A SIZE-DEPENDENT CELL CAPTURE AND RELEASE CHIP USING MULTIPLE VARIABLE MEMBRANE BARRIERS

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ABSTRACT

We present a simple size-dependent cell capture and release chip using multiple variable membrane barriers, concentrically arranged around the central inlet port. The previous cell separators using multiple fixed filters perform the size-dependent cell capture, but require additional structure and process for the release of the captured cells. The present cell chip, however, is capable to capture the cells by their sizes using the multiple membrane barriers and release the captured cells in size order by controlling the height of deformable barriers.

KEYWORDS

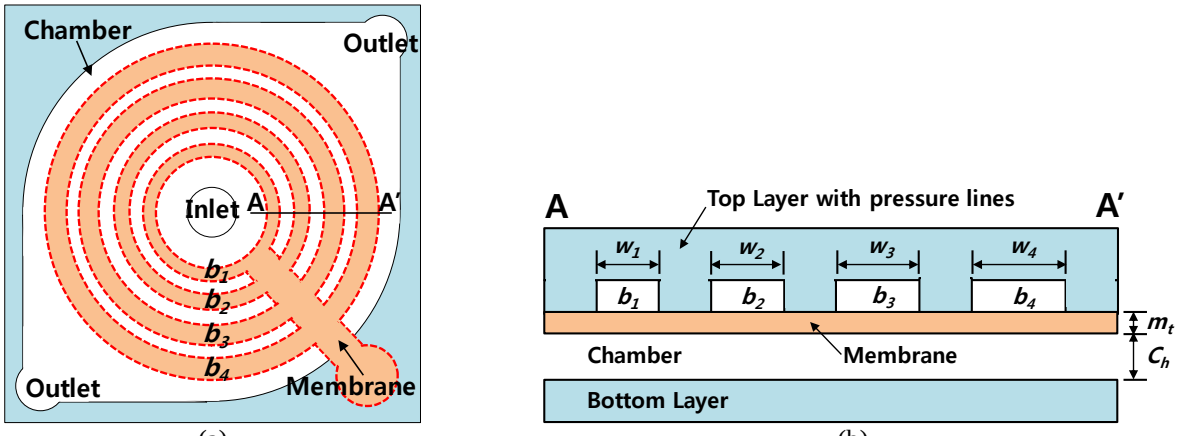
Size-dependent cell capture and release, Variable membrane barrier

INTRODUCTION

Integrated cell analysis systems[1, 2] have received increased attention for point-of-care (POC) diagnostics and drug screening. One of key functions in these systems is separation for the elimination of unnecessary bioparticles. For the development of effective separators, selective separation and recovery of targeted cells from the mixture is essential. The previous cell separators [3-5] using multiple fixed filters perform size-dependent cell capture, but have difficulty on recovering separated cells. They required additional structures and processes to recover the captured cells. In this study, we present a simple cell capture and release chip using multiple variable membrane barriers. It is capable of not only simple size-dependent cell capture, but also captured cell release in size order by controlling height of deformable membrane barriers.

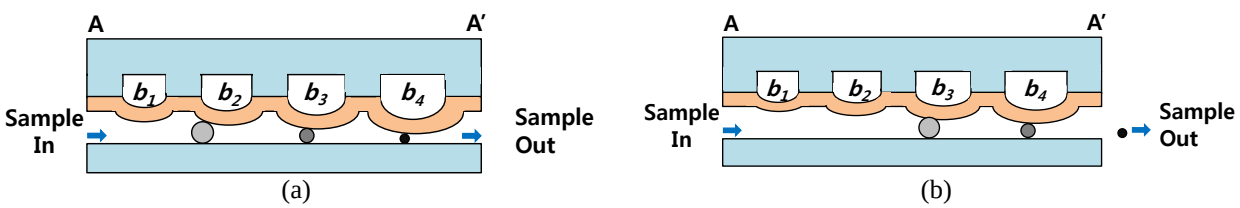
DESIGN AND FABRICATION

Figure 1 shows the overall layout and cross-sectional view of the present chip. The chip is composed of top layer with pressure lines, membrane, and bottom layers. For the size-dependent cell capture, the variable membrane barriers are formed by applying pressure into the top layer (Fig. 2a). The four membrane barriers (b_1~b_4) concentrically spread out from the inlet port with the gradually increased widths (w_1~w_4) of 182, 188, 194, and 200 μm, respectively. The membrane thickness is designed as 90 μm. At the pneumatic pressure of 80kPa, the increase of



(a) (b)

Figure 1. A size-dependent cell capture and release chip using multiple variable membrane barriers: (a) top view; (b) cross-sectional view of A-A'.



(a) (b)

Figure 2. Principle of the cell capture and release chip: (a) variable membrane barriers formed for size-dependent cell capture; (b) variable membrane barriers reduced for size-dependent cell release.

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Table 1. The threshold pneumatic pressure of membrane barriers to capture 10.3 μm- diameter polystyrene beads

Membrane barriers	Threshold pressure(kPa)
b_1	122.8±2.2
b_2	99.2±2.2
b_3	77.3±1.0
b_4	63.0±0.8

the barrier heights from the inlet to outlet is designed to be 2 μm. For the captured cell release, the variable membrane barriers are lowered by reducing the applied pressure (Fig. 2b). The chip is made by the PDMS molding and plasma bonding process. Figure 3 shows the fabricated device.

EXPERIMENTS

In the experimental study, we demonstrated the bead capture and release capability using two different polystyrene beads (diameter = 6.51±0.43 and 10.32±0.39 μm) immersed in 0.5% BSA (Bovine Serum Albumin) solution. The bead solution was supplied by syringe pump at the flow rate of 100 μl/min. Table 1 shows the threshold pneumatic pressure to capture 10.32 μm-diameter beads for each membrane barrier (b_1~b_4). At the pneumatic pressure of 80kPa, 10.32 and 6.51 μm-diameter beads were captured at b_3 and b_4 barrier, respectively (Fig. 4). Figure 5 shows the selective release of the captured beads (Fig. 5a) according to the different pneumatic pressures. At the reduced applied pressure range of 77~80 kPa, some of 10.32 μm-diameter beads were released from b_3 barrier and recaptured at b_4 barrier while 6.51 μm-diameter beads were still captured at b_3 barrier (Fig. 5b). At the pressure between 63~77kPa, the rest of 10.32 μm-diameter beads at b_3 barrier were completely released and recaptured at b_4 barrier as shown in Fig. 5c and d, and the 6.51 μm-diameter beads at b_4 barrier were released. Below 63kPa, 10.32 μm-diameter beads were released from b_4 barrier.

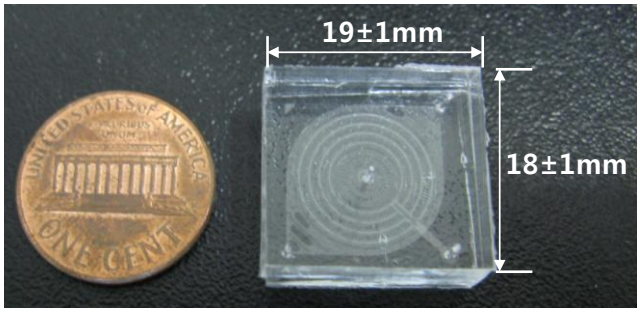

Figure 3. The fabricated chip.

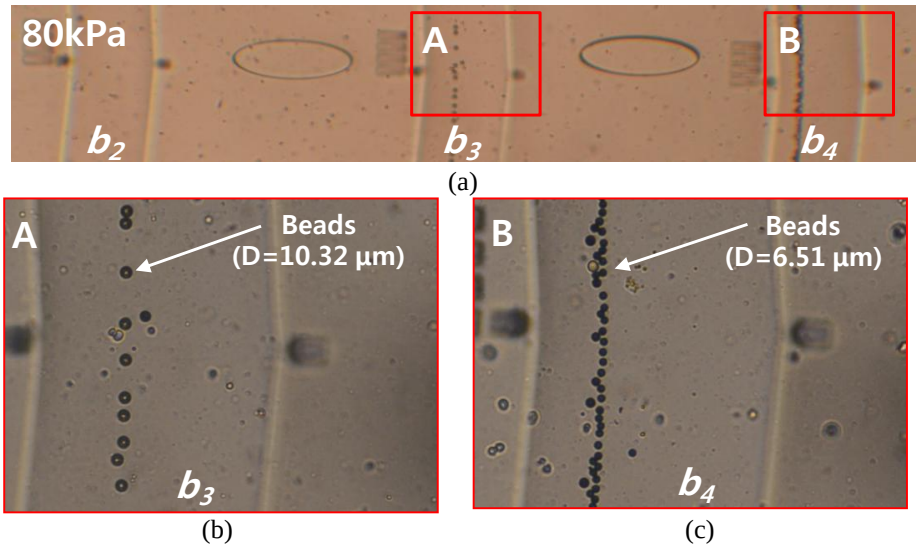

Figure 4. The beads captured by the variable membrane barriers: (a) top view of b_2~b_4 barriers; (b) enlarged view of A, showing b_3 barrier; (c) enlarged view of B, showing b_4 barrier.

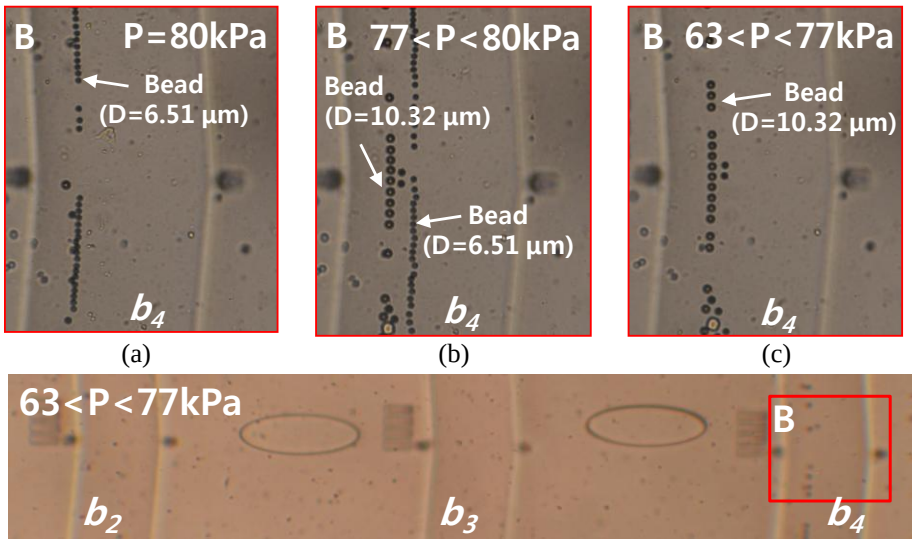

Figure 5. The beads released from the variable membrane barriers:(a-c) Enlarged view of b_4 barrier at the different pneumatic pressures (d) Top view of b_2~b_4 barriers at the pressure condition of (c).

CONCLUSION

We proposed the size-dependent cell capture and release chip using multiple variable membrane barriers. The present chip capable not only to capture cells according to its sizes, but also to release them in order, will be applicable for integrated cell analysis systems.

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