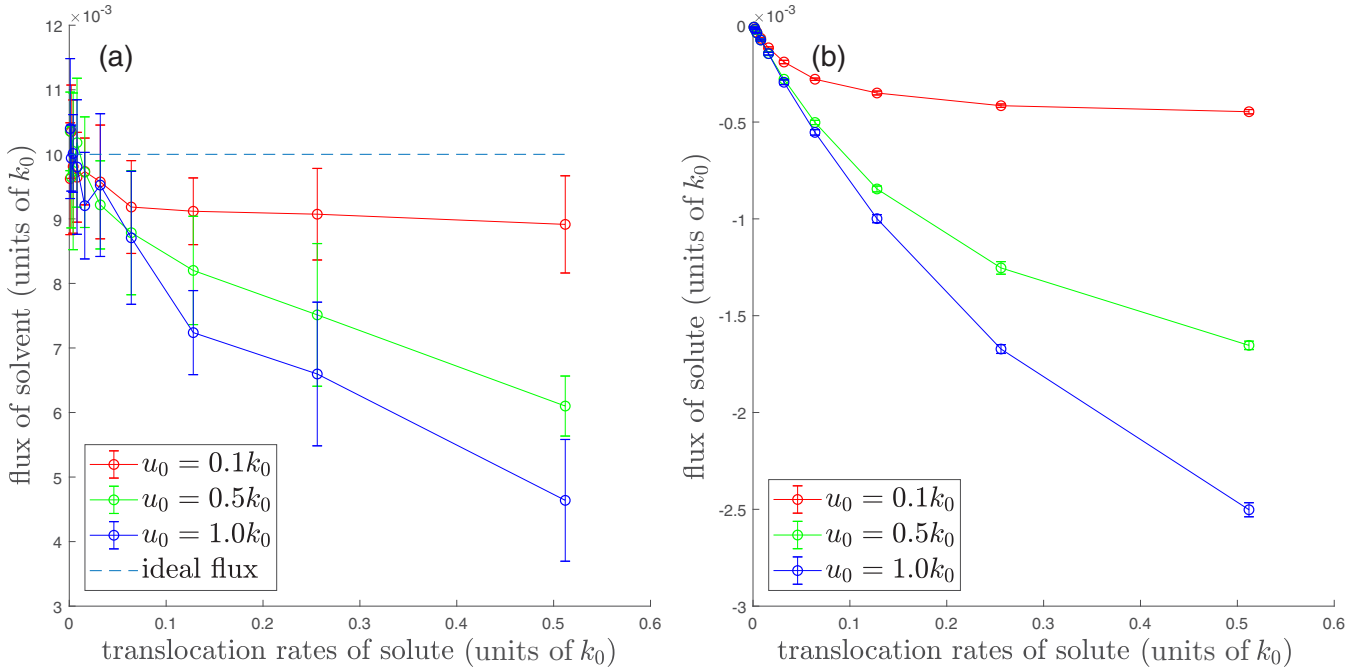

FIG. 5. The flux of solvent (a) and solute (b) as a function of the translocation rates of the solute. The dashed line in (a) refers to the flux of solvent in an ideal osmotic system. The components in the two reservoirs are the same as those described in the previous section. The translocation rates, including u_1, w_1, vary simultaneously as shown on the x axis.

Since the entrance and exit rates are constant, the maximum driving force of the solvent and solute also remains the same. Accordingly, the translocation rates of solute become important intermediate parameters of the penetration process.

The potential of narrow CNT arrays in osmosis has been supported in both simulation [38] and experiment [39]. The discussion indicates that the entrance rate of solute determines the maximum separation efficiency of the single-file pore. To increase the reflection coefficients of the membrane, surface modifications at the entrance of the pore may be an effective method to increase the energy barrier for the solute. This approach has been applied in the previous investigations, with a significant increase in salt rejection observed [38,40].

E. Applications in the actual osmotic process

An important assumption of the K-K equations is that the two reflection coefficients are equal in value based on the Onsager relation. Therefore, in experiments, if the osmotic flux is less than the ideal value, it is believed that both values of the two reflection coefficients are less than 1 and the solute molecules are able to penetrate the pore. However, the spatial structure of the protein, i.e., AQP1, indicates that the narrow channel can hardly allow penetration of these solute molecules [11]. This anomalous phenomenon has caused widespread controversy. It is speculated that this may be related to the hourglass entrance of the channel, as shown in Fig. 6. To study the entrance effect, we check the performance of a single-file pore with four sites and varying accessible depth.

Figures 6(b) and 6(c) shows a representative pore and the osmotic flux in all situations. The x axis represents the solute-entrance binding energy. We can see that as long as the solute molecules can enter the pore, the flux is less than the ideal value and σ_o is less than 1. As the binding energy and the available depth increases, the probability of the solute molecules entering the pore also increases. Since the solute molecules cannot exit the pore from the other side, they still must return to the reservoir from the left side. During this period of time, the effective flux for all the species is zero. Therefore, the longer the solute stays in the pore, the smaller the osmotic flux observed. Meanwhile, σ_o in the K-K equations is less than 1, while σ_s is always zero. In the extreme situation where the attraction between the solute and the pore's entrance is sufficiently strong, the entrance can be "blocked" by the solute. MD simulations [36] have shown that the CNT can be blocked by cations via attraction between the ion and aromatic rings.

This phenomenon does not indicate that the Onsager relation is violated. In contrast, several limitations may be encountered when using the K-K equations, an empirical model, for single-file osmosis. Therefore, the structure of the pore entrance may play a crucial role in osmotic flow. The discussion may help to understand the unequal values for the reflection coefficients in the AQP1 experiments [11]. Moreover, the discussion suggests that the asymmetric entrance region of the pores can induce rectified osmosis under the same osmotic pressure gradient [42].

V. CONCLUSION

In conclusion, the roles of the solute can be reflected in two aspects. First, the imbalance in the solute entrance rates in the opposite directions affects the entrance of the solvent. Therefore, the driving force in osmosis is implemented by the entrance or rejection of solute at the entrance of the pore. Second, after entering the pore, the solute molecule must overcome

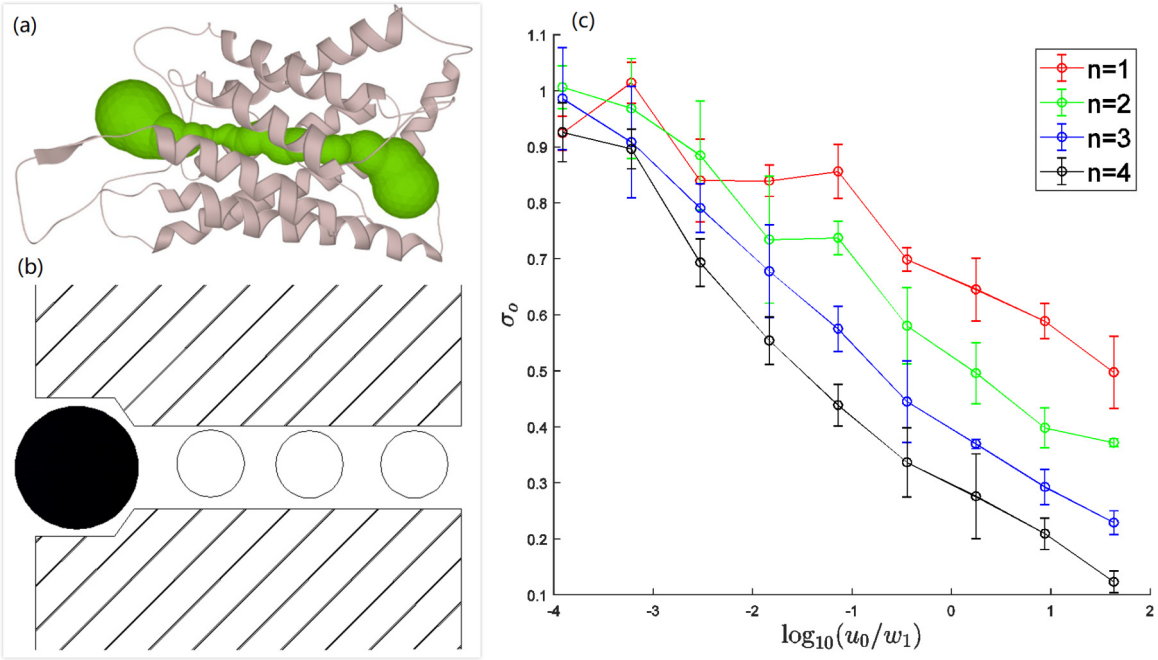

FIG. 6. (a) The three-dimensional structure of AQP1 with a schematic transmembrane pore shown in green [41]. The pore is single-file in the middle with hourglass entrances on both sides. (b) A simplified single-file pore with an accessible site for the solute. (c) The reflection coefficients in Eq. (7) measured by the volume flux, as a function of the solute's accessible depth and the solute-entrance attraction. In all situations, $X_{L,1}$ and $X_{R,1}$ are 0.01 and 0, respectively.

the barrier between the present site and a neighboring site to complete the next hopping event. Accordingly, the entrance structure and the pore-solute interaction can greatly affect the actual flux in osmosis. We hope the discussion in this work can help clarify the debate regarding the observation of unequal reflection coefficients in experiments.

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