Fabrication of a Synthetic Nanopore Ion Pump

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We present a synthetic nanodevice, which transports potassium ions against their concentration gradient if stimulated with external field fluctuations. It consists of a single, conical pore, created in a thin polyethylene terephthalate film. The pumping mechanism is similar to one of longitudinally oscillating deterministic ratchets.

The process of charge pumping, i.e., the transport of charge against the direction of electrochemical potential, has recently attracted considerable attention concerning the flow of electrons and ions (cf. [1–6], and references therein). The concept of a "force-free" motion in temporally and/or spatially asymmetric systems, known as ratchets (cf. [4]), has provided a new possibility of analyzing and designing the devices, which pump the charges. The intrinsic asymmetry of the ratchet system can produce a net flow, also against the electrochemical potential, even if the time average of the fluctuating macroscopic force acting on the system is zero [4,7,8]. An experimental realization of this concept for the flow of negatively charged *micrometer-sized* colloid beads through asymmetric polymer channels has been reported recently [9]. In this Letter, we present the first nanoscale miniaturization of this system. The micro-sized beads are replaced by metal ions and instead of an asymmetric polymer *microchannel* we have a single asymmetric *nanopore* produced in a polymer film. The device reported here can be used for the separation of various ions.

To produce the nanopores, we used the track etching technique based on irradiation of the substrate material, e.g., polymer foils, with energetic heavy ions, and subsequent chemical etching [10]. Circular polyethylene terephthalate (PET) foils (Hoechst, Hostaphan, RN12) of 30 mm diam and 12 μm thickness were irradiated in the center with single Au^{18+} ions of energy $2.2 \cdot 10^9$ eV at the linear accelerator UNILAC (GSI, Darmstadt). For single-ion irradiation, the ion beam is strongly defocused, and a metal mask with a circular aperture of 0.1 mm diam is placed in front of each sample. The irradiation is stopped as soon as a detector located behind the foil registers the passage of the first single ion. Since each ion produces an etchable track, the etching of a single-ion irradiated foil results in the formation of a one-pore membrane [11]. To obtain a conical shape of the pore, the foil was placed between two chambers of a conductivity cell and etched from one side, as shown in Fig. 1(a). The other chamber of the cell was filled with a stopping medium containing a neutralizing electrolyte [12]. The moment of break-

through, indicating that the etchant penetrated the foil completely, is detected as an increase of the current recorded with two Pt electrodes. To obtain nanopores, the etching has to be stopped shortly after the breakthrough. Longer etching leads to a gradual increase of the pore opening. The asymmetric shape of the pore has been visualized by scanning electron microscopy (SEM) [13]. The diameter of the large opening of the pore is approximately 500 nm (measured by SEM), whereas the aperture of the cone tip has a diameter of approximately 2 nm (as estimated from conductivity measurements). Cleavage of polymeric chains during etching produces ca. one carboxylate group per nm^2 on the inner surface of the pore [14]. At neutral pH, the pore walls are therefore negatively charged, and the pore is cation selective [13]. A high
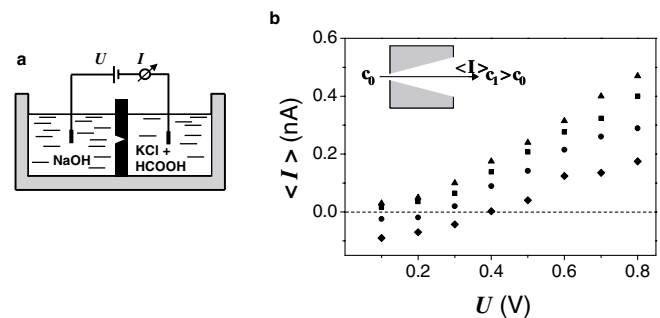

FIG. 1. (a) Scheme of the experimental setup with the conductivity cell. During etching the left compartment is filled with an etchant (NaOH). The solution of KCl and formic acid protects the other side of the membrane against etching. The volume of each compartment is approximately 1 cm^3. (b) Net ion current through a single nanofabricated conical pore. $\langle I \rangle$ is an average of the signal recorded for electric ac field of frequency 0.01 Hz, and variable amplitude. Triangles present $\langle I \rangle$ for symmetric electrolyte conditions on both sides of the membrane: 0.1 M KCl, pH 7; squares, circles, and diamonds represent the current recorded for increasing concentration difference 0.1/0.25, 0.1/0.75, and 0.01/1 M KCl, respectively, with the higher KCl concentration on the wide side of the pore. The inset shows the shape of the pore schematically, an arrow indicates the direction of the net current.

transference number for cations of ca 0.9. indicates that 90% of the measured current is due to cations flow. At pH close to the isoelectric point of the track-etched PET membrane, equal to 3.8 [15], the surface of the pore becomes neutral.

After etching, the chambers of the conductivity cell were washed with the stopping medium and distilled water, and subsequently filled with different KCl solutions. For ion current measurements, we used a salt bridge and Ag/AgCl electrodes at the distance 0.5 cm from the membrane. The dc voltage was replaced by an ac voltage (Grundig, AFG 100 Arbitrary Function Generator) of a frequency in the range from 0.1 to 0.005 Hz, and current-voltage (I-U) characteristics were measured. These frequencies are lower than the frequencies of conformation transitions of the polymer and relaxation processes. At symmetric electrolyte conditions on both sides of the membrane at pH 7, the system rectifies the current, with a preferential flow of potassium ions from the narrow towards the wide opening of the cone [Fig. 1(b)]. When increasing the electrolyte concentration on the side with wide opening, counteracting the transport asymmetry with the diffusion flow, the I-U characteristic does not change its direction. As $|I(U)|$ is not equal to $|I(-U)|$, a net current (averaged over a full period) $\langle I(t) \rangle$ is created, even though the time-averaged electric field is zero, U being the external electric field strength. Figure 1(b) shows $\langle I(t) \rangle$ for different amplitudes of the ac field. When the concentration difference becomes larger, the pumping diminishes. However, even for a 100-fold concentration difference and an amplitude of the external field larger than 400 mV, the net current is positive. An important parameter describing the performance of the nanodevice is the energy efficiency, defined as the ratio *power out/power in* [16]. For the estimation of its value we disregarded the capacitance of the system. *Power in* supplied by the ac electric field can then be calculated on the basis of the square of the effective voltage divided by the resistance of the pore equal to 1 GΩ. Having measured the output of the system in the form of an ion current, *power out* is given by the product of the square of the measured dc signal and the pore resistance. For symmetric electrolyte conditions on both sides of the membrane at $U = 500$ mV, the efficiency reached 40%. With the concentration difference 0.25 M/0.1 M KCl, the efficiency for the same ac field amplitude is ca. 30%. A 7.5-fold concentration difference diminishes the efficiency to ca. 10%. Note that a rigorous determination of the energy efficiency would require information about the probability for an ion to pass through the energy barrier starting from both sides of the pore.

We have found that the pumping phenomenon is determined by the size of the narrow opening, the surface charge of the cone, as well as the frequency of the ac field. When the narrow cone opening is ≥ 15 nm the current-voltage characteristic becomes linear, indicating

that the pore loses both its rectifying and pumping properties. At KCl solutions buffered to pH 3, the pore is neutral and does not pump either. We have also found that the system of a single conical pore pumps the potassium ions only for very low frequencies of the ac field, up to ~ 1 Hz. We presume that this is a consequence of the micrometer-scale length of the pore: the PET pore is 1000 times longer than a biochannel. Our future research will be directed towards diminishing the effective length of the pump.

We would like to note that the phenomenon of ion pumping induced by the oscillating electric field has already been reported for a system of a biological pump (Na$^+$-K$^+$-ATPase) [6], which transports the ions (K$^+$, Rb$^+$, and Na$^+$) in the direction of their increasing concentration gradient in the absence of other energy sources [16–19]. The biological pumping was found to be determined by electric field sensitive conformations of ATPases [16,19]. Although functionally similar (i.e., pumping when exposed to an oscillating external field), our system is structurally different from a biological pump. To describe the pumping performed by the synthetic conical pore, we consider our system as a ratchet. In fact, the similarities between molecular pumps and ratchets (cf. Sect. 4.6 of Ref. [8]) have already been established.

Consider a conical channel with negative charges distributed uniformly (with density ρ) on the internal walls of the cone and a positive unit charge (K$^+$ ion) located at the cone axis. As the phenomena described above occur in the electrolytic solution, we assume here that the charges interact through a screened electrostatic (Debye) potential $U(r) = r^{-1} \exp(-\lambda r)$. With these assumptions and with the geometry shown in Fig. 2, the force acting on the ion is

$$F(z) = -2\pi\rho \int_0^L dz' \frac{z - z'}{R^3(z, z')} [1 + \lambda R(z, z')] e^{-\lambda R(z, z')}$$
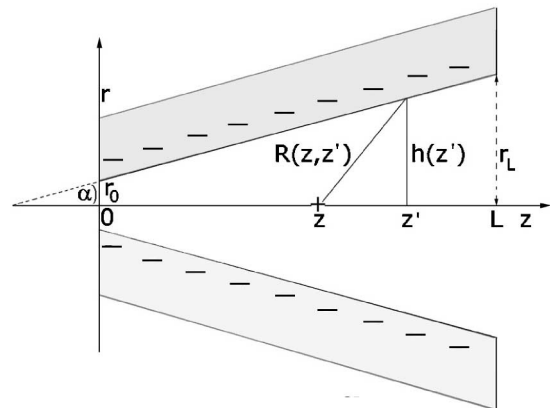$$\text{for } z > -r_0 L/(r_L - r_0), \quad \text{otherwise,} \qquad (1)$$

FIG. 2. Schematic axial cut through a channel. For the sake of clarity, the proportions differ from these of a real pore.

$$F(z) = -2\pi\rho\,[z/R_0^3(z)][1 + \lambda R_0(z)]e^{-\lambda R_0(z)} \quad (2)$$

[20], where

$$R(z, z') = \sqrt{h^2(z') + (z - z')^2}, \qquad R_0(z) = \sqrt{r_0^2 + z^2}$$

$$h(z) = r_0 + (r_L - r_0)z/L. \quad (3)$$

Figure 3 shows $F(z)$ (solid line), and the corresponding potential $V(z)$: $F = -[\partial V(z)/\partial z]$ (dashed line) for the PET pore. Note that a periodic repetition of $V(z)$ would form a typical ratchet potential.

The equation of motion of an ion driven by an oscillating periodic force reads as follows:

$$m\ddot{z} + \gamma\dot{z} = F(z) + A\sin(\Omega t + \phi). \quad (4)$$

m denotes the ion mass, ϕ is the phase, $\Omega = 2\pi/\tau$, where τ stands for the period of the ac field. The term $\gamma\dot{z}$ describes friction (damping). For $A \neq 0$, ϕ determines the initial conditions of an individual ion. For $t = 0$, the external voltage applied equals $A\sin(\phi)$. The direction in which the ion will move along the z axis in the next instant depends on the sign of this expression, and its absolute value determines the velocity of the ion.

This equation was solved numerically. In the absence of the driving field, the damping effect brings the cations to their equilibrium position z_{eq} inside the channel near the narrow end. When $\gamma = 0$, the solution of the equation $\ddot{z} = F(z)$ [$F(z)$ given by Eq. (2)] has intrinsic oscillations, and the position of the ion is not stable.

Figure 4 shows trajectories for different values of the phase ϕ. Note that the average trajectory is related to the effective current (heavy line in Fig. 4). Averaging over initial velocities $v = \dot{z}$ (with Maxwellian distribution), rather than over ϕ leads to similar results. As initial positions (for $t_0 = 0$) we took $z_0 = -15$ nm and $z_0 =$

12 015 nm, i.e., the positions outside the pore, very close to the pore's entrances. The initial velocity was taken $\dot{z}(t_0 = 0) = 0$. The results in Fig. 4 clearly show that most of the ions travel from the cone tip to the wide opening of the channel, resulting in net pumping in this direction.

In the theory of Brownian ratchets, the current is usually defined as the average velocity of the traveling particle. It seems to us that in our case the better estimation of the current is given by the sum [21] of the average velocities of particles starting near both ends of the channel:

$$I \sim \Delta\langle v\rangle = \langle v(z_0 = -\epsilon)\rangle + \langle v(z_0 = L + \epsilon)\rangle, \quad (5)$$

where $\langle\cdots\rangle$ denotes the average over ϕ and over the trajectory (up to maximal time shown in Fig. 4). Figure 5 shows that $\Delta\langle v\rangle$ decreases with increasing pore diameter, which is in accordance with our experimental data. This conclusion has also been supported by the analysis of the position of the ions, which pass the pore starting from both entrances, after a given time T (Fig. 5).
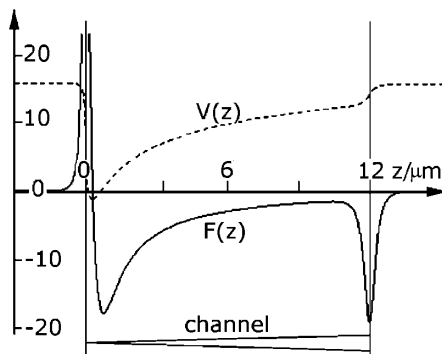

FIG. 3. The force $F(z)$ (solid line) and the corresponding potential $V(z)$ (dashed line) acting on a unitary positive charge at the position z on the axis of the conical channel, as given by Eq. (1) and (2). Vertical lines show the locations of channel openings; the scheme of the pore corresponds to the PET pore: $2r_0:2r_L:L = 2:500:12\,000$. Vertical scale in arbitrary units, charge density $\rho/m = 3.6$, Debye inverse screening length $\lambda = 0.003$ nm^{-1}.
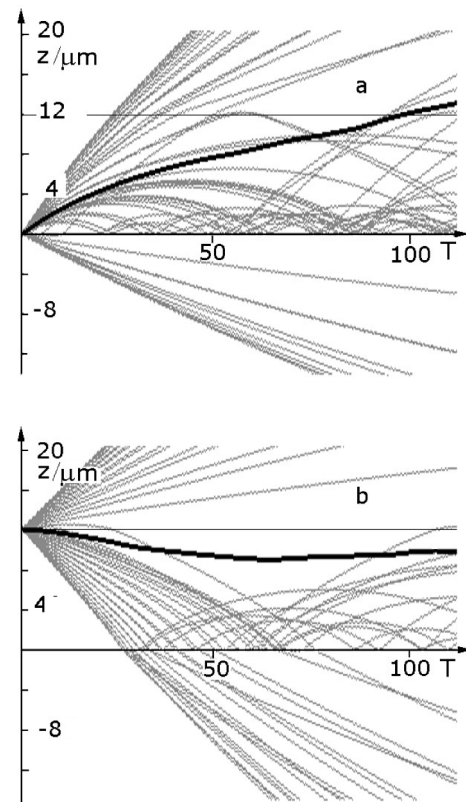

FIG. 4. Trajectories through the channel of a positive ion starting from the initial position located outside the pore (a) close to the narrow aperture, $z = -15$ nm, and (b) close to the wide opening, $z = 12\,015$ nm. Gray lines: individual trajectories for different values of the phase ϕ, heavy line: trajectory averaged over ϕ. $A/m = 70$, $\lambda = 0.003$ nm^{-1}, $\rho/m = 3.6$, $\gamma/m = 0.005$, $r_0 = 1$ nm, $r_z = 250$ nm, $L = 12$ μm, $T = \Omega t/2\pi$.
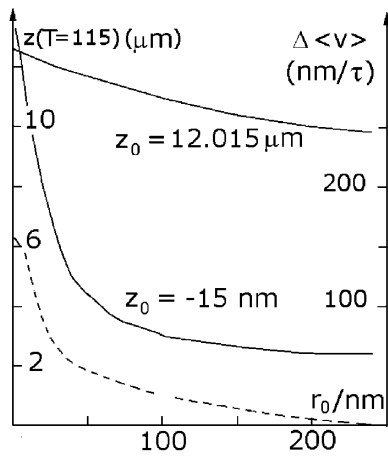
FIG. 5. Dependence of the pumping on the diameter of the narrow aperture of the channel. Solid lines: positions of the ions after the time $T = 115$ starting outside the pore, close to both pore entrances (left-hand scale). Dashed line: the net velocity, defined by Eq. (5) (right-hand scale). $T = \Omega t/2\pi$, Δv is expressed in (nm/period).

Our model also predicts the dependence of the ion pumping on the amplitude of the oscillating force A [Fig. 1(b)], and on the damping γ. The dependence of the pumping effect on the density of the charges located on the channel walls (not shown due to lack of space) has been experimentally shown for an extreme case: for pH 3, ρ becomes zero, our system cannot be considered as a ratchet any more and it stops pumping. Moreover, it is possible to fine-tune various model parameters to enhance the effects shown in Fig. 4 and 5. Especially, decreasing the damping effect should lead to an enhancement of pumping. This may be checked experimentally by examining the pumping phenomenon at solutions of different viscosities and/or ions of different masses. This would also provide a possibility of separating ions pumped with different pumping efficiencies.

In this Letter we have shown that a synthetic asymmetric nanopore acts as an ion nanopump, transporting potassium ions against their concentration gradient. Moreover, it has been demonstrated that the ion-pumping mechanism is similar to that of longitudinally oscillating ratchets: the presence of a periodic driving field in Eq. (4) is equivalent to periodic shifting ("rocking") of the potential $V(z)$ (Fig. 3) along the z axis. The deterministic motion and the simple type of asymmetry of the potential (resulting directly from simple electrostatics) are sufficient to explain qualitatively the observed behavior. We regard our work as useful for the future study and design of asymmetric nanodevices. We were able to show that every sufficiently small asymmetric and charged nano-pore will rectify the ion current and will exhibit pumping properties.

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[20] For $z < r_0$, the ion does not see the inside of the channel, therefore it interacts only with negative charges at the left (narrow) aperture of the channel—we assume that the channel walls are screening the charges.
[21] Note that the signs of average velocities are opposite, which can be inferred from the shapes of trajectories shown in Fig. 4.