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Mini Review

Recent Development of Single Beam Acoustic Tweezer

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Abstract

Microparticle manipulation tools are considered to be a powerful tool for bio-related applications. Here, various manipulation techniques, such as optical, magnetic and acoustic approaches, are introduced. Among them, the acoustic-based method does show its own superior characteristics. The recent development of the acoustic-based method, particularly Single Beam Acoustic Tweezer (SBAT), is reviewed. The content covers device designs and fabrication methods. Some examples of the applications for cells are also highlighted. Finally, the future directions of the acoustic manipulation tool are discussed.

Keywords: Acoustic tweezer; Ultrasound; Manipulation; Red blood cell; Breast cancer cell

Mini Review

Microparticle manipulation tools have attracted great attention because of their extensive applications in biophysics, chemistry, and biomedical engineering. Optical tweezers developed in 1970s were firstly introduced to demonstrate the trapping and manipulation of a microparticle [1]. With using the steep gradient of radiation force generated from a highly focused laser beam, optical tweezers have become an extremely useful tool to trap and manipulate many tiny objects, e.g., cells, molecules, DNA, bacteria, etc [2-4]. Although optical tweezers exhibit absolute advantages in resolution and accurate manipulation of tiny objects, they do have some drawbacks: (1) the properties of targeted cells or biological objects may be changed or even damaged by inducing local heat from the highly focused laser beam; (2) the approach is commonly limited to optical purified objects; (3) the optical setups are complex and expensive; (4) the maximum trapping force is a few hundred pico newtons. Consequently, many alternative techniques have been proposed to overcome the drawbacks. Nevertheless, some techniques, such as magnetic tweezers [5] and electrophoresis-based method [6], still rely on the specific nature of trapped objects. Compared to these proposed techniques, an acoustic-based method is mostly not limited to the nature of objects. They offer stronger trapping force, which are still relatively safe to biological objects. In addition, the acoustic setup is much simpler with lower cost.

The initial research on the acoustic-based method was reported using two opposing acoustic beams to capture latex spheres and frog eggs [7]. Recently, many different acoustic-based manipulation techniques have been reported such as Surface Acoustic Wave (SAW) and Bessel beams. Microparticles and even an organism were demonstrated to be manipulated using a 37-MHz SAW device [8]. However, single object manipulation is not easy to achieve if there is more than one object placed in the pool. A single microparticle was demonstrated to be manipulated using the Bessel beam [9], however, the configuration of device is relatively complex with a limited trapping space. In contrast, an acoustic microbeam [10] may be the promising alternative method because it can control the movement of single objects arbitrarily in two dimensions. This kind of acoustic device is termed Single Beam Acoustic Tweezer (SBAT).

The mechanism of SBAT is similar to that of optical tweezers. Both analytical and experimental studies have shown that SBAT could trap the objects with a size either larger or smaller than an acoustic wavelength that are termed Mie regime or Rayleigh regime, respectively. Although most analytically studies ignored the attenuation and the possible streaming effect in the medium [11,12], it can be concluded that the trapping performance could be affected by many factors such as device performance (frequency, beam width, sensitivity) and targeted object characteristics(shape, size, acoustic properties). To meet the criteria for performing efficient manipulation, the SBAT should have low f-number (f#) and high sensitivity.

Previously, several methods were studied to develop the SBATs including a press-focused method, a self-focused method, and a lens-focused method. Among these methods, the self-focused method may be the easiest approach to develop low f#(~1) SBATs, but the sensitivity of the SBATs is usually poor due to the weak performance of sputtered material. Lens would lead to attenuation in the high frequency range (>80 MHz), resulting in the degradation of sensitivity. The press-focused method may be the most suitable technique to develop the most sensitive SBATs with lower f#s(<1) [13]. It was reported that 96- and 30- MHz SBATs could trap small lipid particles of a size at 50 and 120 μm in distilled water, respectively [14,15]. Recently, 200-MHz SBATs with an f# of 1.6 were developed successfully to trap a single polystyrene microsphere with a size down to 5 μm [16]. The single microsphere could be manipulated along with the random movement of the SBAT within the range of hundreds of microns in distilled water two-dimensionally. The manipulation was demonstrated to be highly efficient that only caused little disturbance to other microspheres nearby.

Since the size of microparticle manipulated has approached the cellular level, biomedical applications have been demonstrated using the developed SBATs. One of the applications is to study the deformability of Red Blood Cells (RBCs) [17]. The approach was very similar to that using optical tweezers [18]. Before the experiment, fresh blood samples were drawn from a healthy donor. Both 5 μm microspheres and RBCs were washed and diluted in Phosphate-Buffered Saline (PBS). The resultant solution was kept in room

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temperature to allow cells and microspheres attach together. A RBC being stuck on the Mylar film (a substrate of chamber) and adhered with a microsphere was chosen under a microscope. The RBC deformation was induced by acoustically manipulated the microsphere using a 200-MHz SBAT. With the random movement of SBAT, the RBC was stretched to deform in different degrees. This demonstrates that the SBATs can do the similar work of cell deformation as the optical tweezers.

Besides the cell deformation, SBATs were also employed to study the cancer cell membrane properties [19]. The method is similar to the above mentioned one. A 5 μm fibronectin-coated microsphere was trapped and attached to a single breast cancer cell (MCF-7) by the 200-MHz microbeam. The cell membrane was then stretched by controlling the movement of the microsphere when the SBAT was turned on and off. The demonstration suggests that the SBATs may be a potential tool to evaluate the cancer cell stiffness or probe local mechanical properties of cancer cells. Since the SBATs could offer a high-frequency high-sensitive ultrasound microbeam, cell stimulation is also their sideline application. High-Frequency Ultrasound microbeam Stimulation (HFUMS) is a kind of non-contact technique to stimulate a single cell at a micrometer scale. Breast cancer cells have been studied as the target cells to be stimulated by a 200-MHz f#1.6 SBAT [20]. With using live-cell fluorescence imaging, calcium ions influx was found to be induced in breast cancer cells. The effect was found to be much significant in invasive breast cancer cells (MDA-MB-231) compared to noninvasive breast cancer cells (MCF-7). This suggests the potential of acoustic microbeam devices to identify the invasiveness of breast cancer cells.

In recent years, research attention and significant progresses have been made on the development of high-quality SBATs. Other than the traditional SBATs, different transducer configurations have also been developed for acoustic tweezing applications. Phased array transducer is one of the recent examples that could electronically steer the acoustic beam to manipulate the target objects without the mechanical movement of device [21]. However, due to the fabrication difficulty and complexity of phased array transducers, the frequency is usually limited to 40 MHz that is not capable of manipulating an individual microparticle and cell. Thus, further improvement on the device or beam forming method is required. Besides, the physical properties of the target cells cannot be evaluated quantitatively without realizing the force generated from the SBATs. Since the frequency of commercial hydrophones is limited to 60 MHz, the force calibration at further high-frequency range is desired and challenging. More efforts should be made to quantify the force generated from the SBATs. The other important front is the three-dimensional manipulation, which is again very challenging.

Conclusion

The potential of SBATs has been shown in various biomedical applications, such as acoustic manipulation, cell deformation, cell stimulation, etc. Previously, the effort was mainly put on the understanding of trapping mechanism as well as on the development of high-performance acoustic devices. Nevertheless, further efforts are required to bridge the relationship between the physical performance of SBATs and the biophysical characteristics of biological samples being interrogated. Moreover, to explore more biomedical applications, novel types of acoustic devices are still highly desired to develop so as to perform much efficient manipulation with higher trapping intensity and deeper penetration depth.

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