A SIMPLE YET EFFECTIVE MICROFLUIDIC SYSTEM FOR TRAPPING AND RELEASING SINGLE MICROBEADS

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ABSTRACT

In recent years bead-based microarrays have been widely used for biochemical applications due to several advantages (e.g, higher binding capacity, resettability, etc.) in comparison with static microarrays using biomolecules immobilized on a static solid surface as probe molecules. This paper introduces a simple yet effective microfluidic system with trapping and selective releasing of single microbeads for bead-based microarray applications. We suggest a simplified trap-and-release method that uses a pneumatically driven valve as a removable trap which allows both trap and release functions to be performed by a single component.

KEYWORDS: dynamic microarray, trap-and-release, single microbead, pneumatically-driven valve

INTRODUCTION

Recently, microfluidic-based trap-and-release techniques for single particles such as microbeads and biological cells have been developed to observe their dynamic responses and to sort particles of interest in continuous flow. For quantitative and high-throughput analyses, several groups introduced trap-and-release integrated dynamic microarray systems [1-3]. However, their systems require separate techniques (i.e., optical-based microbubble retrieval and dielectrophoresis) to achieve releasing capability and require somewhat complicated device fabrication. In this regard, we have proposed a hydrodynamic trap-and-release technique of single particles using dual-function pneumatic valves which are integrated into a single layer with a microchannel [4]. In this study, we propose a dynamic microarray system with an all-in-one valve system for high-throughput studies (e.g., screening and diagnostic). In addition, we suggest step-by-step movement of trapped microbeads for selectively retrieving microbeads of interest.

THEORY

Fig. 1 shows our trap-and-release mechanism of single microbeads. First, a sheath flow is used to regulate the position of introduced microbeads, aligning them onto the sidewall (Fig. 1a). Next, the microbead will go toward the pneumatically operated valve functioning as a trap because the center point of the microbead flows inside the main stream entering into the trap (Fig. 1b) [5]. Once the microbead is trapped, the virtual width (w_v) become wider than the microbead radius because of an increase of the hydraulic resistance toward the trap. Then, following microbeads flowing inside the virtual stream will enter the loop channel. In this way, traps are filled sequentially. Microbead release can be achieved simply by removing applied pressure as shown in Fig. 1c. Microbeads of interest can be selectively retrieved with the all-in-one valve system by re-trapping all released microbeads inside the following traps as shown in Fig. 1c and 1d. Selective retrieval can then be achieved by step-by-step movement of microbeads.

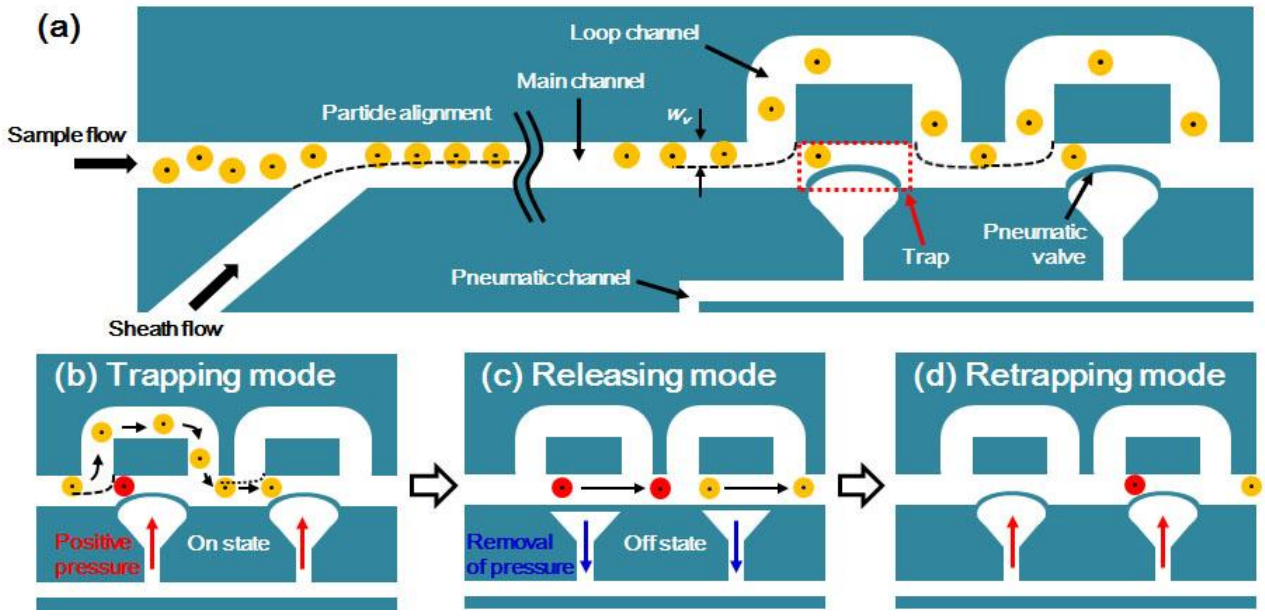

Figure 1. Schematic top views of trap-and-release mechanism of single microbeads. a) A Schematic view showing the microfluidic device consisting of multiple traps b) Trapping mode c) Releasing mode d) Re-trapping mode

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ANALYSIS

In our mechanism, the virtual width should be less than the microbead radius before a microbead trap. Additional inflow of sequential microbeads toward the trap should be blocked, so the virtual width after a microbead trap should be larger than the microbead radius. We developed a theoretical model to predict the virtual width to satisfy the mechanism. According to continuity equation based on conservation of mass, the virtual width is proportional to the flow rate entering into the loop channel. When the flow of a non-compressive Newtonian fluid is pressure-driven, steady and laminar, the flow velocity profile under aspect ratios above ~ 1 (i.e., channel height to width ratio) will be parabolic. Then, the virtual width can be expressed as a function of flow rates as follows:

$$2\left(\frac{w_V}{w_M}\right)^3 - 3\left(\frac{w_V}{w_M}\right)^2 + \frac{Q_L}{Q_M} = 0 \qquad (1)$$

where w_M is the main channel width, and Q_L and Q_M are flow rates entering into the loop channel and the main channel, repectively. From the Hagen-Poiseuille flow problem, the flow rate can be replaced by a pressure difference between channel ends and the hydraulic resistance of the micro-channel. Equation (1) can be then changed to a function of hydraulic resistances as follows:

$$2\left(\frac{w_V}{w_M}\right)^3 - 3\left(\frac{w_V}{w_M}\right)^2 + \frac{R_T}{R_T + R_L} = 0 \qquad (2)$$

where R_L and R_T are hydraulic resistances of the loop channel and the trap, respectively. After determining proper values of the virtual width depending on the microbead size, geometric dimensions can be determined from the required values of hydraulic resistances calculated from equation (2). (Note that the hydraulic resistance is a function of geometric shape and dimension of the micro-channel.)

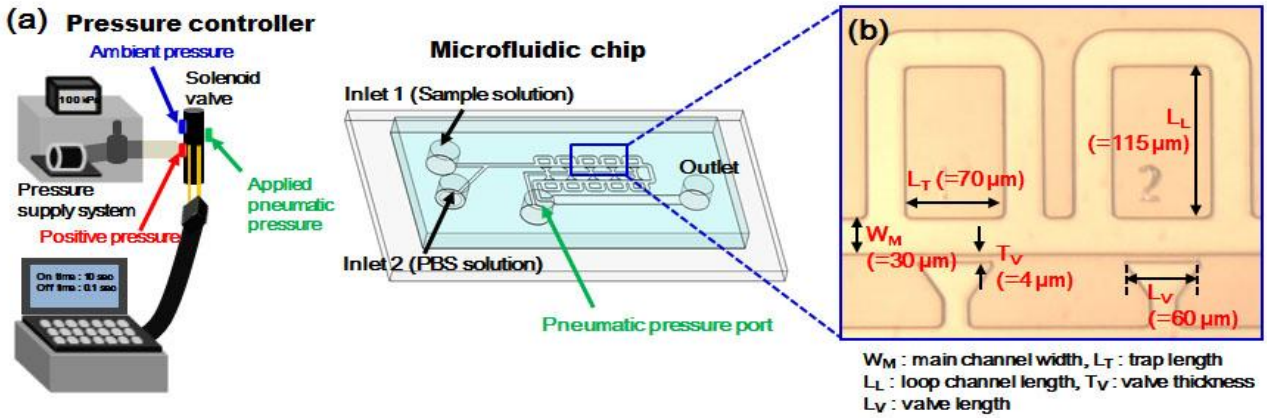

Figure 2. a) Experimental setup consisting of a pressure controller and a microfluidic device b) Close-up image of the boxed region in (a) showing geometric dimensions of the trap

EXPERIMENTAL

Fig. 2a shows the experimental setup which is composed of the pneumatic pressure controller and the polydimethylsiloxane (PDMS)/glass microfluidic chip. The pneumatic pressure controller provides electrical switching of application of either positive or ambient pressure. Geometric dimensions of the microfluidic chip are designed to sufficiently increase the value of the virtual width when the trap is filled (Fig. 2b), resulting in following microbeads bypassing through the loop channel.

RESULTS AND DISCUSSION

Fig. 3a shows successful trapping of single microbeads of 21 μm diameter when the applied pressure is 180 kPa, and sample and sheath flow rates are 100 μl/h and 300 μl/h, respectively. Furthermore, fig. 3b shows that our trapping mechanism offers high trapping efficiency for a single microbead array (N=60). For determining the conditions for re-trapping released microbeads, we characterized the relationship between the main flow rate and the duration of the "OFF" valve state (Table 1). As the main flow rate increased, shorter durations were required for re-trapping released microbeads at the next trap. Fig. 3c shows the re-trapping mode of a single microbead that is accomplished at a the main flow rate of 100 μl/h and a duration of 20 ms.

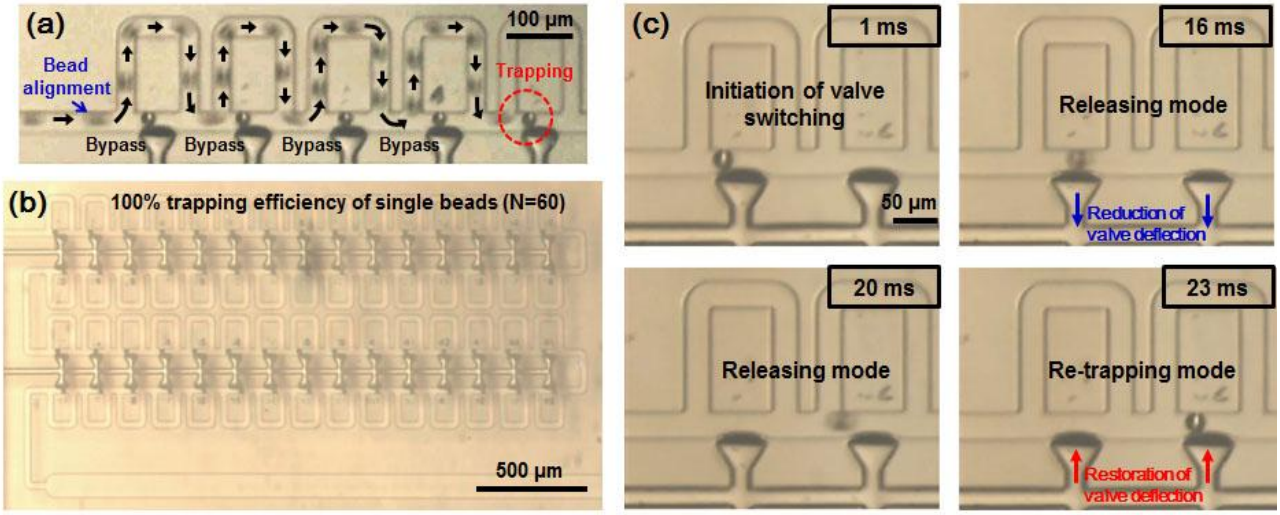

Figure 3. (a) Superimposed high-speed image of trapping mode of a single microbead (b) Single microbeads trapping experimental result (c) Sequence of high-speed images of re-trapping experimental result

Table 1. Relationship between main flow rate and duration of "OFF" valve state in re-trapping mode (× : no movement, ● : re-trapping at next trap, ○ : passage through next trap)

Flow rates [μl/h]	Duration of "OFF" valve state [ms]					
	10	20	50	80	110	140
10	×	×	●	●	●	○
100	×	●	○	○	○	○

CONCLUSION

We demonstrated a simple and novel method for trapping and selectively retrieving single microbeads in an array format. In this work, our microarray device was composed of 60 traps but more traps for quantitative assays can be integrated into a single device due to the independence of each trap. We believe that our method will provide a streamlined system with its integration of trap-and-release functions and simple fabrication procedure.

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