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# Rapid prototyping of microfluidic chips in COC

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**Abstract**
We present a novel, cost-efficient process chain for fast tooling and small-lot replication of high-quality, multi-scale microfluidic polymer chips within less than 5 days. The fabrication chain starts with a primary master which is made by well-established cleanroom processes such as DRIE or negative SU-8 resist based surface micromachining. The formation of undercuts in the master which would complicate demolding is carefully avoided. Secondary PDMS masters or epoxy-based masters which are more suitable for common polymer replication schemes such as soft-embossing, hot-embossing or injection molding are subsequently cast from the primary masters. The polymer replica are mainly made of COC and show excellent fidelity with the conventionally micromachined master while displaying no degeneration, even after more than 200 cycles. The use of other polymers such as PMMA is also possible. The process chain further includes surface modification techniques for overall, long-term stable hydrophilic coatings and for local hydrophobic patches as well as a durable sealing based on thermal bonding.

## Introduction

While most pioneering work in the field of microfluidics relied on silicon microfabrication, the present state of microfabrication provides a broad spectrum of techniques for processing a variety of materials, in particular polymers. This trend to use polymer chips in microfluidics is driven by cost-efficient replication techniques such as hot embossing [1–4, 8] or injection molding [5–10] as well as the huge variety and the favorable pricing of polymers [11]. However, the manufacturing of microstructured metal masters is a complex and rather lengthy process, making it often impractical for an economically efficient prototyping.

The functionality and reliability of microfluidic devices are tightly linked to the geometrical tolerances in the channel geometry, surface roughness and surface energy. These properties of the replica are, in turn, directly impacted by the geometric tolerances and the surface quality of the reverse master structures. As the master has to be repeatedly demolded from the polymer replica, smooth tool surfaces as well as the avoidance of undercuts and a low physico-chemical adherence between the master and the replica minimize the frictional forces on the master, thus facilitating demolding and extending the lifetime of the tool. In addition to the replication of the polymer devices, the surface modification and the sealing of the channel network have to be integrated into a comprehensive prototyping chain.

Substrates fabricated by direct writing methods such as micromilling or laser ablation [12, 13] reveal a poorer

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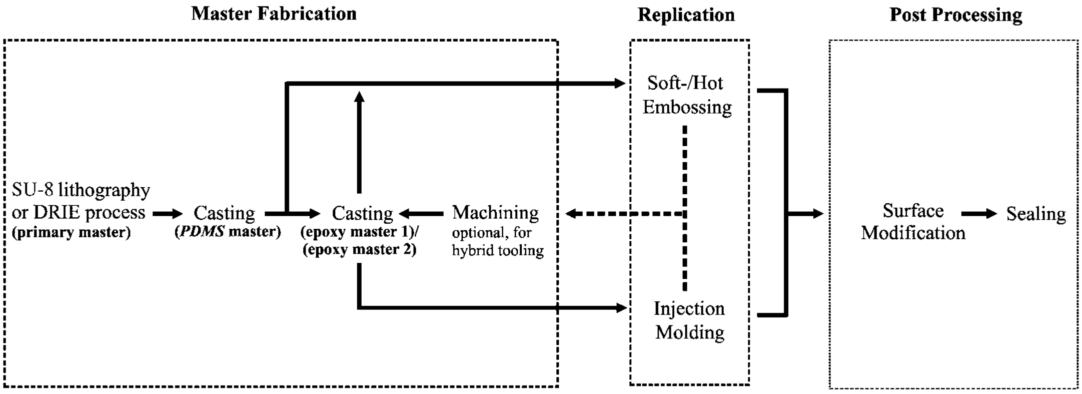

**Figure 1.** Fabrication chain for microfluidic polymer chips. First, a master is made out of PDMS which can be optionally transferred into an epoxy master for subsequent replication of the polymer chips by embossing or injection molding. During post-processing, the microfluidic chips are surface modified and finally sealed.

surface quality and material characteristics in comparison to devices which are replicated from masters originating from photolithographical procedures such as silicon bulk micromachining or surface micromachining employing high-aspect-ratio resists such SU-8 [14–16].

In a typical conventional procedure for obtaining the secondary master, a photolithographically structured primary master features a conductive layer seeding the electroplating [17] in a galvanic bath. A high control over the electrochemical process is critical for an accurate topographical reproduction of the structures. The duration of the electroplating process is proportional to the thickness of the grown metal layer and thus very time-consuming for high structures (several days up to weeks). While enhanced current densities speed up the growth [18], they also tend to increase the formation of internal stress. If no stress reducing agents are used, the additional stress may lead to warped metal masters exhibiting insufficient surface quality. After the primary master is overgrown with the metal, the backside of the electroplated secondary master is post-processed by mechanical procedures. To reduce the time for the testing of novel microfluidic designs while limiting the risks of artifacts from a ‘quick-and-dirty’ electroplating process, an alternative technique for generating a high-quality secondary master with a sufficient lifetime for a small-lot replication is required.

This work focuses on the prototyping of polymer disks in a standard 12-cm compact disc (CD) format for lab-on-a-disk [19–22] systems or other lab-on-a-chip substrates possessing comparatively large surface areas [23–25]. The design of the incorporated microfluidic structures typically displays three different depths. The reservoirs account for the largest depths of about 250 $\mu$m, followed by about 80 $\mu$m deep metering chambers, capillary ducts and channels for other purposes. The smallest channel depths of only about 35 $\mu$m are needed for hydrophobic or hydrophilic capillary barriers or they may serve as aggregation steps for beads.

In order to achieve microstructures of high geometrical precision over the large-area disk, complex structures are generated by a multi-layer SU-8 [26] lithography [27] or deep reactive ion etching (DRIE) into a primary master. This primary master is transferred by a casting process into a secondary PDMS elastomer master which is suitable for the replication into polymer substrates by soft embossing [28]. Furthermore, by casting an epoxy resin into the PDMS mold, the epoxy master 1 can be used as a master for hot embossing or injection molding. The replicated chips made of *cyclo-olefin copolymer* (COC) can optionally be processed by conventional machining techniques to integrate macro structures and again transferred back into another epoxy master (epoxy master 2). Finally, the replicated COC substrates are surface modified to create locally varying wetting conditions in channels. In the final step, the substrates are sealed by thermal bonding with a novel 2-component foil.

Figure 1 shows the process chain for the fabrication and functionalization of polymer disks [29]. All techniques presented here are characterized by their compatibility to an integrated process chain which allows the rapid fabrication of polymer microfluidic chips within less than 5 days.

The individual steps of the prototyping chain are explained in the following sections. First, two alternative microfabrication schemes, SU-8 lithography and DRIE, are introduced for the fabrication of a multi-layer primary master. Next, the transfer of the primary master into a PDMS master or optionally into an epoxy master (epoxy master 1) is explained. Then, the fabrication of a multi-scale epoxy master (epoxy master 2) by a hybrid tooling process based on micro-machining is described. In the following sections, the replication of polymer chips by soft embossing, hot embossing or injection molding is presented. The last sections describe methods for a long-term stable, overall hydrophilization of the COC substrates, the spatial definition of localized hydrophobic patches, and the bonding with a sealing layer.

## Master fabrication by SU-8 lithography

Multi-layer SU-8 structures for the primary masters are realized by successive deposition, pre-baking and exposure of several SU-8 layers on top of each other, followed by a final, simultaneous development [15, 27]. Our 3-layer structures exhibit a maximum aspect ratio of about 2 as prescribed by the subsequent demolding of PDMS. The following process parameters are applicable to thicknesses of composite layers of SU-8 2100 [30] and SU-8 2025 [14, 31] up to 300 $\mu$m. The process starts with the deposition of a thick SU-8 2100 bottom

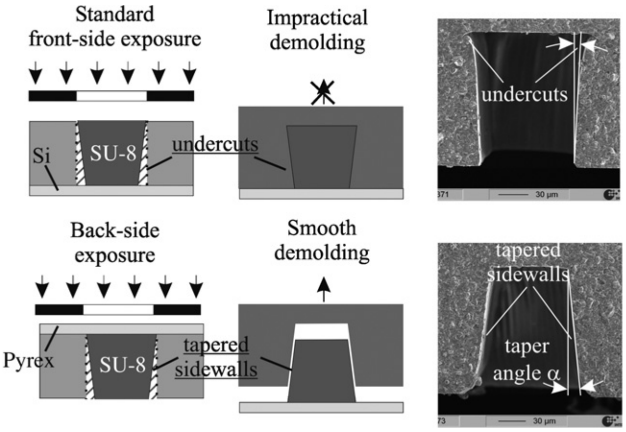

**Figure 2.** Top: standard front side exposure of negative resist tends to form undercut structures at underexposed sidewalls. Bottom: backside exposure reversed the effect to form tapered sidewalls (taper angle $\alpha = 6^\circ$) which allowed facile demolding.

layer. Using a standard spin coater, the resist is spread on a four-inch silicon wafer at a frequency of 500 rpm for 15 s. The spinning frequency is subsequently elevated to define the final layer thickness according to the data sheets supplied with the resist.

After pre-baking on a hotplate at $T = 95$ °C for 30 min, the first layer is exposed to 365 nm UV light at an intensity of 450 mJ $\mathrm{cm}^{-2}$ for 60 s. Since the minimum feature sizes in our structures are in the range above 30 $\mu$m, even low-cost transparency masks (2650-dpi) may be used. Relaxing the resist by a pulsed exposure supports the dissipation of accumulated Joule heat and nitrogen. Cross linking of exposed areas is induced by the post-exposure bake at $T = 95$ °C for 35 min. The deposition of further layers proceeds according to the same protocol at adapted spinning rates for SU-8 2025 layers. In the last step, all SU-8 layers are simultaneously developed at room temperature for about 20 min.

Tapered structures with sloped sidewalls support a smooth removal of the mold. However, standard front-side illumination tends to form undercuts in the negative SU-8 2100 resist due to a decreasing intensity of the UV-light towards the deeper layers of the photoresist. During demolding, the undercuts tend to interlock the replicated structures with the master. In our novel fabrication method, we expose the resist from the backside through a transparent Pyrex wafer [32]. This way, the structures are tapered towards the top, thus reversing the inclination of the parasitic undercuts (figure 2). With an irradiation intensity of 315 mJ $\mathrm{cm}^{-2}$ for 50 s, an optimum taper angle of 6° could be achieved in our experiments.

## Master fabrication by DRIE

As an alternative to SU-8 based surface machining, deep reactive ion etching [33] (DRIE) can be utilized. DRIE is a well-qualified bulk micromachining process, allowing a very precise and reproducible fabrication of microfluidic structures. The taper angle of the sidewalls can be adjusted within a range between $-5^\circ$ and $+5^\circ$ by tuning the switching times, total cycle time, gas flows as well as the DC bias [34].

Two levels can be etched with our established process into the silicon wafer by using two different mask layers, each of which may independently be structured and removed. The design of the microfluidic structures is also limited to an aspect ratio of about 2 due to the demolding. Figure 3 shows the realization of a 2-level structure using thermal silicon oxide and photo resist as mask layers. After performing all etching steps and removing all mask layers, a final $C_4F_8$ passivation step (2 min) coats the wafer with an approximately 200 nm thin PTFE layer to facilitate the detachment of the PDMS mold from the silicon wafer in the following casting steps (figure 1).

Besides the high precision and reproducibility of the microfluidic structures, another main advantage of the DRIE approach is the high robustness of the bulk micromachined wafer. While it is hard to clean an SU-8-on-silicon master without detaching the brittle structured surface layers, the bulk micromachined wafer could be cleaned several times, even with use of brushes, in an ultrasonic bath or by applying standard cleaning solvents.

## PDMS-based mold inserts

Due to their interesting material characteristics in terms of flexibility, transparency and self-adhesive properties [35, 36], elastomers such as *poly-dimethyl siloxane* (PDMS) [37, 38] are nowadays widely used in the microfluidics community. With its high thermal stability up to $T = 250$ °C, PDMS has also been employed as a material for embossing tools. The PDMS-based replication of microstructures by embossing into polymers such as *cyclo olefin copolymers* (COC), *polymethyl methacrylate* (PMMA), *polycarbonate* (PC) or *polystyrene* (PS) is also referred to as soft embossing [39].

The choice of the elastomeric material *Elastosil RT 607 A + B* (Wacker Chemie GmbH, 81737 Munich, Germany) for the PDMS master compromises between the low viscosity of the liquid compounds for optimum filling of the microcavities during casting and the comparably high hardness of the cured matrix displaying a Shore A value of 40. The compounds A and B are thoroughly mixed at a ratio 1:9 by stirring according to the datasheets [40]. The mixture is evacuated for 5 min to suppress the formation of air pockets in the cured silicone. It is then poured over the primary master which is fixed in the center of a round, open cavity with an inner diameter of 12 cm (compact disk format). It is then cured for 5 min.

Afterwards, the backside of the PDMS master is planarized to minimize wedge-errors in subsequently embossed replicas by placing a flat metal stamp on top of the cast material during the curing step at 70 °C for 3 h. The flexible polymer replica can then easily be peeled off from the primary master. Figure 4 shows a microstructured mold insert made from *Elastosil RT 607* in the compact disc format (diameter: 12 cm).

## Epoxy-based mold inserts

The high shear stress and temperatures (up to 200 °C) typically associated with injection molding of polymers impose challenging demands on the mechanical and thermal stability of the mold inserts. The use of PDMS masters for the harsh conditions during this process is limited by the flexibility

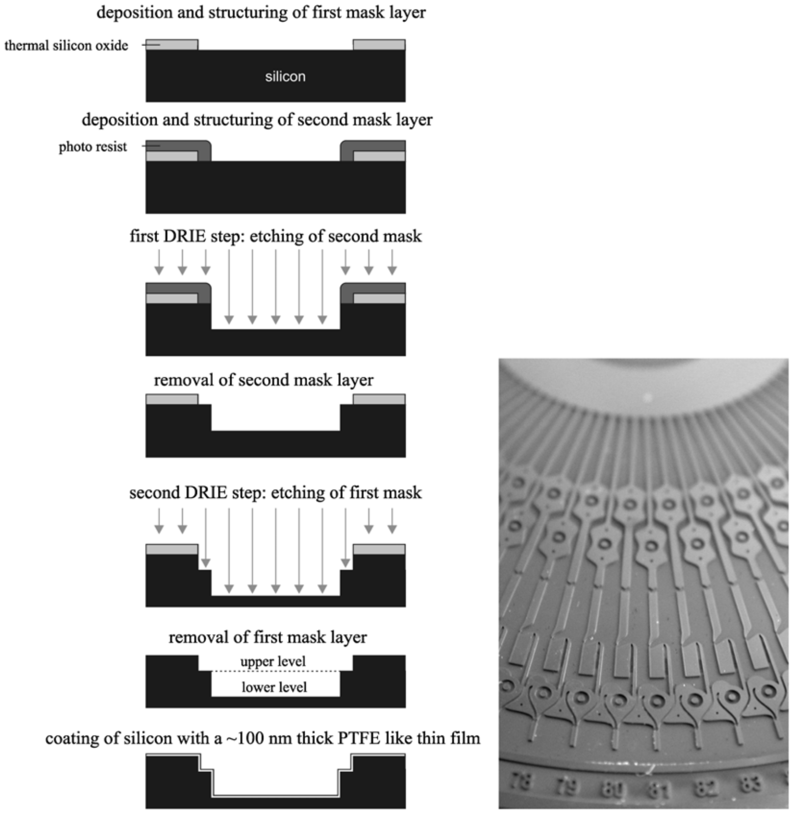

**Figure 3.** Fabrication of the primary master by the DRIE approach. Left: process flow; right: photograph of a DRIE-based Si master exhibiting parallelized microfluidic structures which are arranged according to the rotational symmetry of the disk.

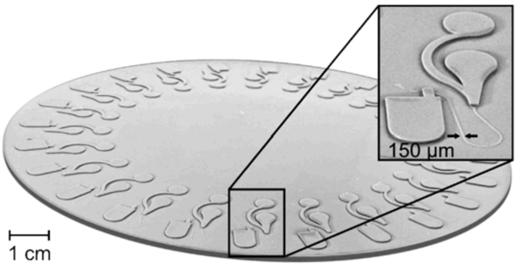

**Figure 4.** PDMS master featuring several microfluidic structures assembled in parallel according to the symmetry of the disk. The structures exhibit reservoirs with a height of 250 $\mu$m and narrow channels possessing a height of 35 $\mu$m and a width of 150 $\mu$m. The insert endures at least 20 cycles of the hot embossing process.

and abrasion rates of the material becoming noticeable after more than about 100 cycles [41]. The high-performance epoxy resin *Weidling C* [42] containing aluminum powder (10% by weight) combines an easy fabrication via simple casting technique as well as the required material properties. Its low viscosity of about 25 000 mPa s ensures optimum filling of microcavities. The resin cures at low volume shrinkage and builds a stiff matrix with a temperature stability of up to 220 °C.

In order to avoid bonding between SU-8 and epoxy resin at direct molding, the positive SU-8 structure is first cast into a negative silicone mold (PDMS master) and subsequently cast in the final (positive) epoxy resin tool (epoxy master 1) (figure 5). The flexible silicone mold (PDMS master) can easily be peeled off from the epoxy master (epoxy master 1). Following the protocol in the datasheets, the epoxy is cured for 12 h, followed by annealing for 14 h at 120 °C where the epoxy gains its thermal stability. The versatile epoxy master 1 can then be used both, for hot embossing and injection molding.

## Hybrid tooling

The SU-8 lithography and DRIE etching delivers high-precision structures with a height ranging between 0.5 $\mu$m and 300 $\mu$m. Mechanical stress induced by the intrinsic volume shrinkage due to cross-linking of the resist during the post exposure bake prohibits the use of this process for structure heights in the range of millimeters. However, in particular in microfluidics, it is often desired to integrate larger macroscopic structures in the order of a few millimeters next to small structures in the micrometer scale. While the microfluidic functions based on, e.g., capillary effects or small diffusion lengths associated with the microstructures, the microliter volume contains by the macroscopic structures may work as reservoirs for sample uptake and batch-mode inertial mixing [43].

The casting technique offers a simple method to integrate both features into one mold insert. Therefore, macrostructures are precision milled [44] next to the microstructures which are already replicated in a polymer (COC) piece. The so obtained negative multi-scale image in the polymer is then once more cast into the epoxy resin (epoxy master 2)

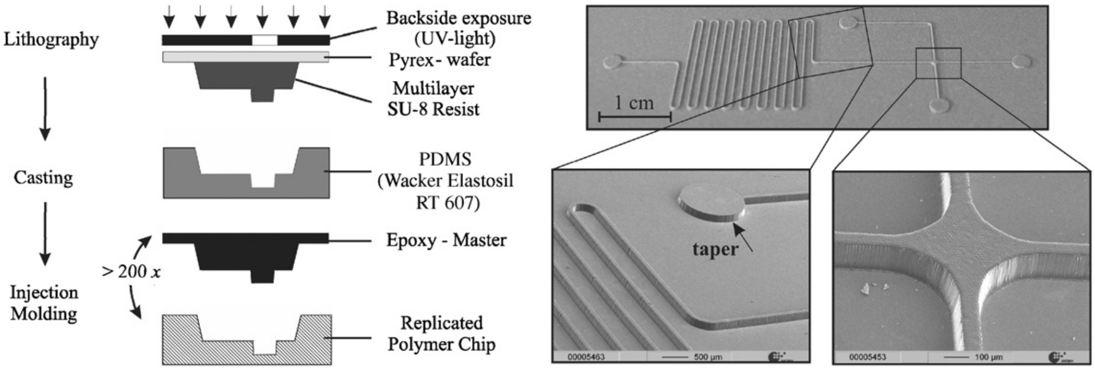

**Figure 5.** Left: fabrication process for epoxy masters (epoxy master 1). Structures are patterned on a Pyrex wafer by backside SU-8 lithography, cast in PDMS and subsequently cast in a mechanically and thermally stable epoxy resin (epoxy master 1). The epoxy master 1 can be used both in hot embossing and injection molding. Right: epoxy master 1 featuring a microfluidic structure displaying two different channel heights. The width amounts to 160 $\mu$m and the heights are 35 $\mu$m and 150 $\mu$m, respectively. Note the slightly tapered sidewalls and the good surface quality.

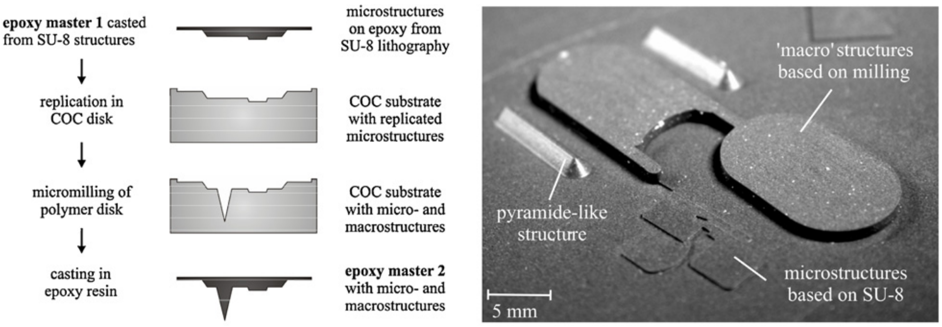

**Figure 6.** Left: fabrication process for multi-scale, hybrid epoxy masters (epoxy master 2). The polymer disk is replicated from a first epoxy master (epoxy master 1) and post-processed by micromilling which forms the larger structures. A negative image of these structures on the polymer disk is then retransferred the epoxy resin (epoxy master 2), which can be used for many replication cycles. Right: segment on an epoxy master 2 showing a microfluidic unit featuring microstructures based on SU-8 lithography and 'macro' structures which are formed by micromilling. The microstructures display a minimum width of the 100 $\mu$m and two height levels of 40 $\mu$m and 160 $\mu$m, respectively. The macrostructures possess a uniform height of 1.5 mm. The pyramid-like structures are defined by milling using a tool tapered at an angle of 45°.

(figure 6). After curing, the epoxy master 2 is isolated by dissolving the polymer (in this case of COC in Toluene for about 10 h). The chemical dissolution procedure is chosen as a mere mechanical demolding often fails due to a strong bond between the cured epoxy and the polymer.

This way, a multi-scale epoxy master 2 featuring macroscopic and microscopic structures is fabricated by hybrid tooling using SU-8 technology and conventional milling. Apart from the scale of the structures, also conical, pyramid-like structures as they are used for internal beam-guidance structures [45, 46] can easily be realized using a proper milling tool (figure 6).

## Replication by embossing

The PDMS masters are replicated into polymer disks (*TOPAS* 5013, Ticona GmbH, 65451 Kelsterbach, Germany) by embossing techniques. To this end, the disks are first assembled with the PDMS mold insert in a closed cavity made of brass. The cavity consists of a round bottom plate, a frame and a cover plate. A tight fit between the PDMS mold and the framing holder is important to avoid deflection of the elastic PDMS mold during embossing. After covering with the plate, the entire assembly is heated under a vacuum (∼1 mbar) up to 175 °C in a hot embossing machine.

Beyond the material specific glass transition temperature ($T_g$ = 130 °C for TOPAS 5013), the melted polymer fills the cavities of the mold insert upon applying a load of $F$ = 3 kN for 5 min at 175 °C. Vacuum conditions during the entire process prevent trapping of air pockets in the cavities. Planarity and parallel alignment of the pressing plates of the hot press is important to avoid wedge-errors in the replicated piece. After solidification of the polymer, the disk is cooled down to room temperature while maintaining a constant force. The structured disk can easily be peeled off from the elastic PDMS mold insert after embossing.

## Replication by injection molding

Mold inserts for injection molding made from low-viscosity epoxy resins eliminate the rather complex and time-consuming electroplating of conventional metal masters. In order to demonstrate injection molding using low-cost epoxy-based mold inserts, various microfluidic structures of typical geometries (channel height 160 $\mu$m, width 150 $\mu$m) are replicated on the footprint of a microscope slide (width 26 mm,

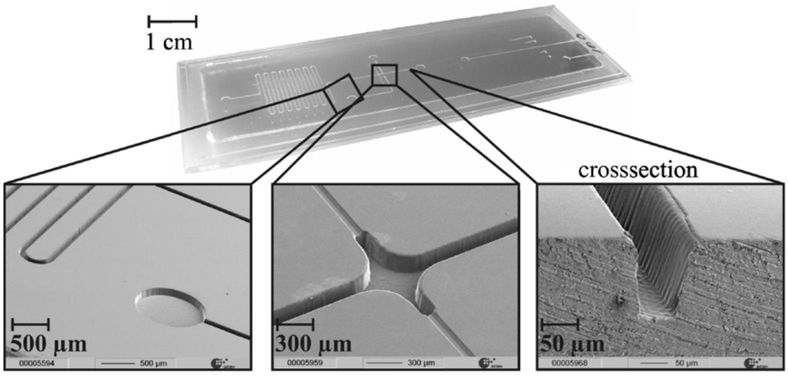

**Figure 7.** Polymer substrate in the format of a microscope slide featuring microstructures replicated in COC. The cycle time of injection molding amounts to 5 s only.

**Table 1.** Maximum deviation of channel geometries in relation to the master and the maximum surface roughness of the different process steps.

| Process step | PDMS master | Epoxy master | Embossed COC chip | Injected molded COC chip |
|---|---|---|---|---|
| Master for casting/molding | SU-8 master | PDMS master | PDMS master | Epoxy master |
| Maximum deviation of channel width | 0.6% | 0.3% | 0.9% | 0.3% |
| Maximum deviation of channel height | 2% | 0.3% | 0.7% | 0.6% |
| Maximum channel roughness | 10 nm | 270 nm | 15 nm | 300 nm |
| Maximum substrate roughness | 15 nm | 30 nm | 20 nm | 30 nm |

length 76 mm, thickness 1 mm) from *polystyrene* (PS) and COC (figure 7). The cycle time remains below 5 s. By optimizing the injection protocol, excellent dimensional conformance between the epoxy master and the replicated polymer and a low surface roughness ($<1$ $\mu$m) was achieved. The mold inserts showed no wear, even after more than 200 cycles. Investigations of replicated polymer surfaces by energy dispersive x-ray spectrometry provided no evidence for abrasion residues of the epoxy master on the polymer surface.

## Process evaluation

The geometrical fidelity as well as the surface roughness of the mold inserts and the replicated polymer substrates are characterized. The fidelity of the channel widths and heights are measured using a needle prober. The surface roughness at the bottom of the channels and on the unstructured substrate is characterized using a white-light interferometer. The data presented in table 1 are derived from at least three measurements of several channel features on different mold inserts/chips. The maximum deviation of the channel dimensions (width: 80–160 $\mu$m, height: 35–150 $\mu$m) in relation to the respective master represents a measure of quality for each replication step. As shown in table 1, the maximum deviations of the channel dimensions are small ($<2\%$) and were therefore neglected in our case since no change in functionality could be observed.

The surface roughness stays below 20 nm when standard front side SU-8 lithography is applied to structure the silicone mold insert for the soft embossing process since the channel roughness is determined by the surface quality of the polished wafer surface. In the case of the backside exposure which are required for the epoxy masters, an elevated surface roughness up to about 270 nm on the SU-8 structures occurs which transforms through the casting process to the final replicated polymer piece.

The surface quality at the channel sidewalls depends on the resolution of the photolithographic mask. In the present work, we use cheap foil masks made by a high-resolution, 2650-dpi laser printer. This leads to a visible roughness of the replicated channel side walls which, however, did not have any observable impact on the microfluidic operations, e.g., contact angle according to the raw COC material.

## Global hydrophilic surface coating

The wettability of the surface is crucial to the function of microfluidic devices. Two different approaches for realizing hydrophilic and hydrophobic surface coatings are outlined. Bare COC surfaces display from slightly hydrophobic contact angles (95° for DI water) and hence do not show any self-priming capability. The COC material is still used owing to its low background fluorescence which is interesting for fluorescence readout of assays. To create a hydrophilic surface, the microstructured COC substrate is selectively modified by attaching hydrophilic and hydrophobic polymers.

For the hydrophilization of the plain disk, *polyhydroxyethyloxazoline* (PEtOx) containing *benzophenone* groups is used to coat the plasma activated substrate ($O_2$ plasma, 100 W for 1 min) either by spin or dip coating techniques. Upon UV irradiation at 356 nm, photo-crosslinking occurs between the photoactive *benzophenone* groups within the polymer and the COC surface. The contact angle of PEtOx surface against DI water experimentally

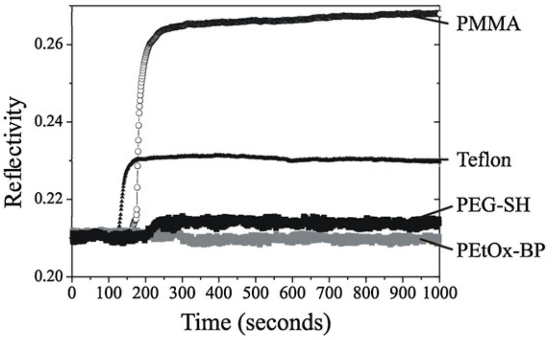

**Figure 8.** Kinetics of fibrinogen adsorption onto various surfaces measured by surface plasmon resonance spectroscopy.

determined to be 50°. This layer remains stable, even after several fillings with solvents.

The protein adsorption is evaluated by surface plasmon resonance (SPR) on different polymer surfaces. The reflectivity $R$ is a measure of the adsorbed amount of protein over time. Model reactions are performed on a lanthanum slide covered with gold and coated with a thin layer of PMMA. Fibrinogen, which is a very important blood protein displaying high adsorption, is chosen as a model protein. The results in figure 8 give clear evidence for a spontaneous, irreversible adsorption of fibrinogen onto the unmodified PMMA surface.

Subsequently, the surface is modified by different hydrophilic and hydrophobic polymers. The protein adsorption onto the surface coated by a *fluoropolymer* (*Teflon*) is significantly lower than the untreated PMMA surface. As expected, further test reactions performed with hydrophilic *polyethylenglycol* (PEG) and *polyhydroxyethyloxazoline* (PEtOx) exhibit the lowest protein adsorption.

## Localized hydrophobic patches

After hydrophilization with PEtOx, hydrophobic fluoropolymer-based solutions (*TEFLON AF* [47]) dissolved in *3M Fluorinert FC77* [48] are placed at specific positions in a given channel. An accurate positioning of these patches is decisive for the hydrophobic flow control in the channel network, in particular in centrifugal microfluidics. To this end, the parasitic spreading of solution along the hydrophilic channels must be suppressed.

Among various approaches, wetting the tip of a felt pen [49] with a hydrophobic solution and 'writing' the coating into the channels yielded the most satisfying results for prototyping. On the one hand, the tip can be accurately positioned; on the other hand the dispensed volume is minimized to avoid spreading after deposition by capillary effects.

The contact angle between the Teflon treated surface and DI water measures 115°. Figure 9 shows a segment of the polymer disk featuring soft embossed channel segments at three different depths. A well-defined hydrophobic patch is defined at the exit of a chamber by the felt-pen writing technique.

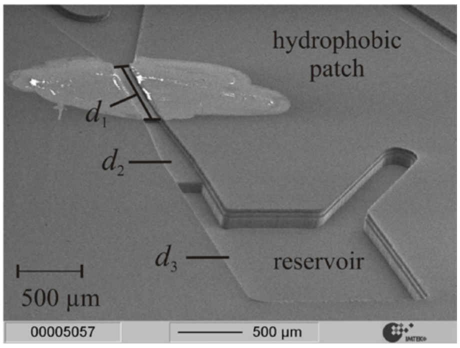

**Figure 9.** Segment of the multi-level disk showing a hydrophobic patch in a channel featuring several depths of $d_1 = 45$ $\mu$m, $d_2 = 80$ $\mu$m, $d_3 = 260$ $\mu$m to confine an upstream reservoir. The structures are replicated in COC by soft embossing from a PDMS mold which is cast over an SU-8 multi-layer master. Note the exact positioning of the hydrophobic patch covering the shallow channel segment only.

## Sealing

The challenge in sealing microchannels is, on the one hand, to establish a pressure-tight bond between substrate and cover which does not distort the cross section, e.g., by channel deformation or the sagging of the cover lid. On the other hand, the compatibility of materials and processes with the surface coatings and the exclusion of unstable reagents (e.g. out-gassing glue or solvents) impact the functionality of bioanalytical devices. Various approaches for sealing of microstructured polymer substrates with cover plates by UV-curable adhesive bond [50], plasma activated bond [51, 52] or temperature diffusion bonding [53, 54] have been reported. We chose the temperature diffusion bonding technique. The strength of the bond is based on the interlink of the polymer chains when the surfaces are closely put together and locally heated beyond their glass transition temperature $T_g$.

The contact pressure as well as the process temperature strongly affects the bonding strength. The optimum set of parameters constitutes a compromise between the bonding strength, promoted by a high process pressure and temperature, and the geometric stability of the channel cross section suffering from the molten substrate the thermal expansion of the cover lid. In order to minimize the thermal expansion, we developed a composite cover foil featuring two layers of different $T_g$ and different thickness: a thin *TOPAS* 8007 'gluing' layer ($T_g = 75°$) with a small thickness of 3–5 $\mu$m is defined by spin coating *TOPAS* 8007 (5% wt dissolved in toluene) at 5000 rpm on a 500 $\mu$m thick *TOPAS* 6013 foil with a $T_g$ of 130 °C. Annealing the composite at 75 °C for 1 h drives out the remaining solvent.

The substrate material consists of *TOPAS* 5013 ($T_g = 130$ °C) which is microstructured by soft embossing. When the composite foil is pressed on the substrate at a temperature fairly above 75 °C but lower than 130 °C, the thin *TOPAS* 8007 melts to establish a vigorous bond to the substrate. The thick and temperature-stable back layer composed of *TOPAS* 6013 provides sufficient mechanical stability to prevent sagging of the lid. Also the structures on the substrate prove to be stable at these temperatures.

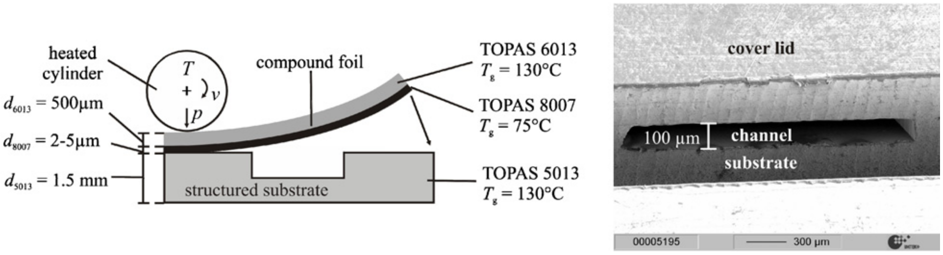

**Figure 10.** Left: lamination process. A composite foil featuring two layers of different $T_g$ and thicknesses is bonded to the substrate by a heated cylinder (temperature *T*), pressure and feed rate $v$. Right: cross section of a microchannel with a height of 100 $\mu$m and a width of 1.2 mm which is thermally sealed by the 2-component foil. The technique provides both a tight bond between cover and the substrate due to the thin adhesion layer as well as an undistorted cross section due to the mechanically rigid foil.

The sealing was carried out on a lamination machine [55] featuring two steel cylinders which are covered with a protective elastomer layer. The two cylinders are pressed together by a pneumatic pressure of 5 bar and heated up to 120 °C while rotating at a feed rate of 30 cm $\text{min}^{-1}$. These settings may vary when using different setups. The cross section of a sealed channel is depicted in figure 10.

The bonding strength of the sealing is characterized by pressurizing a sealed cavity with a diameter of 2 mm using nitrogen with increasing pressure until the cover foil peels off. Experiments show that the bond withstands a pressure of more than 4 bar. This critical bonding strength is much higher than the maximum pressure (about 1 bar) which occurs on our centrifugal platform.

## Conclusion

We presented a comprehensive prototyping chain including fast tooling and replication of typical, multi-layer and multi-scale microfluidic structures into large-format polymer substrates including stable surface modification and sealing. This allows us to test and to improve microfluidic designs and layouts with fast turn-around times.

At the beginning of the chain, primary, multi-level masters with favorable taper angles are made by SU-8 surface micromachining on Pyrex wafers or DRIE on silicon wafers. These primary masters are then cast into secondary PDMS masters and optionally secondary epoxy masters (epoxy masters 1) for the subsequent replication into large-format polymer substrates by soft embossing, hot embossing or injection molding. A hybrid tooling technology is shown to fabricate multi-scale structures into a further epoxy master (epoxy master 2). The fabrication process assures a very high geometrical accuracy and no change of surface properties.

The process chain also features common post-processing steps for microfluidic substrates. First, a stable hydrophilic PEtOx layer is applied by dip coating and subsequent UV-crosslinking to support capillary priming and to block undesired protein adsorption on the channel walls. Next, a technique to accurately place hydrophobic patches at channel constrictions is presented, e.g. to realize common capillary burst valves. Finally, a sealing technology based on thermal bonding of a 2-component foil to the polymer substrate is described. This bonding scheme excels with a high bonding strength paired with minimal thermally and mechanically induced deformation of the channel cross section.

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