Selective Single-Beam Acoustic Tweezers for Cell Manipulation

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Abstract:

Structured sound waves, mechanical waves carrying energy and momentum flux, are frontiers in advancing our understanding of cell mechanobiology. The acoustical tweezers enable biocamplatical, contact and label free manipulation of single cells and microorganisms. Focused sound beams can exert acoustic radiation force and torque that can be used for mechanical property probing and mechanosensitive ion channel activation at powers much lower than their optical counterpart. The external actuation of the mechanosensitive ion channel can act as switches for manipulation of specific cell activities in an electrical-to-chemical mediator manner.

Summary of Research:

We developed a vortex-based acoustic tweezer that can be operated from a single transparent piezoelectric transducer and can be fully integrated to a standard microscopy environment [1,2].

These vortices-based tweezers enable spatially selective manipulation of cells at single cell resolution. Furthermore, we have also developed and fabricated conventional ultrasound focusing lenses but on transparent transducers that are also easily integrated on top of the microscope objective to monitor the sound effects on biological cells [3]. (Figure 1)

To examine the feasibility of vortex-based and focused acoustic tweezers, we have built a fully integrated acoustic tweezer platform on a Nikon Ti microscope (Figure 2) and successfully performed single cell manipulation, positioning (Figure 4) and characterized it in terms of cell viability and exerted force (Figure 3). Figure 4.a shows the capability of the device in manipulating a single 7-micron diameter particle inside a microfluidic device. Figure 4.b shows the selective manipulation of a 15 μm particle using an acoustic tweezer in a microfluidic chamber observed through a standard microscope. As shown, the selected particle marked with a red circle is moved among the other particles marked in yellow, blue and green which do not move. And Figure 4.c is a representation of single budding yeast manipulation and rotation over the course of 0.3 seconds.

Conclusions and Future Steps:

Single beam acoustic tweezers that operate at biomedical ultrasound frequencies have the potential to be integrated into current conventional optical setups. Such level of integration significantly alleviates the tedious single cell manipulation procedures and lets young researchers work more efficiently on analyzing data instead of mastering working with complicated tools. It is also important to study and understand the new mechanotransduction pathways, cell reaction to stress, stress communication between cells, electromagnetic radiation consequences of mechanical stimuli, among many others that these new techniques make possible.

For the future steps, our hypothesis is that, by engineering a reliable mechanotransduction pathway that is responsible for actuating a specific signal pathway, we will be able to realize an efficient non-invasive and remote interface for on demand communication with biological entities at cellular level. Engineering focalized structured sound waves and sensitive impedance measuring sensors are the key technologies for a reversible mechanotransduction based interface between cell and electronics.

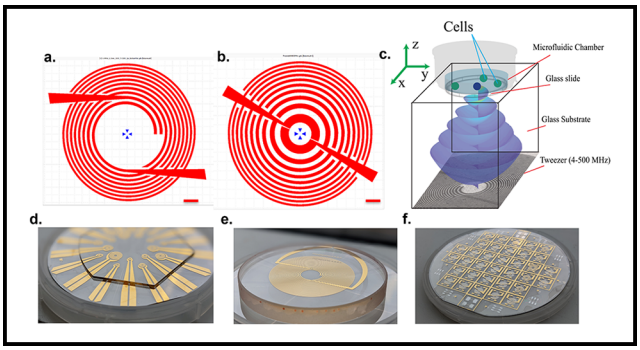

Figure 1: The acoustic tweezer and lens design. a. The intertwined spiral electrode pattern obtained from the approximate equations for frequency of 100 MHz and focal distance of 1235 µm. b. The Fresnel pattern of electrodes for acoustic focusing for f = 100 MHz and focal length of 1000 µm. Scale bar is 50 µm. c. The schematic showing the composition of the acoustic tweezer. The electrode patterns on the active piezo substrate creates a spherical vortex that propagates into the glass medium and focalizes it before it reaches the cover glass and PDMS chamber that holds the cells. The fluidic chamber on top of the acoustic tweezers is held in place by applying silicone oil as a coupler. d-f. Representative images of acoustic tweezers for manipulation of eukaryotic cells at ~ 50 MHz, embryonic female cells at ~ 5 MHz and yeast cells at ~ 200 MHz frequency.

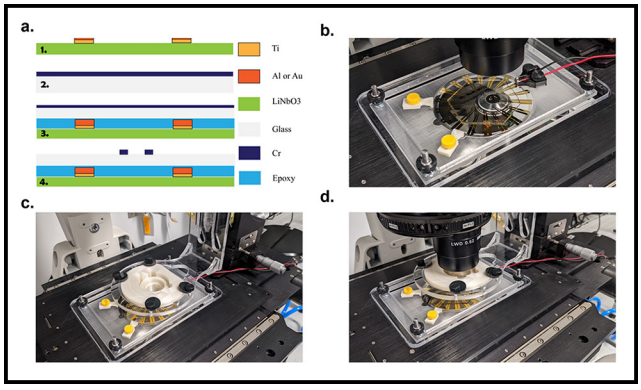

Figure 2: Acoustix tweezer fabrication and integration. a. Shows the fabrication steps. b-d. Shows the integration of the acoustic tweezer to a Nikon TE-300 microscope and 3D manipulator position that controls the fluidic chamber.

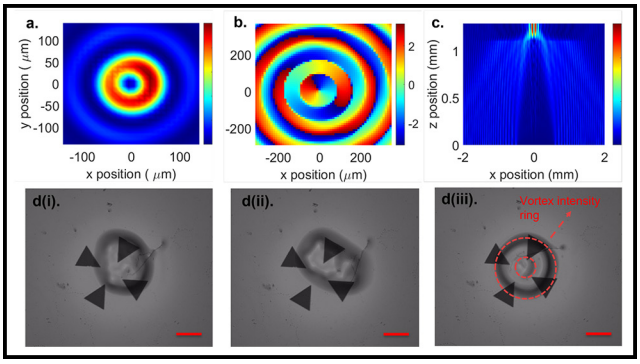

Figure 3: Numerical simulation and experimental observations. a. Intensity and b. phase prediction using angular spectrum method in the xy plane. c. intensity prediction using angular spectrum method in the xz plane. d(i)-(iii) observation of intensity profile variation during a frequency sweep to identify the acoustic tweezer resonant frequency. Scale bar is 40 µm.

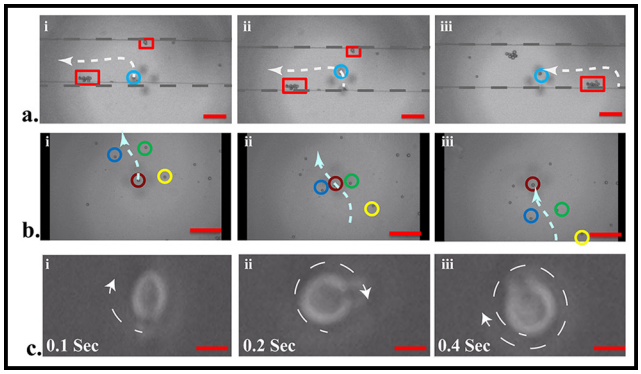

Figure 4: a. Selective manipulation of a 7 µm particle inside a microfluidic device. b. Isolation and manipulation of a 15 µm particle inside a microfluidic chamber. c. Single yeast manipulation and rotation in a microfluidic channel.

References:

[1] M. Baudoin, J.-C. Gerbedoen, A. Riaud, O. B. Matar, N. Smagin and J.-L. Thomas, Sci Adv, 2019, 5, eaav1967.

[2] M. Baudoin, J.-L. Thomas, R. A. Sahely, J.-C. Gerbedoen, Z. Gong, A. Sivery, O. B. Matar, N. Smagin, P. Favreau and A. Vlandas, Nat. Commun., 2020, 11, 4244.

[3] P. S. Balasubramanian, A. Singh, C. Xu and A. Lal, Sci. Rep., 2020, 10, 3075.