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Fabrication of porous polymer monoliths covalently attached to the walls of channels in plastic microdevices

UV-initiated grafting of plastic tubes and microfluidic chips with ethylene diacrylate followed by the preparation of porous polymer monoliths has been studied. The first step affords a thin grafted layer of polymer with a multiplicity of pendent double bonds that are then used in the second step for covalent attachment of the monolith to the wall. As clearly seen on scanning electron micrographs, this procedure prevents the formation of voids at the monolith-channel interface a problem that has always plagued approaches involving bulk polymerization in nontreated channels due to the shrinkage of the monolith during the polymerization process and its lack of compatibility with the material of the device. Irradiation with UV light through a photomask allows precise patterning specifying both the area subjected to surface modification and the location of the monolith within specific areas of the device.

Keywords: Microchip / Microfluidic / Miniaturization / Monolith / Porous polymer
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1 Introduction

Current microfluidic devices, also called micrototal analysis systems (µTAS) or 'lab-on-a-chip', are largely fabricated using inorganic substrates such as glass, silica, and quartz in which the desired network of channels and other features are obtained using etching processes. The popularity of these materials stems from the ease of design and fabrication of both prototypes, and small series of microfluidic chips, using the standard methods of microelectronics such as patterning and etching [1–3]. However, to avoid the high cost of the multistep wet fabrication of these microfluidic devices, the use of thermoplastic polymer materials together with inexpensive 'dry' techniques such as injection molding or hot embossing is desired. Consequently, the development of polymeric substrates for microfluidic devices has become a priority.

In applications that largely rely on interactions with the solid surface such as chromatographic separations, heterogeneous catalysis, and solid-phase extraction, the low surface-to-volume ratio typical of open microchannels is a serious problem since the microdevices can only handle minute amounts of compounds. We have recently developed procedures enabling the "molding" of monolithic porous polymer matrices *in situ* within the capillaries and microchannels of fused-silica and glass microchips leading to a considerable increase in their available surface areas [4–8]. Using the well-known silane primer reagent 3-(trimethoxysilyl)propyl methacrylate it is possible to functionalize the walls of the channels within the inorganic substrates thus enabling covalent attachment of the monoliths to the channel surface in a glass chip as shown in Fig. 1. Given the notoriously poor material compatibility of most polymeric materials, it is likely that poor bonding of the monoliths to the native walls of plastic devices will be observed, and that voids may even develop at the monolith-channel interface thereby making the devices ineffective. Therefore, the plastic channel surface must be modified prior to the *in situ* preparation of the monolith. Unfortunately, no surface primer reagent as simple as 3-(trimethoxysilyl)propyl methacrylate is currently available for the treatment of polymer surfaces.

The current literature presents countless examples of surface modifications of synthetic polymers that may help achieve a firm bond between the chip wall and the porous polymer monoliths created within the channels of a plastic device [9–15]. Good bonding between the wall and monolith is necessary in order to prevent the formation of voids at the monolith-wall interface. Examples of surface modification techniques include surface treatment using cold plasma discharge [9, 10] or transamidation using lithiated diamines with the subsequent reaction of the amine groups has been used for the modification of

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Abbreviations: BuMA, butyl methacrylate; **COC**, cyclic olefin copolymer; **DMPAP**, 2,2-dimethoxy-2-phenylacetophenone, **EDA**, ethylene diacrylate, **EDMA**, ethylene dimethacrylate, **HEMA**, 2-hydroxyethyl methacrylate, **MMA**, methyl methacrylate; **PP**, polypropylene, **SEM**, scanning electron microscope

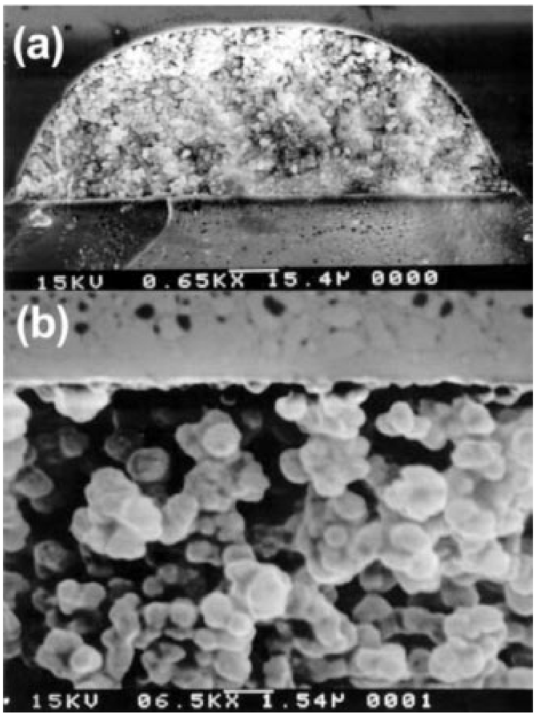

Figure 1. SEM images of a porous polymer monolith inside a commercial glass microchip. The channel surface was treated with 3-(trimethoxysilyl)propyl methacrylate to achieve good adhesion of the monolith to the wall. Magnification (a) 650 and (b) 6500.

channels in microfluidic devices [11]. However, the latter procedure is only suitable for methacrylate ester polymers. Grafting, which is widely used for the modification of polymer surfaces [12], appears to be the method of choice. Although numerous grafting approaches have been demonstrated, most are not suitable for microfluidic devices since grafting should be confined to selected areas. This requirement favors processes in which grafting is triggered through a mask by UV light [13–15]. This report describes a simple method that features UV-initiated reactions mediated by benzophenone. First, the wall surface of a commercially available polymer is photografted with a thin interlayer polymer and then the monolith is prepared *in situ via* UV-initiated polymerization. Using this method, dramatic improvement in adhesion of the monoliths to the plastic devices is achieved.

2 Materials and methods

2.1 Materials

Butyl methacrylate (99%, BuMA), methyl methacrylate (99%, MMA), 2-hydroxyethyl methacrylate (98%, HEMA), ethylene diacrylate (90%, EDA), ethylene dimethacrylate (98%, EDMA), 1-dodecanol (98%), cyclohexanol (99%), benzophenone (99%, BP), and 2,2-dimethoxy-2-phenylacetophenone (99%, DMPAP) were purchased from Aldrich (Milwaukee, WI, USA). The monomers were purified by passing them through a bed of basic alumina (Brockman activity I, 60–325 mesh) to remove inhibitors and distilled under reduced pressure. Polypropylene (PP) micropipette tips (100 µL) were obtained from Eppendorf (Westbury, NY, USA). Cyclic olefin copolymer plates (Topas 8007 X-10, COC) were obtained as gift from Ticona (Summit, NJ, USA).

2.2 Microfluidic chip

The microfluidic chip shown in Fig. 2 consists of two parts. The top plate includes 130 µm wide and 45 µm deep microchannels with a “double-T” geometry that were micromilled using a standard CNC (computer numerical control) milling machine and access holes drilled at the ends of each channel. The featureless planar bottom plate is thermally bonded at a temperature of 68°C and a pressure of 3.5 MPa for 40 min to the top plate to afford the completed chip. The Nanoport fittings (Upchurch Scientific, Oak Harbor, WA, USA) were glued to the chip using an epoxy glue Polybond33 (Nbond Adhesives International, Littleton, CO, USA).

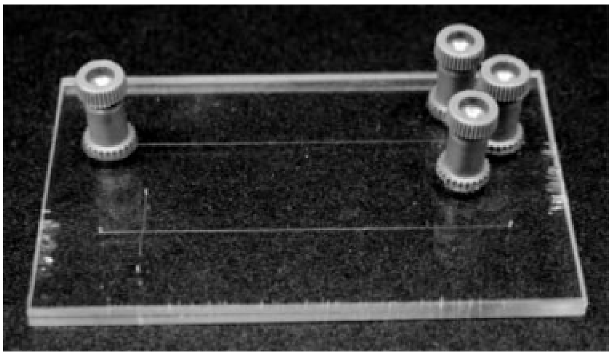

Figure 2. Microfluidic chip prepared by micromilling of COC plates and thermal bonding. The Nanoport fittings were subsequently glued to the access holes of the chip.

2.3 Photografting of inner surface of PP tubes and COC channels

PP micropipette tips were used as a model for the plastic capillaries and microchannels since their shape considerably facilitates their handling. The tube with an inner diameter of 800 µm was filled to a height of about 5 mm with the bulk monomer or a mixture of monomers using capillary action. A 3 mm diameter steel rod was inserted into the chuck of an overhead stirrer, the filled pipette tip was affixed to its tapered end and irradiated from a distance of 25 cm for a specific time while rotated at 50 rpm in an almost horizontal position to assure equal irradiation of the contents. Once the reaction was complete, the tubes were washed with acetone, extracted in the same solvent for 12 h, and dried in a vacuum oven at room temperature for 24 h. The channels of the COC microchips were filled with a mixture of EDA and MMA and their surface pretreated by photografting for 10.5 min followed by rinsing with methanol at a flow rate of 0.25 μL/min for 2 h.

2.4 Preparation of porous polymer monolith inside PP tubes and COC microchips

The surface-modified tubes were filled again by capillary action to a height of about 5 mm with the nitrogen-purged monomer mixture consisting of HEMA (24 wt%), EDMA (16 wt%), 1-dodecanol (29 wt%), cyclohexanol (31 wt%), and DMPAP (1 wt% with respect to monomers). Using the assembly described in Section 2.3, the revolving capillary containing the polymerization mixture was irradiated from a distance of 25 cm for 20 min. The monoliths were then extracted in three portions of methanol for 24 h, and dried in a vacuum oven at 40°C for 12 h. For scanning electron microcope (SEM) images, 2.5 mm long samples were cut from the tube. The channels of the COC microchips were filled with the nitrogen purged monomer mixture consisting of BuMA (24 wt%), EDMA (16 wt%), 1-decanol (60 wt%), and DMPAP (1 wt% with respect to monomers). The sections of the microchip that should not contain the monolith were covered with a photomask, consisting of black electrical tape, and the microchip was irradiated from a distance of 30 cm for 3 min. The monolith in the channel was washed with methanol pumped through at a flow rate of 0.10 μL/min for 12 h. For SEM images the microchip was first cooled in liquid N2, then broken with a hammer into 10–20 mm long samples and dried in a vacuum oven at 40°C for 12 h.

3 Results and discussion

A number of thermoplastics such as polycarbonate, poly(methyl methacrylate), polydimethylsiloxane, poly (butylene terephthalate), and polyolefins such as polyethylene, polypropylene, the copolymer of 2-norbornene and ethylene ("COC"), and hydrogenated polystyrene have already been used for the fabrication of microfluidic devices. All of these thermoplastics are highly hydrophobic and, therefore poorly suited to handle biopolymers such as proteins and peptides unless their surface is made more hydrophilic or otherwise modified. To modify their surfaces, we have recently designed a new photografting approach [16], which is amenable to polymers with sufficient UV transparency. This concept is now extended to the surface functionalization of plastic microfluidic channels. As illustrated schematically in Fig. 3, a microchannel represented by a tube (a) is filled with a divinyl monomer or a mixture of monovinyl and divinyl monomers that contain benzophenone and then UV-irradiated (b). This grafting step is carried out under conditions that only proceed to very low conversions. After removal of the excess monomer from the channel, a grafted polymer layer containing a number of unreacted double bonds remains chemically attached to the surface (c). This channel is then filled with a polymerization mixture suitable for the preparation of the desired porous polymer monolith and irradiated with UV light to initiate polymerization. The residual double bonds at the channel surface are incorporated in the growing polymer chains, thus covalently bonding the monolith to the wall (d).

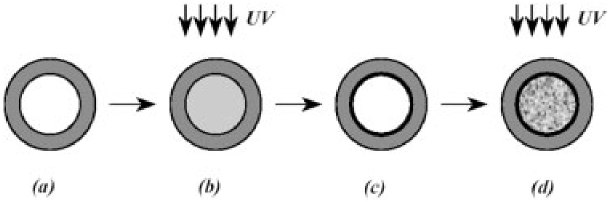

Figure 3. Schematic of the photoinduced surface modification and preparation of a monolith in a polypropylene tube. (a) The tube is filled with a benzophenone solution in diacrylate and irradiated; (b) A grafted compatibilizing polymer layer containing reactive vinyl functionalities is created at the surface; (c) This modified tube is then filled with the polymerization mixture; (d) *In situ* UV-initiated polymerization is carried out to produce the monolith.

3.1 Preparation of monolith in PP tube

We first demonstrated the approach using easily handled PP tubes. The inner surface of the PP tube is modified *via* grafting of EDA followed by the preparation of a porous poly(methyl methacrylate-*co*-ethylene dimethacrylate) monolith using the method we developed earlier [8, 17]. Figure 4 shows SEM images of the monolith inside the PP tube and the corresponding PP surfaces after removal of the monoliths. Figure 4a shows the monolith prepared in a bare tube to better demonstrate the effect of surface grafting. In the absence of surface treatment no bonding is observed. Large voids are seen between the polymer matrix and the PP tube as a result of the shrinkage that occurs during polymerization and the subsequent drying. The monolith is loose within the tube and can slip out of the tube without applying any force, leaving behind no visible traces at the PP surface (Fig. 4a, bottom). A 2 min photografting step with EDA avoids the formation of cross-linked polymer within the channel and enables a

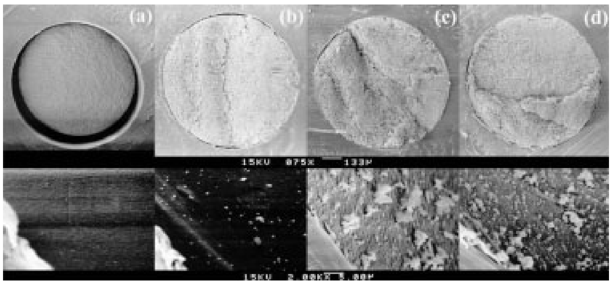

Figure 4. SEM images of porous polymer monoliths inside a PP tube (upper row) and the PP surface after removing the monolith (lower row). Conditions: (a) no surface modification; (b)–(d) surface-modified using photografting (b) with EDA; (c) EDA-methacrylate; (d) and EDMA-MMA.

better attachment of the monolith to the PP surface as shown in Fig. 4b. However, application of a small amount of pressure to the monolith suffices to make it loose and slip out of the tube. Examination of the PP surface after monolith removal shows only a small number of microglobules at the PP surface, indicating that covalent attachment was only achieved to a very small extent. This suggests that the very short reaction time used in order to avoid the rapid cross-linking of the pure diacrylate monomer within the tube, is not sufficient to achieve the desired extent of surface modification. The grafting time can be extended to about 3 min by using a 1:1 mixture of EDA and methacrylate. The images of Fig. 4c indicate good binding of the monolith to the PP surface, as also confirmed by the strength of the bond between the monolith and the tube. After forcing the monolith out, the examination of the PP surface shows that it is covered with a thin skin of globular polymer interspersed with larger residual pieces of monolith. The monovinyl monomer, methyl acrylate, used in the grafting solution decreases the cross-linking density of the grafted surface layer and enables it to swell within the polymerization mixture used for the preparation of the monolith. The best results, shown in Fig. 4d, were obtained after grafting with a 1:1 mixture of EDMA and MMA. Since grafting of methacrylates is slower than that of acrylates, this approach extends the irradiation time to 12 min. Once again, the monolith fills the cross section of the tube completely and no void is seen. Not unexpectedly, its removal from the tube proved to be very difficult. The features at the inner surface after removal of the monolith are similar to those observed earlier in Fig. 4c. However, the skin is significantly thicker, which correlates well with the longer grafting time, and indicates that excellent covalent binding of the monolith to PP has been achieved. Comparative experiments with monoliths prepared within PP tubes without rotation during the UV irradiation afforded equal results. This confirmed that the rotation is not required to achieve good binding. This clearly simplifies procedures during the preparation of monoliths in chips.

3.2 Preparation of monolith in COC microchip

The preparation of a plastic microfluidic chip with an embedded monolith is the ultimate application of surface modification followed by *in situ* polymerization. Figure 5a shows an SEM micrograph of the cross section of a COC microchip. Once again, the walls of the channel were UV-grafted with poly(EDA) and the poly(BuMA-*co*-EDMA) monolith was then prepared using UV irradiation through a mask. The micrograph in Fig. 5b, which shows a high magnification view of the top of the monolith within the channel after delamination, clearly shows that the monolith is attached to the COC wall. Indeed, no movement or loss of adhesion of the monolith was observed when a pressure of 1.4 MPa was applied during its washing with methanol using pressurized flow.

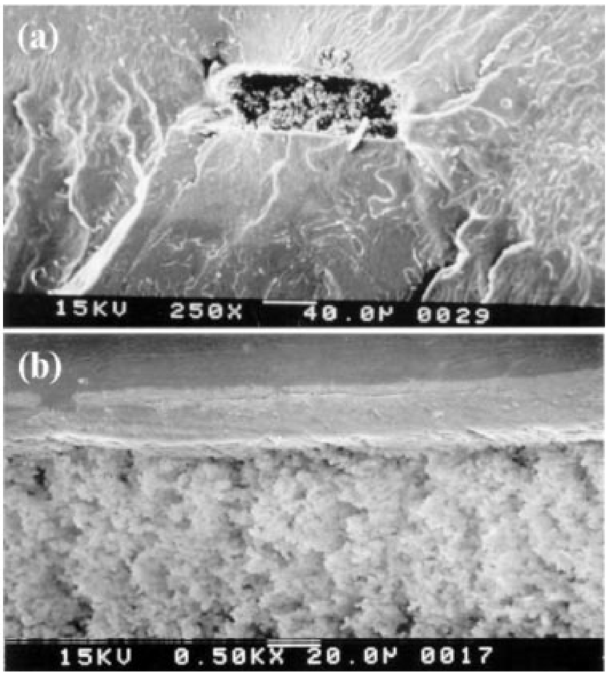

Figure 5. SEM images of (a) the cross section and (b) the delaminated channel showing porous polymer monoliths inside a COC microchip.

4 Concluding remarks

UV-initiated photografting within the channels of a plastic microfluidic device is a simple and versatile approach that enables the surface modification required for the attachment of the monolithic polymer. Further refining of this procedure, if required, could be achieved by varying the type of divinyl monomer, the irradiation time, and by adding a solvent. We expect that this approach will facilitate the design and preparation of numerous new functional elements that are instrumental to the development of complex microanalytical systems. In contrast to the present state-of-the-art glass chips that are produced using the typical microfabrication techniques used in microelectronics, thermoplastic materials are more suitable for mass production using technologies such as injection molding and hot embossing. We believe that our approach opens new avenues that may help in the development of low-cost functional microdevices and systems for a variety of specific applications.

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