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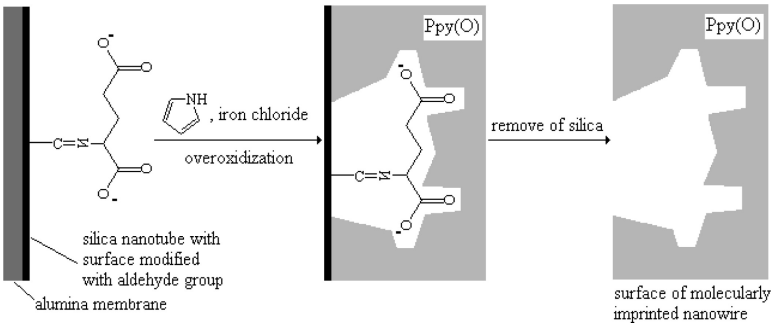

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Surface Molecularly Imprinted Nanowires for Biorecognition

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The molecularly imprinted polymers (MIPs) approach has already been used successfully for mimicking natural receptors and for the synthesis of polymers carrying binding sites with high affinity toward drugs, small analytes, peptides, and proteins.[1] The stability, ease of preparation, and low cost of these MIPs make them particularly attractive.[2] Among present MIPs, imprinting a matrix with binding sites situated at the surface has many advantages: the sites are more accessible, mass transfer is faster, and the binding kinetics is faster. However, these materials are not widely used because their preparation is less straightforward and requires specially adapted protocols.[3] Mosbach and co-workers introduced a remarkably clever protocol for creating surface imprinting based on oriented immobilization of the template molecule on porous silica beads prior to polymerization.[4] Unfortunately, such surface-imprinting material is shapeless, and its application is limited.

Herein we present a novel method for the preparation of surface molecularly imprinted size-monodisperse nanowires (Figure 1). The imprinted molecule (glutamic acid in this paper) is immobilized on the pore walls of a silane-treated nanoporous alumina membrane. The nanopores are filled with the monomer mixture (pyrrole in this paper), and the polymerization is then initiated. The alumina membrane is subsequently removed by chemical dissolution, leaving behind polypyrrole nanowires with glutamic acid binding sites situated at the surface.

Template synthesis in nanoporous alumina membranes is a common method for producing nanotubes and nanowires.[5] A commercial alumina membrane having pores of 100 nm diameter was used for this study. A sol−gel template synthesis method was used to deposit silica nanotubes within the pores of the alumina membranes.[6] The inner walls of the silica nanotubes were then modified with functional aldehyde groups by reaction with trimethoxysilylpropyl aldehyde. The aldehyde groups react spontaneously with the amino group of the glutamic acid, resulting in the attachment of glutamic acid to the inner walls of the silica nanotubes.

The glutamic acid-containing alumina membrane was immersed into a cooled 0.2 M aqueous pyrrole solution, prepared from freshly distilled pyrrole for 1 h. An equal volume of cooled oxidant solution was then added. The mixture was left for polymerization for 12 h. Polypyrrole preferentially nucleates and grows on the pore wall. The TEM and SEM results (Figure 2) verify the formation of polypyrrole nanowires with controlled size in the alumina template membrane. The diameter of the nanowires is determined by the pore diameter of the template membrane.

Molecularly imprinted overoxidized polypyrrole has been proven to be a promising material for molecular recognition of amino acids by Nagaoka.[7] In our experiment, the alumina membrane was first dissolved with dilute phosphoric acid. The resulting polypyrrole nanowires with silica nanotubes at the surface were then dispersed in aqueous 0.1 M NaOH and further overoxidized at + 1.5 V vs Ag|AgCl.[7] The overoxidation of polypyrrole nanowires can create a cavity that is more complementary to glutamic acids; this complementary cavity can be easily created by overoxidation dedoping of anionic glutamic acid. Finally, the imprinted overoxidized polypyrrole nanowires were isolated by dissolving away the surface silica nanotubes with HF solution and then purified by repeated cycles of centrifugation and washing with water.

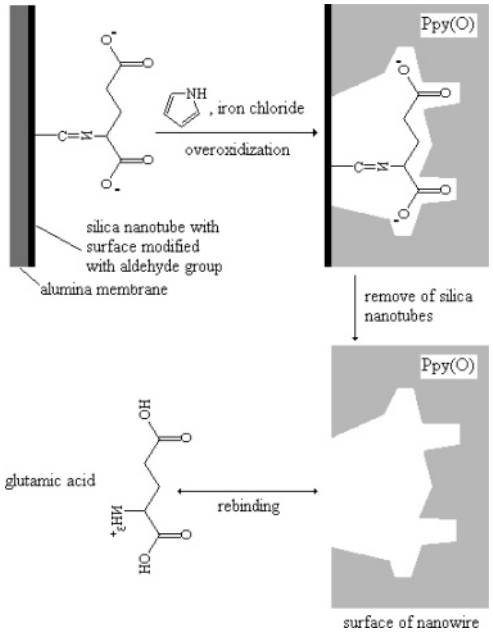

Figure 1. Schematic representation of the molecular imprinting approach employing immobilized template and a sacrificial solid nanotube support.

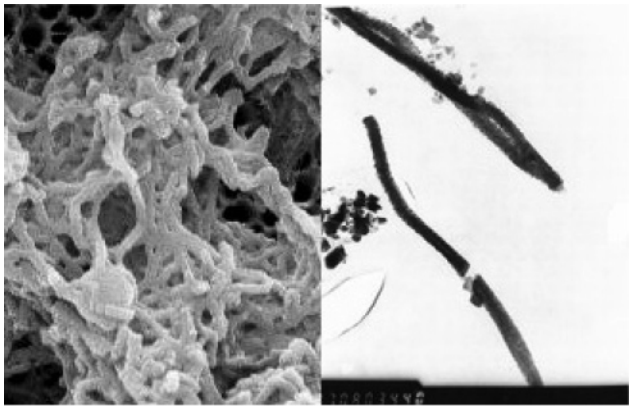

Figure 2. Scanning electron micrograph (SEM) and transmission electron micrograph (TEM) of 100-nm-diameter polypyrrole nanowires after the removal of alumina template membranes.

The glutamic acid recognition ability of the imprinted overoxidized polypyrrole was investigated by the steady-state binding

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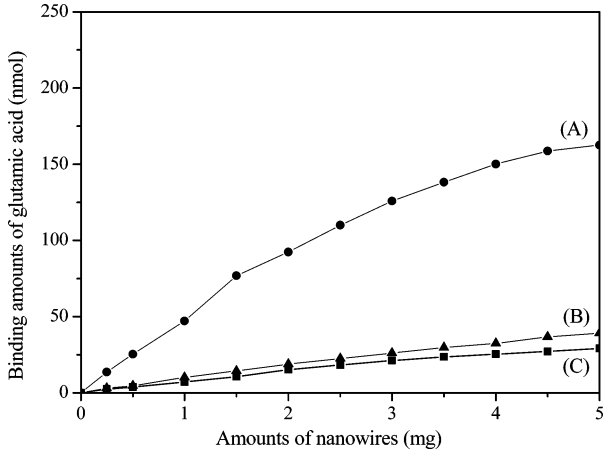

Figure 3. Binding profiles of glutamic acid as a function of the nanowires concentration: (A) glutamic acid-imprinted nanowires, (B) glycine-imprinted nanowires, and (C) control nanowires. The points represent mean values of three measurements.

method. The polymer nanowires were suspended in water, and appropriate volumes of the suspension were added into 1.5 mL test tubes, followed by addition of glutamic acid, pH 1.7 KCl−HCl buffer, and water to give a total volume of 1 mL. The samples were incubated on a rocking table for 1 h at room temperature. After removal of the nanowires by ultrafiltration, the target molecule in the filtrate was determined by *o*-phthalaldehyde fluorometry.[7] As shown in Figure 3, the imprinted nanowires indeed exhibit a higher capacity for glutamic acid than the control nanowires formed in the absence of an imprinting glutamic acid. At a nanowires concentration where the MIP binds 50% of the amino acid, the control polymer binds only 7%. To elucidate the effects of the shape and functionality of the imprinting template, an additional kind of nanowires was synthesized using alumina membrane onto which glycine was coupled. As can be seen in Figure 3, the binding capacity of this kind of nanowires was only slightly higher than that of the control nanowires. This result indicates that the functionalities on the glutamic acid molecule are responsible for the observed imprinting effect.

The glutamic acid-imprinted nanowires also show a high selectivity for glutamic acid over the related compounds phenylalanine and arginine, which have cross-reactivities of less than 8% relative to glutamic acid (see the Supporting Information). This result is similar to that obtained with bulk polymers imprinted with the free template molecule.[7] The general kinetic profile of binding glutamic acid to molecularly imprinted polypyrrole nanowires was also investigated (see the Supporting Information). It can be seen that the imprinted polypyrrole nanowires show a very fast rate of uptake, with a saturation time less than 20 min. This means that the surface imprinting greatly facilitate diffusion of the analyte to the binding sites.

In conclusion, we report a unique kind of imprinted material: relatively monodisperse nanowires with a moderately high surface area and imprinted binding sites located at, or close to, the surface. These nanowires can be dissolved in aqueous media, and their applications should therefore be compatible with procedures in which biological antibodies might otherwise be used. For example, the analyte molecule can be tagged with various markers, such as fluorescence probes and enzymes, whereby the problem of steric hindrance is avoided. Furthermore, these surface-imprinted nanowires are likely to be suitable for imprinting and recognition of large-molecular-weight peptides and proteins. This related work is currently being undertaken in our laboratory. Such nanowires would greatly increase the usefulness of MIPs for immunoassays and related applications. Meanwhile, the phenomena involved during imprinting at the liquid−solid interphase remain to be studied in more detail.

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Supporting Information Available: Experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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