# Biomimetic potassium selective nanopores

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**Teaser:** A nanopore decorated with crown ether and DNA is selective to potassium ions over sodium ions at concentrations up to 1 M.

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**Abstract**: **Reproducing the exquisite ion selectivity displayed by biological ion channels in artificial nanopore systems has proven to be one of the most challenging tasks undertaken by the nanopore community, yet a successful achievement of this goal offers immense technological potential. Here we show a strategy to design solid-state nanopores that selectively transport potassium ions and show negligible conductance for sodium ions. The nanopores contain walls decorated with 4′-aminobenzo-18-crown-6 ether and ssDNA molecules located at one pore entrance. The ionic selectivity stems from facilitated transport of potassium ions in the pore region containing crown ethers, while the highly charged ssDNA plays the role of a cation filter. Achieving potassium selectivity in solid-state nanopores opens new avenues toward advanced separation processes, more efficient biosensing technologies and novel biomimetic nanopore systems.**

## INTRODUCTION

Since the discovery of biological channels and their importance in physiological processes, scientists have attempted to create robust man-made structures that exhibit transport properties mimicking those of their biological counterparts.(*1-4*) Responsiveness to external stimuli and exquisite ionic selectivity are two of the most exciting properties for which efficiency remains unmatched by solid-state nanopores.(*5*) Stimuli in the form of electrical potential modulation, chemical interactions, or mechanical stress can induce so called gated channels to switch between ion conductive and closed states. Biological channels are also frequently able to differentiate between ions of the same charge so that, for example, potassium-selective channels can transport potassium ions thousands times faster than sodium ions.(*6, 7*) Matching biological gating and ion selectivity capabilities in a synthetic nanopore platform could not only enable new sensing technologies but also lay the groundwork for a deeper understanding of ionic and molecular transport at the nanoscale with simple and robust model systems.

Gating has been successfully achieved in a number of man-made systems. Current rectification(*8*) and voltage-responsive pore opening(*9-11*) were demonstrated in polymer and solid state nanopores having walls modified, for example, with single-stranded DNA (ssDNA), or polymer brushes. Transport properties of nanopores can also be made responsive to pressure(*12-14*), temperature (*15*) or molecules present in a solution, thus mimicking the behavior of ligand-gated channels.(*2, 16-18*)

The ability to efficiently transport one monovalent cation over another monovalent cation underpins key cellular processes such as signal propagation in neurons but is very challenging to achieve in artificial nanopores. One example includes anodic alumina membranes filled with silica that were rendered potassium selective via non-covalent attachment of crown ethers.(*19*) Graphene with crown-ether-like nanopores was also proposed as a platform that could be made selective for a specific ion.(*20*) In addition, the literature has shown a few examples of lipid-bilayer-supported synthetic constructs prepared by supramolecular self-assembly to stack crown-ether molecules on top of each other and create a channel.(*21-25*) These synthetic pores, however, display only modest cation/cation selectivities. In a similar approach, self-assembly of rigid macrocycles formed hydrophobic nanopores in a lipid bilayer, which exhibited excellent selectivity towards protons over potassium ions and no measurable conductance in NaCl or LiCl.(*26*) Due to their hydrophobic character, however, the macrocycle-based channels exhibited only very low, pS conductivities in ionic strength as high as 4 M.

To our knowledge, cation/cation selectivity has not been reproduced yet in solid-state nanopores. This type of nanopore, which doesn't involve a lipid bilayer, offers the advantages of tunable geometry and surface properties and are far more robust than lipid-bilayer inserted channels. Thus, solid-state nanopores permit exploration into a wider range of electrochemical conditions and easier integration into fluidic devices.

In this manuscript, we demonstrate a solid-state nanopore that preferentially conducts potassium ions over sodium ions at concentrations up to 1 M and with selectivities far surpassing those previously reported in any other man-made nanopore platform. The

mechanism of ionic selectivity is based on facilitated transport (*27*) of potassium ions through a nanopore with an effective opening of less than 2 nm, whose walls are decorated with 18-crown-6 ether molecules. In polar solvents such as water, the crown ethers are known to selectively bind and release potassium ions quickly, allowing for their transport.(*28, 29*) We chose 4′-aminobenzo-18-crown-6 ether due to the presence of an amino group that permits easy attachment to a carboxylated surface.(*30*)

## RESULTS AND DISCUSSION

### Potassium selectivity is achieved via attachment of crown ether

Figure 1a shows the fabrication of single nanopores and the types of chemical modifications the structures were subjected to. The pores used in this study were formed in 30 nm thick films of silicon nitride by dielectric breakdown.(*31-33*) Transport characteristics of the as-prepared pores were measured in 1 M and 100 mM solutions of KCl and NaCl (Figure S1). The pore walls and the membrane surfaces were then modified with triethoxysilylpropylmaleamic acid (TESPMA), which led to the attachment of carboxyl groups and the reduction of the pore diameter by a few nanometers (Table S1).(*34*) Carboxylated nanopores were again tested in 1 M KCl, 100 mM KCl and NaCl solutions, and the pore resistance obtained from I-V curves in 1 M solutions were used to size the pore diameter assuming a cylindrical geometry (Supplementary Information). All reported pore diameters in this work are therefore calculated after TESPMA functionalization. Due to possible deviation of the pores' shape from a cylinder, calculated diameters should be considered as average or effective diameters. Following carboxylation, nanopores were subjected to one of two modification strategies. (i) The

first sub-set of nanopores (n=3) was decorated with 4′-aminobenzo-18-crown-6 using 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) coupling chemistry (Figure 1b) (*30*). (ii) The second sub-set of nanopores (n=6) was modified from one side with ssDNA oligomer, and the other side with crown ether (Figure 1c). This asymmetric functionalization scheme was motivated by the goal of combining voltage-gated transport and cation/cation selectivity in a single synthetic pore that mimics the structure and double functionality of potassium gated channels.(*6, 7*) Reported selectivity of our pores towards potassium ions are defined here as the ratio of currents in KCl and NaCl solutions measured at 1 M, 100 mM and 10 mM concentrations with a voltage of +1 V across the membrane. The positive sign of electric potential difference corresponds to a working electrode on the side of the membrane with ssDNA; thus, for positive voltages, cations enter the pore from the DNA side and move towards the pore opening containing crown ethers.

Figure 1b shows recordings for a 1 nm wide nanopore modified with crown ether only. These include the ion selectivities before and after each modification step for all studied concentrations and the current-voltage curves in 1 M KCl and 1 M NaCl solutions. Selectivity towards potassium ions is evident only after attachment of crown ether so that the ionic current at +1 V in KCl solutions becomes at least 10 times higher than in NaCl solutions. The pore shows current rectification, thus the selectivity calculated at positive and negative voltages is different (Figure S2). Before implementing the asymmetric functionalization scheme (ii), we tested also the ionic selectivity of a pore subjected to crown modification only from one side. Current recordings for this pore

(Figure S3) revealed that a partly modified pore still preferentially conducts potassium ions.

**DNA plays a role of a cation filter**

In our pore design inspired by voltage-gated ion channels, grafting of ssDNA was localized to the membrane surface and pore mouth through the selection of a 30-mer ssDNA, which is too large to diffuse inside the nanopore.(*35, 36*) We expected the high density of negative charges on the DNA to increase the cation concentrations at the pore entrance, thus causing the process of binding/releasing of ions from the crown ether to be the limiting step in the ion transport process. Note that potassium channels in a cell membrane also feature negative surface charges at one entrance, which are believed to increase local ionic concentrations and pore conductance.(*7*) Example recordings for a 1 nm wide pore subjected to ssDNA/crown ether modification is shown in Figure 1c. In 1 M KCl, this pore exhibited potassium currents that were nearly 80 times higher than currents recorded in 1 M NaCl. Note that the potassium selectivity is induced by the presence of crown ether molecules; the highly charged DNA functions only as a cation filter, preventing anions from passing through.(*37*) We believe DNA does not contribute to the ability of the pore to distinguish between potassium and sodium ions, because a nanopore modified only with ssDNA exhibits comparable conductance in KCl and NaCl (Figure S4).

**Potassium selectivity is based on facilitated transport**

We hypothesized that the selectivity observed in the two nanopores shown in Figure 1 is based on facilitated transport of $K^+$ ions,(*27*) which undergo binding/unbinding to crown ethers on the pore walls. In addition, we speculated that the effective pore opening after TESPMA (1 nm) is narrow enough to be fully occupied by the crown ether groups after EDC chemistry, thus preventing non-selective 'bulk transport' of sodium ions through the middle section of the pore. Pore diameter is therefore predicted to play a very important role in determining the magnitude of $K^+$ selectivity.

Toward validating our hypothesis, we considered six ssDNA/crown-ether modified nanopores as well as three nanopores that contained only crown ether. In Figure 2, we plotted the ratios of ionic currents recorded in KCl and NaCl solutions as a function of pore size determined after the carboxylation step. Clearly, $K^+$ ion selectivity decreases exponentially with the increase of the pore diameter and disappears for pore sizes larger than 3 nm. Importantly, thanks to the combined action of facilitated transport and negligible bulk transport, we could achieve $K^+/Na^+$ selectivities up to 84, which surpass those reported in other synthetic nanopores by about one order of magnitude. Note that pores with effective diameter below 1 nm could have been too narrow to allow for the attachment of crown ether along the pore length. In the case of very narrow pores, the chemical modification could be restricted mostly to the membrane surface/pore entrance, which was sufficient to render the nanopores potassium ion selective.

Another striking finding is the increase of $K^+$ selectivity with salt concentration for the majority of nanopores with diameter below 2 nm, a dependence that contradicts

expectations from an electrostatics-based selectivity mechanism. In order to understand this observation, we looked in detail at the concentration dependence of sodium and potassium currents (Figures 3, S5). Sodium currents in < 2 nm nanopores are nearly concentration independent, which suggests that the nanopores are indeed too small to allow for significant non-selective transport of sodium through the pore middle region. Potassium currents on the other hand do depend on the bulk concentration, thus the ratio of currents in potassium and sodium is lower at lower concentrations.

Figure 2 also offers comparison between pores modified only with crown ethers and those with both DNA and crown ether functionalities. Even though both types of nanopores can exhibit ratios of currents in KCl and NaCl solutions > 78, the crown-ether-only modified pores lose their selectivity more rapidly with the increase of pore size. This observation supports our prediction that DNA would act as a cation selectivity filter and/or contribute to further narrow the size of any non-selective transport pathway at the pore center. Overall, our finding suggests a larger robustness of the potassium selectivity in the presence of DNA.

Like the pores modified only with crown ether, pores functionalized with both ssDNA and crown ether displayed current rectification and different selectivities with voltage sign. The difference in $K^+/Na^+$ selectivity between positive and negative voltages can be explained considering that crown ethers acquire a positive charge in the presence of cations.(*37*) Consequently, a DNA/crown ether nanopore system features oppositely charged membrane surfaces, which can give rise to a diode behavior.(*8*) Continuum

modeling with the Poisson-Nernst-Planck equations shows that for positive voltages ionic concentrations in the pore are higher, and that the electric potential decays nearly linearly across the entire pore length (Figures S6, S7). Negative voltages on the other hand cause the formation of a depletion zone with a localized voltage drop. Thus, the resulting weak voltage gradient in the crown-ether-modified region induces a smaller selectivity.

Finally, we looked at the voltage dependence of potassium ions selectivity. All pores examined exhibited a selectivity increase at larger positive voltages, the magnitude of which is strongly dependent on pore size (Figure 3). The sensitivity of selectivity to voltage was maximized at a pore diameter of ~1 nm and decreased for both larger and smaller pores.

**Selectivity of DNA/crown ether modified nanopores in KCl and NaCl mixtures.** The measurements shown above were performed with only one type of salt was present in solution. Additional experiments were therefore designed to test the performance of the $K^+$ selective nanopores in mixtures of two salts, KCl and NaCl. The current recordings were performed in solutions in which the total concentration of cations was kept at the constant level of 1 M. The following mixtures were studied: 0.8 M KCl + 0.2 M NaCl, 0.7 M KCl + 0.3 M NaCl and 0.5 M KCl + 0.5 M NaCl. In addition, measurements in 1 M KCl and 1 M NaCl were performed. Figures 4, S8 shows current-voltage curves obtained in mixtures and in individual salts together with the magnitudes of the current at +1 V as a function of KCl concentration. The pore examined had an

effective opening diameter of 1 nm and was modified with crown ethers and DNA. In order to calculate selectivity of the nanopore in salt mixtures we recalled that sodium currents did not depend on NaCl concentration in the range between 10 mM and 1 M (Figure S5). Selectivity can be then obtained as a ratio of current observed in a given mixture and the current magnitude recorded in 1 M NaCl. Our measurements revealed that even though selectivity dropped from ~20 in 1 M KCl to ~5 in 0.8 M KCl and 0.2 M NaCl, the pore remained selective when the salts were present at equal concentrations (0.5 M). Recorded ionic currents dropped proportionally to the selectivity change upon addition of sodium ions.

**Phenomenological model with voltage-dependent $k_{on}$ and $k_{off}$ help explain potassium selectivity of nanopores**.

Toward validating the claim that the pore behavior discussed thus far can be explained by crown-ether mediated transport, we developed a simple model, which neglects the presence of DNA and any surface charge effects. We assumed a pore with walls decorated by crown ethers arranged in a ring, which interact with cations through binding/unbinding events governed by $k_{on}$ and $k_{off}$ rate constants. For simplicity, we focused only on transport through a single crown-ether layer (Figure 3a). Both $k_{on}$ and $k_{off}$ constants depend exponentially on voltage, $V$, according to: $k_i = k_{i0} e^{-\frac{d_{ce} eV}{L_p k_B T}}$, $i$=*on, off,* where $\frac{d_{ce}}{L_p}$ corresponds to the fractional potential drop an ion experiences as it approaches and binds to a crown ether, $L_p$ is the pore length, $e$ the unit charge, and $k_B$ the Boltzmann constant.(*18, 38, 39*) The total current in the crown ether region can then

be calculated from the total time, $\tau$, an ion takes to pass through the pore, $\tau = \frac{1}{k_{on}C} + \frac{1}{k_{off}}$, the charge density calculated from the percent of bound cation/crown ether complexes, the ion concentration *C*, and the pore radius, $R_p$. To approximate a leakage current, the model assumes bulk transport in the center of the pore if $R_p > R_{mod}$, where $R_{mod}$ is the constant radial thickness of the crown-ether-modified region. We set the pore length $L_p$ equal to 30 nm to match the experimental system. The model was then fit to the combined experimental dataset of current *versus* voltage for the nanopore shown in Figure 1c, and selectivity *versus* pore diameter for all ssDNA/crown ether modified pores (Figure 2a) while keeping $R_{mod}$ constant at 0.25 nm. Best fit values of parameters are summarized in Table 1. Fitted $d_{ce}$ suggests a reasonable spacing between crown ethers of one to a few nm, while the binding constants, especially for $K^+$, differ significantly from those seen in a bulk system.(*28*) While at first unexpected, this result appears to be supported by previously reported theories that binding/unbinding kinetics of close packed macrocycles under nanoscale confinement can deviate substantially from bulk behavior.(*22, 23*)

**Table 1**. Values of parameters used to fit the experimental data of potassium selectivity and ion current values (Figures 2-4)

| $k_{off0,K}$ [$s^{-1}$] | $k_{on0,K}$ [$s^{-1}M^{-1}$] | $\frac{k_{on0,K}}{k_{off0,K}}$ [M] | $k_{off0,Na}$ [$s^{-1}$] | $k_{on0,Na}$ [$s^{-1}M^{-1}$] | $\frac{k_{on0,Na}}{k_{off0,Na}}$ [M] | $d_{ce}$ [nm] |
|---|---|---|---|---|---|---|
| $\mathbf{9.9 \times 10^8}$ | $5.1 \times 10^9$ | 5.15 | $9.2 \times 10^6$ | $1.1 \times 10^8$ | 11.95 | 1.9 |

The model is able to successfully capture several key trends observed in the experimental data, the first of which is the diameter dependence of selectivity *versus* pore diameter (Figure 2a). As expected, the selectivity decreases for large pores due to leakage current while plateauing at a maximum for small pore diameters where the leakage current becomes negligible. Next, the model reproduces well the exponential current dependence on voltage along with reasonably accurate current magnitudes (Figure 3c,d). Our set of equations also replicate the experimentally observed weaker concentration dependence for NaCl *versus* KCl current, which we attribute to $Na^+$ transport being limited by the concentration independent $k_{off}$. In addition, the model clearly portrays how the voltage dependence of the $K^+/Na^+$ selectivity changes with pore diameter (Figure 3d). At small enough pore size, the leakage current drops to zero and the selectivity becomes voltage independent since both $K^+$ and $Na^+$ binding rates respond to voltage similarly. As the pore diameter gets too large, the leakage current begins to dominate and, thus, the selectivity becomes less sensitive to voltage. Finally, our phenomenological model explains the decrease of ionic current and selectivity when sodium ions are added to a potassium chloride solution. Since the absorption equilibrium constant $k_{on}/k_{off}$ for $Na^+$ is larger than for $K^+$ ions and $k_{off,\,Na}$ is two orders of magnitude lower than $k_{off,\,K}$, a large fraction of crown ethers are occupied by tightly bound sodium ions rather than efficiently transporting fast-releasing potassium ions. Thus, competitive binding of sodium slows down potassium transport. Overall the ability of this simple model to reproduce all observed trends in the data strongly supports the proposed facilitated transport mechanism, and this simple set of equations may prove to be useful in the design of future biomimetic pores.

## CONCLUSIONS

In conclusion, we presented a solid-state nanopore system decorated with crown ethers, which render the pores highly selective toward potassium ions when the pore diameter is sufficiently small. We found that placement of ssDNA at one pore entrance made the system selectivity more robust by concentrating cations at one entrance. Future studies will focus on equipping such a potassium selective pore with a voltage-gated component to enable voltage-regulated pore opening. We will also identify experimental conditions and different types of crown ethers, which may offer highly efficient potassium ion transport even in salt mixtures.

## MATERIALS AND METHODS

**Preparation of nanopores**.

Single nanopores were prepared by the process of dielectric breakdown(*31-33*) in low-stress silicon nitride ($SiN_x$) membranes (50 x 50 $\mu m^2$, 30 nm thickness) purchased from Norcada Product. Before the pore fabrication, the chips were washed in piranha solution (1:3 $H_2O_2$ : $H_2SO_4$) at 100°C for 30 minutes, followed by rinsing in 18 MΩ water.

In the dielectric breakdown process, both chambers of a custom made PDMS conductivity cell were filled with a strongly acidic solution of 1 M KCl (pH 1.6).(*32, 33*) The dielectric breakdown was performed with 12 V applied with two Ag/AgCl pellet electrodes. The electric field chosen, 0.4 V/nm, is close to the minimum magnitude needed to create nanopores by this technique, which assures formation of one pore only.(*31, 40*) The pore formed after ~60 minutes; the process was stopped after the current increased by ~100 nA above the baseline current. The pore diameter was estimated based on the pore

resistance found from current-voltage curve recorded in 1 M KCl in the voltage range between -1V and +1V. Note, that the total resistance is a sum of the geometrical pore resistance and access resistance.(*41*) The opening diameter (D) was then estimated using the following equation:(*33*)

$$D = \frac{G}{2\sigma}\left[1 + \sqrt{1 + \frac{16\sigma L}{\pi G}}\right] \qquad \text{eq. (1)}$$

where *G* is the slope of the I-V curve, $\sigma$ stands for the solution conductivity, and *L* is the pore length (30 nm). The shape of the pores was assumed cylindrical thus the calculated diameters are considered effective/average diameters.

Current-voltage curves were measured with Axopatch 200B and Digidata 1322A (Molecular Devices, Inc.) using sampling frequency of 10 kHz with 0.1 V voltage steps. At each voltage step, the current signal was recorded for 100 s. The current values reported are averages of the whole time series except the first and last 5 seconds of the recordings. Two pellet Ag/AgCl electrodes were used for all current measurements.

**Modification of nanopores with Triethoxysilylpropylmaleamic acid (TESPMA)**.

The modification solution was prepared by adding 50 mg of Triethoxysilylpropylmaleamic acid (TESPMA) to 5 mL of ultrapure water containing acetic acid (50 µL); the solution was stirred for 1 h at room temperature. Nanopore silicon nitride chips were immersed in the solution at room temperature for 1 h. After washing in de-ionized water, the chips were heated at 80 °C for 20 min.(*34*) TESPMA modified nanopores were re-sized in 1 M KCl using the same procedure as described above.

**Attachment of crown ethers and DNA.**

After carboxylation, silicon nitride chips were subjected to chemical modification with 4-aminobenzo-18-crown-6 (4-AB18C6) crown ether and DNA. Both molecules were attached using N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide (EDC) mediated chemistry to link amino groups to carboxyls. To this end, silicon nitride nanopore chips were first activated from both sides using a solution of 0.01 M EDC and 0.02 M N-hydroxysulfosuccinimide (S-NHS) in 0.1 M MES buffer, pH 5.5. The activation time was kept constant at 30 min, which was followed by a thorough wash of the membrane with 0.1 M MES buffer solution from both sides. Attachment of crown ether molecules was performed overnight by incubation of the chips in a solution of 0.01 M 4-aminobenzo-18-crown-6 (4-AB18C6) in 0.1 M MES buffer, pH 5.5.(*37*) One nanopore was modified with the crown ethers asymmetrically; this modification was performed in a conductivity cell so that one chamber of the cell contained the crown ether solution, while the other side contained only 0.1 MES buffer, pH 5.5; the asymmetric modification was expected to result in the attachment of the molecules only to ~a half of the pore length.

DNA oligomer of the following sequence was purchased from Integrated DNA Technologies (Coralville, IA): 5- /5AmMC12/CAC CCA CAA CCA CCA ACA CAC ACC ACC ACC -3. The amino group with a linker was shown before to allow attachment of DNA oligomers to carboxylated surfaces.(*9*) Obtained amount of the oligomer was dissolved in 0.1 M pH 5.5 MES buffer to reach DNA concentration of ~0.5 mM. All DNA modifications were performed in a conductivity cell. One side of the chip was in contact with the DNA solution and the other side with the solution of crown ether. The reaction

occurred overnight. Properties of DNA and 4-AB18C6 modified nanopores were examined in KCl solutions buffered to pH 8.

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**Supplementary Materials.**

Supplementary material for the article is available at:

The material contains additional experimental results and details on modeling.

Figure S1. Example current-voltage curves of nanopores shown in Figure 1 in the main manuscript before crown ether attachment.

Figure S2. Selectivity of nanopores shown in Figure 1 of the main manuscript towards potassium ions at -1V.

Figure S3. Ion selectivity at 1V of a nanopore modified with crown ether from one side only.

Figure S4. Ion current through a 1 nm in diameter nanopore modified with DNA from one side.

Figure S5. Ion currents through a nanopore shown in Figure 1c of the main manuscript as a function of KCl and NaCl concentrations. The nanopore was modified with crown ether and DNA.

Figure S6. Scheme of a modeling system used to predict local ionic concentrations and electric potential in a nanopore.

Figure S7. Results of numerical modeling of ionic concentrations and electric potential in a nanopore shown in Figure S6. Poisson-Nernst-Planck equations were solved numerically.

Figure S8. Current-voltage curves of a nanopore shown in Figure 4 of the main manuscript.

Table S1. Pore opening diameters calculated according to eq. (1) in the main manuscript for all nanopores considered in the manuscript.

## Figure Captions

**Figure 1. Designing potassium selective solid-state nanopores**. (a) Single nanopores with tunable opening diameter were created in 30 nm thick silicon nitride films by the process of

dielectric breakdown. The first modification step led to the attachment of carboxyl groups. The second modification involved either symmetric attachment of 4′-aminobenzo-18-crown-6 ether (b), or asymmetric modification with the crown ether and ssDNA (c). (b) Current-voltage curves in 1 M KCl and 1 M NaCl recorded for a 1 nm in diameter pore whose walls were decorated with crown ether, as shown in the scheme. The graph on the right summarizes ratios of currents in KCl and NaCl at 1 V before and after each modification step for the same nanopore. Ratios of currents for the nanopore before and after carboxylation are calculated based on the recordings in 100 mM of the salts. (c) Current-voltage curves in 1 M KCl and 1 M NaCl for a 0.6 nm wide nanopore modified with crown ether and ssDNA. Selectivity of the nanopore is shown as ratios of ionic currents in KCl and NaCl solutions measured at the same conditions as in (b).

**Figure 2**. **Selectivity of nanopores towards potassium**. (a) Experimental ratios of ion currents in KCl and NaCl solutions for 6 independently prepared nanopores subjected to chemical modification with crown ethers and ssDNA. Data for three different bulk concentrations of the salts are shown. The model fit is shown as dashed lines. (b) Experimental data of potassium selectivity for three nanopores modified only with crown ether. Standard deviations of currents for individual voltages are shown in I-V curves in Figures 1, S5.

**Figure 3. Phenomenological model of the potassium selectivity of solid-state nanopores.** (a) Scheme of the modeled system with geometrical parameters used in the model. (b) Diameter dependence of the selectivity sensitivity ($m_S$) to voltage. $m_S$ is defined here as the slope of a linear fit of $Log(I_k/I_{Na})$ *versus* voltage for 1 M KCl and NaCl solution concentrations. (c) Current *versus* voltage curves at three different bulk KCl concentrations for the same pore shown in Figure 1c. (d) Current *versus* voltage curves at three different bulk NaCl concentraitons for the same pore as (c). Symbols are for experimental data, while dashed lines

represent model predictions using the parameters listed in Table 1. Standard deviations of currents for individual voltages are shown in I-V curves in Figure S5.

**Figure 4. Ion current measurements in mixtures of KCl and NaCl for a 1 nm in diameter nanopore modified with crown ethers and DNA**. (a) I-V curves in all conditions examined; (b) Ratio of the ionic currents in mixed salt solutions and in 1M NaCl solution as a function of KCl concentration at +1 V and a constant total salt concentration of 1 M. Inset: magnitude of the ion current as a function of KCl concentration under the same conditions. Dashed lines show model predictions using the parameters given in Table 1 for a 1 nm diameter pore.

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