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New ‘monolithic’ templates and improved protocols for soft lithography and microchip fabrication

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Abstract

We report a new method for fast prototyping and fabrication of polydimethylsiloxane (PDMS) and plastic microfluidic chips. These methods share in common the preparation of monolithic masters which includes the fabrication of the planar support, the ‘negative pattern’ of the microchannels and the fluidic connectors. The monolithic templates are extremely robust compared to conventional ones made of silicon and *SU-8*, and easier to produce and cheaper than all-silicon or electroplated templates. In contrast to the above-mentioned methods, our process allows one to cast both micrometre- (e.g. the microchannel) and millimetre-sized structures (e.g. the fluidic connection to the outer world) in a single fabrication step. The ‘monolithic template’ strategy can be used to fabricate both elastomeric (e.g. poly(dimethyl siloxane (PDMS)) polyester thermoset masters and glassy polymeric (e.g. cyclic olefin copolymer (COC)) devices. In this study we also report on one step fabrication of elastomer chips and on surface modifications of the above mentioned monolithically fabricated masters in order to improve separation of the chip from the template.

1. Introduction

The recent development of genomics and proteomics has raised strong challenges for bioanalytical sciences, and created an urgent need of fast, high throughput and cheap methods for multicriterion analysis. Microfluidics is a very promising domain for this family of applications, allowing for the integration, miniaturization and automation of complex protocols in ‘lab-on-a-chip’ devices. The strategy underlying this field amounts to integrating into a single planar device, typically of the size of a CD-ROM or smaller, submillimetre-scale channels in which the different operations necessary for an analysis will be performed automatically. This new generation of bioanalytical systems is currently the subject of intense worldwide research.

The first generation of microfluidic systems was prepared by methods directly borrowed from microelectronics, and was often made in silicon. This material, however, is expensive, non-transparent, and also has semiconductor properties that may not be suitable for some applications (e.g. electrophoresis). Alternatively, several groups used fused silica or glass to overcome these limitations, and indeed the largest quantity of microfluidic systems currently commercialized is glass made, especially in the Agilent 'Bioanalyzer' system. Current glass macrofabrication methods, however, remain rather expensive, and it requires a complex infrastructure, including a hazardous fluoridric acid treatment unit, high temperature oven, and clean room facilities.

Although glass will probably keep some ranges of applications, in particular thanks to its resistance to a large range of chemicals and to high temperature, the present trend of microfluidics is largely oriented towards polymer materials. The use of other materials, and in particular thermoplastics, is also increasing rapidly, thanks to the possibility of mass-producing disposable low-cost chips (Kim *et al* 2001, Kricka *et al* 2002). Several organic polymers have been recently reported for developing microsystems for bioanalysis: polystyrene, epoxies (in particular *SU-8*), polycarbonate, polyimide, poly(methyl methacrylate) (PMMA), and cyclic olefin copolymer (COC) (Becker and Gartner 2000, Boone *et al* 2002).

Injection moulding of polymeric materials requires expensive equipment, but allows fabrication of a large number of devices in a short time (McCormick *et al* 1997). Research in microfluidics, however, generally requires frequent modification of chip designs, so injection moulding, which is extremely cost-effective for mass production, is not well adapted on the laboratory scale. It requires, in particular, the fabrication of an expensive microfabricated metal tool for each new chip design. Thus, research laboratories are in strong need of methods adapted for the fast prototyping of a few to a few tens of chips. Ideally, these methods should be fast, require minimum work and equipment, and be adaptable to various materials (Xia and Whitesides 1998). Laser ablation enables one to directly 'write' microstructures on polymer surfaces, but in a sequential way, which makes this process both slow and expensive (Jensen *et al* 2004). In addition, on many polymers the bottom of laser etched channels has a relatively high roughness. Another convenient method for fast prototyping uses a photopolymerizable material, directly patterned by UV light through a mask (Beede *et al* 2000). However, the resolution of this method is rather poor, typically around 10–20 μm .

At present, fast prototyping in poly(dimethylsiloxane) (PDMS), as pioneered by the Whitesides group, remains by far the most popular method (Jackman *et al* 1995). Complex high density chips are now also developed commercially (Fluidigm.com). This technique has also been used to pattern non-planar surfaces (Xia and Whitesides 1998). Hard structured PDMS thin films can be used to improve the resolution of features and to reach dimensions down to 50 nm (Schmid and Michel 2000, Odom *et al* 2002).

PDMS fast prototyping, as indeed several other methods for chip fabrication like hot embossing or injection moulding, involves first the fabrication of a master, with relief patterns representing the negative of the microchannels to be made. Then, the thermocurable elastomer is cast on the master. In principle, the master could be used indefinitely, but in practice the number of chips that can be cast from a master strongly depends on the master's robustness. The simplest and most common masters used at present in laboratories are made of photolithography resin *SU-8* photopatterned on glass or silicon. These masters, however, are rather fragile, the strength of the bonding between the resin and glass is limited, and they rarely last for more than a few tens of chips. There are more elaborate methods for templating preparation such as all-silicon, or two-step preparation of a nickel master by electroless plating, but from the point of view of convenience this is a step back to the expensive and cumbersome approaches necessary for hot embossing. Here, we present a new family of masters, combining

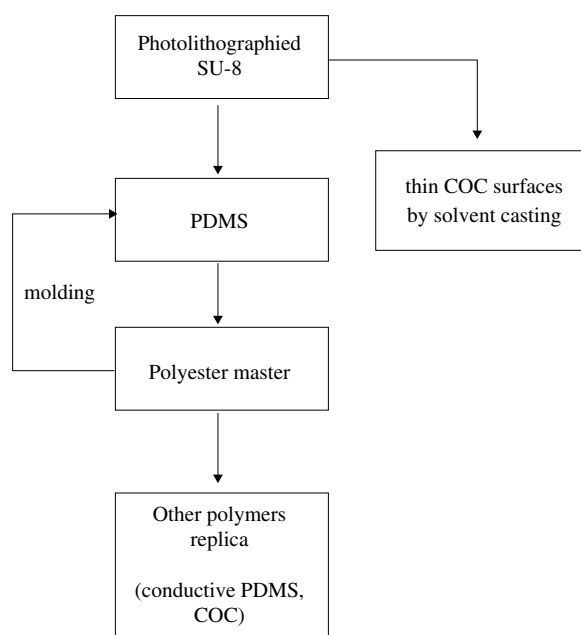


Figure 1. Block diagram of the different routes for fabricating polymeric microstructured surfaces.

the simplicity of *SU-8* ones with a much higher robustness. These masters allow the casting of typically several hundred to several thousand PDMS replicas. As shown below, they are also robust enough to permit hot embossing, without the need of an expensive nickel tool. Finally, they also simplify the moulding process, since millimetre structures like injection holes can be cast together with the microchannels in a single step.

In contrast with the previously described methods, our process, described in detail in section 2, involves lithographic ‘negative’ patterning of *SU-8* resist on a glass substrate, subsequent moulding of a ‘positive’ PDMS replica on it, followed by the fabrication of a ‘negative’ replica using polyester resin, and the replication of the final device from other polymers (such as thermally conductive PDMS and cyclic olefin copolymer (COC)) using the polyester master. In our study, the final microstructured surfaces have been obtained by using various polymers and different fabrication protocols, as shown in the schematic view in figure 1. A gas-phase silanation is performed on the plasma-oxidized polyester template to avoid sticking of the polyester master to the moulded polymeric device. The ‘negative’ replica fabricated using polyester resin is mechanically and chemically very stable and can be re-used many times. We present in section 3 different types of microstructures prepared with such templates.

2. Experimental section

Materials, reagents and solvents. Toluene (HPLC grade) and isopropanol (HPLC grade) were obtained from SDS. Hydrogen peroxide (30%) was obtained from VWR international and sulfuric acid (95%) was obtained from Normapur. Cyclic olefin copolymer, TOPAS 8007, pellets were obtained from Ticona GmbH (Germany, Oberhausen). 750-R Zeonor plates were purchased from Zeon Chemicals (France). Sylgard 184 PDMS resin, curing agent 184,

and the thermally conductive Sylgard Q3-3600 (parts A and B) were obtained from Dow Corning. Polyester resin and catalyst were purchased from Dalbe (France, Saint Denis). All materials, reagents and solvents were used without further purification. Heptadecafluoro-1,1,2,2,-tetrahydrodecydimethylchlorosilane was obtained from Gelest (Germany).

Photolithography. Circular glass slides were cleaned for 20 min in freshly prepared Piranha solution (H_2O_2 (30%) and H_2SO_4 (95%) 1:1 v/v). Glass slides were dried in the oven at 120 °C and then placed in a UV/ O_3 plasma cleaner for 10 min. Deposition of SU-8 2010 (Microchem Corporation, USA) was performed by spin-coating first at 800 rpm for 30 s then 2000 rpm for 60 s. After drying the photoresist layer at 90 °C for 10 min, and then letting it cool down to room temperature, the next step is putting the mask (printed by SLG, France) on top of the photoresist layer and exposing it to UV light for 12 s using a contact mask aligner (MJB3, from Carl Süss). After a post-exposure baking for 10 min at 90 °C and cooling down to room temperature the developing step removes unexposed photoresist. The profiles of the templates have been obtained by a profilometer (XP-1, Ambios Technologies).

PDMS casting. PDMS was mixed with the curing agent in the ratio 10:1 (w/w) and degassed with a hydraulic pump for 10 min to remove the bubbles. Then the mixture was gently poured on the photolithographed SU-8 and cured for 16 h at 60 °C.

Fabrication of thermally conductive chips. The PDMS template was placed in a PTFE container at 150 °C for 30 min. Parts A and B of the thermally conductive resin were mixed in the ratio 1:1 (w/w) and degassed using a water pump for 15 min. The mixture was gently poured on the PDMS template and again degassed in the PTFE container for 10 min. Finally, the container was cured for 1 h at 100 °C.

Fabrication of the polyester masters. The PDMS template was placed in a PTFE container at 150 °C for 30 min. The polyester resin and the catalyst were mixed in the ratio 100:2 (w/w) and degassed for 2 min with a rotary vane pump. The mixture was gently poured on the hot PDMS template. After 20 min the PDMS and the polyester were easily separated.

Fabrication of the thin cyclic olefin copolymer chips. 1 g of cyclic olefin copolymer was dissolved overnight in 15 g of toluene with gentle shaking. The polymer solution was degassed for 4 h by sonication at room temperature. The lithographically patterned SU-8 master was placed in a PTFE container and the COC solution was poured on it, followed by curing at 130 °C for 6 h. The thickness of the COC chip depends on the COC quantity injected into the mould. The SU-8 master and copolymer chip were separated by putting them in liquid nitrogen for 3 s.

Fabrication of PDMS chips from a polyester master. The procedure for fabricating PDMS devices from a polyester master is equivalent to the procedure for fabricating PDMS chips from the SU-8 master (see above).

Silanation of the polyester master. The polyester master was abundantly rinsed with isopropanol and dried in nitrogen gas. It was oxidized in an air plasma for 5 min (Harrick Plasma, USA) in vacuum. Gas-phase silanation was subsequently applied to the polyester master as described elsewhere (Pallandre *et al* 2004). The unreacted silane on the polyester master was removed by rinsing with isopropanol. Finally, the polyester master was dried with nitrogen gas.

COC melting. The silanized polyester master was placed for 24 h in a vacuum oven (Bioblock Scientific) at 160 °C with the COC pellets on it. Prior to melting the pellets, the temperature of the oven was held at 65 °C for two to three hours with continuous pumping to create a primary vacuum. The temperature of the oven was then increased to 160 °C and held there for 24 h. Finally, the set-up was cooled to room temperature (by simply turning off the temperature controller of the oven) before releasing the vacuum and separating the devices.

Hot embossing of Zeonor plates. Zeonor plates were hot embossed for 3 min at 70 °C and under a force of 0.5 ton using a temperature controlled manually operated 15 ton hydraulic press (Specac, UK). The Zeonor plate and the polyester template were held between two 5 mm thick glass plates to apply uniform pressure and to prevent the template and the device from coming in direct contact with the heater plates. The glass plates were dipped in a 50% solution of Teflon-AF (Dupont, USA) and dried before embossing. This step is necessary to prevent the embossed Zeonor plate from sticking to the glass.

3. Results and discussion

3.1. Monolithic fabrication of masters

Figure 2 schematically illustrates the process steps used to fabricate the masters monolithically. Flexible transparency masks with the microfluidic design printed on them are used to pattern *SU-8* resist on clean glass slides. A two-component PDMS resin is cast and cured on the 'negative' *SU-8* master, as described later in the experimental section. Fluidic connections to the microchannels are fabricated at this stage in the same PDMS casting step by appropriately positioning screws in a specially designed curing chamber. Figure 3 shows the curing chamber (on the left) during fabrication of the PDMS device and a 'negative' polyester template (on the right) fabricated subsequently using the PDMS device as a replication template. The polyester template, and all the subsequent polymer devices fabricated from it, 'inherit' the fluidic connections during their replication. Filling the gap deliberately allows us to realize one-step integrated membrane valves (Unger *et al* 2000) when using screws with a polished end adjusted only a few microns apart from the channel structure on the master (see figure 4).

An alternative fabrication protocol with fewer process steps was also considered, in which thin COC devices (see figure 5) were directly cast from a COC solution on the lithographically patterned *SU-8* substrate in the same curing chamber. The separation of the COC device from the glass master was achieved by quenching the whole system in liquid nitrogen. However, this technique has some inherent problems as indicated by the breaking of the glass master several times during quenching.

Different polymeric resins (such as two-component polyester or thermally conductive PDMS) can be cast on the PDMS template (figure 6) to obtain elastomeric and thermoset templates. It is also possible to fabricate polyester masters with different thicknesses by appropriately choosing the amount of resin during the casting step. Moreover, each 'negative' polyester template can again be used to generate hundreds of PDMS devices by simple moulding (see figure 1). The polyester resin used in our process is a hard thermoset polymer which is not reshaped by heating or affected by common solvents in microfabrication. Therefore, it is also a strong candidate for fabricating surfaces that are chemically highly stable.

Another group has also indicated the possibility of directly fabricating entire microfluidic chips using polyester with a similar approach (Fiorini *et al* 2003). However, the main advantage of our approach lies in the ability to simultaneously fabricate polyester structures with a wide range of aspect ratios as illustrated in figure 7. This figure shows a polyester template and a PDMS chip created using this template. Both images in figure 7 show a single microchannel surrounded by two rectangular structures of millimetre dimensions for inserting tiny magnets. This PDMS microdevice has been used for DNA separation in self-assembled magnetic columns (Minc *et al* 2004).

3.2. Plastic microchip fabrication from polyester master

COC (Topas pellets or Zeonor plates) is a well known polymeric material for microfabrication (Becker and Locascio 2002). COC has relatively low glass transition temperatures (typically

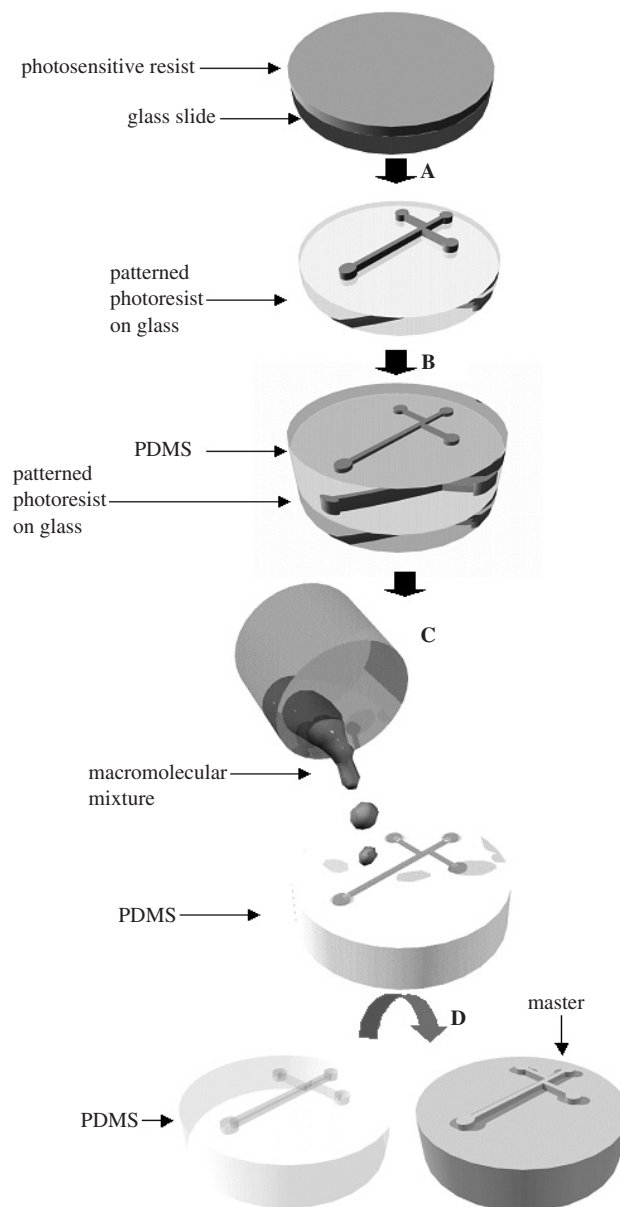


Figure 2. Schematic diagram of the fabrication method to obtain masters for replication. (A) Spin-coated *SU-8* photoresist is lithographically patterned through a mask. (B) PDMS is cast and cured on the *SU-8* patterned glass slide. (C) The PDMS replica is separated from the patterned glass and the polymeric resin is cast on PDMS. (D) Finally the polyester master is cured and separated from the PDMS mould.

between 70 and 120 °C) and can be thermally processed. These COC polymers are biocompatible, but remain a little too hydrophobic to be well suited for aqueous applications (the measured static water contact angles are around 90° for untreated surfaces of both polymers). However, surface modification of these bare polymer surfaces, in order to limit the

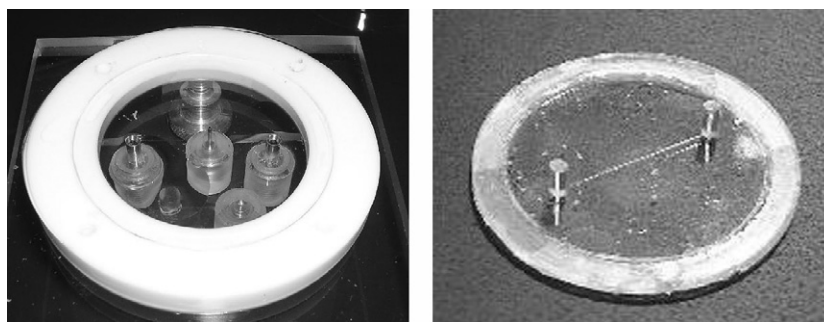


Figure 3. (Left) Photograph of the curing chamber for PDMS showing the system of specially positioned screws that allows 'monolithic' fabrication of fluidic connections to the microchannel in a single casting step. (Right) Photograph of a 'negative' polyester template with the 'inherited' fluidic connections. It was fabricated using the PDMS device as a 'positive' template.

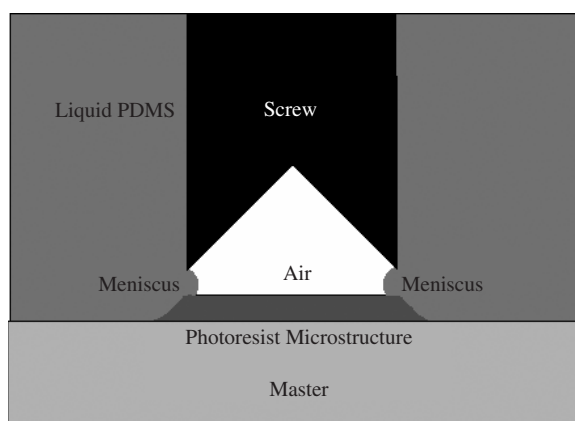


Figure 4. A trapped air bubble avoids the wetting of the gap between the screw defining the connection vial and the microstructure of the master. A concave shape at the lower end stabilizes the bubble in order to assure a good reproducibility even if the distance to the microstructure is of the order of 1/10 mm. If the lower end of the screw is flat and polished the bubble escapes and a thin PDMS layer is built.

hydrophobicity and the unspecific adsorption of analytes, still remains a big challenge. Recent developments in the field of surface chemistry indicate the possibility of tuning the surface properties of polymers, especially with COC (Rohr *et al* 2003, Li *et al* 2005).

Figure 8 illustrates different methods for fabricating polymeric microdevices using the 'negative' polyester template. In one approach, COC pellets are put on top of the polyester master and melted to obtain micropatterns in COC. In another method, COC plates are hot embossed with the microfluidic pattern in a hydraulic press using the hard polyester template.

In the first replication method, COC pellets (with a glass transition temperature $\sim 85^\circ\text{C}$) are heated at $\sim 160^\circ\text{C}$ for 24 h in vacuum on a fluorosilanized polyester template. At this high temperature, the pellets fuse together and the entire mass becomes flowable (Lamonte and McNally 2000). It then fills the volume around the polyester template to generate the pattern of microchannels. Continuous pumping is employed during the process to expel bubbles trapped between fused pellets. Figure 9 shows an optical micrograph of $420\ \mu\text{m}$ square patterns on the COC surface.

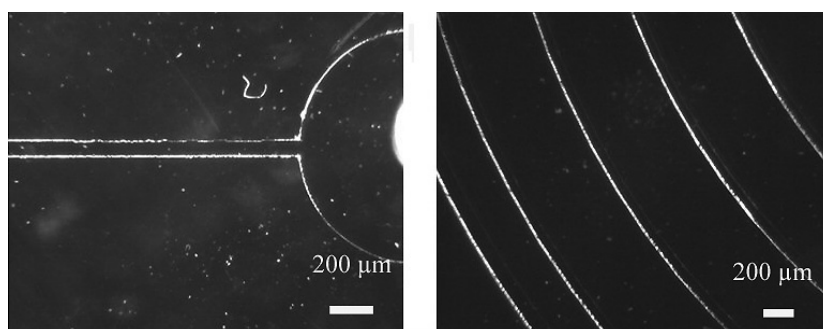


Figure 5. Micropatterns in thin cyclic olefin copolymer (COC) devices obtained by direct casting of COC solution on lithographically patterned *SU-8* on glass slides. This is an alternative protocol with fewer process steps.

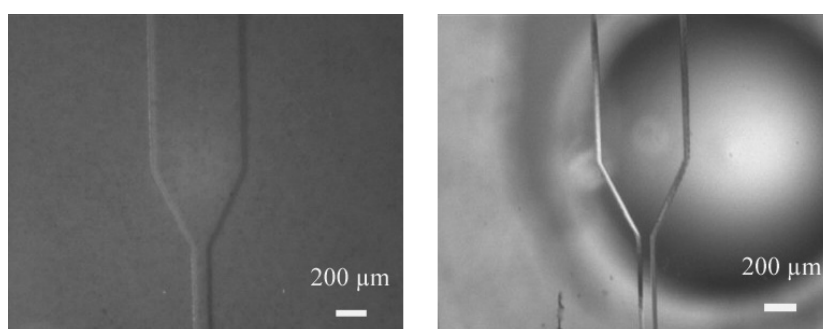


Figure 6. Images of 'negative' elastomeric and glassy masters prepared from a 'positive' two-component PDMS template by micro-transfer moulding. (Left) Thermally conductive PDMS (elastomeric master). (Right) Two-component polyester (thermoset master).

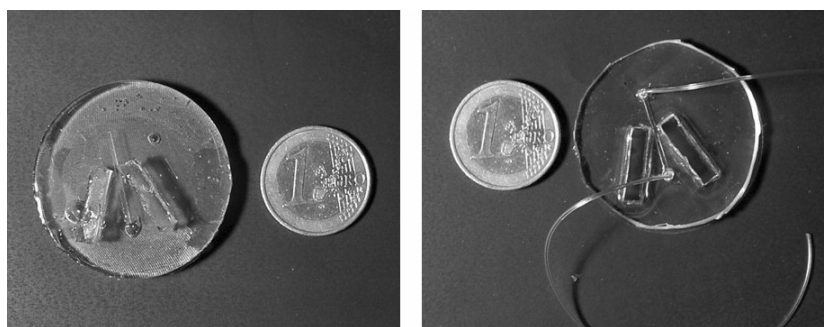


Figure 7. Images of devices with both micrometre and millimetre-sized aspect ratios. (Left) The 'negative' polyester master. (Right) The PDMS microdevice replicated using this polyester master.

We found it difficult to separate the COC surface from an untreated polyester surface. Therefore, a gas-phase silanation with perfluoroalkylsilane is performed on the plasma-oxidized polyester master in order to obtain a hydrophobic and non-adhesive surface. The surface modification of the polyester surface is characterized by static water contact angle measurements as shown in table 1.

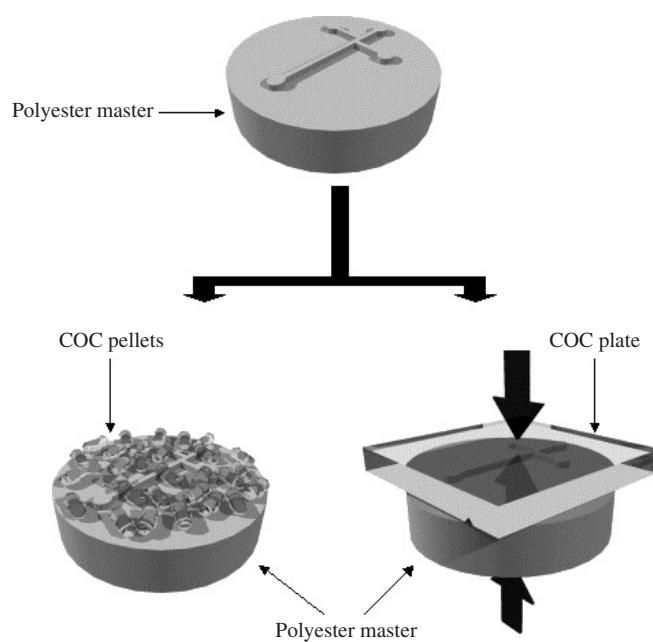


Figure 8. Schematic diagram representing fabrication of plastic microchips, by melting COC pellets at 160 °C in a vacuum oven (left) or by hot embossing a COP plate at 70 °C using a hydraulic press (right).

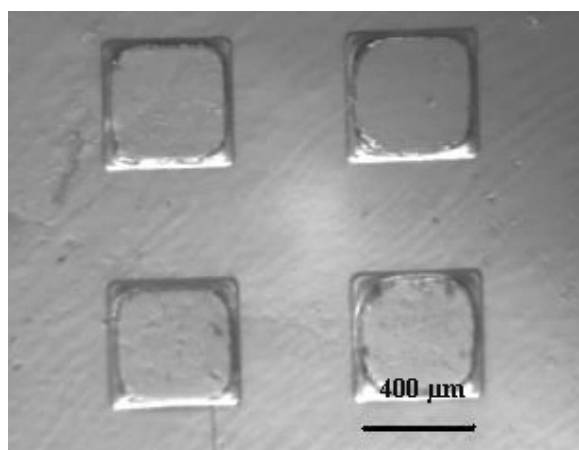


Figure 9. COC surface obtained by melting COC pellets on a fluorosilanized polyester surface in a vacuum oven.

The water contact angle measurements clearly show that the hydrophobic nature of the native polyester surface can be tuned by appropriate surface treatment. The observed droplet profiles are found to change from the bare polyester surface to the silanized one. The water contact angle on the plasma-oxidized polyester cannot be determined as the surface is too hydrophilic (complete spreading of the droplet). However, the surface treatments drastically improve the separation of the replicated devices from the template.

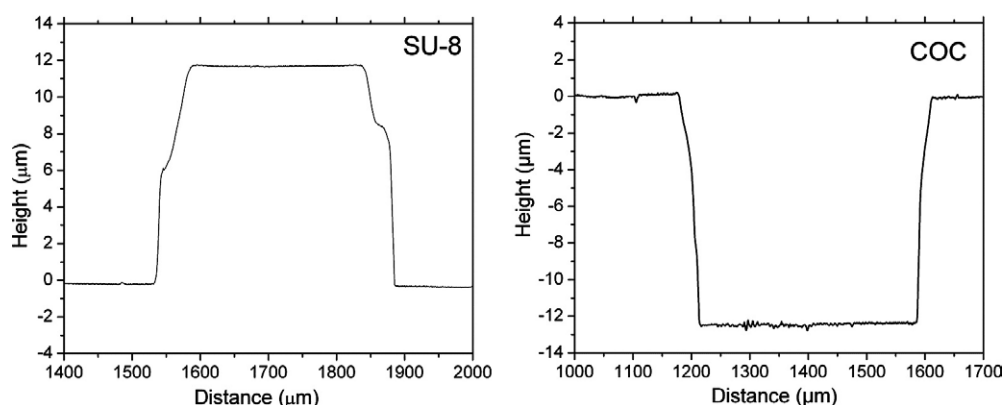


Figure 10. Surface profiles of the first replication template and the final device showing the fidelity of replication. (Left) Profile of the lithographically patterned *SU-8* on a glass substrate. This is the first replication template. (Right) Surface profile of the final COC device obtained by melting COC pellets on a silanized polyester master.

Table 1. Static water contact angle values at various stages of the polyester surface treatment.

	Bare polyester surface	Plasma-oxidized polyester surface	Silanized polyester surface
Initial angle (deg)	75	<10	89
Receding angle (deg)	68	<10	78

To estimate the fidelity of replication, the depths of the channels in the replication templates and the final device were measured by a profilometer. Figure 10 shows the surface profiles of the lithographically patterned *SU-8* master (used in the first replication step) and the final COC device obtained by melting pellets. From the profilometry data it is clear that the fidelity in template replication is excellent since the 12 μm high structures have been measured on both surfaces.

A thermoset polymer, such as the polyester resin used in this study, is capable of withstanding reasonably high temperatures and pressures without being reshaped. Therefore it can be used as a template for replication by hot embossing. Zeonor COC plates (with a glass transition temperature of 68 $^{\circ}\text{C}$) are hot embossed in a press at $\sim 70^{\circ}\text{C}$ for 3 min under a force of 0.5 ton using a silanized polyester master. Figure 11 shows the optical microscope image of an embossed Zeonor plate. The advantage of hot embossing over polymer melting lies in extremely short process times.

4. Conclusions

In summary, we have demonstrated a reproducible method for fabricating monolithic polymer masters for the microfabrication of microdevices by replication. The master's fabrication is achieved by a combination of simple process steps that do not require any specific equipment, such as moulding of PDMS and casting of polyester resin. Another group has also indicated the possibility of directly fabricating entire microfluidic chips using polyester (Fiorini *et al* 2003). However, the main advantage of our approach lies in the ability to simultaneously fabricate structures with a wide range of aspect ratios. This protocol also offers the possibility of fabricating large-area devices. Finally, silanation of polyester templates has been used

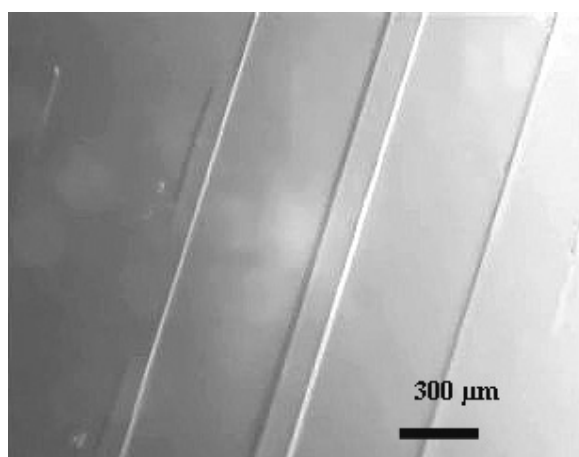


Figure 11. Optical microscope image of a hot embossed Zeonor plate. The central microchannel is 140 μm wide and 12 μm deep.

to drastically reduce the adhesion between the template and the replicated polymer device. This way, in contrast with *SU-8* on silicon masters, the monolithic masters can also be used for solvent casting, hot embossing or pellet melting. The monolithic character of the master strongly increases the resistance of the microstructures, and prevents delamination upon demoulding, currently a problem with *SU-8* on substrate masters. Indeed, for most embossing, casting or moulding applications (except extended mass productions), monolithic polyester masters are robust and versatile enough to replace metallic ones, with the strong advantages of cost efficiency and ease of fabrication. We thus believe that they can find numerous applications in microfluidic research.

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