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Host–guest supramolecular chemistry in solid-state nanopores: potassium-driven modulation of ionic transport in nanofluidic diodes†

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We describe the use of asymmetric nanopores decorated with crown ethers for constructing robust signal-responsive chemical devices. The modification of single conical nanopores with 18-crown-6 units led to a nanodevice whose electronic readout, derived from the transmembrane ion current, can be finely tuned over a wide range of K^+ concentrations. The electrostatic characteristics of the nanopore environment arising from host–guest ion-recognition processes taking place on the pore walls are responsible for tuning the transmembrane ionic transport and the rectification properties of the pore. This work illustrates the potential and versatility of host–guest chemistry, in combination with nanofluidic elements, as a key enabler to achieve addressable chemical nanodevices mimicking the ion transport properties and gating functions of specific biological channels.

Introduction

During the past decade, chemists and materials scientists have exploited biological principles as guidance in developing new strategies that would lead to advanced devices with a broad impact in multiple fields.[1] For instance, different research groups have sought inspiration from biological pores to develop new classes of devices with adjustable molecular transport functionalities.[2] In this context, the advent of track-etching techniques has helped this exciting area of nanotechnology move forward.[3] One of the most intriguing aspects of asymmetric nanopores is their ability to rectify the ion transport flowing through them, thus resembling the well-known voltage-gated biological channels.[4] One of the central features that determines the rectifying characteristics of the conical nanopores is the accurate control over the surface charge of the pore walls.[5] The efficiency by which many biological pores regulate the ionic transport through biological membranes using different chemical species as a trigger has been a source of inspiration for chemists to mimic such processes using solid-state nanopores.[6] In particular, with regard to chemical triggers of biological relevance, potassium ions can be considered of crucial interest as they modulate the activity of muscles and nerves whose cells are equipped with ion channels for transporting this chemical species with a high degree of specificity.[7] The development of potassium-responsive nanofluidic devices has been pioneered by Jiang and co-workers.[8] These authors exploited the versatility of G-quadruplex DNA strands immobilized onto a synthetic nanopore to undergo a potassium-responsive conformational change that ultimately induces a change in the effective pore size. They showed that the responsive characteristics of the nanopore system can be regulated by the stability of the G-quadruplex structure by adjusting the potassium concentration.[7] Devising strategies to manipulate ion transport through nanopores functionalized with K^+-tunable moieties is a key step toward the design of complex functional devices driven by the presence of specific cations. Substantial progress in molecular recognition chemistry has brought about the possibility of designing host compounds, which would have a high degree of molecular recognition, equivalent to the receptors of a biomembrane. For instance, cations are known to be transported through lipid membranes with the aid of synthetic macrocyclic polyethers as well as antibiotics or even natural ionophores such as monensin and nigericin.[9] This carrier-facilitated ionic permeability can also be induced by using synthetic macrocyclic polyethers commonly referred to as crown ethers.[10]

Crown compounds are quintessential elements in supramolecular host–guest chemistry as they are able to bind alkali and alkaline earth cations in their cavities in a very specific manner in aqueous environments.[11–13] For instance, Heins *et al.*[14] studied the effect of adding crown ethers in the solution along with the salt ions finding that the rectification

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properties of asymmetric nanopores increased when the ethers were placed only in one side of the nanopore due to the formation of a junction potential. Taking into account these concepts and being aware of the attractive features of host–guest chemistry we were particularly intrigued by the possibility of triggering and modulating the rectification properties of solid-state nanopores by incorporating ion recognition elements in their inner architecture.[15] Herein, we describe the construction of potassium-responsive nanofluidic diodes whose rectifying properties are easily modulated by the specific formation of K^+-crown ether complexes over a wide range of ion concentrations and even in the presence of other alkaline ions.

Results and discussion

Single bullet-like nanopores with a tip diameter (d) of ∼30 nm and a base diameter (D) of ∼410 nm were fabricated by irradiation of polyethyleneterephthalate (PET) films with single swift heavy ions as described by Pérez-Mitta *et al.*[16] Chemical etching of the tracks generated by the ions along their trajectories resulted in the generation of carboxyl ($-COO^-$) groups on the channel surface. These groups were derivatized with crown ethers by reacting with a solution containing a mixture of *N*-(3-dimethylaminopropyl)-*N*0-ethylcarbodiimide (EDC) and *N*-hydroxysulfosuccinimide (sulfo-NHS). Subsequently, the sulfo-NHS ester molecules were further covalently coupled with 4′-aminobenzo-18-crown-6 (Fig. 1). As is well known 18-crown-6 units function as ligands for some metal cations with a particular affinity for potassium cations. In this regard, our conceptual paradigm relies on the use of specific host–guest interactions between 18-crown-6 units and potassium ions in order to control the charge density on the pore wall with the concomitant influence on their transport and rectification properties. Fig. 2 shows *I*–*V* curves of a single asymmetric nanochannel fully derivatized with 18-crown-6 units in the presence of NaCl and KCl solutions.

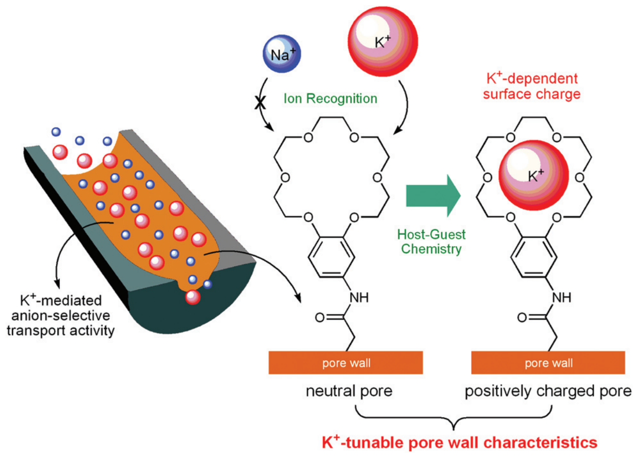

Fig. 1 Schematic depiction corresponding to the asymmetric nanochannel modified with 18-crown-6 units. The chemical structure of the crown ether and the host–guest equilibrium associated with the K^+-dependent behaviour of the supramolecular device are also indicated.

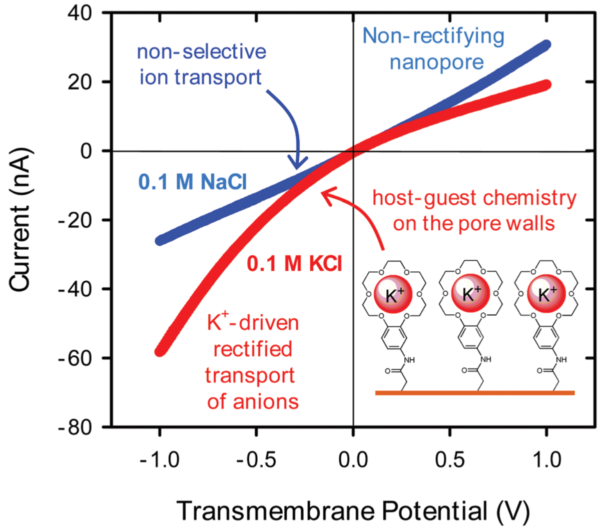

Fig. 2 Transmembrane current–potential curves of an asymmetric nanochannel fully derivatized with 18-crown-6 units in the presence of 0.1 M NaCl (blue trace) and 0.1 M KCl solutions (red trace).

The direction of rectification in asymmetric channels is solely based on the polarity and magnitude of surface charges. Once the carboxylate groups are derivatized with crown ethers, no effective negative charges operate on the pore walls. As a result, considering that Na^+ is not complexed by 18-crown-6 groups, in the presence of 0.1 NaCl the nanopore behaves as a non-rectifying device (Fig. 2). However, this situation changed when a KCl solution was used instead of NaCl. It can be observed that in the presence of K^+ ions, the channel surface charge was switched from neutral to positive, resulting in the rectified passage of anions through the nanopore, *i.e.* anion selectivity. The host–guest ion recognition process taking place on the nanopore walls is responsible for the generation of a tunable nanofluidic device with K^+-dependent surface charges. Contrary to what happens in the presence of Na^+, K^+ ions are recognized, complexed and supramolecularly confined on the pore walls, thus prompting the generation of net positive charges on the pore walls.

The next goal was to achieve a fine-tuning of the surface charges through the interplay of fixed negative and positive charges. In the pore walls the grafted crown ethers can coexist with unreacted carboxylate groups if the reaction time for amidation is decreased in order to avoid their full conversion. As a result, the pore walls display negative carboxylate groups and 18-crown-6 units that in the presence of K^+ can generate surface-confined positive charges that ultimately can neutralize the excess negative charges due to the neighboring carboxylate groups. Contrary to the latter example in which K^+ triggered the rectified transport of anions, in this case the strategy relies on the use of K^+ to tune the rectified transport of cations by modulating the excess negative charges on the pore walls.

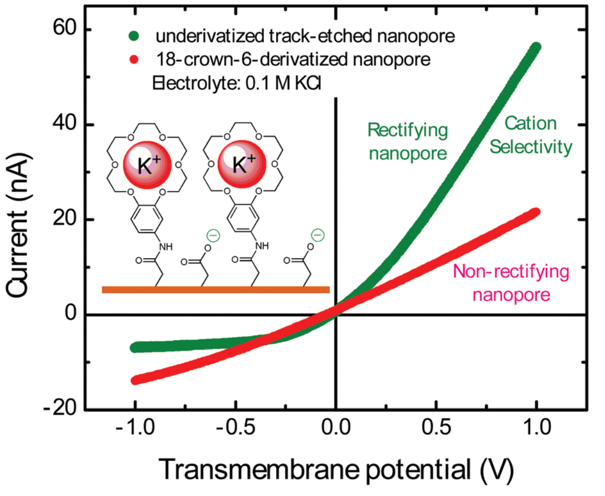

Fig. 3 (a) Transmembrane current–potential curves corresponding to an underivatized track-etched asymmetric nanochannel (green trace) and an asymmetric nanochannel partially derivatized with 18-crown-6 units (red trace) in the presence of 0.1 M KCl.

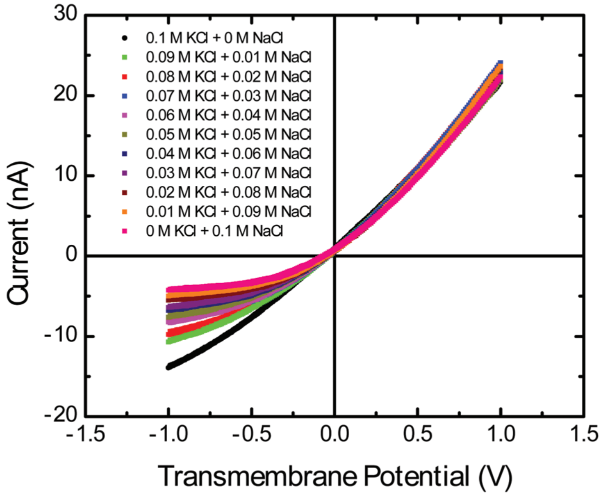

Fig. 4 Transmembrane current–potential curves corresponding to an asymmetric nanochannel partially derivatized with 18-crown-6 units in the presence of different amounts of K^+ and Na^+ ions. Note that the total concentration of the uni-univalent electrolyte is constant.

Fig. 3 shows in the same plot the *I–V* response of an underivatized track-etched single nanochannel and a similar nanochannel partially derivatized with 18-crown-6 units, both of them in the presence of 0.1 M KCl. The underivatized nanochannel displays the typical cation-selective rectified response originating from the exposed carboxylate groups on the pore walls. On the other hand, an asymmetric nanochannel exposing carboxylate and 18-crown-6 groups displays almost no rectification properties as a result of the "neutralization" of fixed charges on the pore walls. Even though negative charges are fixed and, in principle, are independent of the nature of the cations, the ion recognition of K^+ leads to a marked decrease in the rectification properties of the pore, *i.e.* the total negative charges are decreased. For instance, the quasi-linear behaviour of the *I–V* plot (Fig. 3, red trace) indicates that the pore surface of partially derivatized nanofluidic diodes becomes neutral in the presence of K^+. We should note that experiments were performed using a set of nanopores displaying slight differences in the nanopore diameter. This might lead to some differences in terms of total ionic currents measured in different configurations.

The chemical richness of the host–guest chemistry operating in the nanopore lies in the fact that the potassium concentration acts as an accurate chemical parameter responsible for setting well-defined electrostatic conditions on the pore walls. Hence, when the K^+ concentration is increased at a constant ion concentration, the population of net negative charges fixed on the pore walls decreases, thus giving rise to a neutral pore (Fig. 4).

As expected, upon gradually increasing the fraction of potassium ions in the electrolyte bath the rectification properties of the nanofluidic device start to decrease as a result of the variation of net fixed charges on the pore walls, a process that could be referred to as supramolecular surface neutralization.

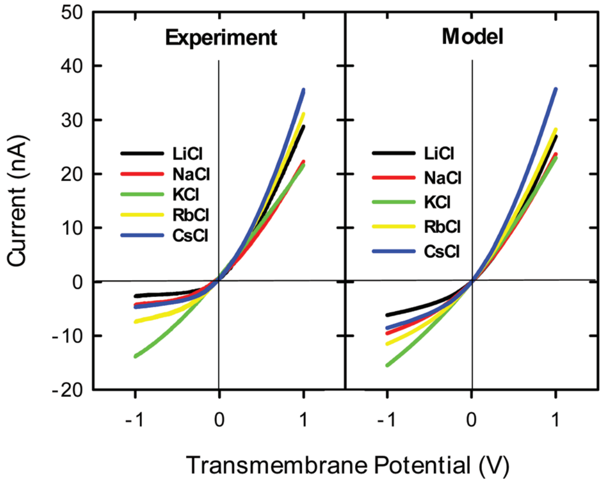

Fig. 5 (Left) Experimental *I–V* curves of an asymmetric nanochannel partially derivatized with 18-crown-6 units in the presence of different alkaline ions. (Right) Theoretical results obtained from a Poisson–Nernst–Planck (PNP) model. The fitting procedure provides an estimate of the average surface charge of the nanopore.

It is important to note that this recognition process ultimately leads to the emergence of well-defined rectification properties in the presence of a very specific chemical stimulus.

To demonstrate the specificity of this approach we performed similar experiments using different alkaline ions. Fig. 5 displays the *I–V* curves of a nanochannel partially derivatized with 18-crown-6 units in the presence of 0.1 M solutions of different chloride salts of alkaline metals. As expected, the functional response of the nanopore is extremely sensitive to the nature of the cation. The experimental results were described theoretically in terms of a continuous model based on the Poisson and Nernst–Planck (PNP) equations with the aim of estimating the effective surface charge of the nanopore walls in the presence of different alkaline cations (see the ESI† file for further details). A comparison between theory and experiment reveals an excellent agreement between the PNP theory and the experiments. Hence, from the modelling of the I–V response we were able to estimate that the nanopore surface charge in the presence of K^+, Na^+, Rb^+, Cs^+ and Li^+ corresponds to 0.1, 0.25, 0.275, 0.5 and 0.5 e nm^{-2}, respectively. The observed trend is in excellent agreement with the affinity of 18-crown-6 units to alkaline ions: $K^+ > Na^+ \sim Rb^+ > Cs^+ \sim Li^+$.

Conclusions

In summary, we showed the integration of ion-recognition elements into asymmetric single nanochannels to obtain highly functional chemical nanodevices. In particular, the use of crown ethers as recognition elements provides a unique tool to manipulate and finely tune the surface charge of the pore walls in a very specific manner. Our experimental evidence describing the use of surface-grafted 18-crown-6 groups and exploiting the K^+ dependent chemical equilibrium of these recognition units demonstrates that fine-tuning of the ionic transport by presetting the environmental K^+ concentration is achievable and enables a high degree of control over the ion transport properties of the system. In other words, the effective surface charge of the nanofluidic device can be adjusted *via* regulation of the environmental K^+ concentration, thus indicating that the crown ether-decorated nanopore enables the tuning of the rectified permselective transport in close resemblance to a K^+-actuated "electrostatic nanovalve". In this context, dressing the inner walls of the nanochannel with different "hosts" could introduce a facile chemical route to create "multiplexed" nanofluidic channels with potential applications for estimating ion concentrations or to deplete a certain specific ion in the presence of others. We consider that these results can lead to new strategies for designing "smart" nanofluidic devices based on the interplay between the chemical richness of host–guest supramolecular chemistry and the remarkable physical characteristics of asymmetric nanopores.

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