A RESETTABLE HIGH-DENSITY MICROFLUIDIC PARTICLE TRAPPING SYSTEM

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ABSTRACT

Microfluidic bead-based microarrays offer an ideal platform for chemical and biological applications, such as bio-molecule detection, diagnostics and drug screening. Despite the numerous advantages inherent to dynamic bead-based microfluidic arrays, current microparticle trapping methods remain limited in terms of trapping density and device resettability. Here we present a simple, resettable microparticle arraying system by utilizing geometric designs in microfluidics to manipulate microscale hydrodynamics. Under forward fluidic flow, arrays of individual 15 μm diameter microbeads immobilize in designated trapping positions between microposts. Under backward fluidic flow, the arrayed microbeads release rapidly to reset the microfluidic device.

INTRODUCTION

Dynamic Microarrays

There are two fundamental classes of microarrays: static and dynamic microarrays. Static microarrays consist of bio-molecules or chemicals immobilized on a static substrate [1]. Alternatively, dynamic microarrays consist of bio-molecules or chemicals immobilized on mobile substrates, such as microparticles (e.g. microbeads) [2]. Dynamic microarrays offer a superior platform compared to static microarrays due to several advantages, including faster reaction times due to larger surface areas of the microparticles, reduced background noise, and the ability to ‘mix-and-match’ particles corresponding to different screenings [3-5]. Also, the constant mixing of solutions and particulate substrates in

microfluidic channels results in faster reaction kinetics compared to the diffusion-based mixing of static systems. One caveat of particulate-based microfluidic platforms is that the microparticles must be visualized for signal detection (e.g. via flow cytometry). However, for systems that preclude expensive, high-maintenance flow cytometry equipment, alternative technologies are required to immobilize microparticles for signal detection.

Microparticle Trapping Techniques

Microfluidic particulate arraying methods provide an effective alternative to flow cytometry for bio-molecule detection applications [6]. Currently, there are a limited number of passive, hydrodynamic techniques for immobilizing microparticles [7-10]. For example, to immobilize cells, Khademhosseini et al. use microwells for cell docking [8], while Di Carlo et al. integrate elevated U-shaped ‘weir’ trapping structures into a microfluidic system [9]. In terms of microbeads, Kim et al. use microfilters composed of micropillars to immobilize microbeads [10]. Although the aforementioned techniques enable the immobilization of microparticles in microfluidics, they lack the ability to achieve high-density arrays of individual microparticles (i.e. without particle-particle contact). To independently array microparticles (i.e. one particle per trap), Tan et al. employ a ‘trap-and-release’ microfluidic system, and have demonstrated effective trapping of microbeads [3] and hydrogel-encapsulated cells [11]. To further improve microparticle trapping density of individual microparticles, we have previously presented a hydrodynamic

Figure 1: Conceptual illustrations of Resettable Micropost Array Trapping (μPAT). (A) Under forward fluidic flow, microparticles array at the designated trapping sites between microposts. (B) Under backward fluidic flow, microparticles release to reset the microarray. W_T and W_B denote the top width and the bottom width, respectively.

microbead trapping technique [12]. However, these techniques are limited in terms of device resettability. If resettability cannot be achieved, a new device is required for each particulate-based microarray run, which greatly increases the cost, time and labor associated with these dynamic microarray techniques.

Microparticle Release Techniques

Simultaneously achieving both high-density arrays of microparticles as well as microdevice resettability has remained a significant challenge [11-13]. Complex techniques have been implemented to release microparticles from trapping sites. For release during forward flow rates, lasers have been used to heat aluminum plates in order to generate microbubbles [3, 11]. As the bubble increases in size, the microparticle is displaced from the trapping site and re-enters the main fluid flow. This technique is ideal for releasing individual microparticles of interest; however, thermal bubble generation is inefficient for resetting an entire microarray (i.e. with thousands of arrayed microparticles). Furthermore, the trapping sites downstream from the released microparticle must be occupied; otherwise the particle will be re-trapped in a vacant downstream trap [3, 11]. For release during backward (alternatively reverse) flow rates, pneumatic valves have been employed to prevent the immobilization of particles at the backs of the original trapping sites to facilitate the release of microparticles [14]. Similarly, accurately placing microfeatures can also redirect microparticles for release during backward flow [13]. In contrast to the prior techniques, here we show that by tuning simple geometric microfluidic designs, both high-density particle trapping and device resettability can be accomplished.

MICROPOST ARRAY TRAPPING (μ PAT)

Microbead Trapping

The μ PAT technique consists of arrays of rectangular microposts which direct flow between the microposts to resolve trapping sites (Fig. 1A). Microbead trapping occurs under forward fluidic flow rates. Initially, flow between the microposts in the upstream area have lower fluidic resistance, which facilitates the transportation and immobilization of microbeads at the designated trapping sites. When microbeads immobilize at each trapping location, flow is diverted from the occupied trap, yielding increased flow rates to the remaining vacant sites. This process continues until beads are immobilized at all of the trapping sites, which redirects fluid flow, and therefore additional microbeads, to the next array of traps (Fig. 1A).

Microbead Release

Microbeads release under backward fluidic flow rates to reset the microfluidic device. Resettability is achieved through modifying two simple dimensions – the top width (W_T) and the bottom width (W_B). Initially, the microbeads are released from the trapping sites. When the microbeads enter other arrays of traps, the microbeads bypass all of the traps instead of re-arraying at the bottom side of the traps. By directing microbeads to an outlet location, the device can be reset for additional experiments with new sets of microbeads, thereby enabling the use of a single microdevice for multiple bead-based experiments.

DESIGN

The foundation of resettable μ PAT is that for an equivalent input flow rate, W_T and W_B can be tuned to control both the trapping mode and the resetting mode for an array. Specifically, the microchannel widths must be optimized to ensure that microbeads ultimately: (i) immobilize in the designated trapping

Figure 2: Two-dimensional COMSOL Fluid Velocity Field Simulations and Conceptual Schematics of Fluidic Forces on Microbeads for Resettable μ PAT. (A) Trapping Case. (B) Resetting Case. W_T and W_B denote the top width and the bottom width, respectively. The magnitude of the input velocity is 7.83×10^{-3} m/s for both cases.

sites for the trapping mode, and (ii) bypass the back (bottom) sides of the trapping sites for the resetting mode. For the trapping case, W_T must be high enough such that the fluid flow bypassing a trapped bead does result in the bead being displaced from the trap

(Fig. 2A). However, if W_T is too high, microbeads will not bypass the occupied trapping sites and instead array on top of previously trapped beads, resulting in bead-bead contact. For the resetting case, W_B must be minimized to increase the fluidic forces in the microchannel to prevent microbeads from immobilizing at the back sides of trapping sites (Fig. 2B). However, the minimization of W_B is limited by the polydispersity of the microbeads. Additionally, altering either microchannel width directly impacts the overall flow pattern. Thus, in order to optimize the μ PAT system to achieve both modes, both W_T and W_B must also be tuned with respect to each other.

FABRICATION

The resettable μ PAT systems can be manufactured using a number of high-aspect ratio microfabrication techniques to fabricate devices in a material of choice (e.g., glass, polymers, etc.). For this study, the μ PAT systems were fabricated via standard photolithography and soft lithography methods. Briefly, an 18 μ m layer of SU-8 negative photoresist was spin-coated onto a clean Si wafer. Using a photomask, the μ PAT and microchannel patterns were UV exposed onto the layer of photoresist via contact photolithography. The wafer was then developed to become a positive master for the micromolding process. Next, the silicone elastomer, polydimethylsiloxane (PDMS), was mixed at a 10:1 ratio and poured onto the master. After curing of the PDMS, the elastomer was removed from the master. Individual devices were cut and then punched with holes at inlet and outlet locations. Glass slides were washed in successive dishes of Acetone, Isopropanol and DI water, while the PDMS devices were washed in successive dishes of Isopropanol and DI water. The glass slides and PDMS devices were dried with a Nitrogen gun, and then exposed to UV ozone. Lastly, the PDMS devices were thermally bonded to the glass slides. For the current μ PAT system, the microposts were 15 μ m in width and length, and 18 μ m in height.

RESULTS

Resettable μ PAT was achieved as microbeads immobilized at the designated trapping sites under forward fluidic flow rates, and released from the trapping sites to reset the microarray under backward fluidic flow rates (Fig. 3). Experimental results for μ PAT resettability corresponding to differing dimensions of W_T and W_B are shown in Figure 4A. For cases where W_B was too high (i.e. $W_B \geq 30$ μ m), microbeads ultimately immobilized at the back of the trapping sites when the flow was reversed (Fig. 4). However, one of the results of decreasing W_B is that the fluidic shear stress at the edge of microbeads located at the back of the trapping sites can be increased (Fig. 2B). By reducing W_B , microbeads were transported in the direction of the shear stress, ultimately bypassing the potential trapping sites located at the back sides of the traps to reset the microdevice (Fig. 3 and Fig. 4A). This also provides insight into the observation that for cases with higher fluid flow rates, and therefore higher fluidic shear stresses, device resettability was enhanced (Fig. 4). By adjusting W_T and W_B such that $W_T = 45$ μ m and $W_B = 25$ μ m, 100% device resettability was accomplished (Fig. 3 and Fig. 4A).

CONCLUSIONS

In this work, we have successfully demonstrated our novel resettable hydrodynamic microparticle immobilization technique – μ PAT – for achieving: (i) high-density and high-throughput arraying of microbeads, and (ii) microarray resettability for a microfluidic device. High-density trapping enables the acquisition of high numbers of data points (i.e. immobilized microparticles)

Figure 3: Sequential Micrographs of μ PAT Resetability. Under backward fluidic flow, microparticles release to reset the microarray. Scale Bar = 100 μ m

from a single experiment, without sacrificing device ‘real-estate.’ Microdevice resettability is particularly advantageous since multiple bead-based experiments can be run using a single microfluidic device, thereby significantly reducing the costs, time and labor associated with fabricating multiple devices. Here we tune simple geometric dimensions in microfluidics to array and immobilize microbeads under forward fluidic flow rates, and release the microbeads to reset the arrays under backward fluidic flow rates. While the current system was designed to array 15 μ m diameter microbeads, the μ PAT technique offers a scalable methodology for trapping and releasing particles of any size. Thus, for chemical and biological applications, such as biomolecule detection, diagnostics and drug screening, where dynamic particulate-based microfluidic platforms are ideal, our system offers a simple, yet powerful technique for realizing resettable, high-density microparticle arraying.

Figure 4: Microdevice Resetability. (A) Percentage of vacant sites located at the back (bottom) sides of trapping sites during backward fluid flow rates of 0.03 $\mu\text{l/min}$ (black) and 0.16 $\mu\text{l/min}$ (gray) for μPAT with differing geometric dimensions. 100% = Full Microdevice Resetability. (B) Microphotos of microbeads immobilized at the back sides of trapping sites during backward fluid flow rates for μPAT with differing geometric dimensions. W_T and W_B denote the top width and the bottom width, respectively. Scale Bar = 100 μm

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