# Ion-Current Rectification in Nanopores and Nanotubes with Broken Symmetry**

By *Zuzanna S. Siwy**

This article focuses on ion transport through nanoporous systems with special emphasis on rectification phenomena. The effect of ion-current rectification is observed as asymmetric current–voltage (I–V) curves, with the current recorded for one voltage polarity higher than the current recorded for the same absolute value of voltage of opposite polarity. This diode-like I–V curve indicates that there is a preferential direction for ion flow. Experimental evidence that ion-current rectification is inherent to asymmetric, e.g., tapered, nanoporous systems with excess surface charge is provided and discussed. The fabrication and operation of asymmetric polymer nanopores, gold nanotubes, glass nanocapillaries, and silicon nanopores are presented. The possibility of tuning the direction and extent of rectification is discussed in detail. Theoretical models that have been developed to explain the ion-current rectification effect are also presented.
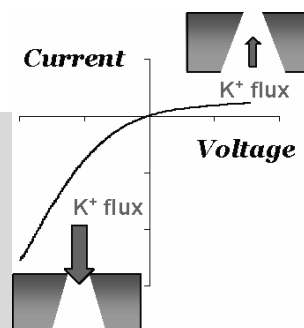
1. Introduction

Transport through nanopores has attracted broad interest from scientists in various fields. This interest stems from the crucial role that transport phenomena through biological channels and pores play in many physiological processes in living organisms.[1,2] Nanopores have also started to play a major role in contemporary biotechnology, because many separation and sensing processes require pores with nanometer-sized openings.[3,4] The properties of nanopores are, however, not well understood yet. As predicted by Richard Feynmann, when objects have dimensions on the nanometer scale, one should be prepared to observe new effects that cannot be explained by classical physics.[5] Nanopores have indeed surprised researchers with transport properties that have not been recorded in their microscopic counterparts.

In this article I want to discuss one particular transport effect that has been observed in asymmetrically shaped, e.g., tapered, cone-shaped, nanopores and nanocapillaries, which is due to their nanometer-sized openings. It has been found that these asymmetric nanopores and nanocapillaries rectify ion current, although the concentration and pH of the electrolyte in contact with the two pore openings are the same. The rectification is observed as asymmetric current–voltage (I–V) curves, with the currents recorded for one voltage polarity higher than the currents recorded for the same absolute value of voltage but of opposite polarity. Such a diode-like I–V curve indicates that there is a preferential direction for ion flow.

There are several nanoporous systems that have been shown to exhibit this rectifying behavior. The first class comprises biological channels and pores present in lipid cell membranes.[1,6] Another rectifying nanoporous system consists of artificial nanopores inserted into a lipid bilayer.[7,8] Our group and others have shown that entirely synthetic systems can also rectify ion current. We have prepared nanopores in polymer films[9–11] as well as gold nanotubes[12] that are ion selective and rectify the ion current if they are conical in shape and have excess surface charge. Wei et al. have shown that glass capillaries can exhibit similar transport properties.[13] Nanopores in silicon nitride prepared by ion sputtering are also asymmetric in shape and their I–V curves are similar to those found for the polymer pores, metal tubes, and glass capillaries.[14]

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In this article, I focus on abiotic nanopores and revisit mechanisms suggested to explain the asymmetric *I–V* curves. The sections present the fabrication of nanoporous systems together with experimental and theoretical examinations of their transport properties. I also suggest experiments that could help elucidate the physical phenomena underlying ion transport in nanopores.

Microfluidic systems, which rectify flow of microparticles such as colloids and polystyrene beads, have been described, e.g., by Marquet et al. and Kettner et al.[15,16] and will not be considered in this article.

2. Synthetic Systems Rectifying Ion Current

2.1. Asymmetric Nanopores in Polymer Films

Single nanopores in polymer films have been prepared by the track-etching technique, which is based on the irradiation of a material with swift heavy ions and subsequent chemical etching of the latent tracks.[17] What sets apart the track-etching technique from conventional lithographic methods is the single-particle recording. It involves one swift heavy ion, which penetrates the foil and produces one latent track. After chemical developing, this one latent track results in the formation of one pore. Counting the number of ions that penetrated the foil makes it possible to design membranes with a preassigned number of pores and pore densities down to one pore per square centimeter. We worked with 12 μm thick poly(ethylene terephthalate) (PET; Hostaphan RN12, Hoechst) and polyimide (Kapton 50HN, DuPont) foils. The polymer films were irradiated with single heavy ions of energy of 11.4 MeV per nucleon at the linear accelerator UNILAC at the Gesellschaft für Schwerionenforschung (GSI) Darmstadt, Germany.[18] Chemical etching of the single-ion irradiated foils leads to the formation of single-pore membranes. Membranes that have only one pore present an optimal system for studying transport properties on the nanoscale, because one can directly observe the behavior of just one pore without having to average the effects of a whole ensemble of pores.

The track-etching technique allows very easy control over the shape of the pores.[17] The track of a heavy ion is cylindrical in shape, and the geometry of the pores is controlled by the etching conditions. Details of chemical etching procedures, which lead to cylindrical, conical, and double-conical nanopores are given in the Experimental section.

Figure 1 shows scanning electron microscopy (SEM) images of the large openings of conical nanopores, which we prepared in PET and Kapton foils at the GSI. The small openings are below SEM resolution.
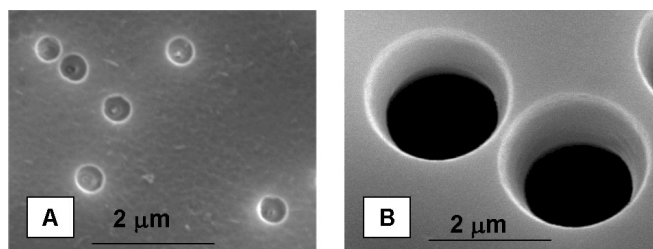

Figure 1. SEM images of the etched side of PET (A) and Kapton (B) foils, showing the large opening of the conical pores. The samples were irradiated at a fluence of 10^7 ions cm^{-2} with Bi (PET) and U (Kapton) ions, and subsequently etched anisotropically from one side. The small openings are below the SEM resolution. Reprinted from [11], with permission. Copyright 2003, Elsevier.

The cylindrical and asymmetric shape of the nanopores in PET and Kapton has been confirmed by imaging cross-sections of the membranes as well as by preparing metal replicas of the nanopores.[19] In the latter method, one uses the fact that electroless deposition and electrodeposition of a metal inside a membrane leads to the formation of wires that assume the shape of the pores.[20–22]

Chemical etching of both polymeric materials results in the formation of carboxylate groups on the pore walls and on the surface of the membranes. The average density of carboxylate groups in these two materials has been estimated to be ~ 1.5 groups nm^{-2}.[23] A direct consequence of the presence of carboxylate groups is the possibility of regulating the surface charge by immersing the membranes in electrolyte solutions buffered to various pH values. For example, at neutral and basic conditions, the carboxylate groups are deprotonated and the net surface charge is negative. Lowering the pH to values close to the isoelectric point of the track-etched surface neutralizes the surface charge.[11]

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2.1.1. Current–Voltage Curves of Conical Polymer Nanopores

Figure 2A shows *I–V* curves of a single PET nanopore, recorded under symmetric electrolyte conditions, for three concentrations of KCl.[9–11] A positive voltage in our electrode configuration indicates that the anode is placed on the side of the membrane with the large opening of the pore. At negative volt-
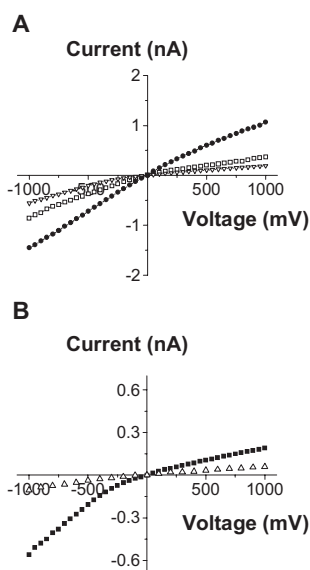

Figure 2. Transport properties of a single conical pore in a PET membrane. A) *I–V* characteristics recorded under symmetric electrolyte conditions at pH 8 and 3 M KCl (●), 1 M KCl (□), and 0.1 M KCl (▽); B) *I–V* curves of a single conically shaped nanopore (the same nanopore as in (A)) recorded with 0.1 M KCl buffered to pH 8 (■) and pH 3 (△). The diameters of the pore openings are ∼ 3 nm and 0.6 μm, respectively.

ages the cathode is on the side with the large pore opening. If we define the degree of rectification as a ratio of absolute values of currents recorded at a given negative voltage and at the same absolute value of a positive voltage, one can see that the rectification becomes stronger at lower KCl concentrations.[11]

The rectification properties have also been found to be dependent on the electrolyte pH. At basic and neutral pH values, in which the polymer membranes have excess negative surface charge, the pores rectify the current. At pH 3, the net surface charge is zero and conical nanopores exhibit linear *I–V* curves (Fig. 2B).

A diode-like *I–V* curve indicates that there is a preferential direction for ion flow. PET and Kapton nanopores have been found to be cation selective with transference numbers for cations as high as 0.9.[11] This indicates that 90 % of the ion-current signal is due to potassium ions. Considering the convention of the applied voltage, we have determined the preferential direction of cation flow is from the small opening towards the large opening of the conical pore.

We have also checked that the rectification property indeed results from the nanometer dimensions of the pore openings. We found that the rectifying effect occurs only in pores with the diameter of the narrow opening smaller than ∼ 20 nm.

2.1.2. Current–Voltage Curves of Double-Conical Nanopores

Figure 3 shows *I–V* curves recorded for a double-conical nanopore in PET with a restricted opening of 2 nm inside the pore, prepared at the GSI. The thickness of the membrane was 12 μm, and the length of the short cone is ∼ 20 nm. Similar to the behavior of tapered-cone pores, the effect of ion-current
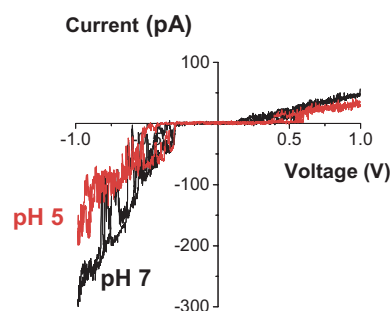

Figure 3. *I–V* curves of a double-conical nanopore in PET foil, recorded in 0.1 M KCl and at pH 5 and 7. The narrowest part of the nanopore is ∼ 2 nm in diameter.

rectification has been observed with double-conical nanopores as well. However, the *I–V* curves of these double-conical pores showed a new feature, namely the existence of a voltage range at which the pore was not conductive. Additionally, strong ion-current fluctuations have been observed;[24,25] therefore, the *I–V* curves of the double-conical nanopores must be analyzed using a high time resolution of 250 Hz. In Figure 3, two voltage sweeps are shown for 0.1 M KCl at pH 7 and at pH 5. For lower pH, at which the excess surface charge of the pore is smaller, the range of zero current is wider.

The physical basis of this effect is not fully understood yet. We presume that this zero-conductivity region is related to the presence of so-called dangling ends of the polymer chains, which are created on pore walls during the fabrication process, i.e., during irradiation with heavy ions and etching with sodium hydroxide.[11,23,26] It is not known how long the dangling ends are, but even if they consist of just one building block of PET, their length would be ∼ 1 nm. The polymer ends have carboxylate groups; therefore, they can respond to electric fields,[9] changing the effective diameter of the pore and even closing it. Pore blocking occurs in pores with double-conical geometry; because the narrowest part of the pore is located inside, it can be occluded by dangling ends from both sides.

The effect of the zero-conductivity region is not observed with double-conical pores in Kapton. The irradiated and etched Kapton foil is known to be much smoother than the PET foil.[11] Additionally, the chemical structure of Kapton is based on a planar sequence of aromatic groups, rendering the material rigid. It is therefore not expected that scissioned polymeric chains perform any significant motion.

2.2. Cylindrical Polymer Nanopores with Asymmetric Surface-Charge Distribution

The observation that conical nanopores rectify ion current only when the pore walls possess an excess surface charge has led us to further experiments with cylindrical nanopores. We have recorded *I–V* curves from a single cylindrical nanopore whose surfaces were in contact with KCl solutions of the same concentration but buffered to different pH values.[27] One side of the membrane was in contact with 0.1 M KCl at pH 9, which made the surface of the membrane and the pore walls close to the entrance negatively charged. The other side of the membrane was in contact with 0.1 M KCl, pH 3—that surface was deprived of any excess surface charge. The *I–V* characteristics of this pore are shown in Figure 4. Positive voltage indicates that the anode was on the side of the membrane with the pH 3 KCl solution. The shape of the *I–V* curve is clearly asymmetric
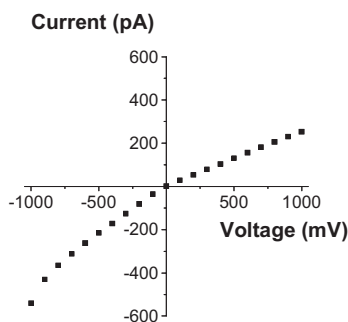

Figure 4. *I–V* curve of a single cylindrical pore in PET with diameter 10 nm and length 12 μm. The concentration of KCl on both sides of the membrane was 0.1 M, buffered to pH 9 on one side and to pH 3 on the other.

and suggests that the side of the membrane in contact with basic KCl solution could be treated equivalently to the small opening of a conical pore. The side of the membrane in contact with the acidic solution would then correspond to the wide entrance of a conical nanopore.

It is important to note that a similar behavior of ion-current rectification has been observed with a geometrically symmetric protein nanopore carrying charges of opposite signs at the two entrances.[7] Our measurements suggest that it is indeed the electrostatic asymmetry at the two openings of a nanopore that is responsible for the rectification behavior. The occurrence of rectification seems therefore to be independent of the membrane material as well as of the specific chemistry of charges on the nanopores.

2.3. Composite Polymer Membranes with Cylindrical Pores

A many-pore system that exhibits ion-current rectifying properties has also been designed. Dietrich Woermann's system consists of two PET membranes with different pore diame-

ters and, consequently, transference numbers for cations.[28] The membranes used to prepare this system were 10 μm thick, had a pore density of ~2×10⁸ pores cm⁻², and diameters of ~100 nm. The membranes were obtained by the track-etching technique. The effective diameters of the pores in one membrane were diminished by filling them with polyelectrolyte gel, which carried SO_3^- groups. Woermann did not characterize the effective size of these modified nanopores quantitatively; however, their nanometer dimensions were confirmed by measuring their high transference number for cations. The other membrane with 100 nm pores was not modified, and this membrane has been shown to be non-selective for either cations or anions. The two membranes were brought into contact using water and clamped together between two chambers of a conductivity cell filled with 0.05 M NaCl.[28] This composite system rectifies the ion current with the preferential direction of cation flow from the modified membrane towards the non-selective membrane, that is, in a similar way to that shown for conical nanopores.

2.4. Conical Gold Nanotubes

Previous experiments with polymer nanopores have shown that the presence of excess surface charge on the pore walls is the crucial parameter that controls ion-current rectification. Chemical etching of the tracked surface of PET and Kapton results in formation of carboxylate groups; however, the chemistry of the etched polymer surfaces is more complicated. Etching PET in NaOH causes formation of both carboxylate and alcohol groups. Additionally, as discussed in Section 2.1.2., cut and etched polymer chains form so-called dangling ends, which can move freely when in solution. The existence of dangling ends, which respond to external electric fields, might also induce another mechanism of ion-current rectification, namely, a change in the effective pore opening induced by the electric field.[9]

In order to examine the mechanism of ion-current rectification, we felt that it was important to simplify the surface chemistry of the pore walls, which we decided to perform by electroless plating of gold onto the polymer surfaces. The process of electroless plating with gold consists of three steps:[29,30] i) sensitization of the pore surface with tin; ii) subsequent reduction of silver; and iii) reduction of gold with formaldehyde as a reducing agent. In the laboratory of Prof. Charles R. Martin at the University of Florida, Gainesville, we plated conical nanopores in PET with gold, thereby reducing the diameter of the small opening from ~20 nm to 5–10 nm.[12]

The gold tubes alone have allowed us to check the importance of surface charge in the ion-current rectification effect. It is known that Cl⁻ ions strongly adsorb to Au surfaces and that the electrosorption valence is –1. When a gold tube is immersed in KCl, its net surface charge is therefore negative.[12,29,30] If KF is used as an electrolyte, the net surface charge is zero, because F⁻ ions do not adsorb to Au surfaces.
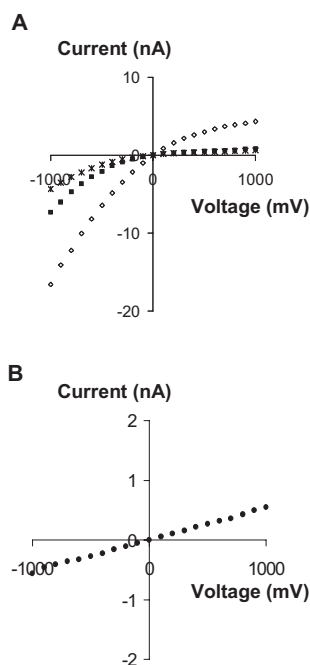
A

Current (nA)

B

Current (nA)

Figure 5. Transport properties of a single conical gold nanotube with opening diameters of 10 nm and 0.6 µm [12]. A) *I–V* characteristics of a single gold tube under symmetric electrolyte conditions: (◇) 1 M KCl, pH 6.6; (■) 0.1 M KCl, pH 6.0; (×) 0.1 M KCl, pH 3.0. B) *I–V* characteristic of a single gold tube recorded in 0.1 M KF, pH 6.6.

A

Current (nA)

B

Current (nA)

Figure 6. *I–V* characteristics of single Au tubes modified with thiols. The tubes have opening diameters of 10 nm and 0.6 µm. A) Characteristic of a single Au nanotube modified with 2-mercaptopropionic acid, measured in 0.1 M KF, pH 6.6 (□) and pH 3.5 (●); B) *I–V* characteristics of a single Au tube modified with mercaptoethylammonium, recorded in 0.1 M KF, pH 6.6. Reprinted with permission from [12]. Copyright 2004, American Chemical Society.

Figure 5A presents *I–V* curves recorded for a single gold nanotube in KCl solutions of various concentrations and pH.[12] The rectification again depends on the KCl concentration, however the tube rectifies at pH 3, at which value an Au surface is still negative. The latter result indicates that the transport properties of the nanotubes are indeed governed by the gold layer.

The transport characteristics of gold nanotubes in KF solutions are significantly different. The net surface charge is zero and Au tubes do not exhibit rectification (Fig. 5B).

Covering polymer membranes with gold gave us the freedom to perform additional chemical modifications. We used the effect of spontaneous chemisorption of thiols to a gold surface.[30,31] To further investigate the dependence of the ion-current rectification effect on the excess surface charge of gold tubes, we modified the tubes with short-chain thiols, which carry both negative and positive charge.[12] Figure 6A shows *I–V* curves recorded in KF of neutral and acidic pH (adjusted with sulfuric acid) for a single gold nanotube modified with 2-mercaptopropionic acid. At neutral pH, the surface has an excess negative charge due to deprotonized carboxylate groups and the tube rectifies the current. Lowering the pH results in protonation of carboxylate groups and the gold tube exhibits a linear *I–V* relationship. Modification with mercaptoethylamine results in a positively charged Au tube, which rectifies ion current in the opposite direction to tubes with negatively charged surfaces (Fig. 6B).
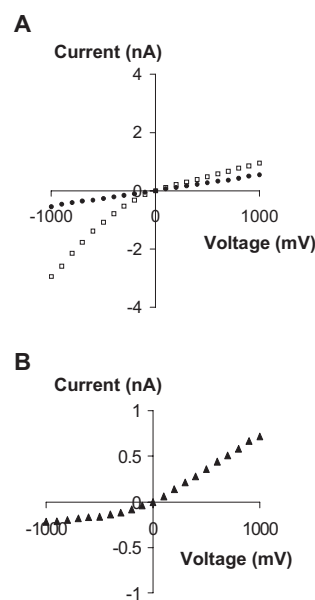
2.5. Glass Nanopipettes Rectifying Ion Current

The nanopores presented in the previous sections had a limiting diameter less than 20 nm and rectified ion current at high KCl concentrations. Another abiotic system that has been shown to exhibit asymmetric *I–V* curves at much lower KCl concentrations consists of glass nanopipettes with openings of between 20 and 200 nm. Wei et al. pulled the nanopipettes from quartz tubes:[13] the conditions of pulling the pipettes regulate the final opening of the glass capillaries. These nanopipettes have been routinely applied in patch-clamp studies and scanning ion conductance microscopy.[1,32] It is important to indicate the convention of applying voltage.[13] The sign of the voltage was established using the same convention as for the polymer nanopores, i.e., positive voltages indicate an anode on the base of the pipette, negative voltages indicate an anode at the tip of the pipette.

The character of *I–V* curves for these nanocapillaries has been found to depend very strongly on the KCl concentration. For KCl concentrations greater than and equal to 0.1 M, the capillaries behaved as ohmic resistors. For lower concentrations, however, clearly nonlinear *I–V* curves were observed (Fig. 7): ion currents recorded for positive voltages were significantly smaller than currents recorded for negative voltages.

Similar to the polymer nanopores, the quartz pipettes also have surface charge, regulated by the pH of the electrolyte with which the pipettes are in contact. Consequently, the *I–V* curves of the quartz pipettes have ion-current characteristics
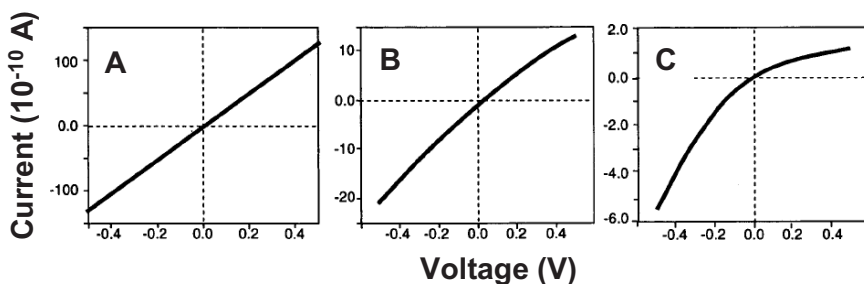
Figure 7. *I–V* curves of a nanocapillary of radius ~ 20 nm at A) 1 M KCl, B) 0.1 M KCl, and C) 0.01 M KCl. Measurements were performed at a scan rate of 20 mV s⁻¹. Reprinted with permission from [13]. Copyright 1997, American Chemical Society.

dependent on the electrolyte pH. At pH 3, which is close to the isoelectric point of the quartz surface, the *I–V* curves become linear.[13]

2.6. Asymmetric Nanopores in Si₃N₄

Another interesting single-nanopore system has been created in silicon nitride by the Harvard Nanopore Group with Profs. Daniel Branton, Jene Golovchenko,[14,33] and Michael Aziz.[33] An argon beam of 3 keV energy was used in the preparation process together with a setup that implements a feedback-controlled ion-sputtering system. It was found that irradiation of silicon nitride with argon at room temperature causes a lateral flow of the material. A pore of diameter ~ 0.1 μm was the starting point of the fabrication process. This pore was subsequently exposed to the argon beam at room temperature, causing a gradual closing of the pore to nanometer dimensions. The diameter of the pore was controlled by monitoring ions transmitted through the opening. Single pores with diameters as small as 1.8 nm were obtained.[14,33] As a result of the preparation process, the pores are asymmetric in shape, i.e., the diameters on both sides of the membrane are different. This system has also been shown to rectify the ion current in a pH- and electrolyte-concentration-dependent manner.[14]

2.7. Conical Gold Nanotubes with Diameters Larger Than 30 nm with Chemisorbed Single-Stranded DNA

The nanoporous systems described in the previous sections rectified the ion current when the pore diameter was comparable to the thickness of the electrical double layer. At the University of Florida in the laboratory of Prof. C. R. Martin, we prepared conical gold nanotubes with diameters larger than 30 nm, which rectified current at a relatively high KCl concentration of 0.1 M. The tubes were prepared as described above by electroless plating of conical nanopores in a polymer membrane. The tubes' surfaces were subsequently modified with single-stranded DNA (ssDNA) that possessed a thiol group attached via an alkyl chain.[34] We used 15-, 30-, 45-, and 60-mer DNA oligomers. Before the DNA modification, the tubes exhibited linear *I–V* curves; however, with DNA at-

tached to the tubes' walls, the tubes rectified the current. A stronger rectification was observed with longer DNA chains.[34]

3. Models of Ion-Current Rectification Observed with Nanoporous Systems

Several mechanisms have been suggested to explain the ion-current rectification effect observed in synthetic nanoporous systems. We present four approaches developed to explain the behavior of the nanopores and nanotubes described in Sections 2.1.–2.5. as well as the model that has been suggested for the system of DNA–Au nanotubes shown in Section 2.7.

3.1. Models for Ion-Current Rectification in Nanopores with Diameters Comparable to the Thickness of the Electrical Double Layer

3.1.1. Electrostatic Model Based on the Concepts of a Rocking Ratchet and an Electrostatic Trap

The ratchet model has been formed on the basis of experimental observations of conditions at which the nanoporous systems rectify ion current. Let us summarize the experimental facts: the rectification is observed with asymmetric nanopores if i) the opening diameter of the tip is comparable to the thickness of the electrical double layer, ii) there is an excess surface charge on the pore walls, and iii) the interactions of ions with the pore walls, induced either by the size of the openings or surface charge, are asymmetric at the two entrances of the pores. It has also been shown that the sign of the surface charge determines the direction of ion-current rectification (see Fig. 6): rendering the surface charge positive or negative made the nanotubes rectify in opposite directions. This observation provided evidence that the rectification effect originated from electrostatic interactions between the ions passing through the nanopore and the pore walls. Interactions of ions with the pore walls are also the basis of pore selectivity, because, e.g., excess negative surface charge allows mainly cations to enter the pore, while anions are rejected.[29,35]

In order to model the profile of an electrostatic potential inside a conical pore, we have considered a cation moving along

the pore axis and interacting with negative charges on the pore wall.[36–40] We assumed Debye-type interactions between ions. Note that interactions of passing ions with the surface charges of the pore occur only if the pore is sufficiently narrow, with a diameter comparable to the thickness of the electrical double layer. This is caused by the short-range character of electrostatic interactions in an electrolyte solution, resulting from a strong screening induced by the presence of other ions.[35] To calculate the electrical potential of a cation at a given position z at the pore axis, we used the following formula[36–38]

$$V(z) = -2\pi\rho \int_0^L dz' h(z') e^{-\lambda R(z,z')} / R(z,z') \tag{1}$$

where ρ is the surface-charge density at the pore wall, R is the distance between the cation on the pore axis and negative charges on the pore walls (see Fig. 8A), L stands for length of the pore, $h(z')$ is the radius of the pore at point z' (Fig. 8A) and λ indicates the inverse screening length related to the thickness of the electrical double layer. The integration indicates that the potential of a cation at a given position z results from interac-
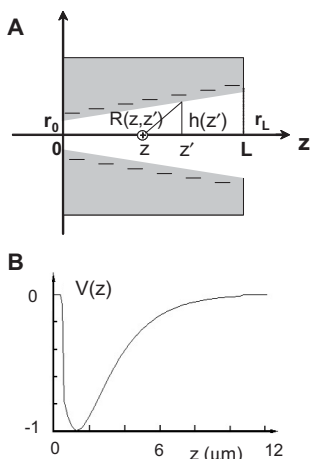

Figure 8. A) Scheme of an axial cut of a conical pore (not in proportion); B) profile of the electrical potential, $V(z)$, inside a tapered-cone pore, calculated from Eq. 1. Reprinted with permission from [37]. Copyright 2003, American Association of Physics Teachers.

tions with carboxylate groups on the entire surface of the pore. The problem has been treated in two-dimensional and three-dimensional space.[37] For conical nanopores, without any voltage applied from the outside, the shape of the internal potential has been shown to be asymmetric and toothlike, reminiscent of the shape of a ratchet potential (see Fig. 8B).[36,37,41–44] A similar character for the internal potential has been found for cylindrical pores with asymmetric surface-charge distribution.[27] The potential minimum is situated at the tip of a conical nanopore. In the case of the cylindrical nanopores (Sec. 2.2.) this potential minimum is located at the membrane side with negative charge. Assuming a simple superposition of the externally applied voltage with the internal electric field, one can obtain the resultant potential profiles for the two polarities of the applied voltage. Figure 9 shows that for positive voltages, a trap of electrostatic
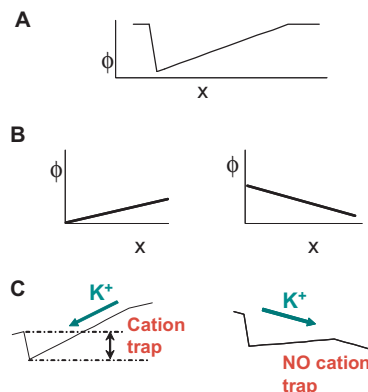

Figure 9. Ratchet model for ion-current rectification in a conical nanopore with excess negative surface charge on the pore walls. A) Schematic representation of the electric potential for cations inside a nanopore without external voltage; B) solution voltage drop for cations, left: positive voltage, right: negative voltage; C) profile of the electric potential resulting from superposition of the profile shown in (A) with the two profiles from (B). Applying positive voltages results in formation of an electrostatic trap and consequently lower ion current. Reprinted with permission from supplementary material to [12]. Copyright 2004, American Chemical Society.

origin is created, causing an "off" state of the pore, i.e., low conductivity. Applying voltage of the opposite polarity does not lead to formation of the trap and the ion currents are higher.

A quantitative model for the *I–V* curves has also been developed, with the following relation for ion flux[37]

$$J = D \frac{c_0 e^{\beta W(0)} - c_L e^{\beta W(L)}}{\int_0^L dz \, e^{\beta[W(z)+V(z)]}} \tag{2}$$

where c_0 and c_L are KCl concentrations on either side of the membrane, D stands for the diffusion coefficient of ions inside the pore, $W(z)$ is the potential inside the nanopore at position z, originating from the applied voltage, and β is the ratio of ion mobility and the diffusion constant.

3.1.2. Model of Ion-Current Rectification Based on the Electrochemical Properties of the Tip of a Conical Nanopore

Another model of ion-current rectification has been developed by Dietrich Woermann and applied to the data of an ion current passing through single conical pores in PET with diameters comparable to the thickness of the electrical double layer.[45,46] Woermann divided the pore into three regions: the tip at the small opening of the pore, a transition zone, and the bulk region at the base of the cone. The regions differ in profiles of ion concentrations, which in turn result from excess surface charge on the pore walls. At the tip region, the influence of the surface charge on the ion concentrations is the strongest. This zone is also characterized by a very high (approaching one) transference number for cations. Therefore, this part of the pore rejects anions, in our case chloride ions. For the bulk region of the pore, the model assumes that the concentrations of cations and anions are the same as in the bulk solution and the transference numbers for cations (t^+) and anions (t^-) are equal. The situ-

ation at the transition zone is more complex because its characteristics depend on the polarity of the applied voltage.

With the cathode at the large opening of the pore, the ion current, treated as stationary, transfers mainly K$^+$ through the pore. As a result, the transition zone changes its t^+ to a higher value, which in turn has to result in lowering t^-. Because electroneutrality must be fulfilled, Woermann claimed that the cation current from the tip-to-base direction increases the concentration of KCl in the lumen and close to the tip of the pore. When a voltage of the opposite polarity is applied, the cations are transferred from the wide opening of the pore towards the tip, in other words from the region of low t^+ to the region of higher t^+. The transition zone decreases its t^+ compared to the situation with the opposite voltage polarity. In this case, according to Woermann, the mean KCl concentration in the pore decreases and consequently a lower value of ion current is measured.

The following semi-quantitative formula for the *I–V* relationship has been derived to describe the transport properties of a conical nanopore

$$U = I\left\{\left[\frac{1}{L_{EE}^{(a)}} + \frac{1}{L_{EE}^{(b)}}\right] + \left[\frac{\left(t_s^{(a)} - t_s^{(b)}\right)^2}{\langle c_s \rangle \left(\omega_s^{(a)} - \omega_s^{(b)}\right)} \cdot \frac{1}{F^2}\right]\right\} \qquad (3)$$

where U is the applied voltage, $L_{EE}^{(a)(b)}$ stands for the electrical conductivity at two parts of the pore, marked as a (tip) and b (base), t_s is the transference number in the tip and bulk part of the nanopore, ω_s indicates the phenomenological diffusive-transport coefficient of the solute, s, and c is the molar concentration of electrolyte.

The above formula is obtained assuming that the driving force acting on the system is small, so that the system can be treated as stationary and linear.

The *I–V* curve predicted by Equation 3 consists of two straight lines with different slopes for positive and negative voltages. Qualitatively, the model indeed predicts the ion-current rectification observed with narrow pores.

3.1.3. Quantitative Description of Ion Current Through a Nanopore by the Poisson and Nernst–Planck Equations

A quantitative description of ion currents through a single conical nanopore has been developed by Cervera et al.[47] They based their model on the Poisson, Nernst–Planck, and continuity equations

$$J_i = -D_i(\nabla c_i + z_i c_i \nabla \varphi), \quad i = +,- \qquad (4)$$

$$\nabla^2 \phi = \frac{F^2}{\varepsilon RT}(c_- - c_+) \qquad (5)$$

$$\nabla J_i = 0, \quad i = +,- \qquad (6)$$

where J_i, D_i, and z_i are the ion flux, the diffusion coefficient, and the charge number of ionic species i, and ε is the dielectric permittivity of the solution inside the pore.

The equations have been solved in spherical coordinates with the origin at the cone apex. Because of a small opening angle of the conical nanopores, ~1.5°, the ion fluxes were assumed to have only a radial component. The profiles of ion concentrations are average values at a cross section of a conical nanopore of a given radius. The ion concentrations and potentials at the entrances of the nanopore, setting boundary conditions for solving the equations, were determined from the Donnan equilibrium relations.

The model has been applied to polymer nanopores and gold nanotubes with diameters of the small opening of ~10 nm.

The models of Cervera et al.[47] and Woermann[45,46] give a similar physical interpretation for ion-current rectification, i.e., the two branches of an *I–V* curve of a conical nanopore correspond to different concentrations of KCl inside the pore, and different selectivity of the pore towards cations. Figure 10 shows profiles of the electric potential and ion concentrations

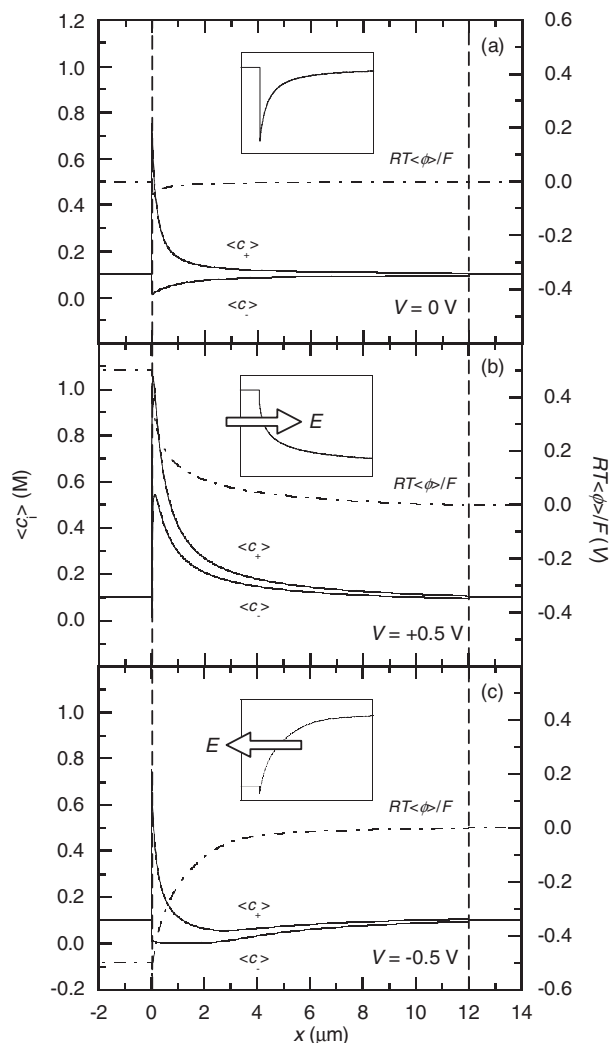**Figure 10.** Average ion concentrations and electrical-potential profiles at A) $V = 0$ V; B) $V = 0.5$ V (high-conductivity state); C) $V = -0.5$ V (low-conductivity state). The insets show magnifications of the tip regions. The polarity of the external voltage was adjusted in a manner opposite to the convention used in the measurements shown in Figs. 2,3,5,6. Reprinted with permission from [47]. Copyright 2005, EDP Sciences.

at no external voltage applied and at two polarities of the external voltage for a gold nanotube with negative excess surface charge. The polarity of external voltage was adjusted opposite to the convention used in the measurements shown in previous sections: positive voltage corresponds to the anode placed at the small opening of the nanotube. The ion-concentration profiles inside the nanotube clearly indicate that at positive voltages the concentrations of K+ and Cl– are higher than at negative voltages. Additionally, at positive voltages the pore distinguishes very weakly between cations and anions. This observation has not yet been checked experimentally.

It is important to note that the profile of the electrostatic potential has indeed been confirmed to have the shape of a ratchet potential (Fig. 10A). The remarkable outcome of the analysis is that with the single adjustable parameter of surface-charge density, the authors have been able to adjust the major properties of these ion-current-rectifying systems. They described in a quantitative way the ohmic behavior of nanopores and nanotubes without excess surface charge as well as a reversal of the direction of rectification when the excess surface charge changed sign. The values of other parameters such as diffusion coefficients were taken from a bulk solution of infinite dilution. This assumption is certainly not valid for very narrow pores with diameters close to the thickness of the electrical double layer. Nevertheless, this quantitative model helps one to grasp the basic physics of the rectification effect, confirming the decisive role of electrostatic interactions in transport phenomena through nanopores.

3.1.4. Model of Ion-Current Rectification Developed for Glass Micropipettes

Ion-current rectification observed in glass nanocapillaries has been explained by Wei et al. on the basis of ion selectivity at the tip region and structural asymmetry of the nanopipettes.[13] These two conditions—permselectivity and structural asymmetry—have been found to be prerequisite for ion-current rectification. The model can be applied to capillaries studied in a situation where their opening diameter is comparable to the thickness of the electrical double layer.

Wei et al. approximated a capillary using a short cylindrical segment connected to two cones of different curvature radii β_1 and β_2.[13] The two openings of the cylindrical part of the capillary also differ in access radii. The asymmetry in the I–V curves, according to the model, comes from differences in limiting transport rates of potassium ions flowing into and out of the capillary.

The formula for ion current at the two polarities of applied voltage was derived from the Nernst–Planck equation; convective transport has not been taken into account.[13]

3.2. Rectification Based on the Existence of an Electromechanical Gate

Conical gold nanotubes, prepared as described in Section 2.7., with openings larger than 20 nm, were the starting

point for designing a system into which ssDNA could be introduced. Because of the relatively large diameter of the opening and high KCl concentrations used in the experiments, these tubes could not rectify ion current according to the electrostatic models discussed in the previous section. As shown by Harrell et al.,[34] DNA oligomers, chemisorbed on the pore walls and surface of the membrane, play the role of an electromechanical gate that responds to the applied voltage.[6] DNA chains are negatively charged therefore they will move in the electric field, changing the effective diameter of the nanopore. Figure 11 presents the principles of operation of this type of rectifier schematically. Placing an anode close to the small opening of the pore results in formation of an "on" state of the
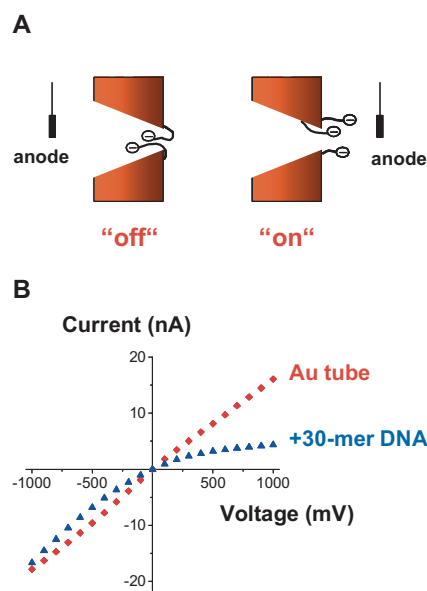

Figure 11. Ion-current rectifier with an electromechanical gate. A) Schematic representation of how the rectifier operates; B) I–V characteristics of a single conical gold tube before and after modification with thiolated ssDNA. The small opening of the gold tube is ~40 nm, the large opening 5 μm. Reprinted with permission from [34]. Copyright 2004, American Chemical Society.

pore, with an opening that is larger than in the case with the anode placed on the large side of the pore when an "off" state of the pore is realized.[34]

To provide additional evidence for this mechanism, Au tubes have been modified with hairpin DNA, which, similar to linear DNA, is also heavily negatively charged but much stiffer.[48] As expected, the Au tubes modified with hairpins did not rectify the ion current.[34]

4. Discussion of Electrostatic Models for Pores of Diameters Comparable to the Thickness of the Electrical Double Layer

The previous section presented four models formulated to explain the effect of ion-current rectification in nanoporous

systems of diameters comparable to the thickness of the electrical double layer. I would now like to discuss similarities and differences among the various approaches as well as suggest experiments to help elucidate which rectification mechanism is in operation in asymmetric nanopores.

All the models of ion-current rectification are based on interactions of the ions passing through the narrow pores with the excess surface charge on the pore walls. When the net surface charge becomes zero, the models predict an ohmic behavior of the systems. The first difference between the models appears when we compare the quantities on which the physical descriptions are based. The approaches of Woermann,[45,46] Cervera et al.,[47] and Wei et al.[13] are based on macroscopic quantities of salt concentration inside the pore. The models of Woermann and Cervera et al. predict that the two branches of an *I–V* curve with lower and higher ion current values correspond to lower and higher KCl concentration in the pore, respectively. Depending on the polarity of the voltage, cations are transferred from the region of the pore with a high value of t^+ to the region with a low value of t^+, or in the opposite direction. The key points in the Woermann model are i) dependence of t^+ of the transition zone of conical pores on the polarity of the external voltage, and ii) requirement of electroneutrality. Higher t^+ of the transition zone at negative voltages results in increasing the KCl concentration inside the pore. The opposite polarity diminishes the t^+ value of the transition region causing lowering of the KCl concentration in the pore.

The Woermann model predicts a linear *I–V* curve, with different slopes for positive and negative voltages. The experimental data are, however, more complex. Fitting the two branches of an *I–V* curve by a power-law function results in an exponent lower than one for positive voltages and higher than one for negative voltages (Fig. 12). The Woermann model is also based on numerous parameters that are very difficult to approach experimentally.
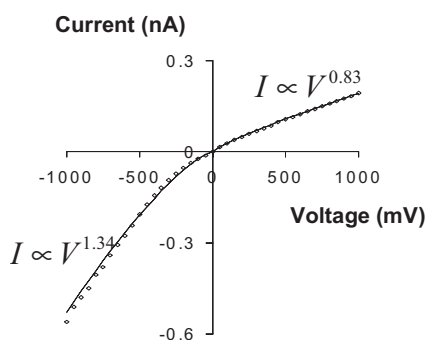
Current (nA)

$$I \propto V^{0.83}$$

$$I \propto V^{1.34}$$

Voltage (mV)

Figure 12. *I–V* curve for a single conical PET pore recorded under symmetric electrolyte conditions of 0.1 M KCl, pH 8. The experimental data (◇) have been fitted with power-law functions.

Woermann divides the channel into three regions differing in transference numbers and ion concentrations. Wei et al. also distinguish three parts of the pore, although the criteria for finding the three regions are different.[13] Wei et al. divide the channel into a cylindrical, permselective part connected to two conical zones of different cone-opening angles. The transition zone of the Woermann model could be related to the cylindrical, permselective part in the description by Wei et al. The cylindrical part does not, however, change its permselectivity at two different polarities of the applied voltage but is "supplied" in a different way with potassium and chloride ions at positive and negative voltages. The difference in the access of the ions results from the presence of two conical zones of different opening angles, which causes different limiting rates in and out of the capillary.

The Woermann model, however, gives more insight into the physical situation inside the pore and it could qualitatively explain the rectification effect observed in cylindrical nanopores with asymmetric surface-charge distribution. Such cylindrical pores could also be divided into three regions: i) a region close to the entrance of the pore in contact with a basic KCl solution; ii) a region close to the other entrance of the pore bathed in KCl solution of pH 2; and iii) a transition region between the other two zones. The first region is characterized by a high transference number, while the second region is not selective for cations. According to the Woermann model, the transition region would have t^+ dependent on the polarity of the applied voltage.

The model of Wei et al. is based on the geometrical asymmetry of the systems, and it would have to be modified in order to explain the data of rectifying cylindrical pores.

The description of Cervera et al. is similar in its physical implications to the Woermann approach; however, their model is quantitative and does not require the fitting of so many parameters. To render the experimental data Cervera et al. needed to adjust just one parameter of clear physical definition, i.e., the excess surface-charge density on the pore walls. It is a remarkable result that with the parameter values of a bulk electrolyte solution, they were able to model the main properties of ion current through nanopores. The assumptions that the authors made to solve the equation, would not, however, be valid in truly nanometer-sized pores. For these pores, one cannot use bulk values of parameters such as the diffusion coefficients for potassium and chloride ions. It has been found that the diffusion coefficient for ions can be reduced by up to 50 % if the diameter of the pore is very small.[49] The diffusion coefficient of ions inside a nanopore is also dependent on whether the pore is cation or anion selective.[50] It is not straightforward to extrapolate the model of Cervera et al. to other experimental conditions and much smaller pores. For example, the model does not provide an intuitive notion of what will happen when the pore geometry is changed to, e.g., double conical.

As mentioned above, these three models are based on macroscopic quantities such as ion concentration. Let us calculate the number of ions that are in the part of a conical nanopore in which 50 % of the total resistance is focused.[51] For a conical pore with opening diameters of 600 nm and 3 nm and a length of 12 μm, 50 % of the pore resistance is observed in the first 50 nm from the tip. Assuming that the pore is filled with 0.1 M KCl, one can calculate that there are only 24 potassium ions in that volume, which makes averaging in terms of ion concentration questionable.

The ratchet model deals with interactions of ions with charges on the pore wall. It models the internal potential of ions inside a nanopore originating from the excess charges on the pore walls. The knowledge of the potential enables one to calculate the ion-concentration profiles inside a nanopore, the rates at which ions translocate the pore, and ion current.[52,53] I would like to emphasize that the model assumes operation of the system far from equilibrium; the system is driven out of equilibrium by the external force and thermal fluctuations. The ratchet model postulates the existence of an electrostatic trap for one polarity of the external voltage. It allows, therefore, the formulation of a direct link between the structure of the pore and its transport properties.

Rectification observed with conical nanopores and tubes as well as cylindrical pores with asymmetric surface-charge distribution can be explained very easily by the ratchet model. The symmetry of the electric potential in both these systems has been broken either by the geometry in case of conical pores or surface charge for cylindrical nanopores. The ratchet model gives an intuitive feel of the physics of ion-current rectification, valid even for very narrow pores. It shows the possibility of influencing the rectifying properties of nanopores by local changes in the chemical structure of the nanopore.

There are still many experiments to be conducted that would give more insight into transport properties of nanometer-sized pores. The simplest set of experiments, which has not yet been performed, would be to study the correlation between the cone's opening angle and its rectification degree. The models of Wei et al.[13] and Woermann[45,46] imply that for smaller opening angles the rectification should increase, because the access resistance at the two pore openings would have a greater difference.

An interesting system has also been discussed by Rischel and Flyvbjerg.[54] They considered a conical nanopore with a surface charge focused at the tip, while pore walls inside the pore were deprived of any excess surface charge. It would be interesting to check whether such a system is sufficient to produce ion-current rectification. Performing experiments with these pores would also give more insight into the influence of the access resistance on the rectification phenomenon.

We would also like to experimentally study the predictions of Woermann[45] and Cervera et al.[47] on the difference in selectivity of a conical nanopore at two polarities of applied voltage. The proper method of studying this issue requires using an equal concentration of ions on both sides of the membrane, because it has been found that the selectivity of a nanopore depends on the electrolyte concentration.[50,52] One way of performing this experiment would be to replace a fraction of ions by radioactive markers, and check whether the ratios of cations and anions translocated for the two voltage polarities are different.

In experiments performed so far we have focused on potassium ions. We do not know yet whether the nanopores can distinguish between various monovalent cations, e.g., sodium and potassium, or lithium and cesium.

To gain more insight into interactions of ions with the pore walls, one should also perform studies with polyvalent cations.

With monovalent ions, one can assume that the translocating ions do not affect the shape of the internal electric potential. We expect that polyvalent cations will bind temporarily to carboxylate groups on the pore walls, and will lead to interesting new transport properties resulting from the nonlinear addition of internal and external electric fields.

5. Conclusions

We have presented synthetic nanoporous systems that exhibit the property of ion-current rectification. Mechanisms formulated to explain the rectification effect have also been revisited. The common feature of all rectifying systems is broken symmetry, achieved by tuning the geometrical and/or chemical properties of the nanopores. More experiments are needed to elucidate the mechanism of ion transport through nanopores.

The next challenging step in research on the nanoporous systems will be to apply them for detection and separation of charged molecules such as DNA and proteins, with application of the ratchet mechanism.[41–43]

6. Experimental

Irradiation with Single Heavy Swift Ions: The irradiation with single ions was performed at the Gesellschaft für Schwerionenforschung (GSI), Darmstadt, Germany. We used mainly U, Bi, and Au ions of energy of 11.4 MeV per nucleon (UNILAC, Darmstadt). In order to achieve control of the irradiation down to one ion, the ion beam was strongly defocused and a metal mask with a 0.1 mm diameter aperture was placed in front of each foil stack [18]. Individual ions passing through the samples were registered by a particle detector behind the samples. The irradiation with precisely one ion per sample was possible via a chopper system shutting off the beam within several microseconds.

Chemical Etching: Etching conditions of the irradiated foils determine the shape of pores. To obtain cylindrical pores, one applies a procedure that assures fast penetration of the etchant along the track with minimum non-specific etching of the material. To produce cylindrical pores in PET, we etched the irradiated foils in 3 M NaOH at 40 °C. Cylindrical pores in Kapton were prepared by etching the foil in sodium hypochlorite buffered with boric acid to pH 9 [55].

Tapered-cone pores were obtained by asymmetric etching of the irradiated foils in an etchant that assured a strong non-specific etching of the polymeric material [9–11,56]. Etching was performed in a conductivity cell from one side only, while the other side of the foil was protected by a so-called stopping medium, which neutralized the action of the etchant. To obtain conical pores in PET, we etched the irradiated foils in 9 M NaOH, and as the stopping medium we used 1 M KCl and 1 M formic acid [56]. Asymmetric etching of Kapton was performed in sodium hypochlorite with a 13 % active chlorine content of highly basic pH (~pH 12.6). As a stopping medium we used 1 M KI, which reduces hypochlorite ions active in the etching process to chloride ions [10].

Double-conical nanopores were prepared in a two-step process: i) short pre-etching of an irradiated foil from both sides; and ii) subsequent etching from one side, while protecting the other side of the membrane with stopping solution. The resulting pores consisted of a short conical part of several tens of nanometers in length, supported by a long cone, which played the role of a mechanical support for the short cone.

Current–Voltage Recordings: *I–V* curves were recorded using a Keithley 6487 picoammeter/voltage source (Keithley Instruments, Cleveland, OH). The voltage was stepped between –1 V and +1 V with 50 mV steps, lasting 5 s. The *I–V* curves of double-conical pores were

studied with a current/voltage converter of pA sensitivity controlled by software written in LABVIEW 5.0 (National Instruments) [23]. The output was digitized at 166 kHz using the National Instruments PCI-MIO-16XE-10 card, and sampled at 250 Hz.

Measurements of the Opening Diameter of Polymer Nanopores: The diameter of the nanopores was found by an electrochemical method using the relation between the resistance of a pore and its dimensions [56]. The resistance is directly proportional to the length of the pore, L, and inversely proportional to its cross-sectional area, A

$$R = \frac{1}{\kappa} \frac{L}{A} \tag{7}$$

where κ is the specific conductivity of the electrolyte filling the nanopore. In this method we assume that the conductivity of the electrolyte inside the pore is the same as in the bulk solution. Because of the presence of carboxylate groups on the pore walls [11,23] and the resulting excess surface charge, the measurements of the pore diameter should be performed in conditions at which the thickness of the electrical double layer can be neglected, i.e., at high electrolyte concentrations and pH close to the isoelectric point of the surface [35,57].

The relation we used to determine the diameter of the small opening of a conical nanopore, d, is [56]

$$d = \frac{4LI}{\pi\kappa DU} \tag{8}$$

where D is the diameter of the large opening of the pore and I is the ion current measured for the applied voltage U.

Pores with effective diameters as small as 2 nm were prepared by track-etching.

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