Published in final edited form as:

Eur Phys J Spec Top. 2014 December ; 223(14): 3063–3077. doi:10.1140/epjst/e2014-02319-3.

On the applicability of entropy potentials in transport problems

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Abstract

Transport in confined structures of varying geometry has become the subject of growing attention in recent years since such structures are ubiquitous in biology and technology. In analyzing transport in systems of this type, the notion of entropy potentials is widely used. Entropy potentials naturally arise in one-dimensional description of equilibrium distributions in multidimensional confined structures. However, their application to transport problems requires some caution. In this article we discuss such applications and summarize the results of recent studies exploring the limits of applicability. We also consider an example of a transport problem in a system of varying geometry, where the conventional approach is inapplicable since the geometry changes abruptly. In addition, we demonstrate how the entropy potential can be used to analyze optimal transport through a tree-dimensional cosine-shaped channel.

1 Introduction

Entropic effects in transport description arise as a natural consequence of the constraints on the coordinate space available for diffusing particles. Whenever transport of particles takes place in the presence of three-dimensional non-uniform confining geometries, the description of the particle dynamics in terms of the one-dimensional Smoluchowski equation (if applicable) effectively introduces entropy potentials to account for the variation in confinement geometry along particle's path through the structures. Such structures with varying confinement geometry are ubiquitous in both technology and biology. Transport in zeolites, gels, as well as in porous media used in chromatography and other separation techniques are among well-known technological examples. Most biological cells are extremely crowded with organelles, vesicles, different protein assemblies and other structures. This creates natural confinements which influence the equilibria and kinetics of intermolecular reactions leading to unexplored and often unexpected effects. Proteinaceous structures embedded in cell and organelle membranes – the so-called ion channels – offer a class of probably the smallest structures where the main concepts of the confined diffusion are still applicable.

It is well-known that ion channels of classical electrophysiology, i.e., the channels of excitable membranes, usually have narrow constrictions in their lumens to discriminate between different ions in solution. The selectivity involves not only discrimination between anions and cations but between ions of the same charge, most notably sodium and

potassium. The narrow passages in the lumens of ion-selective channels are devised to allow for the tight contacts between the permeating ion and the channel protein residues, which compensate for the loss of favorable interactions of the ion with water upon its dehydration and also for the entropic costs. However, as it follows from more recent structural studies, constrictions are characteristic even for large metabolite-transporting channels that display very low ion selectivity.

One of most important examples is the voltage dependent anion channel (VDAC) from the outer mitochondrial membrane, a major conduit of ATP, ADP, and other metabolites in and out of mitochondria [1]. Traditionally considered to be a crude filter at the border between a mitochondrion and the rest of the cell, it is now getting recognition as a major player in mitochondria metabolism regulation through its interactions with cytosolic proteins [2]. The major scaffold of VDAC structure is a beta-barrel of about 2 nm radius. Based on this, one might think that the shape of the water-filled VDAC pore is nearly cylindrical. Though the true structure of the functional VDAC is still under extensive ongoing debates, recent structural studies point out that this is not the case. The available folding pattern of mouse VDAC1 determined by x-ray crystallography shows that the alpha-helical N-terminus of the VDAC molecule is located inside the pore, thus changing its effective geometry probed by translocating particles to that of an hourglass [3].

The shape of the VDAC pore in respect to a translocating ATP molecule was recently probed in molecular dynamics simulations [4]. Using the results of x-ray crystallography [3] it was demonstrated that the effective radius along the channel pore axis changes dramatically, from about 2 nm at the entrances to 0.8 nm at the constriction zone produced by the helix of the N-terminus (Figure 1). This means that an ATP molecule at the entrance of the channel has to climb a significant entropy barrier on its way through the channel. Indeed, in order to translocate in the absence of any driving forces except for the concentration gradient (ATP concentration in the intermembrane mitochondrial space is higher than in the cytosol), the molecule should first partition into a $(2/0.8)^2$ times smaller cross-section area. Intuition suggests that in the absence of attractive interactions between the molecule and channel walls to compensate for the entropy loss, the probability of ATP translocation through the channel will be small, thus rendering the channel ineffective for ATP and other metabolites transport. Molecular dynamics simulations allow for determination of not only the effective radius, but also for the potential of mean force along the channel pore axis. This is very useful information, since it allows one to understand the role of specific protein residues in interactions between a particular solute and the channel, thus shedding light on the channel specificity to metabolite. Unfortunately, currently available maximum simulation times do not allow one to approach the translocation process per se for unbiased diffusion of molecules in the channel. Therefore, such crucial parameters as the solute translocation probability and characteristic times, which determine the channel efficiency, are still out of reach of molecular dynamics simulations and call for analytical treatment.

2 Continuum diffusion model of solute dynamics in the channel

During the past decade we have developed an analytical approach [5–11] which allows one to calculate the translocation probability and characteristic times for the range of problems an example of which is illustrated by Fig. 1. The approach is based on the analysis of the particle diffusion in a channel of length L in terms of the Green's function $G(x, t; x_0)$ which is the probability density of finding the particle at point x at time t on condition that it was at x_0 at $t = 0$, and it has not escaped from the channel during time t . The Green's function satisfies the Smoluchowski equation in the channel, $0 < x, x_0 < L$,

$$\frac{\partial G(x, t; x_0)}{\partial t} = \frac{\partial}{\partial x} \left\{ D_{ch}(x) \exp(-\beta U(x)) \frac{\partial}{\partial x} [\exp(\beta U(x)) G(x, t; x_0)] \right\} \quad (1)$$

with the initial condition $G(x, 0; x_0) = \delta(x - x_0)$, $0 < x < L$, and radiation boundary conditions at the channel ends, $x = 0$ and $x = L$ (Figure 2),

$$\begin{aligned} \frac{\partial}{\partial x} [G(x, t; x_0) \exp(\beta U(x))] \Big|_{x=0} &= \frac{k_0}{D_{ch}(0)} G(0, t; x_0) \exp(\beta U(0)), \\ - \frac{\partial}{\partial x} [G(x, t; x_0) \exp(\beta U(x))] \Big|_{x=L} &= \frac{k_L}{D_{ch}(L)} G(L, t; x_0) \exp(\beta U(L)) \end{aligned} \quad (2)$$

Here $U(x)$ and $D_{ch}(x)$ are the potential of mean force and particle diffusion coefficient inside the channel, and $\beta = 1 / (k_B T)$ with k_B and T having their usual meanings of the Boltzmann constant and absolute temperature. The rate constants k_0 and k_L characterize the escape efficiency; $k = \infty$ and $k = 0$ correspond to absorbing and reflecting channel ends, respectively. For the channel with identical circular openings of radius R on both ends, these rate constants are [11]

$$k_0 = k_L = k = \frac{4D_b}{\pi R}, \quad (3)$$

where D_b is the particle diffusion coefficient in the bulk.

Though, in the general case, it is impossible to solve Eqs. (1) – (3) analytically, the most important characteristics of the particle life in the channel can be calculated explicitly. One of such characteristics is the translocation probability. It can be shown that for the channel with $k_0 = k_L$ and on condition that $U(0) = U(L)$, the probabilities to translocate from the left to the right, $P_{tr}(0)$, and from the right to the left, $P_{tr}(L)$, are equal to each other and given by [10]

$$P_{tr}(0) = P_{tr}(L) = \frac{1}{2 + \frac{4D_b}{\pi R} \int_0^L \frac{\exp(\beta U(x))}{D_{ch}(x)} dx}. \quad (4)$$

This is a special case of more general expressions for the translocation probability,

$$P_{tr}(0) = \frac{k_L \exp(-\beta \Delta U)}{k_0 + k_L \exp(-\beta \Delta U) + k_0 k_L \exp(-\beta \Delta U) \int_0^L \frac{\exp(\beta U(x))}{D_{ch}(x)} dx},$$

$$P_{tr}(L) = \frac{k_0}{k_0 + k_L \exp(-\beta \Delta U) + k_0 k_L \exp(-\beta \Delta U) \int_0^L \frac{\exp(\beta U(x))}{D_{ch}(x)} dx}, \quad (5)$$

where $U = U(L) - U(0)$ is the difference in the potential of mean force between the two channel ends.

Other important parameters are different characteristic times spent by the particle in the channel. Among them are the mean return times (for a particle which enters and leaves the channel from the same side), translocation time, and lifetimes of the particle in the channel. For the translocation time we found that, surprisingly, it is direction independent, $\tau_{tr}(0) = \tau_{tr}(L) = \tau_{tr}$, even when the channel is biased, $U \neq 0$. As shown in Ref. [9] this time is given by

$$\tau_{tr} = \frac{\int_0^L \left[1 + k_0 \int_0^x \frac{\exp(\beta U(y))}{D_{ch}(y)} dy \right] \left[1 + k_L \exp(-\beta \Delta U) \int_x^L \frac{\exp(\beta U(y))}{D_{ch}(y)} dy \right] \exp(-\beta U(x)) dx}{k_0 + k_L \exp(-\beta \Delta U) + k_0 k_L \exp(-\beta \Delta U) \int_0^L \frac{\exp(\beta U(x))}{D_{ch}(x)} dx}. \quad (6)$$

Moreover, not only the mean but even the probability density of the translocation time is direction independent [12]. On the contrary, the mean lifetimes in the channel may depend on the side from which the particle enters the channel. Even for the unbiased channel, they may still be side dependent and, as shown in Ref. [9], are given by

$$\tau(0) = \frac{\int_0^L \left[1 + k_L \int_x^L \frac{\exp(\beta U(y))}{D_{ch}(y)} dy \right] \exp(-\beta U(x)) dx}{k_0 + k_L + k_0 k_L \int_0^L \frac{\exp(\beta U(y))}{D_{ch}(y)} dy},$$

$$\tau(L) = \frac{\int_0^L \left[1 + k_0 \int_0^x \frac{\exp(\beta U(y))}{D_{ch}(y)} dy \right] \exp(-\beta U(x)) dx}{k_0 + k_L + k_0 k_L \int_0^L \frac{\exp(\beta U(y))}{D_{ch}(y)} dy}. \quad (7)$$

Eqs. (6) and (7) give the mean times for arbitrary dependences of the potential of mean force, $U(x)$, and particle diffusion coefficient, $D_{ch}(x)$, on the particle coordinate in the channel, x , assuming that $U = 0$. More general formulas for the translocation probability and characteristic times are available in Refs. [9, 10].

For a simplified case of a symmetric cylindrical channel characterized by a rectangular potential well of the depth U_0 (Fig. 2, dashed line) and a position-independent diffusion coefficient $D_{ch}(x) = D_{ch}$, the expressions for the translocation probability and average lifetime in the channel simplify and take the form

$$P_{tr} = \frac{1}{2 + \frac{4D_b L}{\pi D_{ch} R} \exp(-\beta U_0)} \quad (8)$$

and

$$\tau = \frac{\pi RL}{8D_b} \exp(\beta U_0). \quad (9)$$

Using this simplification and introducing particle-particle repulsive interaction as a requirement that the channel can be occupied by only one particle at a time, we showed that the particle flux through the channel is [7, 8]

$$J = \frac{2D_b R(c_1 - c_2)}{\left[1 + \frac{\pi R^2 L(c_1 + c_2)}{2} \exp(\beta U_0)\right] \left[1 + \frac{2D_b L}{\pi D_{ch} R} \exp(-\beta U_0)\right]}, \quad (10)$$

where c_1 and c_2 are the particle concentrations on the two sides of the membrane (Fig. 2).

Figure 3 shows the flux for the following parameters: $L = 5$ nm, $R = 0.2$ nm, $D_b = 2 D_{ch} = 3 \cdot 10^{-10}$ m²/s, with $c_2 = 0$ and c_1 specified in the graph. As expected, the flux is a nonmonotonic function of the well depth. Indeed, at the well depth that maximizes the flux there should be a compromise between sufficiently high translocation probability, Eq. (8), and not too long particle lifetime in the channel, Eq. (9), as the particle in the channel, according to our model, does not allow other particles to enter. The optimal depth is given by

$$U_{opt} = \frac{k_B T}{2} \ln \left[\frac{4D_b}{\pi^2 D_{ch} R^3 (c_1 + c_2)} \right]. \quad (11)$$

Eq. (11) shows that the optimal well depth decreases with the increasing bulk concentration of the translocating particles. A more detailed analysis leads to an intuitively clear result: at the optimal channel parameters the particle lifetime in the channel should be approximately equal to the mean inverse frequency of particle attempts to enter the channel.

3 Entropy potentials and limitations of their applicability

To apply this approach to the problem of ATP translocation through VDAC channel (Fig. 1) formulated in the Introduction we have to account for the position dependence of the channel radius, $R(x)$, by introducing the entropy potential defined as

$$U_{ent}(x) = -k_B T \ln \frac{A(x)}{A(0)} = -2k_B T \ln \frac{R(x)}{R(0)}, \quad (12)$$

where $A(x)$ is the cross-sectional area of the channel, $A(x) = \pi(R(x))^2$, with $U_{ent}(0) = 0$. In the presence of only steric interactions, $U(x) = U_{ent}(x)$, the substitution of the expression in Eq. (12) into Eq. (1) leads to the familiar Fick-Jacobs equation [13] for the one-dimensional particle propagator in the channel, if we assume that $D_{ch}(x) = \text{const}$.

This approach has been applied to the analysis of ATP translocation through VDAC channel [4]. Assuming that diffusion in the channel is somewhat slower than that in the bulk, $D_b = 2 D_{ch}$, and using in Eqs. (4) and (12) the effective channel radius for an ATP molecule plotted in Fig. 1, the following estimate for the probability of ATP translocation through the VDAC channel was obtained: $P_{tr} \simeq 0.045$. According to this estimate, the entropy barrier due to the

constriction in the middle of the channel significantly reduces the translocation probability – only one of about every twenty molecules that reach the channel entrance makes it to the other side of the membrane successfully.

It is clear that the maximum translocation probability for the passive diffusion is 0.5. As it follows from Eq. (4), one of the ways to approach this maximum is to increase the diffusion coefficient of the particle in the channel relative to its value in the bulk. Such a situation, however, does not agree with conclusions of many studies which point in the opposite direction, namely, that diffusion in the channel is somewhat hindered compared to that in free solution. The other way is to increase the ratio of the channel radius to the channel length. This strategy is also inherently deficient, for the reason that the length of the channel cannot be smaller than the membrane width of about 5 nm, and channel radius cannot be too large because such a channel would be of large non-selective conductance thus compromising the cell membrane barrier function. Many well-known examples demonstrate that Nature explores a different strategy in which solute-specific channels exhibit strong attractive interactions to the corresponding solutes [14]. Similarly, in a recent molecular dynamics study of ATP moving within the confines of the VDAC pore, it was found that the corresponding potential of mean force along the pore axis is negative and reaches many $k_B T$ in absolute value [4]. Substitution of this potential of mean force in Eq. (4) gives $P_{tr} \simeq 0.43$. This is an order of magnitude increase in the translocation probability given above, which was calculated for the channel where attractive interactions with the channel walls were artificially switched off.

These results demonstrate that the combination of the analytical description briefly reviewed above and the data on the potential of mean force obtained in molecular dynamics simulations allows one to evaluate the most important transport parameters of the channel. To use this approach for the structures with the confinement geometry varying along the channel axis, one has to include into consideration both components of the potential of mean force: the “energetic contribution” which comes from Coulomb, van der Waals, Keesom, hydrogen bonding, and other interactions, and the “entropic contribution” stemming from the varying channel geometry. In the absence of any other fields, the entropy potential in the Smoluchowski equation, Eq. (1), accounts for the lateral confinement thus reducing the problem to the one-dimensional diffusion treated within the formalism of the Fick-Jacobs equation [13]. The range of the applicability of the latter and the necessary corrections have been actively discussed for the last decade initiated by Zwanzig’s pioneering paper [15].

The validity criteria for the description in term of the entropy potential can be grouped into three different categories:

- i. there is a limitation on the “rate” of the confining geometry variation along the channel axis;
- ii. there is a limitation on the relative “wavelength” of geometry variation;
- iii. in the case of a biased diffusion in the presence of an external driving force, there is a geometry-dependent limitation on the force strength.

The limitation on the rate of geometry variation attracted the most attention so far, being studied in a growing number of publications. The Fick–Jacobs equation was first generalized by Zwanzig [15], who showed that when the tube radius is a slowly varying function of x , $|dR(x)/dx| \ll 1$, the diffusion coefficient entering into Eq. (1) can be approximated by

$$D_{ZW}(x) = \frac{D_0}{1 + (1/2)(dR(x)/dx)^2}, \quad (13)$$

where D_0 is the particle diffusion coefficient in a purely cylindrical tube. Later, based on heuristic arguments, this result was generalized by Reguera and Rubi [16] to read as

$$D_{RR}(x) = \frac{D_0}{\sqrt{1 + (dR(x)/dx)^2}}. \quad (14)$$

A general theory of reduction to the effective one-dimensional description was developed in a series of papers by Kalinay and Percus [17–21], Martens and colleagues [22, 23], and others [24–26]. In a Brownian dynamics simulation study of diffusion in a long conical channel [27], it was demonstrated that the generalized Fick–Jacobs equation with $D(x)$ given by Eq. (14) is valid for

$$|dR(x)/dx| \leq 1, \quad (15)$$

thus significantly extending the range of applicability of the generalized Fick–Jacobs equation.

The limitation on the geometry variation wavelength was recently analyzed [28] in Brownian dynamics simulations of diffusion in structures shown in Figure 4, which gives a sequence of corrugated tubes made of conical sections with the same minimum diameter, $\min 2R_{\min}$, and the same rate of radius variation, $|dR(x)/dx| = \lambda$, but with different periods of this variation, $2L_V$. The sequence starts with a structure composed of relatively long conical sections and progresses towards structures made of shorter and shorter sections. It is seen that as the period decreases, the structure gets closer to a regular cylindrical tube of radius $R_{\min}$ and, in the limit of infinitely short periods represents a smooth cylinder. One's intuition is that for sufficiently short wavelengths,

$$L_V/R_{\min} \ll 1, \quad (16)$$

the corrections introduced by Eqs. (13) and (14) are not necessary. Figure 5 shows that this is exactly the case. It gives the comparison of the effective diffusion coefficients obtained from Brownian dynamics simulations and predicted by the Lifson–Jackson formula [29],

$$D_{\text{eff}} = \frac{1}{\langle \exp(-\beta U_{\text{ent}}(x)) \rangle \langle \exp(\beta U_{\text{ent}}(x)) / D_{RR}(x) \rangle}, \quad (17)$$

where $U_{\text{ent}}(x)$ and $D_{RR}(x)$ are given by Eq. (12) and Eq. (14), respectively. In our case $|dR(x)/dx| = \lambda$, and Eq. (17) leads to a simple algebraic expression

$$D_{eff} = \frac{D_0}{\sqrt{1+\lambda^2}} \frac{1 + \frac{\lambda L_V}{R_{min}}}{1 + \frac{\lambda L_V}{R_{min}} + \frac{1}{3} \left(\frac{\lambda L_V}{R_{min}} \right)^2}. \quad (18)$$

From Fig. 5 one can see that while at relatively large values of the ratio L_V / R_{min} , the effective diffusion coefficient follows predictions of Eq. (18), small ratios do not require any corrections for the radius variation at both $\lambda = 0.5$ and $\lambda = 1.0$.

Finally, the geometry-dependent limitations on the strength of the driving force were analyzed, both in numerical simulations and analytically, by Burada and colleagues [30, 31] for biased motion of Brownian particles in 2D and 3D periodic channels of varying cross section. As the derivation of the Fick-Jacobs equation is based on the assumption of essential equilibration in the direction transverse to the transport direction [13], it is clear that this assumption is further jeopardized by the drag experienced by the particles under the action of the applied force. In this case, the corrections to the diffusion coefficient include not only derivatives of the channel radius, as in Eqs. (13) and (14), but also derivatives of the external potential [21]. As the present article focuses on unbiased diffusion, we direct the reader to the original studies.

4 Channels with abruptly changing cross-sections

Concluding our discussion, we consider a channel of length L and radius R with a constriction zone of length l , $l < L$, and radius r , $r < R$, in its center, shown in Figure 6. Since the channel radius changes abruptly, we cannot use the results for the translocation probability in Eqs. (4) and (5), and for the mean particle lifetimes in the channel, Eq. (7). Nevertheless, the translocation probability and different characteristic times can be found in this case using a general approach to this class of problems developed in Refs. [32, 33]. Here we give the final results (Berezhkovskii and Bezrukov, unpublished) for the limiting case of $l \ll r, R$, and L , where the constriction can be considered as an infinitely thin partition with a circular aperture of radius r in its center.

As might be expected, the presence of the partition leads to the decrease of the translocation probability which is given by

$$P_{tr} = \frac{1}{2 + \frac{4D_b L}{\pi D_{ch} R} + \frac{2D_b R}{D_{ch} r f(r/R)}}, \quad (19)$$

where function $f(z)$ monotonically increases from unity to infinity as z increases from zero to unity [34],

$$f(z) = \frac{1 + 1.37z - 0.37z^4}{(1 - z^2)^2}. \quad (20)$$

As $r \rightarrow R$, $f(r/R)$ tends to infinity, and Eq. (19) leads to

$$P_{tr} = \frac{1}{2 + \frac{4D_b L}{\pi D_{ch} R}}, \quad (21)$$

which is identical to the translocation probability given by Eq. (4) with $D_{ch}(x) = \text{const} = D_{ch}$ and $U(x) = 0$. As $r \rightarrow 0$, more specifically, $r \ll R^2/L$, the translocation probability takes the limiting form

$$P_{tr} \simeq \frac{D_{ch} r}{2D_b R}, \quad (22)$$

which is independent of the channel length L . In this limiting case the partition aperture is so small that the time required for the particle to find the aperture significantly exceeds its equilibration time in the half-channel.

The mean particle lifetime in the channel with the partition in the middle is insensitive to the presence of the partition and is given by Eq. (9) with $U_0 = 0$ since there is no potential well in the channel,

$$\tau = \frac{\pi R L}{8 D_b}. \quad (23)$$

It is worth mentioning that the translocation probability is independent of the location of the partition inside the channel, whereas it can be shown that the mean lifetime monotonically increases as the partition moves from the channel entrance to its exit. Finally we mention that the above results for the infinitely thin partition can be generalized for partitions of finite widths.

To summarize, one can find the translocation probability and mean particle lifetimes in a channel of smoothly varying geometry by Eqs. (4), (5), and (7) with the diffusion coefficient corrected according to Eq. (14). These formulas fail when the geometry changes abruptly. Indeed, analysis of the translocation probability based on Eqs. (4) and (12) shows that at a however small radius r of the constriction, its contribution to the integral in Eq. (5) could be minimized by decreasing the constriction length l . This is possible, because of the fact that for small constriction lengths the contribution is linear in l . This is obviously not true in the case of a sharp cylindrical constriction shown in Fig. 6. The translocation probability and mean particle lifetime are given now by Eqs. (19) and (23) and do not depend on the constriction length in the limit of small l .

5 Transport through a cosine-shaped channel

As a new illustration we apply the concepts discussed above to analyze the flux through a cosine-shaped channel. For such a channel the x -dependence of the channel radius has the form

$$R(x|x_0) = \bar{R} + \frac{1}{2} \Delta R \cos\left(2\pi \frac{x_0 + x}{L}\right), \quad 0 \leq x, x_0 \leq L, \quad (24)$$

where x_0 is a parameter determining the channel shape, $R = (R_{\max} + R_{\min})/2$ is the mean channel radius, $R = R_{\max} - R_{\min}$ is the amplitude of the radius variation, with $R_{\max}$ and $R_{\min}$ denoting the maximum and minimum channel radii along its axis, respectively. The value of x_0 determines the channel shape with the radii of channel openings changing in the same range, from $R_{\max}$ to $R_{\min}$. In Figure 7 insets we show two limiting shapes of the channel corresponding to the maximum ($x_0 = 0$, $x_0 = L$) and minimum ($x_0 = L/2$) channel openings. Our goal is to analyze how the flux through such a channel depends on the channel shape, i.e., on x_0 , assuming that $c_1 = c$ and $c_2 = 0$.

In the case of non-interacting particles the flux, $J(x_0)$, is a product of the flux entering the channel and the translocation probability. Using the Hill-Berg-Purcell formula [35, 36] we can write the entering flux as $4D_b R(0|x_0)c$. The translocation probability is given by the expression in Eq. (4) in which $R = R(0|x_0)$ and $U(x) = U_{ent}(x) = -2k_B T \ln[R(x|x_0)/R(0|x_0)]$. In addition, we assume that the x -dependence of the intra-channel diffusion coefficient is due to the variation of the channel radius. Then the integral appearing in Eq. (4) is

$$\int_0^L \frac{\exp(\beta U(x))}{D_{ch}(x)} dx = [R(0|x_0)]^2 K, \quad (25)$$

where K is a constant in the sense that it is independent of x_0

$$K = \int_0^L \frac{dx}{[R(x|x_0)]^2 D_{ch}(x)}. \quad (26)$$

Eventually, we can write the flux as

$$J(x_0) = \frac{2D_b R(0|x_0)c}{1 + \frac{2D_b}{\pi} R(0|x_0)K}. \quad (27)$$

This flux is a monotonically increasing function of $R(0|x_0)$. Since $R(0|x_0)$ is a monotonically decreasing function of x_0 for $0 \leq x_0 \leq L/2$, $J(x_0)$ also monotonically decreases with x_0 in this interval. Therefore, the flux through the cosine-shaped channel has a maximum and a minimum for the channel shapes corresponding to $x_0 = 0$ and $x_0 = L/2$, respectively. Fig. 7 shows the flux for the cases of a position-independent diffusion coefficient and the corrected one given by Eq. (14). The channel parameters are chosen to obey the condition of the correction validity in Eq. (15) which, in the case of the shape described by Eq. (24), transforms into $R \leq L/\pi$.

6 Concluding remarks

The focus of the present paper is on the applicability of the concept of the entropy potential for the description of transport in confined systems of varying geometry. Although this concept naturally arises in one-dimensional description of equilibrium distributions in such systems, its applicability to the analysis of transport requires some caution. Several applicability criteria from those explored in the literature up to date are discussed. A general

consideration of these issues in the first four sections is complemented by the analysis of optimal transport for a cosine-shaped channel in Section 5.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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.

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Figure 1.

The effective radius of the voltage-dependent channel of the outer mitochondrial membrane [1] for an ATP molecule, $R(x)$, obtained in the recent molecular dynamics simulations [4] which used the results of an x-ray crystallography study [3] for the channel structure. The radius was calculated from the total area available for the center of the ATP molecule at a particular position along the channel axis. The insets above the curve show three positions of the molecule advancing from the left to the right, with the arrows pointing to the corresponding x values.

Figure 2.

A schematic illustration of a channel traversing the membrane (top) and the potential of mean force, $U(x)$, along the channel axis x (bottom). An example of a rectangular potential well that occupies the entire channel is shown by the thick dashed line.

Figure 3.

The flux through the channel, Eq. (10), depends on the strength of channel-particle interactions in a non-monotonic way. For the particular channel geometry (see the text) and the range of the particle concentrations specified in the figure, the depth of the rectangular well that optimizes the transport is around 6 to 10 $k_B T$ per molecule. Blockage of the channel, which is often a mechanism of channel regulation in nature [2], is achieved at higher well depths.

Figure 4.

Going to the shorter and shorter wavelengths, $L_V/R_{\min}$, at the conserved minimum channel radius, $R_{\min} = \text{const}$, and the radius variation rate, $dR(x)/dx = \text{const}$, one transforms a strongly corrugated channel (top) into a smooth one at $L_V/R_{\min} \rightarrow 0$ (bottom).

Figure 5. The dependence of the effective diffusion coefficient on the characteristic wavelength of the corrugation, L_V/R_{min} (Fig. 4), for the two values of the radius variation rate, $\lambda = dR(x)/dx$, specified in the figure. Solid lines show the prediction of Eq. (18); symbols are the results of Brownian dynamics simulations [28].

Figure 6.

A schematic illustration of a cylindrical channel with an abrupt cylindrical constriction in the center (top). The constriction creates a sharp rectangular entropy barrier (bottom) of length l and height $U = 2k_B T \ln(R/r)$.

Figure 7.

The flux $J(x_0)$, Eq. (27), as a function of the cosine “phase” x_0 , Eq. (24), for the following parameters: $L = 5$, $R = 1$, $R = 1.5$ (corresponding to the images in the insets given for $x_0 = 0$, $x_0 = L/2$, and $x_0 = L$) and $c = 1$. Upper solid (red) line shows the results for a position-independent diffusion coefficient $D_{ch}(x) = D_b = D_0$. Lower solid (black) line is calculated for the case when the intra-channel diffusion coefficient is given by Eq. (14).