SOFT-LITHOGRAPHY-BASED HIGH TEMPERATURE MOLDING METHOD TO FABRICATE WHOLE TEFLON MICROFLUIDIC CHIPS

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ABSTRACT

In this work, we present a high-temperature (up to 350 °C) thermal molding method using PDMS master to fabricate microstructures (e.g., high-aspect-ratio and 3D) in Teflon with high resolution and fidelity at down to sub-micron scale. In addition, we demonstrate a convenient strategy for bonding Teflon plates and can easily fabricate whole Teflon microfluidic chips, which are extremely chemical-inert, anti-fouling and biocompatible.

KEYWORDS: soft-lithography, Teflon PFA, PDMS, chemical-resistant microfluidic chip

INTRODUCTION

With its great advantage in fabrication gained from soft-lithography, poly (dimethylsiloxane) (PDMS) has become the most popular material for preparing microfluidic devices. However, its poor chemical compatibility significantly limits its use in organic solvent-contained applications. On the other hand, fabrication of glass devices requires expensive facilities, hazardous chemicals and long processing time, and it is hard to create certain features (e.g., high-aspect-ratio and 3D) in glass. Other plastics have been explored for microfluidic devices, but most of them have similar problems with PDMS when organic solvents are involved. The backbone of PDMS chain has been fluorinated as chemical-inert microchip material, but it is not commercially available and not easy to synthesize. A potential group of materials are commercially available semi-crystallized perfluoropolymers that are optically transparent and extremely chemical-inert. However, microfabrication on them with hot embossing is very difficult mainly because of their high glass transition temperatures.

Here, we present a hot embossing method using special PDMS masters that can withstand high temperature. The PDMS is cured at a mild temperature and, after our optimization, can be used at high temperature up to 350 °C. This high temperature of the PDMS extends the application of soft lithography to almost all thermoplastics; it is also convenient to fabricate high-aspect-ratio and 3D microstructures. The gas permeability of PDMS facilitates replication with high fidelity at down to sub-micron scale; replication of bottom-up structures is also plausible. With this method, we used perfluoroalkoxy (Teflon PFA), a commercially available optically transparent material with similar chemical inertness as polytetrafluoroethylene (Teflon PTFE), as the material for the fabrication of microchips. We optimized the fabrication process of whole Teflon chips, and demonstrated its compatibility with organic solvents that are incompatible with PDMS and other polymers. We also showed anti-fouling property and biocompatibility of the PFA microchannels. Compared with glass, Teflon chips are much cheaper, more convenient to fabricate and mass produce, easier to generate various complex microstructures, and can be recycled for use. The entire fabrication process can be accomplished with a single hotplate or an oven without involving expensive equipment or harsh chemicals.

EXPERIMENTAL

We conducted molding of commercial PFA plates (Yuyisong Inc., China) against PDMS masters on a hot compressor (TM-101F, Taiming Inc., China). We prepared the PDMS masters by spin-coating a thin layer of PDMS (5:1 in weight of prepolymer: cure agent, ~500 μm thick) on SU-8 templates on silicon wafers. After curing at 70 ºC, we peeled off the PDMS membranes and placed them onto glass slides for baking in a 250 ºC oven for 1 h (Fig 1A). We embossed the PFA substrate on the hot compressor at 270 ºC for 2 min (Fig 1B). We placed the PFA substrates between two pieces of 5 mm thick glass plates that are coated with 50 μm thick PDMS, and fixed the entire stack with four clamps. Then we placed the whole stack into a 260 ºC oven (SX2-4-10A, Ruifeng, China) or on a 285 ºC hotplate (Digital plate, USA). After bonding for 1 h, the system was cooled down to room temperature and PFA tubes were connected to the chip for inlets and outlets.

RESULTS AND DISCUSSION

In MEMS and microfluidics, microstructures are conventionally fabricated in photoresists with photolithography and then transferred into the wanted materials. Of all the transferring techniques, soft lithography is a powerful technique that uses PDMS masters to transfer microstructures into PDMS and many other materials (e.g., hydrogels); it can mold microstructure with very high fidelity down to the nanoscale. Because of their relatively high melting temperatures, Teflon plastics require ~250-300 ºC to process their molding. For example, high-fidelity PFA replication needs at least 260 ºC, approximately the melting point of the PFA. However, even at 250 ºC, a PDMS master produced with conventional formula (A:B=10:1 ratio in weight of prepolymer and cure agent) leads to significant bubble generation in the Teflon replica. We varied the PDMS prepolymer ratio to obtain different cured PDMS. When the formula of PDMS was changed to 5:1 and the cured PDMS was further treated at 250 ºC for 1 h, no bubble in the Teflon replica was observed after hot embossing at 270 ºC. Moreover, the cured PDMS generated by the new formula is more rigid, which facilitates the embossing process. We have used the same PDMS mold for more than 30 times without cracking or other failing. When more PDMS prepolymer A is added (A:B=3:1), the formed PDMS masters were easy to crack and fail to transfer microfeatures to Teflon. We

recommend the PDMS prepolymer formula of A:B=5:1 for making PDMS masters in the hot embossing of Teflon. The PDMS masters with this formula can perform well even at 350 ºC; this high temperature is good for embossing most thermoplastics. We also found that thin PDMS master (< 500 μm) generated smoother surfaces in the Teflon replica, probably because thermal expansion of PDMS along the vertical direction is minimized at this thickness.

We carried out several experiments to evaluate the performance of our method. First, we measured the feature heights of a PDMS master and the impression depths of its PFA replica, and found them perfectly matched with each other. Furthermore, we fabricated microscale features on surfaces of Teflon slides. It was convenient to achieve large scale flawless release with our method. The molded channels and other features showed very sharp edges and perpendicular sidewalls (Fig. 2A, B). The pillars in Fig 2C were measured to be 2.5 μm in diameter, with a 4:1 aspect ratio. The PFA mold showed a high fidelity to its PDMS master, both in dimension and in shape (Fig 2D).

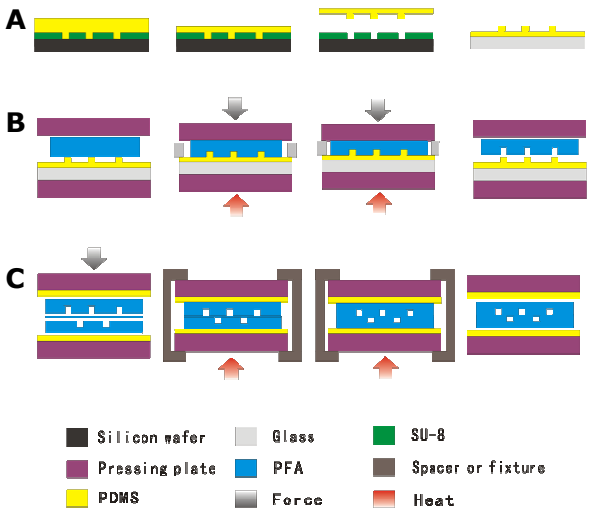

Figure 1: Fabrication process of the Teflon microfluidic chip. (A) Fabrication of the PDMS master. (B) Molding process of the FEP channel. (C) Bonding process of the multilayer PFA chip.

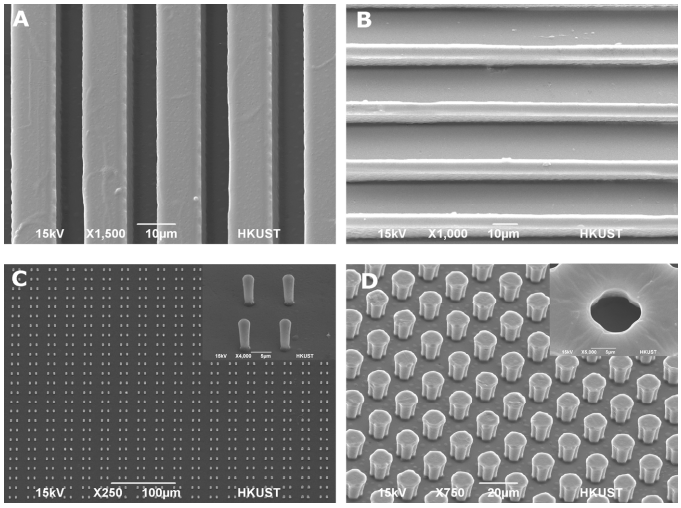

Figure 2: SEM photos of molded Teflon. (A) 25 μm deep channels array.(B) 25 μm high weirs array. (C) 2.5 μm diameter 10 μm high posts array. The inset is a close-up perspective SEM image. (D) 25 μm high "flower" posts. Insert is a SEM image of the PDMS master, after molding.

Our method also showed excellence in 3D molding. Figure 3A shows PFA patterns molded from an initial SU-8 master fabricated using two-step exposure. As the PDMS is flexible, we can even mold "bottom up" structures. Using an over exposed SU-8 master, we successfully fabricated very uniform complicated matrix of 3D PFA structures, which could be considered as a layer of interconnected hollow structures (Fig 3B,C). As the PFA presents an outstanding non-sticking property, the method showed great performance and very delicate microstructures over a large area can be easily achieved (Fig 3D).

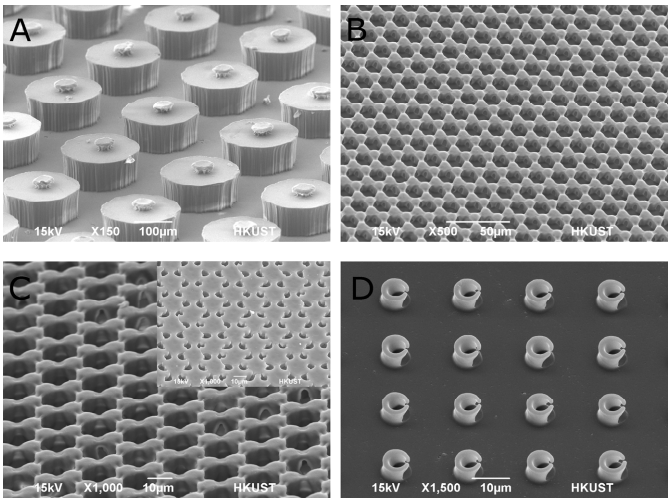

Figure 3: SEM images of 3D molded Teflon. (A) "Poises" generated from a master of overexposed SU-8 posts on 100 μm high SU-8 posts. (B) From overexposed SU-8 triangle post array. (C) Perspective SEM image of B. The inset is its PDMS master after embossing. (D) Hollow microstructures with horizontal arms molded from underexposed SU-8 using an initial master with circle ring patterns.

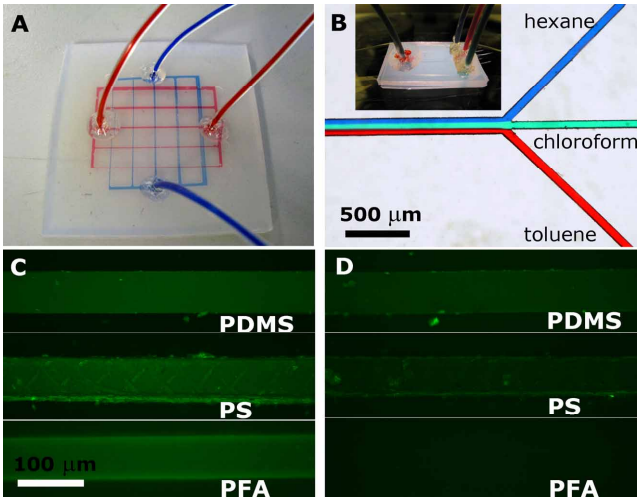

Figure 4: (A) PFA chip with two layer microchannels. (B) Laminar flow of dyed solvents in whole-Teflon multilayer chip. We flow hexane (dyed in blue), toluene (dyed in red) and chloroform (dyed in green) in a PFA channel. (C) Fluorescence images of microchannels filled with 100 μg/mL GFP. (D) Fluorescence images of the channels in figure C after washing with buffer.

We also successfully bonded Teflon chips at 260 ˚C. The bonded whole-FPA channels were tested under pressure as high as 1 MPa pressure without any failing. We found that placing one PFA substrate onto another PFA piece and then heating them without pressure failed to bond them, and applying pressure continuously during thermobonding also failed because the channels collapsed easily. We found that screw clamps are the key to bond the FPA channels successfully. Because PFA has a larger linear expansion factor than the clamps, certain pressure is spontaneously generated during heating from room temperature. In this way, the two PFA pieces are pressed hard to each other at high temperature and the pressure is released when they are bonded, which greatly reduces possible deformation of the microchannels and microstructures on the PFA pieces. The yield of the bonding process was greatly improved to near 100 %. Obviously, both replication with PDMS masters and thermobonding of the Teflon chip are more convenient than the generation of glass or silicon chips.

Compared with other polymeric materials of microfluidics (e.g., PDMS, PMMA and SU-8), PFA presents extreme chemical capability and robustness over a broad range of temperature from -100 °C to 220 °C. In addition, cleaned PFA chips, even with channels in them, can be directly reused for another thermomolding process without leaving any bubble inside. Although it absorbs visible light more than glass or PDMS, its transparency is good for common optical experiments, especially when the thickness of the microchip is less than 2 mm. Fig 5B shows a laminar flow of some organic solvents, which are incompatible with PDMS and many other polymers, in a PFA chip.

Perfluoropolymers are broadly used as non-stick coatings and in superclean process. We carried out an experiment with green fluorescent protein (GFP) to illustrate the anti-fouling property of PFA microchannels: we filled different microchannels with 100 μg/mL GFP that are fabricated in PDMS, PS and PFA, respectively; after 10 min, we rinsed the channels before detection. Significant fluorescence was observed in the PDMS and PS microchannels, indicating severe non-specific adsorption of the protein, while no fluorescent signal was detected from the PFA channel.

Because Teflon plastics are broadly employed as bio-friendly materials, we performed long-term cell-culturing in the PFA microchip. After infusion of cell culture, HepG2 cells quickly settled down and spread out within 1 h. Figure 5B also demonstrates successful embedding of microstructures inside sealed PFA microchannels. The cells grew well in the microchannels, however, the proliferation rates is lower than on an open PFA substrate. The cells tended to grasp the microposts that existed on the 3D channel surface. The cells were cultured in the PFA microchannels for 120 h and less density of cells were found in the channels with 3D channel surfaces.

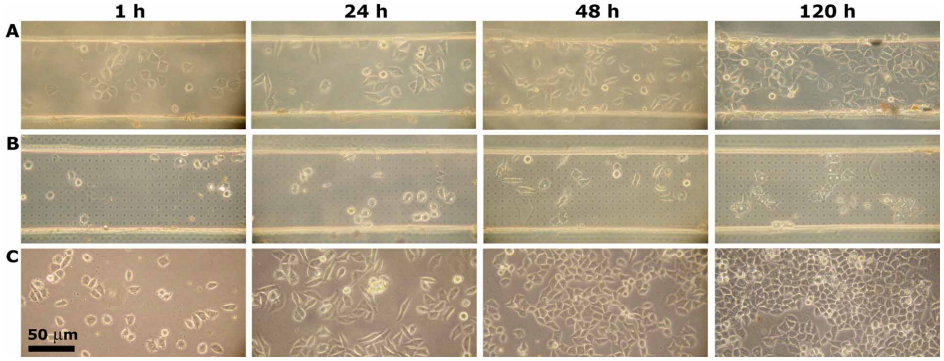

Figure 5: Microphotos of cell culturing experiment on Teflon PFA chips: (A) in 100 μm wide, 100 μm deep and 2 cm long PFA channel. (B) in 100 μm wide, 100 μm deep and 2 cm long PFA channel, with 5 μm diameter, 10 μm high microposts on its bottom surface. (C): on a PFA flat surface open to air.

CONCLUSION

We demonstrate a soft-lithography-based, high-temperature thermomolding and bonding method for fabricating Teflon microfluidic chips with high fidelity, sub-micron resolution, easy mold release and compatibility for fabricating complex microstructures. By combining ease, flexibility and low-cost in fabrication with extreme chemical inertness, super-cleanness and biocompatibility, Teflon chips can be a better alternative to glass chips and will greatly expand the research fields of PDMS microfluidic devices.

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