Published in final edited form as:

Chem Phys. 2010 October 5; 375(2-3): 523–528. doi:10.1016/j.chemphys.2010.04.040.

Fluxes of non-interacting and strongly repelling particles through a single conical channel: Analytical results and their numerical tests

Alexander M. Berezhkovskii,

Mathematical and Statistical Computing Laboratory, Division of Computational Bioscience, Center for Information Technology, National Institutes of Health, Bethesda, MD 20892

Mark A. Pustovoit, and

St. Petersburg Nuclear Physics Institute, Gatchina, 188300 Russia

Sergey M. Bezrukov

Program in Physical Biology, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD 20892

Abstract

Using a diffusion model of particle dynamics in the channel, we study entropic effects in channel-facilitated transport. We derive general expressions for the fluxes of non-interacting particles and particles that strongly repel each other through the channel of varying cross section area, assuming that the transport is driven by the difference in particle concentrations on the two sides of the membrane. For a special case of a right truncated cone expanding in the left-to-right direction, we show how the fluxes depend on the geometric parameters of the channel and on the particle concentrations. For non-interacting particles the flux is direction-independent in the sense that inversion of the concentration difference leads to the inversion of the direction of the flux without changing its magnitude. This symmetry is broken for repelling particles: The flux in the left-to-right direction exceeds its right-to-left counterpart. Our theoretical predictions are supported by three-dimensional Brownian dynamics simulations.

1. Introduction

Membrane channels are typically not cylinders. Quite the opposite, as a rule their cross section areas vary along the channel axes. This paper is focused on the question of how this may affect channel-facilitated transport of noninteracting particles and particles that strongly repel each other. We analyze the problem assuming that the particle motion in the channel can be described as one-dimensional diffusion along the channel axis in the potential of mean force. In the framework of this one-dimensional diffusion model, variation of the channel cross section area leads to two consequences: (i) variation of the entropic contribution to the potential of mean force and (ii) variation of the particle diffusion coefficient.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

The entropic contribution to the potential of mean force arises naturally if one considers the effective one-dimensional distribution of non-interacting point particles. The one-dimensional equilibrium density of such particles at point x of the channel axis is defined as

$$c_{eq}(x) = \int_{A(x)} C_{eq}(x, y, z) dy dz, \quad (1.1)$$

where $A(x)$ is the cross section area of the channel at given x . In the absence of the particle interaction with the channel, the particles are uniformly distributed over the cross section, and their three-dimensional concentration in the channel is identical to that in the bulk, $C_{eq}(x, y, z) = C_b$. Therefore, the one-dimensional concentration is given by $c_{eq}(x) = C_b A(x)$. The ratio of the one-dimensional equilibrium concentrations at points x and x_0 can be written in the form of the Boltzmann formula

$$\frac{c_{eq}(x)}{c_{eq}(x_0)} = \frac{A(x)}{A(x_0)} = \exp \left[-\frac{U_{ent}(x) - U_{ent}(x_0)}{k_B T} \right]. \quad (1.2)$$

Here k_B and T have their usual meanings of the Boltzmann constant and absolute temperature, correspondingly, and $U_{ent}(x) - U_{ent}(x_0)$ is the difference in the entropy potential,

$$U_{ent}(x) - U_{ent}(x_0) = -k_B T \ln \frac{A(x)}{A(x_0)}. \quad (1.3)$$

Counting the entropy potential from its value at x_0 , i.e., choosing $U_{ent}(x_0) = 0$, we arrive at

$$U_{ent}(x) = -k_B T \ln \frac{A(x)}{A(x_0)}. \quad (1.4)$$

For the channel of a constant cross section area, $A(x) = \text{const}$, the entropic contribution to the potential of mean force vanishes, $U_{ent}(x) = 0$.

Variation of the particle diffusion coefficient in the one-dimensional description of diffusion in systems of varying cross section was discovered by Zwanzig [1], who studied reduction to the effective one-dimensional description in terms of the Fick-Jacobs equation [2]. For cylindrically symmetric tubes Zwanzig showed that the reduction is justified when the tube radius, $r(x)$, is a slowly varying function of x , $|dr(x)/dx| \ll 1$. He found that the particle diffusion coefficient entering into the effective one-dimensional description differs from the particle diffusion constant in the bulk solvent, D_b . Moreover, this diffusion coefficient is position-dependent. The expression for the effective diffusion coefficient derived by Zwanzig (Zw) reads

$$D_{Zw}(x) = \frac{D_b}{1 + (1/2)(dr(x)/dx)^2}. \quad (1.5)$$

Later, based on heuristic arguments, this expression was generalized by Reguera and Rubi (RR) who suggested the following formula [3]

$$D_{RR}(x) = \frac{D_b}{\sqrt{1+(dr(x)/dx)^2}}. \quad (1.6)$$

In a recent numerical study [4] it was shown that this formula works well when $r(x)$ satisfies $|dr(x)/dx| \leq 1$. This is much weaker constraint on the rate of variation of the tube radius than $|dr(x)/dx| \ll 1$ suggested by Zwanzig [1]. One can find an interesting discussion of the reduction to the effective one-dimensional description in a series of papers by Kalinay and Percus [5–8]. Detailed analysis of entropic effects in drift and diffusion of non-interacting particles in two-dimensional systems has been carried out by Hanggi and colleagues [9–12]. The question of effective one-dimensional description of transport in such systems was also addressed in [13,14].

There are several recent papers devoted to the relation between channel-facilitated transport and underlying intra-channel dynamics of the transported particles [15–28]. The focus of the present paper is on entropic effects, which are due to variation of the channel radius, in transport of non-interacting particles and particles that strongly repel each other. To our knowledge this aspect of transport has never been discussed in the literature, except for our recent brief report [29].

To be more specific, we analyze fluxes through a conical channel in a membrane separating the left (L) and right (R) reservoirs containing diffusing particles in concentrations c_L and c_R , respectively (Fig. 1). For such a channel the x -dependence of the channel radius, $r_{ch}(x)$, is given by

$$r_{ch}(x) = a + \lambda(x - x_L), \quad x_L < x < x_R, \quad (1.7)$$

where a is the minimum radius and $\lambda = dr_{ch}(x)/dx$ is the dimensionless parameter that characterizes the rate of growth of the channel radius, $\lambda \geq 0$. Counting the entropy potential from its value at the narrow end of the channel at $x = x_L$, we can write Eq. (1.4) as

$$U_{ent}(x) = -k_B T \ln \frac{A_{ch}(x)}{A_{ch}(x_L)} = 2k_B T \ln \frac{a}{r_{ch}(x)} = -2k_B T \ln \left(1 + \lambda \frac{x - x_L}{a} \right), \quad (1.8)$$

where we have used the relation $A_{ch}(x) = \pi r_{ch}^2(x)$. For such a channel Eq. (1.6) takes the form

$$D_{RR}(x) = \frac{D_b}{\sqrt{1+\lambda^2}}, \quad (1.9)$$

which shows that $D_{RR}(x)$ is a constant.

We derive expressions for the left-to-right and right-to-left fluxes, $J_{L \rightarrow R}$ and $J_{R \rightarrow L}$, for both non-interacting particles and particles that strongly repel each other, assuming that $c_L = c$, c_R

$= 0$ and $c_R = c$, $c_L = 0$, respectively. These expressions show how the fluxes depend on the geometric parameters of the channel as well as on the particle concentration. The concentration dependence is linear for non-interacting particles and non-linear when particles strongly repel each other. In our analysis we model the particle-particle repulsion by the requirement that a particle can enter only the empty channel and cannot enter when the channel is occupied by another particle.

Main results of this paper are expressions for the fluxes through a conical channel given in Eqs. (2.4), (3.12) and (3.13). As might be expected the left-to-right and right-to-left fluxes of non-interacting (ni) particles are identical, $J_{L \rightarrow R}^{(ni)} = J_{R \rightarrow L}^{(ni)}$. This is a consequence of detailed balance. The situation is different for strongly repelling (sr) particles. For the geometry shown in Fig. 1 we find that $J_{L \rightarrow R}^{(sr)} > J_{R \rightarrow L}^{(sr)}$. This might seem surprising since the right entrance into the channel is larger than the left one. However, a particle passing through the channel in the right-to-left direction has to climb up the entropy barrier, while a particle passing in the opposite direction slides down the entropy hill. Both qualitative and quantitative considerations of the flux asymmetry are given in Sec. 3.

We will see that analysis of the entropic effects in transport can be handled in the framework of the general approach developed in [28]. Transport through conical channels may be considered as the simplest example illustrating the importance of the entropic effects. The same approach can also be used to study transport through channels of arbitrary shapes. Note that it has been demonstrated that many biological channels have shapes that are much more complicated than that of a simple cone [30–32]. At the same time many artificial channels are nearly conical [33,34]. Our analytical results for the fluxes are tested by comparison with fluxes found in three-dimensional Brownian dynamics simulations. This comparison shows very good agreement between analytical and numerical results.

The outline of this paper is as follows. We find the fluxes of noninteracting and strongly repelling particles in Sections 2 and 3, respectively. Some concluding remarks are made in the final section.

2. Transport of non-interacting particles

The left-to-right flux of non-interacting particles, $J_{L \rightarrow R}^{(ni)}$, can be written as a product of the flux entering the channel from the left reservoir, $k_{on}^{(L)} c$, and the translocation probability, $P_{L \rightarrow R}$. The latter is the probability that a particle entering the channel from the left reservoir does not come back and escapes to the right reservoir. This probability is derived in the framework of a one-dimensional diffusion model of the particle motion in the channel in [35]. Adapting the result derived in [35] to the case of entropy potential, one can obtain

$$P_{L \rightarrow R} = \frac{k_{on}^{(R)}}{k_{on}^{(L)} + k_{on}^{(R)} + \frac{k_{on}^{(L)} k_{on}^{(R)}}{D_{ch}} \int_{x_L}^{x_R} \frac{dx}{A_{ch}(x)}}, \quad (2.1)$$

where $D_{ch} = D_{RR}(x) = D_b / \sqrt{1 + \lambda^2}$, Eq. (1.9), and

$$k_{on}^{(I)} = 4D_b r_{ch}(x_I), \quad I = L, R. \quad (2.2)$$

Thus, the flux is

$$J_{L \rightarrow R}^{(ni)} = k_{on}^{(L)} c P_{L \rightarrow R} = \frac{k_{on}^{(L)} k_{on}^{(R)} c}{k_{on}^{(L)} + k_{on}^{(R)} + \frac{k_{on}^{(L)} k_{on}^{(R)}}{D_{ch}} \int_{x_L}^{x_R} \frac{dx}{A_{ch}(x)}}. \quad (2.3)$$

From this expression one can see that the right-to-left flux, $J_{R \rightarrow L}^{(ni)}$, is given by the same expression, and, hence, $J_{L \rightarrow R}^{(ni)} = J_{R \rightarrow L}^{(ni)}$, as it must be to satisfy the condition of detailed balance.

Carrying out the integration one can obtain the flux as a function of the geometric parameters of the channel (Fig. 1). Denoting the channel length by l , $l = x_R - x_L$, we can write the flux as

$$J_{L \rightarrow R}^{(ni)} = J_{R \rightarrow L}^{(ni)} = \frac{4\pi a(a + \lambda l) D_b c}{\pi(2a + \lambda l) + 4l \sqrt{1 + \lambda^2}}. \quad (2.4)$$

This expression for the flux of non-interacting particles through a conical channel is one of the main results of this paper.

For $\lambda = 0$, the flux in Eq. (2.4) reduces to the flux of non-interacting particles through a cylindrical channel (cc) of radius a ,

$$J_{cc}^{(ni)} = \frac{2\pi a^2 D_b c}{\pi a + 2l}. \quad (2.5)$$

For $l \gg a$ this leads to the well known result

$$J_{cc}^{(ni)} = \frac{\pi a^2 D_b c}{l}, \quad a \ll l, \quad (2.6)$$

which can be obtained based on the steady-state picture of the particle concentration profile in the channel. According to this picture (when $c_L = c$, $c_R = 0$) the effective one-dimensional concentration of the particles, $c_{1d}(x)$, linearly decreases with x from $\pi a^2 c$ at the left end of the channel to zero at its right end,

$$c_{1d}(x) = \pi a^2 c \frac{x_R - x}{l}, \quad x_L < x < x_R. \quad (2.7)$$

Using this in the definition of the steady-state flux through the channel, $-D_{ch} dc_{1d}(x)/dx$, and the fact that for a cylindrical channel $D_{ch} = D_b$, one can recover the result in Eq. (2.6).

The expression in Eq. (2.6) is appropriate only for long channels. It fails when the channel length is comparable with its radius, so that the general expression in Eq. (2.5) should be

used. In the limiting case of a very short channel (very thin membrane) the expression for the flux in Eq. (2.5) further simplifies and takes the form

$$J_{cc}^{(ni)} = 2aD_b c, \quad l \ll a. \quad (2.8)$$

This expression also has a transparent interpretation. When $c_L = c$, $c_R = 0$, the flux in Eq. (2.8) is the number of particles entering the channel from the left reservoir per unit time, $4aD_b c$, multiplied by factor $1/2$, which is the probability of ending up in the right reservoir for a particle that starts from the hole in an infinitely thin membrane.

We illustrate the dependence of the flux through the conical channel, Eq. (2.4), on λ in Fig. 2 where we show the ratio of this flux to the flux through the cylindrical channel of radius a and of the same length l as the conical channel, Eq. (2.5). The ratio is given by

$$\frac{J_{L \rightarrow R}^{(ni)}}{J_{cc}^{(ni)}} = \frac{J_{R \rightarrow L}^{(ni)}}{J_{cc}^{(ni)}} = \frac{2(1 + \lambda l/a)(\pi + 2l/a)}{2\pi + (\pi\lambda + 4\sqrt{1 + \lambda^2})l/a}. \quad (2.9)$$

Fig. 2 gives this flux ratio as a function of λ for different values of the dimensionless channel length, l/a , $l/a = 5, 10$, and 20 . In this figure we also show the flux ratio found in Brownian dynamics simulations. One can see very good agreement between the theoretical and numerical results.

Simulations were performed as described earlier [4] with the following modifications. The two reservoirs connected by the channel had the shape of a parallelepiped and were large enough to ensure that the simulation results were independent of their size. In particular, for the chosen channel parameters, $a = 5$ and $L = 50$, we took the side of the “empty” cubical reservoir to be 200. The “particle containing” reservoir dimensions were $\Delta x = 50$, $\Delta y = \Delta z = 200$. The particle was considered to pass through the channel when it left the empty reservoir through one of its walls except for the wall containing the channel mouth. At the same moment a new particle entered the particle containing reservoir at the point determined by the periodic boundary conditions, thus keeping the total number of the particles in the system fixed. One simulation run contained 400 such passages; the flux was calculated as this number of passages divided by the total simulation time. Three runs with different initial particle configurations were performed for each set of parameters to obtain the mean and the standard deviation of the flux. In simulations of strongly repelling particles (discussed below), when a particle was the channel, the entrance of other particles was prohibited. The probability of finding the channel occupied was calculated as the ratio of the time when the channel contained a particle to the total simulation time.

3. Transport of strongly repelling particles

When analyzing transport of particles which strongly repel each other we model the repulsion by the requirement that a particle being in the channel makes it impossible for another particle to enter the channel. This implies that the channel can not be occupied by more than one particle. The left-to-right and right-to-left fluxes of strongly repelling particles through such a singly-occupied channel are given by [26–28]

$$J_{L \rightarrow R}^{(sr)} = J_{L \rightarrow R}^{(ni)} P_{emp}^{(L)}, \quad J_{R \rightarrow L}^{(sr)} = J_{R \rightarrow L}^{(ni)} P_{emp}^{(R)}, \quad (3.1)$$

where $P_{emp}^{(L,R)}$ are the probabilities of finding the channel empty in the two cases analyzed in the paper.

The probabilities $P_{emp}^{(L,R)}$ can be expressed in terms of the mean lifetimes of the channel in the empty and occupied states, $\tau_{emp}^{(L,R)}$ and $\tau_{oc}^{(L,R)}$,

$$P_{emp}^{(I)} = \frac{\tau_{emp}^{(I)}}{\tau_{emp}^{(I)} + \tau_{oc}^{(I)}}, \quad I=L, R. \quad (3.2)$$

The mean lifetimes $\tau_{emp}^{(L,R)}$ are given by

$$\tau_{emp}^{(I)} = \frac{1}{k_{on}^{(I)} c}, \quad I=L, R. \quad (3.3)$$

We use this to write the probabilities in Eq. (3.2) as

$$P_{emp}^{(I)} = \frac{1}{1 + k_{on}^{(I)} c \tau_{oc}^{(I)}}, \quad I=L, R. \quad (3.4)$$

The mean lifetimes $\tau_{oc}^{(L,R)}$ are nothing else than the mean lifetimes in the channel of the particles entering the channel from the left and right reservoirs, respectively, $\tau_{inside}^{(L,R)}$. These times are derived in the framework of the one-dimensional model of the particle dynamics in the channel in [36]. Adapting the results derived in [36] to the case of entropy potential, one can obtain

$$\tau_{oc}^{(L)} = \tau_{inside}^{(L)} = \frac{V_{ch} + \frac{k_{on}^{(R)}}{D_{ch}} \int_{x_L}^{x_R} A_{ch}(x) \left[\int_x^{x_R} \frac{dy}{A_{ch}(y)} \right] dx}{k_{on}^{(L)} + k_{on}^{(R)} + \frac{k_{on}^{(L)} k_{on}^{(R)}}{D_{ch}} \int_{x_L}^{x_R} \frac{dx}{A_{ch}(x)}} \quad (3.5)$$

and

$$\tau_{oc}^{(R)} = \tau_{inside}^{(R)} = \frac{V_{ch} + \frac{k_{on}^{(L)}}{D_{ch}} \int_{x_L}^{x_R} A_{ch}(x) \left[\int_{x_L}^x \frac{dy}{A_{ch}(y)} \right] dx}{k_{on}^{(L)} + k_{on}^{(R)} + \frac{k_{on}^{(L)} k_{on}^{(R)}}{D_{ch}} \int_{x_L}^{x_R} \frac{dx}{A_{ch}(x)}}, \quad (3.6)$$

where V_{ch} is the channel volume,

$$V_{ch} = \int_{x_L}^{x_R} A_{ch}(x) dx = \pi a^2 l \left(1 + \frac{\lambda l}{a} + \frac{\lambda^2 l^2}{3a^2} \right). \quad (3.7)$$

Explicit expressions for the times in Eqs. (3.5) and (3.6) can be obtained by carrying out the integrations and using the relation in Eqs. (2.2) as well as the relation $D_{ch} = D_b / \sqrt{1 + \lambda^2}$. The results are

$$\tau_{oc}^{(L)} = \tau_{inside}^{(L)} = \frac{\pi l \left[3\pi a(a + \lambda l) + 2l \sqrt{1 + \lambda^2} (3a + \lambda l) + \pi \lambda^2 l^2 \right]}{12D_b \left[\pi(2a + \lambda l) + 4l \sqrt{1 + \lambda^2} \right]} \quad (3.8)$$

and

$$\tau_{oc}^{(R)} = \tau_{inside}^{(R)} = \frac{\pi l \left[3\pi a(a + \lambda l) + 2l \sqrt{1 + \lambda^2} (3a + 2\lambda l) + \pi \lambda^2 l^2 \right]}{12D_b \left[\pi(2a + \lambda l) + 4l \sqrt{1 + \lambda^2} \right]}. \quad (3.9)$$

Substituting probabilities $P_{emp}^{(L,R)}$, Eq. (3.4), into the expressions for the fluxes, Eqs. (3.1), and using the relations in Eqs. (2.3), (3.5), and (3.6) one can obtain

$$J_{L \rightarrow R}^{(sr)} = \frac{J_{L \rightarrow R}^{(ni)}}{1 + k_{on}^{(L)} c \tau_{inside}^{(L)}} = \frac{k_{on}^{(L)} k_{on}^{(R)} c}{k_{on}^{(L)} (1 + c V_{ch}) + k_{on}^{(R)} + \frac{k_{on}^{(L)} k_{on}^{(R)}}{D_{ch}} \int_{x_L}^{x_R} \left[1 + c \int_{x_L}^x A_{ch}(y) dy \right] \frac{dx}{A_{ch}(x)}} \quad (3.10)$$

and

$$J_{R \rightarrow L}^{(sr)} = \frac{J_{R \rightarrow L}^{(ni)}}{1 + k_{on}^{(R)} c \tau_{inside}^{(R)}} = \frac{k_{on}^{(L)} k_{on}^{(R)} c}{k_{on}^{(L)} + k_{on}^{(R)} (1 + c V_{ch}) + \frac{k_{on}^{(L)} k_{on}^{(R)}}{D_{ch}} \int_{x_L}^{x_R} \left[1 + c \int_x^{x_R} A_{ch}(y) dy \right] \frac{dx}{A_{ch}(x)}}. \quad (3.11)$$

Explicit expressions for these fluxes are

$$J_{L \rightarrow R}^{(sr)} = \frac{4\pi a(a+\lambda l)D_b c}{\pi(2a+\lambda l)+4l \sqrt{1+\lambda^2}+\pi a c \left[V_{ch}+2l^2 \left(a+\frac{\lambda l}{3}\right) \sqrt{1+\lambda^2} \right]} \quad (3.12)$$

and

$$J_{R \rightarrow L}^{(sr)} = \frac{4\pi a(a+\lambda l)D_b c}{\pi(2a+\lambda l)+4l \sqrt{1+\lambda^2}+\pi(a+\lambda l)c \left[V_{ch}+2l^2 \left(a+\frac{2\lambda l}{3}\right) \sqrt{1+\lambda^2} \right]}. \quad (3.13)$$

These expressions are the second main result of our paper. The first one is the expression for the left-to-right and right-to-left fluxes of non-interacting particles, Eq. (2.4).

The ratio of the fluxes given in Eqs. (3.12) and (3.13),

$$\frac{J_{L \rightarrow R}^{(sr)}}{J_{R \rightarrow L}^{(sr)}} = \frac{\pi(2a+\lambda l)+4l \sqrt{1+\lambda^2}+\pi(a+\lambda l)c \left[V_{ch}+2l^2 \left(a+\frac{2\lambda l}{3}\right) \sqrt{1+\lambda^2} \right]}{\pi(2a+\lambda l)+4l \sqrt{1+\lambda^2}+\pi a c \left[V_{ch}+2l^2 \left(a+\frac{\lambda l}{3}\right) \sqrt{1+\lambda^2} \right]} \quad (3.14)$$

shows that

$$J_{L \rightarrow R}^{(sr)} \geq J_{R \rightarrow L}^{(sr)}. \quad (3.15)$$

The two fluxes are equal only when $\lambda = 0$. In this limiting case both fluxes reduce to the flux through a cylindrical channel of radius a and length l ,

$$J_{cc}^{(sr)} = \frac{4\pi a^2 D_b c}{(\pi a+2l)(2+\pi a^2 l c)} = \frac{J_{cc}^{(ni)}}{1+V_{cc}c/2}, \quad (3.16)$$

where $V_{cc} = \pi a^2 l$ is the volume of the cylindrical channel. Flux $J_{cc}^{(sr)}$ is smaller than its counterpart for non-interacting particles, $J_{cc}^{(ni)}$, because of the inter-particle repulsion.

The left-to-right flux exceeds the flux in the opposite direction because the probability of finding the channel empty is greater when the particles go from the left reservoir to the right one, $c_L = c$, $c_R = 0$, than when they go in the opposite direction, $c_L = 0$, $c_R = c$, $P_{emp}^{(L)} > P_{emp}^{(R)}$. To see this consider the ratio of these probabilities

$$\frac{P_{emp}^{(L)}}{P_{emp}^{(R)}} = \frac{1+k_{on}^{(R)} c \tau_{inside}^{(R)}}{1+k_{on}^{(L)} c \tau_{inside}^{(L)}}, \quad (3.17)$$

in which

$$k_{on}^{(L)} = 4D_b a, \quad k_{on}^{(R)} = 4D_b (a + \lambda l) \quad (3.18)$$

and the times $\tau_{inside}^{(L,R)}$ are given in Eqs. (3.8) and (3.9). One can see that both $k_{on}^{(R)}$ and $\tau_{inside}^{(R)}$ are greater than $k_{on}^{(L)}$ and $\tau_{inside}^{(L)}$, respectively, when $\lambda > 0$. However, the two times are close and their ratio does not exceed 1.5 while the rate constant $k_{on}^{(R)}$ may be much greater than $k_{on}^{(L)}$ (when $\lambda l \gg a$).

In Fig. 3 we show the ratio $J_{L \rightarrow R}^{(sr)} / J_{R \rightarrow L}^{(sr)}$ as a function of λ for channels with $l/a = 5, 10$, and 20 . One can see a good agreement between analytical and numerical results.

Next we discuss the λ -dependences of the left-to-right and right-to-left fluxes of strongly repelling particles. These dependences are given by the ratios of the fluxes in Eq. (3.12) and (3.13) to the flux through a cylindrical channel of radius a and length l , Eq. (3.16), which corresponds to $\lambda = 0$,

$$\frac{J_{L \rightarrow R}^{(sr)}}{J_{cc}^{(sr)}} = \frac{(\pi a + 2l)(2 + \pi a^2 l c)(a + \lambda l)}{a \left\{ \pi(2a + \lambda l) + 4l \sqrt{1 + \lambda^2} + \pi a c \left[V_{ch} + 2l^2 \left(a + \frac{\lambda l}{3} \right) \sqrt{1 + \lambda^2} \right] \right\}} \quad (3.19)$$

and

$$\frac{J_{R \rightarrow L}^{(sr)}}{J_{cc}^{(sr)}} = \frac{(\pi a + 2l)(2 + \pi a^2 l c)(a + \lambda l)}{a \left\{ \pi(2a + \lambda l) + 4l \sqrt{1 + \lambda^2} + \pi(a + \lambda l)c \left[V_{ch} + 2l^2 \left(a + \frac{2\lambda l}{3} \right) \sqrt{1 + \lambda^2} \right] \right\}}. \quad (3.20)$$

In contrast to the case of non-interacting particles (see Fig. 2), these ratios are non-monotonic functions of λ . We plot the ratios in Eqs. (3.19) and (3.20) in Fig. 4 for channels with $l/a = 5, 10$, and 20 . Symbols in this figure show the values of the ratios found numerically in Brownian dynamics simulations. These values are in a reasonably good agreement with the values predicted by the theory.

Note that the effect of the flux symmetry breaking is due to the inter-particle repulsion. We model the repulsion by the requirement that the channel cannot be occupied by more than one particle. Therefore, the higher is the channel occupancy, the stronger is the effect. The occupancies, which are nothing else than probabilities of finding the channel occupied, $P_{oc}^{(I)}$, are given by

$$P_{oc}^{(I)} = 1 - P_{emp}^{(I)} = \frac{k_{on}^{(I)} c \tau_{oc}^{(I)}}{1 + k_{on}^{(I)} c \tau_{oc}^{(I)}}, \quad I = L, R. \quad (3.21)$$

These probabilities increase with the increase of the channel volume. Therefore, $P_{oc}^{(I)}$ monotonically grow with λ and are always larger than their counterparts for cylindrical channels, $\lambda = 0$, of radius a and the same length l . We have shown that $P_{emp}^{(L)} > P_{emp}^{(R)}$. As a consequence, $P_{oc}^{(R)} > P_{oc}^{(L)}$. One can see that in Fig. 5, which presents $P_{oc}^{(R)}$ and $P_{oc}^{(L)}$ as functions

of λ for the channels of different lengths, $l/a = 5, 10$, and 20 . Solid lines in Fig. 5 are theoretical predictions drawn using the relations in Eqs. (2.2), (3.8), (3.9), and (3.21), while symbols are numerical results obtained in Brownian dynamics simulations. One can see a good agreement between the two.

Finally we note that at equilibrium the probabilities $P_{emp}^{(L)}$ and $P_{emp}^{(R)}$ in the expression for the fluxes, Eq. (3.1), should be replaced by the equilibrium probability of finding the channel empty, P_{emp}^{eq} . As a result, the expressions for the fluxes take the form

$$J_{L \rightarrow R}^{(sr)} = J_{L \rightarrow R}^{(ni)} P_{emp}^{eq}, \quad J_{R \rightarrow L}^{(sr)} = J_{R \rightarrow L}^{(ni)} P_{emp}^{eq}. \quad (3.22)$$

Since $J_{L \rightarrow R}^{(ni)} = J_{R \rightarrow L}^{(ni)}$, the fluxes in Eq. (3.22) are identical, as it must be according to the condition of detailed balance.

4. Concluding remarks

This paper is devoted to entropic effects in transport of non-interacting and strongly repelling particles through single membrane channels of varying cross section area. Using a conical channel (Fig. 1) as the simplest example we derived expressions for the left-to-right and right-to-left fluxes through the same channel driven by the same, but oppositely directed, concentration difference, $c_L = c$, $c_R = 0$ and $c_L = 0$, $c_R = c$, respectively. These expressions for the fluxes are given in Eqs. (2.4), (3.12), and (3.13).

The left-to-right and right-to-left fluxes are equal to one another for noninteracting particles, $J_{L \rightarrow R}^{(ni)} = J_{R \rightarrow L}^{(ni)}$. For particles that strongly repel each other $J_{L \rightarrow R}^{(sr)} > J_{R \rightarrow L}^{(sr)}$ in spite of the fact that the right entrance into the channel is larger than the left one (Fig. 1). Another distinction between the fluxes of noninteracting and strongly repelling particles is in their qualitatively different dependences on parameter λ , $\lambda = dr_{ch}(x)/dx$, which determines the growth rate of the channel radius. The dependence on λ is monotonic for non-interacting particles, Fig. 2, and non-monotonic for particles that strongly repel each other, Fig. 4.

The expressions for the fluxes in Eqs. (2.4), (3.12), and (3.13) have been obtained in the framework of the one-dimensional diffusion model of the particle intra-channel dynamics [28]. Our theoretical predictions are verified by three-dimensional Brownian dynamics simulations without any adjustable parameters.

Finally, we note that the obtained results are of importance not only in understanding regulation of the membrane transport. They may also be relevant to the description of many systems where the constrained motion of the Brownian particles underlies their functional properties. Those may include technologically important applications such as liquid chromatography, catalysis, and osmosis.

Acknowledgments

This study was supported by the Intramural Research Program of the NIH, Center for Information Technology and Eunice Kennedy Shriver National Institute of Child Health and Human Development. M.A.P. also thanks the Russian Foundation for Basic Research (Project 08-02-00314a) and the State Programs "Quantum Macrophysics", "Strongly Correlated Electrons in Metals, Superconductors, Semiconductors and Magnetic Materials", and "Neutron studies of matter" for partial support.

References

1. Zwanzig R. *J Phys Chem* 1992;96:3926.
2. Jacobs, MH. *Diffusion Processes*. Springer; New York: 1967.
3. Reguera D, Rubi JM. *Phys Rev E* 2001;64:061106.
4. Berezhkovskii AM, Pustovoit MA, Bezrukov SM. *J Chem Phys* 2007;126:134706. [PubMed: 17430055]
5. Kalinay P, Percus JK. *Phys Rev E* 2005;72:061203.
6. Kalinay P, Percus JK. *J Chem Phys* 2005;122:204701. [PubMed: 15945758]
7. Kalinay P, Percus JK. *Phys Rev E* 2006;74:041203.
8. Kalinay P, Percus JK. *J Stat Phys* 2006;123:1059.
9. Reguera D, Schmid G, Burada PS, Rubi JM, Reimann P, Hanggi P. *Phys Rev Lett* 2006;96:130603. [PubMed: 16711977]
10. Burada PS, Schmid G, Talkner P, Hanggi P, Reguera D, Rubi JM. *BioSystems* 2008;93:16. [PubMed: 18462863]
11. Burada PS, Hanggi P, Marchesoni F, Schmid G, Talkner P. *CemPhysChem* 2009;10:45.
12. Burada PS, Schmid G, Hanggi P. *Phil Trans R Soc A* 2009;367:3157. [PubMed: 19620115]
13. Yariv E, Dorfman KD. *Phys Fluids* 2007;19:037101.
14. Laachi N, Kenward M, Yariv E, Dorfman KD. *Europhys Lett* 2007;80:50009.
15. Bauer WR, Nadler W. *Proc Natl Acad Sci USA* 2006;103:11446. [PubMed: 16861303]
16. Kolomeisky AB. *Phys Rev Lett* 2007;98:048105. [PubMed: 17358819]
17. Kolomeisky AB, Kotsev S. *J Chem Phys* 2008;128:085101. [PubMed: 18315084]
18. Chou T. *Phys Rev Lett* 1998;80:85.
19. Chou T. *J Chem Phys* 1999;110:606.
20. Chou T, Lohse D. *Phys Rev Lett* 1999;82:3552.
21. Lu D, Grayson P, Schulten K. *Biophys J* 2003;85:2977. [PubMed: 14581200]
22. Kosztin I, Schulten K. *Phys Rev Lett* 2004;93:238102. [PubMed: 15601207]
23. Zilman A, Di Talia S, Chait BT, Rout MP, Magnasco MO. *PloS Comp Biol* 2007;3:e125.
24. Zilman A. *Biophys J* 2009;96:1235. [PubMed: 19217844]
25. Zilman A, Pearson J, Bel G. *Phys Rev Lett* 2009;103:128103. [PubMed: 19792464]
26. Berezhkovskii AM, Bezrukov SM. *Biophys J* 2005;88:L17. [PubMed: 15626697]
27. Berezhkovskii AM, Bezrukov SM. *Chem Phys* 2005;319:342.
28. Bezrukov SM, Berezhkovskii AM, Szabo A. *J Chem Phys* 2007;127:115101. [PubMed: 17887882]
29. Berezhkovskii AM, Pustovoit MA, Bezrukov SM. *Phys Rev E* 2009;80:020904.
30. Cowan SW, Schirmer T, Rummel G, Steiert M, Ghosh R, Pauptit RA, Jansonius JN, Rosenbusch JP. *Nature* 1992;358:727. [PubMed: 1380671]
31. Song LZ, Hobaugh MR, Shustak C, Cheley S, Bayley H, Gouaux JE. *Science* 1996;274:1859. [PubMed: 8943190]
32. Doyle DA, Cabral JM, Pfuetzner RA, Kuo AL, Gulbis JM, Cohen SL, Chait BT, MacKinnon R. *Science* 1998;280:69. [PubMed: 9525859]
33. Kosinska ID, Goychuk I, Kostur M, Schmid G, Hanggi P. *Phys Rev E* 2008;77:031131.
34. Howorka S, Siwy Z. *Chem Soc Rev* 2009;38:2360. [PubMed: 19623355]
35. Berezhkovskii AM, Pustovoit MA, Bezrukov SM. *J Chem Phys* 2002;116:9952.
36. Berezhkovskii AM, Pustovoit MA, Bezrukov SM. *J Chem Phys* 2003;119:3943.

Figure 1.

Conical channel in a membrane separating the left (L) and right (R) reservoirs containing diffusing particles in concentrations c_L and c_R , respectively. We consider flux $J_{L \rightarrow R}$ when $c_L = c$, $c_R = 0$ and flux $J_{R \rightarrow L}$ when $c_L = 0$, $c_R = c$ for non-interacting particles and particles that strongly repel each other.

Figure 2.

Fluxes of non-interacting particles as functions of λ , normalized to the fluxes through the cylindrical channel, Eq. (2.9). The curves from bottom to top show the fluxes for $l/a = 5, 10$, and 20 at $c = 2.5 \cdot 10^{-5}$ and $a = 5$. Corresponding numerical results are shown by triangles and squares, representing the left-to-right and right-to-left fluxes, respectively.

Figure 3.

Flux ratio for strongly repelling particles $J_{L \rightarrow R}^{(sr)} / J_{R \rightarrow L}^{(sr)}$ as a function of λ . The curves are drawn according to Eq. (3.14) with the same parameters as for Fig. 2. The length of the channel increases from $l/a = 5$ for the bottom curve to $l/a = 20$ for the top one. Symbols show the values obtained in Brownian dynamics simulations.

Figure 4.

Fluxes of strongly repelling particles as functions of λ normalized to the fluxes through the cylindrical channel. The curves are drawn for the left-to-right flux according to Eq. (3.19) (panel **A**) and for the right-to-left flux according to Eq. (3.20) (panel **B**) with the same parameters as for Fig. 2. The initial slopes of the curves increase with the increasing channel length l/a . Symbols show the values obtained in Brownian dynamics simulations. At $\lambda > 0.5$ the curves from top to bottom show the fluxes for $l/a = 5, 10$, and 20 , respectively.

Figure 5.

Occupancies of the channel as functions of λ for the same parameters as in previous figures. Panel **A** corresponds to the left-to-right flux; panel **B** – to the right-to-left flux. The length of the channel increases from $l/a = 5$ for the bottom curves to $l/a = 20$ for the top ones. Symbols show the values obtained in Brownian dynamics simulations.