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Micromolding in Capillaries for the Generation of Molecularly Imprinted Polymer Filaments and Microstructures

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ABSTRACT

The technique of micromolding in capillary has been employed to prepare molecularly imprinted polymer microfilaments, and to pattern MIP structures on silicon wafers. The approach relies on crosslinked poly(dimethylsiloxane) that contains relief structures as a mold to define the shape and size of the imprinted polymers. This article describes the processes leading to the fabrication of free-standing MIP micromonoliths and covalently immobilized MIP microstructures on silicon wafers. The limitations of the technique are also discussed.

The development of miniaturized systems for chemical, analytical and diagnostic applications has attracted great interest recently.[1,2,3] Significant advantages in speed, efficiency and control can be gained through the application of such miniature systems in laboratory testing. Micro devices have been fabricated to perform a variety of chemical and enzymatic reactions and in chip capillary electrophoresis separation. Much effort has also been devoted to shrinking analytical instruments such as high performance liquid chromatography,[4] combinatorial library screening system,[5] and biosensors.[6,7]

Molecular recognition and interactions play central roles in these applications. Molecular imprinting, a technique for the synthesis of polymeric materials with analyte-specific recognition properties, is an attractive alternative to natural recognition systems such as antibodies and receptors.[8,9,10] The ability to generate molecularly imprinted polymer (MIP) microstructures on devices should open new possibilities towards the development of miniaturized systems for chemical, analytical and diagnostic applications. The added advantages of long-term stability and chemical resistivity of MIPs may make these "intelligent chips" attractive for instrument and device fabrication.

We have employed a soft lithography[11,12] technique, micromolding in capillaries (MIMIC),[13,14] to fabricate MIP microstructures on silicon wafers. In MIMIC, an elastomeric stamp is placed in an intimate contact with the solid substrate. The recessed microchannels on the stamp form a network of empty capillaries. When a low-viscosity fluid precursor is placed in close contact at one end, it spontaneously fills the channels by capillary actions. Curing of the fluid leaves patterned microstructures on the substrate surface (Figure 1). An attractive feature of this technique is that the size and shape of the MIPs can be easily controlled and altered by those on the PDMS stamps. In addition, the process can be carried out conveniently in a chemical laboratory. Once the master mold is made, many elastomeric stamps can be cast and used repeatedly.

Figure 1. Schematic illustration for the fabrication of polymer microstructures using the technique of micromolding in capillaries.
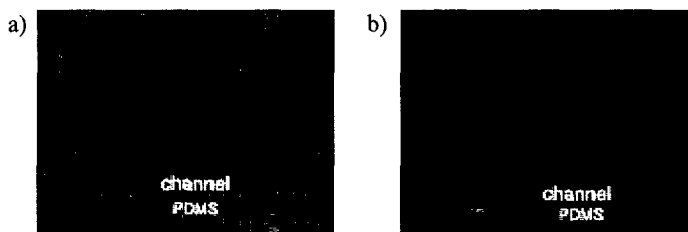
Poly(dimethyl siloxane) (PDMS) has been widely used as the stamp material. PDMS can be released easily from patterned structures and substrates due to its high elasticity and low surface energy. It is also transparency to UV light, down to 300 nm, and is therefore compatible with the photochemical polymerization procedures employed in MIP synthesis. Alternative materials such as polyimide,[15] polyurethane and Novolac (phenol-formaldehyde) resin[16] have also been used to make stamps.

PDMS stamps are fabricated by casting a mixture of a PDMS prepolymer (Sylgard 184, Dow Corning) and the corresponding curing agent on a master mold. The master mold contains the inverse features of the stamp, and is made by conventional photolithography. In our studies that thick features (20-100 μm) were needed, SU-8 negative photoresists (MicroChem Corp.) were used to make master molds. The surface of the master mold was treated with a fluorinated silane, for example $C_6F_{13}CH_2CH_2SiCl_3$, to ensure facile release of the PDMS stamps.

A major limitation of this technique is that the crosslinked PDMS stamp tends to swell in many organic solvents that include chloroform, methylene chloride, toluene and tetrahydrofuran. These solvents have been widely used as the porogen in the synthesis of molecularly imprinted polymers, with chloroform and toluene especially popular in non-covalent imprinting systems where it is critical for the solvents not to interfere with the hydrogen bonding/ionic interactions between monomers and template molecules. We found that PDMS stamps swelled dramatically in these solvents and subsequently lost the conformal contact with the substrate. We have successfully fabricated MIP microstructures with dimethylformamide (DMF) as the solvent in both an acrylic acid-based[17] and a polyurethane-based[18] imprinting system. On the other hand, solvents that do not swell PDMS stamps include alcohols and water. Alcohols have low surface tension and wet the surface of PDMS and the wafer substrate. They are most useful in MIMIC and should therefore be very appropriate for imprinting systems that employ alcohols as the solvent. Water is another solvent that does not cause swelling of the PDMS stamps. However, water has a high surface tension and it does not wet hydrophobic surfaces. A small amount of alcohol (~5%) can be added to the aqueous solution to promote the liquid flow through the channels,

The swelling of PDMS stamps by solvents was studied using DMF and acetonitrile. The effect of swelling was evaluated by measuring the width of the PDMS ridges and the microchannels after polymerization. The imprinting solution contained 4-vinylpyridine (4-VP, monomer), ethylene glycol dimethacrylate (EGDMA, crosslinker), 2,4-dichlorophenoxyacetic acid (2,4-D, template molecule), 2,2'-azobisisobutyronitrile (AIBN, initiator), and the solvent. The solution was photopolymerized inside the microchannels with a 450 W medium pressure Hg lamp at 0 °C for 2 h. Optical images were taken on the area of stamps before the imprinting solution was introduced and after the imprinted polymers were formed inside the microchannels (Figure 2). It was found that after polymerization, the width of the PDMS ridges increased whereas the width of the channels decreased. This indicated that as the PDMS was swollen by the solution, it expanded thus reducing the size of the channels. This swelling effect was more

pronounced for acetonitrile as compared to DMF. With acetonitrile as the solvent, the width of the PDMS ridges increased by 12% and that of the channels containing the polymers decreased by 14%. For DMF, the expansion and shrinkage were 5% and 7%, respectively. Note that besides the solvent, the organic monomers also contribute to the swelling of the PDMS stamps. 4-Vinylpyridine was especially problematic.

Figure 2. Optical micrographs of a) section of a PDMS stamp placed on a silicon wafer; b) the same area after the imprinted polymers were formed inside the channels. Acetonitrile was used as the solvent. The width of the PDMS ridges and the channels was measured using a free imaging software (Scion Corporation). About 6-8 measurements were taken and averaged. The PDMS stamps were fabricated from a master mold that contains features with a 20 μm x 20 μm cross-sectional dimension.

The polymers synthesized inside the channels can be isolated from the assembly as freestanding microfilaments. When the PDMS stamp was placed directly on the silicon wafer, the polymers formed would partially adhere to the substrate or the PDMS, and they were difficult to remove even after treating with HF. To avoid this problem, a PDMS thin layer was spin cast and cured on the wafer before the PDMS stamp was placed on the substrate. Therefore, the polymers were sandwiched between two PDMS, and could be released after the PDMS was removed. Two approaches were employed to facilitate the release of the MIP microfilaments: to dissolve PDMS with tetrabutylammonium fluoride in THF,[17] or to swell PDMS with a solvent such as toluene.[18] In the later case, the polymers were released from the PDMS after the PDMS were physically deformed. The imprinted polymers could then be centrifuged and extracted with solvents to remove template molecules for subsequent analysis.

In order to make MIP microfilaments of good quality, the amount of solvent used in the free radical polymerization was reduced dramatically. This was probably because the solvent was difficult to escape from the confined microchannels. As a result, the pore size, pore volume, and distribution of the MIPs will be affected. In addition, these MIP microfilaments may have different surface morphology as compared to MIPs prepared by the conventional method due to the surface property and the large surface areas provided by the PDMS microchannels. Studies are underway to characterize these MIP microfilaments.

Compared with MIPs prepared by bulk polymerization in large test tubes, this technique produces a much smaller quantity of materials. With a cross-sectional dimension of 20 μm x 20 μm and the spacing of 20 μm between channels, a PDMS stamp of 1 cm x 1 cm in size produces a maximum of 1.5 mg of MIP, assuming the density of the MIP to be ~1 g/cm^3. To prepare a

larger amount of materials is time consuming. One approach is to use several PDMS stamps simultaneously on a substrate.

The technique could be modified for the synthesis of MIP membranes. In this case, a drop of the imprinting solution was applied on the PDMS film that was spin cast on a wafer or glass surface. A flat PDMS block was then placed on the solution and the assembly was allowed to photopolymerize. The thickness of the MIP membrane was controlled by the amount of imprinting solution applied. We have successfully synthesized MIP membranes using the imprinting system described above (4-VP, EGDMA, 2,4-D, AIBN, acetonitrile). However, these membranes were quite fragile. After solvent extraction, they frequently fractured into small fragments.

We have employed the technique of MIMIC to fabricate MIP microstructures on silicon wafers for the construction of a MIP-based waveguide sensor. A polyurethane-based imprinting system was adapted and the details of the studies are described in a separate publication in this Proceeding.[18] In this type of application, it is desirable that the polymers be covalently attached to the substrates so that the device can withstand subsequent processing conditions. To achieve this, the wafers were treated with aminopropyltrimethoxysilane. The amino groups copolymerized with the isocyanate groups in the monomer feeds, thus forming covalent bonds between the polymer and the wafer. For acrylate-based MIPs, reagent such as (meth)acryloxypropyltrimethoxysilane can be used to treat the surface of the wafer.

MIMIC has been employed by others for the fabrication of functional microelectronic devices such as transistors and diodes.[11] A limitation of the technique is that it relies on the *interconnected* capillary channels in order for the fluid to flow through. For non-interconnected patterns, one solution was to create access holes through the PDMS stamp.[19] When the liquid was fed through the access holes, it was forced into the closed capillary patterns by the evaporation of solvent from the filled capillaries. However, if the device contains a large amount of non-interconnected patterns, the process can be extremely slow and inefficient.

In summary, MIMIC has been selected as the fabrication technique for the generation of MIP microstructures. Although the technique has a number of limitations, its simplicity, flexibility, and ease of use proved to be advantageous over other microfabrication methods. Using this approach, we have synthesized free-standing MIP microfilaments and created patterned MIP microstructures on silicon wafers. The integration of MIPs with microfabrication may lead to new types of functional devices with potential applications in separation, sensing and diagnostics.

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