

FABRICATION OF MULTILUMEN MICROFLUIDIC TUBING FOR *EX SITU* DIRECT LASER WRITING

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ABSTRACT

Among the numerous additive manufacturing or “three-dimensional (3D) printing” techniques, two-photon Direct Laser Writing (DLW) is distinctively suited for applications that demand high geometric versatility with micron-to-submicron-scale feature resolutions. Recently, “*ex situ* DLW (*esDLW*)” has emerged as a powerful approach for printing 3D microfluidic structures directly atop meso/macroscale fluidic tubing that can be manipulated by hand; however, difficulties in creating custom *esDLW*-compatible multilumen tubing at such scales has hindered progress. To address this impediment, here we introduce a novel methodology for fabricating submillimeter multilumen tubing for *esDLW* 3D printing. Preliminary fabrication results demonstrate the utility of the presented strategy for resolving 743 μm -in-diameter tubing with three lumens—each with an inner diameter (ID) of 80 μm . Experimental results not only revealed independent flow of discrete fluorescently labelled fluids through each of the three lumens, but also effective *esDLW*-printing of a demonstrative 3D “MEMS” microstructure atop the tubing. These results suggest that the presented approach could offer a promising pathway to enable geometrically sophisticated microfluidic systems to be 3D printed with input and/or output ports fully sealed to multiple, distinct lumens of fluidic tubing for emerging applications in fields ranging from drug delivery and medical diagnostics to soft surgical robotics.

KEYWORDS

Direct Laser Writing, Additive Manufacturing, Two-Photon Polymerization, 3D Printing, Multilumen Tubing

INTRODUCTION

Additive manufacturing technologies have gained increasing interest in the microelectromechanical (MEMS) and microsystems communities as a route to overcome the geometric restrictions of conventional microfabrication methods (*e.g.*, photolithography, soft lithography) [1-3]. In particular, DLW—a two-photon polymerization (2PP)-based 3D manufacturing technique in which a femtosecond laser is used to selectively crosslink photoresists in a point-by-point and/or layer-by-layer fashion—allows for geometrically complex microstructures to be fabricated with feature resolutions down to the 100 nm range [4-6]. For microfluidic applications, however, one challenge of DLW is that the high feature resolutions are inherently ill suited for printing the macro-to-micro fluidic interfaces (*i.e.*, fluidic access ports) that are critical to fluidic loading,

retrieval, and control processes [7-9]. One pathway to overcome this issue is by means of “*esDLW*”.

Building on the works of previous investigators in optics and photonics fields in which DLW was used to print 3D optical elements (*e.g.*, lenses and micromirrors) directly onto optical fibers and photonic components [10, 11], researchers have developed microfluidic analogues of these approaches in the form of *esDLW* protocols that involve DLW-printing microfluidic entities directly onto (and fluidically sealed to) meso/macroscale fluidic components and systems [12-18]. At present, researchers have devised and harnessed *esDLW* strategies to 3D print a wide array of geometrically complex microfluidic components onto fluidic tubing for applications including soft microrobotics [13-15], drug delivery *via* hollow microneedle arrays [16], and biochemical delivery and sampling [17]. The utility of such *esDLW* approaches, however, remains limited by the challenges in fabricating custom, multilumen fluidic tubing at submillimeter length scales—challenges that have contributed to the vast majority of these previous efforts being based on the use on single-lumen fluidic tubing or capillaries [12-17]. Thus, new approaches for manufacturing *esDLW*-compatible, submillimeter-scale multilumen fluidic tubing are in critical demand.

CONCEPT

In this work, we present a novel multilumen tubing fabrication strategy that involves five key steps. First, a straight microchannel is molded from a Fused Filament Fabrication (FFF) filament using the silicone elastomer, polydimethylsiloxane (PDMS), such that the ID of the channel will correspond to the outer diameter (OD) of the multilumen tubing (**Fig. 1a, b**). Second, alignment components—manufactured *via* “liquid crystal display (LCD)” 3D printing—are placed at the inlet and outlet of the PDMS microchannel as a means to control the position of the internal channels of the tubing (**Fig. 1c**). Next, fused silica capillaries are threaded through the alignment components and PDMS channel (**Fig. 1c**). The channel is then filled with a liquid-phased photomaterial (**Fig. 1d**). Lastly, the system is exposed to UV light to polymerize the photomaterial and the tubing is extracted from the mold and the alignment components (**Fig. 1e**). Thereafter, the multilumen tubing can be used as desired, such as for *esDLW* strategies in which 3D microfluidic structures—for example, a “MEMS” structure with distinct embedded microchannels (**Fig. 1f**)—are printed atop the tubing with distinct ports interfaced to corresponding lumens.

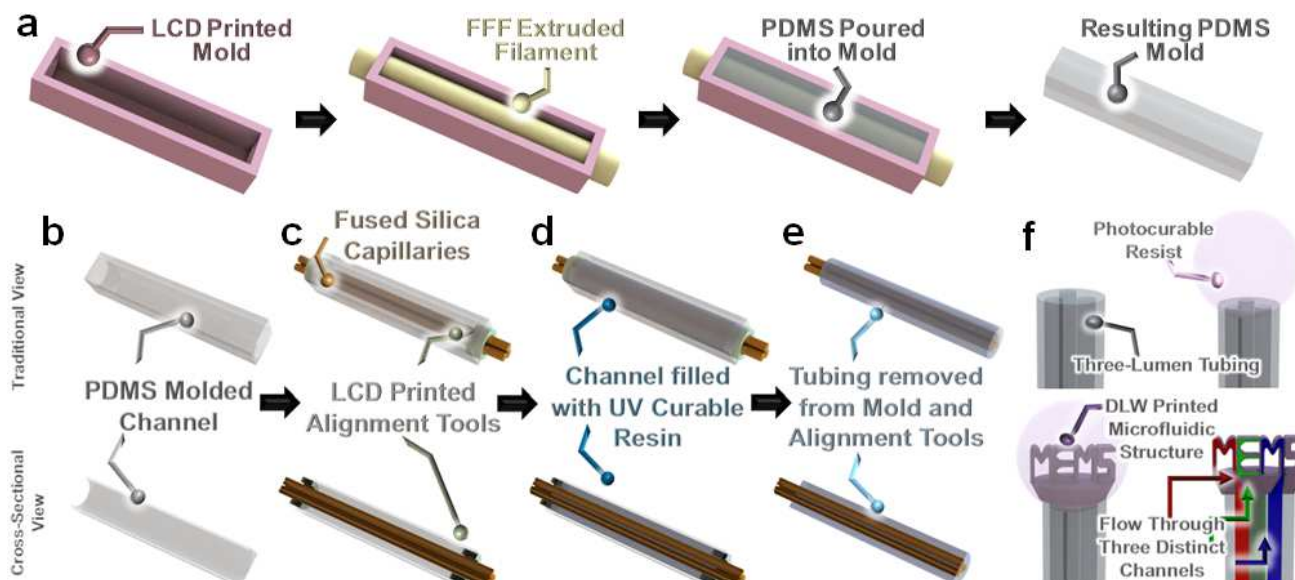


Figure 1: Conceptual illustrations of the multilumen tubing fabrication strategy and the esDLW printing process. (a) A “Liquid crystal display (LCD)” 3D printed mold is filled with PDMS after placement of a fused filament fabrication (FFF) extruded filament to maintain the shape of the inner channel during curing. (b) The resulting PDMS channel is used to control the dimensions of the multilumen tubing. (c) Fused silica capillaries are threaded through the PDMS channel, and each end is plugged with an LCD 3D printed alignment component to secure the capillaries in place. (d) The channel is filled with photocurable resin. (e) Following exposure to UV light, the tubing is extracted from the mold and alignment components. (f) The esDLW process for 3D microprinting a “MEMS”-inspired microfluidic structure directly atop the multilumen tubing such that each letter’s microchannel input is sealed to a distinct, corresponding lumen.

MATERIALS AND METHODS

PDMS Mold

The exterior mold for the PDMS microchannel was fabricated using an LCD 3D printer (Mars 3 4K, ELEGOO, Shenzhen, China) and a flexible resin (F80 Elastic Resin, Resione, Dongguan Gosaid Technology Co, China). An FFF 3D printing apparatus comprising a v6 HotEnd and extruder (Titan Universal Extruder, E3D, UK) was used to extrude custom diameter filaments from a thermoplastic polyurethane (Giantarm, ShenZhen Getech Technology, China) such that the OD of the filament corresponds to the ID of the PDMS microchannel and, in turn, the resulting OD of the final multilumen tubing. Extrusion parameters such as temperature and speed were controlled in real-time *via* the software, Pronterface. The filament was threaded through corresponding holes of the LCD-printed mold. PDMS (Sylgard 184 Elastomer, DOW Corning, NY, USA) was mixed at a 10:1 base-to-curing ratio, degassed in a vacuum, poured over the filament into the mold, and then cured on a hot plate at 75 °C for 6 hours. After curing, the PDMS mold was removed, and the thermoplastic filament was extracted, resulting in a PDMS mold with an internal microfluidic channel.

Alignment Components

To control the location of the fused silica capillaries, an LCD 3D printer was used to manufacture hollow tubes from photocurable resin (Microfluidic Resin, CADWorks, ON, Canada). These alignment components were designed using the computer-aided design (CAD) software, SolidWorks (Dassault Systèmes, France), such that: (i) their OD was slightly larger than the ID of the PDMS channel, and (ii) their ID allowed for three fused silica capillaries to be held tightly together in the center of the

PDMS channel. Specifically, the OD of each alignment component was designed to be 1 mm, and the single channel ID was 450 μm . The CAD files were exported at STL file and then imported in slicing software (CHITUBOX, Shenzhen, China) to prepare for 3D printing.

Multilumen Tubing Fabrication

To manufacture the multilumen tubing, three fused silica capillaries were threaded through an alignment component and the PDMS channel. A second alignment component was positioned at the opposite end of the PDMS channel such that each end of the mold had an alignment component centering the three fused silica capillaries (Molex LLC, Lisle, IL) inside the channel. The photocurable resin, 3D Rapid Tuff (Monocure 3D, Sydney, Australia), was used to encapsulate the fused silica capillaries. To reduce dust and particulates in the tubing during printing, the resin was first centrifuged for 10 min at 3,000 rpm, after which the supernatant was removed and stored in a UV-blocking conical until use. A 5 mL syringe was loaded with the cleaned resin and used to fill the interior of the PDMS channel. A UV pen at a wavelength of 405 nm was used to photocure the resin around the capillaries. After the entire length of the channel had been fully cured, the multilumen tubing was manually extracted from the PDMS mold and the alignment components were removed from both ends of the tubing.

3D Microprinting *via* esDLW

A 3D model of a “MEMS”-inspired structure with three distinct embedded microchannels was designed using SolidWorks, exported as an STL file, and then then imported into the computer-aided manufacturing (CAM)



Figure 2: Photographs captured during the multilumen tubing fabrication process. (a) PDMS mold. (b) PDMS mold following placement of the alignment components and three fused silica capillaries. (c) PDMS channel filled with photocurable resin. (d) UV exposure. (e) The extracted multilumen tubing. Scale bar = 4 mm.

software, DeScribe (Nanoscribe GmbH, Karlsruhe, Germany), to prepare files for printing. Before printing atop the tubing, flow through each channel was confirmed by pushing DI water through each capillary independently. The multilumen tubing was mounted into a custom-made holder and the print surface was cleaned by rinsing in propylene glycol methyl ether (PGMEA) followed by two successive rinses with isopropyl alcohol (IPA) and the dried with compressed N₂ gas before the photocurable resist, IP-Q (Nanoscribe), was deposited atop the tubing.

The tubing and holder were then loaded into the Nanoscribe Photonic Professional GT2 DLW system. To ensure a seal between the surface of the multilumen tubing and the “MEMS” microstructure, the interface of the tubing was found manually, and the print was started roughly 50 μm below the surface of the tubing. Following *esDLW* printing, the tubing and holder were removed from the printer, and the structure was developed by soaking and backfilling each capillary with PGMEA for 2 hours and then IPA for 2 hours before being air dried overnight.

Optical Characterization

A scanning electron microscope (TM4000 Tabletop SEM, Hitachi, Tokyo, Japan) was used to measure cross-sectional slices of the multilumen tubing and image the resulting 3D “MEMS” *esDLW*-printed microstructure. To demonstrate independent flow through each distinct input channel, Methylene Blue, Rhodamine B, and Green Fluorescent Microparticles were each loaded into a separate flow channel and a fluorescent microscope (Axio Observer.Z1, Zeiss, Germany) connected to a charge-coupled device (AxioCam 503 Mono, Zeiss) was used to image the fluids in their corresponding lumens.

RESULTS

Multilumen Tubing Fabrication and Discrete Lumen Microfluidic Characterization

Images captured during the multilumen tubing fabrication process are presented in **Figure 2**. SEM imaging revealed the tubing OD to be roughly 750 μm with IDs of each lumen to be smaller than 70 μm (**Fig. 3a, b**). Notably, the OD of the tubing is determined by the OD of

the initial filament used for molding the microchannel, so the specific dimensions of the tubing can be modified as desired. To evaluate the fluidic independence of the lumens, we performed microfluidic experiments in which distinct fluorescently labelled fluids were loaded into each lumen. Results from fluorescence micrographs did not reveal any indications of crosstalk or undesired leaked among the discrete lumens (**Fig. 3c–f**), suggesting sufficient encapsulation of the fused silica capillaries and, in turn, the effective production of three-lumen tubing.

esDLW 3D Printing Compatibility

Because a core motivation of the presented work is for the multilumen tubing to support *esDLW* printing protocols, we performed an initial study of this capability by DLW-printing a 3D “MEMS”-inspired microstructure onto the fabricated three-lumen tubing. Sequential CAM simulations and fabrication results of the point-by-point, layer-by-layer *esDLW* printing process are presented in **Figure 4a** and **b**, respectively. The total print for this structure was under 25 min. SEM micrographs of the fabricated “MEMS” structure atop the multilumen tubing provide preliminary evidence of effective adhesion of the print to the top surface of the multilumen tubing (**Fig. 4c**). Future work is still needed, however, to not only assess the burst pressure dynamics for the print-to-tubing interface, but also evaluate the ability to load distinct fluids into the corresponding distinct embedded channels of the structure.

CONCLUSION

This work presents a proof-of-concept demonstration of a novel strategy for fabricating custom multilumen tubing to, for example, serve as the substrate for *esDLW*-based microfluidic components and systems. Here, we fabricated 750 μm -in-diameter tubing comprising three discrete lumens; however, it should be noted that the tubing dimensions and the number of lumens can be readily modified to meet application-specific requirements. Nonetheless, these results represent an important first step toward realizing increasingly sophisticated microfluidic components that necessitate multiple, discrete channels for emerging microfluidic and micropneumatic applications.

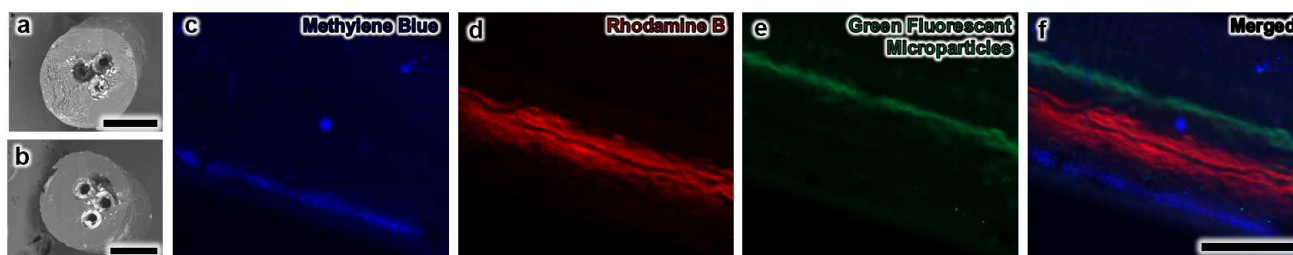


Figure 3: Multilumen tubing fabrication results. (a, b) SEM micrographs of tubing cross sections. Scale bar = 400 μm . (c–f) Fluorescence micrographs of distinct fluorescence signatures. Scale bar = 250 μm .

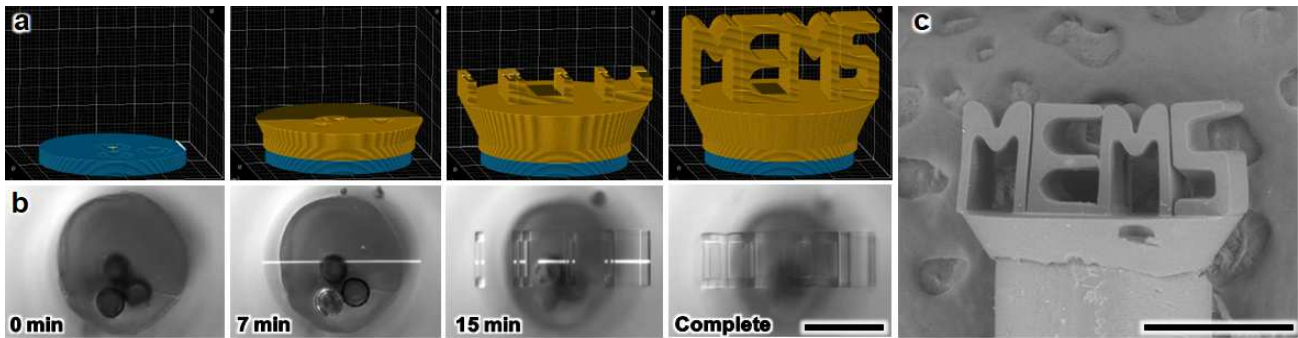


Figure 4: Fabrication results for esDLW-printing a “MEMS”-inspired microstructure atop the multilumen tubing. (a, b) Sequential (a) simulations and (b) corresponding micrographs of the esDLW-printing process. (c) SEM micrograph of fully developed microstructure. Scale bars = 500 μm .

ACKNOWLEDGMENTS

The authors greatly appreciate the contributions of Terrapin Works technical staff and members of the Bioinspired Advanced Manufacturing (BAM) Laboratory at the University of Maryland, College Park. This work was supported in part by U.S. National Institutes of Health Award Number 1R01EB033354, U.S. National Science Foundation Award Number 1943356, and the National Science Foundation Graduate Research Fellowship Program under Grant No. DGE 2236417. Any opinions, findings, and conclusions or recommendations expressed in this material are those of the authors and do not necessarily reflect the views of the National Science Foundation.

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