Rapid manufacture of modifiable 2.5-dimensional (2.5D) micro-structures for capillary-force-driven fluidic velocity control

Electronic Supplementary Material 1

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One major challenge in the microfluidic field is to fabricate microfluidic systems in a rapid and inexpensive way. Despite the brilliant achievements gotten in µTAS over the past twenty years, significant barrier is still presented for its access to ordinary labs. Early microfluidic devices are mainly fabricated on hard materials like silicon or glass, with extensively steep fabrication cost. In the late 1990s, G. M. Whitesides *et al.* revolutionized manufacture methodology through introducing PDMS as the microfabrication materials.[21,22] This smart method indeed simplified microfabrication process and heightened the microfluidic accessibility to non-specialized labs, but it relied in a master mold commonly fabricated by photolithography. Nowadays, photolithography is still the main workhorse in fabricating master molds, which are applied for structural definition into various materials including PDMS elastomer,[23,24] silicon wafer,[25] or glass slide.[26,27] A standard photolithography requires various instruments (spin coater, UV transmitter, oven and hot plate, etc.), various reagents (photoresist, developer and washing reagent, etc.), an optical mask, and a clean room,[28] with extremely high manufacture cost involved.

To solve this challenge, a variety of benchtop based straightforward processes have been addressed recently. Yuen *et al.* utilized desktop digital craft cutter to carve software designed micropattern into double-sided tape, which can be further assembled to tape-based microchips.[18] Kim *et al.* presented a microfabrication technique by spin coating PDMS onto double-sided tape, which is then cut to the desired microfluidic pattern by a knife plotter.[29] All these straightforward prototyping techniques are fast and cost-effective, without the use of photoresist, optical masks and clean room that are indispensable in traditional photolithography. Similarly, herein the multi-tape-lithography also relies in benchtop based straightforward processing on the tape. As a result, all staff required in the 2.5D microfabrication methodology as introduced here, is only one office printer, single-sided tape, double-sided tape, a knife, an oven (or hotplate), PDMS elastomer, and a glass slide. Except for PDMS, all other tools and materials can be easily found in an ordinary chemistry or biology lab, without necessity of any costly laboratory investment. As a result, this 2.5D microfabrication methodology can be easily adopted by many potential µTAS users from wide range of fields such as chemistry, biology, pharmacy and medicine, etc., who may be limited in access to professional microfabrication instrumentation.

In contrast with other classical microfabrication techniques, such as CNC micromachining, laser ablation, inkjet printing, injection molding, photolithography, dry etching, and hot embossing, etc., no any professional microfabrication facilities or specialized skills beyond the scope of other fields are involved here. Furthermore, the height, width, and length of microchannels of the 2.5D tape master, can be easily modified without the necessity of fabricating a new mould every time. So for the case that a series of similar microstructures are required for parallel experiments or applications, one same mater mound can be repeatedly modified and utilized after stricter-modification, without the necessity of fabricating a new master mould every time, and consequently, multilayer-tape lithography can dramatically heighten the microfabrication efficiency. In contrast, master mould can't be further modified once fabricated in traditional fabrication techniques (e.g., photolithography, dry etching, and inkjet printing).

Theoretically speaking, for any 2D and 2.5D microstructures with straight microchannels no less than 500 µm in width, we can directly utilize the commercial scalpel to manually fabricate through "multilayer-tape lithography". There are lots of academic literatures applying microsystems containing microchannels no less than 500 µm in width. Most of them can be fabricated by commercial scalpel. For extremely complicated micronetworks with microchannel lower than 500µm in width, we suggest to use digital craft cutter instead of scalpel, which has already been widely adopted for the microstructural definition on various tape-like substrates by many other groups.[2,18,30] Two topological microchips with Y-structure channel and parallel channels are fabricated to address the multilayer-tape lithography here. Even if only three functionalized applications from them, they definitely have many other potential applications than what are demonstrated here. For instance, a Y-shaped microchip with same channel width (500 µm) and similar height (120 µm) and length (1 cm) as the first functionalized Y-shaped microchip in our manuscript was also reported by A. van den Berg *et al.*,[31] which was successfully utilized for the co-cultures of human endothelial cells and embryonic stem cell-derived pericytes for microvascular formation. This further proves the microsystem fabricated by "multilayer-tape lithography" can be utilized for various potential applications, but not simply limited to what's shown in this manuscript. As for the second and third functionalized microchips, successful programmable spontaneous flow proves 2.5D multilevel channel itself can efficiently control programmable sequential autonomous flow, promising as a powerful approach for the construction of self-imbibing & activated micropump for cost-effective, disposable, and programmable autonomous POC diagnostic chip. But in contrast, varied surface modification may be required to form similar sequential self-powered pumping in parallel 2D microchannels. For instance, sucrose solution has been utilized to treat 2D microchannels for programmable autonomous flow in one microchip consisted of parallel microchannels.[8,9] By waiving working liquid and porous wicking material in previous self-powered pumping system,[2] our methodology also acts as easier approach to automate analytical sample. The 2.5D multilevel microchip can also be further utilized for sequential and autonomous injection of controlled volumes of multiple solutions into the same microchannel, simply by replacing the parallel microchannels to adjacent capillary network as reported by Novo *et al.*[7] All these proofs confirm the multilayer-tape lithography as introduced here, can be utilized for various applications like autonomous POC diagnosis.

For a brief summary, our work is consisted of four most important ingredients. The first is the introduction of multilayer tape for rapid fabrication of 2.5D lithographical master; the second is the easy modification of the tape-master both in 2.5D and 2D level; the third is sequentially autonomous liquid transport by 2.5D microchannels; the fourth is totally benchtop and straightforward processing with high accessibility to potential μTAS users limited to professional microfabrication instrumentation. Compared with traditional methods, this novel multilayer-tape lithography possesses great advantages, especially for 2.5D microchannel fabrication and downstream applications. For example, it eliminates time-consuming and labour-intensive aligning problems internally associated with traditional 2.5D microfabrication techniques. Furthermore, since there is no photoresist-related operation (spin coating, soft bake, UV explosion, hard bake, developing, rinsing, and post bake, etc.) involved, multilayer-tape lithography can be used to fabricate 2.5D-microfluidic masters much faster than traditional approaches relying on photolithography, such as the "stacking method". A 2.5D master containing multilevel channels with varied heights may require hours to fabricate by the "stacking method," but herein they can be fabricated in minutes. For the microfabrication of 2.5D microchannels with width of lower than 500μm, digital craft cutter instead of scalpel can be utilized, which has been proven as mature techniques for the microstructural definition on tape-like materials according to various previous reports.[2,18,30] In most traditional microfabrication techniques, microstructure like the height of the channel is impossible to be modified once it is fabricated. On the contrary, in the technique here, modification of the micro-structure can be easily made on the master both in 2.5D level (channel height can be changed at 50 μm unit here) and 2D level (channel length is changed by 10 mm in our case) for new micro-structure and new application. Because new micro-structures can be easily realized on modifying the existing master, without the necessity of fabricating a new master every time, this advantage can dramatically heighten fabrication efficiency and decrease fabrication cost. Finally, we find that a new type of channel-height-controlled programmable autonomous flow can be easily realized and controlled by differentiate the height of a series of micro-channels in both 2.5D chips, fabricated by our technique within minutes.

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