MANIPULATING SINGLE PARTICLES USING STANDING SURFACE ACOUSTIC WAVES

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ABSTRACT

Techniques that can noninvasively and dexterously manipulate single particles, cells, and organisms are invaluable for many applications in biology, chemistry, engineering, and physics. Here, we demonstrate "acoustic tweezers" that can trap and dexterously manipulate single microparticles, cells, and entire organisms (*i.e.*, *Caenorhabditis elegans*) in a microfluidic chip. These acoustic tweezers utilize the wide resonance band of chirped interdigital transducers to achieve real-time control of a standing surface acoustic wave field, which enables flexible manipulation of most known microparticles. The low power density requirement by our acoustic device renders the technique noninvasive and amenable to miniaturization. Cell-viability tests were conducted to verify the non-invasive nature of this approach.

KEYWORDS

Cell manipulation, surface acoustic waves, microfluidics, lab on a chip.

INTRODUCTION

In 1986, Arthur Ashkin, Steven Chu, and colleagues first demonstrated trapping of single particles with a laser beam, known as optical tweezers[1]. Optical tweezers have since been used to manipulate many kinds of micro/nano objects, including dielectric spheres, cells, bacteria, viruses, DNA, and molecular motors[2–4]. However, the excellent precision and versatility for a number of functionalities of optical tweezers rely on high power laser beam and complex, potentially expensive optical setups that are difficult to maintain and miniaturize. Other popular particle-manipulation techniques also have potential drawbacks: magnetic tweezers require targets to be pre-labeled with magnetic materials, a procedure that affects cell viability[5]; electrophoresis/dielectrophoresis based methods are strictly dependent on the polarizability of the particles and the conductivity of the background medium, and utilize electrical forces that may adversely affect cell physiology due to current-induced heating and direct electric-field interaction[5-8]. In this regard, acoustic-based particle manipulation methods present excellent alternatives thanks to the fact that acoustic-based methods are relatively non-invasive to biological objects and work for most microparticles regardless of their optical, electrical, or magnetic properties. To date, many particle-manipulation functions (*i.e.*, focusing, separating, sorting, and patterning) have been realized through acoustic-based approaches[9–11]. None of these approaches, however, have achieved the capability of manipulating single microparticles or cells along an arbitrary path. The acoustic tweezers presented here represent the first acoustic manipulation method to precisely control a single microparticle in two-dimensions.

EXPERIMENT

Figure 1 illustrates the working mechanism and structure of our device. A polydimethylsiloxane (PDMS) channel was bonded to a lithium niobate (LiNbO$_3$) piezoelectric substrate asymmetrically between two orthogonal pairs of chirped interdigital transducers (IDTs). Chirped IDTs have a gradient in their finger period (Fig. 1a) which allows them to efficiently resonate at a wide range of frequencies[12]. Each pair of chirped IDTs was independently biased with a radio frequency (RF) signal to generate identical surface acoustic waves (SAWs), which then interfere with each other to form a standing SAW on the substrate. The standing SAW field generates an acoustic radiation force acting on suspended particles within. The acoustic radiation force drives particles to nodes or anti-nodes in the pressure field, depending on their elastic properties[7]. Most objects, including polystyrene beads, cells, and *C. elegans*, are pushed to nodes in the pressure field because of density and/or compressibility variations relative to the background medium[7, 9]. Figure 1b shows a schematic of the standing SAW and related pressure field along one dimension (*x*-axis) of the device. We refer to the stationary pressure node in the centre of the IDTs as the 0 order node (shown as a long dash dot line in Fig. 1b), progressing to the 1st order, 2nd order, 3rd order, etc. outward from the centre. Because absolute node location ($x_n = n\lambda/2$ for nth order pressure node, λ is the SAW wavelength) is directly related to the SAW wavelength which is directly related to the signal frequency ($f = c/\lambda$, where c is the SAW propagation

velocity on the surface of substrate), all higher-order ($n > 0$) pressure nodes can be moved simply by altering the applied signal frequency. The node displacement (Δx_n) can be described by: $\Delta x_n = n(\lambda_1 - \lambda_2)/2 = n(c/f_1 - c/f_2)/2$, as shown in Fig. 1b for a frequency change from f_1 to f_2. Using chirped IDTs with varying input RF frequency, we can shift the location of the pressure nodes, thus moving a single particle/cell/*C. elegans* which is trapped in the pressure node. Using our manipulation technique, we have achieved a velocity as high as ~1600 μm/s for 10-μm fluorescent polystyrene bead, corresponding to a force as high as 150 pN.
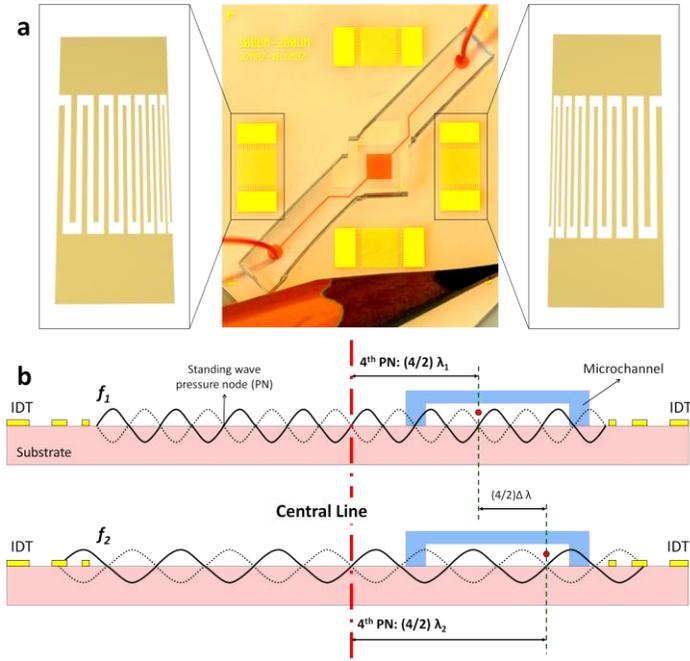
Figure 1 a, *Schematic illustrating a microfluidic device with orthogonal pairs of chirped IDTs for generating standing SAWs.* *b*, *standing SAWs generated by driving chirp IDTs at frequency f_1 and f_2. When particles are trapped at the nth pressure node, they can be translated a distance of ($\Delta\lambda/2$)n by switching from f_1 to f_2. This relationship indicates that the particle displacement can be tuned by varying the pressure node where the particle is trapped.*
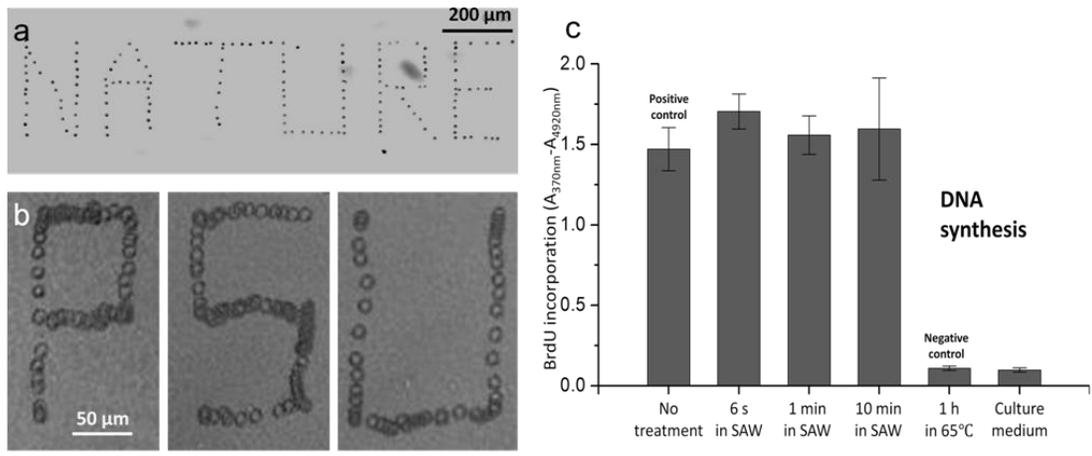
Figure 2 a, *Stacked images used to demonstrate independent motion in x and y using a 7-μm fluorescent polystyrene bead to write the word "NATURE". **b**, Stacked images showing dynamic control of a bovine red blood cell to trace the letters "PSU". **c**, Hela cell DNA synthesis measurement to verify the cell proliferation.*

To demonstrate single particle/cell manipulation in two dimensions, we tuned the input frequency of both pairs of orthogonally arranged chirped IDTs (as shown in Fig. 1a). Each pair of chirped IDTs independently controls particle motion along a single direction, thus the orthogonal arrangement enables complete control in the device plane. The dexterity of this approach is shown in the layered image in Fig. 2a, where a 7-μm polystyrene particle is trapped and moved along a path to write "NATURE". Figure 2b presents the capture and subsequent manipulation of single bovine red blood cell to trace the letters "PSU", demonstrating the applicability of the acoustic tweezers to biological samples. Additionally, we examined the proliferation of HeLa cells in high-power (23 dBm) standing SAW fields for 6 s, 1 min, and 10 min. The results (see Fig. 2c) indicate that after 10 min exposure to the acoustic field, no significant physiological damage was induced to the cell.

Finally, our acoustic tweezers can also simultaneously manipulate large numbers of particles. Parallel manipulation of multiple particles can be achieved with clusters of particles at a single pressure node, single particles at different pressure nodes, or clusters of particles at distinct pressure nodes (see Fig. 3). These results show that while the acoustic tweezers are capable of dynamically manipulating single particles/cells/organisms, they are also capable of simultaneously manipulating more than tens of thousands of particles over a variety of length scales.
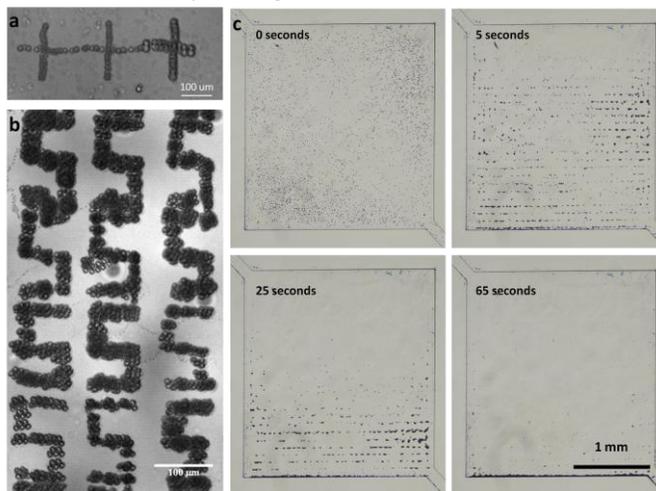
*Figure 3 a, stacked image of the parallel manipulation of 3 bovine red blood cells to write a cross. **b**, stacked image of the parallel manipulation of arrays of 15- μm polystyrene particle clusters to write an array of "S". **c**, simultaneously move tens of thousands of 15- μm polystyrene particle towards the same direction and functions as particle concentration.*

The low power consumption and simple structure/setup of our technique can be integrated with a small RF power supply and basic electronics to function as a fully integrated, portable, and inexpensive particle-manipulation system. If combined with flow-based microfluidics, the device could sort, identify, and characterize cells and other biological particles. Additionally, the acoustic tweezers' non-invasiveness, versatility, and dexterity render them an excellent microfluidic platform for a wide range of applications in both the biological and physical sciences.

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