THREE DIMENSIONALLY-PRINTED (3DP) MICROFLUIDIC DEVICES

O.H. Paydar^{1*}, C.N. Paredes², and R.N. Candler^{2,3}

¹Biomedical Engineering Interdepartmental Program, ²Department of Electrical Engineering,

³California NanoSystems Institute

University of California, Los Angeles, USA

ABSTRACT

This paper introduces the use of three-dimensionally printed (3DP) molds for rapid fabrication of complex and arbitrary microchannel geometries unattainable through existing soft lithography techniques. These molds are printed directly from computer-aided design (CAD) files, making rapid prototyping of microfluidic devices possible in hours. These 3D-printed structures enable precise control of various device geometries, such as the profile of the channel cross-section and variable channel heights in a single device. We report fabrication of complex 3D channels in a polydimethylsiloxane (PDMS) polymer. Device characterization, including surface roughness and resolution, are assessed.

INTRODUCTION

Soft Lithography

Polymer-based microfluidic devices have revolutionized biomedical research and diagnostics due to the many advantages that elastomers have over rigid materials, such as silicon or glass [1-3], with polydimethylsiloxane (PDMS) being the most common elastomer used in microfluidic devices. PDMS is well suited to microfluidics due to its potential for fast prototyping, low cost, and gas-permeability. Additionally, PDMS is optically transparent (240 nm - 1100 nm), nontoxic, electrically insulating, impermeable to liquids, and the PDMS prepolymer conforms to the contours of the master-mold with high fidelity (~10's nm).

Presently, the fabrication of a mold requires silicon wafers with positive surface relief structures [4, 5], typically a photoresist, to shape the PDMS prepolymer. Defining these microstructures requires cleanroom access, microfabrication tools, extensive training, and expensive reagents. Moreover, this method, based on integrated circuit (IC) fabrication processes, is constrained to planar structures. The simplest 3D structures require multiple lithography steps, precise layer alignment, and are typically limited to extrusions of 2-D geometries. Consequently, complex three-dimensional (3D) structures, including vias [6, 7] and multi-tier devices [8], remain a fabrication challenge.

Innovative alternatives to cost-prohibitive microfluidic device fabrication include a high-resolution shrink film device with high aspect ratio (HAR) channels [9] and inkjet-printed devices [10-12]. The shrink film devices suffer from similar design limitations to those made by IC processes, including single channel heights and lack of 3D shape control. The inkjet-printed microfluidic devices provide another inexpensive alternative, but are still limited to planar channels defined on the surface of a glass slide. While these solutions do provide a cost-effective approach to microfluidics, they do not fully address the needs of 3D microfluidics. A three-dimensional fabrication method would allow for the possibility of increased port density and device complexity, improved through-channel (via) formation, and the possibility of more physiologically relevant geometries, such as channels with round cross sections.

Rapid Prototyping— Three Dimensional (3D) Printing

Commercially available rapid prototyping technologies, specifically 3D printing, have been available for nearly a decade. However, recent advances (e.g., biocompatibility, multi-material

printing) and improved resolution enable, for the first time, rapid prototyping of structures that can be used to mold PDMS microchannels with tens of microns resolution and nearly arbitrary topography (e.g., variable channel height and cross section profile). These molds are printed directly from computer-aided design (CAD) files, making rapid prototyping of microfluidic devices possible in hours. Three-dimensional printed structures enable precise control of various device geometries, such as the profile of the channel cross-section and varying channel heights in a single device. Three-dimensional printed microfluidic devices will give researchers unprecedented design flexibility to quickly and inexpensively create more complex channels.

Figure 1. Three-dimensional (3D) printing process using the Objet24 printer. Model (yellow) and support (white) photopolymers are dispensed and immediately UV-cured in 28-micron layers. The gel-like support material is removed with pressurized water, revealing the final device. The resolution limit of this technology is 600x600x900 dpi— capable of ~45 μm line widths. Reprinted with permission from Objet Geometries Ltd.

Similar rapid-prototyping technologies including stereolithography are capable of milli- and micron-scale manufacturing. As a serial writing process, this technology has encountered throughput issues in the past, although recent advances may help overcome this limitation [13].

MATERIALS AND METHODS

Design, Print, and Pour

Microchannel molds are printed directly from computer-aided design (CAD) files (Autodesk Inventor, Autodesk, Inc., San Rafael, CA, USA), making design and rapid prototyping of devices possible in hours. The fully automated printing process simultaneously jets a photocurable polymer and a support material in 28- μm layers (Figure 1). Each layer of the model and support material is immediately UV-cured. Upon completion of the printing process, a high-pressure water jet exposes the final device design by dissolving the gel-like support material. The 3D printed device becomes the replica mold master and replaces time consuming, expensive microfabrication (Figure 2).

Figure 2. Conventional and 3D printed mold fabrication processes. (a) Conventional master-mold fabrication requires cleanroom access, and multi-layer devices require several iterations of photolithography. (b) For 3D printed molds, a CAD file is directly exported to the 3D printer for mold fabrication.

A base-to-catalyst mixture (9.1% w/w) of silicone elastomer (Sylgard 184, Dow Corning, Midland, MI, USA) was poured onto the master, desiccated, and cured at 75°C. The device was removed from the mold and access holes were punched into the device to define the inlet(s) and outlet(s). To complete the process, the device was treated with O₂ plasma and bonded to a glass substrate.

Characterization—Surface Roughness

Because PDMS conforms to the contours of the mold with high fidelity, it was imperative to characterize the surface topology. Limitations of printer resolution due to droplet size or droplet spreading during curing can lead to leakage or lack of faithful reproduction of design features. To investigate these limitations, surface roughness of 3D printed samples (2.5-mm²) was quantified and compared to surface roughness measurements of conventional replica-mold materials, silicon and photoresist (SU-8). The printer provides two options for surface finish, glossy and matte, both of which were characterized.

The surface roughness measurements were taken with an optical profiler (Wyko NT3300, Veeco, Fullerton, CA, USA). Vertical scanning interferometry (VSI) resolves the surface topography by detecting the interference between emitted light and the reflected beam. Because of poor reflectivity, the 3D printed samples were sputter coated with a 100-Angstrom layer of chromium/gold. The average of the absolute value of deviation from the mean surface height is used as a measure of the surface roughness, R_a .

Design of Microfluidic Devices

The 3D printing process was used to fabricate three types of devices molds—gradient generators, size-exclusion filters, and double helices. The molds were used to fabricate PDMS devices to demonstrate the ability to fabricate functional devices with control of 3D geometry, as discussed in the following section.

RESULTS AND DISCUSSION

Three-dimensionally printed devices, regardless of finish, have predictably rougher surface topology than traditional microfluidic molds (Figure 3). Because microfluidic channels are molded from photoresist relief structures, we compared the roughness of the SU-8 sample with the 3D printed material. The

surface roughness of both matte and glossy samples were an order of magnitude larger than conventional microfabricated templates.

Figure 3. Vertical scanning interferometry (VSI) of microfluidic master materials. The glossy (a) and matte (b) 3D printed surface roughness, R_a , is an order of magnitude larger than the channel-defining SU-8 feature (c). Silicon (d) is also represented. All dimensions are given in nanometers.

Fortunately, the periodic minima and maxima (figure 3a)—a consequence of the jetting process—that define the surface topology do not affect the ability of the device to bond to glass, likely due to the low elastic modulus of PDMS.

Characterization of 3D-Printed Devices

Characterization of a replica-molded, 3D-printed gradient generator designed with 150-μm-wide square channels highlighted important design considerations. A scanning electron microscope (SEM) image of the gradient generator outlet (Figure 4) clearly illustrates enlarged channels. As can be seen, spreading occurred during the 3D printing process, leading to a 133% increase in channel diameter. To avoid channels reflowing into one another, the CAD was modified to account for the droplet spread and the separation between channels was increased.

Figure 4. Scanning electron micrograph (SEM) at the outlet of a 3D-printed mold of the gradient generator. Channels designed to be 150- μm -wide have spread to 350 micrometers. This 133% increase was a result of the photocurable polymer spreading prior to the UV cure. Arrows represent the direction of fluid flow after the PDMS was cast and the device was completed.

After removing the PDMS from the 3D printed master and attaching connectors to the inlets and outlet of the device, the three input streams were filled with red, yellow, and blue dyes. Flow rates below 100 $\mu\text{L}/\text{min}$ generated a gradient at the device outlet, but because laminar flow dominates in this regime, larger flow rates resulted in the same three-color streams at the outlet.

Figure 5. Three-dimensional printed (3DP) gradient generator. The device was designed with 150 μm -wide channels. Inset shows the color gradient generated between the red, yellow, and blue input streams.

Unlike conventional microfluidic device fabrication, the manufacturing of 3D printed master-molds for multi-tier devices is no more difficult than the fabrication of simple 2D geometries.

A relatively simple multi-level structure, which would require four separate exposures and precise alignment with conventional

microfabrication was designed and printed in less than one hour. This step-structure (Figure 6) was designed with an initial 400- μm -tall inlet and each successive step reduces the channel height by 150 μm . This type of device is representative of size-exclusion filters where changes in the channel height can funnel different sized particles into separate collection reservoirs.

The ability to design arbitrary channel heights could open up new design spaces for microfluidic devices, such as size-based particle filters or biomimetic channels that reproduce the exact shape of blood vessels.

Figure 6. (a) Computer-aided design (CAD) schematic of multi-tier device (i.e. size-exclusion filter). Steps were integrated into the design and printed. Each step is 150 μm shorter than the previous. (b) The molded PDMS device with three different channel heights ranging from 100 to 400 μm .

Figure 7 shows the full capability of the 3D printing technique, where double helices have been fabricated in PDMS. Each strand of the double helix structure was designed in CAD as a 1-mm diameter circular channel with a 5-mm pitch (Figure 7a). The strands were anchored onto the same base and their inner surfaces were separated by 2 millimeters. The PDMS prepolymer was cast around the device shaping the helical channels. The mold was removed following the curing process. Removal of the mold was not difficult because the mold material was observed to impede full curing of the PDMS. The PDMS would fully cure after contact with the mold was removed. For illustration purposes, a single channel was filled with dye (Figure 7b). The channels were then filled with different colored dyes to emphasize the ability to create over- and underpasses (Figure 7c).

Of particular importance, the channels were fully defined in the PDMS polymer. This technique allows the user to bypass O_2 plasma treatment and avoid bonding the device to glass, which further simplifies the device manufacturing process. It also allows for the channel to be fabricated from the same material, as opposed to bonding PDMS onto a substrate. However, without oxygen plasma treatment, the untreated PDMS remains hydrophobic (109°) and obstructs flow. To overcome this potential challenge the device can be submerged in 1 M NaOH for 24 hours. The resulting surface treatment is more stable than radio-frequency plasma or corona discharge and relieves the flow obstruction of native PDMS [14].

The Advantage over 2D Fabrication Technology

Three-dimensional printing facilitates increased microchannel complexity and simplifies fabrication at a low cost (< \$1/mol of material costs). In addition to the technical advantages, this economical alternative can help accelerate research progress by increasing access to a once-limited field.

Figure 7. Truly 3D microchannels developed from 3D printed molds. (a) PDMS surrounding the mold. Each strand of the double helix was designed to have a 1 mm diameter and a 5 mm pitch. (b) A single channel filled with colored water. (c) Both channels filled with solutions, emphasizing the ability to create over- and underpasses.

CONCLUSION

Microfluidic structures fabricated through traditional soft lithography processes are limited to rectangular extrusions of high-resolution 2D structures. While 3D printed structures do not currently possess the resolution of photolithographically defined structures, they do enable enhanced control of device geometries, such as the profile of the channel cross-section and varying channel heights in a single device. Because of this design flexibility, 3D printed microfluidic technology will give researchers the ability to quickly and inexpensively create channels with unprecedented shape and complexity.

FUTURE WORK

Future efforts will focus on the creation of high-density embedded channel networks. The process requires selectively dissolving the 3D printed material without damaging the surrounding PDMS structure. Also, we will continue investigating resolution limits of the 3D-printed mold technology and methods to improve this resolution.

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CONTACT

*O.H. Paydar, tel: +1-317-332-3302; omeed.paydar@ucla.edu