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PERSPECTIVE

Construction of biomimetic smart nanochannels with polymer membranes and application in energy conversion systems

Liping Wen,^{a,b} Ye Tian,^{a,b} Jie Ma,^{a,b} Jin Zhai^{*ab} and Lei Jiang^{a,b}

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Learning from nature has inspired the creation of intelligent devices to meet the increasing needs of the advanced community and also to better understand how to imitate biology. As one of biomimetic nanodevices, nanochannels or nanopores aroused particular interest because of their potential applications in nanofluidic devices, biosensing, filtration, and energy conversions. In this review we have summarized some recent results mainly focused on the design, construction and application in energy conversion systems. Like biological nanochannels, the prepared smart artificial nanochannels fabricated by ion track-etched polymer membranes and smart molecules show a great potential in the field of bioengineering and biotechnology. And these applications can not only help people to know and understand the living processes in nature, but can also inspire scientists to study and develop novel nanodevices with better performance for the mankind.

1. Introduction

Nanochannels (frequently mutual use to nanopores), embedded within cell membranes in living systems, are formed of membrane proteins and the corresponding complexes that open (ions are allowed to pass) and close (ion transport is blocked) in

response to ambient stimuli by gating mechanisms to selectively transport ions through cell membranes, which are necessary for performing proper cellular and biological processes.^{1–5} However, such nanochannels and their embedding lipid bilayers are susceptible to deterioration in changing external environments such as pH, temperature, mechanical stress, etc. To overcome the drawback, much effort has been focused on the construction of artificial nanochannels that emerged as “abiotic” analogues to mimic the function of biological nanochannels.⁶ Early work in this field used biomolecule α -hemolysin nanopores as nanodevices to sensing, measuring DNA sequence and filtrating.^{7–10} The latter focus has gradually moved towards solid-state

^aOrganic Solid Laboratory, Center for Molecular Sciences, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, P. R. China

^bKey Laboratory of Bio-Inspired Smart Interfacial Science and Technology of Ministry of Education, School of Chemistry & Environment, Beihang University, Beijing 100191, P. R. China.
E-mail: zhaijin@buaa.edu.cn



Liping Wen

current scientific interests are mainly focused on construction and application of biomimetic smart nanochannels.



Ye Tian

Ye Tian is currently an assistant professor at the Institute of Chemistry, Chinese Academy of Sciences (ICCAS). She received her BS degree from Northeast Normal University (Changchun, China) in 2006. Then she joined Prof. Lei Jiang's group as a PhD candidate. She received her PhD in physical chemistry from ICCAS in 2011. Her current scientific interests are focused on biomimetic smart single nanochannels.

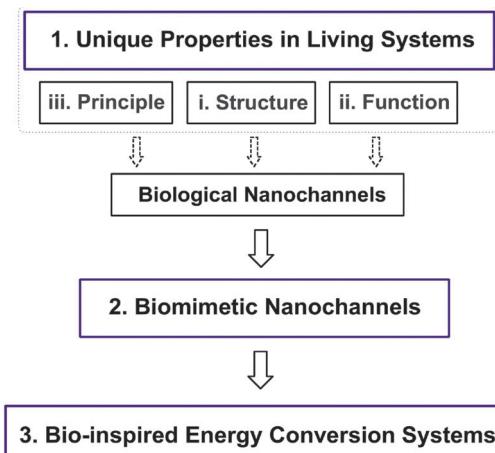


Fig. 1 The design and fabrication of BSNC and application in energy conversion whose inspiration comes from the living systems.

nanochannels due to their higher durability. These solid-state nanochannels can be made by organic materials,^{11–13} inorganic materials^{14,15} or hybrid materials.^{16–18} Among these nanochannels,



Jie Ma

Jie Ma acquired his BS degree in physics from Peking University (Beijing, China) in 2003 and his PhD degree in microelectronics from the Institute of Microelectronics, Chinese Academy of Sciences (Beijing, China). He is currently an assistant professor at the Institute of Chemistry, Chinese Academy of Sciences. His research interests are the novel design and construction of biomimetic materials and systems, especially surface materials with special wetting and liquid propelling properties, and micro/nano-fluidic systems.



Jin Zhai

Professor Jin Zhai received her PhD. degree in inorganic chemistry (1999) from Peking University. Then she worked as a postdoctoral fellow at the Institute of Chemistry, Chinese Academy of Sciences (ICCAS). She joined ICCAS in 2001 and in 2009 the School of Chemistry and Environment, Beihang University (BUAA) as a full professor. Her scientific interests are focused on the photoelectric conversion materials with micro- and nanostructures, bio-inspired interfacial materials and has published over 80 papers.

ion track-etched nanochannels in polymer membranes have been found to show some properties similar to biological channels, such as selectivity, voltage-dependent current fluctuations, ionic rectification current and ionic gating.^{19–23} More importantly, these nanochannels are easy to functionalize due to their functional groups on the inner surfaces of the nanochannels. Herein, we present a strategy for the design and construction of biomimetic smart nanochannels (BSNC) with ion track-etched polymer membranes, and their application in energy conversion systems.^{24–27}

This review is organized into five sections. The first section gives a brief introduction to nanochannels (natural ones as well as synthetic ones) including a strategy for the design and construction of BSNC and applications in energy conversion systems. The second section summarizes a comprehensive overview of design and construction of synthetic nanochannels including materials, fabrication procedures and modification methods. The third section provides some samples of BSNC: single responsive nanochannels, dual responsive nanochannels, while the fourth section presents two concrete examples of energy conversion systems based on the BSNC. Lastly, we will give our conclusions.

2. Design and construction of BSNC with ion track-etched polymer membranes

Biomimetics means taking ideas from nature and developing novel materials and devices whose functions are the same as in living systems. It contains a bionic principle,^{28,29} bionic structure,^{30–32} bionic function,^{33,34} etc. As shown in Fig. 1 we provide three principles for the construction and application of BSNC: (i) selection of a unique property found in living systems, which can serve as “bio”-inspiration; (ii) design and construction of BSNC whose inspiration comes from the nanochannels in living system; (iii) application of these BSNC in energy conversion systems whose inspiration stems from the principle of living systems.^{35–37}

2.1 Unique functions in living systems

Nanochannels, as a vital part of the living organisms can be defined as channels with at least one cross section dimension in



Lei Jiang

Lei Jiang is currently a professor at ICCAS, and Dean of School of Chemistry and Environment, Beijing University of Aeronautics and Astronautics. He received his PhD degree (1994) from Jilin University (Tiejin Li's group). He then worked as a postdoctoral fellow in Prof. Akira Fujishima's group in Tokyo University. In 1996, he worked as a senior researcher in Kanagawa Academy of Sciences and Technology under Prof. Kazuhito Hashimoto. He joined ICCAS in 1999. In 2009, he was elected academician of CAS. His scientific interests are focused on bio-inspired, smart, multiscale interfacial materials.

the nanometre range. Nanochannels, such as cation ion channels (Fig. 2A–E), anion ion channels (Fig. 2F) and neutral nanochannels (Fig. 2G) in natural cells can open and close precisely in response to ambient stimuli to complete normal physiological activities. For example, H^+ channels play important roles in the process of photoelectric conversion of the retina.^{38,39} The Cl^- channel is vital to sperm fertilizing capacity and male fertility.^{40,41} These important functions can be realized by the features including ionic selectivity, ionic rectification and ionic gating. Selecting unique properties in biological systems and using them as bio-inspiration can make people obtain smart materials and devices. Recent progress provides a series of nanochannels which can realize the unique functions in living systems in respond to external stimuli, *e.g.*, pH,^{42–49} ions,^{50–53} temperature,^{54,55} ligand^{56,57} and electricity.⁵⁸

2.2 Fabrication of artificial solid state nanochannels with polymer membranes

Solid-state synthetic nanochannels^{59–67} emerged as “abiotic” analogues to mimic the function of biological nanochannels. Herein we only introduce one kind of solid-state nanochannels which are fabricated by ion track-etched polymer membranes. Before etching, polymer membranes should be first irradiated with heavy ions that can create damage zones on the polymer membranes which were chemically etched to obtain nanochannels. The shapes and structures of the etched channels depend on how much faster the track is etched in comparison to the bulk materials, which are removed isotropically in the process of etching.⁶ The etching process is shown schematically in Fig. 3A. The opening angle φ of the resulting channel is determined by the ratio v_{track} and v_{bulk} . The higher the track-etched velocity v_{track} , the more cylindrical the channel is. In order to develop a single channel with a specific shape and size, one should select an appropriate apparatus, etchant

and monitoring of the etching process so as to stop it at the right time. The etching conductivity cell is shown in Fig. 3B (left) in which a polymer membrane is separated between two halves of the cell. To create a cylindrical or dual conical channel, both halves of the cell are filled with etchant, and a voltage of typically 1 V is applied across the membrane to constantly monitor the current flow through it during the etching process. Before etching through, the membrane has an infinitely large resistance, and no current flow from it. Once the channel opens, a sudden current jump can be observed. Herein we can obtain the needed shapes and sizes of the nanochannels by changing the conditions such as etching time, etchant temperature, *etc.* If using an asymmetric track-etching technique, one can obtain a single conical nanochannel in polymer membranes (Fig. 3B right). The fabrication procedure is demonstrated as follows: etching proceed from one side only, the other half of the cell contains a stopping reagent that can neutralize the etchant as soon as the channel opens, thus slowing down the further etching process. The popular polymers used to prepare conical nanochannels and their corresponding conditions are shown as follows: to the poly(ethylene terephthalate) (PET) membrane, 9 M NaOH solution is used as etchant and 1 M KCl/HCOOH as stopping reagent; to polyimide (PI), NaClO is used for oxidative etching, neutralized on the opposite side of the membrane by KI; for polycarbonate (PC), the typical etching conditions for the production of cylindrical pores are 6 M NaOH at 50 °C. Conical geometries can be obtained by increasing the bulk etch rate either by addition of 20–30% methanol to 9 M NaOH used at room temperature or by applying higher voltages during the etching process. As the materials that are prepared for solid state nanochannels can not respond to some stimuli, one should modify some smart materials on the inner surfaces of the nanochannels and obtain smart functions.

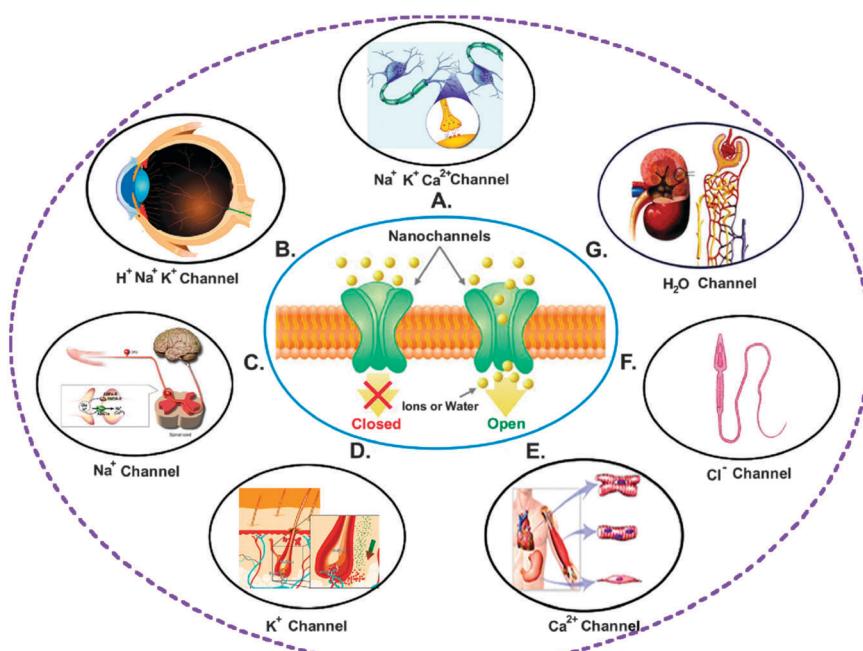


Fig. 2 Types and unique functions of nanochannels in living systems: (A–E) cation ions nanochannel; (F) anion ions nanochannel; (G) neutral molecule channel.

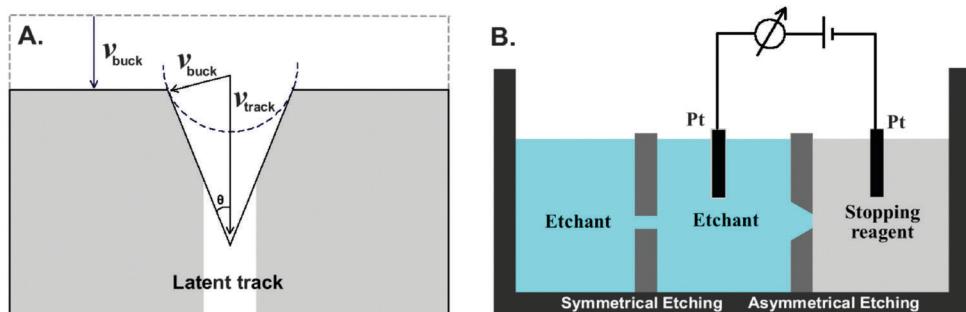


Fig. 3 Schematic of an etched ion track and an etching conductivity cell.

2.3 Characterization of nanochannels fabricated by ion track-etched polymer membranes

Many methods can be used to characterize the properties of solid state nanochannels, such as scanning electron microscopy (SEM), atomic force microscopy (AFM), *etc.* A typical SEM image of nanochannels in ion track-etched PET membrane with $\sim 10^{7-8}$ channels cm^{-2} are shown in Fig. 4 from which one can measure the diameter of the base side of nanochannels. Except for this method, conductance measurements can also be applied for characterization of nanochannels. The conductance measurements were performed in the same conductivity cell used for the fabrication of single conical nanochannels in ion tracked polymer membranes, as shown in Fig. 3B. The polymer membrane containing a single conical nanochannel was mounted between the two halves of the conductivity cell, and both halves were filled with electrolyte solutions. Ag/AgCl electrodes were placed into each half-cell solution, and a picoammeter/voltage source (Keithley 6487, Keithley Instruments, Cleveland, OH) was used to apply the desired transmembrane voltage and obtain the measurement values. Associated with the data of SEM images and conductance values, one can estimate the tip diameter that can be evaluated by an electrochemical measurement of the ionic conductance, and the nanochannel filled with 1 M potassium chloride solution as electrolyte *via* the following equation:

$$d_{\text{tip}} = \frac{4LI}{\pi k(c)UD} \quad (1)$$

where d_{tip} is the tip diameter, D is the base diameter; $k(c)$ is the special conductivity of the electrolyte. For 1 M KCl solution at 25 °C is 0.11173 $\Omega^{-1} \text{ cm}^{-1}$. L is the length of the channel, which could be approximated to the thickness of the membrane after chemical etching. U and I are the applied voltage and the

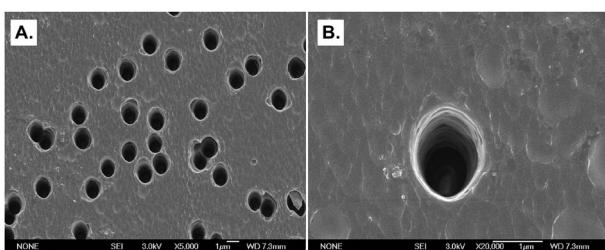


Fig. 4 SEM images of nanochannels in a track-etched PET membrane with $\sim 10^{7-8}$ channels cm^{-2} .

measured ionic current in the pore conductivity measurement, respectively.

2.4 Stimuli-responsive molecules and materials and modification techniques for fabrication of BSNC

Two routes can be used for the design and preparation of BSNC: (i) fabrication of smart nanochannels with functional materials directly; (ii) indirect method, modifying functional molecules and materials on the inner surfaces of the prepared nanochannels. To a simple responsive nanochannel, the first route is always used by us. While for the more complex responsive systems or functional materials in which nanochannels cannot be easily prepared, the second route may be the better choice, because modifying functional materials and molecules on the inner surfaces of the nanochannels is convenient and easy to make nanochannels smart. Herein, no matter which route is chosen to fabricate BSNC, the design and synthesis of suitable smart molecules are necessity. Fig. 5 lists some smart molecules described in the literature, *i.e.*, pH-, ions- temperature- electricity- and photo-responsive.⁶⁸⁻⁷⁵ The nanochannel's properties such as selectivity,¹³ ionic rectification current^{48,76-79} and gating^{3,43,45,52,80} can be changed by modifying these smart molecules on the inner surface of the synthetic nanochannel. Fig. 6 lists some popular modification approaches which are reported by the groups of Jiang,^{45,46,81} Siwy,⁸² Martin,⁸³ Azzaroni,⁸⁴ *etc.* Besides these methods, self-assembled monolayers (SAMs) from smart molecules with proper functionality have also been used for surface modification. Depending on the design, the synthesis and the combination of these responsive and functional materials with the synthesis solid state nanochannels, single responsive and even dual/multi responsive BSNC are possible. Some examples are listed in the next section.

3. Examples of a series of responsive nanochannels based on polymer membranes

Biological nanochannels can use their unique protein complex to selectively transport ions. Inspired by living systems, researchers have fabricated a series of smart nanochannels that can respond to external stimuli. Examples of these responsive nanochannels are shown as follows.

3.1 Single-responsive nanochannels

3.1.1 pH-responsive nanochannels. Among the many types of BSNC, pH-responsive nanochannels have been widely studied due to their important physiological functions in the

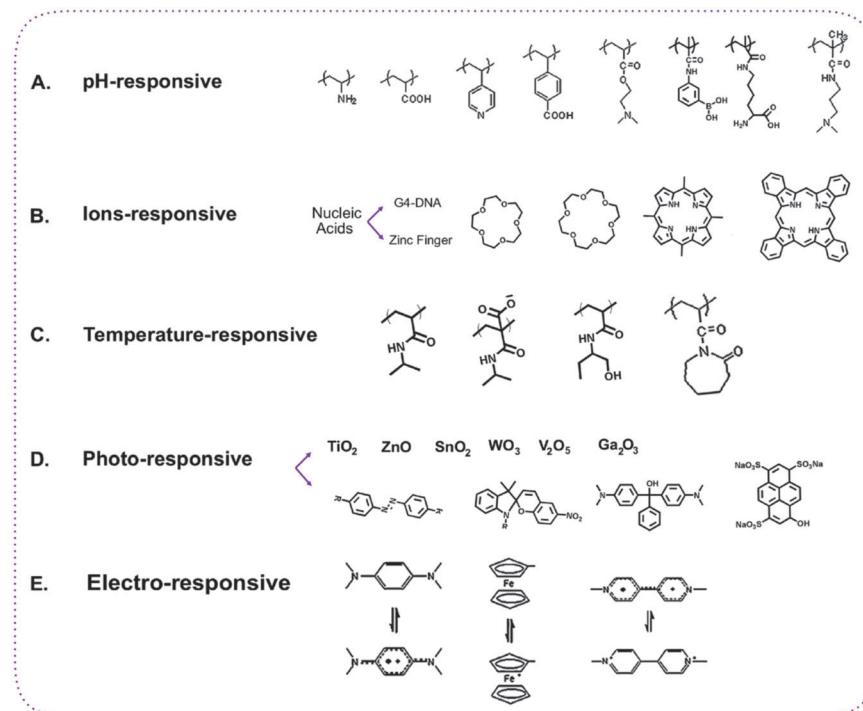


Fig. 5 Responsive molecules: (A) pH-responsive; (B) ion-responsive; (C) temperature-responsive; (D) photo-responsive; (E) electro-responsive molecules.

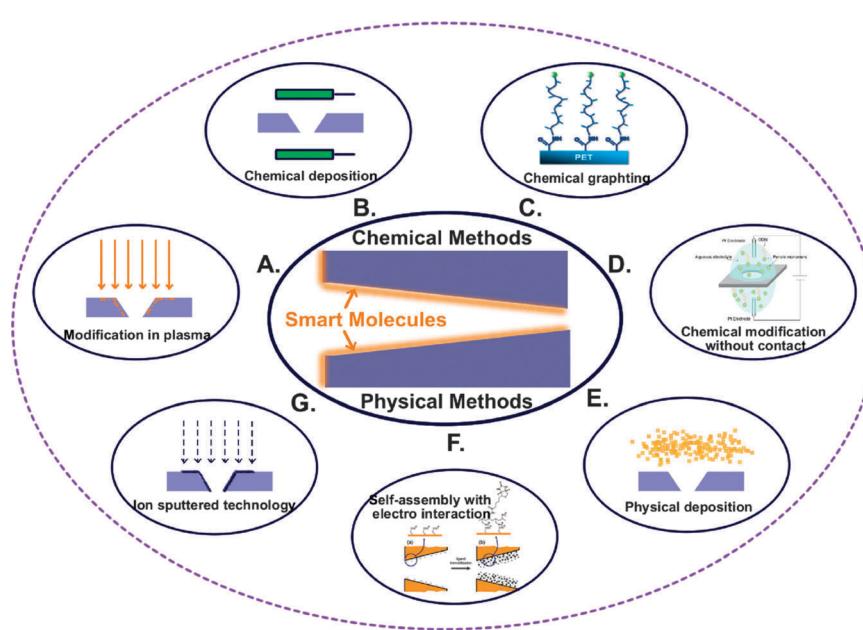


Fig. 6 Modification of responsive molecules onto the inner surfaces of nanochannels: (A) Plasma modification methods; (B) electroless deposition; (C) chemical modification; (D) contactless electrofunctionalization; (E) physical deposition; (F) electrostatic self-assembly; (G) ion sputtering technology.

living systems. Such a system can be easily obtained either by changing the surface charges or modifying the pH-sensitized molecules onto the inner surface of synthetic nanochannels. For example, Siwy reported single conically shaped nanochannels fabricated by ion track etching polymer membranes.⁴⁴ They found that the nanochannels behave as an ionic rectification current, where the cation ions flow from the narrow entrance to

the wide aperture of the channel. And such rectification is pH sensitive. When the pH values of the electrolyte are higher than the isoelectric point of the etched polymer surface, the surface will be negatively charged; otherwise the surface is protonized for adsorption of protons and loses its rectification properties (Fig. 7A). In 2007, also the Siwy group presented a single asymmetric nanochannel whose inner surface was patterned

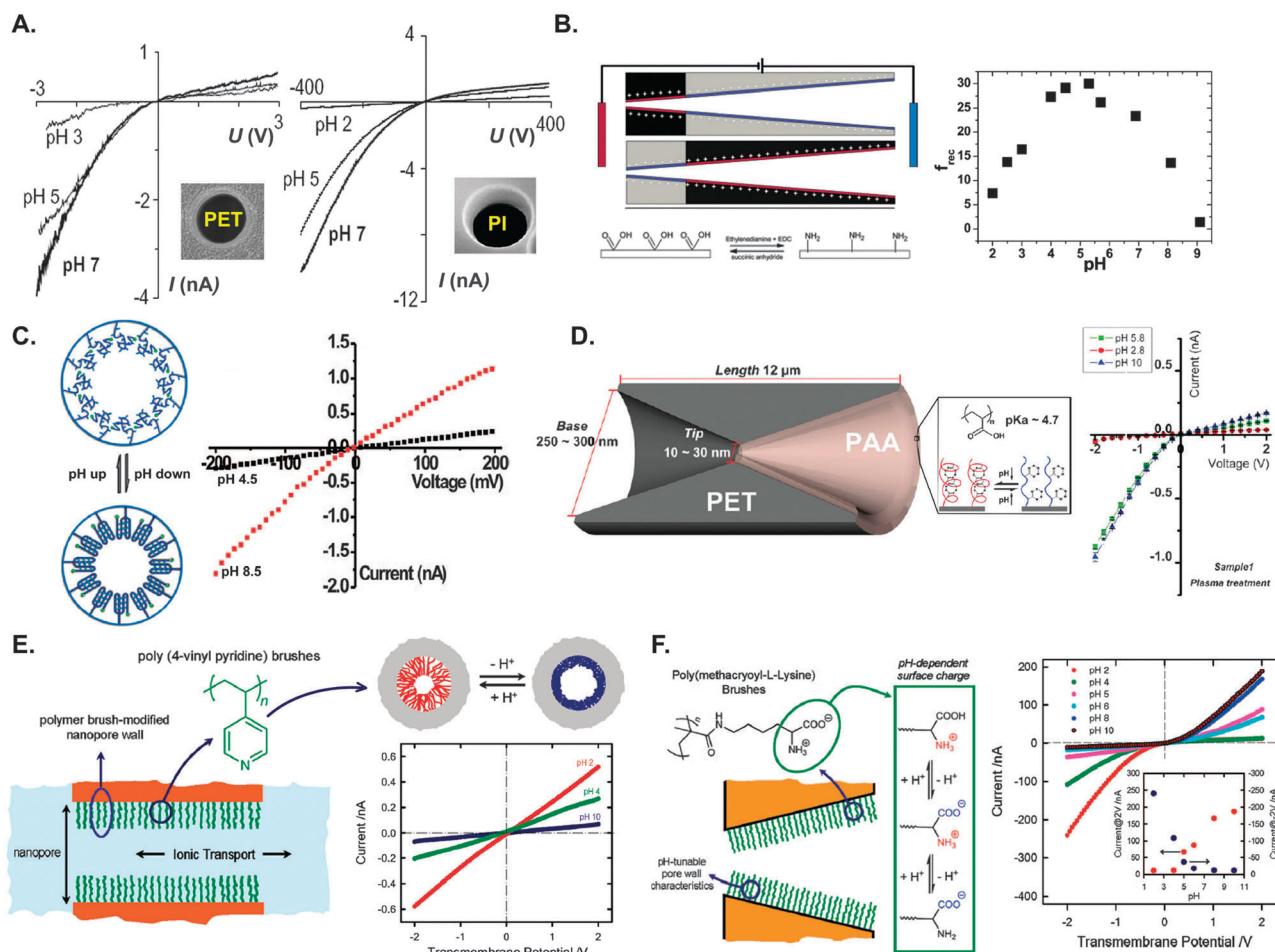


Fig. 7 pH-responsive nanochannels: (A) I - V characteristics of the original PET and PI single nanochannels recorded at symmetric electrolyte conditions. The measurements were performed in 0.1 M KCl at different pH. Adapted with permission from ref. 44. Copyright (2003) Elsevier; (B) Up: patterns of surface charge that lead to the formation of a nanofluidic diode; Down: dependence of the rectification degree f_{rec} at $\pm 2/-2$ V for a nanofluidic diode that was performed in 0.1 M KCl. Adapted with permission from ref. 82. Copyright (2007) American Chemical Society; (C) I - V properties were recorded under symmetric electrolyte conditions at pH 4.5 (black) and 8.5 (red) with the PET single nanochannel modified with DNA motors. The image describing DNA conformation is responsive to pH. Adapted with permission from ref. 45. Copyright (2008) American Chemical Society; (D) I - V properties of the single nanochannel with plasma asymmetric chemical modification under different pH conditions. Adapted with permission from ref. 46. Copyright (2010) Wiley-VCH; (E) I - V characteristics of a single cylindrical nanochannel modified with PVP brush in 0.1 M KCl at different pH. Adapted with permission from ref. 43. Copyright (2009) American Chemical Society; (F) Schematic describing the polymer brush-modified conical nanochannel. I - V curves corresponding to a single conical nanochannel modified with poly(methacryloyl-L-lysine) brushes measured at different pH values (using 1 M KCl as electrolyte). Adapted with permission from ref. 48 Copyright (2009) American Chemical Society.

after chemical modification to partially transform carboxyl groups into amino groups so that a sharp boundary between positively and negatively charged regions was created.⁸² This rectification property is not a typical pH responsive change of the original conically shaped nanochannel, and there is a maximum value in the middle range of the pH change from acidic to alkaline (Fig. 7B).

On the basis of these works, Jiang and Wang *et al.* developed a pH gating with a single asymmetric PET nanochannel and pH-sensitive DNA motors.⁴⁵ In low pH solution, the DNA motors fold into a densely packed rigid quadruplex i-motif structure that partially decreases the effective diameter of the nanochannel (Fig. 7C, left and down). While in high-pH solution, the i-motif structure DNA motors relax to a loosely single-stranded molecule with more negative charges, which

enhances the total ion conductance (Fig. 7C, left and up). The difference in ionic conductivity at the different pH values is shown in Fig. 7C (right). They thought the fabricated nanochannel-DNA system can provide an artificial counterpart of switchable protein-made nanochannels, which closely mimic the gating mechanism of acid sensing ion channels. On the basis of the pH-responsive DNA-nanochannel system, other pH gating ionic transport nanochannels has been developed by Jiang's group *via* an asymmetric plasma modification (Fig. 7D).⁴⁶ Such a pH-responsive nanochannel system can control both the asymmetric and the gating ionic transport properties. Fig. 7D shows I - V properties of the nanochannel after asymmetric modification, and there was a remarkable increase in the transmembrane ionic current when the pH changed from 2.8 to 10. This asymmetric ionic transport property displays

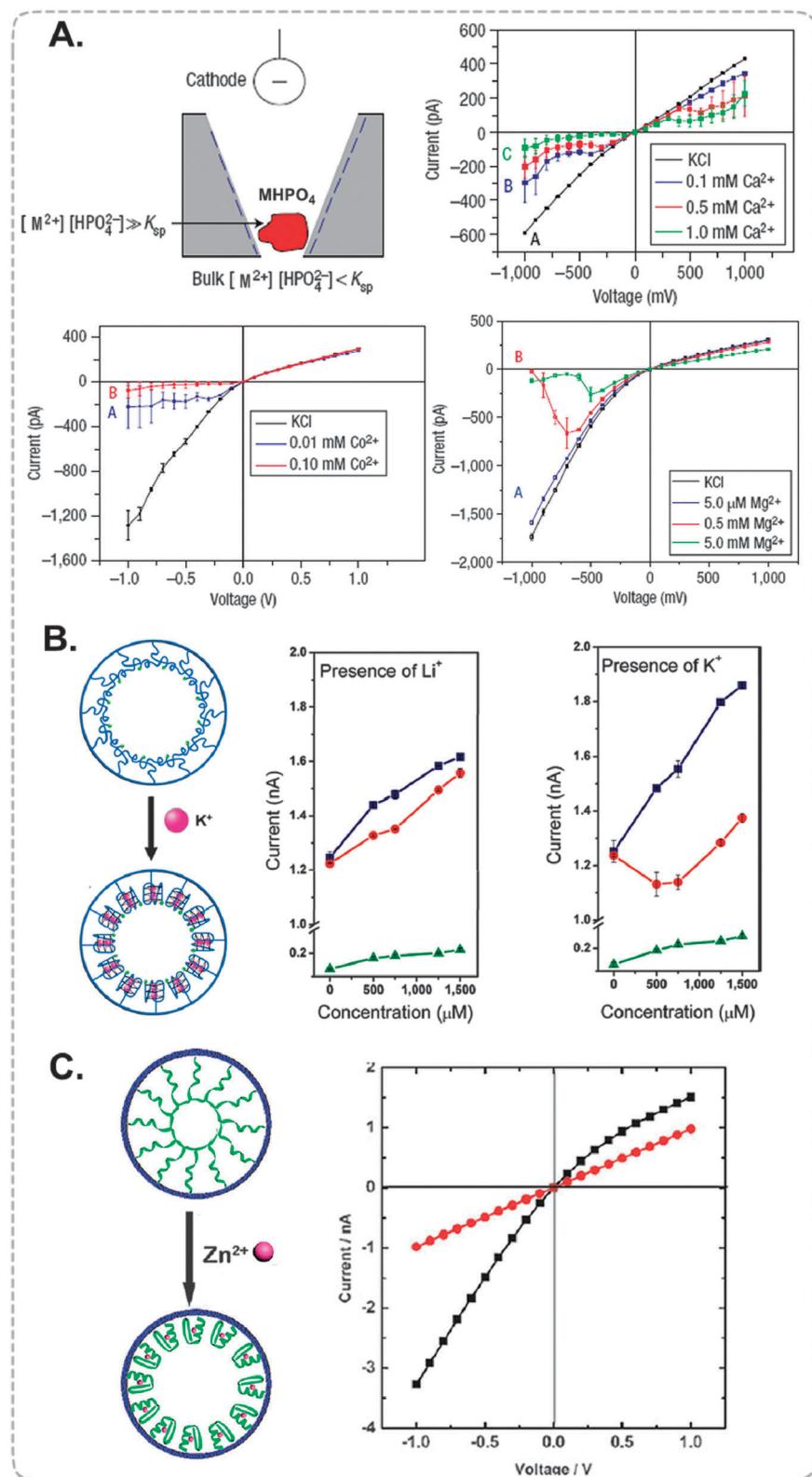


Fig. 8 Ion-responsive nanochannels: (A) calcium induced voltage gating in a single conical nanochannel. $I-V$ curves were recorded in 0.1 M KCl with 2 mM PBS buffer alone (black trace) and with varying divalent cation concentrations. Adapted with permission from ref. 94 Copyright (2008) Nature Publishing Group; (B) A biomimetic potassium responsive nanochannel that was constructed with G-quadruplex DNA and synthetic nanochannel. Current–concentration (Li^+ and K^+) properties of the single nanochannel before and after DNA motors attached onto the channel wall in Tris-HCl (5 mM, pH 7.2, at 23 °C). Adapted with permission from ref. 50. Copyright (2009) American Chemical Society; (C) a biomimetic zinc activated nanochannel: $I-V$ curves were measured in 0.1 M KCl before (black) and after (red) zinc fingers immobilization. Adapted with permission from ref. 51 Copyright (2010) The Royal Society of Chemistry.

the advanced feature of controlling over the pH-tunable asymmetric and the pH gating. At the same time, Szleifer and Azzaroni *et al.* developed a proton-gated nanochannel with a single cylindrical polymer nanochannel and pH-responsive polymer brushes (Fig. 7E, left).^{43,85} And the transmembrane ionic current can be controlled accurately by manipulating the proton concentration in the solutions. The mechanism shows the ionic current gating can be switched from an “off” state to an “on” state in response to a pH drop (Fig. 7E, right and up). The I - V curves of the single nanochannel modified with polyvinylpyridine (PVP) brushes at different pH was observed under the same applied bias. By changing the surface charges, they could control the channel conductivity and the gating switches. Then, they demonstrated several pH-tunable asymmetric single nanochannels by an integration of polymer brushes or amphoteric molecules into the inner surfaces of the synthetic nanochannels. Such pH-gating systems can display pH-tunable rectifying characteristics by simply varying the environmental pH (Fig. 7F, left).^{48,86,87} They found that at pH 2 the I - V curve displayed a well-defined rectification behavior which would imply the permselective transport of anionic species through the positively charged nanochannel (Fig. 7F, right). Moreover, they used a combined experimental and theoretical approach to address this topic. The results showed that the charge transport properties of single conical nanochannels functionalized with polymer brushes were highly dependent on the number of polymers assembled on the channel wall. They considered that modification of nanochannels, nanopipets, and nanoelectrodes using charged brushes, was also of importance in “soft nanotechnology”, provided that structural complexity, induced by nanoconfinement, could define the functional properties of self-assembled polymeric nanostructures.

3.1.2 Ion-responsive nanochannels. Metallic ions such as potassium,^{88,89} calcium,^{90,91} sodium⁹² and zinc⁹³ play crucial roles in modulating the normal body function by regulating within a certain range. Inspired by these nanochannels, Siwy and their co-workers demonstrated a calcium-induced voltage gating nanochannel by an addition of small amounts of divalent cations to a buffered monovalent ionic solution, which results in an oscillating ionic current through a conical nanochannel.^{52,53,94} They thought such behavior was caused by the transient formation and redissolution of nanoprecipitates, which temporarily block the ionic current through the channel (Fig. 8A). I - V curves were measured before and after adding Ca^{2+} in the presence of PBS, and they found nonlinear behavior occurred in the I - V curves; that is, larger amplitudes of voltage induced smaller ionic fluxes. While the calcium is substituted with other divalent cations such as cobalt and magnesium, similar results were obtained due to the formation of cations hydrogen phosphate precipitates (Fig. 8A). In 2009, Jiang and their co-workers developed a biomimetic potassium responsive single nanochannel that had an ion concentration effect and provided a nonlinear response to K^+ at a concentration ranging from 0 to 1500 μM (Fig. 8B).⁵⁰ The effective channel size was modulated by a potassium-responsive conformational change G-quadruplex (G4) DNA that immobilized onto the inner surface of a single nanochannel. On naked conditions, the conductance trends were similar regardless of adding K^+

or Li^+ (Fig. 8B). However, there was a remarkable difference after G4 DNA modification with the addition of K^+ . This nonlinear response phenomenon could be attributed to the structures of G4 DNA changing with K^+ addition, which can change the effective channel size and the transmembrane current. They later reported a biomimetic zinc activated nanochannel that was obtained by immobilizing zinc fingers into single polymeric nanochannels.⁵¹ Fig. 8C shows the naked single PET nanochannel that presented a slightly ionic rectification current due to its negative charge and conical shape. After modification with the peptides, the current decreased markedly, which could be charged by the volume exclusion mechanism resulting from the large-sized peptides. The artificial nanochannels prepared here not only mimic the biological ion channels from the conformational change mechanism, but also open up new avenues to exploit other systems with different intriguing functions.

3.1.3 Temperature-responsive nanochannels. Nanochannels activated by temperature changes are vital to the physiological process. Inspiration from these ion channels, many studies about thermal-responsive nanochannels have been developed based on thermal-responsive polymers and nanochannel membranes.^{54,55,95–100} Compared with pH- and ion-responsive nanochannels, such a system shows no ionic rectifying properties due to the uncharged polymer chains. Recently, both the Jiang⁵⁵ and Azzaroni⁵⁴ group reported simultaneously a temperature-responsive nanochannel based on an ion track etched polymer membrane. The biomimetic nanochannels all exhibit open-closed switching in the ionic permeability in response to the temperature by temperature-responsive poly(*N*-isopropylacrylamide) (PNIPA) brushes modified onto the inner surfaces of the nanochannel (Fig. 9A). At low temperature ($T < \text{LCST}$), PNIPA brushes remain swollen, thus decreasing the effective nanochannel size which is associated with the low conductance. Raising the temperature ($T > \text{LCST}$), the PNIPA brushes suffer a transition from a swollen to a collapsed state, thus leading to an increase of the effective size of the nanochannel (Fig. 9A) which is evidenced as an increase in conductance. Therefore, the thermal-responsive brushes act as a thermal-driven macromolecular gate controlling the ionic flow through the nanochannel. Asymmetry I - V curves are observed at low temperature and show ionic rectifying behavior, while the I - V curves become linear and ohmic if the temperature is elevated (Fig. 9B). If the temperature is down to room temperature, the I - V curves show ionic rectification again. Therefore, such a thermal-responsive nanochannel is reversible. It can be clearly seen that this temperature-responsive nanochannels pave a new way for controlling the preferential direction of ion transport in nanofluidics by modulating the temperature, which has the potential to build novel nanomachine with smart fluidic communication functions for future lab-on-chip devices.

3.1.4 Electro-responsivne nanochannels. Like other kinds of BSNC, electro-responsivne nanochannels can also be obtained by modifying the electro-responsive molecules and materials onto the inner surface of synthetic nanochannels. The dipole or charge will be changed when a potential is applied on these molecules and materials, such as metal, ferrocene and conductive polymers.^{70,101} For example, Martin and Siwy *et al.* reported a

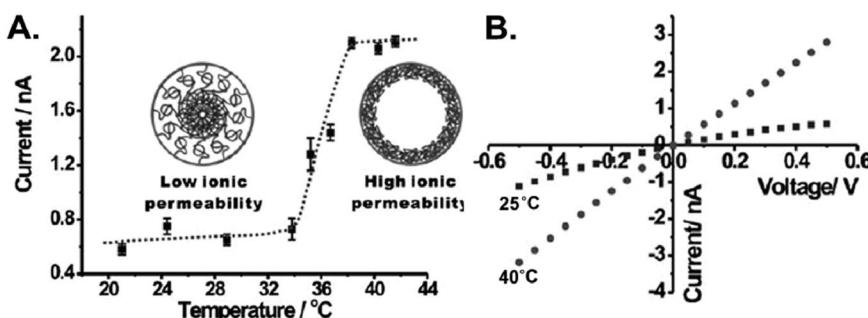


Fig. 9 Temperature-responsive nanochannels: (A) temperature dependence of the ionic current through the PNIPA-modified single metal-polymer nanochannel; (B) I - V curves measured on single conical gold-coated nanochannels with PNIPA modification at 25 °C (■) and 40 °C; Adapted with permission from ref. 55. Copyright (2010) Wiley-VCH.

nanochannel that can rectify the ion current *via* electromechanical mechanisms.¹⁰² Such a device is based on a conical gold single nanochannel and some single-stranded DNA molecules attached to the nanochannel's wall. Before modification, rectification can not be observed, because the diameter of tip side nanochannels is much larger than the thickness of the electrical double layer, while the DNA-containing nanochannels can rectify the ion current (Fig. 10A), that is, the DNA-containing nanochannels show an on-state at negative transmembrane potentials (anode facing the tip side of nanochannel) and an off-state at positive potentials (Fig. 10B). It was supposed that the electrophoretic insertion of the DNA into (off-state) and out of (on-state) the nanochannel entailed the ionic rectification phenomenon. When DNA chains are inserted into the channel opening under the force of an applied potential, they will partially occlude the way for ion transport and yield weak ionic conductance. Then an off-state is obtained. Even in the on-state, the DNA chains also partially occlude the size of the nanochannel and increase the nanochannel resistance. Recently, Siwy's group developed an ionic transistor based on single conical nanochannels in a polymer membrane with an insulated gold thin film "gate".¹⁰³ The transmembrane current can be changed from the rectifying behavior of a typical conical nanochannel to the almost linear behavior seen in cylindrical nanochannels by changing the electric potential at the "gate." The mechanism for this change in transport behavior is thought to be the enhancement of concentration polarization induced by the gate.

3.1.5 Ligand-responsive nanochannels. Living cells use protein nanopores and channels to communicate chemically and electrically with the extracellular environment.⁴ The protein channels open and close in response to stimuli such as changing the presence of a specific small-molecule ligand. Nowadays, several studies have been focused on developing abiotic nanochannels that mimic these gating functions.^{56,57} For example, Martin's group investigated the effects of chemical ligands complexed 18-Crown-6 (18C6) that can dramatically change the ionic transport properties of such conically shaped abiotic nanochannels.⁵⁶ They found that, when adding 18C6 to the electrolyte solution on one side of a conical nanochannel membrane, ionic rectification current can be found flowing through the nanochannel. And such chemical rectification is only observed when the cation of the electrolyte is complexed by 18C6 (*e.g.*, K⁺), and the diameter

of the tip side of conical nanochannel is the same as the molecular dimensions. This chemical rectification can either augment or diminish the inherent electrostatic rectification observed with the tip side diameter of nanochannels. Fig. 11A shows I - V curves with the 18C6 added to the solution facing the tip side of the conical nanochannel. When positive transmembrane potentials are applied, the positively charged K⁺-18C6 complex is driven electrophoretically away from the membrane surface, and the 18C6 has no effect on the I - V curve. Charge is carried through the nanochannel by free K⁺ ions migrating from base to tip (upper inset, Fig. 11A). When negative transmembrane potentials are applied, both the excess uncomplexed K⁺ and the positively charged K⁺-18C6 complex are driven electrophoretically into the tip side of the nanochannel. In this case, the measured current at any applied potential decreases with an increasing concentration of 18C6. Fig. 11B shows analogous I - V curves for 18C6 added to the solution facing the base side of the conical nanochannel. When negative transmembrane potentials are applied, the positively charged K⁺-18C6 complex is driven electrophoretically away from the membrane surface, and the 18C6 has no effect on the I - V curve. Charge is carried through the nanochannel by free K⁺ ions migrating from tip to base (upper inset, Fig. 11B). When positive transmembrane potentials are applied, both the excess uncomplexed K⁺ and the positively charged K⁺-18C6 complex are driven electrophoretically into the tip side of the nanochannel (lower inset, Fig. 11B). Again, they find that when the complex is driven into the nanochannel, the measured current at any applied potential decreases with an increasing concentration of 18C6. Therefore, when the K⁺-18C6 complex is driven electrophoretically into the nanochannel, the current decreases with an increasing 18C6 concentration, and this is true whether the complex is driven into the nanochannel from tip to base (Fig. 11A) or from base to tip (Fig. 11B). For these experiments, the diameter of the tip side of nanochannel is comparable to the diameter of the 18C6 complex. In 2011, Jiang and Li *et al.* reported a simple enantioselective sensing device based on a single artificial β -cyclodextrin-modified nanochannel system. This nanodevice shows a highly selective recognition of histidine enantiomers through monitoring of ionic current signatures. The operating principle of the chiral-responsive system is shown in Fig. 11C. After the mono-6-amino- β -CD molecules were immobilized into the nanochannel, the functionalized nanochannel system exhibited excellent chiral recognition capability

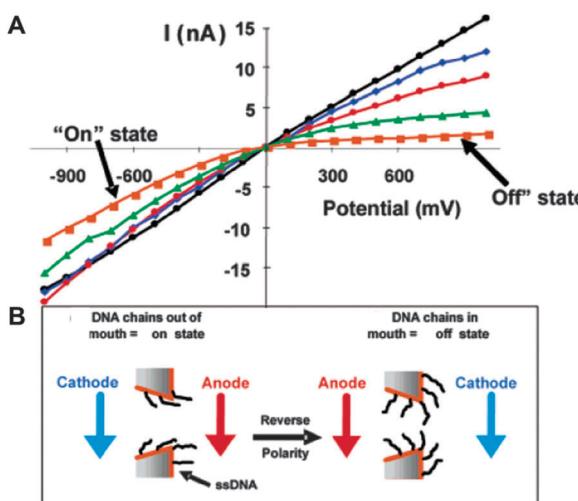


Fig. 10 Electro-responsive nanochannels: (A) I - V curves for the DNA-modified single metal-polymer nanochannel containing no DNA (black) and attached 12-mer (blue), 15-mer (red), 30-mer (green), and 45-mer (orange) DNA motors; (B) schematics showing the electrode polarity and DNA chain positions for on and off states. Adapted with permission from ref. 102 Copyright (2004) American Chemical Society.

toward L-His, which was manifested *via* the changes in the ionic current flowing through the nanochannel. When the β -CD-modified nanochannel is exposed to a solution of L-His, the transmembrane ionic current will decrease to some extent. In comparison, no significant changes happened in the ionic current if they modified D-His or other aromatic amino acids on to the inner channel wall. Fig. 11D and E show the current changes in the nanochannel before and after β -CD modification at -2 V upon the addition of L-His or D-His solutions with different concentrations under the same conditions. The transmembrane ionic currents for the unmodified channel exhibited no obvious changes upon treatment with L-His or D-His in the concentration range 0 to 1 mM (Fig. 11D). When these measurements were repeated with the β -CD-modified channel, a clear difference in the results for the two enantiomers was observed (Fig. 11E). The ionic currents decreased gradually with increasing L-His concentration from 0 to 1 mM, whereas the current remained almost constant for D-His. Therefore, the modified nanochannel system can provide a novel platform to discriminate chiral His on the basis of rectified ionic currents, which can move a potential step toward the ability to simulate the process of chiral recognition in living organisms. On the basis of these findings, they believe that artificial nanochannel systems offer a real promise for preparing practical chiral-sensing devices that could be employed in a biological environment.

3.2 Dual-responsive nanochannels

Many stimuli-responsive nanochannels exhibiting ionic rectification current have been fabricated, while these nanochannels can only be responsive to one kind of external stimulus. According to the strategy of fabricating single-responsive nanochannels, dual/multiple-responsive nanochannels have been reported by modifying multiple-responsive molecules onto the inner surfaces of nanochannels. For example, Siwy's group reported nanofluidic diodes with highly nonlinear I - V characteristics which

offer a unique possibility to construct different biosensors.¹⁰⁴ Such a system is based on local changes of the surface charge on walls of single conical nanochannels induced by the environmental stimuli, such as pH and special ligand. With the ligand binding on the channel wall, the ion-current rectification can be changed (Fig. 12). A prototype of a sensor for the capsular poly(γ -D-glutamic acid) (γ -DPGA) from *Bacillus anthracis* is presented (Fig. 12A and B). The nanochannel used for the sensing was locally modified with the monoclonal antibody for γ -DPGA. The resulted conical sensor, containing the antibody, showed a very strong dependence of its I - V behavior on the pH of the bulk solution (Fig. 12A down). At pH 8, the rectification was the same as for an unmodified channel, indicating that at these conditions the monoclonal antibody was negatively charged. Placing the system in an acidic solution resulted in reversed rectification and significant increase of the rectification degree, providing evidence of the formation of a bipolar diode junction. After the channel was modified with the bacterial γ -D-glutamic acid, the ionic rectification current can only be detected in one direction for all examined pH conditions (Fig. 12B, down), and the pH values change the magnitude of ionic currents especially for negative voltages. Very recently, Siwy's group developed another functional nanochannel by decorating with horseradish peroxidase (HRP) enzyme for detecting small molecules hydrogen peroxide, H_2O_2 (Fig. 12C).¹⁰⁵ The success of the HRP immobilization on the channel surface is confirmed by measuring the pH-dependent I - V curves of the system (Fig. 12D), because immobilization of the HRP enzyme caused partial blockage of the channel observed as lowering of the transmembrane ionic current. After modification, the measured I - V curves additionally exhibited hysteresis at positive voltages. The currents for voltages increasing from 0 to +2 V were significantly higher than the recordings for the voltage sweep from -2 to 0 V (Fig. 12E). They attributed the current changes to the appearance of cationic products of the redox reaction that occurred in the presence of HRP, ABTS, and H_2O_2 . Therefore, one can develop sensors by a modification of the special ligand that can influence the surface charge and then the ionic rectification current of the functional conical nanochannels.

In 2010, Jiang's group presented an integrated ionic gate and rectifier within an asymmetric single nanochannel *via* modifying the pH and temperature dual responsive copolymer brushes poly(*N*-isopropyl acrylamide-*co*-acrylic acid) (PNIPAA) (Fig. 13A).¹⁰⁶ At *ca.* 25 °C, the nanochannel works on a low conductance. When temperature is raised to *ca.* 40 °C, the nanochannel switches to a high ion conductance. The off/on state results from the temperature-triggered conformational transition of the attached copolymer brushes. The charge properties of the copolymer brushes, combined with the asymmetrical pore geometry, render the nanochannel a pH-tunable ionic rectifier (Fig. 13B). The thermal gating ratios of this nanochannel remain approximately the same in the pH range from 3.6 to 9.4, but the ionic current rectification ratios increase with pH, which show a trend to saturation at high pH. Furthermore, the temperature controlled ionic gate works properly in the pH range from 3.6 to 9.4 and the pH-controlled ionic rectifier works equally well at both low (25 °C) and high (40 °C) temperatures. Almost at the same

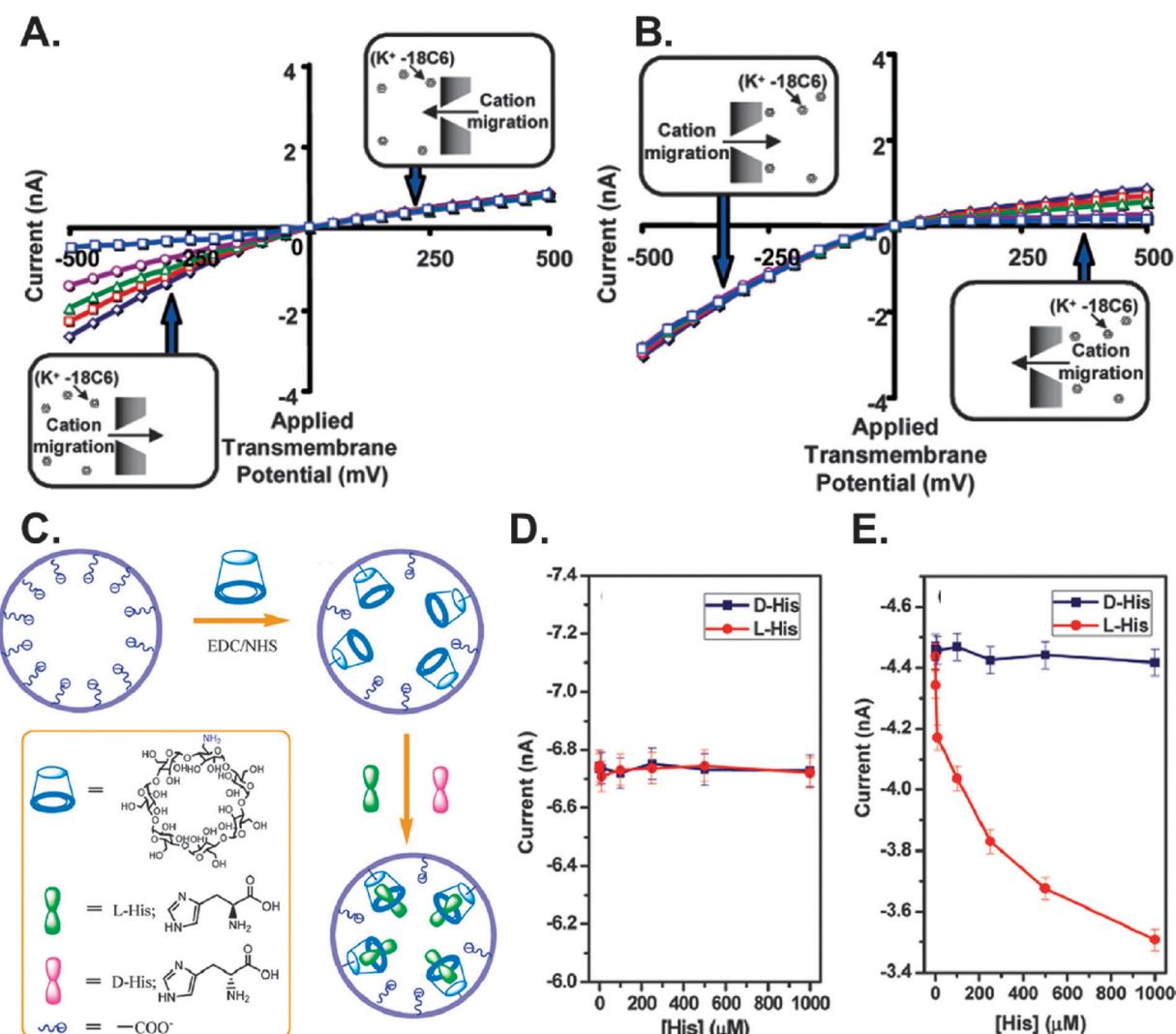


Fig. 11 Ligand-responsive nanochannels: I – V curves for a conical nanochannel with a tip diameter around 1.5 nm, and with 18C6 added to the 1 M KCl solution facing the tip (A) or base (B) of the conical nanochannel. The concentration of 18C6 was 0 mM (blue), 5 mM (red), 10 mM (green), 25 mM (pink), or 50 mM (grey). Adapted with permission from ref. 56. Copyright (2005) American Chemical Society; (C) principle of chiral recognition of His. The modified nanochannel works as a chiral receptor for His, as selective binding of L-His to the inner wall of the nanochannel; (D) current–concentration (I – C) properties of the single nanochannel (D) before and (E) after β -CD was attached to the inner channel wall. The large difference in the enantiomeric ionic currents makes the β -CD-modified nanochannel practically useful as a sensor for the *enantiomer* selective recognition of L-His. Adapted with permission from ref. 57. Copyright (2011) American Chemical Society.

time, another asymmetric dual responsive nanochannel that controls over pH and temperature was created by using an asymmetric chemical modification approach (Fig. 13C).¹⁰⁷ A negative correlation between the ionic current rectification ratio and the temperature with various pH was shown in the system (Fig. 13D), while the ratio of the nanochannel before modification stayed nearly 1 with different temperature and pH. Obviously, the chemical modification strategy could be applied to incorporate other stimuli-responsive materials for designing smart multifunctional nanofluidic systems resembling the “live” creatures in nature.

4. Application of BSNC in energy conversion systems

In recent years, advancements in nanotechnology have led to the development of new methods for fabricating nanochannels

according to advanced requirements. Like biological nanochannels in living systems, the obtained nanochannels always have some properties such as ion current rectification, cation selectivity and gating, which can be used in many fields including sensing,^{108–112} filtrating,^{58,113–116} and energy conversion.^{117–121} Among various potential applications of interest in nanochannels, herein, we only introduce the BSNC based on an ion track etching membrane for energy conversion. For example, Wang’s group reported a power generation system with a single track-etched nanochannel by measuring the streaming currents and conductance.²⁴ Their experimental results indicate that both the efficiency and output power depend on the electrolyte concentration and the dimension of the pore. And the highest efficiency of 5% was obtained in nanochannels with small radii of 31 nm. Recently, Jiang’s group reported a photoelectric conversion system based on

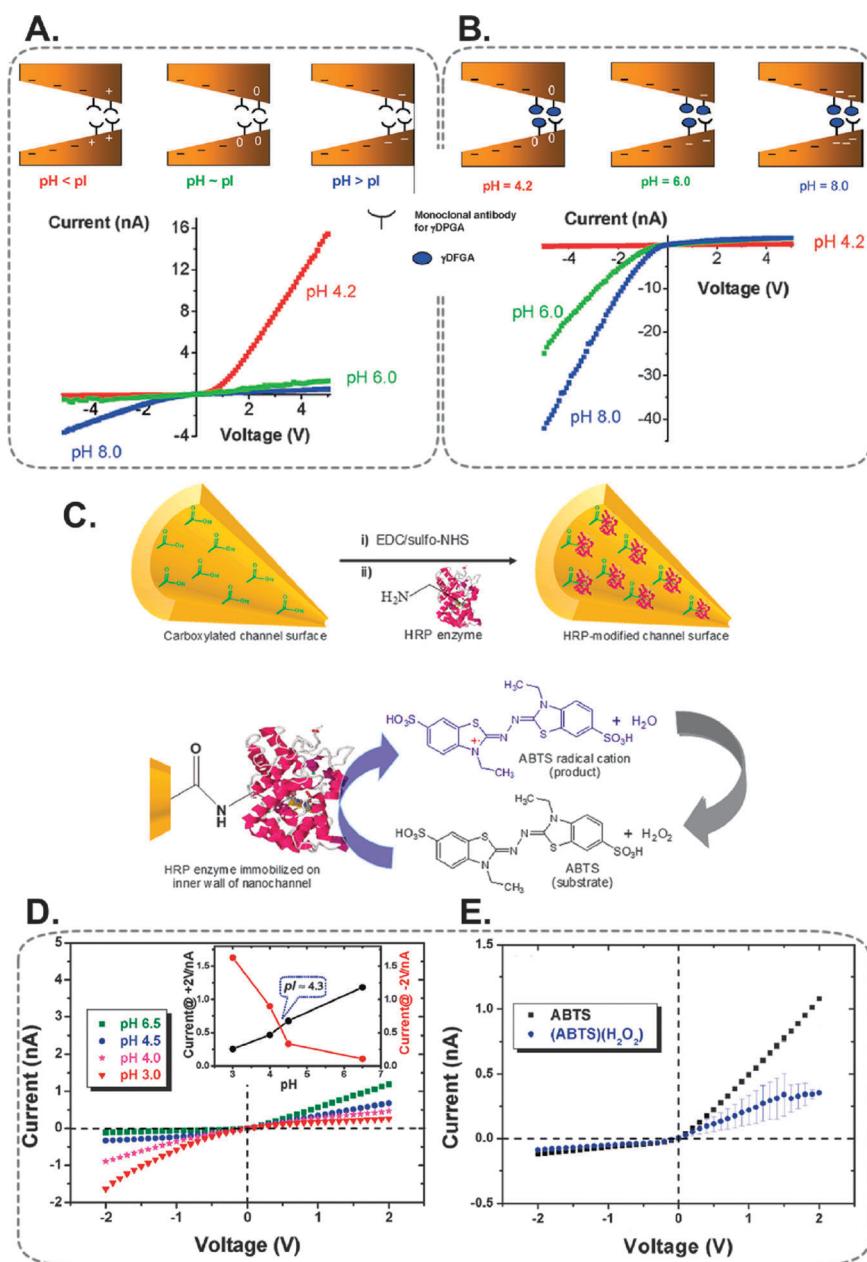


Fig. 12 Dual responsive nanochannels: (A) a conical nanochannel modified with a monoclonal antibody to the nanochannel, the measurements were performed in 10 mM KCl and at various pH values; (B) a nanochannel with mAb F26G3 was incubated with a solution of γ -DPGA, and the measurements were performed in 10 mM KCl and at various pH values. Adapted with permission from ref. 104. Copyright (2009) American Chemical Society: (C) Schematic and mechanism of the system modified horseradish peroxidase (HRP) enzyme on the inner surfaces of a single conical nanochannel *via* carbodiimide coupling chemistry; (D) I – V characteristics of a single conical nanochannel in 0.1 M KCl buffered to different pH values as indicated after functionalization of the channel walls with HRP enzyme. The inset in (D) summarizes the changes of ion currents with solution pH at +2 V (black symbols) and -2 V (red symbols) for the HRP-modified system. The pH value at which positive and negative currents have the same magnitude indicates pI of the HRP enzyme; (E) I – V characteristics of a single HRP-modified channel recorded in the absence (square) and in the presence (blue dot) of 0.5 mM hydrogen peroxide in 0.1 M KCl solution containing 1.5 mM ABTS substrate. Adapted with permission from ref. 105. Copyright (2011) American Chemical Society.

smart gating proton driven nanochannels whose inspiration come from the photoelectric conversion of retina (Fig. 14A). The schematic of the photoelectric conversion system was shown in Fig. 14B. Two pieces of membranes with proton-driven nanochannels were inserted between part I and part II, and between part II and part III; and an anion-exchange membrane was situated between part I and part III, respectively. Platinum

electrodes were used in their photoelectric conversion system. The light driven proton pump (HA) in part I can release protons and corresponding anions when the HA are irradiated with UV light. Then, the generated protons will transport across the membrane from part I to part II in turn, which contributes to the diffusion potential (E_{diff}). At the same time, the anions A^- that have diffused to part III can also accept

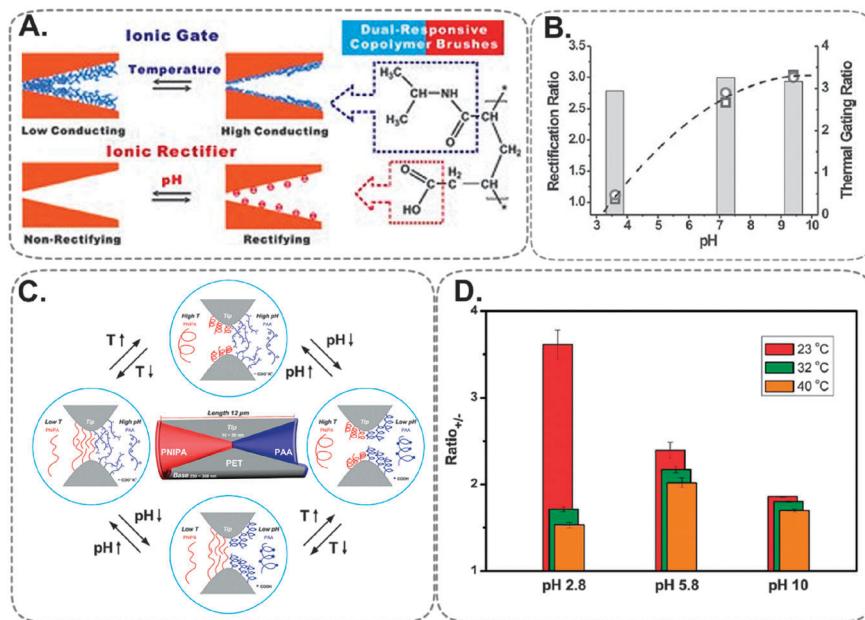


Fig. 13 Dual responsive nanochannels: (A) schematic and mechanism illustration of the system that is fabricated by chemical modification poly(*N*-isopropyl acrylamide-co-acrylic acid) copolymer brushes on the inner surfaces of cone-shaped PI nanochannels. (B) Ionic current rectification ratio and thermal gating ratio measured in electrolytes at different pH. Adapted with permission from ref. 106. Copyright (2010) Wiley-VCH. (C) A biomimetic asymmetric dual responsive single nanochannel system. (D) Ionic current rectification of the single nanochannel measured at 2 V. Adapted with permission from ref. 107 Copyright (2010) American Chemical Society.

protons to recover to the original HA molecules that can re-supply the HA molecules. The cyclic transport of HA molecules and their disassembled ions transported across the membranes can bring about a production of E_{dif} . The typical response properties of the photoelectric conversion are shown in Fig. 14C and D. They found the E_{dif} and the I_p tended to be constant without irradiation. Once irradiation started, both parameters shifted in the negative direction and reached their maximum values within 30 min. If the light was removed, all values decreased rapidly and recovered to their original state within 45 min. When the HA molecules in part I were irradiated again, both E_{dif} and I_p peaks arose again but the maximum values were weaker than that of the first cycle. Moreover, Wang, Jiang *et al.* presented a fully abiotic single-pore nanofluidic energy-harvesting system that can efficiently convert Gibbs free energy in the form of a salinity gradient into electricity (Fig. 14E).²⁶ The inspiration comes from electric eels. The maximum power output with the individual nanochannel approaches 26 pW, which were one to three orders over the previous ion exchange membranes. They think the harvested power can be delivered to the external circuit and drive an electrical load resistor (Fig. 14F). The power consumption on the external electrical load resistor (R_L) is calculated as $P_L = I_R^2 R_L$, where the electrical current I_R increases with the concentration gradient and decreases with the load resistance (Fig. 14G). P_L also increases with the concentration gradient, but reaches its maximum with a moderate load resistance (R_m) (Fig. 14H). To demonstrate the origin of the net diffusion current, the ion distribution and the resulting diffusion current density (j) were calculated from the pore axis along the radius of the nanochannel cross section. The concentration gradient was 1000 mM/1 mM. In highly charged

nanochannels, the radiation distribution proves that the diffusion current stems from the separation of cations from anions within the electrical double layer associated with the negative charge on the pore wall (Fig. 14I). Obviously, smart gating nanochannels played a key role in the process of power generation regardless of whether in the photoelectric conversion systems or in the salinity gradient into electricity. If we prepare more smart nanochannels, more energy conversion systems will be obtained in the future.

5. Conclusions

This paper gives a brief introduction of recent progress in biomimetic smart nanochannels (BSNC). A strategy for the design and construction of BSNC was proposed and examples of these BSNC, including those can respond to external single stimuli such as pH, ions, temperature, electricity and even light as well as those that can respond to external dual stimuli such as pH/temperature were presented. As can be anticipated, multi stimuli-responsive BSNC will be prepared soon on the basis of this strategy. Although a series of BSNC have been developed, a very complex problem on BSNC such as stable, reversible, durable and grafting density *etc.* related work still remains to be done from the experimental and theoretical point. Only in this way can we make our BSNC more significant and smart, and use them in practical applications.

Inspired by the energy conversion of the retina and electric eel, scientists developed BSNC and applied them in an energy conversion system.^{25,26} Although the efficiency is not high enough to apply them in practical applications, the significance is to provide a novel approach for the development of a new energy conversion system. Nanochannel-based energy conversions are

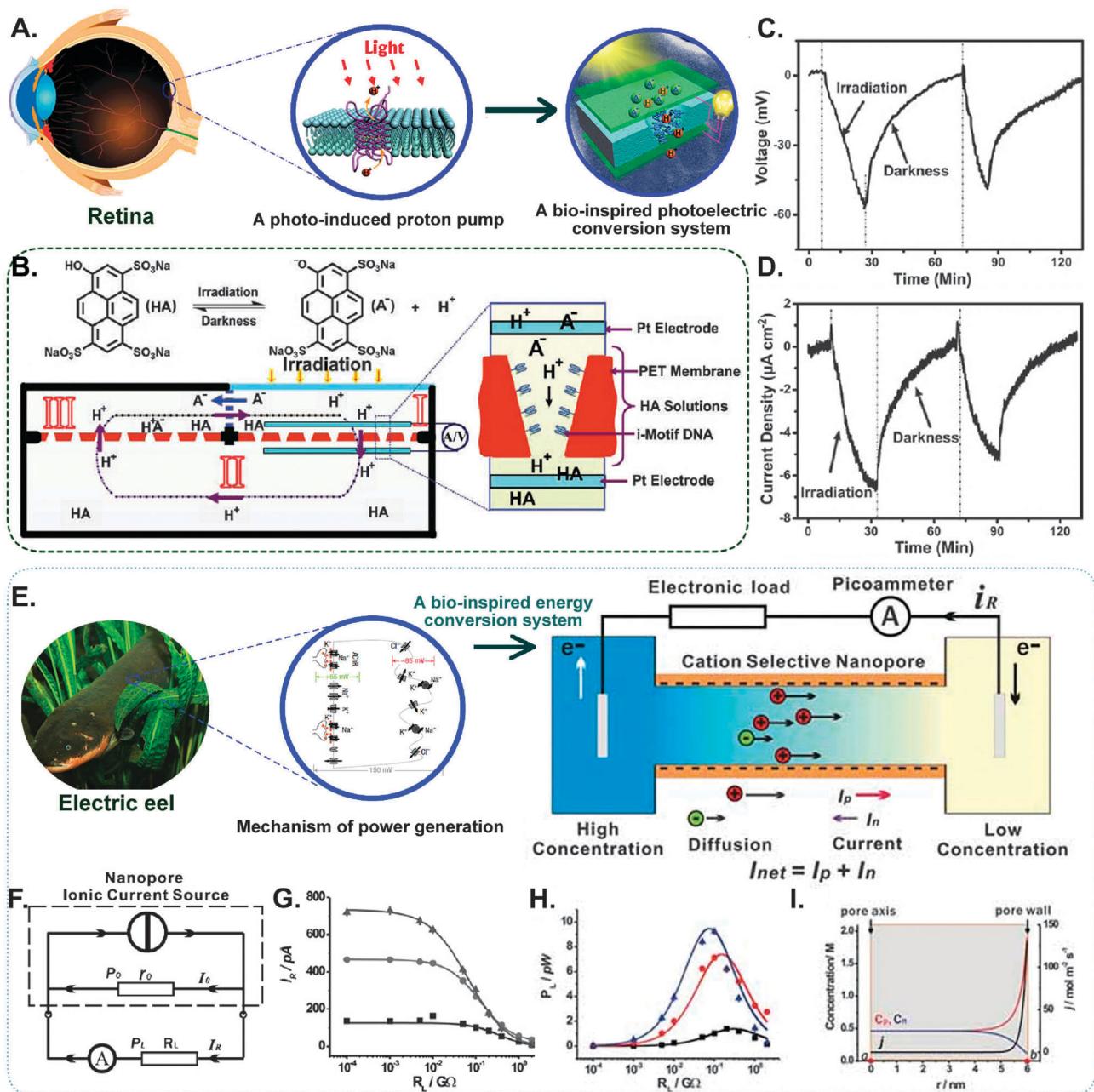


Fig. 14 Bio-inspired energy conversion systems: (A) a bio-inspired photoelectric conversion system whose inspiration comes from a photo-induced proton pump in the retina; (B) mechanism of the photoelectric conversion system, which is constructed using a photoelectrochemical cell containing three parts, and only part I could be irradiated by outside light. 8-Hydroxypyrene-1,3,6-trisulfonate (HA) was utilized as light-driven proton pumps. The generated protons could transport across the membrane between part I and part II and resulted in a charge imbalance on both sides of the membrane, thus creating a E_{dif} ; (C, D) $J-t$ and $V-t$ characteristics of the optimized photoelectric conversion, which was obtained by irradiation of the HA molecules in part I; adapted with permission from ref. 25. Copyright (2010) Wiley-VCH; (E) bio-inspired by the power generation of an electric eel, an energy conversion system has been developed by using preferential ion diffusion across single ion-selective nanopores driven by the concentration gradient; (F) the equivalent electronic circuit model. (G, H) I_R and P_L on R_L as a function of resistance; (I) the mechanism for j generated from the charge separation within the electrical double-layer (p for cations and n for anions). Adapted with permission from ref. 26. Copyright (2010) Wiley-VCH.

attractive for the development of energy conversion not only because the principle is novelty as compared to the traditional energy conversion systems, but also many instances in energy conversion efficiency can be improved by optimizing the properties of BSNC. Therefore, for future progress much effort should be focused on applying those fabricated smarter

BSNC into real world applications, such as imitation and preparation of the proton pump in photosynthesis for energy conversions; imitation and preparation of biomimetic potassium channels for transferring electric signals in the nervous system; imitation and preparation of the biomimetic water channel for filtrating fresh water, etc.

Acknowledgements

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