Nanochannels

DOI: 10.1002/anie.201104904

Building Bio-Inspired Artificial Functional Nanochannels: From Symmetric to Asymmetric Modification

*Xu Hou, Huacheng Zhang, and Lei Jiang**

biomimetics · nanochannels · nanostructures · nanotechnology

Over millions of years, complex processes of intelligent control have evolved in nature. Learning from nature is a continuing theme in the development of smart materials and intelligent systems. For example, biological nanochannels, which are typically ion channels, play a very important role in basic biochemical processes in cells. Inspired by ion channels, in which the components are asymmetrically distributed between the membrane surfaces, the generation of biomimetic smart nanochannels is a broad and varied scientific research field. The design and development of new biomimetic channels includes the use of different shapes of channels, different stimuli-responsive molecules, and different symmetric/asymmetric modification methods. In this Minireview, we summarize recent developments in building functional nanochannels by applying various symmetric and asymmetric modifications.

1. Introduction

The transport of ions across cell membranes is a prerequisite for many biological processes. Life depends on the continued flow of ions into and out of cells. Biological nanochannels, which include ion pumps and ion channels, are used by cells to transport ions across membranes.[1] Various components of biological nanochannels are not uniform in distribution, and their structures are also asymmetric (Figure 1 a).[2] The bio-inspired study of the design and development of artificial biomimetic channels has been receiving a great deal of attention.[3] Artificial functional nanochannels have emerged as possible candidates for mimicking physiological processes in biological nanochannels. Moreover, research in this field boosts the development of bio-inspired intelligent nanomachines for real-world applications, such as biosensors, molecular filtration, and nanofluidic devices.[4]

[*] Dr. X. Hou
National Center for Nanoscience and Technology
Beijing 100190 (China)
H. Zhang, Prof. L. Jiang
Institute of Chemistry, Chinese Academy of Sciences
Beijing 100190 (China)
E-mail: jianglei@iccas.ac.cn

Artificial micro/nanochannels in organic or inorganic membranes have been well studied for the purposes of building smart materials for various applications,[5] such as track-etched polymer membranes, carbon nanotubes, the integration of biological nanopores or ion channels into artificial membrane materials for filtration, nanomedicine, and biosensing.[6] However, we still need a single-channel system to provide an optimal system for studying the transport properties of different ions or molecules. This system can also provide many potential smart platforms, for applications such as detecting single molecules, because one can directly observe the behavior of a single functional channel without having to average the effects of multiple channels.[4b,7] The present research towards bio-inspired artificial functional nanochannels is still in its early stages. It will be enhanced greatly by the development of chemistry, nanotechnology, and biotechnology methods that are capable of producing more smart functional molecules and variations in the chemical, physical, and biological properties of the confined channel space.

This Minireview is focused on symmetric and asymmetric modifications of single track-etched polymer nanochannels for building bio-inspired artificial nanochannels. This review is organized into four sections. The first section gives a brief introduction of the strategy for the design of symmetric/

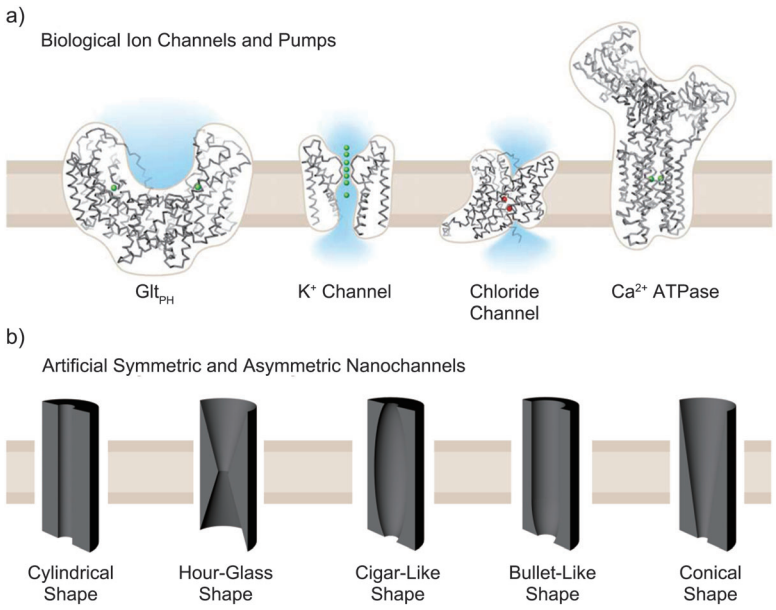


Figure 1. a) Architectures of different ion channels and ion pumps.[2] b) Different shapes of polymer nanochannels.

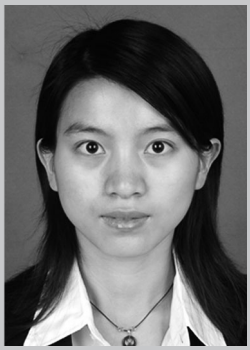
asymmetric modifications of bio-inspired artificial nanochannels. The second section summarizes symmetric modification methods that have been used in channels in recent years and the third section examines asymmetric modification methods. The last section is an outlook towards future challenges in the development of artificial functional nanochannels. This review uses the well-developed examples of ion-track-etched polymer nanochannels with different shapes (Figure 1b) to demonstrate the feasibility of the design strategies for building functional nanochannels by various symmetric and asymmetric modifications, which may also be extended to other materials.

Herein, we suggest three routes for the design and preparation of various artificial functional nanochannels: symmetric/asymmetric design for the shapes of the nanochannels, the physicochemical modification of the inner surface of nanochannels, and the above two methods combined in a co-design strategy (Figure 2). In these three routes, the asymmetric design idea provides more flexible approaches for building various functional nanochannels. In this Minireview, the asymmetric design reflected mainly in the asymmetric physicochemical modification. The approaches for the preparation of nanochannel materials have been described in detail by Apel et al.,[8] Gyurcsanyi,[9]Matile and co-workers,[10] Dekker,[3c] and Martin and co-workers,[11] and will not be considered in this review.

2. Symmetric Modification of Nanochannels

Symmetric modification of nanochannels is the most commonly used method due to the advantage of simple and direct implementation of modification of the entire inner surface of the nanochannels. It is universally suitable for making a variety of modifications to materials. It is also noteworthy that this modification method can take advantage of the symmetric/asymmetric shape of the nanochannel itself to achieve symmetric/asymmetric regulation of ion transport inside the nanochannel. The major symmetric modification methods are illustrated by the following examples: electroless deposition,[12] chemical modification by functional molecules in solution[13] and self-assembly.[14]

Xu Hou received his B.S. degree (2006) from Sichuan University where his scientific interest was materials for tissue engineering. He completed his Ph.D. (2011) at the National Center for Nanoscience and Technology, China, under the direction of Prof. Lei Jiang. His current scientific interests are focused on the design and fabrication of biomimetic smart single nanopores/nanochannels.



Huacheng Zhang is currently a Ph.D. student at the Institute of Chemistry, Chinese Academy of Sciences (ICCAS). She received her B.S. degree (2009) from Xi'an Jiao Tong University. Her current scientific interests are focused on the fabrication of smart nanofluidic devices and theoretical modeling of ionic/molecular transport in functional single nanopores/nanochannels.

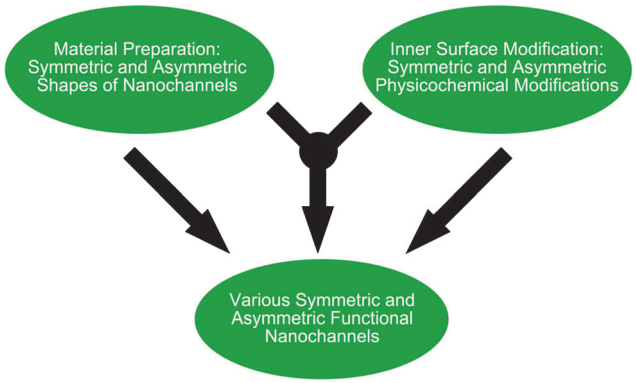


Figure 2. The symmetric/asymmetric design and preparation of bio-inspired artificial functional nanochannels.

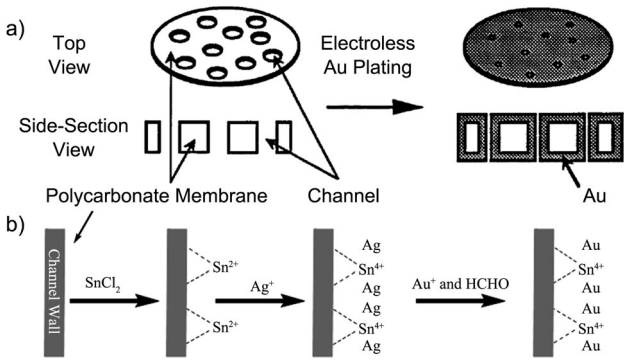


Figure 3. a) Diagram of electroless gold plating of nanochannels.[12] b) Chemical processes of gold electroless deposition.[16]

2.1. Electroless Deposition

Electroless deposition is a nongalvanic type of plating method that involves several simultaneous reactions in an aqueous solution. It occurs without the use of external electrical power.[15] According to the principle of redox reactions, the use of strong reducing agents in a solution that contains metal ions results in reduction of the metal ions to metal atoms and deposition of the metal atoms onto a surface to form a dense coating. Various metals can be used for modification of nanochannels by electroless deposition, such as gold, nickel, silver, copper, palladium, and platinum. Typical chemical reaction equations for this process are shown in Table 1.

Table 1: Typical metals used for modification by electroless deposition and the related reaction equations.

Reductant	Metals	Reaction equations	Ref.
Formaldehyde	Au, Cu	$2\,Au^{+}+HCHO+3\,OH^{-}\rightarrow HCOO^{-}+2\,H_2O+2\,Au$	[12,16–17]
Hypophosphite	Ni, Pd	$Ni^{2+}+2\,H_2PO_2^{-}+2\,H_2O\rightarrow Ni+2\,H_2PO_3^{-}+2\,H^{+}+H_2$	[18]
Borohydride	Pt, Au	$2\,Pt^{2+}+BH_4^{-}+4\,OH^{-}\rightarrow 2\,Pt+BO_2^{-}+2\,H_2+2\,H_2O$	[15,19]
Hydrazine	Ag, Ni	$4\,[Ag(NH_3)_2]^{+}+N_2H_4\rightarrow 4\,Ag+4\,NH_3+4\,NH_4^{+}+N_2$	[15,20]

Lei Jiang is currently a professor at ICCAS, and Dean of the School of Chemistry and Environment, Beijing University of Aeronautics and Astronautics. He received his B.S. degree (1987), M.S. degree (1990), and Ph.D. degree (1994) from Jilin University. He then worked as a postdoctoral fellow in Prof. Akira Fujishima's group at Tokyo University. In 1996, he worked as a senior researcher in the Kanagawa Academy of Sciences and Technology under Prof. Kazuhito Hashimoto. He joined ICCAS in 1999. In 2009, he was elected academician of the Chinese Academy of Sciences. His scientific interest is focused on bio-inspired, smart, multiscale, interfacial materials.

Based on this approach, Martin and co-workers reported a metal-polymer composite nanochannel (Figure 3a), which provides a good basic platform for the further functional modification of the inner surface of the channel.[12] As shown in Figure 3b, the processes of modification by electroless deposition of the polymer nanochannel are divided into two steps: The first step is pretreatment of the track-etched polymer template by coating the inner surface of the nanochannels with a catalyst. Secondly, the pretreated template is immersed in the plating solution. Metal ions react with a reducing agent at the surface of the template. After electroless plating with the metal, the diameter of channels decreases. However, the second plating step can take a long time to achieve small enough diameters in the channels, and several toxic solvents are also used.[16]

2.2. Chemical Modification by Functional Molecules in Solution

In this Minireview, chemical modification mainly refers to the chemical reactions between the inner surface of the nanochannel and functional molecules in a solution to create new covalent bonds. At present, there are two main methods for chemical modification of nanochannels. The first one is based on functional groups (for example, −COOH) in the nanochannels reacting with decorating molecules to form covalent bonds (for example, −C(O)−NH−). Based on this method, Jiang and co-workers developed a pH-gating, asymmetric, single polyethylene terephthalate (PET) nanochannel by using a DNA molecular motor that was attached to the channel by a two-step chemical reaction (Figure 4a).[13b] During the preparation of the PET nanochannel, negatively charged carboxyl groups were created on the inner surface of the nanochannel, which is a process that can also be performed with other similar materials, such as polyimide (PI). After modification, the diameter of the nanochannel also decreases, and different sizes of decorating molecules can be used to regulate the sizes of the channels. Table 2 shows several decorating molecules that have been used for chemical modification of polymer nanochannels, and some typical examples are shown in Figure 4b. Recently, Azzaroni and co-workers reported the design and preparation of several pH-responsive nanochannel systems by chemical

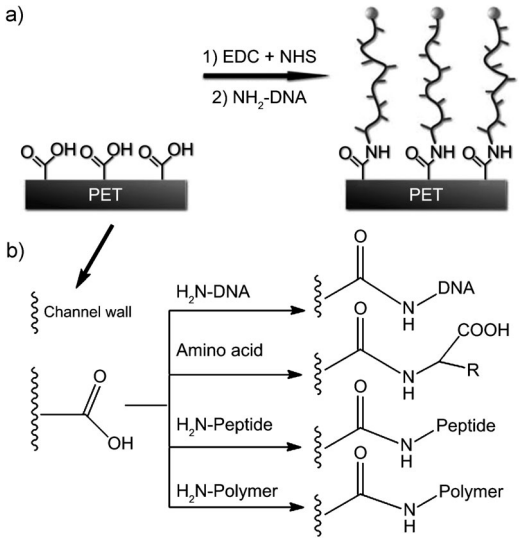


Figure 4. a) Immobilization of a DNA motor onto the inner wall of a nanochannel by chemical modification.[13b] 1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide hydrochloride (EDC) and *N*-hydroxysuccinimide (NHS) are used for activating the carboxylic acid groups. b) Several typical decorating molecules used in chemical modification of nanochannels.

Table 2: Decorating molecules used in chemical modification of polymer nanochannels by functional molecules in solution.

Nanochannels	Decorating molecules	Ref.
PET	H_2N-DNA	[13b, 22]
PET	L-lysine and L-histidine	[21a]
PET	Poly(2-methacryloyloxy)ethyl phosphate)	[21b]
PET	3-aminopropylphosphonic acid	[23]
PET	β-cyclodextrin	[24]
PI	Poly(*N*-isopropylacrylamide)	[25]
PI	Amine-PEO_3-biotin[a]	[26]
PI	Poly(methacryloyl L-lysine)	[21c]
PI	Peptide nucleic acid (PNA)	[27]

[a] PEO = poly(ethylene oxide).

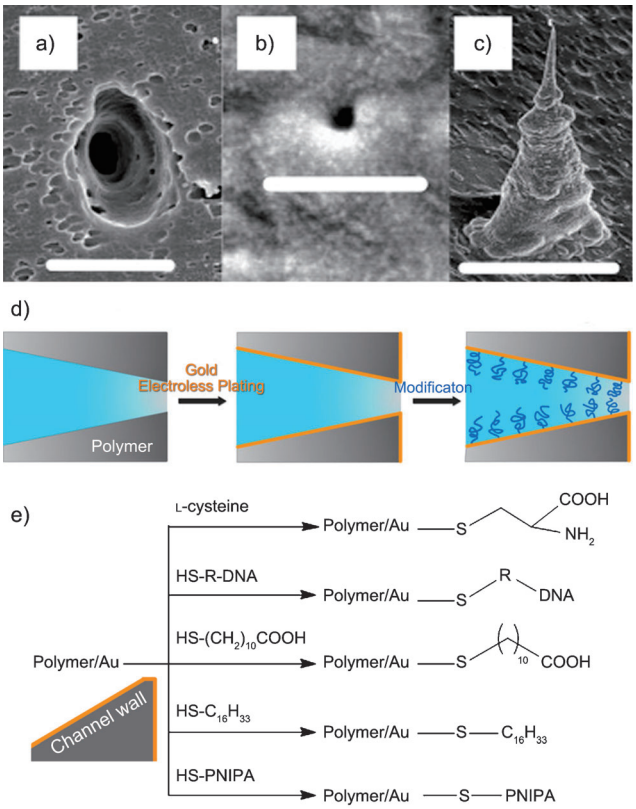


Figure 5. a–c) Electron micrographs of a single conical nanochannel after electroless modification with gold. Scale bar 5 μm.[29a] d) Immobilization of functional molecules onto the inner wall of a nanochannel by electroless modification and surface chemisorbing thiols. e) Several typical thiol self-assembled functional molecules for modifying the inner surface of a polymer/gold nanochannel.

Table 3: Several functional self-assembled thiol molecules for decorating Au-polymer composite nanochannels.

Nanochannels[a]	Decorating molecules	Ref.
PC	HS-$C_{16}H_{33}$ and HS-C_2H_4-OH	[30]
PC	HS-$(CH_2)_{10}$COOH	[31]
PC	Cysteine	[32]
PC	Thiol-DNA	[29a]
PC	Thiol-PNA	[33]
PC	Thiol-antibody fragments	[34]
PC	11-mercaptoundecanoic acid and biotin	[35]
PC	Thiol- and disulfide-bearing ionophores	[36]
PET	HS-PNIPA	[29b]
PET	HS-R-biotin,[b] HS-antibody, HS-protein G	[13a]

[a] PC = polycarbonate. [b] R = $-(CH_2)_2C(O)NH(CH_2)_6NH-$.

modification to obtain functional nanochannels for achieving control of ionic transport.[21]

The second method for chemically modifying nanochannels is based on self assembly of functional thiol molecules to form Au–S covalent bonds after the electroless deposition of gold onto the inner surface of the nanochannel (Figure 5 a–d). This method has been widely used in developing many functional surfaces,[28] and in the past few years has also been utilized for functionalizing nanochannels. For instance, Martin and co-workers as well as Jiang and co-workers have developed single nanochannels that are responsive to electrical potential and temperature.[29] Table 3 shows several self-assembling thiol molecules, and some typical examples are shown in Figure 5 e.

Relative to the second method, the first method is direct covalent chemical modification. It has no metallization process, thus, the surface of the channels remains organic in nature, which is more closely analogous to biological channels. However, the second method is advantageous for making nanodevices, as these channels are stable with a metalized surface, and the density of the chemical modification can be better controlled as a result of the formation of a thiol/gold self-assembled monolayer. Furthermore, the second method is also slow, with functionalization times as long as one day.

2.3. Self-Assembly

From a physicochemical point of view, modification by self-assembly is different from covalent modification with self-assembled thiol compounds. It is based on specific molecular interactions between specific groups of the inner surface of the nanochannels and functional molecules, such as electrostatic interactions[14b,37] or intermolecular forces (hydrogen bonding[27] and van der Waals forces[38]), separately or together, to achieve functionalization of the inner surface of the nanochannels.[26] However, the range of physicochemical modification that can be obtained is limited.

Azzaroni et al. reported layer-by-layer assembly of polyelectrolytes into an artificial single nanochannel that rectifies ionic current and was prepared by the electrostatic self-assembly of multiple layers of functional molecules inside the channel[14b] (Figure 6a). They also reported a biosensor that contains functionalized, single, asymmetric PI nanochannels, which functions by self-recognition of ligands between a protein recognition ligand (biotin) and a specific protein molecule receptor (streptavidin, Figure 6b).[26]

3. Asymmetric Modification of Nanochannels

Asymmetric functional modification of nanochannels is still in its early stages. In general, asymmetric modification methods are also adequate for symmetric modification. However, asymmetric modification could potentially provide new ideas for developing smart nanochannel systems as a result of complex modification approaches to precisely functionalize diverse but specific local areas of the channels with different functional molecules. It provides more design ideas for building multiple functional nanochannel systems. The typical asymmetric modification methods are illustrated by the following examples: ion sputtering,[39] physical/chemical evaporation,[40] modification with plasma,[41] and asymmetric modification by functional molecules in solution.[42]

3.1. Ion Sputtering

Ion sputtering is a process whereby atoms are ejected from the cathode (target) as a result of bombardment of the target surface by accelerating positive ions, the energy from which passes to the surface atoms of the cathode. After atoms leave the cathode, they are deposited on the substrate, which is a momentum transfer process. Magnetron ion sputtering as a high-speed and low-temperature sputtering technology has many advantages, such as strong combination between the coating layer and the substrate, the uniform and dense coating layer, and easy control of the process.

Recently, Jiang and co-workers reported the fabrication of stable, single asymmetric nanochannels with controllable ionic rectification by asymmetric modification with ion sputtering.[39a] As shown in Figure 7a, each side of the nanochannel was independently sputtered to control the pore size for studying ion transport properties. The properties of nanochannels that have been functionalized by double-sided sputtering have also been studied. Asymmetric modification approaches impart a significant increase in the ionic rectification properties of the nanochannel, which is difficult to achieve by symmetric modification. On the basis of the above study, Jiang and co-workers further utilized a symmetric, hour-glass-shaped single nanochannel with asymmetric sputtering of different metal ions to develop ionic rectifier systems (Figure 7b), which moves one step further toward the development of functional nanochannel systems for real-world applications.[39b] Moreover, gold and platinum are easily modified by thiol chemisorption, thus, these nanochannels open up new avenues to further investigate more sophisticated biochemical asymmetric systems by combining them with DNA, peptides, and proteins.

3.2. Physical/Chemical Evaporation

Modification by electron-beam evaporation is a typical physical vapor-deposition technology. It is widely used for advanced surface modification. The working principle is based on bombarding a target anode with an electron beam that is given off by a charged tungsten filament under high vacuum. The electron beam causes atoms from the target to transform into the gaseous phase. These atoms then precipitate into the solid state, which coat the surface of the substrate with a thin layer of the anode material. Characteristics of this method are fast deposition and a clean surface after modification. In particular, the coating layer is strongly adhered to the substrate, and the choice of substrate material is unlimited.

Based on this technology, Siwy and co-workers successfully prepared an ionic transistor by asymmetric electron-beam evaporation.[40a] As shown in Figure 8, titanium as the adhesive layers, gold as the gate electrode, and SiO_2 as the insulating layer were all deposited on the side of a conical nanochannel with a small opening. The gold layer serves as the gate electrode, which is used to supply the chosen potential at the surface of the nanochannel. By changing the electric potential that is applied to the gate, the current through the channel can be changed from the rectifying behavior of a typical asymmetric conical nanochannel to the almost linear behavior of a symmetric nanochannel.

Initiated chemical vapor deposition is a chemical vapor-deposition method that directly translates free radical polymerization into a chemical vapor deposition process.[43] The process does not involve any solvents, hazardous byproducts, or other contaminants, and so it is environmentally benign. Because the reactants are delivered in the vapor phase, the modification process is not subject to surface tension limitations, and uniform, pinhole-free coatings can be formed on essentially any substrate. Based on the above method, Asatekin and Gleason successfully developed functional polymeric nanochannels for hydrophobicity-based separations.[40b]

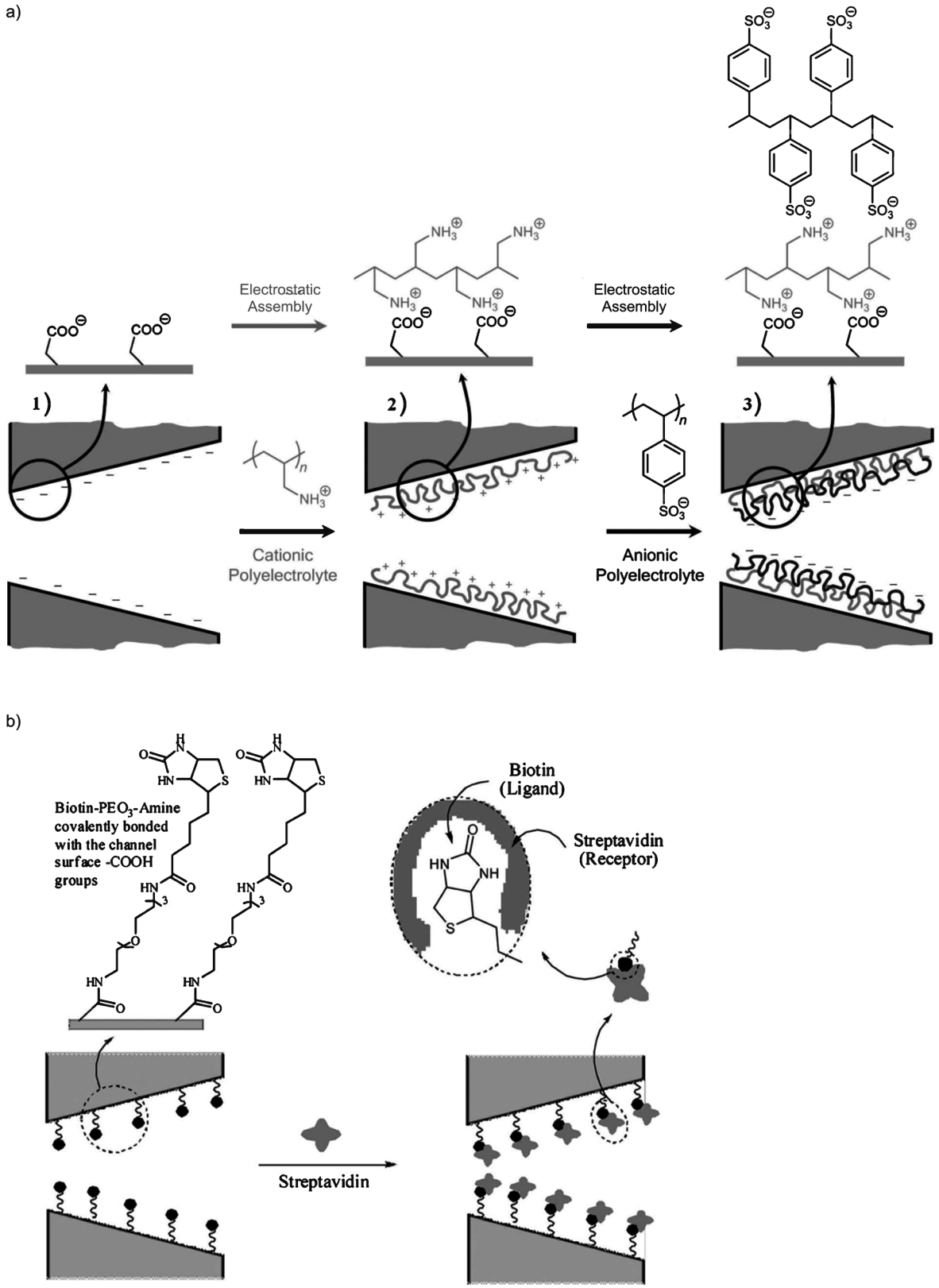


Figure 6. a) Illustration of sequential nanochannel modification through layer-by-layer assembly of polyelectrolytes: 1) As-synthesized nanochannel; 2) (Poly(allylamine hydrochloride) (PAH))$_1$(poly(styrenesulfonate) (PSS))$_0$-modified nanochannel; 3) (PAH)$_1$(PSS)$_1$-modified nanochannel.[14b] b) Representation of an asymmetric nanochannel functionalized with biotin-PEO$_3$-amine and subsequent biospecific, noncovalent binding of a streptavidin analyte.[26]

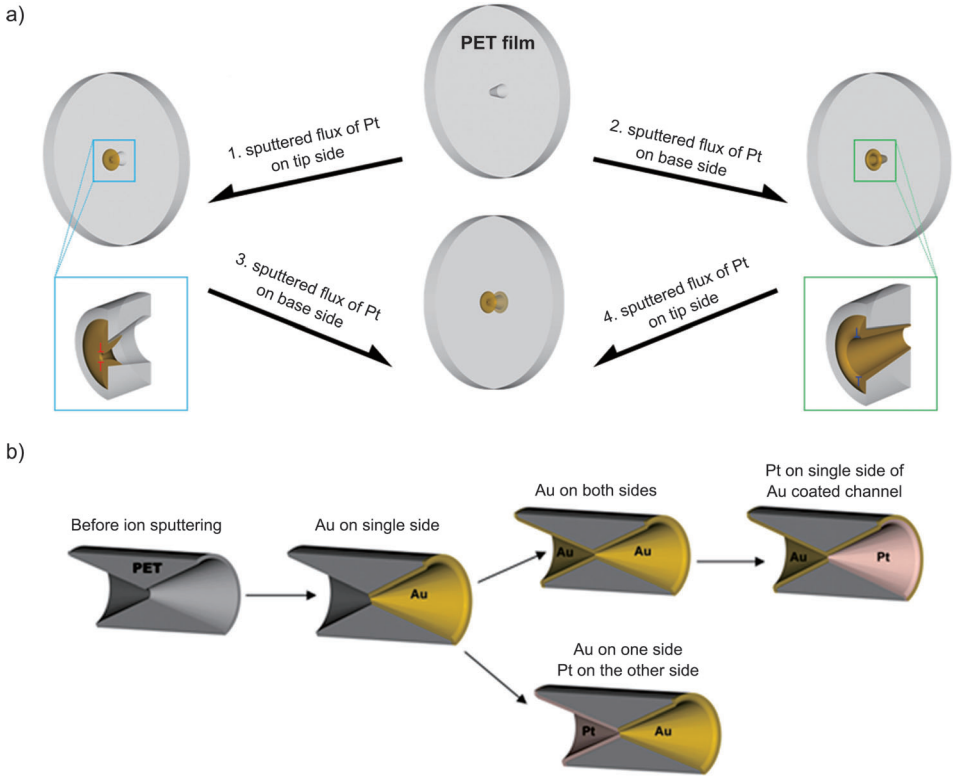


Figure 7. Metal-polymer composite asymmetric nanochannels. a) The experimental design.[39a] b) Four hour-glass shaped nanochannels composed of gold or platinum deposited on different sides of the nanochannels.[39b]

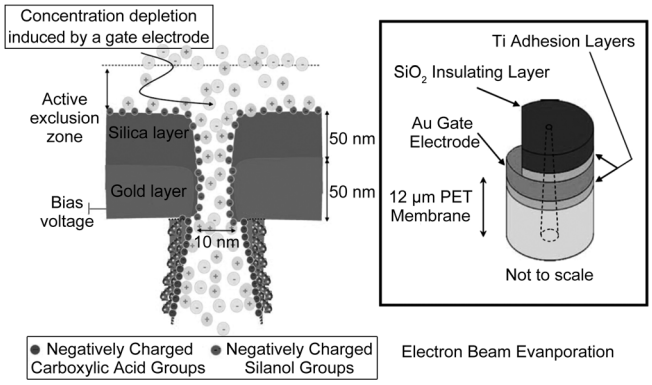


Figure 8. Conical nanochannel with metal and SiO_2 layers.[40a]

3.3. Modification with Plasma

Modification with plasma offers an effective method for nanoscale surface engineering of materials, which can functionalize a specific local area precisely, whether by symmetric or asymmetric chemical modification. This can provide a variety of nanoscale features and properties for developing advanced nanomaterials. The principle is based on plasma modification of polymer materials and can effectively produce large amounts of free radicals in the surface layer. The newly generated free radicals continue to react to form functional groups. However, the structures that are obtained by plasma modification within the nanochannels are not well characterized, and the density of functional groups is not well understood.

Jiang and co-workers reported building a pH-gating single nanochannel for ionic transport by using asymmetric chemical modification with plasma to achieve the asymmetric modification of a symmetric channel.[41a] Most recently, Jiang and co-workers further utilized this method to develop a biomimetic, asymmetric, dual-responsive single nanochannel by using asymmetric plasma modification approaches to functionalize two sides of the channel with different functional molecules. This method provides simultaneous control over the pH- and temperature-dependent asymmetric ion-transport properties inside the channel (Figure 9).[41b]

3.4. Asymmetric Chemical Modification by Functional Molecules in Solution

Asymmetric chemical modification by functional molecules in solution is based on the minimum concentration requirements of the chemical modification reaction, and the different reagent concentration distribution inside the symmetric/asymmetric confined space of the nanochannels. Therefore, the different shapes of the nanochannels can be used to achieve a different concentration distribution and, consequently, symmetric and asymmetric chemical modifications of the nanochannels.

Vlassiouk and Siwy developed the above method for asymmetric modification of nanochannels to build a nano-

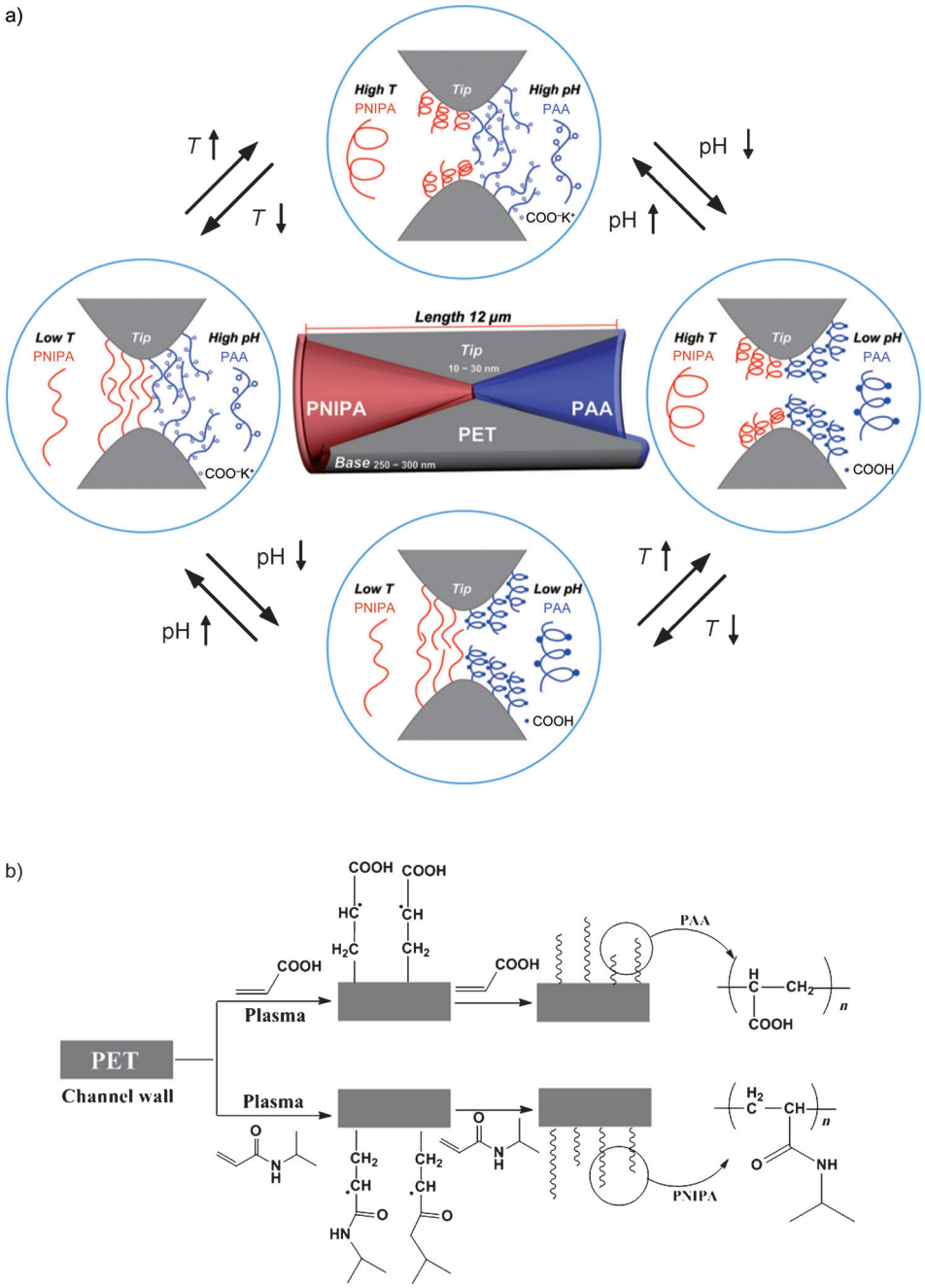


Figure 9. a) A biomimetic asymmetric pH/Temperature responsive single nanochannel produced by asymmetric plasma modification. One side of the nanochannel was treated by plasma-induced grafting of *N*-isopropylacrylamide in the vapor phase, which became a temperature-responsive polymer, PNIPA, after plasma-induced graft polymerization. The other side of the nanochannel was treated by plasma-induced grafting of distilled acrylic acid in the vapor phase, which became a pH-responsive polymer, polyacrylic acid (PAA), after plasma-induced graft polymerization.[41b] b) Plasma polymerization modification processes of the inner surface of the nanochannel.

fluidic diode that relies on a concentration gradient. The concentration gradient is constant in time and is created when a reagent is placed only on one side of the channel.[42a] Figure 10 shows a single conical nanochannel in which the inner surface was patterned so that a sharp boundary between positively and negatively charged regions was created. Later, Siwy and co-workers further utilized this strategy to develop a bipolar ionic transistor by using a single hour-glass shaped nanochannel with asymmetric modification.[44] Recently, Siwy and co-workers also reported a biosensor that is based on the above nanofluidic diodes with highly nonlinear current/voltage characteristics, and the nanodevices allow the isoelectric point of minute amounts of proteins immobilized on the surface of the nanochannel to be determined.[45]

A solution assembly method is also a possible way to achieve asymmetric modification inside nanochannels. Most recently, Xue and co-workers reported that the degree of ionic current rectification of a nanochannel could be finely

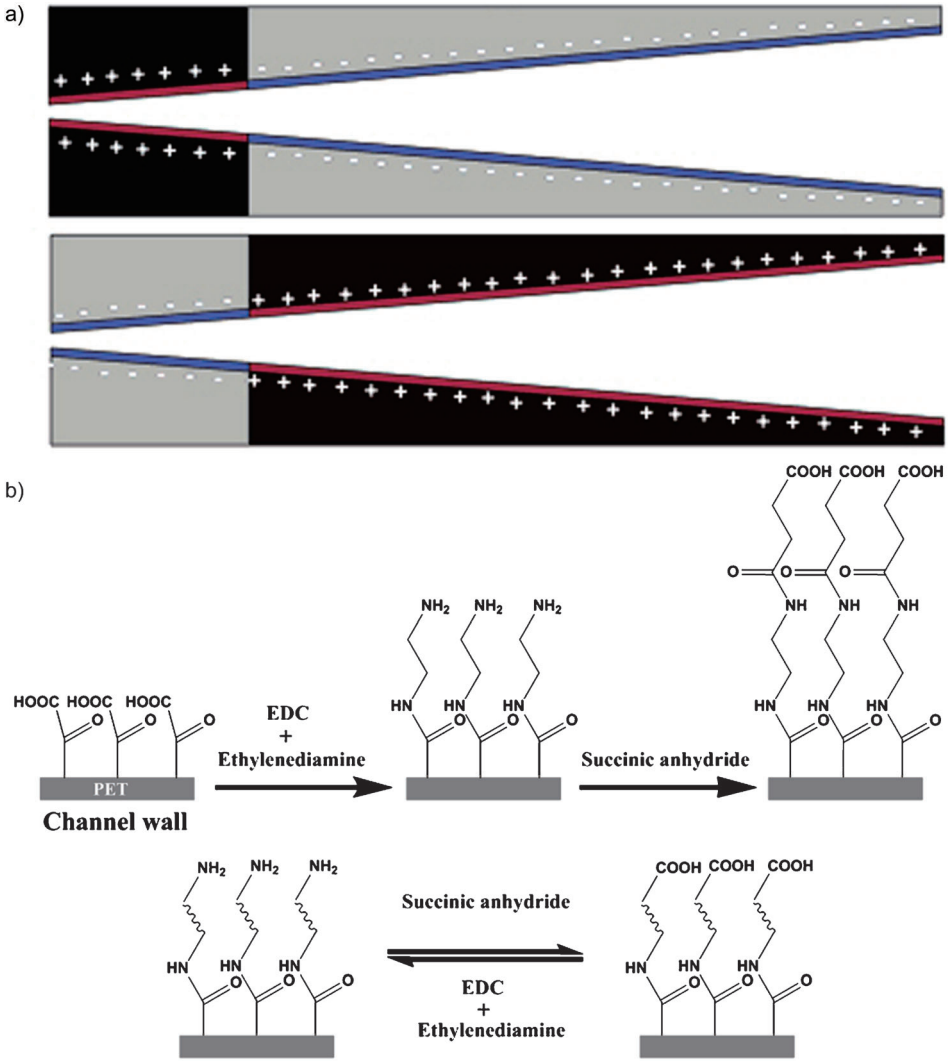


Figure 10. a) Asymmetric chemical modification by functional molecules in solution as applied to transform carboxylic acid groups into amino groups with different concentration gradients onto the inner wall of the conical nanochannels.[42a] b) Chemical modification of the inner surface of the nanochannel by functional molecules in solution. Carboxylic acid groups can be transformed into amide groups with EDC and ethylenediamine, and the resulting surface amines can be transformed to carboxylic acid groups by succinic anhydride.

tuned over with a wide range by controlling the modified region of the channel and the concentration of cationic surfactant hexadecyl trimethylammonium bromide inside the channel.[42b]

4. Summary and Outlook

Building bio-inspired artificial functional nanochannels imparts the ability to actively manipulate and control the transport of ions and molecules that are confined in a nanoscale space. It paves the way for mimicking the process of ionic/molecular transport in biological channels, as well as for boosting the development of bio-inspired intelligent nanomachines for real-world applications. At present, there has been rapid progress in developing artificial nanochannels, and these nanochannels are transforming technology in a variety of different fields, from life science[4c] to energy.[46] However, how to endow these artificial nanochannels with greater functionalization and intelligence is still a challenging task. Inspired by biological channels, this Minireview outlines the design and preparation of various artificial functional nanochannels from symmetric to asymmetric physicochemical modification approaches, and gives many examples to demonstrate the feasibility of the design strategy. Table 4 summarizes the above typical modification methods of the nanochannels and gives a comment on each of these methods.

The ion transport properties of these artificial nanochannels are substantially different from those of macroscopic channels, and understanding these properties requires the application of fundamental physicochemical concepts. The design strategy from symmetric to asymmetric modification could provide platforms for the further development of nanochannel systems. For instance, the transmembrane asymmetric states of the environment are omnipresent in cell membranes. However, at present, most artificial nanochan-

Table 4: Comments on various typical modification methods for nanochannels.

Modification method	Nanochannels	Functional substances	Comments	Ref.
Electroless deposition	PC, PET	Au	Increases the stability of nanochannels by plating a metal layer on the inner surface of the nanochannels and provides a good platform for further binding of all kinds of functional molecules by the self-assembly of thiols and chemical modification. However, this method is time consuming and involves toxic chemicals and heavy-metal salts.	[12, 47]
Chemical modification by functinal molecules in solution	PET, PI, PC, PC(PET)/Au	DNA, biotin, amino acids, polymeric brushes, thiols	The most commonly used method for functionalizing the inner surface of nanochannels though stable covalent bonds, such as C(O)—NH bonds and Au—S interactions.	[13, 21, 27, 32, 48]
Self-assembly	PET, PI	Polyelectrolytes	Changes the inner surface of nanochannels by specific molecular interactions, such as electrostatic interactions and intermolecular forces. These functional nanochannels are greatly influenced by environmental factors because of noncovalent interactions. The range of functionalities that can be obtained is limited.	[42b]
Ion sputtering	PET	Au, Pt	Coats the inner surface of nanochannels by depositing metal layers, increases the stability of the nanochannels, and provides a platform for further binding of all kinds of functional molecules by the self-assembly of thiols. It can be easily and widely used to achieve asymmetric modification of nanochannels. However, the thickness and uniformity of deposited metal layer within the channels is not well understood.	[39]
Electron-beam evaporation	PET	Au, SiO_2	Coats the surface of nanochannels by depositing metal/inorganic layers and can easily get continuous, multiple, nanometer-thick layers of metals.	[40a]
Initiated chemical vapor deposition	PC	Polymers	Coats the inner surface of nanochannels by depositing nanometers thick polymer layers, which can easily and quickly be used to symmetrically/asymmetrically modify any substrate without surface-tension limitations. It is also environmentally benign. However, the stability of the deposited polymer layer is not good.	[40b]
Plasma	PET	Polymer brushes	Controls specific modification of areas of nanochannels by symmetric and asymmetric plasma grafting of various polymers. It is easy and fast to obtain functional nanochannels; however, the modification density is hard to control.	[41]
Asymmetric chemical modification by functional molecules in solution	PET	Antibodies, succinic anhydride, ethylenediamine	Commonly used method for functionalizing diverse but specific local areas of the nanochannels though stable covalent bonds. The shape and the surface charge of the original nanochannels have a great impact on the asymmetric modification of the channels.	[42a, 44–45]
Asymmetric assembly in solution	PET	Surfactants, particles	It is a possible solution method for functionalizing diverse but specific local areas of the nanochannels by physical adsorption of surfactants or particles. This method is cheap, versatile and the materials are reusable.	[42b]

nels have been studied under symmetric stimuli, and how to achieve various smart transport controls under asymmetric stimuli is still in its early stages. Asymmetric modification will provide a useful method for developing functional nanofluidic devices that can operate in complex, asymmetric solution environments.

We hope this Minireview will inspire the active interest of many scientists in the area of building artificial functional nanochannels. We expect that designed asymmetric modification will find broad application as a useful strategy to establish approaches in the development of artificial functional nanochannel systems and facilitate the asymmetric design of other materials.

This work was supported by the National Research Fund for Fundamental Key Projects (2011CB935703, 2010CB934700, 2009CB930404, 2007CB936403) and the National Natural Science Foundation (20974113, 20920102036). The Chinese Academy of Sciences and National Center for Nanoscience and Technology, China are gratefully acknowledged. We also thank Dr. K. Li, Dr. Y. Tian, Prof. D. Qiu (Institute of Chemistry, Chinese Academy of Sciences), L. Zeng, Z. Yang, Dr. F. Yang, and Prof. D. D. Yan (College of Chemistry and College of Physics, Beijing Normal University) for beneficial discussions.

Received: July 14, 2011
Revised: January 13, 2012
Published online: April 13, 2012

[1] B. Hille, *Ion Channels of Excitable Membranes*, Sinauer Associates, Sunderland, MA, **2001**.
[2] E. Gouaux, R. MacKinnon, *Science* **2005**, *310*, 1461 – 1465.
[3] a) Z. S. Siwy, S. Howorka, *Chem. Soc. Rev.* **2010**, *39*, 5067 – 5067; b) A. J. Storm, J. H. Chen, X. S. Ling, H. W. Zandbergen, C. Dekker, *Nat. Mater.* **2003**, *2*, 537 – 540; c) C. Dekker, *Nat. Nanotechnol.* **2007**, *2*, 209 – 215; d) C. R. Martin, Z. S. Siwy, *Science* **2007**, *317*, 331 – 332; e) X. Hou, W. Guo, L. Jiang, *Chem. Soc. Rev.* **2011**, *40*, 2385 – 2401; f) G. L. C. Paulus, S. Shimizu, J. T. Abrahamson, J. Zhang, A. J. Hilmer, M. S. Strano, *AIChE J.* **2011**, *57*, 1104 – 1118.
[4] a) L. T. Sexton, L. P. Horne, C. R. Martin, *Mol. BioSyst.* **2007**, *3*, 667 – 685; b) X. Hou, L. Jiang, *ACS Nano* **2009**, *3*, 3339 – 3342; c) S. Howorka, Z. Siwy, *Chem. Soc. Rev.* **2009**, *38*, 2360 – 2384; d) L. P. Wen, X. Hou, Y. Tian, F. Q. Nie, Y. L. Song, J. Zhai, L. Jiang, *Adv. Mater.* **2010**, *22*, 1021 – 1024; e) D. W. Inglis, E. M. Goldys, N. P. Calander, *Angew. Chem.* **2011**, *123*, 7688 – 7692; *Angew. Chem. Int. Ed.* **2011**, *50*, 7546 – 7550.
[5] L. A. Baker, S. P. Bird, *Nat. Nanotechnol.* **2008**, *3*, 73 – 74.
[6] a) E. N. Savariar, K. Krishnamoorthy, S. Thayumanavan, *Nat. Nanotechnol.* **2008**, *3*, 112 – 117; b) R. H. Baughman, A. A. Zakhidov, W. A. de Heer, *Science* **2002**, *297*, 787 – 792; c) M. S. Strano, C. A. Dyke, M. L. Usrey, P. W. Barone, M. J. Allen, H. Shan, C. Kittrell, R. H. Hauge, J. M. Tour, R. E. Smalley, *Science* **2003**, *301*, 1519 – 1522; d) H. Liu, J. He, J. Tang, H. Liu, P. Pang, D. Cao, P. Krstic, S. Joseph, S. Lindsay, C. Nuckolls, *Science* **2010**, *327*, 64 – 67; e) R. Kawano, T. Osaki, H. Sasaki, M. Takinoue, S. Yoshizawa, S. Takeuchi, *J. Am. Chem. Soc.* **2011**, *133*, 8474 – 8477; f) G. Maglia, M. R. Restrepo, E. Mikhailova, H. Bayley, *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 19720 – 19725; g) S. Majd, E. C. Yusko, Y. N. Billeh, M. X. Macrae, J. Yang, M. Mayer, *Curr. Opin. Biotechnol.* **2010**, *21*, 439 – 476; h) T. Osaki, H. Suzuki, B. Le Pioufle, S. Takeuchi, *Anal. Chem.* **2009**, *81*, 9866 – 9870.
[7] a) A. Mara, Z. Siwy, C. Trautmann, J. Wan, F. Kamme, *Nano Lett.* **2004**, *4*, 497 – 501; b) E. A. Heins, Z. S. Siwy, L. A. Baker, C. R. Martin, *Nano Lett.* **2005**, *5*, 1824 – 1829; c) G. Wang, A. K. Bohaty, I. Zharov, H. S. White, *J. Am. Chem. Soc.* **2006**, *128*, 13553 – 13558; d) G. Wang, B. Zhang, J. R. Wayment, J. M. Harris, H. S. White, *J. Am. Chem. Soc.* **2006**, *128*, 7679 – 7686; e) M. Ali, Q. H. Nguyen, R. Neumann, W. Ensinger, *Chem. Commun.* **2010**, *46*, 6690 – 6692.
[8] P. Y. Apel, I. V. Blonskaya, S. N. Dmitriev, T. I. Mamonova, O. L. Orelovitch, B. Sartowska, Y. Yamauchi, *Radiat. Meas.* **2008**, *43*, S552 – S559.
[9] R. E. Gyurcsányi, *Trends Anal. Chem.* **2008**, *27*, 627 – 639.
[10] A. L. Sisson, M. R. Shah, S. Bhosale, S. Matile, *Chem. Soc. Rev.* **2006**, *35*, 1269 – 1286.
[11] C. C. Harrell, Z. S. Siwy, C. R. Martin, *Small* **2006**, *2*, 194 – 198.
[12] M. Nishizawa, V. P. Menon, C. R. Martin, *Science* **1995**, *268*, 700 – 702.
[13] a) Z. Siwy, L. Trofin, P. Kohli, L. A. Baker, C. Trautmann, C. R. Martin, *J. Am. Chem. Soc.* **2005**, *127*, 5000 – 5001; b) F. Xia, W. Guo, Y. D. Mao, X. Hou, J. M. Xue, H. W. Xia, L. Wang, Y. L. Song, H. Ji, Q. Ouyang, Y. G. Wang, L. Jiang, *J. Am. Chem. Soc.* **2008**, *130*, 8345 – 8350; c) E. N. Savariar, M. M. Sochat, A. Klaikherd, S. Thayumanavan, *Angew. Chem.* **2009**, *121*, 116 – 120; *Angew. Chem. Int. Ed.* **2009**, *48*, 110 – 114.
[14] a) M. Ali, B. Yameen, R. Neumann, W. Ensinger, W. Knoll, O. Azzaroni, *J. Am. Chem. Soc.* **2008**, *130*, 16351 – 16357; b) M. Ali, B. Yameen, J. Cervera, P. Ramirez, R. Neumann, W. Ensinger, W. Knoll, O. Azzaroni, *J. Am. Chem. Soc.* **2010**, *132*, 8338 – 8348.
[15] G. O. Mallory, J. B. Hajdu, *Electroless Plating: Fundamentals and Applications*, American Electroplaters and Surface Finishers Society, Orlando, FL, **1990**.
[16] V. P. Menon, C. R. Martin, *Anal. Chem.* **1995**, *67*, 1920 – 1928.
[17] J. E. A. M. Meerakker, *J. Appl. Electrochem.* **1981**, *11*, 387 – 393.
[18] a) H. Li, H. Lin, S. H. Xie, W. L. Dai, M. H. Qiao, Y. F. Lu, H. X. Li, *Chem. Mater.* **2008**, *20*, 3936 – 3943; b) G. A. Krulik, *J. Chem. Educ.* **1978**, *55*, 361 – 365.
[19] K. P. Pernstich, M. Schenker, F. Weibel, A. Rossi, W. R. Caseri, *ACS Appl. Mater. Interfaces* **2010**, *2*, 639 – 643.
[20] S. Fujikawa, R. Takaki, T. Kunitake, *Langmuir* **2006**, *22*, 9057 – 9061.
[21] a) M. Ali, P. Ramirez, S. Mafé, R. Neumann, W. Ensinger, *ACS Nano* **2009**, *3*, 603 – 608; b) B. Yameen, M. Ali, R. Neumann, W. Ensinger, W. Knoll, O. Azzaroni, *Chem. Commun.* **2010**, *46*, 1908 – 1910; c) B. Yameen, M. Ali, R. Neumann, W. Ensinger, W. Knoll, O. Azzaroni, *J. Am. Chem. Soc.* **2009**, *131*, 2070 – 2071.
[22] X. Hou, W. Guo, F. Xia, F. Q. Nie, H. Dong, Y. Tian, L. P. Wen, L. Wang, L. X. Cao, Y. Yang, J. M. Xue, Y. L. Song, Y. G. Wang, D. S. Liu, L. Jiang, *J. Am. Chem. Soc.* **2009**, *131*, 7800 – 7805.
[23] M. Ali, S. Mafe, P. Ramirez, R. Neumann, W. Ensinger, *Langmuir* **2009**, *25*, 11993 – 11997.
[24] C. P. Han, X. Hou, H. C. Zhang, W. Guo, H. B. Li, L. Jiang, *J. Am. Chem. Soc.* **2011**, *133*, 7644 – 7647.
[25] B. Yameen, M. Ali, R. Neumann, W. Ensinger, W. Knoll, O. Azzaroni, *Small* **2009**, *5*, 1287 – 1291.
[26] M. Ali, B. Schiedt, R. Neumann, W. Ensinger, *Macromol. Biosci.* **2010**, *10*, 28 – 32.
[27] M. Ali, R. Neumann, W. Ensinger, *ACS Nano* **2010**, *4*, 7267 – 7274.
[28] a) S. T. Wang, H. J. Liu, D. S. Liu, X. Y. Ma, X. H. Fang, L. Jiang, *Angew. Chem.* **2007**, *119*, 3989 – 3991; *Angew. Chem. Int. Ed.* **2007**, *46*, 3915 – 3917.
[29] a) C. C. Harrell, P. Kohli, Z. Siwy, C. R. Martin, *J. Am. Chem. Soc.* **2004**, *126*, 15646 – 15647; b) W. Guo, H. W. Xia, F. Xia, X. Hou, L. X. Cao, L. Wang, J. M. Xue, G. Z. Zhang, Y. L. Song, D. B. Zhu, Y. G. Wang, L. Jiang, *ChemPhysChem* **2010**, *11*, 859 – 864.
[30] a) J. C. Hulteen, K. B. Jirage, C. R. Martin, *J. Am. Chem. Soc.* **1998**, *120*, 6603 – 6604; b) K. B. Jirage, J. C. Hulteen, C. R. Martin, *Anal. Chem.* **1999**, *71*, 4913 – 4918.
[31] a) K. Y. Chun, P. Stroeve, *Langmuir* **2002**, *18*, 4653 – 4658; b) J. R. Ku, S. M. Lai, N. Ileri, P. Ramírez, S. Mafé, P. Stroeve, *J. Phys. Chem. C* **2007**, *111*, 2965 – 2973.
[32] a) S. B. Lee, C. R. Martin, *Anal. Chem.* **2001**, *73*, 768 – 775; b) S. B. Lee, C. R. Martin, *Chem. Mater.* **2001**, *13*, 3236 – 3244.
[33] G. Jágerszki, R. E. Gyurcsányi, L. Höfler, E. Pretsch, *Nano Lett.* **2007**, *7*, 1609 – 1612.
[34] B. Y. Kim, C. B. Swearingen, J. A. Ho, E. V. Romanova, P. W. Bohn, J. V. Sweedler, *J. Am. Chem. Soc.* **2007**, *129*, 7620 – 7626.
[35] R. E. Gyurcsanyi, T. Vigassy, E. Pretsch, *Chem. Commun.* **2003**, 2560 – 2561.
[36] a) G. Jágerszki, Á. Takács, I. Bitter, R. E. Gyurcsányi, *Angew. Chem.* **2011**, *123*, 1694 – 1697; *Angew. Chem. Int. Ed.* **2011**, *50*, 1656 – 1659.
[37] H. Alem, F. Blondeau, K. Glinel, S. Demoustier-Champagne, A. M. Jonas, *Macromolecules* **2007**, *40*, 3366 – 3372.
[38] a) R. Schmuhl, A. van den Berg, D. H. A. Blank, J. E. ten Elshof, *Angew. Chem.* **2006**, *118*, 3419 – 3423; *Angew. Chem. Int. Ed.* **2006**, *45*, 3341 – 3345.
[39] a) X. Hou, H. Dong, D. B. Zhu, L. Jiang, *Small* **2010**, *6*, 361 – 365; b) Y. Tian, X. Hou, L. Jiang, *J. Electroceram. Chem.* **2011**, *656*, 231 – 236.
[40] a) E. B. Kalman, O. Sudre, I. Vlassiouk, Z. S. Siwy, *Anal. Bioanal. Chem.* **2009**, *394*, 413 – 419; b) A. Asatekin, K. K. Gleason, *Nano Lett.* **2011**, *11*, 677 – 686.

[41] a) X. Hou, Y. J. Liu, H. Dong, F. Yang, L. Li, L. Jiang, *Adv. Mater.* **2010**, *22*, 2440 – 2443; b) X. Hou, F. Yang, L. Li, Y. L. Song, L. Jiang, D. B. Zhu, *J. Am. Chem. Soc.* **2010**, *132*, 11736 – 11742.
[42] a) I. Vlassiouk, Z. S. Siwy, *Nano Lett.* **2007**, *7*, 552 – 556; b) L. Wang, Y. Yan, Y. Xie, L. Chen, J. Xue, S. Yan, Y. Wang, *Phys. Chem. Chem. Phys.* **2011**, *13*, 576 – 581.
[43] K. K. S. Lau, K. K. Gleason, *Macromolecules* **2006**, *39*, 3688 – 3694.
[44] E. B. Kalman, I. Vlassiouk, Z. S. Siwy, *Adv. Mater.* **2008**, *20*, 293 – 297.
[45] I. Vlassiouk, T. R. Kozel, Z. S. Siwy, *J. Am. Chem. Soc.* **2009**, *131*, 8211 – 8220.
[46] L. P. Wen, X. Hou, Y. Tian, J. Zhai, L. Jiang, *Adv. Funct. Mater.* **2010**, *20*, 2636 – 2642.
[47] Z. Siwy, E. Heins, C. C. Harrell, P. Kohli, C. R. Martin, *J. Am. Chem. Soc.* **2004**, *126*, 10850 – 10851.
[48] B. Yameen, M. Ali, R. Neumann, W. Ensinger, W. Knoll, O. Azzaroni, *Nano Lett.* **2009**, *9*, 2788 – 2793.