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The influence of flow intensity and field frequency on continuous-flow dielectrophoretic trapping

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ABSTRACT

We examine the combined influence of the intensity of pressure driven background flow and the frequency of the applied field on the continuous-flow dielectrophoretic trapping behavior of micro-particles within a micro-channel. Using an embedded interdigitated electrode array, we find that the measured trapping percentage over a continuous frequency range exhibits several curious effects which are strongly dependent on the flow intensity, including an apparent shift of the cross-over frequency and low-frequency dispersion. A numerical and theoretical model accounting for the combined effects of pressure-driven flow, dielectrophoresis and alternating-current electro-osmosis on the equation of motion for the particle is used to qualitatively describe the main experimental results.

1. Introduction

Continuous flow dielectrophoresis (DEP) has been demonstrated as an efficient means for steady separation and/or enrichment of particles (cells/colloids/biomolecules) [1], wherein the sub-population experiencing positive DEP (pDEP) is trapped at the electrodes, while the other, experiencing negative DEP (nDEP), is repelled from them and driven by the background flow toward the outlet, where they can be collected. The interdigitated planar electrode array used herein, is a popular geometric configuration in such systems [2], since it can produce large field gradients even for modest values of the applied voltage, and is effective in both nDEP and pDEP modes. For example, Hughes et al. [3] have previously demonstrated its use as a dielectrophoretic filter for the separation/trapping of particles at the inlet of a microfluidic device in preparation for further analysis. Additionally, similar geometry has also been used to generate the DEP force at the bottom of a micro-chamber used to implement field flow fractionation (FFF), a technique which exploits nDEP repulsion in conjunction with hydrodynamic forces and gravity to separate particles [4]. In the latter case, the repulsive DEP force, acting against gravity, levitates different particles to different heights producing a vertical separation. Depending on their vertical location, the particles then experience differing drag forces from the background parabolic flow profile, ultimately resulting in horizontal separation along the electrode array. The aforementioned experimental studies were also complemented by theoretical analysis of the electric potential, field and DEP forces occurring at such a planar electrode array geometry based on Green's theorem [5,6], Fourier series [7] and finite-element based numerical analysis [8,9].

Following Flanagan et al. [10] we have recently used the interdigitated electrode design to measure the trapping percentage of particles/cells over a wide range of applied frequencies [11]. A simplified theoretical model accounting for a combination of convective and DEP forces on trapping percentage was used to enable the extraction of the effective particle (cell) surface conductivity (membrane and/or cytoplasm conductivities). In the current study we extend [11] to account for varying forced flow intensities and widen the frequency range to values as small as 0.5 kHz. As will be shown below, this enables analysis of the impact of alternating-current electro-osmosis (ACEO) [8,12], which is characterized by an inverse of the RC time on the order of 1–10 kHz, on the trapping efficiency.

Numerous works have examined the influence of background flow intensity on the trapping and separation efficiencies in continuous flow systems [1,2,13–15]. While high flow rates are generally associated with high throughput, increased flow rates can also result in a decrease in trapping percentage, since hydrodynamic shear acts against trapping by p-DEP, suggesting a delicate interplay between these two parameters is necessary for optimization [16]. In an attempt to circumvent this conflict, Markx et al. [17] demonstrated that a higher trapping level could be maintained by appropriate decrease of the solution conductivity.

The aforementioned studies on the relationship between DEP and background hydrodynamics tend to be designed around a

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single frequency, chosen to optimize separation [18] and thus do not consider the frequency dependent behavior of the trapping. Additionally, since this frequency is generally above 20 kHz, ACEO is not apparent. Conversely, studies on optimization of trapping percentage using a combination of ACEO and DEP have generally been performed in the absence of pressure driven background flow [19–23]. With the advent of pressure driven flow, maximum throughput may be increased but the convection of the particles from the edge of the electrodes – where the field gradient is at a maximum – to their center is expected to result in a drop in the trapping percentage as the hydrodynamic force can more easily dominate the weakened DEP [24]. It is thus the intention of this work to examine this interplay in depth, by determining DEP trapping percentages over a broad spectrum of frequencies and flow rates. By characterizing the relative contributions of ACEO, DEP and pressure-driven hydrodynamic forcing on continuous dielectrophoretic trapping as a function of frequency, we aim to provide a comprehensive overview of the relevant forces to be considered when choosing the optimal separation frequency and flow parameters for realistic separation devices.

The materials and methods section is divided into experiments and theory, where the latter section describes the calculation of particle trajectories, ACEO and DEP effects. The results and discussion section is similarly divided between experimental particle trapping spectroscopy results, and the analysis of the respective contributions of ACEO, DEP and background hydrodynamics.

2. Materials and methods

2.1. Experiments

2.1.1. Experimental set-up

The chip consists of two parts: a long straight microfluidic channel ($L = 3$ cm long, $b = 1$ mm wide and $H = 35$ µm height) made of polydimethylsiloxane (PDMS) which is sealed (at the bottom) by a glass slide printed with an interdigitated electrode array (Fig. 1). The array consists of 19 electrode fingers of opposing polarity that are interlocked. The width of each electrode is 32 µm and the gap between two successive electrodes is 18 µm. Commercially available fluorescent polystyrene beads (Fluoro-Max, Thermo-Scientific), 0.5 µm, 2 µm and 3.1 µm in diameter, were diluted to volumetric concentration of 10^{-5}–10^{-3}% in deionized water (DI). Concentrations were chosen such that a sufficient number of particles cross the electrode array within a given time interval. Particle movement was observed using a Nikon TI Eclipse inverted epifluorescent microscope and recorded with either Andor Neo sCMOS camera at a rate of approximately 90 fps or a spinning disk confocal system (Yokogawa CSU-X1) connected to a camera (Andor iXon3). A silicone reservoir (Grace Bio) was attached above the channel inlet. An automated syringe pump (KDS Legato 200 series, KDScientific), connected to the channel outlet via a Teflon tube, was used to control the different flow rates (1–10 µl/min) in withdraw mode.

2.1.2. Quantifying particle trapping percentage

For each flow rate, particles flowing through the micro-channel with the embedded interdigitated electrode array were recorded in two movies, each 5–15 s long, for various ac field frequencies (1 kHz–2 MHz) with a constant applied voltage of 5 V_{pp} for 3.1 µm particles (see Movie#1 in [25]) and 20 V_{pp} for 2 µm particles. Herein, the subscript pp stands for peak-to-peak. The percentage of trapped particles for each frequency was calculated according to

$$Trapping\% = \frac{N_{in} - N_{out}}{N_{in}} \cdot 100, \tag{1}$$

wherein N_{in} and N_{out} are the number of particles entering and leaving the electrode array respectively over a prescribed time interval.

2.1.3. Quantifying ACEO flow velocity

The particle motion on the electrodes themselves was measured by tracking tracer particles, 500 nm in diameter, over frequencies ranging from 0.1–100 kHz while the applied voltage was varied between 1 and 20 V_{pp}. The small size of the particle was chosen so as to reduce the DEP effect and isolate the ACEO flow dynamics. For each frequency, the positions of about 10 particles undergoing convection due to ACEO, i.e. moving from the edge of the electrode toward its center, were visualized using a confocal microscope to better control the focal plane, and the recorded videos were analyzed using IMAGE-J software and the Speckle tracker plugin [26] to extract their velocity profile along the electrode.

2.2. Theory

2.2.1. Particle trajectories

In contrast to our previous publication [11], wherein a simplified approach of a spatially uniform (averaged) DEP force was used to

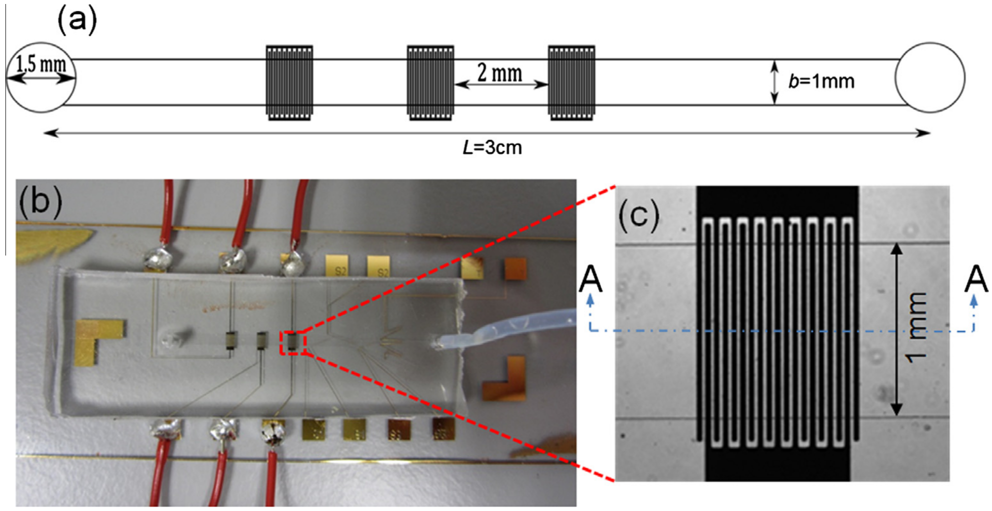

Fig. 1. (a) Schematic description of the microchannel with embedded electrode arrays; (b) a photo of the chip consisting of the microchannel, embedded electrodes, electrical wiring and tubing; (c) close-up of the interdigitated electrode array for DEP characterization.