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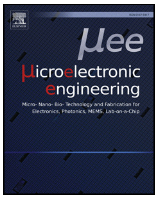

Research paper

Optimization of a suspended two photon polymerized microfluidic filtration system

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ABSTRACT

Two Photon Polymerization (2PP) is a powerful additive manufacturing technology already employed in the field of micro-/nano- engineering. The resolution achieved by 2PP 3D printing systems is in the range of hundreds of nanometers, but the printing volume is limited to few mm^3 and printing times are not negligible. Therefore, it cannot be considered economically efficient with respect to standard clean room technologies or other Stereolitography (SL) techniques. A possible solution to this limitation is the embedding of micro-/nano-features fabricated by 2PP inside a low-resolution object obtained by SL printers. Moreover, 2PP optimized strategies should be adopted to maximize the resolution and maintain a high printing velocity. In this work, a suspended microfilter obtained by a 2PP system has been successfully integrated in a 3D printed microfluidic structure. The microchannel was fabricated by a standard SL printer using a low-cost 3D printing resin, while the suspended microfilter was obtained using a 2PP Micro-3-Dimensional Structuring System (M3D) and a drop of Femtobond D resin. An innovative printing strategy was carried out to maximize the 2PP resolution and optimize the fabrication time. In particular, the X,Y plan was exploited to build the high-resolution mesh, thus obtaining a suspended microfilter that has a final pores size of 4 μm on a considerable area of 0.5 mm^2 in an only 30 min process. Finally, the microfluidic filtration system was carried out and its efficiency was evaluated employing size-controlled fluorescent microparticles.

1. Introduction

In the biological and biomedical field, particle sorting is often a key point both for diagnostic and therapeutic purposes. Among the sorting techniques, label-free is the most attractive since it involves very few preparation steps [1]. Label-free separation is mainly based on the physical properties of the different particles or cells and it can be implemented both with active and passive techniques in microfluidic devices [2]. If the sorting efficiency is adequate for the analysis, passive techniques, as porous filters, are preferable because they do not require additional interfaces with external devices which could introduce challenging coupling of different elements [3]. For applications at the micro-scale, microfabrication represents the favorite solution for filters production since it allows building customized structures which correctly select the particles to be collected [4].

The simplest filtering structure is a single layer membrane, for instance the one described by Yang et al. in 1999 [5]: it was built by silicon micromachining and was studied to collect airborne particles in gaseous flow with a pore range from 6 to 12 μm. Unfortunately, this approach could seem outdated today, since the design of a filter should not only take into account the particles to retain, but also be easily and fully embeddable inside a microfluidic chip with other components [6]. Moreover, the introduction of polymer technology could overcome the disadvantages linked to silicon processing [3]. In this perspective, 3D printing promises to be an effective alternative to micromachining as it allows to print not only a single-layer filter with the desired geometry, but a multi-layer filtrating device embedded in a more complex microfluidic chip. Many researchers have worked in this direction, implementing processes to build micro- and nano- structures with high resolution additive manufacturing techniques. In this regard, two photon polymerization (2PP) represents one of the most suitable processes to build features with a spatial resolution down to 120 nm [7]. Unfortunately, the high resolution is achieved at the cost of long processing times. This is the reason why 2PP is frequently combined with

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faster techniques so that most of the device is obtained by a lower resolution and more efficient approach, while the 3D micro-/nano- feature is printed by 2PP [8], trying to shorten process times [9]. An integration of different fabrication technologies means combining, for example, standard microfluidic fabrication techniques with 2PP to achieve a considerable time and cost reduction, thus maintaining the high resolution capability for the critical features [10]. For example, standard Stereolithography (SL) allows for obtaining micro devices with a resolution of tens or hundreds of micrometers and a higher throughput, with respect to 2PP, employing a low-cost resin. Indeed, previous works [11] have demonstrated the applicability of SL systems to fabricate microfluidics and Lab-On-a-Chip with the advantages to easily pass from the design to the device avoiding the implementation of high cost processes or micromachining technology [12,13]. A similar approach for 3D objects manufacturing by integrating SL and 2PP has been developed in a recent work [14], but this technique is still in its infancy since a multi technology printing system does not exist yet.

In this work, a novel printing strategy exploiting the integration of SL and 2PP technologies to obtain a membrane based microfluidic filtration system has been carried out. Differently with respect to previous works, where the filtering structures were developed on the Z axis to obtain a wall-like single-layer filtrating structure [9,15,16], a horizontal membrane-like multi-layered sieve with pores down to 4 μm was fabricated inside a previously 3D printed microchannel. The adopted novel printing strategy allows for maximizing the printing resolution with respect to printing velocity and then for obtaining a filtrating device with pore dimensions of few microns (e.g. the range of blood cells) avoiding the introduction of supporting structures and optimizing the process to reduce building times. A standard SL was employed to print the bulk microchannel, while micro-/nano- metric structures were fabricated exploiting 2PP. The object printability evaluation was carried out and a microfluidic filtration system was properly fabricated. Finally, to prove the filtering capability, real time sorting tests were conducted using fluorescence microparticles.

2. Experimental

2.1. Microfluidic chip design

The microfluidic filtration system geometry consisted of a single-channel chip with one inlet and one outlet, as reported in Fig. 1a. One of the peculiarities of this structure is that no top and bottom enclosure are present: this strategy was adopted to allow a better cleaning [17] of both the channel lumen and, in a second time, of the filter. Moreover, with an open channel, the difficulty of 2PP resin vehiculation to the polymerization site is avoided [18]. The channel was designed to be 300 μm wide and 300 μm deep. Inlet and outlet had different dimensions: while the outlet was a 450 μm diameter hole, the inlet was a 650 μm diameter hole with a 200 μm high step-like feature that creates a slot for the filter and was designed to hold and support it both during printing and filtration (Fig. 1a). These dimensions and geometries were chosen in accordance with the 2PP printing setup respecting the constraint on the maximum structure height that the apparatus could print (1.1 mm).

The tridimensional layout of the filter was designed in SolidWorks and then converted in a *.STL file for processing.

2.2. Microfilter design

The microfilter consisted in a 50 μm thick circular structure with 800 μm diameter. Its structure was designed to have two main parts, highlighted in Fig. 1b: a solid full ring (grey) and a grid structure (blue and cyan, the actual filter). The 100 μm wide external ring was added to mechanically strengthen the structure and overcome the issue of poor adhesion raised by Baldacchini et al. in a similar work [18]. The full integration inside the 650 μm inlet of the SL printed microfluidic channel was reached by designing the filter to be wider than the inlet. Thus, in the 2PP printing step the laser would describe the ring path inside the microfluidic chip walls allowing a polymerization process at the junction point between the two structures (microfluidics and filter). The second part, enclosed by the outer ring, was composed by two grids: a primary one, in which 20 μm wide rods, extending for the whole microfilter height, formed a matrix of 60 μm wide squared holes. A secondary one, composed by smaller rods orientated alternatively along x and y direction between subsequent layers, which formed a 4 μm porosity inside each of the primary grid holes.

The primary grid (cyan color in Fig. 1b) provided mechanical resistance to the whole filter and to the secondary grid (blue color in Fig. 1b), which represented the real filtering unit. This geometry was generated to combine high filtering surfaces and mechanical stability at the same time.

2.3. Microfluidic chip fabrication

The single channel chip was printed in a SL 3D printer (Microla Optoelectronics s.r.l) equipped with a 405 nm laser source mounted on a galvo scanner. With its minimum feature size of 100 μm on X,Y plane and layer thickness tunable from 20 μm to 200 μm, it can print objects covering a maximum area of 170 × 200 mm^2.

The printing process comprised the following steps: a 175 μm foil of PMMA was positioned on the building platform. This expedient was introduced to perform a better detachment after printing exploiting the lower adhesion of the polymerized resin with PMMA with respect to the building platform material (aluminum). Then, once the resin vat was filled with the commercial resin SpotHT by SpotAmaterials, printing was performed polymerizing the resin layer by layer. In this case, three layers of 100 μm thickness each were printed: the first two had a 450 μm diameter inlet hole while in the last layer a 650 μm concentric hole was polymerized in order to build the step-like feature that would hold the filter. This printer enables the user to set multiple parameters, such as laser power, hatch spacing, hatching pattern and velocity (with different values for internal hatching and borders if desired). The fixed printing parameters (optimized for the SpotHT resin) are reported in Table 1.

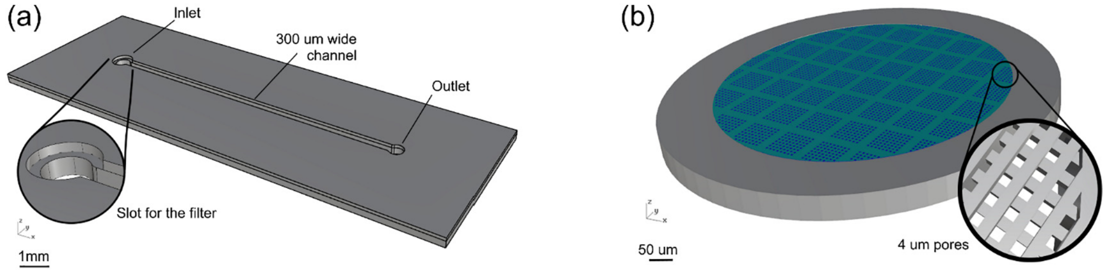

Fig. 1. (a) Microfluidic chip geometry (b) Filter geometry: cyan and blue grid represents the filtrating structure while the grey ring the support structure. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

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