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INERTIAL PARTICLE FOCUSING IN PARALLEL MICROFLUIDIC CHANNELS FOR HIGH-THROUGHPUT FILTRATION

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ABSTRACT

In this study, we introduce inertial microfluidics in straight, parallel channels for high-throughput particle filtration. We show that particles flowing through low aspect ratio rectangular microchannels can be focused into four particle streams, distributed at the centers of each wall face, or into two particle streams, at the centers of the longest channel walls, depending on the particles' size. For high-throughput filtration, we fabricated scalable, single inlet and two outlet, parallel channel microdevices, using a high-density 3D microfluidic PDMS channel manufacturing technology, in a design that allows for easy integration with other downstream on-chip functions we recently described. We demonstrate filtration of 24 μm particles from a suspension mixture in a microdevice with four parallel channels. The filtration efficiency at a non-optimized flow rate of 0.8 ml/min was 82%.

KEYWORDS:

Inertial microfluidics, inertial focusing, 3D fluidic networks, PDMS, particle filtration.

INTRODUCTION

The possibility to control the position of particles in continuous flow in microfluidic channels at very high throughput opens the door to the development of a large set of bioanalytical applications, such as blood cell separation and pathogen isolation. Very recently, inertial-induced forces developed in microchannels have been proposed by ourselves and others as a promising approach for particle focusing, filtration and separation [1][2][3]. In inertial microfluidics, lift forces act on particles and force them across streamlines towards particle size dependent equilibrium positions. Since inertial microfluidics rely on focusing many particles into a few particle streams, particle-particle interaction puts a limitation on the total particle volume fraction – often kept below 1%. For practical blood cell separation applications, the sample needs to be diluted, which limits the total volumetric flow rate. A straightforward way of increasing throughput is through parallelization. 3D fluidic networks allow the recollection of sample fractions of multiple parallel channels into a minimum of outlet ports. However, 3D microfluidic channel interconnections pose a severe manufacturing challenge. We recently introduced a novel technology for the high-yield manufacturing of densely spaced miniaturized vertical vias in PDMS [4]. This method is based on the inhibition of PDMS polymerization through the local depletion of the platinum polymerization catalyst. In this

work, we have improved the technique to reliably produce densely packed PDMS-vias over larger device areas. We also manufactured single inlet/two-outlet parallel-channel inertial focusing microdevices and demonstrate particle filtration in those.

THEORY

In Poiseuille flow, the parabolic velocity profile results in a shear-gradient-induced lift force, F_{LS} , directed down the shear gradient towards the wall, and a wall-induced lift force, F_{LW} , directed away from the wall. Depending on the specific particle size, channel geometry and fluidic conditions, the resulting channel cross-sectional force field, F , can exhibit specific stable regions of zero force magnitude that form equilibrium positions. Assuming point-shaped particles ($R_p \ll 1$), it has been shown that the magnitude of the force vectors F_L in F scale quadratically with the particle Reynolds number, R_p , and linearly with a cross-sectional position dependent lift coefficient, f_c [5]: $F_L = R_p^2 \cdot f_c \cdot \mu^2 / \rho$, in which $R_p = Re \cdot (a/D_h)^2$ is the particle Reynolds number, $Re = r \cdot U_m \cdot D_h / \mu$ the channel Reynolds number, a the particle diameter, $D_h = 2 \cdot w \cdot h / (w + h)$ the hydraulic diameter, w and h the width and height of the channel, U_m the maximum channel velocity and μ and ρ are the viscosity and density of the fluid, respectively.

Figure 1: Particle inertial focusing in flow through straight channels. (a) The shear induced lift force (F_{LS}) and a wall induced lift force (F_{LW}) acting on a particle flowing in a microchannel. (b) Illustration of the cross-sectional equilibrium positions of particles flowing through different channel geometries.

Because the force on the particles scales with the fourth power of the particle size, a , the flow focusing force field is negligible for very small particles. This can be used to separate particles depending on size. At intermediate Re , particles are forced across streamlines and occupy the equilibrium positions positioned along the centres of the faces of the microchannel walls [1]. In a square microchannel, this results in particle focusing in 4 streams, close to the centre of each channel wall (figure

1b). Changing the channel geometry to rectangular cross-section reduces the particle focusing into two streams, close to the centre of the longest channel side wall. This means that for high aspect ratio channels, i.e. with $h > w$, particles are found in two laterally positioned particle streams, as reported in [2]. In our study, we report flow through low aspect ratio channels, i.e. with $h < w$, resulting in particle focusing in two streams in single lateral focusing position along the center of channel (figure 1 b, right).

MATERIALS AND METHODS

Design

We manufactured both single channel and parallel channel devices. All designs feature a channel length of 20 mm and height of 50 μm . The 10 mm upstream parts of the channels have a width of 70 μm , whereas the 10 mm downstream parts of the channels are tapered from width 70 μm to width 200 μm . The tapering was designed to increase the lateral spatial separation of flow streams in the channel. The multi-channel device consists of two PDMS layers, featuring a single inlet and two outlets. The top PDMS layer is designed to separate the side fractions from the channels to outlet 1 and the middle fractions from the channels to outlet 2, as shown in figure 3b. The dual PDMS layers are capped with a thick polycarbonate lid to allow easy attachment of steel tubes as fluidic ports.

Fabrication of devices

The single channel PDMS microdevices were fabricated using a single layer SU-8 mold. The fabrication steps for the 3D multi-channel devices are shown figure 2. A dual level SU-8 mold, pretreated with Teflon AFTM was used, in which the lower mold features define the channels ($h=50\text{ }\mu\text{m}$) and the higher mold features define the vertical vias ($h=150\text{ }\mu\text{m}$). A flexible 250 μm thick polycarbonate (PC) plate was incubated for one hour in a solution of 4% Z-6020 silane (Dow Corning®, US) in methanol and baked for 10 min at 110°C to create an amine surface coating that inhibits PDMS polymerization. PDMS prepolymer was poured onto the dual layer SU8 bottom mold (figure 2a). The PC plate was clamped onto the prepolymer, after which the prepolymer is cured for 30 min at 65°C. During curing, the polymerization is locally inhibited on top of the highest mold features (i.e. the vias positions), as described in [4] and illustrated in figure 2b. The polymerized PDMS adheres better to the PC plate than to the mold. Its flexibility allows the PC-PDMS stack to be peeled off from the mold (figure 2c). The bottom PDMS surface of the PC-PDMS stack is treated with oxygen plasma and bonded covalently to a clean and oxygen plasma treated glass slide. This ensures the adhesion between the PDMS and the glass to be higher than that between the PDMS and the PC. The flexible PC sheet is thereafter peeled off from the PDMS-glass device. The unpolymerized PDMS residues at the via positions follow the PC sheet, thus forming open vias in the PDMS (figure 2d). The top

PDMS layer is prepared from a second SU8 mold and is, after oxygen plasma treatment, bonded to the bottom PDMS layer (figure 2e). A 2 mm thick PC cover lid is milled out and assembled with steel tubes. Finally, a leak-tight bond is formed between the PC lid and the PDMS-top layer (figure 2f) by: incubating the PC lid for one hour in a solution of 4% silane (Z-6020) in methanol; oxygen plasma treating the PDMS top layer; and subsequently clamping the PC lid to the PDMS at 65°C for one hour.

Figure 2. Fabrication steps for the manufacturing of 3D multi channel devices. (a) The PC inhibition plate is applied on the PDMS prepolymer and clamped to the bottom layer mold. (b) During baking, the thin layer of PDMS close to the inhibition layer remains unpolymerized as compared to the PDMS bulk, which polymerizes. (c) The PC-PDMS stack is peeled off from the mold. (d) The PDMS is plasma treated and permanently bonded to the glass slide, after which the PC plate is peeled off. (e) A second, top PDMS layer is aligned and plasma-bonded on top of the bottom PDMS layer. (f) A 2mm thick PC lid with attached steel tubes is bonded on top of the top PDMS layer.

Experimental setup

The device characterization is based on the analysis of fluorescent microspheres flowing through the channels. Internally dyed green and red fluorescent polystyrene microspheres (2, 10 and 24 μm in diameter, Thermo Scientific) were diluted to 0.1-0.5 vol % with deionized water with 1% TritonX-100 (BDH Prolabo). The solutions were pumped with a syringe pump (Harvard Apparatus PHD 2000). The device was mounted onto the stage of an inverted fluorescent microscope and fluorescent streak images were obtained. For filtration characterization, a suspension mixture of 24 μm (green) and 2 μm (red) microspheres was pumped through a 4-parallel-channel device at a flow rate of 0.8 ml/min and collected at the two outlets. The fractions were quantified by a coulter counter (Z2, Beckman Coulter, USA).

RESULTS & DISCUSSION

First we describe particle focusing in single channels. Thereafter, we describe the results of the manufacturing technology for the production of high-density 3D

microfluidic PDMS channels. Finally, we describe particle filtration in parallel channel devices as a proof of principle for high-throughput sample processing.

Particle focusing in flows through straight channels

To investigate the particle focusing characteristics, three different particles sizes ($2\ \mu\text{m}$, $10\ \mu\text{m}$ and $24\ \mu\text{m}$) were flown at several flow rates ($3 < \text{Re} < 110$) through the single channels.

Figure 3: Fluorescence images of $2\ \mu\text{m}$ (left), $10\ \mu\text{m}$ (middle) and $24\ \mu\text{m}$ (right) particles flowing at a flow rate of $200\ \mu\text{l}/\text{min}$ (corresponding $\text{Re}=56$ for $w=70\ \mu\text{m}$) showing inertial focusing. The schematic cross-sections show the particle positions at the outlet of the channels. The $2\ \mu\text{m}$ particles remain unfocused, while the $10\ \mu\text{m}$ particles were focused into 4 streams and the $24\ \mu\text{m}$ particles into two streams.

As can be seen in figure 3, the $2\ \mu\text{m}$ particles remain unfocused, while the $10\ \mu\text{m}$ and $24\ \mu\text{m}$ particles, initially well distributed at the inlet, are focused after 10 mm. $2\ \mu\text{m}$ particles remained unfocused regardless of flow rate, suggesting an optimal particle size with respect to the channel geometry below which no focusing can occur, the latter being in agreement with previous reports [1][2].

Notably, the $10\ \mu\text{m}$ particles are focused in four equilibrium positions whereas the $24\ \mu\text{m}$ particles are focused into two streams at a single lateral position at the center of the channel. The occurrence of four equilibrium focusing positions has previously only been observed in square channel cross-sections [1]. The reduction of focusing particle streams from 4 to 2 when changing from a square to a rectangular channel cross-section was previously attributed to be channel geometry only, but our findings indicate a particle size dependency in addition to the channel geometry dependency. The ability to differentially focus particles at different equilibrium positions could be utilized in particle sorting applications.

3D multi channel device fabrication

As illustrated in figure 2, we have adapted a previous manufacturing protocol [4] to produce vias over large areas. In contrast to previous work, we used a more flexible inhibition plate material (a thin polycarbonate sheet) on which the monolayer of the silane inhibitor was immobilized. This flexibility enabled us to successfully transfer PDMS structures with a footprint area of $900\ \text{mm}^2$, whereas using a glass plate as inhibition plate, as described previously [4], resulted in the glass-PDMS stack being stuck to the mold and practically impossible to remove without destroying the PDMS structures. Figure 4a shows the PDMS vias in an 8 parallel channel device, filled with red dye for visualization. The vias manufacturing yield was repeatedly 100%, without residual membranes blocking the vias. Figure 4b shows two layers of PDMS channels, aligned and bonded. The final step of bonding the PC lid to the top PDMS layer resulted in low yields but when successful, the bond was leak tight. A successfully fabricated 3D device using 4 parallel channels can be seen in figure 4c.

Figure 4: Pictures of 3D multi channel devices. (a) An image of an 8-parallel-channel device with open vias filled with red dye for visualization. (b) Image of the outlet of a 4-parallel channel device, interconnected through vias (left panel). The top PDMS layer (marked by yellow diagonal lines) is aligned and bonded onto the bottom PDMS layer. One of the vias is highlighted (right panel). (c) A 4-channel high throughput filtration device filled with red dye to show the leak-tight bonding of the PC-lid. The distance from the inlet to the outlets is $23\ \text{mm}$ and the total footprint area of the device is less than $100\ \text{mm}^2$.

High throughput particle filtration

A mixture of 24 μm and 2 μm particles was pushed through the 4 parallel channel device at a flow rate of 0,8 ml/min (with corresponding $\text{Re} = 56$) to evaluate the separation efficiency. As expected, the 24 μm particles were focused into the lateral centre position of every channel and could be extracted through outlet 2 (figure 5a), while the 2 μm are unforced and equally distributed in both fractions. The filtration efficiency of the un-optimized flow rate was 82%,. One way to improve the efficiency is to optimize the channel geometry (length and aspect ratio) and flow rate. In addition, we observed clogging in the outlet channels of the top PDMS layer, presumably due to residues of un-polymerized PDMS. Coating the channel system can possibly solve the latter issue.

The non-optimized particle filtration throughput of 0.2 ml/min in each channel, can be compared with 28 $\mu\text{l}/\text{min}$ by Bhagat et al. [2] and 0.2 ml/min per-channel by Mach et al. [6] but the flow-through per microchip footprint area are however unmatched. In addition, the integration level provided by our manufacturing process enables integration of the design with other lab-on-chip components.

Figure 5: Particle filtration in parallel-channel device. (a) Fluorescent image of 24 μm and 2 μm particle suspensions flowing through the filter, showing the 24 μm particles entering to the middle outlet leading to the top layer and outlet 2. (b) The filtration efficiency for the 24 μm beads was 82%, as analyzed by a coulter counter.

CONCLUSIONS

We report inertial microfluidics for high-throughput particle filtration in flows through parallel channels, enabled by a scalable integrated 3D microfluidic network fabrication technology. The uncomplicated device requires neither external force fields nor mechanical parts

to operate which is suitable for low-cost particle focusing, and filtration applications.

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