A LOW-ASPECT-RATIO, ROLL-TO-ROLL HOT EMBOSSED INERTIAL MICROFLUIDIC SORTER

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ABSTRACT

This work presents a low-aspect-ratio (LAR) inertial microfluidic design compatible with roll-to-roll (R2R) hot embossing for size-based cell or microparticle separation in a low-cost and disposable format. The device consists of two segments of LAR channels in which inertial lift forces are used to differentiate lateral positions based on size for separation downstream. Separation of 18µm and 15µm diameter particles was first demonstrated in a conventional PDMS device, and further validated in a thin-film device mass-produced by R2R embossing. The described LAR inertial microfluidic separator is ideally suited as a low-cost, disposable device for point-of-care sample preparation.

KEYWORDS: Inertial microfluidics, roll-to-roll hot embossing, microfluidic sorting

INTRODUCTION

Inertial microfluidics has become a highly active area in recent years for high-throughput sample preparation in biomedical research, cell biology and clinical diagnostics [1]. Most of today's inertial microfluidic designs rely on high-aspect-ratio microchannels to enable focusing or separation of cells [2], which hinders manufacturing of such devices for low-cost, disposable applications, as deep or small structures cannot be easily replicated in thermoplastics and require very expensive tooling. Herein, we report on a low-aspect-ratio inertial separator that offers reliable high-resolution separation of microparticles as well as ease of fabrication. We fabricated our devices using roll-to-roll hot embossing which is an ideal manufacturing process for high-throughput mass-production of disposable, in-expensive microfluidic devices [3]. Our design successfully separated 18µm and 15µm diameter particles in PDMS device fabricated by conventional soft lithography and showed comparable separation in low-cost device fabricated by the R2R process. We expect this LAR inertial microfluidic separator has a great potential for high-performance cell/particle separation for low-cost, disposable sample preparation.

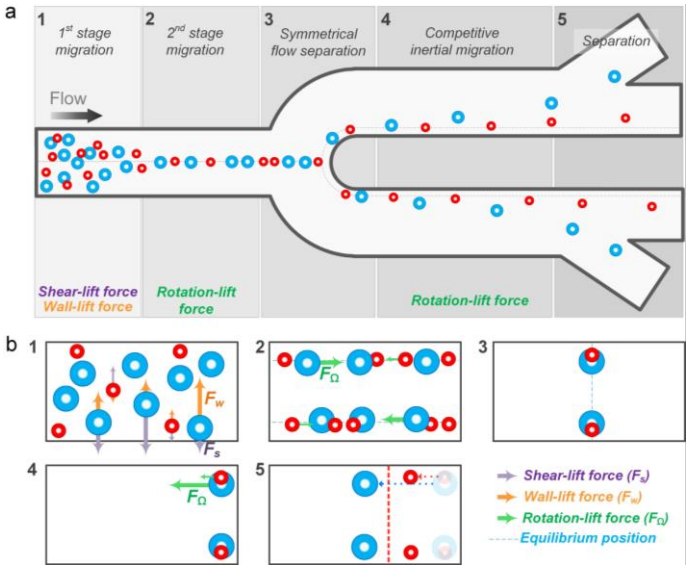

Figure 1: *(a) Schematics of device principle. The design consists of two segments of low-aspect ratio channels in which the lateral positions of particles are gradually manipulated by inertial forces to fulfill size-based separation. (b) Cross-sectional schematic of particle lateral migration subjected to inertial forces at different downstream positions.*

DEVICE PRINCIPLE

Our design concept is based on the principle of 2-stage lateral migration [4], and uses two segments of LAR channels to differentiate particle lateral positions based on size (Fig.1a). In the upstream LAR channel, particles focus along centers of the top and bottom walls (Fig.1b). Downstream, flow is symmetrically split between two LAR channels so that center-focused particles re-equilibrate close to the

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side walls. Particles then once again migrate towards the channel center under the influence of the rotation-lift force. Large particles experience larger force, and thus exhibit high lateral migration velocity than the small particles, leading to differentiation of their lateral positions.

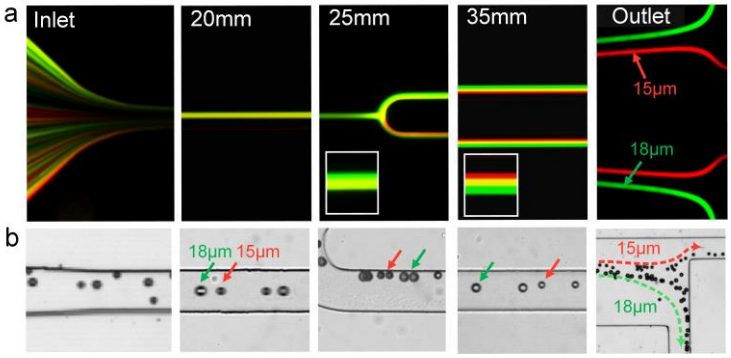

Figure 2: *(a) Fluorescence images and (b) bright field images of focusing and separation of 18 μm and 15 μm particles at five downstream positions showing successful separation in this low-aspect-ratio design.*

EXPERIMENTAL

For design characterization, we used microchannels fabricated in polydimethysiloxane (PDMS) by standard soft lithography. The low cost microchannels were fabricated onto polymethyl methacrylate film (PMMA) using roll-to-roll hot embossing process (Fig. 3a). The embossing parameters were 105°C for the embossing cylinder surface, 85°C for the counter pressure cylinder surface, 20 bars of nip pressure and 0.5 m/min web speed. The chips were sealed with hydrophobic tape (TESA). Fluid access ports of 2 mm diameter were drilled prior to bonding. The overall details of the R2R process are discussed in [3]. The channel cross-sectional images were taken using an optical profilometer (Bruker Corporation). We induced fluorescent particles (Polyscience inc.) into the devices using a syringe pump. We used an inverted epi-fluorescence microscope (IX71, Olympus Inc.) equipped with a 12-bit high-speed CCD camera (Retiga EXi, QImaging) to take fluorescence and bright-field images of particle focusing.

RESULTS AND DISCUSSION

We first demonstrated the concept using a PDMS device fabricated by standard soft lithography. As Fig.2 shows, the mixture of 18μm and 15μm diameter particles were first focused at the center of top and bottom wall in the upstream LAR channel shown as a bright fluorescent streak. As the focused particles enter the downstream LAR channel, they begin to migrate from the corner of the channel to the center. FITC-labeled 18μm diameter particles migrate faster than TRITC-labeled 15μm diameter particles shown as partially separated green and red fluorescent streaks which was separated successfully at the outlet. Line scans of the two fluorescent streaks at different downstream positions indicate that 18μm and 15μm diameter particles were separated with 6μm distance. Experiments in the PDMS device suggest that our concept can be used for separations of microparticles or cells with high size-resolution.

Next, we tested devices fabricated by R2R hot embossing of PMMA. Roll-to-roll process is an ideal approach for mid to large scale manufacturing, which produces low-cost disposable devices. A device

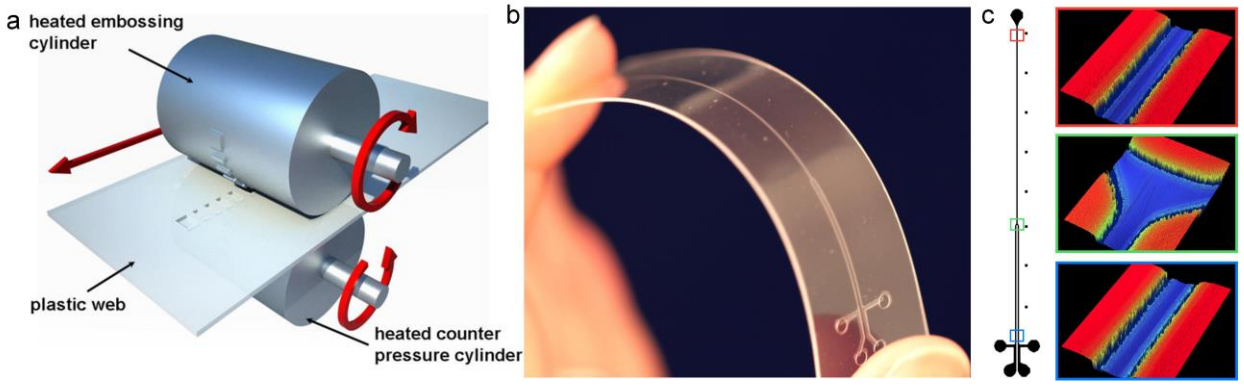

Figure 3*: (a) Schematic illustration of roll-to-roll hot embossing. (b) The low-aspect-ratio design fabricated by roll-to-roll hot embossing. (c) Optoprofilometer images showing the cross-sections of fabricated R2R chip at three downstream positions.*

fabricated with R2R process was illustrated in Fig. 3b. The 3D cross-sectional images of the chip indicate the low-aspect-ratio channel can be successfully replicated using R2R process (Fig. 3c).

We investigated focusing in the R2R channel. Both fluorescent images and bright-field images were taken at the upstream LAR channel and show a tight focusing of 18 µm diameter particles (Fig. 4a). Line scans of fluorescent particle focusing streaks in PDMS and R2R devices indicate that the focusing quality is comparable with only ~1µm difference in full width at half maximum (FWHM) (Fig. 4b). We further studied the particle separation in the R2R device. As shown in the fluorescent images (Fig. 5a), 18µm and 15µm diameter particles were first tightly focused at the center of the channel and then separated as they travel in the downstream LAR channel. The bright field image taken at 60mm downstream clearly shows the separation of the 18µm and 15µm diameter particle streams (Fig. 5b). The particle streaks were separated with >6 µm distance in R2R device indicating comparable separation with PDMS device.

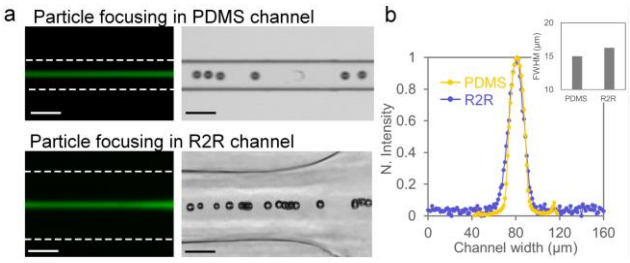

Figure 4: *(a) Experimental observation of particles focusing in PDMS channel and R2R channel indicating comparable focusing quality of microparticles. The scale bar is 75µm. (b) Linescans of particle fluorescence streaks show particles focusing in PDMS and R2R devices are similar. The inset picture shows only ~1µm difference in FWHM.*

CONCLUSION

In conclusion, we report for the first time a low-aspect-ratio straight microchannel inertial microfluidic design for separation of microparticles. The LAR nature brings convenience in fabrication and allows mass-production using R2R hot embossing (which has significant challenges in replicating conventional high-aspect-ratio designs). With the ease of fabrication and robustness of separation, we envision this LAR R2R inertial microfluidic separator as a low-cost, disposable, yet reliable sample preparation device for applications from bench-top biomedical research to point-of-care clinical diagnostics.

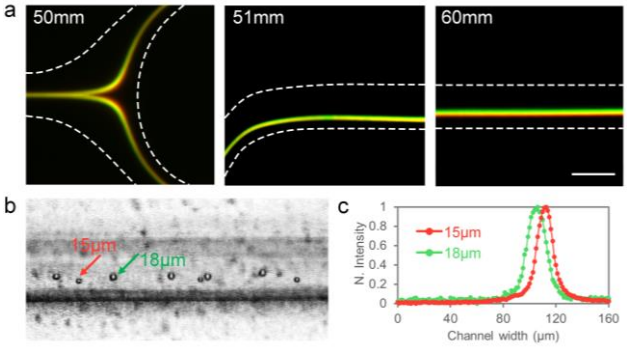

Figure 5: *(a) Fluorescence images of particles focusing in R2R device showing separation of 18 µm and 15 µm particles stream. The scale bar is 160µm. (b) Bright field image and (c) linescan of fluorescence streaks at 60mm downstream.*

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