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Gas-Breathing Polymer Film for Constructing of Switchable Ionic Diodes

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ABSTRACT

Carbon dioxide (CO_2) as one of the major byproduct of cellular metabolism mediates many fundamental behaviors, whose detection is associated with the activation of protein ion channels expressed on the olfactory sensory neurons. Inspired by this biological phenomenon, we developed extraordinary gas-sensitive ion channel, reconfigurable ionic diode and bionic ion pump on the basis of growth of gas-responsive polymer film, which can be rendered hydrophilic with the CO_2 stimulus of and hydrophobic with the N_2 stimulus. In particular, by alternatively purging CO_2/N_2 into the solutions which are placed on both sides of the channel embedded in the polymer membrane, the smart polymer-coated channel can be either closed or opened, which is independent of voltage polarity. Most intriguingly, under the asymmetric stimulation with pH pairs (pH 6.5||pH 9.0) or with gas inputs (CO_2||N_2) for both sides of the channel, change in voltage polarity can switch the channel between close status and open status, leading to construction of reconfigurable fluidic diode. Furthermore, by combination of gas inputs and voltage polarity, each of both gates of the channel can be individually manipulated, which are very important prerequisites for construction of bionic ion pump that can be operated under physiologically mild conditions. It is envisaged that this new progress in bionic pore/channel field will hold great prospects for the application of this kind of biomimetic device in energy storage, sample filtration and seawater desalinization.

Keywords: Ionic diode, Gas-responsive polymer brush, Track-etched membrane.

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INTRODUCTION

Carbon dioxide (CO_2) has been widely involved in natural activities. The ecosystem has evolved a comprehensive set of CO_2-responsive pathways to make a balance. CO_2 as one of the major byproduct of cellular metabolism mediates many fundamental behaviors, whose detection is associated with the activation of protein ion channels expressed on the olfactory sensory neurons [1-9] and transportation through biological gas channel[10, 11]. It will be intriguing to design artificial gas-responsive ion channel, ionic diode and ion pump by mimicking the gas-responsive pathway existing in the living system. Until now, no artificial gas-responsive ion channel, ionic diode and ion pump on the basis of the thin polymer film supported on track-etched membrane have been constructed, although many biomimetic pore/ionic systems have been built up on the basis of immobilization of organic molecules, polymer, and biomolecules onto the pore/channel[12-23].

In recent years, abiotic devices that mimic the function and structure of biological counterparts are alluring increasing attentions. Among these artificial designs, incessant endeavors have been devoted to imitating ion channels, which mainly comprise engineered protein ion channels[24], solid nanopores[20, 25-27] in ultrathin membrane, asymmetric pores[28, 29] in polymer membrane and glass nanopores[30, 31]. Heretofore, many bioinspired ion conducting channels are designed based on artificial nanopore with one gate, which can be switched on and off by various external stimuli such as voltage[32, 33], temperature[34], light[35], ion[36], pressure[37], ATP[38, 39] and pH[40, 41]. More recently, Jiang group invented a biomimetic ion pump based on nanochannel with two gates[13]. In that pioneering study, two different responsive polymer brushes were grafted on each end of the ionic channel and each gate can be switched from on to off or vice versa independently/synchronously by pH stimuli.

Among those external stimuli, pH stimulus is very appealing and easily accessible, which has been applied to change the size, surface charge and wettability of the channels. However, many operation cycles that require repeated addition of acids and bases into the solution can degrade the switching capability of artificial ion channel and ion pump due to the salt accumulation in the solution. While substituting gas stimuli for pH has several distinct advantages: (1) Salt accumulation due to repeated addition of various pH solution can be eliminated, which can diminish the performance of biomimetic device; (2) Drastic conditions such strong acid and strong base can be replaced by much more mild operation conditions; (3) The whole system can be easily restored to previous status even after many cycles of operations. Furthermore, another common feature for previous external-stimuli responsive ion channels is that responsive monolayer is grafted inside the channel[16, 18-20]. When the channel/pore is in close status, the leakage and switching efficiency is highly diameter-dependent. Insufficient growth of responsive polymer leads to the failure and leakage of artificial ion pump, whereas overgrowth of responsive polymers will deteriorate the performance of the channel. It will be more encouraging for scientists to develop more intelligent materials and devices with leakage-free property and high switching efficiency.

In this work, we develop an ionic channel device both of whose entrances are covered by gas-breathing polymer film, which possess the properties of artificial ion channel, ion pump and ionic diode. Each gate of this ionic channel can be manipulated individually or synchronously. Purging CO_2 into buffer solution (pH 7) on both sides of the channel membrane can render the polymer films positively charged and hydrophilic, leading to the ion transport though the polymer films and to the "on" status of the channel. Whereas, the polymer films can be switched back to hydrophobic status and the channel is completely shut down when the solutions on both

sides of the channel membrane were purged with N_2 or replaced with buffer solutions with pH≥7. Except synchronous manipulation of both polymer films on both sides of the channel membrane, each gate can also be individually operated by combination of gas (or pH) and voltage inputs, which are very important prerequisites for construction of bionic ion pump. Most interestingly, under the asymmetric stimulation with pH pairs (pH 6.5||pH 9.0) or with gas inputs (CO_2||N_2), change in voltage polarity can switch the channel between close status and open status, leading to construction of reconfigurable ionic diode. The alternative passing of CO_2/N_2 into the solution can allow each gate of the channel to be operated repeatedly for many cycles, which fully eliminates the salt accumulation and degradation of performance. The second advantage lies in that this approach prevents any leakage and lifts the strict requirement on the size of the channel as well. It is envisaged that this new progress in bionic pore/channel field will hold great prospects for the application of this kind of biomimetic device in energy storage, sample filtration and seawater desalinization.

EXPERIMENTAL SECTION

Fabrication of Channel: PET (polyethylene terephthalate) membranes (diameter = 3 cm, thickness = 12 μm) that had been irradiated with heavy ions of 2.2 GeV kinetic energy to create single track and multi tracks through the membrane were obtained from GSI, Darmstadt, Germany and referred to as the "tracked" membranes. NaOH, HCOOH, Na_2CO_3 and KCl were purchased from Beijing Chemical Reagent Company (Beijing, China). 2A1 was purchased from Dow Corning. All of the chemicals were at least analytical grade. To obtain conically shaped pore, each side of the PET membrane was treated with UV light (4 mW/cm^2) for one hour,

respectively to allow the activation of the polymer foil. Polymer membrane was sandwiched between two half compartments each of which contained etching solution (6 M NaOH) and stopping solution (1 M HCOOH plus surfactant 2A1), respectively and the etching temperature was maintained at 40℃. The whole etching process was controlled by monitoring current through the membrane; one volt potential difference was applied. The current remained zero as long as the pore did not break through the membrane. The current after the breakthrough can be monitored via a picoammeter/voltage source(Keithley 6487, Keithley Instruments, Cleveland, OH), when the desired current was reached, the etching process was stopped by replacing the etching solution with the stopping solution to neutralize the etching solution in the pore. After first step etching, the membranes were thoroughly washed with purified water and dried under nitrogen flow. The membrane after first step etching is immersed into a vial containing 2 M NaOH at 65 for 10 minutes. The diameters of the conically shaped channel are obtained by measuring the corresponding diameters of multi-track membrane etched under the same experimental conditions.

Polymer Film Growth Via Surface-Initiated ATRP: Nascent membranes after chemical etching were immersed in an aqueous solution containing 1% w branched PEI(MW: 25,000) for 8 hours in room temperature, and then the samples are wash with ethanol, followed by Nitrogen flow drying. The surface immobilization of ATRP initiator was adapted from previous published procedures[42]. Briefly, 2-bromopropionyl bromide (10 mM) was coupled via amide linkage to the PEI coated membrane surface in buffered solution (pH 10, 32 mM Na_2CO_3). The reaction mixture that was cooled in the ice bath, and bubbled with N_2 for 30 minutes lasted for 24 h under N_2 protection. Regents for polymer brush growth including H_2O, methanol, 2-(Diethylamino)ethyl methacrylate, CuBr and N,N,N′,N′,N″-pentamethyldiethylenetriamine

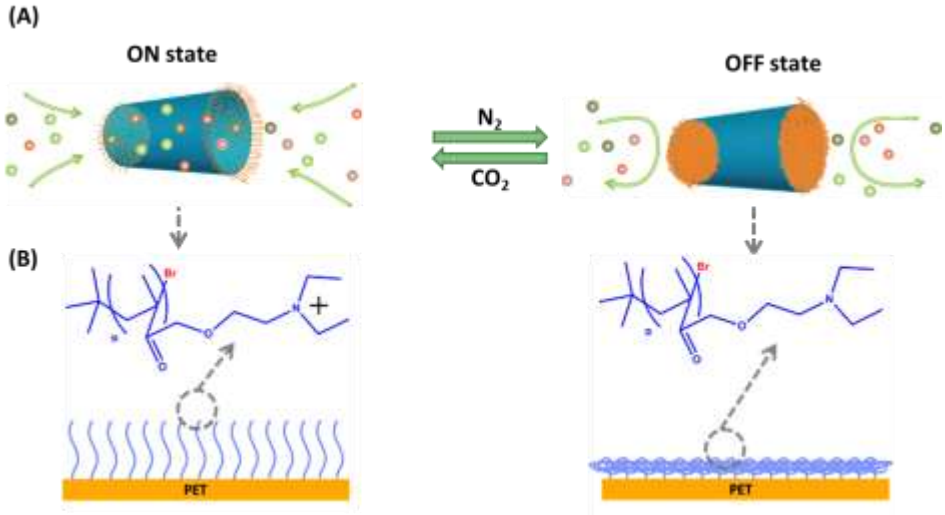
(PMDETA) were purchused from JK Chemical (Beijing, China) and used without further purification. The polymerization reaction takes place for 30 minutes under N_2 protection. After the polymerization, the PET film was washed with methanol and dH_2O for several times to remove the redundant CuBr and the other reagents. Then the PET film was dried in the N_2 flow and put in the vacuum for subsequent characterization.

Current-Versus-Voltage Measurements (I-V curve): The prepared PET film with asymmetrical pore inside was sandwiched between two half components filled with conductive electrolyte in order to measure the I-V curve. The current though the conical-shaped pore was measured with a Keithley 6487 picoammeter (Keithley Instruments, Cleveland, OH) and Ag/AgCl electrodes in a custom-designed electrolyte cell. Transmembrane potentials from -1V to +1V was scanned to obtain each I-V curve. All experiments were carried out in room temperature. Buffered solutions (0.1 M PBS, 0.1M KCl) at pH 3.0, 5.0, 7.0 and 9.0 were used for stimulation. For gas stimulation, buffered solution (0.1 M PBS, 0.1M KCl) at pH 7 after purging of the solution with CO_2/N_2 for desired time was used to open/close the gate, respectively and each gate of the asymmetric pore can be independently operated.

RESULTS AND DISCUSSION

Endowing the artificial pore with switching features responsive to external stimuli has been the scholastic pursuit in the past several years. Until now, several approaches based on pH[40, 41], metal ion[36], voltage[32, 33] and ligand[43] have been built up to mediate the open/close status of the pores. In this study, the gas-responsive polymer film has been adopted to cover both entrances of the ionic channel. Figure 1A illustrates the reversible switching process accomplished via alternatively purging CO_2 and N_2 into the buffer solutions close to the track-etched polymer film. In the presence of CO_2, the pH value of the buffer solution drops, leading to the protonation and

137 extension of the polymer and subsequent "on" status of the polymer film (Figure 1B). Purging
138 the buffer solution with N_2 could displace the CO_2 and leads to the increase of pH value, which
139 provokes the deprotonation of polymer film and drives the polymer film toward hydrophobic and
140 collapsed status. The whole modification process is presented in the supporting materials (Figure
141 S1 in supporting information). Additional XPS and NMR characterizations have also proved
142 each modification step (Figure S2 and S3 in supporting information).



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144 **Figure 1.** (A) Cartoon illustration of "on" status and "off" status of cylindrical channel covered
145 by polymer films under the symmetric stimulation with gas inputs. (B) charged status due to
146 protonation of polymer film and collapsed status due to deprotonation of the polymer film.

147 To prove the successful growth of gas-responsive polymer film on the channel membrane,
148 SEM images were acquired (Figure 2), including the cross section, the top and bottom sides of
149 the channel. Continuous polymer films fully covered both sides of the channel membrane after 1
150 hour growth (Figure 2B and 2C) and the thickness of the polymer film was measured to be 1.6
151 μm (Figure 2F). It is clear that domains with various sizes exist in the polymer film and have
152 much larger size than the channel diameter (200 nm). From the cross section image (Figure 2E),
153 the polymer film growth majorly happened on the faces of the channel membrane and the inside

of the channel was left empty without polymer growth. To the best of our knowledge, growth of gas-responsive polymer film on the channel membrane has not been reported yet.

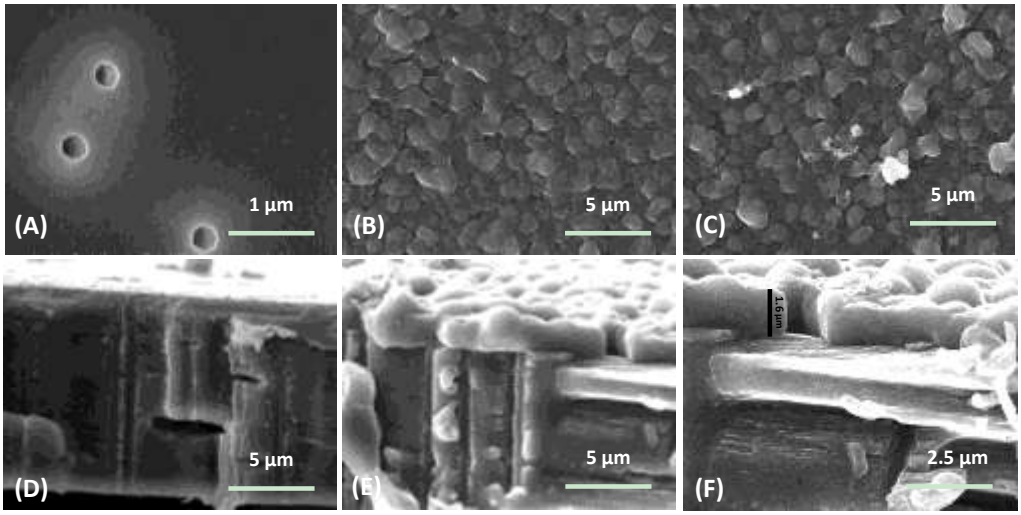

Figure 2. SEM images of cylindrical channels with diameter of 200 nm before and after polymer film growth. The side view (A) of track-etched membrane (A), the top and bottom views (B and C) of cylindrical channel embedded in PET membrane after polymer film growth; Cross section of the cylindrical channel before (D) and after (E and F) polymer film growth. The thickness is measured to be around 1.6 µm.

Gas-responsive polymer film on the track-etched membrane exhibited repetitive switching between hydrophobicity and hydrophilicity (Figure 3). Contact angle measurements (Figure 3) illustrate that the contact angle of water droplet on the nanopore surface showed contact angle of 16.17^{o} after the membrane grafted with polymer film was immersed in pH 5. Whereas after the membrane was immersed in pH 7 buffer and air dried, the contact angle increased to 54.76^{o} (Figure 3B). The contact angle can be further increased if pH 9 solution was used. This result clearly manifested that protonation/deprotonation of the polymer film on the membrane can lead to change in the hydrophilicity/hydrophobicity of the membrane surface. Instead of employment of buffer solutions adjusted with NaOH to certain pH values, buffer solution reversibly purged

171 with CO_2/N_2 can also efficiently switch the membrane status between big contact angel (57.50^o)
172 and small contact angle (20.69^o) (Figure 3A).
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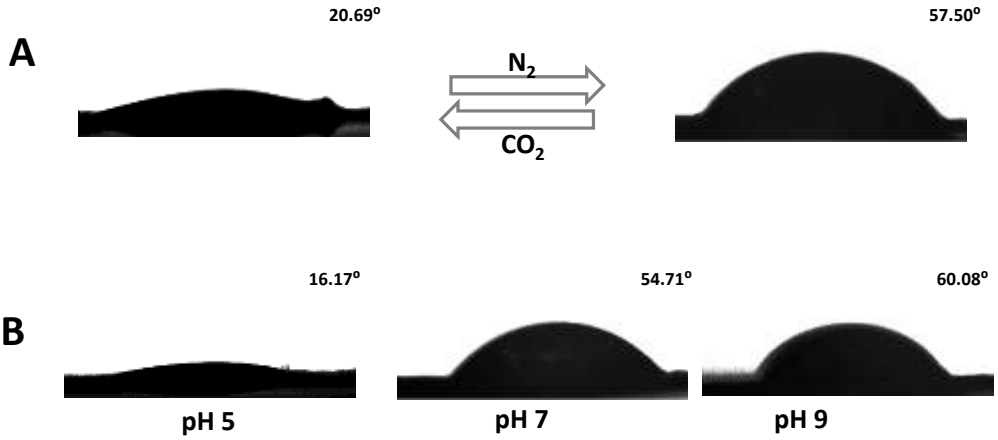

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176 **Figure 3.** Contact angle measurements of the polymer film (PDEAEMA: poly
177 2-(Diethylamino)ethyl methacrylate) grafted onto the channel membrane. (A) Measurements
178 were carried out after polymer film was immersed in neutral electrolyte solutions purged with
179 CO_2 and N_2 for 30 minutes, respectively and was nitrogen dried. (B) Measurements were carried
180 out after polymer film was immersed in each electrolyte solution (pH 5, 7 and 9). 0.1 M PBS
181 containing 0.1 M KCl was applied as the electrolyte solution.

182 Previous study[19] proposed that toggling between hydrophobicity and hydrophilicity can
183 play an extremely important role in opening/closure of the channel on the basis of the pH-tuned
184 polymer brush immobilized into the channel. Unambiguously, it has been clarified that
185 conformation variation is a negligible factor which contributes to the ion transport through this
186 kind of channel. In contradiction with immobilization of the polymer brush inside the channel,
187 the present study entails only growth of gas-responsive polymer film on both sides of the
188 track-etched membrane, which can fully prevent leakage of the channel embedded in the
189 membrane once the channel is switched to "off" status. Notably, several previous nanochannels
190 with responsive property are majorly related with conformation switching of the monolayer

immobilized inside the nanochannel surface. Obviously, this is not the same as our case. As shown in Figure S4 (supporting information), in the presence of different pH values (5, 7 and 9), the morphology of the polymer film characterized by SEM did not show any distinct difference and the channel membrane was consistently covered by continuous polymer film, which means that the conformation switching is not the important factor contributing to ion transport through the channel. Furthermore, the thickness of the polymer film was up to 1.6 μm, which was several times larger than the diameter of the channel embedded in the PET membrane.

Except XPS and NMR characterization of polymer film growth, each step in the modification process was confirmed and characterized with current-versus-voltage curve (I-V curve). In this study, we presented I-V curves for one cylindrical channel with diameter of 200 nm and another conical-shaped channel with tip diameter of 130 nm. The cylindrical channel in the PET membrane was fabricated under the same conditions as those in Figure 2. The I-V curve (black curve in Figure 4A) of the single cylindrical channel without any modification showed linear shape without any rectification, which is measured in 100 mM PBS solution containing 1M KCl at pH 3. Further tandem modification with branched PEI and initiator not exhibited much difference in the current-versus-voltage curves. As compared to cylindrical channel, asymmetric channel after PEI adsorption (red curve, Figure 4C) presented upward curve with strong rectification. For both cylindrical and asymmetric channel, the polymer film growth fully blocked ion transport through the channel when being measured in 0.1 M KCl with pH 7 solution (curves in dark cyan, Figure 4A and C).

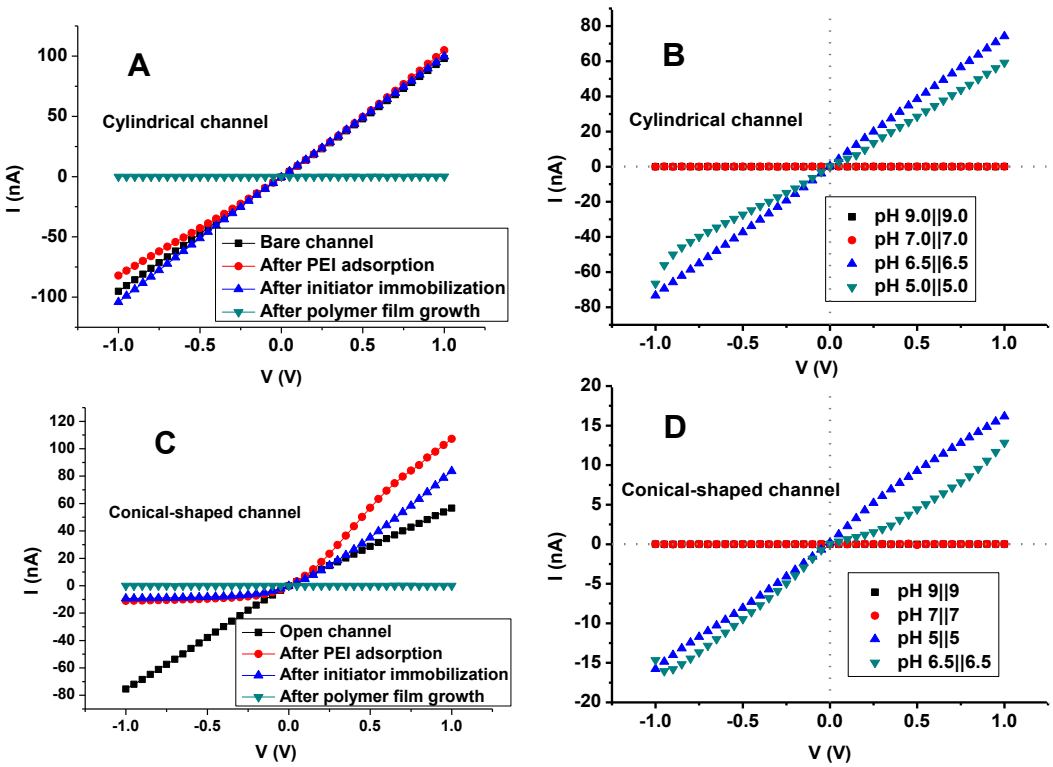

Figure 4. (A) I-V characterization of each modification step for the cylindrical channel with diameter of 200 nm. (B) pH-dependent switching between "on" status and "off" status of the cylindrical channel covered by polymer film. (C) I-V characterization of each modification step for conical-shaped channel with tip diameter of 130 nm and base diameter of 957 nm. (D) pH-dependent switching between "on" status and "off" status of the conical-shaped channel covered by polymer film. Electrolyte solution for experimental measurements in (A) and (C) is 0.1 M PBS containing 1 M KCl at pH 3; Buffer solution for experimental measurements in (B) and (D) is 0.1 M PBS containing 0.1 M KCl at pH 7.

Both cylindrical and asymmetric channel covered with gas-responsive polymer film can be switched on/off by the pH stimuli or gas inputs (Figure 4B and 4D). Ion channel behaviors common to biological nanopore can be faithfully reproduced: when the pH value is above 7, the channel can be fully blocked with symmetric pH 7||7 and 9||9 conditions; when pH value is decreased towards 6.5, the channel can be restored to "on" status with symmetric pH 6.5||6.5 and pH 5||5 conditions. If the on/off current ratio was defined as the ratio of the current

measured at pH 6.5/6.5 to the current measured at pH 9/9, the on/off current ratio corresponding to 1 V was calculated to be 34418 for the cylindrical channel with diameter of 200 nm. Furthermore, the current corresponding to the "off" status measured at 1V was only 2.1 pA, which was defined as the leaking current. To the best of our knowledge, these were the biggest on/off current ratio and the lowest leakage current. As for asymmetric channel with tip diameter of 130 nm and base diameter of 957 nm, the on/off current ratio and the leaking current were 6736 and 1.9 pA, respectively, which is calculated from data in Figure 4D. This is to say, the geometry of the channel was not critical factor for determining the switching efficiency. The quality of gas-responsive polymer film itself could play a crucial rule. The pH-adjusted ion transport through the channel both sides of which were covered with gas-responsive polymer film was highly consistent with the pH-dependent switching between hydrophobicity and hydrophilicty.

Features belong to ionic diode can be exactly reproduced by this channel system symmetrically functionalized with the same gas-responsive polymer films. It has to be noted that previous ionic diodes based on channel were almost accomplished via asymmetric functionalization with differently charged ligands or polymer brushes[13, 14, 16, 44, 45]. In the current study, symmetric growth of the same gas-responsive films was executed on both sides of the channel. As shown in Figure 5A, the upward curve with nonlinear shape was divided into two parts including part I and part II. The corresponding cartoons about the ion transportation were also illustrated on the right side. When the buffer solution at pH 6.5 was placed on the left side of the channel and another same solution at pH 9 was placed on the right side of the channel, the voltage polarity decided the status of the channel. When positive voltage was applied on the right side of the channel (part II in Figure 5A), the slope of the I-V curve corresponded to "on" status ,

which was exactly same as the case when both sides of the channel were placed with buffer solutions at pH 6.5 (Figure 4B). When negative voltage was applied (part I), the channel was completely shut down. The "on" status and "off" status of the channel was exchangeable by swapping the position of the buffer solutions as shown in Figure 5B.

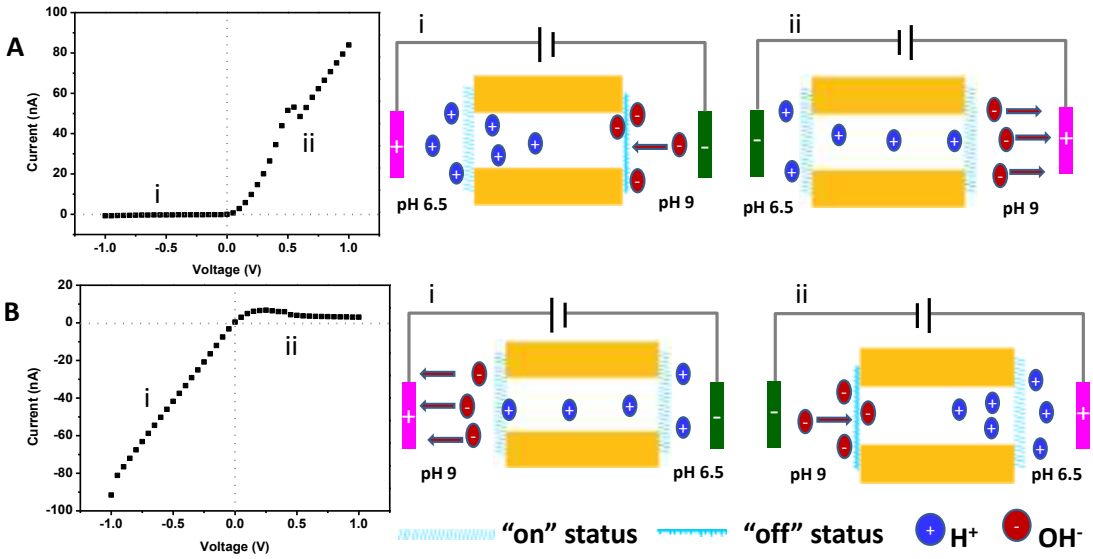

Figure 5. Switchable ionic diode pair (A and B) based on the same cylindrical channel covered by gas-responsive polymer films. Each curve is divided into part I and part II. The corresponding cartoons illustrate the ion transport mechanisms under pH stimulation and voltage polarity. When the OH^- ions accumulate around the polymer film, this gate is shut down due to deprotonation and hydrophobicity; when the OH^- ions decrease and H^+ ions dominate around the polymer film, the gate open up due to protonation and hydrophilicity.

Why did voltage polarity play such a significant impact on the ion transport through the channel when the channel covered by two same polymer films was stimulated under asymmetric pH conditions? To better understand this phenomenon, we have to understand the movement of ions under the applied voltage. When negative voltage (Part I in Figure 5A) was applied in chamber containing the buffer solution at pH 9, the negative ion such as OH^- in the same chamber moved towards the polymer films and the concentration of OH^- around the film increased, leading to closure of the polymer film due to deprotonation and hydrophobicity. When

positive voltage (Part II in Figure 5B) was applied in chamber containing the buffer solution at pH 9, the negative ion such as OH^- in the same chamber moved away from the polymer films and the concentration of OH^- around the film decreased. Although the H^+ ion in another chamber containing electrolyte solution at pH 6.5 moved away from the polymer film adjacent to the chamber which contained the electrode applying positive voltage, its concentration still overwhelms that of OH^-, leading to the "on" status of the polymer film due to protonation of the polymer film and hydrophilicity. This similar mechanism can be also applied to explain the download curve observed in Figure 5B. Now, it is also very clear that by combining stimuli such as pH and gas with voltage polarity, each one of the two gates can be selectively shut down or open up, which is the important prerequisite for construction of ion pump with alternative gates and occluded states.

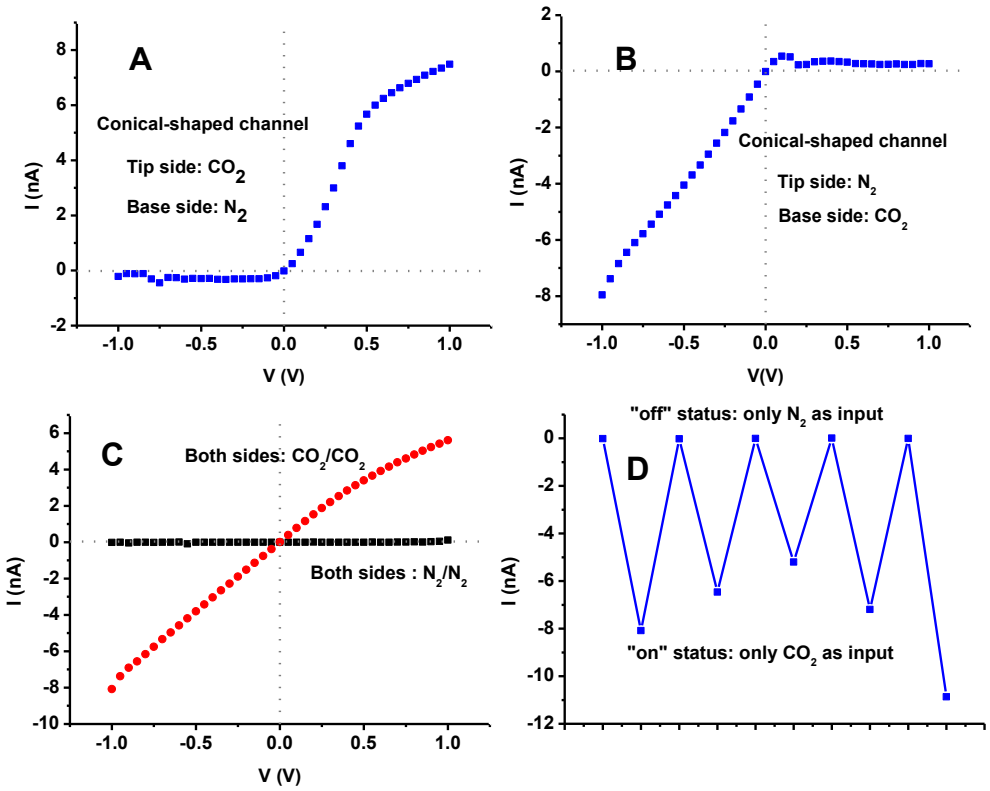

Figure 6. Green gas (CO_2 and N_2) breathing ionic diode (A and B) and ion channel(C). In case (A), the electrolyte solution in the tip side of the conical-shaped channel was purged with CO_2 for 20 minutes and the base side electrolyte solution was purged with N_2 for 20 minutes. In case (B), the electrolyte solution in the tip side of the conical-shaped channel was purged with N_2 for 20 minutes and the electrolyte solution in the base side was purged with CO2 for 20 minutes. In case (C), electrolyte solutions in both sides were purged with CO_2 or N_2. (D) Repetitive switching between "on" status and "off" status upon alternative purging with CO_2 and N_2: each point value was measured by applying -1 V voltage.

Once again, features of this type of diode device which can be explained by the above mechanism can also be realized by asymmetric channel covered by the two same polymer films (Figure S5 and S6, Supporting Information). Most interestingly, this kind of ionic device is not only pH-actuatable but also highly CO_2/N_2-stimulable. By utilization of asymmetric channel as a gas-responsive prototype, we carried out a series of experiments to challenging this kind of channel device with gas stimuli. Upon purging CO_2 into the buffer solution (0.1 M PBS, pH 7, 0.1 M KCl), the pH value changed towards 5; with passing N_2 into the solution, the pH value of

7 was recovered. Once the tip and base side solutions of the conical-shaped channel were purged with CO_2 and N_2, respectively, the I-V curve demonstrated extreme high rectification behavior and unprecedented on/off current ratio with upward nonlinear shape (Figure 6A). One unique feature for this channel device is that the current rectification can be fully inversed. Upon purging N_2 and CO_2 into the tip and base side solutions of the same device, the downward I-V curve with excellent high rectification and on/off current ratio was obtained (Figure 6B). The rectification inversion and current direction were highly reversible, which was only dependent on the gas pair ($CO_2||N_2$ or $N_2||CO_2$). Additionally, as shown in Figure 6C and 6D, more than 5 times switching cycles between "on" status and "off" status have been presented in this study under the alternative stimulation with symmetric gas pair ($N_2||N_2$ and $CO_2||CO_2$).

In this paragraph, we would like to clarify that under the unsymmetrical stimulation, the competition between H^+ and OH^- plays a dominant role in the status of the polymer film. By using conical-shaped channel as prototype, we compared three different pH pairs (pH 5||7, pH 6.5||7, and pH 6.5||9). As shown in Figure S7, only pH 6.5|| 9 among three pH pairs offered the opportunity to observe the ionic diode behavior: the "on" and "off" statuses are determined by voltage polarity. Figure S7A and S7B conclusively affirmed that H^+ won and only "on" status was present, which was indicated by the curve shape of the I-V curve. Therefore, the combination of voltage polarity and the appropriate pH pair is crucial for opening and closure of each polymer film gate.

CONCLUSIONS

In summary, we describe a new ionic diode with both entrances covered by the same gas-responsive polymer films. Under the symmetric stimulation with pH pairs (5||5, 6.5||6.5, 7||7 and 9||9) or with gas pairs (CO_2||CO_2 and N_2||N_2), features common to ion channel can be faithfully reproduced including "on" status and "off" status. Under the asymmetric stimulation with gas pairs (CO_2||N_2, N_2||CO_2), ionic diode based on gas-responsive polymer films supported on channel membrane can be constructed with the unprecedentedly high rectification ratio more than several thousands and the smallest leaking current around several pA. Most importantly, the diameter and geometry of channel are no longer the critical determining factors that influence the switching efficiency and contribute to current leakage, whereas the quality of the ionic device is more reliant on the polymer films. Except construction of artificial ion channel and ionic diode, this new device can also be applied to build ion pump since both gates of this device can be individually manipulated by combination of gas pairs (or pH pairs) and voltage polarity. Therefore, this device developed herein holds great promise in further applications such as energy field, sample filtration and seawater desalinization.

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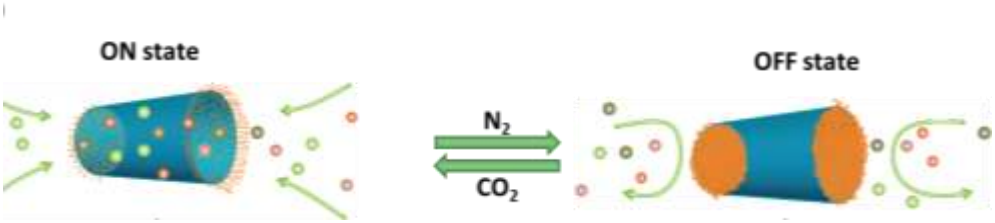
479 **TOC**

480 We describe a new fluidic channel with both entrances covered by the same gas-responsive
481 polymer films. Under the symmetric stimulation with pH pairs (5||5, 6.5||6.5, 7||7 and 9||9)
482 or with gas pairs (CO_2||CO_2 and N_2||N_2), features common to ion channel can be faithfully
483 reproduced including "on" status and "off" status. Under the asymmetric stimulation with gas
484 pairs (CO_2||N_2, N_2||CO_2), fluidic diode based on gas-responsive polymer films supported on
485 channel membrane can be constructed with the unprecedentedly high rectification ratio



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