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DEP CHIP WITH PLANAR MICROELECTRODES ARRAY FOR BIOPARTICLES SEPARATION

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Abstract

This paper presents a microfluidic chip with arc-shape electrode array (ASEA) for separation of different-size particles/Cells based on negative dielectrophoresis (DEP). The DEP chip consists of two parts: first part is a two-channel flow system for focusing particles by a shear flow before enter the ASEA region; the second part is a straight microchannel with several pairs of arc-shape electrodes for generating the dielectrophoretic force perpendicular to the microchannel direction within the each gap between two arc-shape electrodes. The DEP force as a external force for a floating particle, the dielectrophoretic velocity is proportional to the particle size and the gradient of the square of electric field, ∇E^2, from the equilibrium of dielectrophoretic force and viscous drag force under fixed medium conductivity. If the variation of ∇E^2 across the microchannel can be reduced by electrode design, the separation effect thus only depends on particle size. In order to construct such condition of electric field, three typically electrode shapes, trapezoidal shape, convex-arc shape and concave-arc shape, were investigated by numerical simulation. As the simulation results, a convex arc-shape electrode can provide better separation effect due to the larger effective area of DEP force and relative small variation of ∇E^2. Currently, the ASEA and SU-8 microchannel have been fabricated by conventional photolithograph. And, the vertical DEP force was experimentally demonstrated by separation of 19 μm and 8μm Latex beads. The separation function will be further examined by 19 μm and 8 μm Latex beads for the practical case of bladder cancer cells and blood cells. This method can provide a continuous and high throughput separation of different-size bioparticles once they have similar dielectric properties that cannot separated by traditional DEP approach.

Introduction

The separation of different cell subpopulations is one of the fundamental procedures for following processing such as cell culture, cell therapy, diagnostics, and cytological studies in clinical field. For example, a urine sample from a bladder cancer patient usually contains normal and abnormal upper urinary epithelial cells, blood cells and impurities, therefore, the most important procedure is to separate these different kinds of cells for evaluation of cancer stage by cytology. Unfortunately, these cells usually possess quite similar dielectric properties so that cannot easily divide them into different parts by acting positive and negative dielectrophoretic force on different kind of cells, respectively. However, normal and abnormal cancer cells usually have significant difference in the size. Consequently, if a dielectrophoretic separation only depends on the size of particles, the limitation of requiring sample preparation steps like labeling of marker and the problem of sensitive to the medium conductivity can be avoided. The dielectrophoretic velocity for a particle floating in the microchannel can be expressed as from the equilibrium of dielectrophoretic force and viscous drag force; therefore, the velocity is proportional to the square of particle radius if the gradient of the square of electric field keeps constant. According to this theory, S-Y Choi [1] proposed a novel microfluidic device with trapezoidal electrode array for particle separation based on dielectrophoretic force; however, the effective area of DEP force was limited within the small area at top of electrode due to the decreased dramatically across the microchannel, which makes the separation effect only appeared at the front trapezoidal electrode in the array. In order to construct a nonuniform electric field for generating effective DEP force across most area of microchannel, we introduced the convex arc-shape electrode array (ASEA) and examined the capability by numerical analysis and experimental observation.

Experimental

The schematic view of a DEP chip with convex ASEA for generating different DEP velocity for different size particles was illustrated as Fig. 1. Particles were firstly focused by a shear flow, then, were separated by DEP force perpendicular to the microchannel direction. Three kinds of electrode array were investigated here by CFD-ACE+ simulation: (a) trapezoidal; (b) convex arc-shape electrode and (c) concave arc-shape electrode; the width and the distance between two electrodes at top in these models are the same as 60μm and 20μm, respectively. The purpose to understand the effects of electrode shape on resulting electric field. The dimension of each kind of electrode shape and the corresponding electric field were shown in the Fig. 2 and Fig. 3, respectively. The nonuniform electric field resulted in a DEP force perpendicular to the flow direction in the microchannel. The suspending particle will be move to the bottom of ASEA where possessed the lowest electric field as a negative DEP force acting on it. In addition, the electric fields for either trapezoidal or concave arc-shape electrode decreased rapidly as away from the top of electrode. As shown in the Fig. 4, the variation of ∇E^2 across the microchannel for convex ASEA was much smaller than others, which means the effective area of DEP force can be expended to whole microchannel and the ∇E^2 can keep an acceptable range to achieve the separation effect via particle size only. The microfluidic chip was fabricated by using SU-8 and conventional photolithography as illustrated in Fig. 5. There were eight pairs of electrodes in a 200μm width microchannel, and the distance between each electrode was 50μm. The experimental setup of DEP chip with arc-Shape microelectrode array for separation of different-size particles are shown in Fig. 6. A DEP chip with arc-shape electrode array (ASEA) whose width and the distance between two electrodes are 200μm and 50μm, respectively, was examined to separate 19 μm and 8μm particles in Fig. 7. Firstly, we used DI water to flash the flow chamber under high flow rate 1 ml/hr about 1 minute in order to remove the impurities and fulfill the medium in the flow chamber. Then, the particles immersed in DI water and pumped into the flow chamber by syringe pump (KD-210, KD Scientific, Holliston, MA) under 0.06 ml/hr about 1 minute in order to steady flow rate as Fig 7(a). After these suspension particles flowed over the ASEA in the flow chamber, the AC function generator (Agilent 33220A, San Diego, CA) began to apply with 10 Vpp and 50 KHz on the electrode. Particles began to move toward the region of electric field minima by negative DEP force.

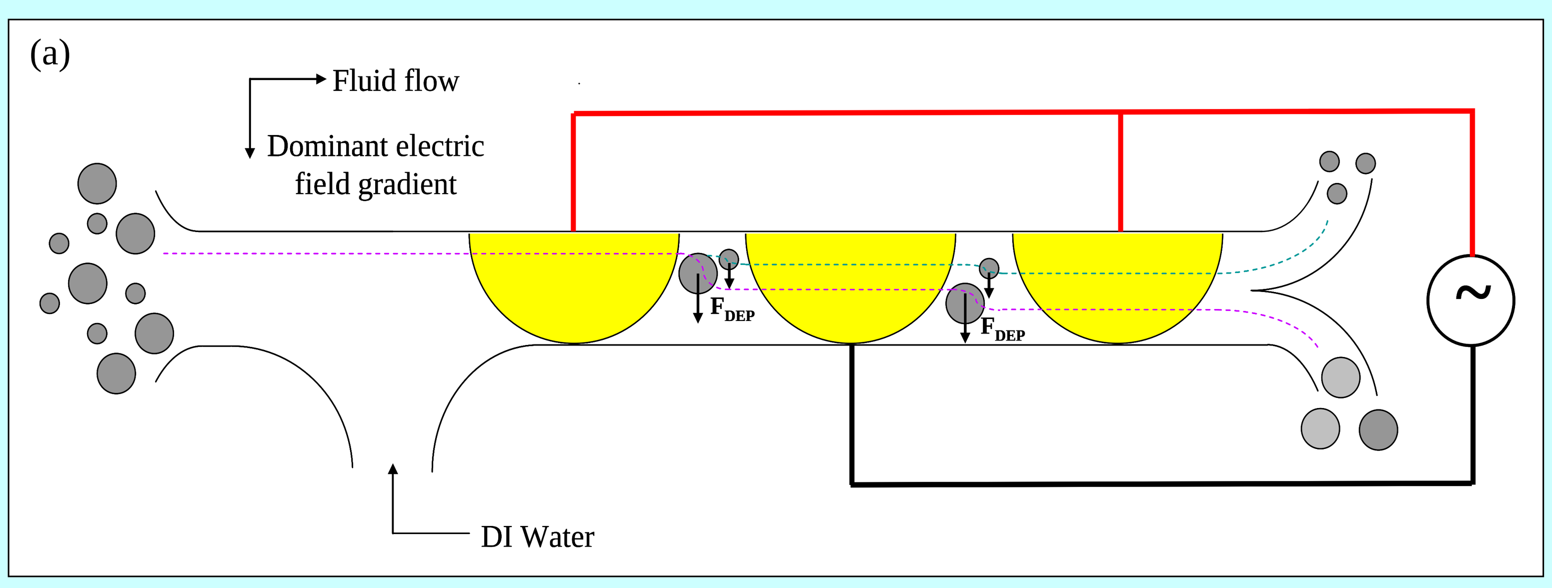

Fig.1. Schematic picture of an arc shape electrode array (ASEA) and its DEP separation. Different size particles are focused by a shear flow before they are separated by a DEP force perpendicular to flow stream between a pair of arc shape microelectrodes. The DEP force acting on the particles depends on the size and the position.

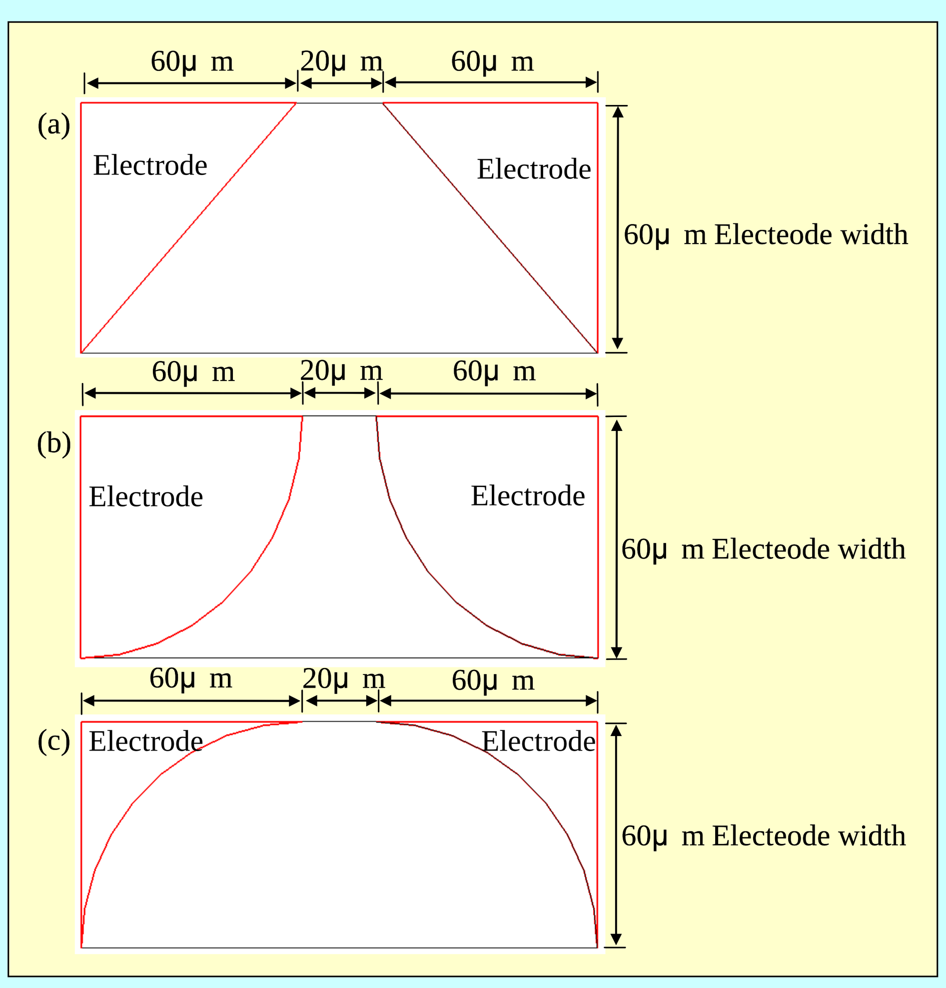

Fig. 2. Three kinds of ASEA design were utilized for numerical simulation.

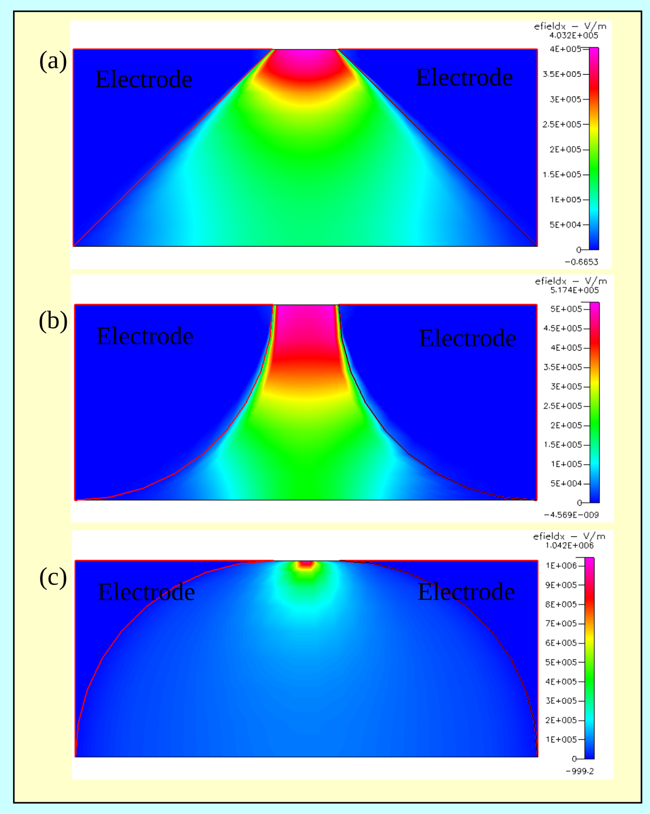

Fig. 3. The density of electric field for 2D models of (a) trapezoidal; (b) convex arc shape electrode and (c) concave arc shape electrode

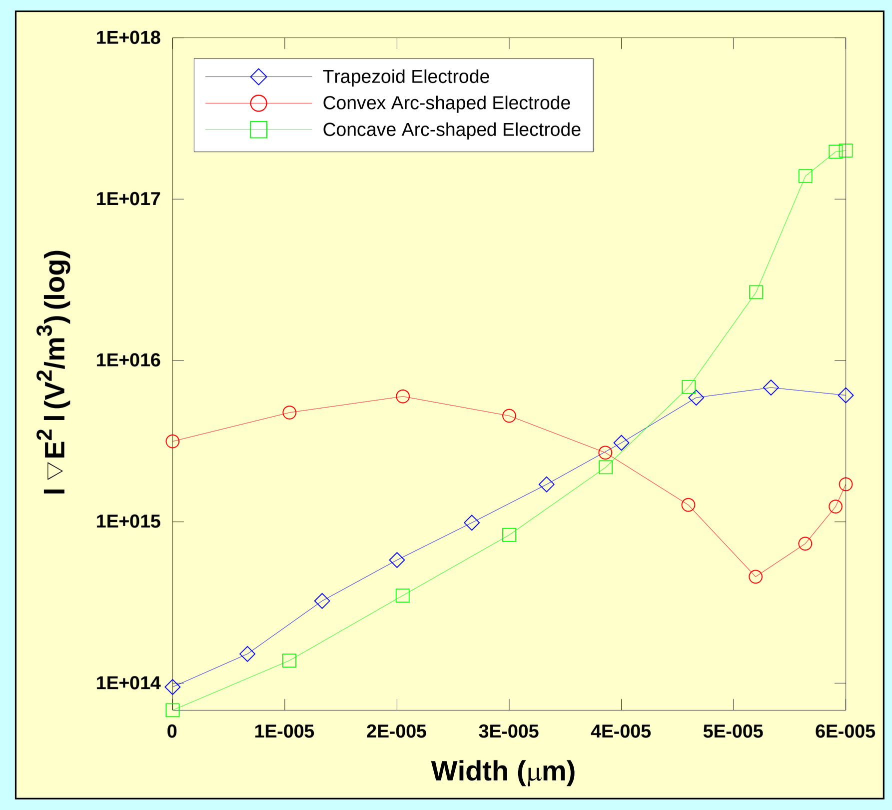

Fig. 4. The gradient of the square of electric field ,∇E^2, along the vertical centerline between two electrodes.

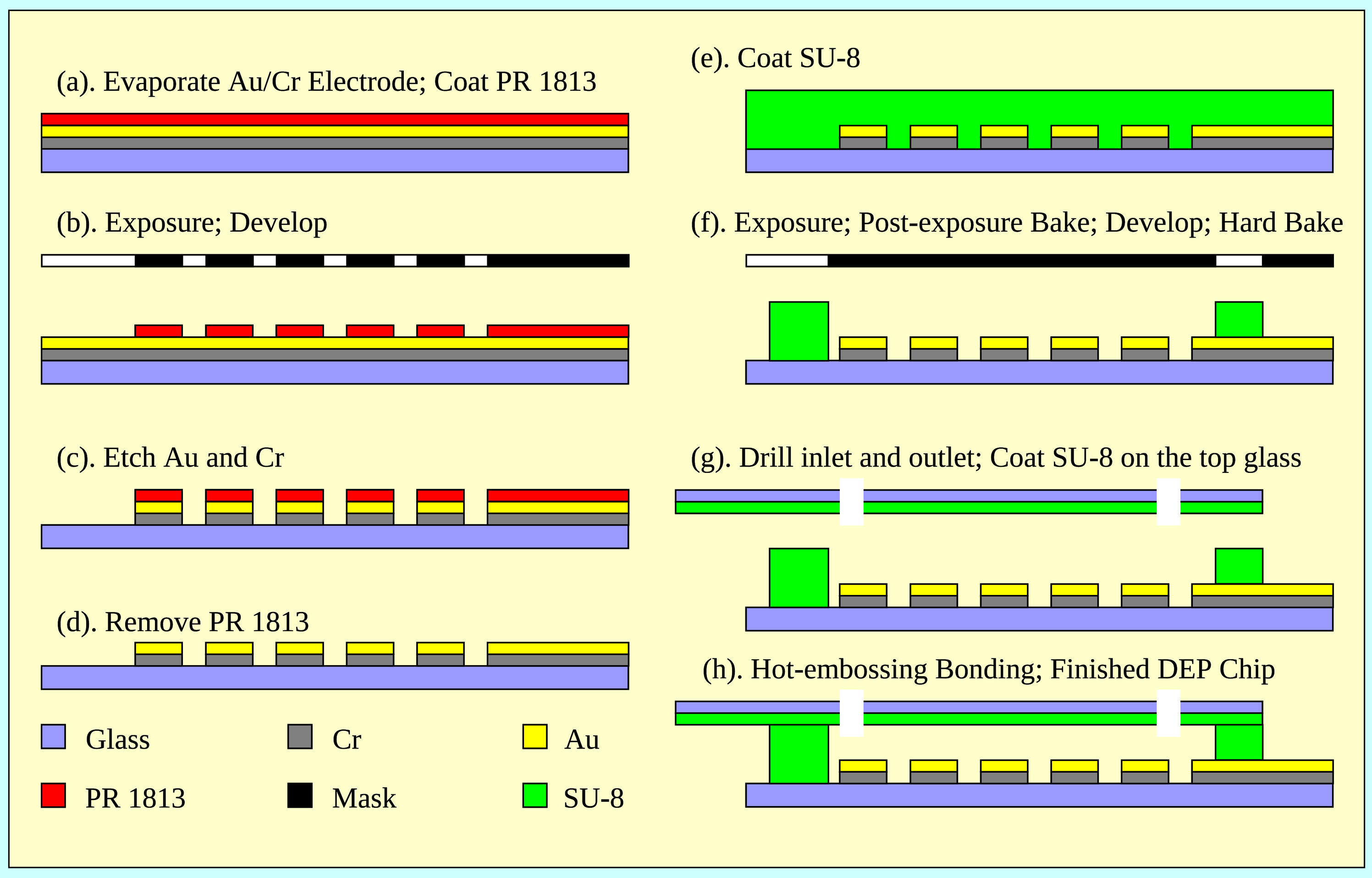

Fig. 5. The micro-fabrication process of DEP chip with arc-Shape microelectrode array.

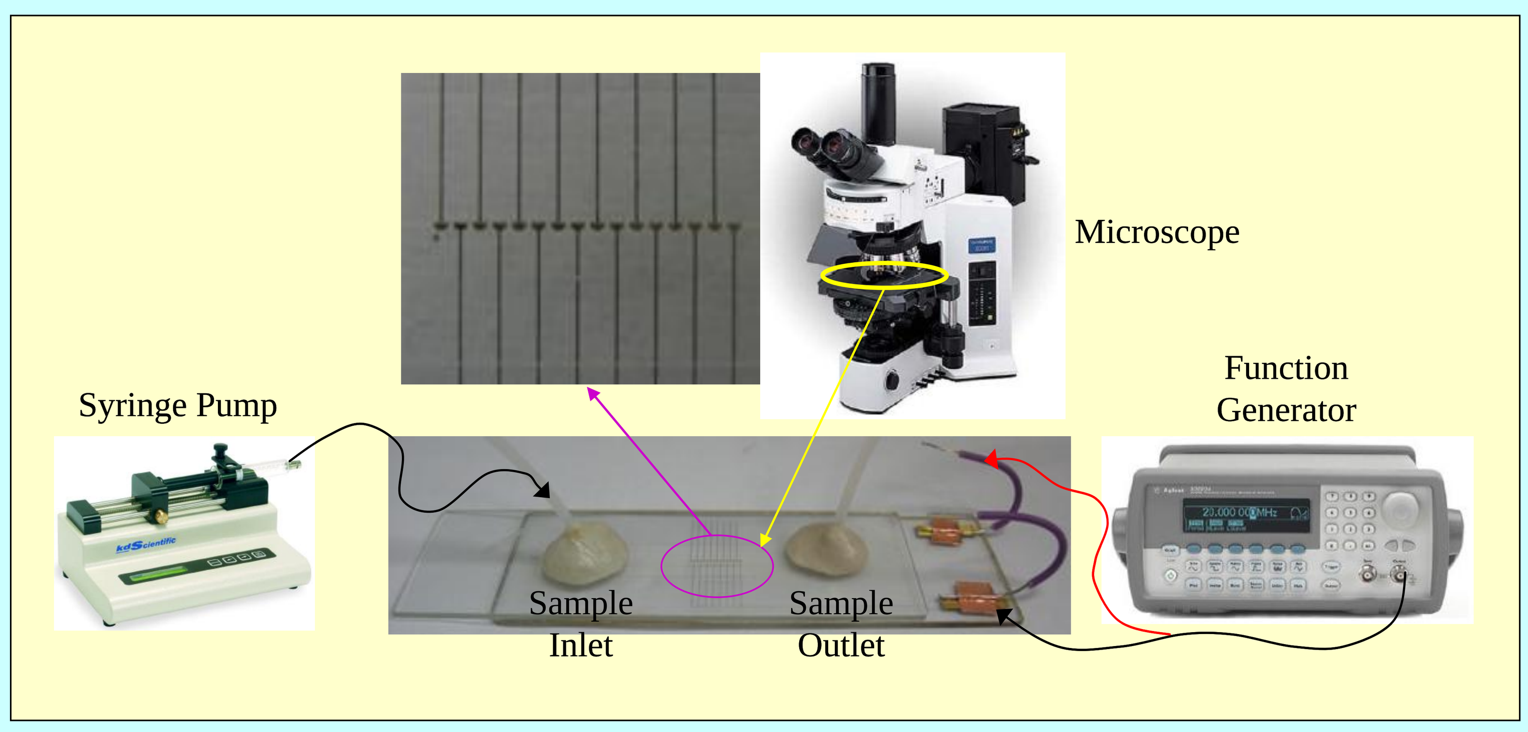

Fig. 6. Experimental setup of DEP chip with ASEA for separation of different-size particles.

Results and Discussion

The experimental results demonstrated that the different-size latex beads could be separated by negative dielectrophoretic force in ASEA at voltage of 10 Vpp, frequency of 50 KHz and flow rate of 0.06 ml/hr from flowing fluid as shown in Fig. 7(b). According to the DEP theory, the particle size can influence magnitude of the DEP force, which means the particle with larger dimensions (19μm) would produce the stronger DEP force on this electrode array, thus, the larger particles could be rapidly moved to the region of electric field minima by negative DEP force. However, the smaller particles not yet reach to the region of electric field minima after eight pairs of convex arc-shape electrodes.

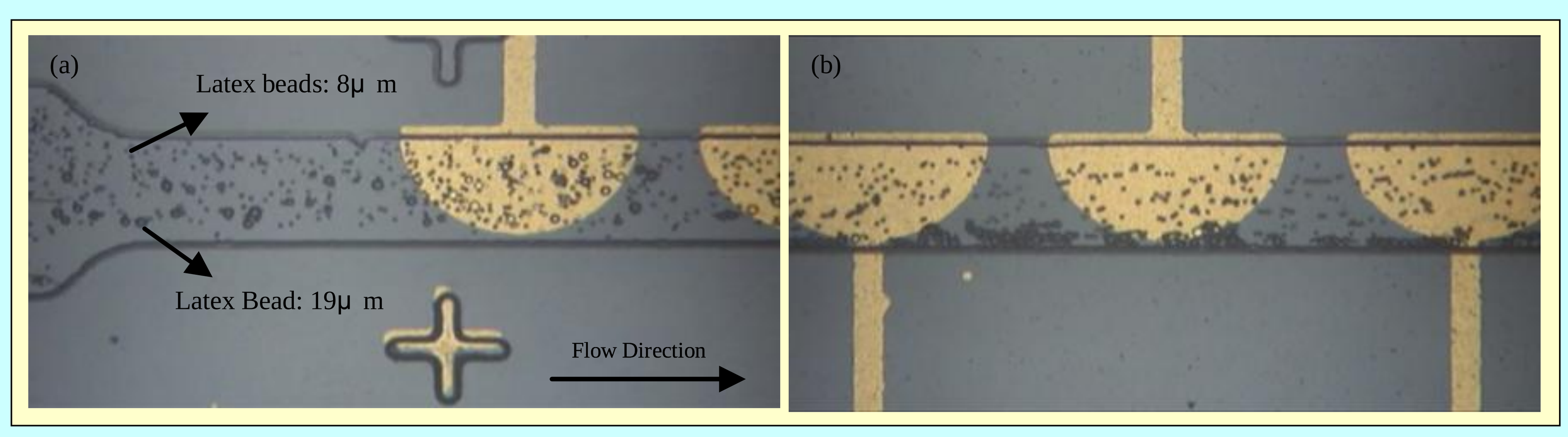

Fig. 7. The optical microscope images of separation of different-size latex beads in ASEA for 25 seconds by negative DEP forcat voltage of 10 Vpp, frequency of 50 KHz and flow rate of 0.06 ml/hr. The latex beads size are 16μm and 9μm, respectively

Conclusion

In this study we have presented the design, simulation, fabrication and measurement of a microfluidic DEP chip with convex-arc shape electrode array (ASEA) for separation of different-size particles. The simulation showed a convex arc-shape electrode can provide better separation effect due to the larger effective area of DEP force and relative small variation of ∇E^2 as the applied AC voltage produced a non-uniform electric field within it. The experimental results also demonstrated that the different-size latex beads could be separated by negative dielectrophoretic force in ASEA from flowing fluid. Besides, the negative DEP force was demonstrated by repelling 19 μm Latex beads to the region of electric field minima at voltage of 10 Vpp, frequency of 50 KHz and flow rate of 0.06 ml/hr after four pairs of convex arc-shape electrodes. The effects of flow rate and the numbers of electrode for separation of different size of bioparticles, such as bladder cancer cells and blood cells will be examined in the future.