Nanochannel and Its Application in Analytical Chemistry

Zenglian Yue, Guoqing Zhao, Bin Peng, Shasheng Huang*
College of Life and Environment & science
Shanghai Normal University
Shanghai, 200234, China
sshuang@shnu.edu.cn http://www.shnu.edu.cn

Abstract: The nanochannels method for the separation and detection of analytes plays an important role in the analytical chemistry and is exhibiting the great potential advantages and promising future. In this review we bring together and discuss a number of nanochannels made of biological and special material. The preparation and application of biological nanochannels are described. Compared with the biological single channel, nanochannels prepared by special material are more selective and have advantages in practical application because these channels are less fragile and more easily modified. Studies of the special material membrane involve in the chemical, bio-technical, medical fields, etc. For the increasing interest in using material channels at present, we demonstrated the synthetic methods of different special material nanochannels and a mount of their applications in analytical chemistry here. The advantages and tendency of nanochannels are discussed as well.

Key-Words: - Nanochannels, separation, preparation, applications

1 Introduction

Traditional separation methods and techniques such as extraction, ion-exchange, chromatography, etc. are confronted with great challenges. How to separate and analyze trance analytes is the focus of the challenges. With the fast development of nanotechnology in 1999s, new thoughts and opportunities have appeared for deep research of separation. Nanochannels are the pores or channels with diameter from 0.1 to 100 nanometers. As an important part of nanoscience, nanochannels technique has become a new growth point. It is exhibiting the great potential advantages and promising future due to the size effect, chemical and physical characteristics.

At present, the studies about nanochannels mainly refer to the biological nanochannels and material nanochannels. The biological nanochannels such as bacterial α-hemolysin (α-HL) a heptameric protein that spontaneously assembles in a lipid membrane has proven in the separation of peptide [1]. A single channel (typically an α-hemolysin channel) also can be used as the sensing element. These sensors can detect individual analyte with channel interactions and convert these stochastic events into a current pulse. Sutherland et al [2] demonstrated that peptide transport through nanopores can also be used to analyze the structure of peptides. Depending on this device, the change in current can be used to determine size and the concentration of the analytical species.

However, lower stability and reproducibility of traditional bilayer membrane limited its practical application. In contrast with the biological single channel, material nanochannels have advantages in practical application, special because these channels are less fragile.

The studies on the special material membrane have received intensive interest since Martin et al. reported gold nanochannels membrane for the separation of small molecules on the basis of molecular size [3]. Generally, material nanochannels are prepared by special materials such as carbon nanochannels, silicon nanochannels, nanochannel array (eg. porous alumina membranes and the polycarbonate tracketched membranes) and so on. The templates of material nanochannels include membrane template, emulsion / micromulsion template and other kinds of templates.

In this article, we will first introduce the general configuration and the preparation of nanochannels. The unique properties of gold nanochannels for chemistry and bioseparation have been summarized. At the same time, some successful examples of nanochanneles membrane that have been applied to chemical and biomolecular species have been introduced. The novel bioseparation method based on nanotubules will also
be described. The objective of this review is to introduce the extremely valuable nanochannels to the biologists and chemists and encourage them to consider nanotubules in their research.

2. Biological nanochannels

2.1 Structure and characteristics of biological nanochannels

Biological nanochannels were first posted in 1999. One of the typical channels is a single $\alpha$-hemolysin in cross-section embedded in a lipid bilayer with a diameter about 1.5-2.6 nm [4]. Ions, water and other small molecules can go through this channel. So it can be used as an ion-channel. The structure of $\alpha$-HL is shown as figure 1.

![Figure 1](image)

The important structure features of $\alpha$-HL are the mouth of the channel (2.6 nm), which leads into a larger vestibule, and the stem of the channel containing a pore with an interior diameter of 2.2 nm. The opening between the vestibule and stem forms the limiting aperture of 1.5 nm diameter, so it can only allow the single strand DNA to go through the channel while the double strand DNA can not. $\alpha$-HL is composed of a ring of 14 alternating lysine and glutamate side chain. So the channel is hydrophilic in the interior while lyophobic in the exterior [5].

2.2 Applications of biological nanochannels

The biophysical characteristics of poly-nucleic acids through the channel were first researched by Kasianowicz and his group [6]. They found that the single molecules of DNA or RNA can be detected as they are driven through the $\alpha$-hemolysin channel by applying an electric field. During translocation, the spread single DNA or RNA can block the channel and transiently block the ion current, resulting in a downward current pulse. The duration of the current pulses is proportional to the length of the polymer molecules. It has proved that this nanochannel can be used to find differing pyridine and purine quickly [4]. Szabo et al. covalenced biotin molecule with the 3.4kDa poly-ethyleneglycol of monomer cysteine -106 radical and then bonded with the deep area of $\alpha$-HL pore. After modification, the ionic current would be lower by 15% [10].

However, the stability of traditional bilayer membrane is not so high and this membrane can not play important role in practice. So, there is much room to improve in acquiring the carrier with more channel selectivity and higher stability. It has been proved that solid supported object as the carrier will be more stable than the single channel. Cornel et al. stablized the ramicidin on the Au surface as a biosensor and studied the transport of electrolyte [11]. Stora et al. studied the bacterial multiplicore channel on the similar surface, and found that the R residue can close the channel [12].

3 Nanochannels of special material

Nanochannels of special material are nanochannel arrays prepared by the template -synthesized method. This kind of special material nanochannels is more selective and producible due to the flexible nanochannels membrane. The application of these nanochannels membrane was expanded due to the modification within the pores. The templates, preparation and application of these channels in the below were shown in table 1.

![Table 1](image)

3.1 The templates of nanochannels

Generally, the membranes such as porous alumina membranes and the track-etched membranes generally can be used as template to make nanochannels. The track-etched membranes prepared by polycarbonate, polycatate or other polymer material membranes are broadly used. At present, it is a general method to synthesize nanomaterials within the pores of porous alu-
minerals. In contrast to traditional electron-etch technology, this method can get the nanomaterial with high aspect ratio. Furthermore, this method described here provides a simple means to alter the diameter of the nanosized pores easily and make the nanomaterial with good thermal stability.

It is possible to use nonaqueous emulsion template to get the ordered macroporous molecule sieve because inorganic oxide is easily hydrolyzed. Imhof and Pine reported a new method for producing highly monodisperse macroporous materials with pore sizes ranging from 50 nm to several micrometres. The result showed that the pore size can be accurately controlled, and that the technique should be applicable to a wide variety of metal oxides and even organic polymer gels [13]. Walsh and his coworkers described a method for synthesizing hollow porous shells of crystalline calcium carbonate (aragonite) that resembles the coccospheres of certain marine algae. They showed that thin cellular frameworks of either mesoporous or macroporous aragonite can be formed from oil–water–surfactant microemulsions supersaturated with calcium bicarbonate. Hollow spherical shells of the honeycomb architecture can be produced by using micrometre-sized polystyrene beads as the substrate for the microemulsion. It proposed that these cellular frameworks originated from rapid mineralization of aragonite, with self-organized foam of oil droplet acting as a structural template, and similar processes could be of general importance in materials chemistry [14].

Zhao et al. reported a morphological control approach using block copolymers, cosurfactants, cosolvents, or the additive of strong electrolytes to selectively form micrometer-sized hard sphere-, fiber-, doughnut-, rope-, egg-sausage-, gyroid-, and discoid-like mesoporous silica SBA-15 with highly ordered large mesopore hexagonal structures [15].

The synthesis of mesoporous materials using surfactants as templates has been studied extensively since 1992 [16, 17]. In 1998, mesoporous silica materials were prepared by HCl-catalyzed sol-gel reaction of tetraethyloxysilicate in the presence of non-surfactant templating compounds, e.g., D-glucose, D-maltose, and dibenzoyl-L-tartaric acid [18]. This new, versatile, low-cost, environmentally friendly non-surfactant templating pathway leads to mesoporous materials with large surface areas and pore volumes as well as narrow pore size distributions. Zheng and Qiu synthesized mesoporous titania materials using non-surfactant organic compounds, such as 2, 2-bis (hydroxymethyl) propionic acid, glycerin and pentaechytritol, as templates via the HCl-catalyzed sol-gel process. The surface area and pore volume increase slightly with increasing content of organic template while the pore size is nearly constant (3.0–4 nm) with narrow distribution about 0.5–0.8 nm [19].

Davis et al. showed how a bacterial superstructure, consisting of a thread of coaligned multicellular filaments of bacillus subtilis, can be used to extend the length scale of inorganic materials patterning [20].

3.2 Preparation of Membrane

Template-synthesized method is often used in synthesizing nanochannels. It uses the porous material as template containing pores whose diameter is varied from micron to nanometer. Electrochemical deposition, chemical deposition, chemical polymerization, sol-gel and chemistry gas deposition methods can be used to deposit the atom or ion on the pore walls to form channels and then remove away the template or leave it as supported matter.

Potentiostatic or galvanostatic method at room temperature can sputter a layer of Au onto one side of membrane to make the surface electrically conductive. This electrodeposition method has been used to prepare metal nanowire of Cu, Pt, Au and Ni. Changing the amount of metal deposition can make the wires with different length. A spot of metal deposition can get short wires while a mass of metal deposition can get long and acicular wires. Zhang et al. used electrodeposition method to fabricate the single-crystalline anatase TiO2 nanowire arrays by anodic oxidative hydrolysis of TiCl4 with AAO(porous alumina membranes) template [21,22].The fabrication of Au and Ni nanowire arrays is also reported. Li et al. used this method to prepare Bi2Te3 and Bi2Te3 derived alloy nanochannel arrays [23].

Electroless metal deposition involves the use of a chemical reducing agent to plate a metal from solution onto a surface. Menon and Martin described detail of electroless deposition of Au on the nanochannels of polycarbonate membrane. The advantage of the electroless method (relative to electrochemical plating) is that the surface to be coated does not need to be electronically conductive. The key feature of the electroless deposition process is that Au deposition begins at the pore wall. Changing the deposition time can get the hollow tubules or stuffed wires. Unlike electrode-
position, by this method it is possible to control the inner diameter by changing the deposition time [24]. Nishizawa et al. synthesized many conductive polymers and prepare the nanochannel or nanowire by controlling the deposition time [25].

Chemical polymerization is performed by immersing the membrane template into the solution including polymeric monomer and polymeric reagent. The inner diameter can be controlled by changing the polyreaction time. The outside diameter is decided by the diameter of template pore. Parthasarathy et al. produced polyacrylonitrile nanochannel by immersing the porous alumina membranes into the solution containing acrylonitrile momomer [26].

Sol-gel chemistry has recently been evolved into a general and powerful approach for producing inorganic materials [27, 28]. This method typically entails hydrolysis of a solution of a precursor molecule to obtain a suspension of colloidal particles (the sol) and then a gel composed of aggregated sol particles. The gel is then thermally treated to yield the desired material. It occurred to us that sol-gel chemistry could be done within the pores of the nanoporous template membranes to obtain tubules and fibrils of a variety of inorganic materials. Martin used this method to make tubules and fibrils composed of polymers, metals, semiconductors, carbon, and Li ion intercalation materials [29-31]. Lakshmi et al. combined the sol-gel and template methods to prepare fibrils and tubules of a variety of inorganic materials including ZnO, WO3 and TiO2 using alumina membrane as a template. They found that single-crystal anatase-phase TiO2 nanostructures can be obtained via this approach and that these nanostructures can be used as efficient photocatalysts [32]. Like other template synthesis methods, changing the immersion time can get the nanochannels or nanofibrils.

Chemical vapor deposition (CVD) is a way to deposit the material onto the template in the vapor. The problem is that the material may block the pores of surface and cannot deposit inside because of the fast deposition speed. Li et al. developed a method for producing pure carbon nanochannel fibers which involved direct spinning of continuous fibers from an aerogel of carbon nanochannels formed by CVD [33]. This process was realized through the appropriate choice of reactants, control of the reaction conditions and continuous withdrawal of the product with a rotating spindle used in various geometries.

3.3 Applications of special material nanochannels

3.3.1 Separation of the small molecule

The nanochannels can be acted as the molecular sieving and the filtration. In 1995, Menon and Martin first reported a commercially available microporous polycarbonate filter with cylindrical nanoscopic pores. The gold nanotubules are prepared via electroless deposition of Au onto the pore walls; i.e., the pores act as templates for the nanotubules [24]. By controlling the Au deposition time, Au nanotubules that have effective inside diameters of molecular dimensions (< 1 nm) can be prepared. Hence, these membranes are a new class of molecular sieves. Only if the diameter is small enough, it is possible to separate the small molecule from the large one. They used the nanotubule of 0.6 nm to separate permeate pair pyridine/quinine, anilin/iun/rhodamineB, MV2+/Ru- (bpy)32+ and the selectivity coefficient was 15000, 130000 and 1500, respectively [34]. The fine structures of organic molecules greatly affected the transport of small organic molecules through the Au-nanotubules. The modification of gold nanotubules expands the difference of transport of VB2 and Try through the nanomembrane [35]. The nanomembrane based on the modification of functional groups can be used to separate and detect rutin [36].

3.3.2 Separation of mixtures containing hydrophobic and hydrophilic molecules

Chemical interactions between the membrane material and the molecule to be transported can also be used to control transport selectivity. The introduction of chemically based transport selectivity into Au nanotube membranes has been accomplished by chemisorbing thiols (RSH) to the Au tubule surfaces. Hulteen et al. reported the ratio of the fluxes for toluene vs pyridine transport in the diameters of 1.5 nm membrane modified with an alkyl (R = C18H33) was greater than 400, suggesting that this membrane might be useful for separating mixtures containing hydrophobic and hydrophilic molecules [37].

The micropore and nanochannel membranes with mimic function were also synthesized. These membranes can be switched from an “off” state (no or low ion current through the membrane) to an “on” state (higher ion current) in response to the presence of a chemical stimulus. The “off” state was obtained by making the membranes hydrophobic by chemisorbing either a C18 silane (alumina membrane) or a C18 thiol...
(Au nanochannel membrane). Water and electrolyte are forbidden from entering these very hydrophobic pores/nanochannels. The transition to the “on” state was induced by partitioning a hydrophobic ionic species (e.g., a drug or a surfactant) into the membrane. The membrane switches to the “on” state because at a sufficiently high concentration of this ionic analyte species, the pores/nanochannels flood with water and electrolyte. A pH-responsive membrane was also prepared by attaching a hydrophobic alkyl carboxylic acid silane to the alumina membrane. Steinle et al. investigated the transport of amiodarone, amitriptyline and bupivacaine in the hydrophobic channels [38].

3.3.3 Separation of protein and DNA

Huang et al. prepared the gold nanotubule with about 55 nm of diameter by chemical deposition of gold on polycarbonate templates membrane. After being modified by cysteine and guanide thiocyanate, the nanomembranes were studied with BSA and IgG as the model molecules. The results showed that guanide thiocyanate facilitated transporting of BSA by 30 to 50 times because of hydrophilic and denaturalization effects whereas IgG almost retained its transporting activity can be obtained [43]. The nanochannels with inside diameter of the silica nanochannels decreases [52].

3.3.4 Separation of chiral drug

Synthetic bio-nanochannel membranes were developed and used to separate two enantiomers of a chiral drug. Lee et al. used alumina films that had cylindrical pores with monodisperse nanoscopic diameters (for example, 20 nanometers). Silica nanochannels were chemically synthesized within the pores of these films, and an antibody selectively bindings one of the enantiomers of the drug was attached to the inner walls of the silica nanochannels. These membranes selectively transport the enantiomer specifically binded to the antibody. The enantiomeric selectivity coefficient increases as the inside diameter of the silica nanochannels decreases [52].

In addition to transmembrane potential and nanochannel diameter, solution pH value plays an important role in determining the transport selectivity. This is because pH determines the net charge on the protein molecule and this, in turn, determines the importance of the electrophoretic transport term. Yu et al. investigated the transport properties of four proteins (lysozyme, bovine serum albumin, carbonic anhydrase and bovine hemoglobinins) with different sizes and pI values [54].

3.3.6 Sensors based on the nanochannels

The nanochannel membranes can also be used as sensors. Martin and his coauthors have shown that electrically conductive polymers with fibrillar supramolecular structures can be prepared by synthesizing the polymer within the pores of a microporous membrane. They compared charge transport rates in fibrillar polypyrrole with the corresponding rates in conventional polypyrrole films. The results showed that the charge transport rates in the fibrillar versions can be significantly higher [55].

Figure2

Martin et al. described an electroless deposition procedure for filling the pores in nanoporous filtration
membranes with metal (gold) nanowires. This method prepared ensembles of gold nanodisk electrodes in which the nanodisks have diameters as small as 10 nm. Cyclic voltammetric detection limits for electroactive species at ensembles containing 10-nm-diameter gold disks can be as much 3 orders of magnitude lower than those at large-diameter gold disk electrodes. Moretto et al. described the construction and characterization of an electrochemical nitrate biosensor based on the ultrathin-film composite membrane concept. This film separated the analyte solution from an internal sensing solution which contained the enzyme nitrate reductase and an electrocatalyst (methyl viologen). The sensor showed good sensitivity to nitrate, with a detection limit of 5.4 µM and a dynamic range which extended up to 100 µM NO₃⁻. Brunetti et al. prepared gold nanoelectrode ensembles (NEEs) used for biosensors based on reductase enzymes — two phenothiazines (Azure A and B) and methylviologen. Compared with macro electrode, NEE can obtained lower detection limits without adsorption of the reduced forms to the electrode surface. And it is the first use of the NEEs for the determination of standard heterogeneous rates constants.

A new kind of nanochannels membrane with conically shaped pores was developed based on the membranes with cylindrical pores. The conically pores membranes can provide dramatically higher rates of transport than analogous cylindrical pore membranes. Apel et al. showed that conical nanopores can be chemically etched into radiation-tracked polymeric membranes. Li et al. investigated plasma etching the surface of a track-etched (vide infra) polymeric membrane (schema1) to obtain conical pores as shown in Fig.3.

Figure 3

Martin research group described resistive-pulse sensing of two large DNAs, a single-stranded phage DNA (7250 bases) and a double-stranded plasmid DNA (6600 base pairs), using a conically shaped nanopore in a track-etched polycarbonate membrane as the sensing element. The conically shaped nanopore had a small-diameter (tip) opening of 40 nm and a large-diameter (base) opening of 1500nm. The phage DNA was driven electrophoretically through the nanopore (from tip to base), and these translocation events were observed as transient blocks in the ion current. They found that the frequency of these current-block events scales linearly with the concentration of the DNA and with the magnitude of the applied transmembrane potential. Increasing the applied transmembrane potential also led to a decrease in the duration of the current-block events.

Sexton et al. added a protein analyte to the solution containing antibody that selectively binds the protein. The complex formed upon binding of the Fab to BSA is larger than the free BSA molecule. So the current-pulse signature for the BSA/Fab complex can be easily distinguished from the free BSA. Furthermore, the BSA/Fab pulses can be easily distinguished from the pulses obtained for the free Fab and from pulses obtained for a control protein that does not bind to the Fab. The current-pulse signature for the BSA/Fab complex can provide information about the size and stoichiometry of the complex.

4 Conclusions

Nanotubules technology is exhibiting the great potential advantages and promising future due to the size effect and chemical physical characteristics. The applications of nanochannels in many fields, such as analytical chemistry, biochemistry, materials science, environmental science, and so on, will undergo more development although some reports on the nanochannels have been published.

Acknowledgment

This work was supported by the National High-tech R&D program (863 program, 2007AA06Z402), Project of Shanghai Municipal Government (08520510400), Shanghai Leading Academic Discipline Project (S30406), and Leading Academic Discipline Project of Shanghai Normal University (DZL706).

References


No.5576, 2198-2200


Table 1. Templates, preparation and application of material nanochannels

<table>
<thead>
<tr>
<th>Different templates of nanochannels</th>
<th>Membrane preparation</th>
<th>applications of special material nanochannels in analytical chemistry</th>
</tr>
</thead>
<tbody>
<tr>
<td>membrane template</td>
<td>electrochemistry deposition</td>
<td>separate the molecular with different size</td>
</tr>
<tr>
<td>emulsion template</td>
<td>electroless deposition</td>
<td>separate mixtures containing hydrophobic and hydrophilic molecules</td>
</tr>
<tr>
<td>micromulsion template</td>
<td>chemical polymerization</td>
<td>separate the molecular with different charge</td>
</tr>
<tr>
<td>other kinds of templates</td>
<td>sol-gel chemistry</td>
<td></td>
</tr>
<tr>
<td></td>
<td>chemical vapour deposition</td>
<td>separate protein/DNA</td>
</tr>
</tbody>
</table>
Figure legends

Figure 1. Cross-section of single α-hemolysin channel embedded in a lipid bilayer.\textsuperscript{4}

Figure 2. The transport of goat anti-bovine IgG and goat anti-cat IgG through Au-Mem and B-IgG-Au-Mem, respectively. \textsuperscript{41}

Figure 3. Surface SEM images of the membrane after (A) chemical etching and (B) after 5min (C) 10min (D) 20 min of plasma etching.\textsuperscript{34}
Figure 1
Figure 2
Figure 3