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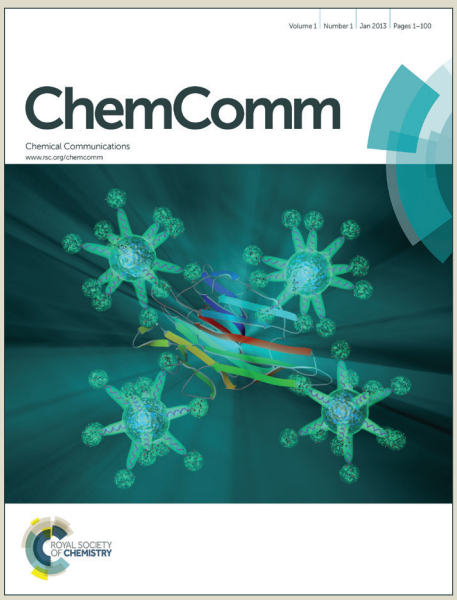





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Cite this: DOI: 10.1039/c0xx00000x

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COMMUNICATION

# Gating of Responsive Multiple Nanochannels by Ultra-Low Concentration of Saccharides

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***Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX***

**DOI: 10.1039/b000000x**

**We report a saccharide recognition system by modifying responsive copolymers on the solid-based multiple nanochannels. The ion transport through nanochannels can be regulated by ultra-low concentration of saccharides, which can switch nanochannels between the "on" and "off" state.**

Molecular recognition through saccharides and cell membranes plays a crucial role in physiological processes, such as immune response, fertilization, communication between the cells, and infections caused by pathogens.[1-4] Understanding the selective uptake and transportation of biomolecules with saccharide moieties through cell membranes is important for both fundamental research and medical treatment. Inspired by the ion pumps and ion channels in cells, artificial nanochannels have attracted increasing attentions because of their applications in the interdisciplinary fields of chemistry, physics, and materials science, especially for biosensing.[5-9] The minimal change on the inner surface of nanochannel can induce corresponding current change through the channel, which can be monitored by electrochemical detector.[10-12] Therefore, after the modification of the inner surface with appropriate functional ligands, nanochannels are capable to efficiently detect a series of biomolecules, such as DNA, proteins, saccharides, and so on.[13-21] The mimicking of saccharide recognition on cell membranes can be achieved by creating a recognition system into artificial nanochannel, which possesses gating mechanism similar to cell membranes. Recently, Li and co-workers reported a pH-gated recognition of saccharides by immobilizing the inner wall of single conical nanochannel with a monolayer of phenylboronic acid, which demonstrates the potential of nanochannels for saccharide recognition.[22] However, saccharides quite resemble water due to their hydroxyl group arrays, making it difficult to recognize saccharides at a low concentration close to *in vivo* condition. The design of more sensitive and reliable systems becomes the biggest challenge.

Responsive polymers are able to undergo physical or chemical changes as responses to small external stimuli in the environmental conditions, which have been widely used for biosensors, bio-separation, controllable drug release, delivery, and so on.[23-25] The integration of responsive polymers with nanochannels leads to the generation of smart devices which can respond to single/multiple external stimuli, e.g., pH, temperature, light, and so on.[26,27] Sun and co-workers have previously reported a kind of saccharide-responsive copolymer interface material.[28-31] Mediated by the cooperative hydrogen bonding (H-bonding) interactions, the recognition of saccharide molecules induces the conformational change of copolymer chains. This process is accompanied by the change of the wettability of the copolymer film. Herein, we report a saccharide recognition system by modifying responsive copolymers on the multiple nanochannels of porous anodic alumina (PAA) membrane. The wettability change of the nanochannel inner surface is triggered by the recognition of saccharide molecules. Therefore, the ion transport through nanochannels can be regulated by ultra-low concentration of saccharides, which can switch nanochannels between the on- and off- state.

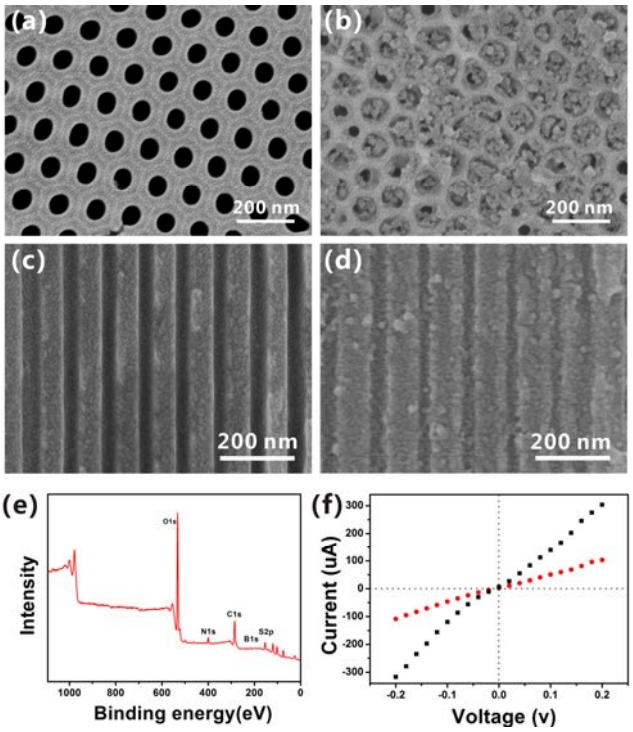


**Fig. 1** (a-d) SEM characterizations of PAA membranes before (a,c) and after (b,d) copolymer modification. (e) XPS spectrum of PAA membrane after copolymer modification. (f) I-V curves for the PAA membranes before (black) and after (red) copolymer modification in 0.5 M NaCl solution.

The fabrication of responsive nanochannels is based on PAA membrane, which is an ideal multiple nanochannel material with high pore density and well-defined tuneable nanochannels.[32,33]

Straight through-hole PAA membranes with an average pore size of 60 nm were employed. PAA nanochannels were chemically modified with chirality-responsive copolymers poly(3-(acryloylthioureido) phenylboronic acid-*co*-*N*-isopropyl acrylamide) [P(ATPBA-*co*-NIPAAm)] through a two-step process. First, the inner surface of nanochannels was functionalized with vinyl group by vinyl trichlorosilane. Then a "thiol-ene" click reaction was carried out between the vinyl group on surface and thiol group of copolymers to obtain responsive nanochannels (details in ESI).[34-37]

The modified nanochannels were characterized by scanning electron microscopy (SEM), X-ray photoelectron spectrometry (XPS), and contact angle measurement. As shown in Fig. 1a-d, the porosity of PAA membrane reduces significantly after modification. The cross section view of the modified nanochannels clearly shows that the polymer brushes are grafted onto the inner wall of nanochannels. Compared with bare membrane (Fig. S1), signals of N1s and S2p with binding energies of 399.4 eV and 162.2 eV appear in the XPS spectrum of modified membrane (Fig. S2 and Fig. 1e), which originate from the responsive copolymers. The recognition of saccharide induces the conformational change of copolymer chains and a subsequent wettability change of the copolymer on surface (Fig. S3). The modified nanochannel was also characterized by measuring the ionic current across the channels.[38] The membrane was mounted in between a two-compartment electrochemical cell. The electrolyte was 0.5 M NaCl solution. The immobilization of responsive copolymers on the inner wall hinders the ion transportation across the nanochannels, and leads to a decrease of in the transmembrane ionic current (Fig. 1f).

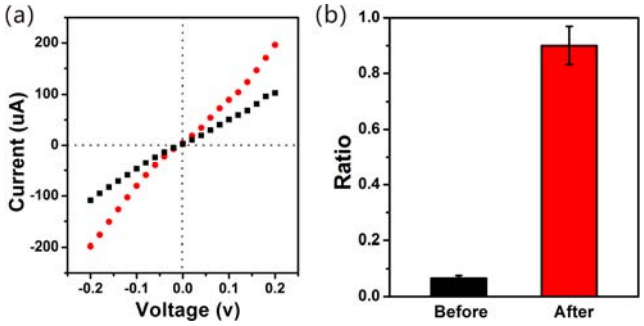


**Fig. 2** (a) I-V curves for the modified nanochannel in the absence (black) and presence (red) of 100 nM glucose. (b) Current change ratios at +0.2 V for the nanochannel in the presence of 100 nM glucose before (black column) and after modification (red column).

The gating of this nanochannel system by saccharides was evaluated. After exposing modified nanochannels in the electrolyte containing 100 nM saccharide for 10 min, the ionic current sharply increases (Fig. 2a). Fig. 2b shows the ionic current change ratios (defined as $(I-I_0)/I_0$) before and after copolymers modification of the nanochannels in the absence and presence of 100 nM glucose. It is evident that the modified channel displays good responsiveness to glucose. Previous studies have indicated that saccharide molecule can bind with saccharide recognition unit phenylboronic acid group in P(ATPBA-*co*-NIPAAm). Mediated by thiourea group, it then interrupts the intramolecular H-bonding within the PNIPAAm chains, making the chains hydrophilic.[29] In the channel system, the recognition of saccharides can be transduced into the electronic signal change. The interaction between saccharide and copolymer improves the hydrophilicity of inner surface and increases the ionic flux through the channel, which results in a switching from low current state (off-state) to high current state (on-state). Moreover, we repeatedly measured the transmembrane ionic current at +0.2 V after immersing the modifed membrane in blank electrolyte for 10 min and in 100 nM glucose solution for 10 min (see Fig. S4). The cycling experiment clearly shows the reversible gating property of the nanochannels.

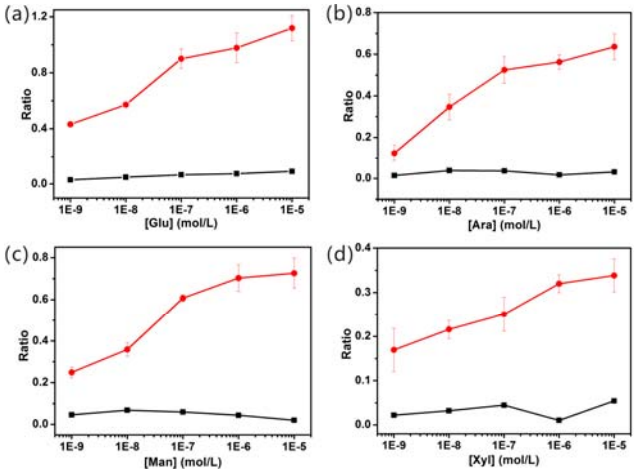


**Fig. 3** Curves of ionic current change ratios at + 0.2 V for nanochannels changing with concentrations in four saccharide solutions. Black curves: bare nanochannels; Red curves: modified nanochannels. (a) glucose (Glu); (b) arabinose (Ara); (c) mannose (Man); (d) xylose (Xyl).

In order to test the generality of this effect, we selected four different saccharides (glucose, arabinose, mannose, and xylose) with different concentrations, and repeated the experiments. Fig. 3 shows curves of ionic current change ratios at +0.2 V for nanochannels before and after copolymer modification changing with concentrations in four saccharide solutions. Although nanochannels exhibit different responsiveness to four saccharides, a similar trend for the changes of ionic current change ratios can be observed. Take glucose for example, when the bare channels were exposed to glucose in the concentration range 1 nM-10 μM, no significant change in the ionic current was found; whereas the ionic current through modified channels gradually increased as the concentration of glucose increased. It should be noted that even the concentration of glucose decreased to 1 nM, the modified channels still exhibited responsiveness with an ionic current change ratio of about 40%.

An important aspect for the recognition of saccharides is the selectivity. We chose four common biomolecules (vitamin C, glycine, urea, and cysteine) and repeated the same experiment under the same condition to evaluate the recognition selectivity of copolymer modified nanochannels. Fig. 4 shows the current change ratios for the nanochannels in electrolyte upon addition of 100 nM vitamin C, glycine, urea, cysteine, and glucose, respectively. It is obvious that the copolymer-modified nanochannel displays convictive saccharide-specific discrimination and no response to other interferents. The high selectivity of modified nanochannels towards saccharides originates from two aspects. Firstly, due to the three-component

design of copolymer, the interaction between the inner surface and saccharides is highly selective. Secondly, the nanochannel-based strategy also significantly enhances the selectivity of this method for complex samples.

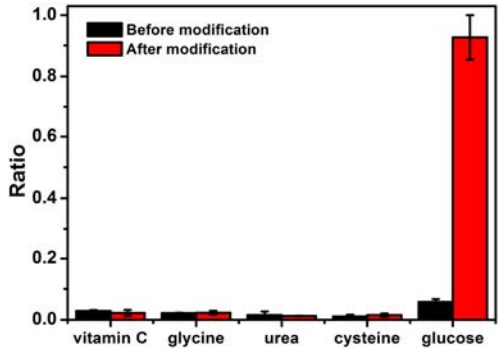


**Fig. 4** Current change ratios for the modified nanochannels in 0.5 M NaCl solution upon addition of 100 nM vitamin C, glycine, urea, cysteine, glucose, respectively.

In conclusion, we have described the construction of a saccharide recognition system based on solid-based multiple nanochannels. Taking advantages of the three-component composition of copolymers and cooperative H-bonding interaction among the functional units, the nanochannels can be gated by saccharides at nanomolar level. This work is a step towards the simulation of the recognition process in living organisms. This artificial nanochannel system also provides a new platform for the development of sensing devices that could be employed in practical applications.

This work was supported by National Natural Science Foundation of China (21105078) and the Fundamental Research Funds for the Central Universities (2013-IV-059).

## Notes and references

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† Electronic Supplementary Information (ESI) available: details of experiments, scheme for the modification of nanochannels, XPS spectra of PAA membrane, contact angle results, cycling experiment results. See DOI: 10.1039/b000000x/

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