A NOVEL APPROACH FOR THE FABRICATION OF ALL-POLYMER MICROFLUIDIC DEVICES

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ABSTRACT
This paper describes a process sequence for the fabrication of all-polymer microfluidic chips based on the multilayer lamination of TMMF dry resist (TOK, Japan) on a pre-patterned PMMA substrate. The sequence provides a simple way to meet major microfluidic requirements like the fabrication of embedded microchannels, nozzles and interconnecting vias as well as their accurate integration into a chip-interface without additional materials and bonding procedures. We demonstrate the applicability of the sequence by manufacturing and testing a 24-channel TopSpot printhead. Additionally, non-cytotoxicity of TMMF was confirmed in cell culture experiments and different methods for surface modification were investigated.

INTRODUCTION
In recent years, polymer materials had a large impact on research and development in microfluidics and BioMEMS [1]. A wide range of techniques for polymer microfabrication by either direct micromachining or replication is available. However, the commercial success of polymer microfluidics requires more than reliable technological platforms and is above all dependent on the interest expressed by life sciences companies to provide access to the market [2]. Although many microfluidic prototypes have been developed in research laboratories, far fewer have been transformed into marketable devices [3]. A critical aspect in this context is the gap between academic approaches, mainly represented by casting of PDMS and SU-8 lithography, and fabrication methods suitable for mass production, e.g. injection molding and mechanical machining [4]. PDMS, for example, enables rapid testing of fluidic designs but the control of its surface properties is insufficient to provide long-term stability [5]. The main disadvantage of SU-8 is the lack of standardization for post-processing steps like stacking of layers, sealing of microchannels and removing the cross-linked resist from its substrate [6].
Micro injection molding, on the other hand, provides few design limitations. The accuracy of injection molded microparts, for example, is limited due to thermal shrinkage of the polymer as a function of the overall chip size. Thus, injection molding is not suitable for high aspect ratio microstructures on large substrates, as often required in microfluidics. Another challenging issue is the precise fabrication of interconnecting vias or dispensing nozzles, which requires a manual removal of a thin residual layer. Furthermore, sharp edges and undercuts should be avoided due to stress peaks and demolding requirements, respectively [7]. Sealing of molded microfluidic channels requires heating above the glass-transition-temperature or the use of adhesive layers and may lead to deformation and clogging. Generally, even when post-processing of injection molded chips can be easily standardized, it remains a challenging issue and a can make up to 80 % of the manufacturing costs [4].
Newly, dry film resists have moved away from their original purpose of providing sacrificial layers for the fabrication of printed circuit boards and were successfully applied as a structural material for BioMEMS. Riston [8], Ordyl SY [9] and the recently introduced negative-tone, epoxy-based TMMF [10,11] offer numerous advantages over liquid resists, the most important of which are their ability to bridge over trenches, low thickness variation and suitability for both prototyping and mass production. So far, dry film resists were mostly applied on silicon or glass substrates and usually an additional bonding step was used to define the fluidic interface and seal the channels. In this paper, we describe an alternative approach based on the multilayer lamination of the dry film directly on a pre-patterned polymer interface. The applicability of the approach was proven by the manufacturing and test of a 24 channel TopSpot printhead used for the fabrication of microarrays [12].

PRINCIPLE AND DESIGN
The main objective was to provide a fabrication sequence that enables the accurate alignment of the microfluidic components to each other and to the interface with the least number of assembly steps. Figure 1 shows the schematic cross-section and the operation principle of the TopSpot printhead.

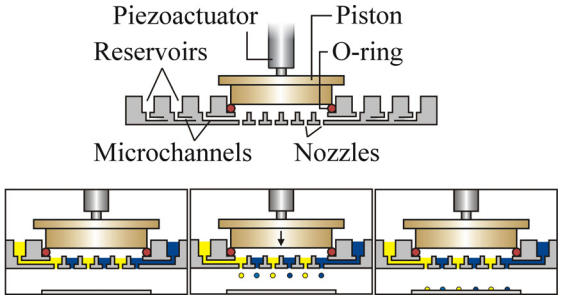

Figure 1: Schematic of the printhead cross-section and TopSpot operation principle.

During actuation, a piezo driven piston generates a pressure pulse by compressing an air chamber which causes the simultaneous ejection of a single droplet out of each nozzle. The outer dimensions of the interface are 36x20x3 mm^3 and are given by the 24 reservoirs with a diameter of 2 mm. A one to one format change from the 4.5 mm pitched reservoirs to the 500 µm pitched microarray grid is provided by capillary microchannels connecting each reservoir to a corresponding nozzle. Due to the need of very homogeneous and precise fabrication of the fluidic components, thermoplastic replication is not feasible. Thus, nozzles and microchannels were fabricated in TMMF dry resist. PMMA was used for the interface since it is a common material for BioMEMS. Figure 2 summarizes all dimensions of the printhead: Microchannels have a cross-section of 110x70 $µm^2$, nozzles and nozzle inlets have a diameter of 50 µm and 200 µm respectively.

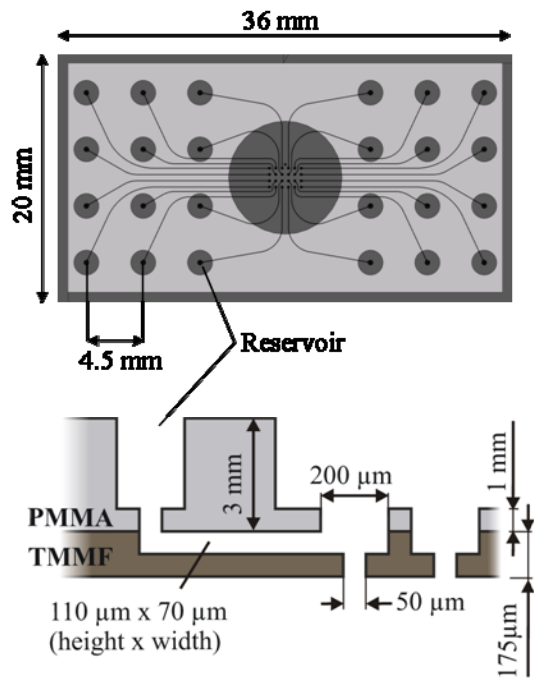

Figure 2: Top view and detailed dimensions (cross-section) of the PMMA/TMMF printhead.

FABRICATION

The fabrication of the PMMA/TMMF printheads is depicted in figure 3.

Chip interface

A PMMA plate with a thickness of 3 mm was first laser-cut into 4-inch wafer format that can hold up to six printheads. Reservoirs, actuation chambers and nozzle inlets (diameter from 8 mm to 0.2 mm) were fabricated by standard machining on a wafer level. Finally, alignment marks were placed outside the chips, at the border of the PMMA substrate.

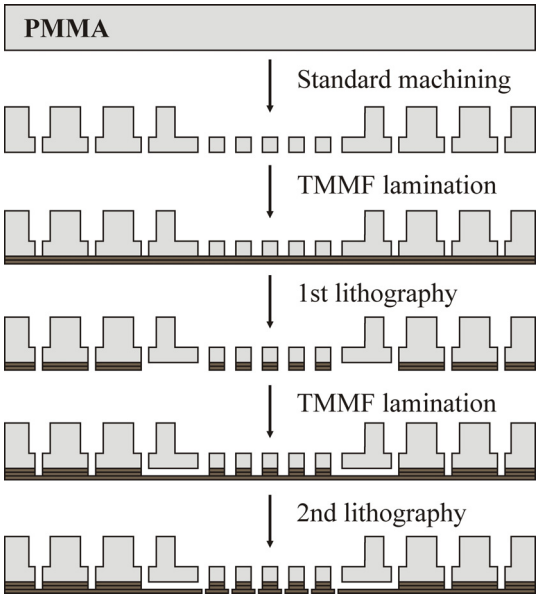

Figure 3: Fabrication process: Standard machining was used for fabrication of the chip-interface and TMMF lithography for fabrication of the fluidic microstructures.

Microchannels and nozzles

TMMF dry resist (55 µm thick, TOK, Japan) was applied on the pre-patterned PMMA substrate via wafer-level lamination. The process was performed on a DuPont laminator (Riston HRL) at a temperature of 60 °C, a pressure of approx. 1 bar and a roll speed of 1 m/min. The process was repeated to create a 110 µm thick TMMF layer. Microchannels running from each reservoir to the corresponding nozzle inlet were patterned using i-line (150 mJ/cm^2) and a printed lithography mask in a contact mode. To prevent mask sticking, the upper coversheet of the resist was removed after exposure. The resist was then heated on a hot plate for 45 min at 90 °C (post-exposure bake) to complete the cross-linking reaction. Subsequently, it was developed in PGMEA (propylene glycol methyl ether acetate) for 7 minutes, rinsed with deionized water and blown dry with nitrogen. Sealing of the microchannels was realized by laminating an additional TMMF layer using the same parameters as above. Again i-line lithography was performed to initiate cross-linking of the lid and pattern a nozzle at the end of each channel. In contrast to the first lithography step, a proximity gap of 20 µm was used and the TMMF protective foil was removed prior to the exposure to avoid scattering effects and improve the resolution. Thus, six 6x4 nozzle arrays were patterned in the sealing lid. The dry film was then post-exposure baked and developed in PGMEA for 15 minutes under ultrasonic actuation. Finally, the substrate was again rinsed with deionized water and blown dry with nitrogen.

Separation
The printheads were separated using a conventional wafer dicing machine. As an alternative, separation was realized by using a CO_2 laser cutting system.

RESULTS AND DISCUSSION
The main requirements for a successful evaluation of the novel approach are (i) the reliable fabrication of basic structures like embedded microchannels and interconnecting vias, (ii) the easy integration of these structures into a chip interface, (iii) the biocompatibility of the used materials and (iv) the availability of methods for surface modification.
Figure 4a shows the processed PMMA/TMMF wafer before dicing. A SEM observation proved the good quality of the process: No channel clogging or sagging of the cover lid (Fig. 4b) and perfectly round nozzles (Fig. 4c) were achieved.

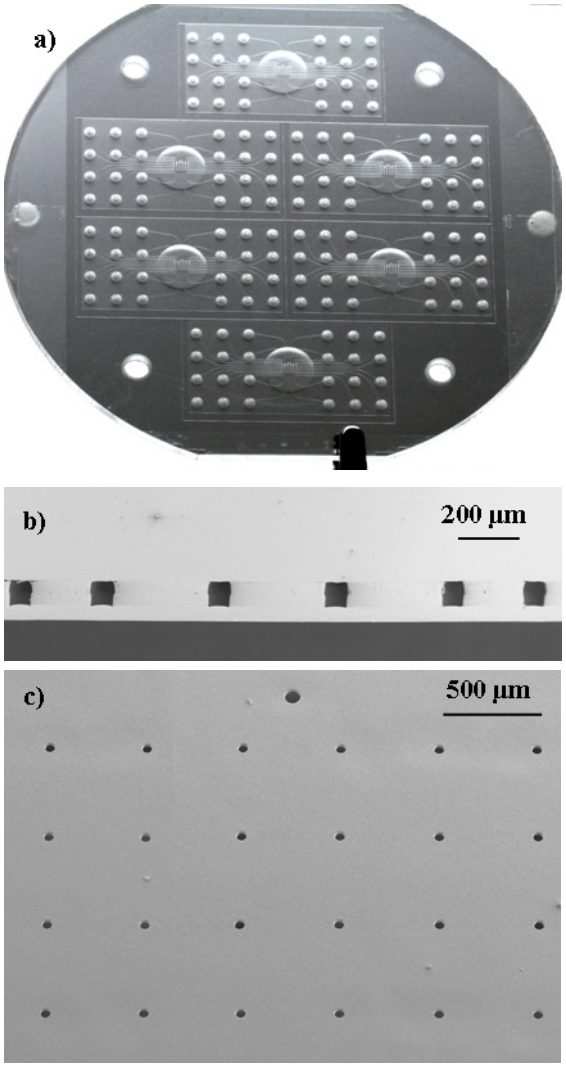

Figure 4: a) TMMF microstructures on a pre-patterned 4-inch PMMA substrate; b) Channel cross-section; c) A 6x4 nozzle array and a vent nozzle patterned in TMMF on a wafer level.

The connection of the microfluidic components with the chip interface is enabled by the adhesion of the dry film on PMMA and its ability to bridge over the reservoirs already patterned on the substrate. The adhesion was tested by applying a pressure of 8 bar which showed no delamination on the interface TMMF/PMMA or TMMF/TMMF. The accurate alignment of the microfluidic structures to the interface was facilitated by alignment marks on the back side of the substrate (back side alignment). The liquid-tight sealing and bonding of the microchannels to the PMMA-interface was checked by filling the printheads with colored ink (Fig. 5).

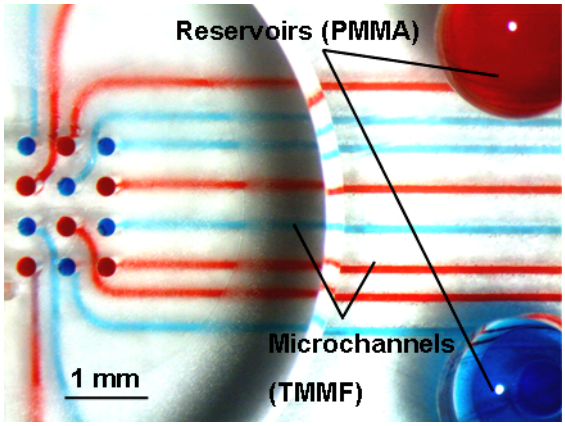

Figure 5: Cross-contamination free microchannels running from the reservoirs to the corresponding nozzles.

Materials for microfluidic applications have to be biocompatible in order to avoid unintentional effects on the biological samples. We applied an elution test method according to ISO 10993-5 to analyze the cellular toxicity of TMMF. A DMEM cell culture medium containing extractables from hard-baked TMMF was applied to a monolayer of L929 cells (mouse fibroblasts) replacing the medium that had nourished the cells until that point. The cells were incubated for 24 h at 37°C. Finally, the amount of LDH (lactate dehydrogenase) released in the test medium was compared to the LDH-amount in the control media. Organo-tin polyvinylchloride (PVC; a known cytotoxic material) and Thermanox™ Coverslips (Nunc) were used as a positive and negative control material, respectively. The test showed no cytotoxic effects of the dry film on the cell proliferation.
Surface modification is essential for microfluidic applications. Using O_2-plasma, the static contact angle of water on hard-baked TMMF was reduced from 84° to less than 20°. This type of hydrophilization is easy to implement and enables self-filling of TMMF-based microchannels. On the other hand,

hydrophobic treatment can be used to prevent surface wetting and enables the reliable droplet ejection out of a nozzle. Using a standard ICP system, a 100 nm Teflon-like layer was deposited from gaseous C4F8 (octafluorocyclobutane) on the TMMF surface. Alternatively, TMMF-hydrophobization could be realized by vapor phase deposition of Tridecafluoro-1,1,2,2-tetrahydrooctyltrichlorosilane (ABCR, Germany). With both methods we achieved reproducible surface properties and a contact angle to water of approx. 105°. In contrast, treatment with hexamethyldisilazane (HMDS) and 1H,1H,2H,2H-Perfluorodecyldimethylchlorosilane (ABCR, Germany) did not change the wetting properties of TMMF.
Eventually, the printheads (Fig. 6a) were tested in terms of capillary filling and dispensing of single droplets (Fig. 6b) by using an E-Vision microarrayer [13].

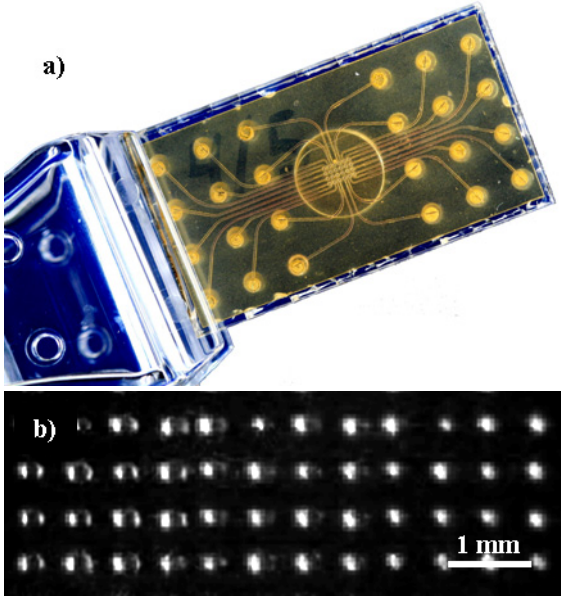

Figure 6: a) A photograph of the PMMA/TMMF printhead; b) Dispensing of single water droplets.

CONCLUSION AND OUTLOOK

The presented combination of standard PMMA machining and TMMF lithography enables the cost-efficient fabrication of high precision structures on large, pre-patterned polymer substrates. The approach targets some of the most challenging issues in the fabrication of polymer BioMEMS. It enables the easy fabrication of multilayer microfluidic systems and their accurate assembly into the chip interface. The approach has been applied for the fabrication of a dispensing device with common microfluidic structures. The main technological challenge will be to provide process repeatability and yield that are sufficient for high-volume production. Beyond that, the future work will concentrate on the characterization of the chemical resistance of TMMF to commonly used sample solutions and the long-term stability of the applied surface treatments.

ACKNOLEDGEMT

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