STRAIGHTFORWARD MODULATION OF TWO DIMENSIONALLY FEATURED MICROFIBERS USING OPTOFLUIDIC SYSTEM FOR MULTIPLEX IMMUNOASSAYS

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ABSTRACT

We present the optofluidic system to generate compositionally featured microfibers. A photopolymerizable core liquid is stably transformed into a microfiber and safely conveyed to the outlet with the help of inert carrier liquid flows. The composition and dimension of microfibers was readily manipulated by changing core liquid materials and the input pressure of flows. Moreover, pneumatic valves were employed to fabricate sequentially segmented microfibers by switching on/off each core liquid flow. Finally, microfibers in the desired configurations are expected to be used to the multiplex biomolecular analysis.

KEYWORDS

Microfibers, Flow lithography, Optofluidics, Immunoassays

INTRODUCTION

Hydrogel microfibers have attracted extensive attentions for biomedical applications including scaffolds for tissue engineering [1], and biological sensors for analytical uses [2]. In particular, the multi-segment microfiber is the key issue due to its feasibility for parallel analysis of active ingredients in numerous conditions [3]. Previous literatures have reported fabrication methods of microfibers *via* electrospinning[4] and extrusion[5] but they are not suitable to make multifunctional microfibers due to the difficulty in precise shape modulation. Flow lithography which uses oxygen layers in polydimethylsiloxane (PDMS) microfluidic device, is a promising method to control shapes and compositions of microstructures [6, 7, 8]. However, it is limited to fabricate only microparticles since the process for microfiber generation requires continuous UV light which causes lack of surrounding unpolymerized solution to convey the bulk microfiber.

Herein, we report double-layer microfluidic platform that generates vertically stacked laminar flows for rectangular hydrogel microfibers with diverse compositions. Inert carrier flows along microchannels helped high-throughput generation of microfibers by preventing undesirable blockage of the channel and conveying the microfiber safely to the outlet. The dimension and chemical composition of microfibers were modulated by changing the flow rates and core liquid materials. In addition, microfibers were sequentially patterned by using pneumatic valves towards further applications in the multiplex immunoassay.

EXPERIMENT

Conventional photolithography was conducted, using the photoresist to make microchannel patterns for both top and bottom layers. Subsequently, PDMS molds were made by curing PDMS prepolymer on microchannel patterns at 70℃. Then, PDMS molds of top and bottom layers were detached from substrates and carefully combined together by using oxygen plasma treatment (Figure 1A). Figure 1B shows PDMS microfluidic device with double layered channels to form vertical laminar flows. Photocrosslinkable core flows and inert carrier flows – poly(ethylene glycol) diacrylate (PEGDA) and poly(ethylene glycol) (PEG), respectively – are stacked in the narrow channel to minimize hydrodynamic mixing and gently expanded at the downstream for the desired width of microfibers.

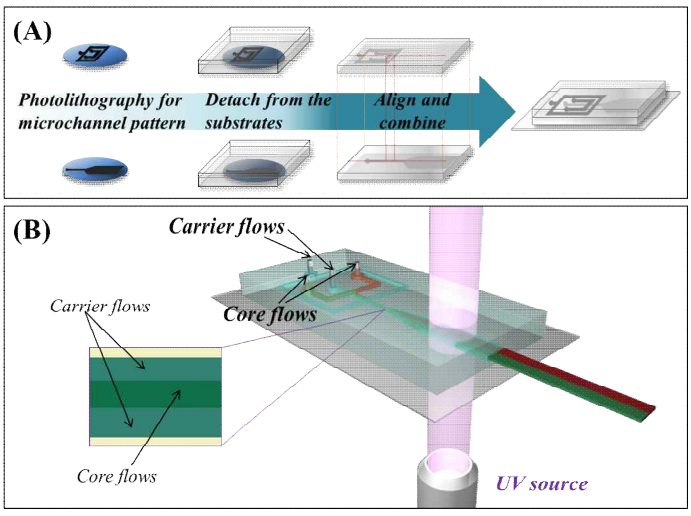

***Figure 1**: (A) Schematic for the fabrication of microfluidic devices. (B) Illustration of microfiber generation.*

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Compositionally featured microfibers were generated by introducing core liquid flows side by side and stacking them one on another (Figure 2A). In order to visualize individual segments, silica particles which were modified with two different fluorescent dyes – tetramethyl rhodamine isothiocyanate (TRITC) and fluorescein isothiocyanate (FITC) – were incorporated to core liquids. As represented in Figure 2B, multi-segment microfibers were readily obtained in the designed features. Since only core liquid flow is polymerized into the microfiber, changing the input pressure ratio of flows can achieve the dimensional control over microfibers (Figure 3). As pressure ratio of core to carrier flows increased, the microfiber thickness also gradually increased. Moreover, pneumatic valves were integrated into the microfluidic device for the controlled shape of microfibers as shown in Figure 4A. The computer aided pneumatic valve which acts as the on-off switch of each core liquid actuates the thin elastomeric membrane around the core liquid channels. Once the pneumatic valve is activated by the pressurized gas, the elastomeric membrane is expanded and ends up blocking the way of the core liquid (Figure 4B). As two pneumatic valves were alternatingly operated, two different core liquid flows containing rhodamine 6G (R6G) and FITC, entered the channel sequentially following the frequency of valve actuation. As can be seen in Figure 4C and D, the sequential flow pattern of core liquid flow was appeared and the UV light was exposed over the microchannel to acquire alternatingly segmented microfiber. The parabolic flow pattern could be due to the velocity profile throughout the channel. The velocity difference of flow in the middle and flow near channel boundary results in U-shaped sequential compartments on the microfiber.

In conclusion, we suggested the optofluidic system for the fabrication of compositionally featured microfibers by generating stratified laminar flows. On-demand control of the dimension and composition was achieved by manipulating the flow rate of liquids and chemical ingredients of core liquid flows. In addition, pneumatic valves were incorporated to fabricate sequentially segmented microfibers. We expect that our system is potentially applied to the biomedical research such as multiplex biosensors and cell scaffolds in tissue engineering by adding different biomaterials into microfibers.

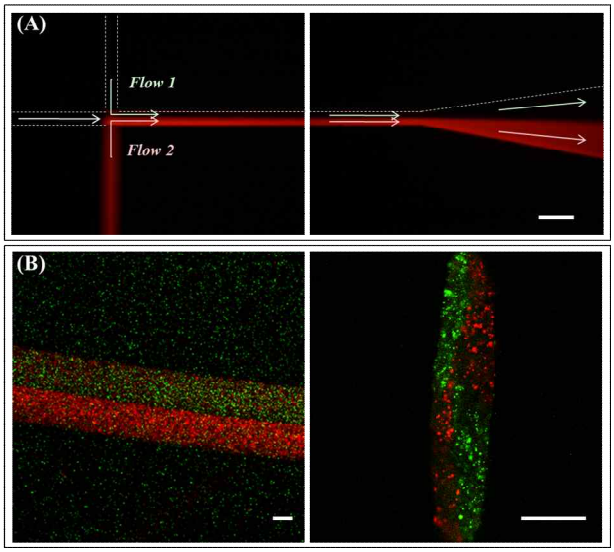

Figure 2*: (A) Fluorescent images of microchannels with the cross junction (left) and the expanded region (right) for two parallel core liquid flows; the red fluorescence was from a core liquid flow containing R6G and the other flow contained FITC. (B) Fluorescent images of a microfiber from the top view (left) and from the cross-sectional view (right). Scale bars for (A) and (B) are 100 μm.*

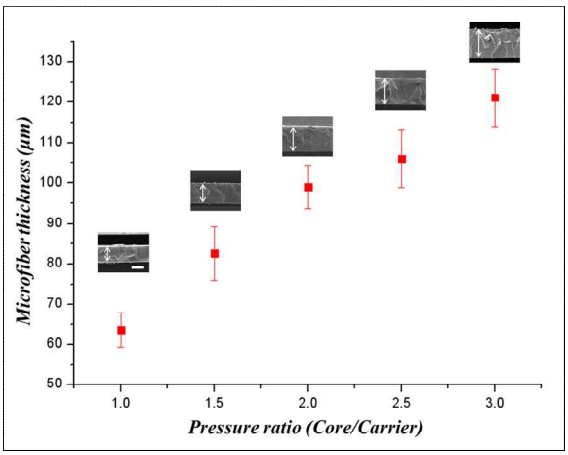

Figure 3*: Thickness of microfibers as a function of the input pressure ratio of core to carrier liquid flows. (Inset) Cross-sectional SEM images of microfibers, representing the tendency of film thicknesses according to the pressure ratio of flows. Scale bar for inset is 100 μm.*

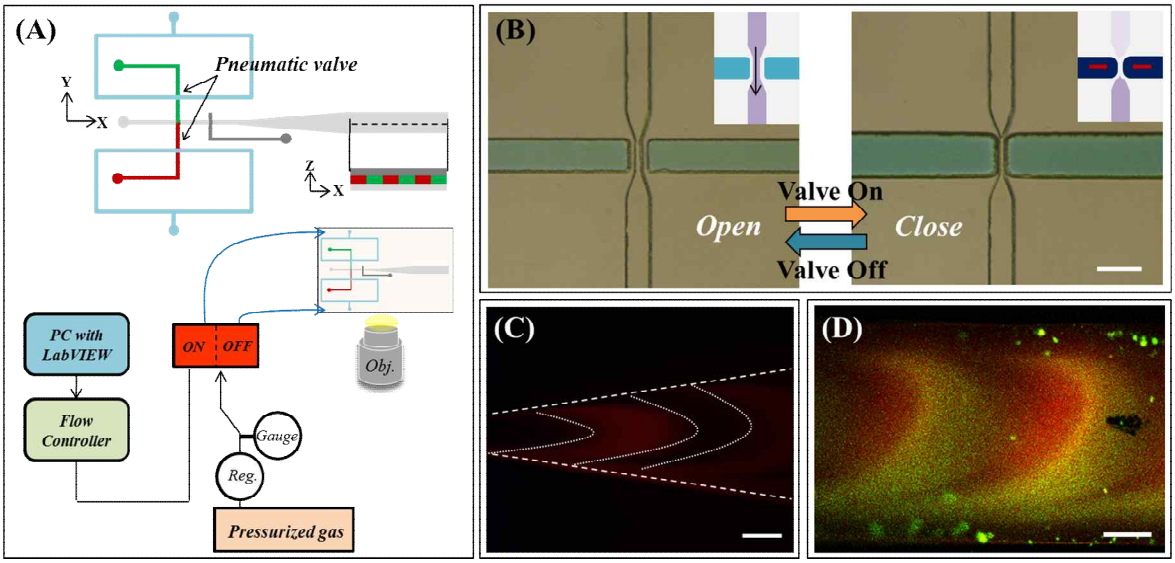

Figure 4: *(A) Schematic illustration of microchannels for sequentially patterned microfibers (top) and the computer aided pneumatic valve system for the on-off switches of core liquid flows. (B) Optical microscope images of pneumatic valves in the 'off' state (left) and 'on' state (right). (C) Fluorescent image of the microchannel in the expanded region; the alternating parabolic flow pattern was visualized with R6G and dotted lines were drawn over the boundary of channel and each flow pattern. (D) Fluorescent image of the microfiber with sequential compartments; the red fluorescent signal from R6G and the green from FITC. Scale bars are 200 μm for (B), 200 μm for (C), and 100 μm for (D).*

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