Learning from Nature: Building Bio-Inspired Smart Nanochannels

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ABSTRACT Learning from nature has inspired the fabrication of novel artificial materials that enable researchers to understand and to imitate biology. Bio-inspired research, in particular, owes much of its current development to advances in materials science and creative "smart" system design. The development and application of bio-inspired nanochannels is a burgeoning area in this field of research. Bio-inspired nanochannels enable many potential approaches to study various biomolecules in confined spaces and in real-time by current measurements. In this Perspective, we describe how these bio-inspired systems can be used to build novel, smart nanodevices with precisely controlled functions. Applications for these systems range from simulating the process of ion transport in living organisms by using biomimetic nanochannels to applying artificial nanochannel systems to investigate the chemistry, structure, size, and conformational states of biomolecules.

Structures from Nature have remarkable properties, many of which have inspired laboratory research. Bio-inspired materials and devices are attracting increasing interest because of their unique properties, which have paved the way to many significant applications.[1−3] Ion channels that exist in living organisms play important roles in maintaining normal physiological conditions and serve as "smart" gates to ensure selective ion transport (Figure 1). Normal body function depends strongly on regulation of ion transport inside these nanochannels. Thus, designing a system that simulates these complex processes in living systems is a challenging task for nanoscience.

Chemical Modification of the Nanochannels. Nanopores[4] can be defined simply as pores having diameters of 1 to 100 nm, with the pore diameter larger than its depth. If the pore depth is much larger than the diameter, the structure is generally referred to as a nanochannel.[5,6] At present, fabrication and application of artificial nanochannels and nanopores are becoming the focus of attention because, compared with their biological counterparts, they offer greater flexibility in terms of shape and size, superior robustness, and surface properties that can be tuned depending on the desired function.[7−9] Chemical modification of the interior surface of the nanochannels with functional molecules that closely mimic the gating mechanisms of biological channels may provide a highly efficient means to control ionic or molecular transport through nanometer-scale openings in response to ambient stimuli, such as applied force,[5] light,[10] pH,[11,12] and specific ions[13,14] (Figure 1, bottom left). These nanochannel−molecule systems can be used to build smart biomimetic structures with more precisely controlled functions in the near future by designing more complex functional molecules.

> Real-world applications require the design and development of smart nanodevices using artificial nanochannels that may respond to a single external stimulus, such as temperature, light, or pH, or to dual or even multiple stimuli.

What challenges remain in the design and implementation of these biomimetic nanochannel systems? There are already many approaches for chemical modification of the interior surfaces of nanochannels, including electroless deposition,[15] solution chemical modification,[16] and electrostatic self-assembly;[17] however, it is still a challenge to functionalize a specific local area precisely, whether *via* symmetric or asymmetric chemical modification. Another important aim is the ability to control precisely the density of grafted functional molecules in terms of surface coverage. Real-world applications require the design and development of smart nanodevices using artificial nanochannels that may respond to a single external stimulus, such as temperature,[18] light,[10] or pH,[6,11,12] or to dual or even multiple stimuli.

Application of Artificial Nanochannels as Biosensors. A single nanochannel presents an optimal system for studying transport properties of different ions or molecules in

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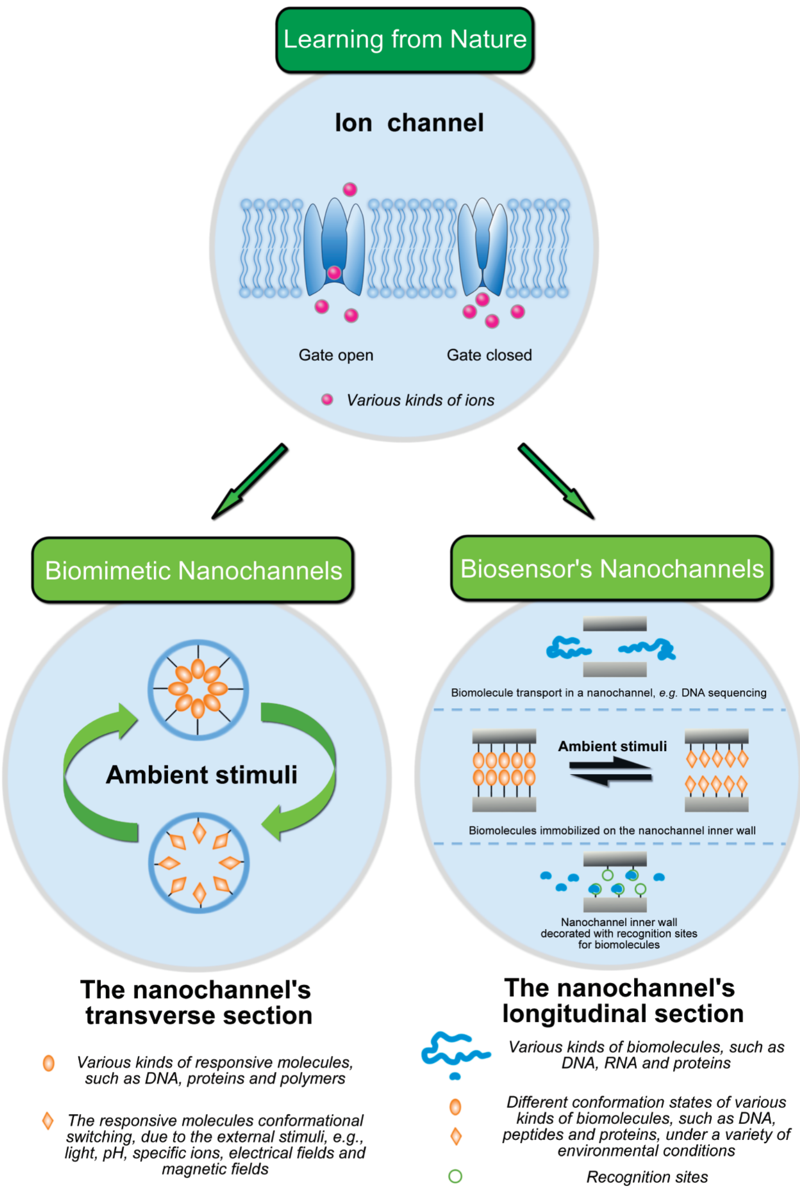

Figure 1. Bio-inspired nanochannel systems: learning from nature means taking ideas from nature and developing novel functional materials based on these concepts. Top: Inspired by natural phenomena, we can design smart artifical nanochannel systems for life science research. Bottom left: We can simulate the process of ion transport in living organisms by using the biomimetic nanochannels. Bottom right: Artificial nanochannel systems can be used to investigate the chemical, structural property, and conformational changes of biomolecules in confined spaces.

confined space because one can observe directly the behavior of a single channel without having to average the effects of multiple channels. The first experiments to use this idea involved the biological nanopore α-hemolysin inserted in a lipid bilayer for the detection of single DNA polynucleotides.[19] Recently, there has been significant interest in the development of artificial nanochannels as sensing elements for chemical and biochemical sensors,[7,20−22] due to their mechanical and chemical stability. They enable single-molecule detection and analytical capabilities that are achieved by the measurement of ionic current blockades caused by different conformations of the molecules through a nanoscale pore or channel. It is expected that the chemistry, size, and conformational states of biomolecules passing through the channel will be reflected in the duration and magnitude of the current.

This approach has been used to investigate a wide range of biomolecular translocation events through artificial nanochannels,[4,23,24] which has led to an increasing understanding of basic physical translocation processes. Moreover, artificial nanochannels provide two potential advantages for biosensing. First, there are numerous interactions between the ions or biomolecules in solution and the targeting molecules on the channel walls as the solution travels the distance of the nanochannel; thus, it is possible to improve signal detection[25] and achieve different quantitative analyses[26] simply by lengthening the channel. The second advantage is that the size, length, and shape of the confined space provided by nanochannels can be controlled precisely by different approaches, such as metered penetration[23] or by ion track-etching technology,[20] thereby providing closer resemblance to physiological conditions. Furthermore, grafting of biomolecules on the inner walls of the nanochannel can mimic *in vivo* conditions (Figure 1, bottom right). For example, the G-rich telomere overhang is attached to the chromosome in confined space *in vivo*, a condition that can be more closely mimicked in an artificial nanochannel, compared to experiments performed in solution.[13] In this way, nanochannels can be used to study conformational changes of biomolecules in confined spaces, from another perspective, compared to biomolecular transport in nanopores.[24] It is worth mentioning that conformational changes may be observed in real-time, due to changes in the detected current caused by the physical blockage of different biomolecular conformational states and changes in the distribution of charge density of biomolecules on the interior surfaces of the nanochannels.

In addition, a simple strategy exists based on specific biomolecular ligands bound to recognition sites on the interior surface of nanochannels, which can then be used as recognition elements for developing a biosensor (Figure 1, bottom right). By designing specific recognition sites, it may be simple to detect various biomolecules by measuring the current drop at a constant potential. This strategy is different from a resistive-pulse nanochannel sensor,[27] in which the analyte is identified by the current–pulse signature. Because biomolecular analytes are comparable in size to the narrowest of nanochannels, binding of the biomolecules leads to blocking the nanochannel, which is detected as a permanent blockage of the ionic current.[17] Although this specific configuration is a "one-use" sensor, if the ligands and recognition sites are only weakly bound, the sensor can be regenerated and used again.[28]

Focus on Biosensing with Artificial Nanochannels. For sensing with nanochannels, there are several existing challenges, which limit their stability, sensitivity, reliability, and practicability. Composite nanochannel materials, such as metal–polymer compounds, are a potential way to increase the robustness of nanochannels.[29] Another necessary consideration is the fabrication of nanochannels with high length-to-diameter ratios, which contributes to the observed translocations and higher temporal resolution.[22] Material contamination is also a significant issue for improving the cycling properties of the sensors and lowering application costs.

Although research toward bio-inspired smart nanochannels is still in its early stages, it will be enhanced greatly by the development of both chemistry and nanotechnology methods that are capable of producing more smart functional molecules and variations in the chemical and physical properties of the confined channel space.

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A breakthrough in biosensing for real-world applications is therefore expected from implementing artificial nanochannels, an area that is still under rapid development.

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