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Electrodynamically actuated on-chip flow cytometry with low shear stress for electro-osmosis based sorting using low conductive medium

Srinivasu Valagerahally Puttaswamy [a], Shilpa Sivashankar [a], Chia-He Yeh [b], Rong-Jhe Chen [a], Cheng Hsien Liu [a,b,*]

[a] Department of Power Mechanical Engineering, National Tsing Hua University, Taiwan
[b] Institute of NanoEngineering and Microsystems, National Tsing Hua University, Taiwan

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ABSTRACT

In the proposed paper, we demonstrate on-chip electrodynamically driven actuator flow cytometry, based on negative dielectrophoretic (nDEP) focus and alternating current electro-osmotic flow (ACEOF) sorting technique. This single chip can perform three different functions such as focusing, transportation of beads/cells to detection site and reloading the unsorted ones with two distinctive phenomena. AC EOF is achieved by the design of the asymmetric electrode pair's array and nDEP is used to focus the beads/cells in-line. The design, simulation and experimental results of the proposed microchip are reported in this paper. The simulation and experimental results reveal well defined stable region for nDEP and ACEOF driving force. The potential severe shear stress damage caused by the sheath flow in conventional flow cytometry is eliminated. In addition, to explore the influence of conductivity of the medium, we have used low conductive formulated medium with conductivity of 81.4 μS/cm. The voltage and the frequency required to manipulate the particles decreased comparatively with the use of this medium.

1. Introduction

Flow cytometry is a powerful technique for the analysis of multiple parameters of individual cells within heterogeneous populations. The analysis is performed by passing thousands of cells per second through a laser beam and capturing the light that emerge from each cell as it passes through. The information regarding the size, type and content of cells can be derived through analysis of scattered light arising from individual cells. Flow cytometry has been used in applications such as immunology [1,2], cancer biology [3,4]. However, for environmental and clinical applications microflow cytometry is the preferred diagnostic tool [5–10]. Many flow cytometers have been fabricated using microsystem technologies among which, some use sheath flows while; others use sheathless flow for focusing [11].

Dielectrophoresis (DEP) is the movement of cells in non-uniform electric field. When the particle is more polarisable than the immersion medium, the resulting force will direct particles towards regions of electric field maxima at electrode edges. This phenomenon is known as positive dielectrophoresis (pDEP). The nDEP occurs when the cell is less polarizable than the suspending medium in a non-uniform electric field, and describes the movement of particles away from high field regions. Under, nDEP the particles are repelled by the electrodes and restricted to an area of low electric field between them. DEP finds a wide range of applications [12] such as, separation and isolation of cells [13,14], cell handling prior to electro fusion [15] or cell sorting [16]. The side effect of DEP is the temperature increase in the high conductivity medium in which the cells are suspended to disturb a favorable cellular environment [17]. The high conductivity medium requires high electric-fields environment to manipulate the beads/cells which might lead to a variety of profound biochemical and biophysical effects, such as apoptosis and cell-lyses [18].

EOF is the motion of liquid, induced by an applied potential across a capillary tube or microchannel. The cause of EOF is an electrical double layer (EDL) that forms at the stationary/solution interface. An electrical potential gradient arises in the vicinity of the solid–liquid interface due to the presence of net charge density. The region containing this electrical potential gradient is called EDL. When an external electrical field is applied to the liquid along the microchannel, the excess cations in the diffuse layer (mobile part) of the EDL will move towards the cathode. Because of the viscous force, these moving cations will drag the surrounding liquid to move with them and thus, result in the motion of a bulk movement. Because thickness of EDL compared with the channel dimension is very thin, the velocity profile of liquid flow is plug-like in the fully developed region. This is so-called EOF in which mean velocity is independent of the cross-sectional area of the channel.

* Corresponding author at: Microsystems and Control Laboratory, Department of Power Mechanical Engineering, National Tsing Hua University, Hsinchu 300, Taiwan. Tel.: +886 3 5715131x33706.
E-mail address: liuch@pme.nthu.edu.tw (C.H. Liu).

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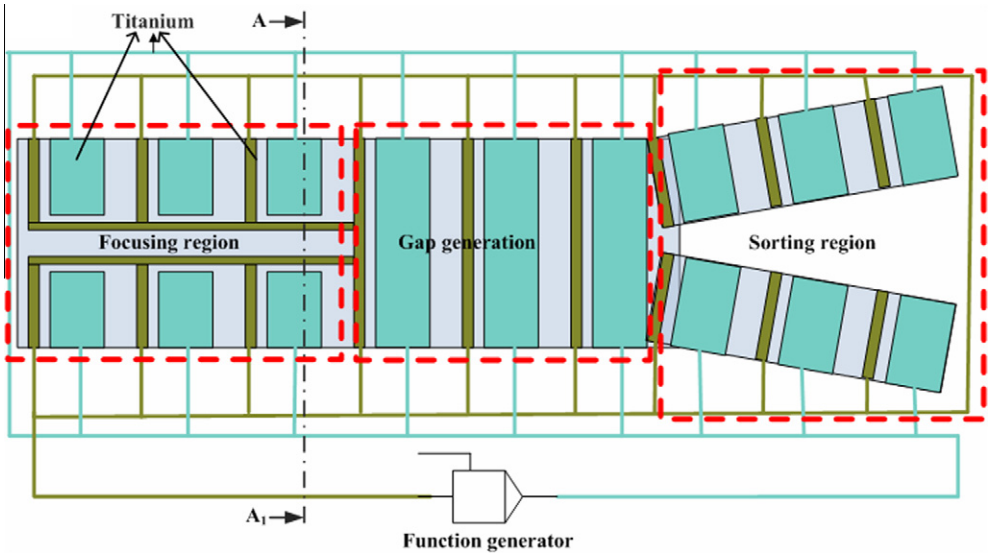

Fig. 1. Schematic diagram of the microchip representing the three regions performing three different functions.

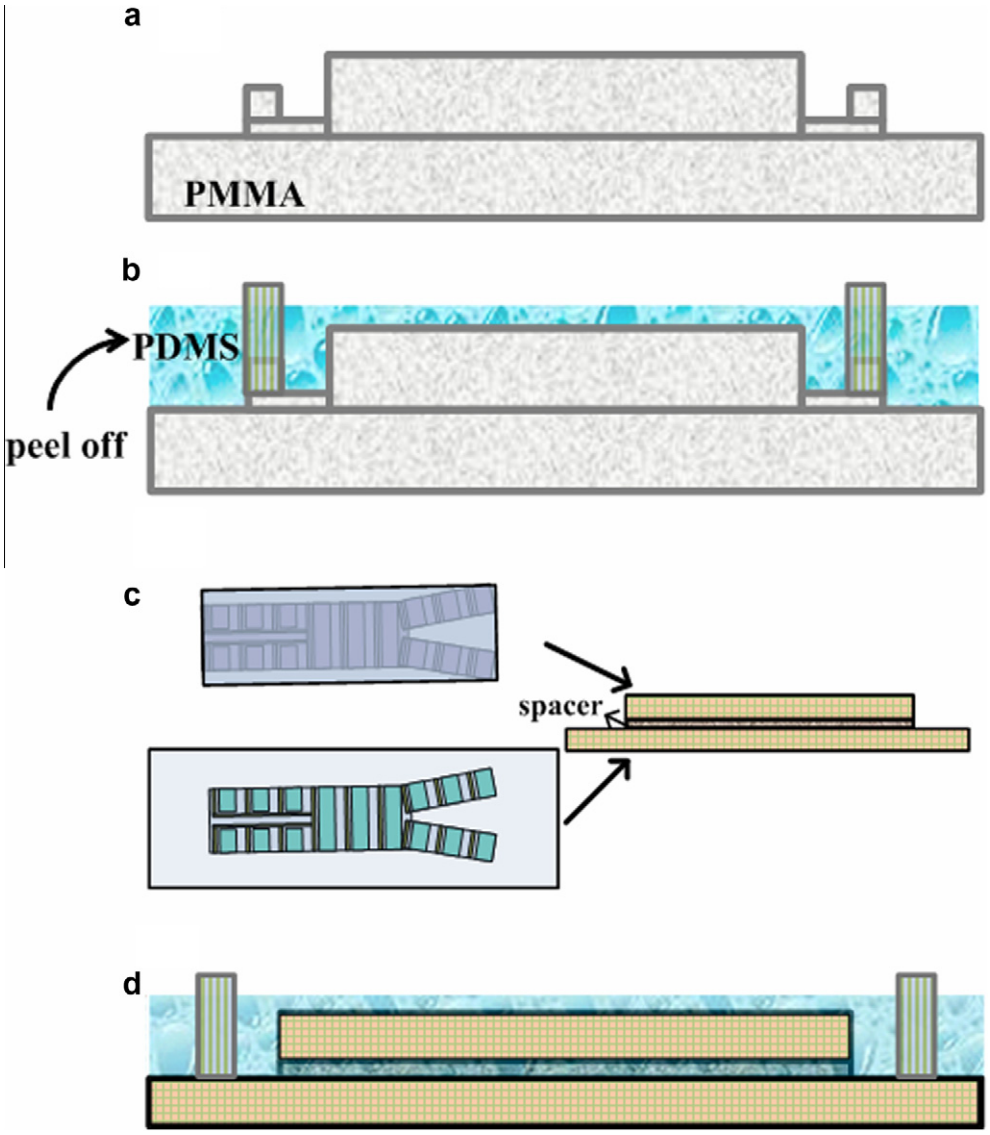

Fig. 2. Fabrication process of the device. (a) Engraved PMMA master mold. (b) PDMS poured on PMMA master mold. (c)The two identical glass substrates are placed one above the other with a PDMS spacer to enhance EOF and nDEP phenomena. (d) PDMS layer permanently bonded with the glass substrate after O_2 plasma treatment.