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Dielectrophoresis based cell switching in continuous flow microfluidic devices

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ABSTRACT

This article presents a novel negative-dielectrophoresis based approach for switching of a focused stream of micro-sized particles, including cells, to desired locations inside a continuous flow microfluidic device. The first section, of the device, focuses the incoming stream of micro-sized particles while the second section switches this focused stream of micro-sized particles. The microfluidic device consists of a glass substrate and a PDMS layer. The microfluidic device is realized using standard microfabrication. Tests are carried out using blood cells to demonstrate the efficacy of the approach in switching a stream of micro-sized particles to multiple locations inside the microchannel.

1. Introduction

Microfluidic devices are used for several engineering applications including separation/sorting of desired micro-sized particles from a heterogeneous mixture of the same [1,2]. Several actuation mechanisms, including dielectrophoresis (DEP), is employed for this purpose. Dielectrophoresis (DEP) is the movement of dielectric micro-sized particles, including cells, towards the maxima or minima of a non-uniform electric field [3–6]. When micro-sized particles move towards the maxima and minima then it is specifically known as positive-DEP (pDEP) and negative-DEP (nDEP), respectively [3,7]. Parameters such as conductivities and permittivities, of the medium and micro-sized particle, as well as the operating frequency influence the preference of micro-sized particles for the extremum of the electric field. The combined influence of these parameters on the preference of micro-sized particles regarding the extremum of the electric field is included in the Clausius-Mossotti (CM) factor; micro-sized particles experience pDEP and nDEP when the CM factor is greater and smaller than zero, respectively. When the above mentioned material properties are held constant, then the change in frequency alters the preference of micro-sized particle for the extremum of the electric field. The frequency at which the micro-sized particle neither experience pDEP nor nDEP is referred to cross-over frequency. Equations (1) and (2) provide the mathematical formulation for the force associated with DEP and CM factor, respectively [3,4]. Both direct current (DC) and alternating current (AC) can be employed for creating the non-uniform electric field necessary for realizing DEP. In the case of DC-DEP the CM factor just depends on the conductivities of the micro-sized particle and the medium as can be inferred from Eq. (2). For AC-DEP, the CM factor depends on both conductivities and permittivities. Nevertheless, at very low ($\omega \rightarrow 0$) and high ($\omega \rightarrow \infty$) operating frequencies the CM factor can be reduced to being function of conductivities and permittivities, respectively.

$$\boldsymbol{F}_{DEP} = \pi \varepsilon_m r_p^3 \, Re[f_{CM}] \left[\left(\vec{i} \frac{\partial}{\partial x} + \vec{j} \frac{\partial}{\partial y} \right) \left(\boldsymbol{E}_x^2 + \boldsymbol{E}_y^2 \right) \right] \tag{1}$$

$$f_{CM} = \frac{(\varepsilon_p - \varepsilon_m) - (\sigma_p - \sigma_m)\frac{j}{\omega}}{(\varepsilon_p + 2\varepsilon_m) - (\sigma_p + 2\sigma_m)\frac{j}{\omega}} \tag{2}$$

Where $\boldsymbol{F}_{DEP}$ (N) is the dielectrophoretic force vector, ε_m (F/m) is the permittivity of the medium, ε_p (F/m) is the permittivity of the micro-sized particle, σ_m (S/m) is the electrical conductivity of the

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medium, σ_p (S/m) is the electrical conductivity of the micro-sized particle, r_e (m) is the radius of the micro-sized particle, f_{CM} (−) is the CM factor, E_x (V/m) is the electric field in the x-direction, and E_y (V/m) is the electric field in the y-direction.

Focusing is a unit operation that is commonly employed in microfluidic devices and it refers to the alignment of randomly ordered micro-sized particles, Fig. 1 a [8]. When the randomly ordered micro-sized particles present in a microchannel are arranged in a plane (vertical or horizontal) then focusing is specifically termed as 2D focusing. Meanwhile, when micro-sized particles present in a microchannel are arranged as a single file then this particular focusing is termed as 3D focusing. Focusing can be realized in microfluidic devices using different actuation mechanisms including dielectrophoresis (DEP), surface acoustic waves (SAW), and hydrophoresis [8].

Switching is another important unit operation in the field of microfluidics and it refers to diverting a stream of heterogeneous/homogeneous micro-sized particles, including cells, towards a desired location within the microchannel as depicted in Fig. 1 b; switching is always performed on a focused stream of micro-sized particles. Review of existing literature reveals that switching and sorting/separation are interchangeably used to refer to the unit operation of splitting of a heterogeneous sample of micro-sized particles into multiple homogenous samples of the same [9–13]. In this article switching solely implies the unit operation depicted in Fig. 1 b and does not constitute splitting a heterogeneous sample into multiple homogeneous samples. Switching is always performed on a focused stream of micro-sized particles so that they experience the same actuation force and in turn undergo equal displacement; thus all switching devices employ focusing. Switching is employed in microfluidic devices for primarily biomedical applications such as medium exchange, washing, and surface functionalization [14–18]. Researchers have employed different actuation mechanisms, including DEP, SAW, and hydrophoresis, to realize switching [17,19]. Employing DEP instead of SAW and hydrophoresis for switching has the advantage of not requiring specialized wafers and sheath flow, respectively [20].

Takahashi et al. [21] demonstrated switching of a hydrodynamically focused stream of polystyrene micro-sized particles between two downstream outlets using DC-DEP. A single pair of finite sized Pt/Ti planar electrodes placed at the junction of the two downstream outlets is used for realizing DC-DEP. The gap between the electrodes is slightly smaller than the microchannel width so that the electrodes slightly protrude into the microchannel. When the electrodes are inactive, the stream of polystyrene micro-sized particles flowed into one of the outlets. On the other hand, when the electrodes are powered (30 V) the stream of polystyrene micro-sized particles gets diverted into the other outlet. Seger et al. [22] developed a microfluidic device for “cell dipping” on a continuous basis. Cell dipping refers to temporarily exposing cells, suspended in a carrier medium, to a desired reagent. Seger et al. executed this on a focused stream of cells using two sets of planar angled-electrodes. The first electrode switches the stream of cells from the carrier medium to the reagent while the second electrode switches the stream of cells back to the carrier medium from the reagent after a specified duration. Wang et al. [23] developed a microfluidic device employing AC-DEP for purposes of switching. The microfluidic device employs a set of three dimensional interdigitated transducer (IDT) electrodes on each of sidewalls of the microchannel. By employing unequal voltages, it is possible to simultaneously focus and switch micro-sized particles between multiple outlets; when the actuation voltage associated with one set of IDT electrodes is maintained smaller than the other, the micro-sized particles can be switched to outlets nearer to the IDT electrodes with lower voltage. The authors demonstrated switching of cells and beads between multiple outlets simply by varying the actuation voltages between 0 and 10 V_{pp} [23]. Tornay et al. [24] developed a microfluidic device employing IDT “liquid” electrodes for AC-DEP based switching of stream of latex micro-sized particles between two media with little mixing of the media. Pt/Ti electrodes are employed in this microfluidic device. In this device the micro-sized particles are focused prior to switching using IDT “liquid’

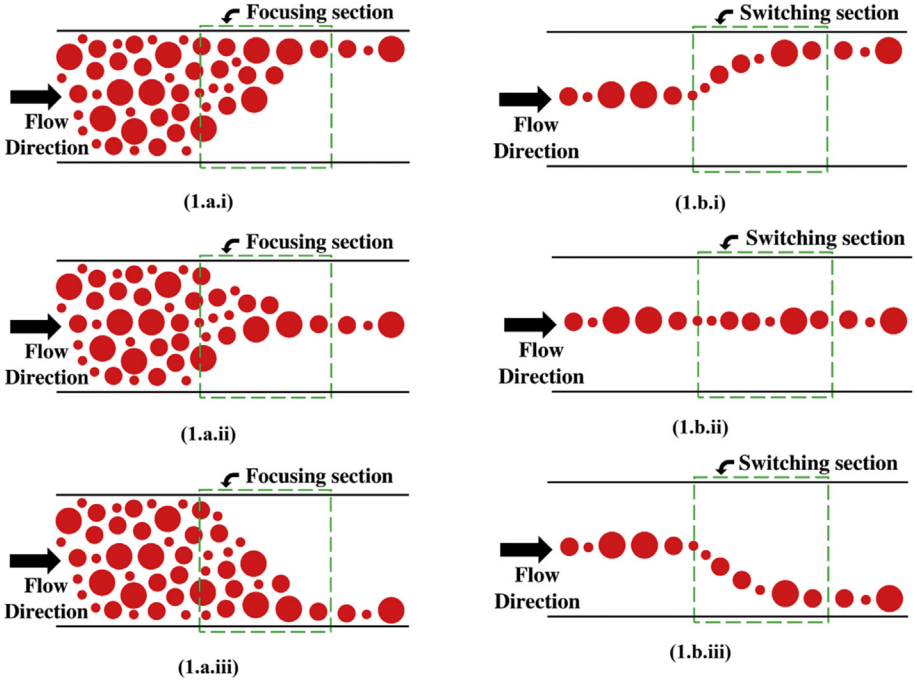

Fig. 1. Schematic representation of unit operation of (1.a) focusing and (1.b) switching wherein the incoming stream of micro-sized particles is directed towards (i) top, (ii) middle, and (iii) bottom of the microchannel.