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High-Throughput Three-Dimensional (3D) Lithographic Microfabrication in Biomedical Applications

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ABSTRACT

Two-photon excitation microfabrication has been shown to be useful in the field of photonics and biomedicine. It generates 3D microstructures and provides sub-diffraction fabrication resolution. Nevertheless, laser direct writing, the most popular two-photon fabrication technique, has slow fabrication speed, and its applications are limited to prototyping. In this proceeding, we propose high-throughput 3D lithographic microfabrication system based on depth-resolved wide-field illumination and build several 3D microstructures with SU-8. Through these fabrications, 3D lithographic microfabrication has scalable function and high-throughput capability. It also has the potential for fabricating 3D microstructure in biomedical applications, such as intertwining channels in 3D microfluidic devices for biomedical analysis and 3D cell patterning in the tissue scaffolds.

Keywords: Two-photon absorption, lithography, SU-8, 3D fabrication

1. INTRODUCTION

Three-dimensional (3D) microfabrication techniques have been used extensively for prototype making. One popular method is two-photon excitation (TPE) microfabrication. The technology of TPE microfabrication [1-3] has been under development for over twenty years. Importantly, this microfabrication technique can utilize a variety of photo-interactions to alter material properties in 3D. TPE microfabrication has found a broad range of applications in the fields such as 3D optical storage [4, 5], tissue scaffold [6, 7], photonic crystal structure [8, 9], and microfluidic devices [10, 11]. One of the limits of TPE microfabrication is its low throughput. TPE typically achieves 3D resolution by focusing ultrafast optical pulses to a diffraction-limited focus using a high numerical aperture (NA) lens. The nonlinear dependence of material responses to the excitation power distribution provides the depth discrimination. Since this fabrication processing is carried out on a point-by-point basis, known as laser direct writing, the throughput of fabrication is ultimately limited by the sequential nature of this method and the mechanical limit of the scanner. Although TPE microfabrication provides very attractive submicron lateral resolution and 3D optical sectioning, the use of the TPE approach is limited to laboratory investigations and prototype fabrication. Therefore, there is a need to improve the throughput of TPE microfabrication to enable commercial mass-production. We introduce 3D lithographic microfabrication technique based on depth-resolved wide-field illumination (DRWFI) [12, 13]. It has found a number of applications in the nonlinear microscopy [14-17] and is also important for 3D microfabrication field since imaging and lithography has duality. During imaging, the sample is located at the object plane of the objective, and image is formed at image-conjugate plane. If the photomask is located at image-conjugate plane, the image of the photomask will be projected on the specimen, which is located in the objective plane of the objective.

In this proceeding, 3D-resolved lithographic microfabrication system is implemented, and its capabilities are demonstrated in terms of 3D microstructures built with SU-8 photopolymer. The potential for biomedical applications such as microfluidics and tissue engineering is also discussed.

2. 3D LITHOGRAPHIC MICROFABRICATION

The schematic diagram of 3D lithographic microfabrication is shown in figure 1. Femtosecond pulsed laser is incident on reflective diffraction grating surface. It disperses light at different angles, depending on corresponding wavelength since optical pulse consists of a packet of wavelengths in spectral domain. After demagnifying lens pair, the optical

pulse is restored where the image conjugate plane for specimen is located. By inserting optical mask, the image gets projected at the focal plane of the objective and the optical pulse is restored. Therefore, maximum photon flux occurs only at the focal plane with patterns formed by the optical mask and 2D microstructure is fabricated only at given depth. Photon flux rapidly decreases far from the focal plane, and this results in generating optical sectioning capability. By moving the objective in axial direction and changing optical mask, another 2D microstructure at different depth, and 3D microstructure are built by stacking up a series of 2D microstructures.

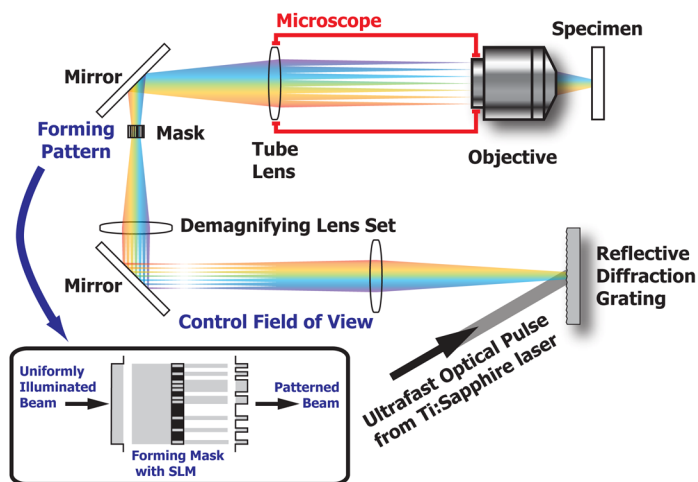


Figure 1. Schematic diagram of 3D lithographic microfabrication system

3. MICROSTRUCTURES WITH SU-8 PHOTOPOLYMER

In this section, several types of 3D microstructures are demonstrated in order to show its scale and high-throughput capability for 3D lithographic microfabrication. SU-8 was chosen as the photopolymer, since its polymerization is working very well with TPE [18]. Cover glass was used as a SU-8 substrate instead of silicon wafer commonly used in order to avoid back reflection on its surface. Since cover glass and SU-8 do not have strong adhesion, 2 μm thick SU-8 layer was first cured on the cover glass. Then, we coated SU-8 thick enough to make the microstructures. All the processes except for the lithography are standard ones. For the lithography process, we used our own 3D lithographic microfabrication system. Figure 2 describes the protocol for SU-8 sample preparation in detail. For SU-8 microfabrication, Titanium Sapphire pulsed laser was used to facilitate two-photon excitation (pulse width is ~ 100 fs and pulse repetition rate is 80 MHz).

First, 2.5D microstructures were made with MIT logos. As seen in figure 3, roughly 1:5 high-aspect-ratio was achieved. Second, 3D structures similar to photonic crystal was generated by stacking up log piles in figure 4(a). In addition, the square with hole pattern was used as an optical mask, and overhanging structure was fabricated by overlapping two 3D structures in different depths. These 3D structure demonstrate that our microfabrication technique has 3D fabrication capability. To show the scalability, we made different scale structures with same photomask by using different magnification objectives. Although the optical resolution was sacrificed since lower magnification objective has lower NA, the structures were clearly scalable, as shown in figure 5. Lastly, we fabricated large area structure to demonstrate high-throughput capability by using fabrication mosaic. The size of each pattern is about 50 μm, and the total dimension is about 1 mm length by 1 mm width by 10 μm height. The fabrication time for these structures is relatively short, compared with laser direct writing method. Currently, fabrication time is limited by pulse peak power; the use of regenerative amplifier may enable high-throughput mass production.

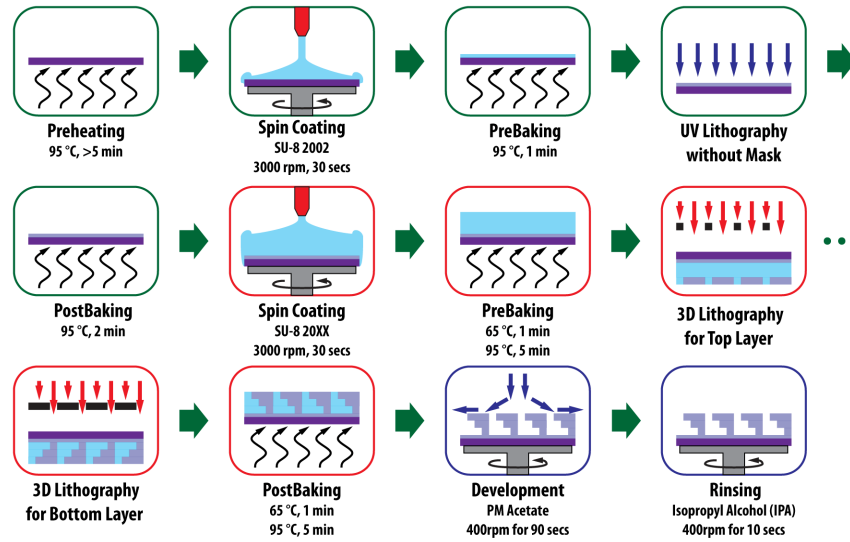


Figure 2. Pictorial description of SU-8 Sample preparation process. Standard protocol for SU-8 was used except for lithography process. To improve the adhesion between cover glass and SU-8, 2 μm thick SU-8 layer was attached on cover glass surface before coating thick layers.

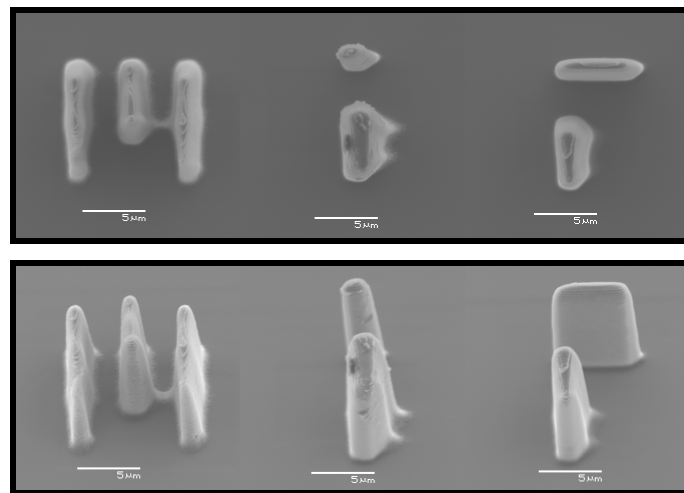


Figure 3. 2.5D structure for MIT logo: top view (top) and isometric view (bottom). The thickness of the SU-8 coating was 15 μm and 2D structures are stacked up with the step size of 500 nm. 40X objective with 1.3 NA oil immersion was used. Energy dose per layer was 94.3 $\mu\text{J}/\mu\text{m}^2$

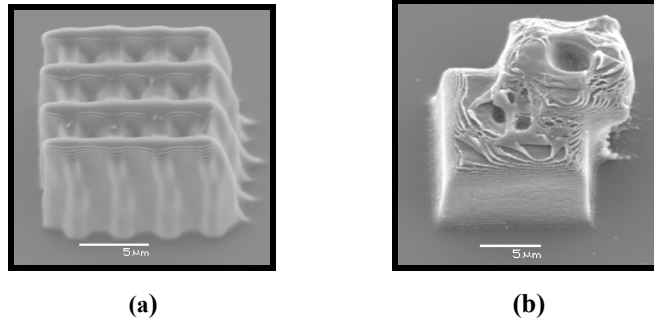


Figure 4. (a) 3D photonic crystal structure and (b) high-aspect-ratio structures. The thickness of the SU-8 coating was (a) 15 μm and (b) 10 μm . 2D structures are stacked up with the step size of (a) 500 nm and (b) 200 nm. 40X objective with 1.3 NA oil immersion was used. Energy dose per layer was (a) 188.7 $\mu\text{J}/\mu\text{m}^2$ and (b) 11.8 $\mu\text{J}/\mu\text{m}^2$

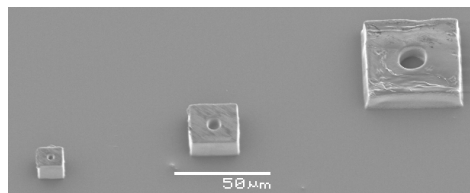


Figure 5. Different scale structures with various objectives. Note that same optical mask was used for all the structure fabrication. Different objectives were used: from left to right, 40X (1.3NA, oil immersion), 20X (0.75NA, air), and 10X (0.5NA, air). The thickness of the SU-8 coating was 15 μm and 2D structures are stacked up with the step size of 500 nm. Energy dose per layer was 188.7 $\mu\text{J}/\mu\text{m}^2$

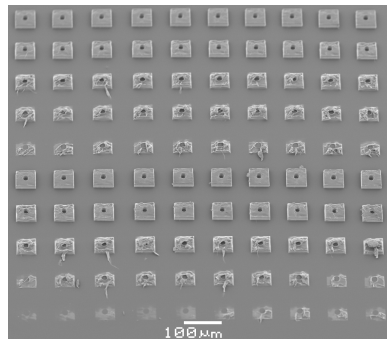


Figure 6. 1 mm by 1 mm large scale structures with translating sample stage (Stitching). The thickness of the SU-8 coating was 10 μm and 2D structures are stacked up with the step size of 500 nm. 10X objective with 0.5 NA air was used. The structures in same row are identical. Each row has different exposure time, or energy dose: from top to bottom, 188.7 $\mu\text{J}/\mu\text{m}^2$, 94.3 $\mu\text{J}/\mu\text{m}^2$, 37.7 $\mu\text{J}/\mu\text{m}^2$, 18.9 $\mu\text{J}/\mu\text{m}^2$, and 9.4 $\mu\text{J}/\mu\text{m}^2$

4. SUMMARY

In summary, we introduced and implemented 3D lithographic microfabrication system based on temporal focusing concept. With our 3D microfabrication technique, depth-resolving fabrication, high-aspect-ratio structure, scalable capability, high-throughput production were demonstrated. Assuming that 3D lithographic microfabrication is possible, we expect many high-throughput applications in the biomedical field since one of its advantages is scalability. Microfluidic device has been very popular and has the potential to deliver very complex biomedical analysis. However, 3D microfluidic device fabrication is currently confined to laboratory setting since there are very few methods for mass

production. Another potential application is cell patterning in tissue scaffold, which is mostly done in 2D. Therefore, 3D lithographic microfabrication has mass production potential for many biomedical applications.

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