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Single-actuator Bandpass Microparticle Filtration via Traveling Surface Acoustic Waves

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ABSTRACT

Microscale separation is an important process for many medical diagnostics and biological analysis applications. Acoustic based microparticle manipulation has the advantages of low power consumption and good biocompatibility, and has been widely exploited in label-free particle and cell separation. However, typically applied forces scale with increasing particle dimensions, making the selective translation and separation of intermediate-sized objects a multi-stage process. In this work, we realize a single surface acoustic wave (SAW) actuated bandpass filter that can selectively sort out particles with dimensions between smaller and larger diameter populations. This bandpass filter takes advantage of the sharply nonlinear force scaling in the regime where the particle diameter is on the order of the wavelength or larger. Two sets of bandpass filtration, 15.2 μm polystyrene particles out of 10.2 μm and 19.5 μm ones, 10.2 μm particles out of 8.0 μm and 11.8 μm ones, have been experimentally demonstrated.

There is need in many medical diagnostics and biological analysis applications for high fidelity and flexible separation of microscopic particles such as biomolecules, cells and polymer particles [1], where conventional lab techniques such as centrifugation are not sufficiently sensitive or suited to microscale systems. Fluorescence-activated cell sorting (FACS) is a classic solution for highly accurate sorting of cells and particles. Although it is an effective and highly specific approach, the fluorescent labeling requires expensive reagents and multi-step sample preparation. Moreover, cells would be killed in the labeling process, which precludes further analyses that require the cells sorted to be viable [2]. Accordingly, various forces have been exploited for label-free microparticle separation including dielectrophoresis [3], magnetophoresis [4], optical tweezers [5], inertial focusing [6] and acoustophoresis [7]. These label-free separation techniques are usually based on the difference of their intrinsic properties such as size, density, shape, deformability, hydrodynamic properties, electric polarizability and magnetic susceptibility. Among these characteristics, size is the most widely used characteristic since the aforementioned forces are commonly proportional to the volume of the microparticles [8] and this parameter is most likely to vary between otherwise similar cells and particles. Because of this scaling, the most straightforward implementation of these size-based separations is to isolate the largest or the smallest particles from a mixed population [9]. However, the target objects may be in the intermediate size of a mixed population or the sample could be confounded with larger aggregates or debris, necessitating multi-step separations [10–12] and increasing the complexity, and thus decreasing the practical usability of these binary separation devices. A straightforward method to sort out a limited range of particle dimensions from a mixed population is therefore of interest for applications in biological research.

Recently, acoustophoresis has become widely used for microparticle separation thanks to not only its high biocompatibility and low power consumption [13], but also its strength in separating microparticles based on their mechanical properties [14]. Though resonant channels actuated by bulk acoustic waves have been successfully applied for continuous manipulation [15–17], surface acoustic waves (SAW) in particular are an acoustic wavemode well suited to microfluidic integration, where a substrate-bound wave on a planar substrate can flexibly generate either standing or traveling wavemodes in a wide variety of microfluidic architectures and be highly localized in specific regions [18]. A particle suspended in fluid experiences a time averaged acoustic radiation force (ARF) while exposed to an acoustic field [19]. Classified by the types of the incident acoustic field, the ARF can be divided into two kinds, one of which is induced by a traveling acoustic wave and the other one induced by standing acoustic wave. Although both of the two types have been demonstrated for label-free size-based microparticle separation [20,21], traveling acoustic field based separation has the advantages of high spatial resolution [22], less restriction on the alignment and no inherent displacement limit of one quarter of the wavelength compared with that based on standing acoustic field [23].

Most of the existing studies on acoustophoresis are conducted at relatively low frequencies, where the particle is smaller than the wavelength in the fluid, corresponding to values of the dimensionless

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number $\kappa = \pi df / c_f < 1.5$, where d is the diameter of the particles, f is the acoustic wave frequency and c_f is the sound speed in the fluid. In this regime, the traveling wave acoustic radiation force on the particle increases monotonically with increasing particle size. Destgeer et al. has demonstrated that the ARF on polystyrene particles rises dramatically with increasing κ value to achieve size-based particle separation with submicron difference within the range $1 < \kappa < 1.3$. However, beyond this range of κ value, the acoustic radiation force can actually decrease for larger particle dimensions, where ARF maxima correspond to particle resonance conditions. The κ values for these maxima are determined by the particle's relative mechanical properties (densities and sound speed) compared to the fluid medium. Though Hasegawa measured this relationship between ARF and κ value with millimeter-sized silica spheres decades ago [24], this strongly nonlinear relationship has not been suitably applied in continuous size-based separation for microscale objects, the target system and application for biological research.

In this study, we for the first time demonstrate a continuous single step bandpass filtration of microparticles using a traveling SAW generated by a single set of interdigital transducers (IDTs), in contrast to previous acoustic bandpass filtrations that require at least two sets of IDTs operating at different frequency and power conditions [10–12]. This simple but novel design of single-actuator bandpass microparticle filter takes advantage of the nonlinear relationship between ARF and κ value when $\kappa > 1$ such that the ARF on intermediate-sized particles could be precisely tuned to become substantially stronger than that on smaller and larger particle populations.

Fig. 1 shows the schematic layout and working principle of the continuous size-based microparticle bandpass filter. A pre-fabricated disposable polydimethylsiloxane (PDMS) microchannel is placed on a piezoelectric substrate (128° Y-cut, X-propagating $LiNbO_3$) patterned with a single set of IDTs, following a similar experimental setup in our previous study [23]. The sample suspension containing a mixture of size-varied particles is introduced through a hydrodynamically focused middle inlet, and sandwiched by two uneven sheath flows from two side inlets. The flow rate ratios of the two sheath flows to the sample flow are adjusted to ensure all the particles will flow into the waste outlet in the absence of any external disturbance. Once an AC signal is applied to the IDTs, a traveling surface acoustic wave (TSAW) propagates along the surface of the piezoelectric substrate and radiates into a PDMS microchannel containing a focused particle suspension. Because of the acoustic damping effect in PDMS, the traveling acoustic wave gradually attenuates along the PDMS/$LiNbO_3$ interface with an attenuation length around 18.2λ_{SAW} [23], where λ_{SAW} is the acoustic wavelength on the substrate. The attenuation length is defined as the distance from the acoustic source to the location where the acoustic displacement attenuates exponentially to 1/e (36.8% of the non-attenuated displacement). The lowest frequency used in this study ($f = 45.52$ MHz)

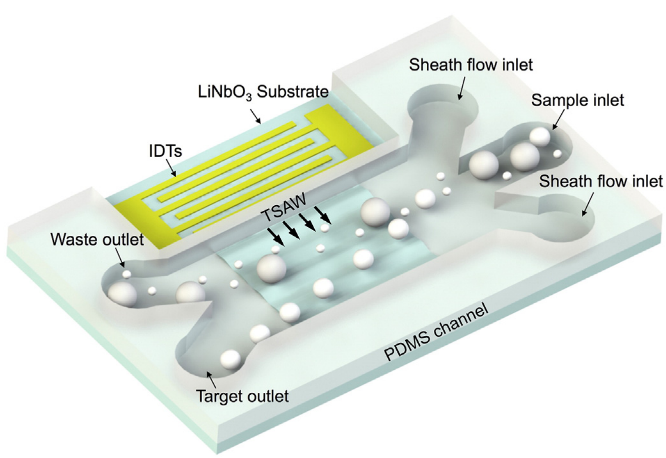

Fig. 1. Schematic layout of the single-IDTs actuated microparticle bandpass filter. A mixture of three particle sizes are asymmetrically focused and flow in the half side of the main channel closer to the IDTs without the application of SAW. When an AC signal is applied to the IDTs, a TSAW field is generated and propagates along the $LiNbO_3$ substrate into the PDMS channel. When the mixed particle populations are exposed in the TSAW field, intermediate-sized particles that experience the largest ARF are translated laterally farthest and flow into the target outlet, while smaller and larger particles continue to flow into the waste outlet.

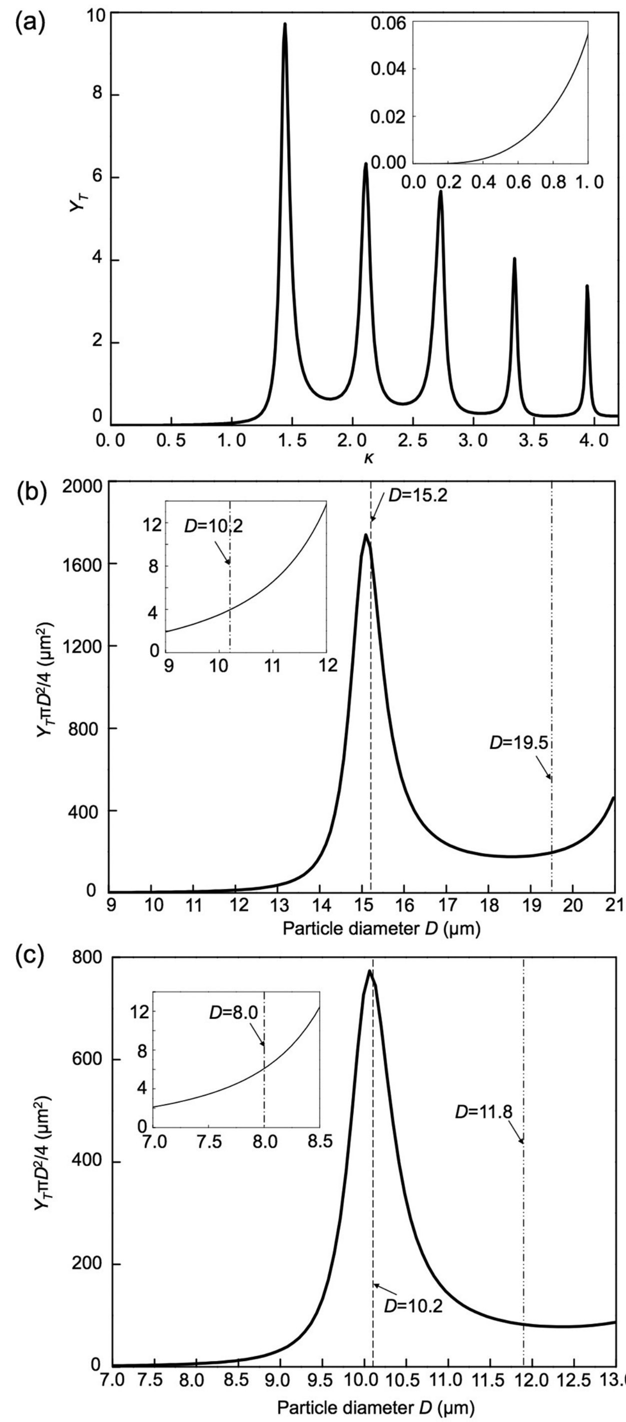

Fig. 2. Theoretical analysis of ARF factor. (a) Curve plot of the ARF factor (Y_T) for spherical polystyrene particles as a function of the κ value. Successive peaks (maxima) and dips (minima) exist along the curve in the $\kappa > 1$ region, resulting from the free vibration resonance of spherical particles. (b) Curve plot of unit-intensity ARF, $P_T = Y_T(d)\pi d^2/4$ as a function of the particle diameter in a 45.52 MHz acoustic field. The theoretical model shows that the particles with size near 15 μm have a much higher P_T value than particles smaller than 14 μm or larger than 16 μm, thus experience higher ARF to implement bandpass filtration. (c) P_T versus d plot for the bandpass filtration of 10 μm particles in a 68.28 MHz acoustic field, which experience a higher ARF than particles smaller than 9.5 μm and larger than 10.5 μm.