Embellishment of microfluidic devices *via* femtosecond laser micronanofabrication for chip functionalization†

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This paper demonstrates the embellishment of existing microfluidic devices with integrated three dimensional (3D) micronanostructures *via* femtosecond laser micronanofabrication, which, for the first time, proves two-photon photopolymerization (TPP) to be a powerful technology for chip functionalization. As representative examples, microsieves with various pore shape and adjustable pore size were successfully fabricated inside a conventional glass-based microfluidic channel prepared by wet etching for microparticle separation. Moreover, a fish scale like microfilter was also fabricated and appointed as a one-way valve, which showed excellent performance as we expected. These results indicate that such embellishment of microfluidic devices is simple, low cost, flexible and easy to access. We believe that, combined with TPP, the application of lab-on-chip devices would be further extended.

Introduction

In the past two decades, microfluidic systems have been intensively investigated due to their broad applications in chemistry, physics, biology and medicine. Comparing with macroscopic settings, microfluidic devices have a series of distinct advantages, such as low materials consumption, simplicity, high safety, high sensitivity, high throughput and high integrity,[1–9] which strongly stimulate the development of new techniques for the fabrication of microfluidic devices. For example, ultraviolet (UV),[10] e-beam,[11] X-ray lithographies,[12] softlithography,[13,14] and nanoimprint[15] methodologies were successfully used to create planar microfluidic channels. In order to further improve the applications of microfluidic chips, efforts were also devoted to fabrications of three-dimensional (3D) structured chips. Through multi-exposure photolithography and soft lithography, 3D microfluidic devices were manufactured and assigned as advective micromixer,[16] immunoassay,[17] and neuron culture platforms.[18] By utilizing replica remolding, complex microfluidic channels were also developed for the use of valves or pumps,[9] the study of cell–cell interactions,[19] computing,[20] and DNA manipulation.[21] Besides, fabrication routes such as X-ray ablation, layer-by-layer printing were also used for 3D microstructure prototyping.[22] Recently, a novel self-folding route was reported for fabrication of real 3D microstructures from precreated 2D micropatterns.[23–25] Using self-assembly, 2D cruciform structures with porosity could be transformed into 3D microcontainers with porous walls,[26,27] which shows great potential for cell encapsulation and separation towards microfluidic appliations.[28] All of these efforts have greatly advanced the developments of functional microfluidic devices. However, up to now, it is still difficult to make refined microfluidic chips with complex 3D topological structures in a designable, flexible, and controllable fashion. Moreover, it is still lacking in nanotechnology for local mending, modification, functionalization and integration of existing microfluidic devices for special applications.

Femtosecond laser direct writing by two-photon photopolymerization (TPP) of resins, due to its powerful capability in 3D fabrication and high spatial resolution, would be a promising solution to this gap.[29–35] Previously, for the first time, we reported that TPP prototyping of nanoshells by using negative tone resin SU-8, shows great potential for fabrication of 3D microfluidic devices.[35] Recently, we found that TPP prototyping was also a powerful technology for embellishing existing microfluidic devices towards advanced functions. Herein, we demonstrate a novel post-embellishment strategy for appending extra functions on traditional microfluidic channels *via* femtosecond laser micronanofabrications. Through careful adjustment of the laser power, transparent microchannels would be well integrated with additional photopolymer functional parts without incompatibility. As a representative example, microsieves with different pore sizes and shapes were successfully created inside the glass microchannel prepared by wet etching for sieving particles with different sizes. In addition, a fish scale-like structure was designed as a one-way valve for microfluidic chips. It is believable that, in the near future, femtosecond laser micronanofabrications would be widely used for embellishing microchips and thus make microfluidic devices almighty in more extensive applications.

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† Electronic supplementary information (ESI) available: Scheme for "wall effect"; scheme for particle movements in one-way microvalve test; SEM images of particles before and after sieving. See DOI: 10.1039/c003264f

Experimental section

1. Fabrication of microchannels

The microfluidic channel was fabricated by conventional wet etching. Briefly, a glass slide was washed by acetone, alcohol and deionized water, and then dried by nitrogen. After deposition of Chrome (30 nm, adhesive layer) and gold (100 nm, sacrificial layer) on the glass slide, a layer of photoresist was spin coated on the sacrificial layer (SL). Required channel patterns could be obtained by ultraviolet exposure under a mask and subsequent development. After orderly removal of exposed SL and then photoresist film, the glass slide was etched by hydrofluoric acid. Finally, a glass chip with channels imbedded was finally obtained. In this work, the channel was 75 μm in width and 15 μm in depth.

2. Embellishment with inside 3D structures

The obtained microfluidic channel was firstly coated with negative resin SU-8 2075 (Microchem, US) on the channel side and then scratched by straight-edged cover glass. Then the microchannels containing SU-8 were prebaked for 40 min at 95 °C for solidification, and cooled down to room temperature subsequently. The 3D structures were designed by 3D MAX, and converted to operable computer data. The laser beam from a femtosecond laser (80 MHz repetition rate, 120 fs pulse width, 800 nm central wavelength) was focused by a 60× oil immersion objective lens (numerical aperture NA = 1.35) to directly write the desired microstructure. After that, the polymer embellished glass chips were put in the oven for 15 min at 95 °C for post-bake. By rinsing the unphotopolymerized resin with SU-8 developer, the designed microstructure was obtained in the microfluidic channel. Finally, we covered the open channel with a cured PDMS (Dow Corning, US) slab, and pressed it for adhesion.

Results and discussions

1. Embellishment of microfluidic channel with microsieves

For illustrating the feasibility of embellishment on existing microfluidic chips, a conventional glass-based microfluidic channel was used as a substrate for building inside 3D microstructures. As shown in Fig. 1, firstly, a "T" shaped microfluidic channel was prepared by wet etching on a glass slide (75 μm in width, and 15 μm in depth, see detailed procedures in the Experimental section). Then the channel was covered with SU-8 2075 photoresist. It is worth pointing out that during TPP fabrication, the 60× oil lens of the 1.35 numerical aperture (NA) makes the work distance of the lens very short, so excess resin has to be scraped off by straight-edged cover slide to protect the lens and meanwhile let the laser focus at the bottom freely without obstacle. After prebake of the resin, we use the femtosecond laser to directly write in the microchannel according to the pre-programmed microstructures. The entire process including the positioning of sites to be addressed was monitored under the Charge Coupled Device (CCD) set, because we had to induce the laser light to focus[36] on the interior of the tiny channel but not on the platform. After that the unphotopolymerized resin was removed by SU-8 developer, and the embellished microstructure was obtained in the microfluidic channel. For further microseparation tests, a PDMS slab was covered to make the channel a closed system. At each end of the "T" shaped channel, there was a hole used for the sample inlet, sample outlet, and waste outlet respectively.

TPP prototyping inside the microchannel is quite different from the processing on a smooth substrate. For example, when we fabricated a simple sieve inside the microchannel under conventional conditions, only collapsed structures were obtained after development (ESI, Fig. S1a†). A possible reason might be due to the interference of the channel walls, here called "wall effect". When the laser wrote at the position near the wall of the channel, the light passed through both the glass wall and the resin. The different refractive index of SU-8 resin (1.58) and

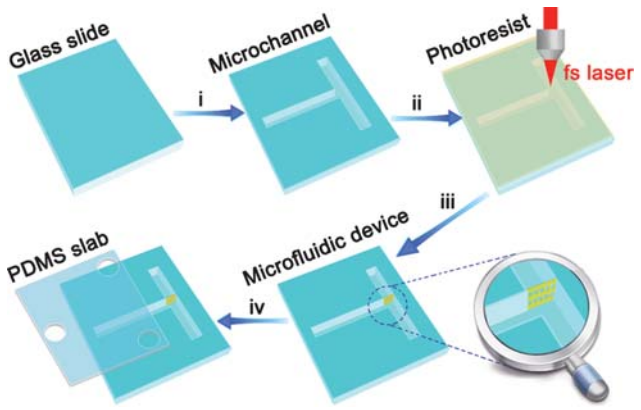

Fig. 1 Schematic illustration of embellishment of a microfluidic system by femtosecond laser micronanofabrication. (i) Preparation of microfluidic channel by conventional wet etching; (ii) surface coating with photoresist of SU-8 and direct writing by femtosecond laser; (iii) developing; (iv) covering of the device with PDMS slab.

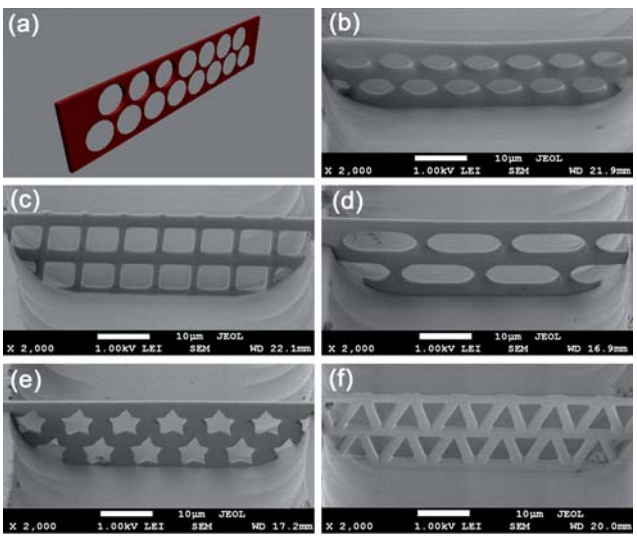

Fig. 2 Microstructrues fabricated by direct writing of TPP inside the channel. (a) 3D structures designed by 3D max. The structures have mainly two elements: a wall with high aspect ratio, and pores in it with different shapes, such as round (b), square (c), round-end rectangle (d), pentagrams (e), and triangle (f). The very high resolution and high aspect ratio showed the powerful capability of fabricating complex 3D structures by TPP.

the glass (1.51)[37] defocused the incident beam (ESI, Fig. S1b right†), and thus laser intensity was not strong enough to reach the threshold of resin polymerization. As a result, the edge of the sieve wafer did not stuck to the wall of the channel, and collapsed easily after development. So the energy of the laser used for fabricating microstructures inside the channel should be higher than that on the flat surface because of the as-formed "wall effect". Under this guidance, we successfully fabricated a well stood sieve wafer in the microchannel (ESI, Fig. S1c†).

In order to show the variety of TPP in embellishing microfluidic chips, microsieves with various high-resolution pores were firstly fabricated inside the microfluidic channel. As shown in Fig. 2, microsieve wafers 1 μm thick, 15 μm high with different pore shapes including round, square, round-end rectangle, pentagram, and equilateral triangle could be easily created according to preprogrammed 3D structures (Fig. 2a). Although the shapes seem to be simple, they include the basic building elements of various complex structures, including straight edge (edges of square and triangle), cambered edge (round), acute angle (triangle), right angle (square), obtuse angle (ESI, Fig.S1c†), and even angle with negative degree (pentagram). The spatial resolution of the structures could achieve as high as a submicrometer.

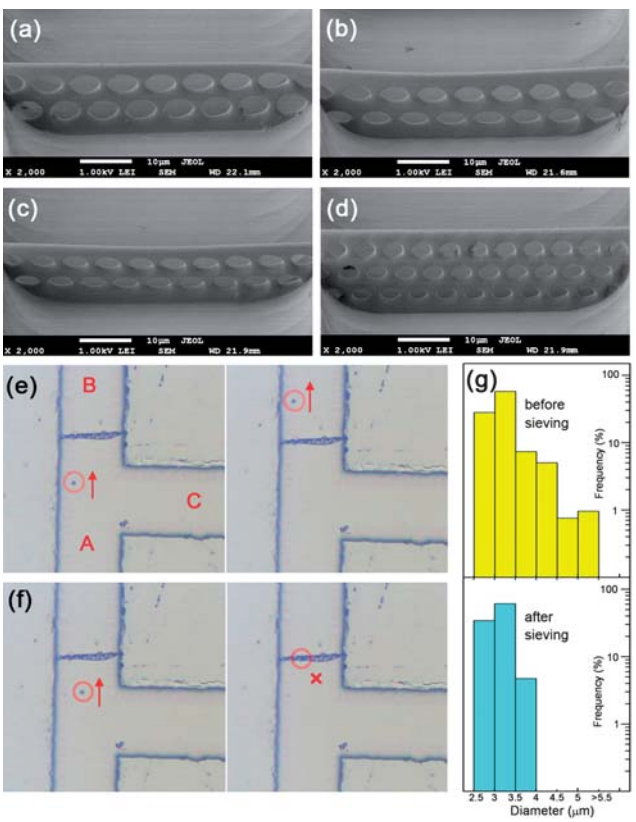

Fig. 3 Microsieves and their working effects in the microchannel. We fabricated sieves with pores of different diameters to sort particles. The diameters of the pores are 5.5 μm (a), 5 μm (b), 4 μm (c), 3.5 μm (d) respectively, and we used the 4.0 μm sieves for further testing (e). If the particle size is smaller than the pores, it would pass the sieve, (f) but if the particle is bigger than the pores, it would be blocked by the sieve. (g) Statistic results of microparticles before and after sieving.

2. Microsieving tests

For microsieving tests, microsieves with round pores were fabricated for the separation of microparticles with diameters in the range of 2.5 to 5.5 μm. In our case, the pore size of microsieves could be adjusted in a certain range. As representative examples, a series of sieve wafers with 6, 5.5, 5, 4 and 3.5 μm pores could be adopted for sieving particles with different sizes (Fig. 3a–d). According to the diameter of the microparticles, we chose the sieve with pores of 4.0 μm diameter for the test. As shown in Fig. 3e, the "T" shape channel (75 μm in width, and 15 μm in depth) embellished with the above mentioned microfliter was coverd with PDMS slab to form close channels, and there were three reservoirs at each end of the channel used for sample inlet (A), sample outlet (B), and waste outlet (C) respectively. By altering the depth of fluid in the reservoirs, we could control the flow direction in the channels. Due to the good wettability to both the PDMS and glass, herein, we used alcohol as the media fluid to deliver the particles. It could be clearly identified from the optical microscopy images that particles smaller than the pores could pass the sieve (Fig. 3e), on the contrary, bigger ones (Fig. 3f) could be headed off. If too many blocked particles assembled at the sieve, we changed the flow direction (A to B, A to C) to remove the particles by altering the depth of the fluid in each reservoir. Statistic results of microparticles before and after sieving (Fig. 3g) show that particles with diameter larger than 4.0 μm have been successfully headed off, exhibiting its excellent separating capacity (ESI, Fig. S2†).

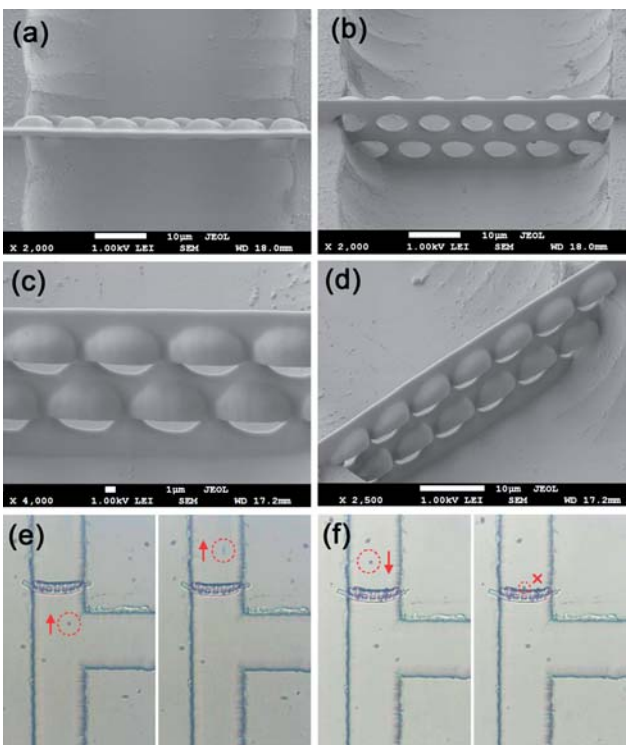

Fig. 4 Fish scale like filters act as one way valves. Top view (a) and side view (b, c, d) of the valve with fish scale like structures. If the particles come from the non-eave direction, they would meet the eaves after they passed the pores. If the particles come from the eaves direction, they meet the eaves before the wall, and they lose their horizontal momentum when they bang against the eaves, and would be blocked by the valve.

3. One-way microvalve

The functionalization of microfluidic chips by TPP prototyping is not only limited to microsieves. For the second case, a fish scale like microfilter was fabricated and designed as a one-way valve. The unique filter wafer contained two major parts: a wall with 5.5 μm of round pores, and eaves half-covering the pores (Fig. 4a–d). When the particles come from the eave direction, they meet the eaves in advance, and lost their horizontal momentums. As a result, they bang against the eaves due to the flow force (ESI, Fig. S3†). On the contrary, if the particles come from the opposite direction, they lost the horizontal momentums after passing the pores, and then they would pass the valve with flow of fluid (ESI, Fig. S3†). In the test, as shown in Fig. 4e, f, this unique one-way microvalve was very employable, exhibiting favourable performance as we expected.

Conclusions

In conclusion, we have found femtosecond laser micro-nanofabrication a powerful technology for functionalizing microfluidic devices with inside 3D microstructures. By using this method, we have built a series of microsieves with round, square, round-end rectangle, pentagram, equilateral triangle shaped pores and adjustable pore sizes of 3.5–6.0 μm inside a vitreous microfluidic channel, which, therefore, imparts the conventional microchannel a separative function. Additionally, through design and fabrication of a fish scale like microstructure (eaves covered pores), the microchannel was functionalized with a one way valve. The above results show that TPP prototyping has already exhibited great potential for mending, modification, functionalization and integration of general microfluidic chips, and probably, it would be widely used in lab-on-chip systems in the near future.

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