Asymmetric nanodiffusion

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The asymmetric diffusion through conical nanopores is described by the diffusional model. Diffusion is several times faster; when the concentration gradient points from the wide towards the narrow opening of the cone than in the opposite direction. The asymmetric diffusion appears either when the diffusion coefficient depends on the concentration or when the diffusing substances interact with the channel (i.e., ions moving through channels with charged walls). These results suggest that asymmetric nanopores can act as molecular (ionic) filters which could be used for retrieving the molecules of a given component from solutions in which its concentration fluctuates strongly, and only occasionally attains high values.

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I. INTRODUCTION

One of the main unsolved problems in nanoscience is how to control the material transport. This aim was achieved long ago in living cells where the active channels pump ions or other substances against their concentration gradients, and passive channels transport the material down concentration gradients [1]. In synthetic nanosystems the most widely known example is the Brownian ratchets [2,3]. Recently, it has been proved also that the synthetic nanopores can rectify the ionic currents [4,5] and pump the ions against their concentration gradients [6].

In all the above-mentioned examples, the asymmetric transport is achieved by the driving of the system by forces external to the system under consideration. In active channels, proteins (ATP-ases) use the energy stored in the ATP to pump ions or other substances against their concentration gradients. They are also able to use this aim of oscillations of external electric fields [7–9], and intrinsic fluctuations of electric fields across the membrane [10]. In some of the passive channels—so-called *voltage-gated* channels, that exhibit a remarkable property of *current rectification*—this effect is obtained by means of excitation of the channel by an externally applied voltage, that results in different magnitudes of the conduction currents in opposite directions [11]. The same objectives (i.e., pumping and rectification) can also be achieved in synthetic nanopores [6,12,13]—nano pumps and rectifiers—which also make use of the energy from external electric fields.

We report here the theoretical description of a new asymmetric transport phenomenon, the asymmetric diffusion through very narrow conical pores. In the presence of concentration gradients, and without the use of external forces which could pump energy into the system, the magnitude of diffusion flow depends on the direction of the concentration gradient. One of possible realizations of this effect has recently been confirmed experimentally [14]. It is worth noting that a similar phenomenon of asymmetry in channel selectivity properties has been reported recently for the bacterial porin OmpF [15]. These results prove that it is possible to construct ionic nanofilters. However, it should be stressed that this effect cannot be used for pumping the material against concentration gradients (except perhaps by means of the so-called co-diffusion [16,17])

Typical synthetic nanochannel [4–6,12–14] is a conical pore of length $L=8-12\ \mu$m, and diameters $d_0=2r_0$ a few nanometers, and $d_L=2r_L$, a few hundred nm (cf. Fig. 1). The biological channels are more narrow and much shorter. The channel connects two compartments containing solutions of concentrations c_0 and c_L, The charge density at the inner surface of the pore can be regulated by changing *p*H of the solution. The pores used in [14] at *p*H 8 are negatively charged with surface charge ρ of about $1.5\ e/\mathrm{nm}^2$ (e—elementary charge); at *p*H 2 the pore's surface is electrically neutral. The setup assumed implicitly in this paper is the same as in our earlier work [12–14]. In the major part of this paper no driving external fields, electric or otherwise, are considered.

We define here the positive direction of the motion of particles (ions) as the direction from left to right—therefore, the diffusion flow is positive when $c_L<c_0$; we also assume that the narrow tip of the pore is situated at the left (cf. Fig. 1).

A convenient measure of the effect of asymmetric diffusion is the quantity introduced in [14]:

$$Q=|J_{\leftarrow}|/|J_{\rightarrow}|, \tag{1.1}$$

where $J_{\leftarrow}$ and $J_{\rightarrow}$ are the currents measured (calculated) for $c_0<c_L$, and $c_0>c_L$, respectively. For the ionic currents flow-

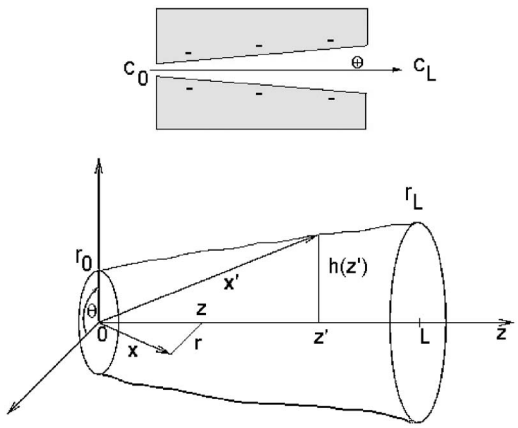

FIG. 1. Schematic sketch of the channel geometry. Not in proportions.

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ing through long narrow charged nanopores measured in KCl solutions, Q is about 2 ± 0.2 for concentration gradients $0.1M/1.0M$ [14].

This paper is organized as follows: Section II presents the diffusion equations in Zwanzig's formulation [18,19] of the so-called Fick-Jacobs equation. Asymmetric diffusion through neutral pores and/or of neutral particles is discussed in Sec. III, and asymmetry of ionic diffusion in electrically charged pores—in Sec. IV. Sec. V contains final remarks and conclusions.

II. DIFFUSION EQUATIONS

We consider the diffusion through the narrow axially symmetric channel of length L. The shape of the channel is defined by its local radius $h(z)$, z being the coordinate along channel's long axis (cf. Fig. 1).

There have been several approaches to the issue of diffusion in confined geometries and/or in irregular channels reported recently (for a review see [20]). We shall use Zwanzig's formulation [18] of the so-called Fick-Jacobs equation, in which the boundary problem in 2 or 3 dimensions, which is a very difficult issue, is replaced by an equivalent one-dimensional (averaged) representation.

The diffusional transport of component i in external fields is described by the Smoluchowski-Nernst-Planck (or generalized diffusion) equation:

$$\frac{\partial}{\partial t}c_i(\mathbf{x},t) = -\,\boldsymbol{\nabla}\cdot\mathbf{j}_i(\mathbf{x},t), \tag{2.1}$$

$$\mathbf{j}_i(\mathbf{x},t) = -D_i\,\boldsymbol{\nabla}\,c_i(\mathbf{x},t) + \mu_i\mathbf{E_i}(\mathbf{x})c_i(\mathbf{x},t), \tag{2.2}$$

with appropriate boundary conditions, where D_i stands for diffusion coefficient, μ_i is the mobility, c_i denotes concentration, $\mathbf{j}_i$ is the mass current density, and $\mathbf{E}_i(\mathbf{x})=-\boldsymbol{\nabla}\phi_i(\mathbf{x})$, ϕ_i is the potential energy of the ith particle in the electric field. (In a more general case the electric field $\mathbf{E}_i$ can be time-dependent.)

The boundary conditions of the confined geometry can be easily taken into account in the following way: define the "entropy barrier" $\psi_0(z,r)$ [18] such that $\psi_0=0$ outside the pore, and inside the pore for $r\leqslant h(z)-r_{particle}$, and is infinitely repulsive for $0<z<L$ and $r>h(z)-r_{particle}$ (the particle radius $r_{particle}$ takes into account the nearest approach distance of the particle to pore's surface), and write Eq. (2.2) in the form

$$\mathbf{j}_i(\mathbf{x},t) = -\,e^{-\beta\psi_i(\mathbf{x})}D_i\,\boldsymbol{\nabla}\,e^{\beta\psi_i(\mathbf{x})}c_i(\mathbf{x},t), \tag{2.3}$$

$$\psi_i(\mathbf{x}) = \tilde{\phi}_i(\mathbf{x}) + \psi_0(\mathbf{x}), \quad \tilde{\phi}_i = \phi_i/\beta D_i, \tag{2.4}$$

where $\beta=1/kT$.

Solution of Eq. (2.1) for both the concentration and the current in the general three-dimensional case, and for the confined geometry shown in Fig. 1, is difficult even for the stationary case. One way of dealing with this issue suggested in the literature [18–21] is to formulate a one-dimensional equivalent. Let $\bar{c}_i(z)$ be the local concentration inside the channel, averaged over channel's cross-section $A(z)=\pi h^2(z)$:

$$\bar{c}_i(z) = \int_{-\pi}^{\pi} d\theta \int_0^{h(z)} dr\; r\; c_i(z,r,\theta)/A(z), \tag{2.5}$$

inside the channel, and $\bar{c}_i(z)=c_{i,bulk}$ otherwise.

According to Zwanzig [18], in the local equilibrium approximation (along the cross-section) the local average concentration $\bar{c}$ satisfies the one-dimensional Smoluchowski equation (in this case equivalent to the so-called Fick-Jacobs equation [18,19]):

$$\frac{\partial}{\partial t}A(z)\bar{c}_i(z,t) = \frac{\partial}{\partial z}A(z)\bar{j}_i(z,t), \tag{2.6}$$

with the current density

$$\bar{j}_i(z,t) = -\,D_i e^{-\beta\phi_{i,eff}(z)}\frac{\partial}{\partial z}e^{\beta\phi_{i,eff}(z)}\bar{c}_i(z,t), \tag{2.7}$$

where [18]

$$e^{-\beta\phi_{i,eff}(z)} = \int_{A(z)}\int dr\; r\; d\theta\, e^{-\beta\tilde{\phi}_i(z,r,\theta)}/A(z). \tag{2.8}$$

The above formula has clear physical meaning for the confining potential ψ_0 (cf. [18,19]) as the effective probability density of finding the diffusing particle inside the channel at the position z along the channel's length. For electrostatic potential and diffusing ions, this Zwanzig-type average would lead to effective electric fields $E_{i,eff}(z)=-\partial V_{i,eff}(z)/\partial z$ [with $\phi_{i,eff}(z)=Z_i e V_{i,eff}(z)$, $Z_i e$ being the ith ion's charge] different for anions ($Z_i<0$) and cations ($Z_i>0$). In a negatively charged channel the absolute magnitude of the effective potential for a cation would be higher (in some cases much higher) than that for an anion. This seems to be dubious from the physical point of view. The use of the effective potential energy $\phi_{i,eff}(z)=\bar{\tilde{\phi}}(z)$ defined by the formula analogous to that for the concentration, Eq. (2.5), ensures that the effective field inside the channel is the same for every ion, and, moreover, yields results, which are more in keeping with experimental data [13].

In one dimension, the overall stationary current is just the current density multiplied by the pore's cross-section: $J_i=A(z)\bar{j}_i(z)$ and does not depend on z. The stationary effective Smoluchowski equation therefore reads:

$$\frac{\partial}{\partial z}e^{\beta\phi_{i,eff}(z)}\bar{c}_i(z) = -\,e^{\beta\phi_{i,eff}(z)}J_i[D_iA(z)]^{-1}. \tag{2.9}$$

When neither the diffusion coefficient nor the potential $\phi_i(z,r)$ depend on the concentration, the solution of Eq. (2.9) is simple:

$$e^{\beta\phi_{i,eff}(z)}\bar{c}_i(z) = e^{\beta\phi_{i,eff}(0)}\bar{c}_i(0) - J_i\int_0^z dz'\,e^{\beta\phi_{i,eff}(z')}/\pi D_i h^2(z'), \tag{2.10}$$

with J_i given by the boundary conditions $\bar{c}_i(0)=c_{i,0}$, $\bar{c}_i(L)=c_{i,L}$:

$$J_i = \frac{e^{\beta\phi_{i,eff}(0)}c_{i,0} - e^{\beta\phi_{i,eff}(L)}c_{i,L}}{\int_0^L dz' e^{\beta\phi_{i,eff}(z')}/\pi D_i h^2(z')}. \quad (2.11)$$

However, in the majority of interesting cases, either the diffusion coefficient is the function, or the internal potential energy is the functional of the local value of the concentration of the diffusing molecules. In these cases, the direct analytic solutions of the Smoluchowski equation (2.6) are unknown. The standard method is the self-consistent iteration of the expressions (2.11) and (2.10): assume as the zero-th approximation some concentration gradient $\bar{c}_i^{(0)}(z)$, e.g., the "bulk" linear solution $c_{i,bulk}(z)=c_0+(c_L-c_0)z/L$, calculate $J_i^{(0)}$ from (2.11), insert the result to Eq.(2.10) to calculate $\bar{c}_i^{(1)}(z)$, insert the result to Eq.(2.11), etc. Note that at every subsequent approximation one needs to calculate also the subsequent local values of $D_i(c(z))$

$$D_i(c(z)) = D_i(c_0) + \frac{D_i(c_L) - D_i(c_0)}{c_L - c_0}c(z), \quad (2.12)$$

from the expansion in Taylor's series and $\phi_{i,eff}(z,[c_i(z)])$ [i.e., $\phi_i(z,r,\theta)$ also]. Still, this method (if convergent) is faster than the numerical solution of Eq.(2.6), which can be cumbersome because of the need to calculate $D_i(z)$ and $\phi_i(z)$ at many intermediate values of the running variable z.

III. NEUTRAL DIFFUSION

Let us consider first the case when there are no interactions ($\phi_i \equiv 0$) between the channel's walls and the diffusing particles. This corresponds either to the diffusion of neutral particles or to the diffusion of charged or polar particles through neutral channels. In this case the only source of the asymmetry sensitive to the direction of the concentration gradient is the concentration-dependent diffusion coefficient $D_i=D_i(c_i(z))$ and Eqs.(2.10) and (2.11) reduce to

$$\bar{c}_i(z) = c_{i,0} - J_i \int_0^z dz h^{-2}(z') D_i^{-1}(z'), \quad (3.1)$$

$$J_i = \pi \frac{c_{i0} - c_{iL}}{\int_0^L dz h^{-2}(z) D_i^{-1}(z)}. \quad (3.2)$$

It is easy to check that for cylindrical pores, $h(z)=r_0 \neq f(z), J_{i,\leftarrow}=-J_{i,\rightarrow}$, and $Q_i=1$.

In the case of neutral diffusion, the procedure described in (3.2) works very well and the self-consistency at the level of about 0.1% is obtained after two-three iterations. The shape of the final concentration distribution $c_i(z)$ (full lines) for both directions of the concentration gradient is shown in Fig. 2, where the dashed lines denote the "bulk" (linear) distribution $c_i^{(0)}(z)$. Although the initial and final concentration profiles are very different, the calculated currents change no more (and in many cases much less) than 20%, and the measures $Q^{(0)}$ and Q remain practically the same.

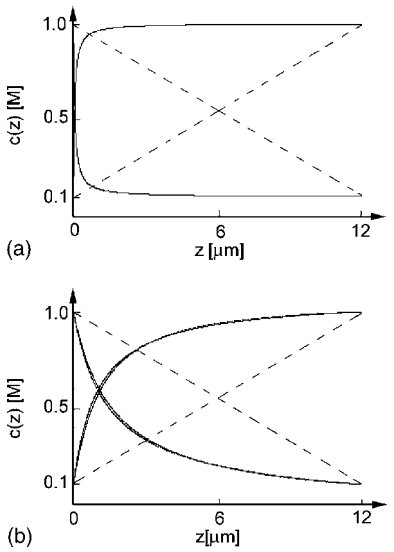

FIG. 2. Iterated distribution of concentrations of the diffusing components inside the neutral conical channel, under concentration gradients $c_0=0.1$, $c_L=1.0M$, and $c_0=1.0$, $c_L=0.1M$. Dashed lines show the linear ("bulk-type") gradients. (a) $r_0=1.0$ nm, $r_L=250$ nm, $L=12000$ nm, $q=0.85$, $Q=1.33$, $J_{\leftarrow}^{(0)}=-40.7 \rightarrow J_{\leftarrow}^{(2)}=-38.2$, $J_{\rightarrow}^{(0)}=30.6 \rightarrow J_{\rightarrow}^{(2)}=32.7\times10^8$ particles/s; (b) $r_0=0.5$ nm, $r_L=5$ nm, $L=12000$ nm, $q=0.5, Q=2.41$, $J_{\leftarrow}^{(0)}=-0.52 \rightarrow J_{\leftarrow}^{(3)}=-0.46$, $J_{\rightarrow}^{(0)}=0.22 \rightarrow J_{\rightarrow}^{(3)}=0.42\times10^8$ particles/s.

The analysis of Eqs.(3.1) and (3.2) shows that the effect, as measured by the quantity Q, will depend on three factors only: the shape of the channel described by the function $h(z)$, the magnitude of the dependence of the diffusion coefficient on the concentration, measured by the parameter $q=D_i(c_{i,high})/D_i(c_{i,low})$ ($c_{i,low}, c_{i,high}$ being the lower and upper outside-the-channel concentrations, respectively; we assume here that the diffusion coefficient diminishes with increasing concentration), and the geometrical asymmetry of the channel, measured by the parameter r_L/r_0 for below-described different shapes of the channel.

Figure 3 shows the dependence of the asymmetry factor Q on the parameter q for three different shapes of the channel (shown in the inset): concave, straight cone, and convex. It is seen that the concave and straight shapes are optimal,

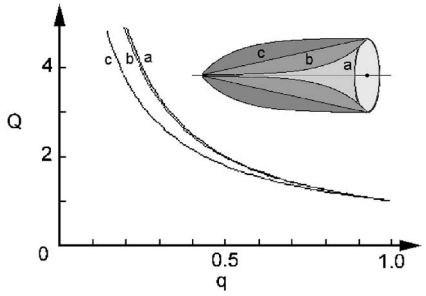

FIG. 3. Dependence of the asymmetry factor Q on the parameter $q=D_i(c_{high})/D_i(c_{low})$, for three different shapes (shown—not in scale—in the inset) of the channel. In all three cases $r_0=1.0$ nm, $r_l=250$ nm, $l=12000$ nm. For short narrow channels the dependence $Q(q)$ is similar.

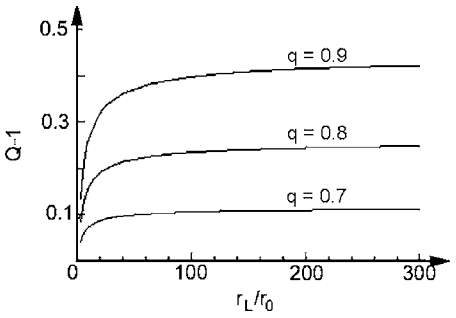

FIG. 4. Dependence of the asymmetry factor Q on the quotient r_L/r_0, for constant r_0 and L, for three different values of the parameter q. In this parametrization the effect depends very weakly on r_0 and L.

whereas the convex-shaped channels being less effective. However, the effect is non-negligible only for not too weak dependence of the diffusion coefficient on the concentration. Now, in most cases the diffusion coefficients depend on the concentration in a fairly weak manner.

For example, for the water solutions of KCl, considered in [14], the literature treats usually the diffusion coefficients of K^+ and Cl^- as independent of concentration and equal to each other (about $2\times10^{-9}\mathrm{m}^2\,\mathrm{s}^{-1}$) (e.g., [20]). On the other hand, the dependence $D(c)$ for KCl can be estimated from the dependence on the concentration of its conductance $\chi(c)$, assuming the validity of the Einstein relation $\mu=D/kT$, and $\chi\sim c\mu, \mu$ being the mobility. Now, for KCl concentrations $0.1M$ and $1.0M$ (used in [14]), $(\chi_{1.0}/c_{1.0})/(\chi_{0.1}/c_{0.1})\approx0.85$ [12,13,22], and therefore also $q\approx0.85$, and, from Fig. 3, $Q\approx1.15$, which implies that there is about 15% contribution of the neutral diffusion effect, and about 85% contribution of the electrostatic effects in the measured [14] asymmetry. Stronger dependence can, perhaps, appear in the case of associating molecules, when the association depends on the concentration, or in other exotic conditions.

Figure 4 presents the dependence of Q on the parameter r_L/r_0, for a straight-cone geometry, and for a few values of the parameter q. The wider the cone's opening angle, the stronger the effect, but the dependence saturates practically for $r_L>100\,r_0$.

Factor Q does not depend on the length of the channel. On the other hand, the length influences the magnitudes of the currents which are inversely proportional to L.

The plausible tentative mechanism of this "neutral" effect might be explained through "density" of particles (flow lines) when the flow is in the direction towards the narrow end, and "attenuation" in the opposite case, which seems to be related to the recently described effect deviations from parallel geometry resulting in nonuniform pressures and density profiles of a liquid along the pore [23]. Formally, this is taken into account in the formulas (3.2) and (3.1) by the factor $1/\pi h^2(z)$. However, it still has not been shown as to what extent the Fick-Jacobs-Zwanzig approximation [18,19], on which these formulas are based, is good enough to explore the fine details of diffusion through asymmetric confined spaces, i.e., whether the effects shown in Figs. 2–4 are real or are merely artefacts of the model. It still requires experimental verification, and if the answer is affirmative, a more detailed theoretical description will be necessary. Still, the comparison of experimental results and model calculations in [12–14] seem to suggest that the models based on this approximation are correct at least in a semi-quantitative way.

IV. IONIC DIFFUSION

The essential results, both experimental and theoretical, concerning the asymmetry of diffusion of electrolytes in charged synthetic nanopores were published in our previous paper [14]. In this section we present some additional analyses and a few corollaries.

The internal potential $V_{int}(z,r)$ inside the charged channel is generated by the charges of charge density $\rho(z)$, located on the channel walls. In general, the density of the charges and the internal potential depend on their location along the channel axis [24]. We assume that the internal potential does not depend on the angle θ (cf. Fig. 1 for explanation of the notation):

$$V_{int}(z,r)=\frac{1}{4\pi\epsilon}\int_0^L dz'\rho(z')h(z')\times\int_{-\pi}^{\pi}d\theta' R^{-1}(z,z',r,\theta')e^{-\lambda R(z,z',r,\theta')}, \quad (4.1)$$

where

$$R(z,z',r,\theta')=|\mathbf{x}-\mathbf{x}'|=\sqrt{[r-h(z')\cos\theta']^2+[h(z')\sin\theta']^2+(z-z')^2} \quad (4.2)$$

is the distance between points x and x', where $\theta=0$, due to the assumed cylindrical symmetry of the channel. ϵ denotes the dielectric constant (for water solutions we assume $\epsilon=80.1\epsilon_0$, ϵ_0 being the vacuum permittivity), $\lambda=1/l_D$ is the inverse Debye (screening) length, factor $h(z')\int_{-\pi}^{\pi}d\theta'=A(z')$ [$h(z)$ being the cone's radius at z'] gives the number of charges per unit length on the channel's circumference, L is the length of the pore, and r_0 and r_L are the radii at the left and right apertures. In the presence of external voltage U (as in Fig. 5) the total potential is the sum of $\phi_{i,int}=Z_ieV_{int}(r,z)$, and of the contribution $\phi_{ext}(z)=[\mathcal{R}(z)/\mathcal{R}(L)]Z_ieU$, Z_ie being the ion's charge, $\mathcal{R}(z)$ the resistance of the cone of length z. Note that this external contribution remains unchanged in the effective potential appearing in (2.9) and (2.11). The validity of Einstein's relation $\mu_i=\beta D_i$, μ_i being the mobility, is assumed.

The nanopores discussed in [14] were wider and much longer than typical biological membrane nanochannels [1]. Therefore, to check whether the effects described there may occur also in biological situations, we calculated the currents for a short and narrow cone of dimensions $(r_0,r_L,L)=(0.5,1.5,6.0)$ nm (cf. Fig. 1), resembling the dimensions of the biological ionic channels. The results are shown in Figs. 5–7 below. Qualitatively, these results are the same as those reported in [14]. The comparison of diffusional currents for the cones (0.5, 1.5, 6.0) nm (Fig. 5(A)) and (1.5, 315, 12000)

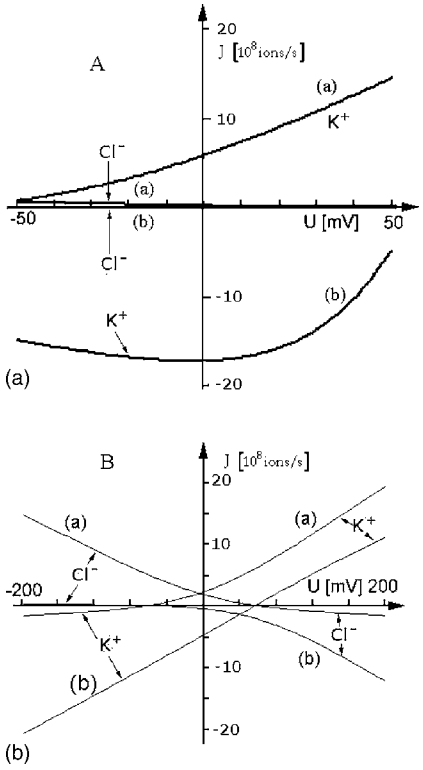

FIG. 5. Diffusional flows $J(U)(10^8$ ions/s) of cations and anions through the conical nanochannels of dimensions (r_0, r_L, L)= (a) (0.5, 1.5, 6.0) nm and (b) (1.5, 315, 12000) nm. $\rho=1.5e$ nm^{-2}, $D_+ = D_- = 2\times10^{-9}$m^2 s^{-1}, (a) $c_0=1.0$, $c_L=0.1$ M, (b) $c_0=0.1$, $c_L=1.0$ M.

nm (Fig. 5(B)) shows that one may expect the asymmetry of the ionic diffusion to be even stronger in short biological channels than in long synthetic ones.

The measurements reported in [14] show that the *electric* currents $I=\Sigma_i Z_i e J_i$ measured at zero voltage (i.e., corresponding to pure diffusion without drift) are different from zero when the channel's surface is charged, whereas the currents flowing through electrically neutral channel are equal to zero (within the experimental error) at $U=0$. Note that this does not mean that the *diffusional flow* is zero in the presence of concentration gradients; $I=0$ means merely that the diffusional flows of anions and cations are equal to each other,

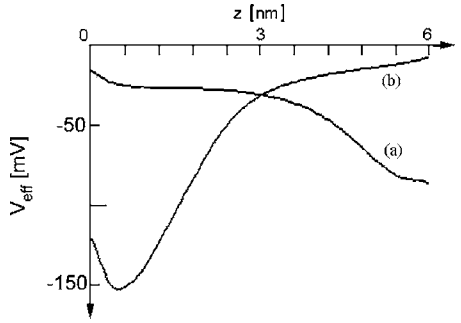

FIG. 6. The effective electric potential inside the charged short conical channel, under concentration gradients (a) $c_0=1.0$, $c_L=0.1$ M, (b) $c_0=0.1$, $c_L=1.0$ M. $r_0=0.5$ nm, $r_L=1.5$ nm, $L=6.0$ nm, $U=0$, $\rho=1.5e$ nm^{-2}.

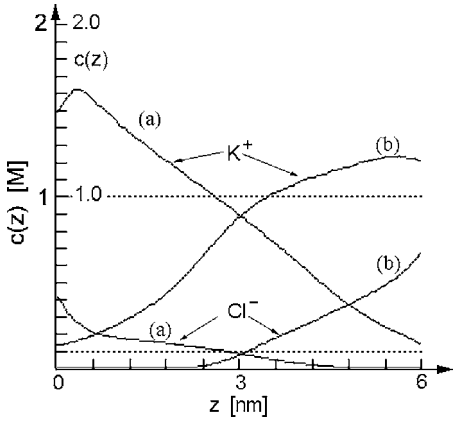

FIG. 7. Concentration gradients inside the charged channel resulting from the confinement in the charged nanopore with internal electric potential as in Fig. 6.

resulting in the zero net electric current. On the other hand, when the nanochannel is charged, $I\neq0$, which means that anionic and cationic diffusional flows are unequal—the channel is cation-selective. This is shown in Fig. 5, where the diffusional currents calculated separately for anions ((Cl^-)) and cations (K+) are presented [25]—the biological-like narrow channel is practically closed for anions, whereas for wider synthetic one the anionic flows are much smaller than the cationic ones.

The most important result found in [14] was that the magnitudes of the currents at zero voltage are different when the direction of the concentration gradient is reversed—the magnitude of the diffusional flow is higher when it flows from the wide towards the narrow aperture of the channel than in the opposite direction. Again, this effect is distinct in Fig. 5. It has also been found that it exclusively appears in charged channels. Moreover, this effect is due to the diffusional flow of cations—anionic flows are higher when the direction of the concentration gradient points from the narrow towards the wide aperture. The latter means that the net charge transferred by diffusion alone (at $U=0$) from one compartment to the other is not zero. Such charge transfer across the membrane will build up the appropriate diffusional potential, which will eventually stop the process, unless the transferred ions are carried away or consumed by some additional processes.

The absence of the effect at pH 2 suggests that the asymmetrical diffusion is related to the electrostatic interactions between ions and the surface charges. More detailed analysis of the mechanism of this effect can be understood on the basis of the properties of the electrostatic fields acting on different ions inside the negatively charged channels.

We have shown in [14] that the principal role is played by the electric potentials $V_{eff}(z)$ and their gradients, the magnitudes of which are much higher for $c_0<c_L$ than otherwise (cf. Fig. 6). As a result, the cations are drawn into the channel more strongly from the wide than from the narrow aperture of the channel. This in itself would not be sufficient for the appearance of the asymmetry in the flows—as what is gained by the cations would be compensated by the anions, for which the effect is opposite. However, in the narrow

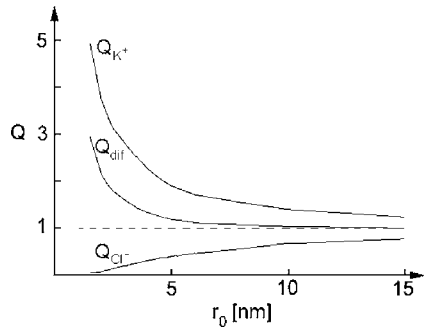

FIG. 8. Diffusional asymmetry factors for cation Q_{K+}, anion Q_{Cl-}, and the whole electrolyte Q_{dif}, for the long channel (1.5, 315, 12000) nm.

nanochannels, the concentration of ions of the same sign as that of the surface charges is depleted, which is due to strong repulsion, whereas that for counter-ions is enhanced. This can be seen from the stationary solution for the concentration, Eq. (2.10), and is illustrated in Fig. 7. Therefore, the above-described action of the electric field on the ions is effectively stronger on cations than on anions, which leads to the asymmetry of the net electric current.

In this context we want to stress that the measured asymmetry, Q_{expt}, is the asymmetry of the *electric* current flowing through the channel and it results mainly from the fact that ions of different sign carry electric currents in opposite directions: $I_{el}=\Sigma_i Z_i F J_i$. The *diffusional* asymmetries Q_i of the ionic diffusional flows are different for different ions, and the overall asymmetry Q_{dif} of the diffusional flows of the whole electrolyte ($J_{dif}=\Sigma_i J_i$) is still different and also different from both ionic and electrical asymmetries. This is illustrated in Fig. 8.

We calculated also the factor Q for the cones with the linear gradients of the surface charge $\rho=\rho(z)$. We found where the situation, when $\rho(z=0)=1.5$ e/nm^2, and $\rho(z=L)=0$ (this would correspond to the experimental situation with pH 8 in the left compartment, and pH 2 in the right compartment), that the effect is almost the same as when $\rho=1.5$ uniformly. On the other hand, when $\rho(0)=0$ and $\rho(L)=1.5$, the effect practically vanishes ($Q=1$). This confirms our earlier observations that practically the whole effect has its source in the narrow part of the channel near the tip.

V. FINAL REMARKS AND CONCLUSIONS

The basic equation of this paper, Eq. (2.6) has been obtained by the projection of the three-dimensional transport process in long narrow channels (confined geometry) onto equivalent one-dimensional process [12,18,19]. Such a procedure results in the factor $\pi h(z)^2$ appearing in the reduced Smoluchowski equation. The procedure is valid when the local equilibrium is established in the radial direction perpendicular to the channel's axis. The first-order correction to this result is the position-dependent correction to the diffusion coefficient: $D_i \rightarrow \tilde{D}_i(z)=D_i/f(z)$ [18,19]. This correction results from both the geometrical effects [described by the shape function $h(z)$] and the presence of the potential $\phi_i(z)$. The geometrical effect is estimated to be $f_g(z)=1+(1/2)h'(z)^2$ (cf. [19] for more details). For the majority of narrow conical pores this correction is negligible [for the short pore (0.5,1.5,6) nm $f_g=1.014$, for longer pores it is still smaller] for more "fancy geometries" it may introduce non-negligible effects. The correction f_ϕ is much more difficult to determine. The formulas given by Zwanzig [18] hold for two-dimensional cases only and require very special properties of the potential $\phi(z,r)$, which are not fulfilled by the electrostatic potential considered in the Sec. IV [26].

The presence of the effect of the asymmetrical diffusion discussed above was established experimentally for the diffusion of electrolytes in charged nanopores. So far there is no verification of the existence of such an effect in neutral conditions. This raises the following question: to what extent are one-dimensional continuous diffusional-type models sufficient for the description of transport through nano-sized channels? These issues are being widely discussed, mainly in the context of the transport phenomena in biological channels [28]. One of main objections is the well-established and rather obvious fact that the particles (ions) can pass through pores of diameter comparable to particles' sizes only in the form of single ions, which seems to exclude the possibility of the continuous (macroscopic-type) description. We want to stress the difference between single-file and our continuum description. On the other hand, the diffusion-type models seem to describe the familiar nanotransport phenomena at least in a semi quantitative way, and are able to reproduce most of their qualitative characteristics. In the following paragraph, we offer our explanation of this seemingly paradoxical situation.

The starting point of all diffusion-type description is the Smoluchowski-Nernst-Planck equation. The original Smoluchowski equation [29] describes the evolution of the (conditional) probability density for finding the Brownian (diffusing) particle moving in an external field. The Smoluchowski equation is isomorphic with the continuity equation together with the first Fick's law (of diffusion in external field). However, in this case it is the *diffusion of probability*. [It was Smoluchowski who first realized that the phenomenological laws of macroscopic diffusion can be applied to probability "because the process of diffusion is the superposition of Brownian motions of the molecules of the substance under consideration".] In other words, the Smoluchowski equation describes the (probability of finding of a) particle performing a random walk in an external field, and therefore is able to describe even the single-ion motion in nanoscale. The description in terms of the concentration of diffusing molecules is just the way of normalizing the probability density, related to the fact that (due to experimental limitations) the *measured* currents are of the order of pico-Amperes, i.e., millions of particles per second.

The effect of the asymmetrical diffusion described in this paper and in [14] may serve for the construction of *nanofilters* (or *nanosieves*), composed of thin polymer films containing many nanochannels of the same orientation. Such filters could be used for retrieving the molecules of a given component from solutions in which its concentration fluctuates strongly, and only occasionally attains high values, as the result of either varying environment, or chemical reactions.

The effect of asymmetric diffusion through the membrane has been demonstrated via numerical simulations [30]. The phenomenon occurs if the diffusing particles are spatially extended and the pores in the membrane have asymmetric structure. The authors suggest that the purely geometric effects may play a role in the potassium ion channel.

Because the anisotropy coefficient in the case of ionic diffusion seems to depend very weakly on channels' sizes when the narrow apertures do not exceed about 20 nm diameter [14], it will not be necessary to control tightly these diameters. On the other hand, the absolute magnitude of the currents, and consequently, the amount of the transported material, are roughly proportional to $\pi r_0 r_L / L$; therefore it would be expedient to use channels of the greatest possible width without diminishing the asymmetry effect. At the same time, it should be remembered that the effect virtually vanishes in wider pores [14], which is the result of short-ranged screened interactions between ions and charges on pores' walls.

To avoid misunderstandings, we re-emphasize the fact that the described effect results from the differences in diffusion rates under the same concentration gradient, and therefore cannot be used, e.g., for pumping the molecules (ions) against their concentration gradient. On the other hand, this fact does not exclude the use of the effect described recently [16,17] of carrying other particles by the diffusing ones, i.e., of the use of so-called co-diffusion.

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