MAGNITUDE AND VARIANCE OF ACOUSTIC ENERGY DENSITY IN MICROCHANNEL ACOUSTOPHORESIS: COMPARISON BETWEEN SINGLE-FREQUENCY AND FREQUENCY-MODULATED ACTUATION

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ABSTRACT

Using a novel light-intensity method, we quantify for the first time the magnitude and spatial variance in acoustic energy density along a microchannel during acoustophoretic focusing of particles with frequency-modulated ultrasound. We compare the distribution in energy density between single-frequency (SF) and frequency-modulation (FM) actuation along the microchannel. In addition, we analyze the field uniformity for the two actuation approaches (SF and FM) by measuring the deviation of the final particle pattern from an ideal straight line. We conclude that the magnitude of the energy density for FM actuation is of the same order of magnitude as for SF actuation, but with much less spatial variance.

KEYWORDS: Acoustophoresis, Frequency modulation, Acoustic energy density, Microchannel

INTRODUCTION

Microchannel acoustophoresis is a powerful and well-investigated method for particle and cell manipulation in lab-on-a-chip devices [1]. The standard actuation method in acoustophoresis is to operate the ultrasound transducer at a single frequency (SF) causing a half-wave resonance across the channel width or height. However, a generic problem with SF operation is the formation of unwanted resonance modes along the channel length. Such spurious-mode three-dimensional resonances are difficult to avoid and cause curved and/or fragmented patterns of acoustophoretically focused particles. This effect often hampers or reduces the efficiency of the intended acoustophoretic function.

We have previously reported a method for cancelling out the spatial variations in acoustophoresis along a microchannel by the use of frequency-modulated (FM) ultrasonic actuation [2]. This method is based on kHz-rate linear frequency sweeps for averaging a set of several single-frequency resonances. Although proven useful in cell applications [3], this method has never been quantified in terms of field strength or improvement in field uniformity.

In this paper, we quantify the acoustic energy density (E_{ac}) along a microchannel during acoustophoretic focusing of particles by measuring the magnitude and spatial variance of E_{ac} using frequency-modulated (FM) ultrasound and single-frequency (SF) actuation.

THEORY

For a half-wave resonance mode across the channel width ($\lambda = 2w$), the simple 1D approximation yields a resonance frequency f and acoustic pressure amplitude p as [4]:

$$f = \frac{c_0}{2w} \quad \text{and} \quad p(y) = p_a \cos(k_y y). \tag{1}$$

Here, c_0 is the sound velocity in the fluid, w is the channel width, y is the coordinate along the channel width w, and $k_y = 2\pi/\lambda$ is the 1D wavenumber (where λ is the wavelength in the fluid).

If we assume a local 1D pressure field according to Eq. 1, the acoustic radiation force on a single particle with radius $a \ll \lambda$ can be estimated by using the following formula:

$$F_y^{\text{rad}} = 4\pi\Phi k_y a^3 E_{ac} \sin(2k_y y), \tag{2a}$$

$$\Phi = \frac{1}{3}\left[\frac{5\tilde{\rho}-2}{2\tilde{\rho}+1} - \tilde{\kappa}\right]. \tag{2b}$$

Here, Φ is the acoustic contrast factor where $\tilde{\rho} = \rho_p / \rho_0$ and $\tilde{\kappa} = \kappa_p / \kappa_0$ are the density and compressibility ratios between the particle (index "p") and the fluid medium (index "0"), respectively. The relationship between the acoustic energy density, E_{ac}, and the acoustic pressure amplitude, p_a, is:

$$E_{ac} = \frac{p_a^2}{4\rho_0 c_0^2}. \tag{3}$$

EXPERIMENTAL METHOD

The microfluidic chip used in the experiments is shown in Fig. 1 and is described in more detail in Ref. 4. In brief, it consists of a light-transparent three-layer structure where the microchannel is etched through the silicon layer (110 µm), which in turn is sandwiched in between two glass layers (200 µm and 1 mm, respectively).

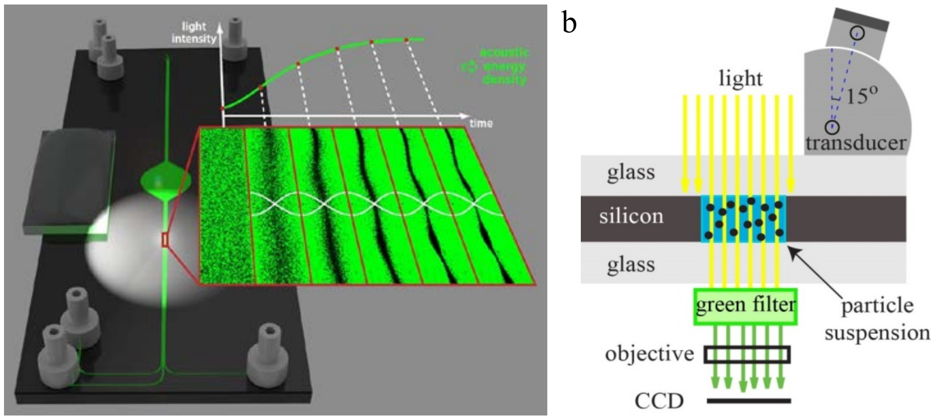

Figure 1: a) Illustration of the chip and the light intensity method for measuring the acoustic energy density. b) Schematic side-view of the device including the transducer with a 15° coupling wedge (not to scale).

The energy-density analysis is based on measuring the transmitted light intensity through the microfluidic channel filled with a suspension of 5-µm-diameter polyamide beads [4], see Figs. 1 and 2. The examined section of the microchannel was 1 mm long, and each experiment was repeated four times. The transducer had a 15°-coupling wedge and was driven at U_{pp} = 20 V and f = 2.19 MHz (SF) or f = 2.19±0.05 MHz, rate 1 kHz, linear sweeps (FM).

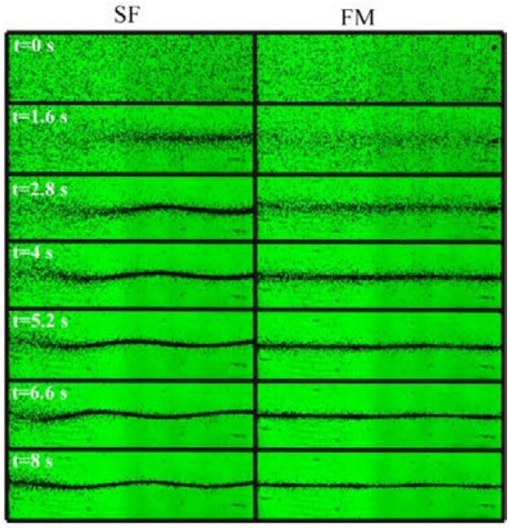

Figure 2: Dynamics of acoustophoresis patterns during the first 8 s when actuating the device with U_{pp}=20 V at single frequency (SF, left panel) and frequency modulation (FM, right panel).

RESULTS AND DISCUSSION

In Fig. 2, we note that the focusing is locally faster at SF actuation, but more uniform at FM actuation. This evolution is quantified in Fig. 3 with the light-intensity method [4]. As seen in the diagram, the axial variance in energy density along the channel is seven times higher for SF than FM actuation, and the final lateral variance in pattern shape after completed focusing is two times higher for SF than FM actuation (cf. Fig. 4). Finally, we investigated the reproducibility of the experiment using the light-intensity method [4]. The uncertainty of the experiments is 10% for SF and 6% for FM actuation (Fig. 5).

CONCLUSIONS

We find in this work that frequency-modulation actuation is suitable for robust acoustophoresis, causing uniform particle patterns with average acoustic energy densities comparable to those obtained using single-frequency actuation but with much less spatial variances. This is particularly important for accurate acoustophoretic cell separation in microchips having branched channel outlets after the separation zone [5]. Another benefit of FM-actuated acoustophoresis is in no-flow applications such as in cell-cell interaction studies in microplates [3].

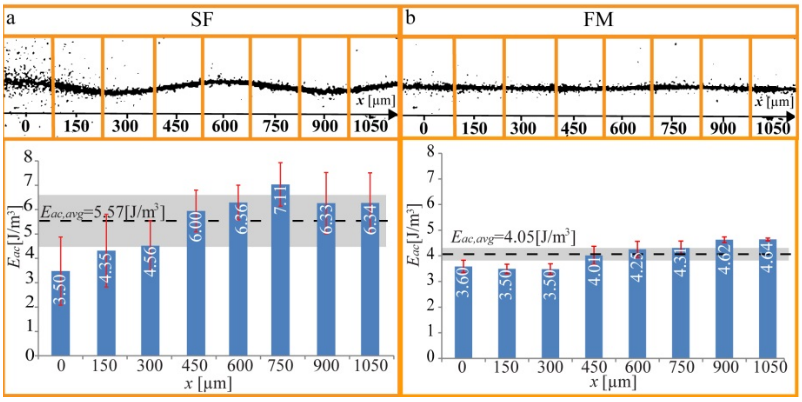

Figure 3: The spatial distribution in energy density along the channel for a) single frequency (SF) and b) frequency modulation (FM) actuation. The averaged energy density for the whole channel, $E_{ac,\ avg}$, is marked with a dotted black line, and the corresponding 1σ standard deviation is marked with a grey band. The red error bars are the standard deviations from the four repetitions of each experiment.

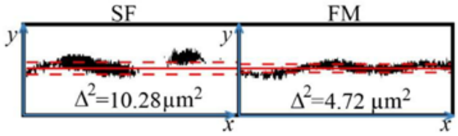

Figure 4: Analysis of the variance, Δ^2, in final pattern shape. The dotted red lines mark the standard deviation (±Δ) of the pattern from an ideal straight line along x around its mean position (y_c) (solid red lines). The variance is here defined as $\Delta^2 = (1/N)\sum_{j=1}^{N}[y(x_j) - y_c]^2$.

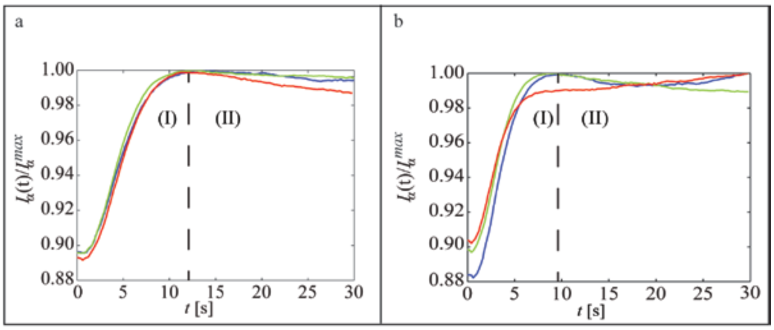

Figure 5: Reproducibility tests of the light intensity method. The diagrams are normalized light-intensity curves for a) single-frequency (SF) actuation, and b) frequency-modulation (FM) actuation. Each experiment was repeated three times.

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