UC Irvine UC Irvine Previously Published Works

Title

An adjustable multi-scale single beam acoustic tweezers based on ultrahigh frequency ultrasonic transducer

Permalink https://escholarship.org/uc/item/8t51r1zz

Journal Biotechnology and Bioengineering, 114(11)

ISSN 0006-3592

Authors

Chen, Xiaoyang Lam, Kwok Ho Chen, Ruimin <u>et al.</u>

Publication Date 2017-11-01

DOI

10.1002/bit.26365

Peer reviewed



HHS Public Access

Author manuscript *Biotechnol Bioeng.* Author manuscript; available in PMC 2023 June 29.

Published in final edited form as: *Biotechnol Bioeng.* 2017 November ; 114(11): 2637–2647. doi:10.1002/bit.26365.

An adjustable multi-scale single beam acoustic tweezer based on ultrahigh frequency ultrasonic transducer

Xiaoyang Chen^{1,5}, Kwok–ho Lam⁴, Ruimin Chen², Zeyu Chen², Ping Yu⁵, Zhongping Chen¹, K. Kirk Shung², Qifa Zhou^{2,3}

¹Beckman Laser Institute & Medical Clinic and Department of Biomedical Engineering, University of California-Irvine, Irvine, California 92612, USA

²Department of Biomedical Engineering and NIH Transducer Resource Center, University of Southern California, Los Angeles, California 90089, USA

³Department of Ophthalmology, University of Southern California, Los Angeles, 90089, USA

⁴Department of Electrical Engineering, The Hong Kong Polytechnic University, Hunghom, Kowloon, Hong Kong

⁵College of Material Science and Engineering, Sichuan University, Chengdu 610064, People's Republic of China

Abstract

This paper reports the fabrication, characterization and microparticle manipulation capability of an adjustable multi-scale single beam acoustic tweezer (SBAT) that is capable of flexibly changing the size of "tweezers" like ordinary metal tweezers with a single-element ultrahigh frequency (UHF) ultrasonic transducer. The measured resonant frequency of the developed transducer at 526 MHz is the highest frequency of piezoelectric single crystal based ultrasonic transducers ever reported. This focused UHF ultrasonic transducer exhibits a wide bandwidth (95.5% at -10 dB) due to high attenuation of high-frequency ultrasound wave, which allows the SBAT effectively excite with a wide range of excitation frequency from 150 MHz to 400 MHz by using the "piezoelectric actuator" model. Through controlling the excitation frequency, the wavelength of ultrasound emitted from the SBAT can be changed to selectively manipulate a single microparticle of different sizes (3 – 100 μ m) by using only one transducer. This concept of flexibly changing "tweezers" size is firstly introduced into the study of SBAT. At the same time, it was found that this incident ultrasound wavelength play an important role in lateral trapping and manipulation for microparticle of different sizes.

Keywords

acoustic trapping; ultrahigh frequency ultrasonic transducer; adjustable multi-scale tweezers; microparticle trapping and manipulation; "piezoelectric actuator" model

Correspondence to Author: Qifa Zhou, telephone: 213-821-2648; fax: 213-821-3897; qifazhou@usc.edu.

Introduction

A device for contact-free manipulation of the microparticle, e.g., cells, molecules, DNA, bacteria, etc, is of great interest for biological and medical applications(Ding et al. 2012; Yang et al. 2009). Many devices have been developed including optical tweezers(MacDonald et al. 2003) and acoustic tweezers(Wu 1991). Optical tweezers can produce forces to manipulate particles with a size from tens of nanometers to tens of micrometers(Grier 2003). However, this technique has its own drawbacks, including photo damage on the target tissues by high intensity focused laser and the requirement of optically purified samples(Lam et al. 2013; Neuman and Nagy 2008). To overcome the issues, acoustic tweezers utilizing single beam(Shung 2012), standing wave(Brandt 2001) and surface acoustic wave(Guo et al. 2016), have been proposed. Among them, a single beam acoustic tweezer (SBAT) which requires only single-sided transducer or array transducers is much attractive, especially in *in-vivo* manipulation, because the SBAT could be applied directly to the skin with the manipulation taking place inside the body(Marzo et al. 2015), or could be placed closer to blood vessels in which microparticles were manipulated after pierced through skin and tissues by using the needle type transducer(Li et al. 2014).

The SBAT has been demonstrated to be capable of manipulating a single red blood cell(Lam et al. 2016), estimating the deformability of cancer cells(Hwang et al. 2014), stimulating breast cancer cells at a micrometer scale(Hwang et al. 2013), trapping and manipulating microparticles in the lateral direction with the size from several microns to hundreds of microns by using different frequency ultrasonic transducers(Hwang et al. 2013; Lam et al. 2012; Lee et al. 2010; Lee et al. 2011; Lee et al. 2009; Zhu et al. ; Zhu et al. 2016). Preliminary analytical studies show that the feasibility of acoustic tweezers and trapping an arbitrarily located object mainly comes from the focused Gaussian ultrasound beam (Azarpeyvand and Azarpeyvand 2013; Lee et al. 2005; Lee and Shung 2006b; Mitri 2015b; Wu and Du 1990). These studies have shown that Gaussian beams can be used for trapping particles in both lateral and axial directions, although the latter is much harder due to the existence of the radiation force from scattering by pushing the particle away from the transducer(Hill 2016; Marzo et al. 2015). To overcome this problem, single Bessel vortex beam was introduced into the study of SBAT, which can produce a negative axial radiation force(Mitri 2009; Mitri 2014a; Mitri 2014b; Mitri 2015a). Besides, the theoretical analysis has shown that the acoustical waves from a uniform vibrating circular piston source can induce a negative radiation force on a sphere with an arbitrary radius placed in the near field(Mitri 2013), while the annular beam can improve the acoustical tweezing performance by producing a negative pulling force in the prefocal and postfocal regions(Mitri 2016). Except for the study of three dimensional (3D) trapping, an excellent microparticle-handling tweezers should be capable of selectively manipulating objects with a large range of size from the concept of tweezers, like ordinary metal tweezers. This is very helpful for the targeted microparticle manipulation, especially when the microparticles with different sizes mix together. Therefore, this paper aims to develop a more advanced SBAT which have the aforementioned capability of selectively manipulating microparticles with wide range of size using only one transducer.

Recently, much effort have been made to develop highly sensitive ultrahigh frequency (UHF) ultrasonic transducers (center frequency >100 MHz) with a low *F*-number (*F*-number= focal length /aperture size)(Cannata et al. 2003; Lee et al. 2010; Lee et al. 2009) since the beam width is inversely proportional to the transducer frequency and proportional to f-number. The smaller beam width allow UHF transducers to trap smaller particles(Lam et al. 2013b). A 200-MHz lens-focused transducer was developed to trap a cell of a size of 15~20 µm diameter(Lee et al. 2011). A 200MHz LiNbO₃ (LNO) crystal lens-less focused transducer was used to manipulate a 5µm diameter microsphere(Lam et al. 2013). A 230-MHz self-focused AlScN film transducer can be used to trap 10µm microspheres and epidermoid carcinoma cell(Zhu et al.). Besides for trapping and manipulating smaller particles, acoustic trapping force calibration of UHF SBAT is another useful approach to evaluate the trapping performance of SBAT(Lim et al. 2016). However, there is less work reported for fully studying the trapping capability of one transducer for microparticles with different size, and systematically exploring the relationships between ultrasound frequency, beam width and particle size. The effect of propagating surface acoustic wave (PSAW) with different frequencies on particles with different sizes have been studied(Skowronek et al. 2013). Thus, these studies would make SBAT more practical as one kind of particle-handling devices. The work provided here may offer an experimental basis for further development of single-beam acoustic handling devices.

Besides, there is less work reported that the operating frequency of UHF transducer using piezoelectric crystals can exceed 300 MHz by using the traditional approach in which the piezoelectric crystals are lapped down to the order of microns. Although the piezoelectric thick film technology provides an alternative solution by controlling the film thickness within the accuracy of a few microns(Chen et al. 2016), the weak sensitivity and poor performance are the main concerns for developing piezoelectric thick film UHF transducers. In this study, the LNO crystal was used to fabricate UHF transducer with the center frequency beyond 300MHz with a modified conventional approach. This center frequency of the developed transducer is the highest among the piezoelectric crystal-based ultrasonic transducers ever reported.

By introducing the "piezoelectric actuator" model, microparticles with a wide range of size could be manipulated by using only one SBAT, i.e. the UHF transducer (>300 MHz). At the same time, the trapping processes have been studied systematically in terms of the ultrasound wavelength and microparticle size.

Materials and Methods

The LNO crystal was used to fabricate the UHF transducers with the center frequency beyond 300 MHz with a modified conventional approach.

Fabrication of UHF transducer

The resonant frequency of ultrasonic transducer is decided by the thickness of piezoelectric element(Zhou et al. 2014; Zhou et al. 2011), so the key to develop the UHF ultrasonic transducer is to fabricate the piezoelectric element with the thickness of several microns. The conventional approach is to directly lap down crystal wafers that are fixed on a glass

by using wax to the desired thickness. However, the limit of the thin thickness by using this approach is about 9 μ m for the LNO crystals(Fei et al. 2016). The further lapping process would break crystal wafers into pieces and easily remove the wafers from the glass due to the decreasing bonding strength between the glass and crystal wafers and the increasing stress concentration on the wafers. Different from the conventional approach, a very lossy conductive epoxy was cast to the LNO crystal as the supporting layer as well as the buffer layer before the lapping process. This polymer can offer better bonding effect and relieve the stress concentration effectively. By using this modified method, the ultrathin LNO crystal wafers with the thickness down to 6~9 μ m could be fabricated. The detailed fabrication process is given below.

The LNO crystal (Boston Piezo-optics, Bellingham, MA) was polished to keep two sides flat with the thickness tolerance of 1 μ m. A very lossy conductive epoxy (E-Solder 3022, Von Roll Isola Inc., New Haven, CT) with an acoustic impedance of ~6 MRayl was cast to the LNO crystal as the backing material by centrifuging at 3000 rpm for 15 min. After cured overnight at room temperature, the backing layer was lapped down to 1-mm thick with the tolerance of 1 μ m. Then the wafers were pasted on the glass (the deviation of glass flatness 1 μ m) with high-temperature (90 °C) wax. Then the LNO crystals were lapped to 6~9 μ m according to the design and simulation. In the lapping process, especially for the final 30 μ m, the flatness of LNO crystal wafer is needed to keep within 1 μ m. The samples were diced along the thickness direction into small squares with dimensions of 0.3 × 0.3 mm².

The acoustic stack was inserted into a polyimide tube (Small Parts Inc., Miramar, FL), which served as an insulating layer. A lead wire was connected to the backing layer by injecting the conductive epoxy to the polyimide tube. The piezoelectric element was fixed into a steel needle housing followed by filling the gap between the element and housing with epoxy (Epotek-301, Epoxy Technology Inc., Billerica, MA). In order to apply the UHF transducer for microparticle manipulation, the tightly focused UHF transducers with a *f*-number of 1.3 (focal depth= radius of ball) were obtained by press-focusing. The UHF transducers were press-focused by a highly polished chrome/steel ball bearing of 0.8 mm diameter at 90 °C. The critical point to obtain the tightly focused acoustic beam is to make sure that the ball was positioned at the center of these samples. Finally, a Cr/Au (500 Å/1000 Å) layer was sputtered across the piezoelectric element and the needle housing to serve as common ground. A 0.8 μ m-thick parylene layer was vapor-deposited on the front face of the transducer to serve as an acoustic matching layer and a protection layer. The final transducer was assembled with an SMA connector.

A cross-sectional view of the design and photograph of the focused UHF LNO transducer with the *f*-number of 1.3 is shown in Figure 1.

Transducer characterization

The performance of the transducer was measured by using the conventional pulse-echo response measurement. During the measurement, the transducer was connected to a pulser/ receiver (JSR Ultrasonics DPR500, Imaginant, Pittsford, NY), which was excited by an electrical impulse at 200-Hz repetition rate, $50-\Omega$ damping and $2.3-\mu$ J energy per pulse. The reflected waveform was received by by a 500-MHz bandwidth receiver with a high pass

5-MHz filter and a low pass 500-MHz filter. An X-cut quartz plate was placed at the focal point as a target. The reflected waveform was digitized by a 12-bit data acquisition board at a sampling frequency of 2 G sample/s.

The acoustic trapping experimental arrangement was described previously(Li et al. 2014), as shown in Figure 2. The focused UHF transducer was set in a cell culture dish of distilled water. The transducer was mounted on a three-axis motorized linear stage ((SGSP 26–50, Sigma KOKI Co., Japan) and controlled by a customized LabVIEW program. A CMOS camera (ORCA-Flash2.8, Hamamatsu, Japan) combining with an inverted microscope (IX-71, Olympus, Japan) were used to record the motion of the trapped particle. Before the trapping experiment, a pulse-echo test was performed to make sure that the target particles were on the focal plane of UHF transducer. In this study, polystyrene microparticles of 3, 5, 6.3, 10, 50 and 100µm mean diameter were used. The transducer was driven in a sinusoidal burst mode by a function generator (Stanford Research Systems, Sunnyvale, CA, USA) and then amplified by a 50-dB power amplifier (525LA, ENI, Rochester, MN). To demonstrate the capability of two dimensional (2D) single microparticle manipulation, the transducer with the trapped particle was moved in a random manner by the motorized stages. The duty factor and pulse repetition frequency were fixed at 1% and 1 kHz, respectively, while the excitation frequency and input voltage were varied in our experiments.

This trapping measurement setup can be also used to measure the maximum displacement of microparticle trapped by transversal radiation force (Fig. 2B). The maximum displacement was defined as how far the transversal radiation force can attract the microparticle from the center of beam(Lee et al. 2009). After the transducer is switched on, an acoustic trap will be immediately formed at the focus and then draw the microparticle to the center of beam by transversal radiation force.

Results and Discussions

Transducer Characteristics

The UHF transducers were designed at ultrahigh center frequencies in the 300~500-MHz range by using PiezoCAD modeling. The resonant frequency of the unfocused UHF transducer was measured at 526MHz (Fig. 3A). However, the corresponding echo response and frequency spectra show that the center frequency of the unfocused UHF transducer decreased down to 391 MHz (Fig. 3B). The relationship between the resonant frequency and center frequency of the LNO UHF transducer fabricated in our lab previously from 100MHz to the present work (275 MHz)(Fei et al. 2016) was also studied in our experiments (Fig. 3C). It was found that increasing the resonant frequency would induce a serious center frequency down-shift especially when the resonant frequency exceeds 300MHz. This is attributed to the high attenuation of high frequency ultrasound wave that is proportional to the square of the frequency of ultrasound wave (Shung 2015) and the bandwidth limitation of the pulser/receiver (Bandwidth: 5 - 500MHz) used in our experiment(Hill et al. 2004). Even though, the resonant frequency of the developed transducer was still the highest among the reported piezoelectric single crystal-based ultrasonic transducers. Meanwhile, the UHF transducer also shows the improved sensitivity with no gain, compared with the previous UHF devices.

In order to apply the 394MHz UHF transducer for microparticle manipulation, the tightly focused UHF transducers with the *f*-number of 1.3 were developed by press-focusing. Since neither calibrated hydrophones nor alternative standardized methods are available for measuring absolute pressure levels at the frequency greater than 60 MHz(Zhu et al.), the lateral beam profile, instead, was measured by scanning a tungsten wire target with the diameter of 4-µm. The measured pulse-echo waveform and frequency spectrum from the wire target are shown (Fig. 3D). It can be found that the center frequency of the transducer is 336 MHz, and the bandwidths at -6 dB and -10 dB were measured to be 44.6% and 95.5%, respectively. Compared with the results obtained from the unfocused LNO UHF transducer, the center frequency of the press-focused transducer was found to further shift down because the relative long focal length of the press-focused transducer leads to the longer distance and time of ultrasound wave propagation, which suffers much from the high attenuation of UHF ultrasound wave. Consequently, the magnitude decreased very quickly at the high-frequency region beyond the maxima while the magnitude decreased slowly at the low-frequency region, especially from -6 dB to -10 dB. With the contribution of low-frequency components, UHF ultrasonic transducer was shown to exhibit a wide bandwidth (95.5% at -10 dB). In general, the bandwidth at -6 dB plays an important role in the axial resolution of ultrasound imaging(Shung 2015). Previous studies about the SBAT mainly focused on the center frequency, and paid little attention on the bandwidth of transducer. In the following sections, the excitation frequency was found to closely relate to the bandwidth. Different from the bandwidth in ultrasound imaging, the bandwidth at the lower value compared to -6 dB becomes more important for the SBAT application. The 4um-diameter tungsten wire phantom image was shown (Fig. 4A). The lateral beam width was determined to be 7 µm by detecting its magnitude value that was reduced by 6 dB from the maximum (Fig. 4B). This measured result is close to the predicted width of 5.95 µm (*f*-number × wavelength).

Particle manipulation (3 – 100-µm)

The aim of this study is to precisely and selectively manipulating microparticles with a wide range of size by using only one transducer. The experimental results proved that the SBAT can manipulate the particles with the size of much larger than and smaller than an acoustic wavelength in Mie regime ($a \gg \lambda$) and Rayleigh regime ($a < \lambda$), respectively. In Mie regime, single microsphere can be manipulated effectively to form a 2D pattern. However, one major disadvantage of trapping in Mie regime is the stronger dependence on the particle shape and the material of particle(Lee et al. 2005; Lee and Shung 2006a; Lee and Shung 2006b). Even though there is a lesser requirement of the particle material and shape in Rayleigh regime(Lam et al. 2016), we found that the ultrasonic transducer may trap several particles when the center frequency of the ultrasonic transducer is too low. Besides, the trapping and manipulating processes become much complicated and challenged when the particle size lies between Mie regime and Rayleigh regime. This means that an optimal frequency is needed to determine for a particular particle size. As a result, the development of a powerful SBAT capable of covering both Mie and Rayleigh regime with a wide range of particle size is desired.

Besides the regime consideration, the SBAT can also be treated as the actuator in which the motion is driven by the electrical signal. This "piezoelectric actuator" model may make SBAT flexible in trapping particles of different sizes. For the study of piezoelectric actuators, there are two general working models: (1) under resonance condition and (2) under non-resonance condition. Under the resonance condition, much larger displacements and vibration velocities of the actuator can be achieved even with lower driving voltage compared to the ones under the non-resonance condition(Yao et al. 2000). In this work, the UHF SBAT was excited not only at the resonant frequency but also at other non-resonant frequencies, while the excitation voltage was changed to offer enough force to move a particle. It was noticed that the range of excitation frequency is closely related to the bandwidth of ultrasonic transducer. Here, it was found that this focused UHF transducer can effectively be excited with the driving frequency from 150MHz to 400MHz, which is close to its range of bandwidth at -10dB (Fig. 3D). Beyond this range, the SBAT was hardly driven by high voltages, and there was a risk of damaging the transducer.

Figure 5 shows the motion of a single 3µm, 5µm, 6.3µm and 10µm particle that could be manipulated effectively without affected neighbor particles under the excitation frequency from 380 MHz to 150 MHz, respectively. It was found that the lower excitation frequency would allow SBAT to manipulate the bigger microparticle. In order to manipulate the bigger particles with the diameters of 50µm and 100µm and avoid damaging the piezoelectric layer, the excitation frequency was increased for manipulate of Higgs. 5C and 5D). This result is very interesting because changing the excitation frequency would allow the UHF transducer to work in different regimes. In other words, the strategy of excitation frequency adjustment could extend the trapping capability of SBAT.

The relationships between the driving conditions in experiments, the calculated wavelength, beam width and particle size, were studied (Table I). During the manipulation experiments, the SBAT was driven in a sinusoidal burst mode by a function generator, and thus the excitation frequency decides the wavelength of ultrasound emitted from the transducer. It was found that higher voltage was required to apply on the transducer to trap the particle when the excitation frequency was further away from the center frequency. This result also shows that the particle trapping process is strongly related to the particle size, the excitation frequency and beam width.

In order to investigate the relationship between the excitation frequency and the particle size, the trapping and then manipulating processes of 3-µm microparticle at different excitation frequencies were studied in detail from two approaches. One approach is to study the maximum displacement of a single 3-µm microparticle at different excitation frequencies (330MHz, 350MHz and 380MHz) with the same input voltage, as shown in Figure 6. The result shows that lowering the excitation frequency would increase the maximum displacement, which can prove that reducing the excitation frequency would increase the range of transversal radiation force. Other approach is to study the maximum number of the trapped 3µm microparticles at different excitation frequencies (Fig. 6D). It was found that reducing the excitation frequencies (Fig. 6D). It was found that reducing the excitation frequency would enable the SBAT to trap more 3µm microparticles from 300MHz to 200MHz.

Besides, the relationship between the excitation frequency and the particle size was also studied, especially when the particle size lie between Mie regime and Rayleigh regime. The SBAT was driven by different excitation frequencies from 400 MHz to 150 MHz to manipulate 3 –10µm particles (Table II). It was found that the SBAT can manipulate not only single but also several particles at the same time. Supplementary Figure 1 and Figure 2 show that reducing the excitation frequency would enable the SBAT to trap more microparticles with the same size. In fact, the excitation frequency for the SBAT determines the number of trapped particles. If the excitation frequency was too high, the SBAT would lose the trapping capability. It appears that there exists a critical frequency for trapping a single particle of a particular size. This critical frequency is lower for trapping the bigger single particle such that the SBAT was found to be able to trap the single particle effectively when the wavelength is bigger than or comparable to the particle size. More particles would be trapped at the same time when further increasing the wavelength.

Working principle of an adjustable multi-scale SBAT

The direct obvious effect of changing the excitation frequency of SBAT is the wavelength, nevertheless, this would also change the focused Gaussian beam width, i.e., decreasing the frequency would increase the wavelength and widen the beam width of the ultrasound wave. The theoretical analysis of the acoustic radiation force in a single focused Gaussian beam evaluated by integrating the time-averaged radiation stress tensor over a surface(Azarpeyvand and Azarpeyvand 2013), indicates that the exerted transversal radiation force generally repels the object away from the beam axis when the wavelength is smaller or comparable to the particle size, except for particles located on the waist plane and laterally within a certain distance from the beam center. This theoretical analysis mentioned above is analyzed in an inviscid fluid. In fact, the dissipative effects should be considered in terms of the radiation force, for example, the viscous effect in the boundary layer and the streaming effect would cause the unstable trap(Mitri 2011; Mitri 2013). What's more, the exertion of transversal radiation forces becomes much easier near the center of the beam by using wider Gaussian beams. Moreover, in their theoretical analysis, it was found that wider beam width of incident ultrasound wave would have smaller transverse radiation force and wider lateral range of that force. This theoretical analysis is very much in accord with our experimental results. The particle trapping with the wider beam width could be performed in much easier and stable ways, particularly when the wavelength is smaller or comparable to particle size. This wider range of transverse radiation force may be the main reason why the wider beam width can trap several particles at the same time.

For the particle size large than the wavelength, it was found that increasing the excitation frequency is beneficial to the trapping and manipulation of the bigger particle (50µm microparticle at 150MHz, 100µm microparticle at 180MHz) as shown in Table I, which can be explained by the Ray approach. However, the theoretical analysis of SBAT in Mie regime mainly focuses on the axial acoustic radiation force rather than the transversal radiation force (Lee et al. 2005; Lee and Shung 2006b). This calculation of transversal radiation force in Mire regime will be further investigated in our lab. Even though, the principle of SBAT is very similar to optical tweezers that are capable of carrying momentum, especially in Mie regime. Both experimental result and theoretical analysis using the Ray approach show that

the transversal radiation force and lateral trapping efficiency of optical tweezers decreases as the particle size decreases in Mie regime(Felgner et al. 1995; Wright et al. 1994). It was also found that the transversal radiation force and trapping stability of optical tweezers sensitively depend on the focused beam width, and decrease with the increase in beam width (Zhang et al. 2007). Similar results were also found in our experiments. This smaller beam width would produce larger transverse radiation force so as to manipulate bigger particle effectively.

Besides the excitation frequency, the duty factor and mechanical properties of microparticle et al. would also influence the effective trapping force of SBAT. Moreover, the trapping force often increases nonlinearly with those excitation parameters(Li et al. 2013). The control of trapping force exerted by SBAT on the microparticles is the key to trap and manipulate microparticles such that too large or too small force cannot trap the targeted microparticle or microparticles effectively.

Based on the above analysis mentioned before, the trapping process can be summarized in Figure 7. The relationships between the particle size, ultrasound wavelength and beam width is shown (Fig. 7A). When the particle size is larger than the incident ultrasound wavelength, the smaller beam width would have stronger trapping capability. When the particle size is smaller than or comparable to the incident ultrasound wavelength, the effect of excitation frequency or beam width on the trapping process is contrary to the former case, and the SBAT trapped several particles at the same time when the excitation frequency was decreased significantly. Based on this relationship and the "piezoelectric actuator" model, an adjustable multi-scale SBAT that is capable of performing manipulation in different regimes can be obtained by controlling the excitation frequency to satisfy the specific condition (Fig. 7B). This study shows that optimizing the width of Gaussian beam and the excitation frequency is helpful to enhance the performance of SBAT. Such SBAT has the capability of selecting the specific size and the amount of particle to trap and manipulate, which is very similar to the ordinary metal tweezers.

Discussions

By using the "piezoelectric actuator" model, the SBAT device can be operated under the resonance/non-resonance mode through controlling the excitation frequency. The resonance/non-resonance operation mode based on the converse effect of piezoelectric material shows that the electromechanical energy conversion efficiency would be lower under the non-resonance condition, and the low energy conversion efficiency can be made up by increasing the input voltage. Moreover, the excitation frequency range is close to the bandwidth of ultrasonic transducer. It was found that increasing the resonant frequency of ultrasonic transducer would cause a serious frequency down-shift due to the high attenuation of high-frequency ultrasound wave, especially when the resonant frequency exceeds 300MHz. However, this frequency down-shift makes UHF ultrasonic transducer exhibit a wide bandwidth (95.5% at -10dB) by containing the other low-frequency components, which allows the SBAT effectively excite with a wide range of excitation frequency from 150MHz to 400MHz. Through controlling the excitation frequency, the wavelength of ultrasound emitted from the SBAT can be changed to selectively manipulate a single microparticle

of different sizes. At the same time, it was found that the incident ultrasound wavelength plays an important role in lateral trapping and manipulation for microparticle of different sizes. When the particle size is bigger than the incident ultrasound wavelength, reducing the ultrasound wavelength or beam width would be beneficial to the trapping process. When the particle size is smaller than or comparable to the incident ultrasound wavelength, increasing the ultrasound wavelength or beam width would make the trapping process easier.

Conclusions

In this work, we report a modified conventional approach in which the 6 µm-thick LNO crystal was lapped down for the fabrication of UHF (Resonant frequency: 526 MHz, Center frequency: 394 MHz) needle-type ultrasonic transducers. By using the "piezoelectric actuator" model, the SBAT device can be operated under the resonance/non-resonance mode through controlling the excitation frequency, while the excitation voltage was changed to offer enough force to manipulate a particle. Moreover, the excitation frequency range of SBAT is close to the bandwidth of ultrasonic transducer. Similar to the usage of ordinary metal tweezers, the flexible beam width and wavelength offer the SBAT being able to selectively manipulate the microparticle with the size range of 3~100 µm through controlling the excitation frequency. Such wide size range was seldom reported in the study of SBAT. This UHF transducer is very helpful for targeted microparticle manipulation from a mixture of particles with different sizes. Besides, the interaction of focused Gaussian beams and wavelength by particles of different sizes was studied in detail. The experimental results should help us to enhance the performance of the existing acoustic trapping techniques and develop more advanced particle-handling devices.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by the National Institutes of Health (Grant No. P41-EB002182), the China Scholarship Council (CSC), and the Hong Kong Research Grants Council (ECS Grant No. 253001/14P).

References

- Azarpeyvand M, Azarpeyvand M. 2013; Acoustic radiation force on a rigid cylinder in a focused Gaussian beam. J Sound Vib. 332 (9) 2338–2349.
- Brandt EH. 2001; Acoustic physics. Suspended by sound. Nature. 413 (6855) 474–5. [PubMed: 11586343]
- Cannata JM, Ritter TA, Chen W-H, Silverman RH, Shung KK. 2003; Design of efficient, broadband single-element (20–80 MHz) ultrasonic transducers for medical imaging applications. IEEE Trans Ultrason Ferroelectr Freq Control. 50 (11) 1548–1557. [PubMed: 14682638]
- Chen X, Fei C, Chen Z, Chen R, Yu P, Chen Z, Shung KK, Zhou Q. 2016; Simulation and fabrication of 0–3 composite PZT films for ultrahigh frequency (100–300 MHz) ultrasonic transducers. J Appl Phys. 119 (9) 1033–926.
- Ding X, Lin S-CS, Kiraly B, Yue H, Li S, Chiang I-K, Shi J, Benkovic SJ, Huang TJ. 2012; On-chip manipulation of single microparticles, cells, and organisms using surface acoustic waves. P Natl Acad Sci USA. 109 (28) 11105–11109.

- Fei C, Chi TC, Chen X, Chen Z, Ma J, Zhu B, Shung KK, Zhou Q. 2016; Ultrahigh Frequency (100 MHz–300 MHz) Ultrasonic Transducers for Optical Resolution Medical Imagining. Sci Rep. 6: 28360. [PubMed: 27329379]
- Felgner H, Müller O, Schliwa M. 1995; Calibration of light forces in optical tweezers. Appl Optics. 34 (6) 977–82.
- Grier DG. 2003; A revolution in optical manipulation. Nature. 424 (6950) 810–816. [PubMed: 12917694]
- Guo F, Mao Z, Chen Y, Xie Z, Lata JP, Li P, Ren L, Liu J, Yang J, Dao M. 2016; Three-dimensional manipulation of single cells using surface acoustic waves. P Natl Acad Sci USA. 113 (6) 1522.
- Hill CR, Bamber JC, Haar GRT. 2004; Physical Principles of Medical Ultrasonics. J Acoust Soc Am. 116 (5) 2707–2707.
- Hill M. 2016; Viewpoint: A One-Sided View of Acoustic Traps. Physics. 9: 3.
- Hwang JY, Lee C, Lam KH, Kim HH, Lee J, Shung KK. 2014; Cell membrane deformation induced by a fibronectin-coated polystyrene microbead in a 200-MHz acoustic trap. IEEE Trans Ultrason Ferroelectr Freq Control. 61 (3) 399–406. [PubMed: 24569245]
- Hwang JY, Lee NS, Lee C, Lam KH, Kim HH, Woo J, Lin MY, Kisler K, Choi H, Zhou Q. 2013; Investigating contactless high frequency ultrasound microbeam stimulation for determination of invasion potential of breast cancer cells. Biotechnol Bioeng. 110 (10) 2697–2705. [PubMed: 23568761]
- Lam KH, Hsu HS, Li Y, Lee C, Lin A, Zhou Q, Kim ES, Shung KK. 2013; Ultrahigh frequency lensless ultrasonic transducers for acoustic tweezers application. Biotechnol Bioeng. 110 (3) 881– 886. [PubMed: 23042219]
- Lam KH, Li Y, Lee C, Zhou Q, Shung KK. 2012. Ultrahigh frequency ultrasound microbeam for biomedical applications. Proc IEEE Ultra Sym. 1994–1997.
- Lam KH, Ying L, Yang L, Lim HG, Zhou Q, Shung KK. 2016; Multifunctional single beam acoustic tweezer for non-invasive cell/organism manipulation and tissue imaging. Sci Rep. 6: 37554. [PubMed: 27874052]
- Lee C, Lee J, Lau ST, Zhou Q, Shung KK. 2010. Single microparticle manipulation by an ultrasound microbeam. Proc IEEE Ultra Sym. 849–852.
- Lee J, Ha K, Shung KK. 2005; A theoretical study of the feasibility of acoustical tweezers: Ray acoustics approach. J Acoust Soc Am. 117 (5) 3273–3280. [PubMed: 15957793]
- Lee J, Lee C, Kim HH, Jakob A, Lemor R, Teh SY, Lee A, Shung KK. 2011; Targeted cell immobilization by ultrasound microbeam. Biotechnol Bioeng. 108 (7) 1643–1650. [PubMed: 21328319]
- Lee J, Shung KK. 2006a; Effect of ultrasonic attenuation on the feasibility of acoustic tweezers. Ultrasound Med biol. 32 (10) 1575–1583. [PubMed: 17045879]
- Lee J, Shung KK. 2006b; Radiation forces exerted on arbitrarily located sphere by acoustic tweezer. J Acoust Soc Am. 120 (2) 1084–1094. [PubMed: 16938994]
- Lee J, Teh S-Y, Lee A, Kim HH, Lee C, Shung KK. 2009; Single beam acoustic trapping. Appl Phys Lett. 95 (7) 073701. [PubMed: 19798424]
- Li Y, Lee C, Chen R, Zhou Q, Shung KK. 2014; A feasibility study of in vivo applications of single beam acoustic tweezers. Appl Phys Lett. 105 (17) 173701. [PubMed: 25422525]
- Li Y, Lee C, Lam KH, Shung KK. 2013; A simple method for evaluating the trapping performance of acoustic tweezers. Appl Phys Let. 102 (8) 84102. [PubMed: 23526834]
- Lim HG, Li Y, Lin MY, Yoon C, Lee C, Jung H, Chow RH, Shung KK. 2016; Calibration of Trapping Force on Cell-Size Objects From Ultrahigh-Frequency Single-Beam Acoustic Tweezer. IEEE Trans Ultrason Ferroelectr Freq Control. 63 (11) 1988–1995. [PubMed: 27834633]
- MacDonald M, Spalding G, Dholakia K. 2003; Microfluidic sorting in an optical lattice. Nature. 426 (6965) 421–424. [PubMed: 14647376]
- Marzo A, Seah SA, Drinkwater BW, Sahoo DR, Long B, Subramanian S. 2015; Holographic acoustic elements for manipulation of levitated objects. Nat Commun. 6: 8661. [PubMed: 26505138]
- Mitri FG. 2009; Negative axial radiation force on a fluid and elastic spheres illuminated by a highorder Bessel beam of progressive waves. J Phys A-Math Theor. 42 (24) 1947–1957.

- Mitri FG. 2011; Potential-well model in acoustic tweezers--comment. IEEE Trans Ultrason Ferroelectr Freq Control. 58 (3) 662–5. [PubMed: 21429858]
- Mitri FG. 2013; Near-field single tractor-beam acoustical tweezers. Appl Phys Lett. 103 (11) 2140–2143.
- Mitri FG. 2014a; Partial-wave series expansions in spherical coordinates for the acoustic field of vortex beams generated from a finite circular aperture. IEEE Trans Ultrason Ferroelectr Freq Control. 61 (12) 2089–97. [PubMed: 25474783]
- Mitri FG. 2014b; Single Bessel tractor-beam tweezers. Wave Motion. 51 (6) 986–993.
- Mitri FG. 2015a; Acoustical pulling force on rigid spheroids in single Bessel vortex tractor beams. Epl. 112 (3) 34002.
- Mitri FG. 2015b; Acoustical tweezers using single spherically focused piston, X-cut, and Gaussian beams. IEEE Trans Ultrason Ferroelectr Freq Control. 62 (10) 1835–1844. [PubMed: 26470046]
- Mitri FG. 2016; Annular spherically focused ring transducers for improved single-beam acoustical tweezers. J Appl Phys. 119 (6) 219–223.
- Neuman KC, Nagy A. 2008; Single-molecule force spectroscopy: optical tweezers, magnetic tweezers and atomic force microscopy. Nat Methods. 5 (6) 491. [PubMed: 18511917]
- Shung KK. 2012; Single beam acoustic tweezer. J Acoust Soc Am. 131 (4) 3533-3533.
- Shung, KK. Diagnostic ultrasound: Imaging and blood flow measurements. Boca Raton, FL: CRC Press; 2006.
- Skowronek V, Rambach RW, Schmid L, Haase K, Franke T. 2013; Particle deflection in a poly (dimethylsiloxane) microchannel using a propagating surface acoustic wave: size and frequency dependence. Anal chem. 85 (20) 9955–9959. [PubMed: 24053589]
- Wright WH, Sonek GJ, Berns MW. 1994; Parametric study of the forces on microspheres held by optical tweezers. Appl optics. 33 (9) 1735–48.
- Wu J. 1991; Acoustical tweezers. J Acoust Soc Am. 89 (5) 2140–2143. [PubMed: 1860996]
- Wu J, Du G. 1990; Acoustic radiation force on a small compressible sphere in a focused beam. J Acoust Soc Am. 87 (3) 997–1003.
- Yang AH, Moore SD, Schmidt BS, Klug M, Lipson M, Erickson D. 2009; Optical manipulation of nanoparticles and biomolecules in sub-wavelength slot waveguides. Nature. 457 (7225) 71–75. [PubMed: 19122638]
- Yao K, Uchino K, Xu Y, Dong S, Lim LC. 2000; Compact piezoelectric stacked actuators for high power applications. IEEE Trans Ultrason Ferroelectr Freq Control. 47 (4) 819–825. [PubMed: 18238614]
- Zhang Y, Liu H, Sun Q. 2007; Transverse optical trapping of spherical particle with strong absorption in a focused Gaussian beam. Proc of SPIE. 6832: 68320K–1.
- Zhou Q, Lam KH, Zheng H, Qiu W, Shung KK. 2014; Piezoelectric single crystal ultrasonic transducers for biomedical applications. Prog Mater Sci. 66: 87–111. [PubMed: 25386032]
- Zhou Q, Lau S, Wu D, Shung KK. 2011; Piezoelectric films for high frequency ultrasonic transducers in biomedical applications. Prog Mater Sci. 56 (2) 139–174. [PubMed: 21720451]
- Zhu B, Fei C, Wang C, Zhu Y, Yang X, Zheng H, Zhou Q, Shung KK. 2017; Self-focused AlScN film ultrasound transducer for individual cell manipulation. ACS Sens. 2 (1) 172–177. [PubMed: 28722425]
- Zhu B, Xu J, Li Y, Wang T, Xiong K, Lee C, Yang X, Shiiba M, Takeuchi S, Zhou Q. 2016; Micro-particle manipulation by single beam acoustic tweezers based on hydrothermal PZT thick film. Aip Adv. 6 (3) 035102. [PubMed: 27014504]



Figure 1.

Biotechnol Bioeng. Author manuscript; available in PMC 2023 June 29.

Author Manuscript



Figure 2.



Figure 3.



Figure 4.



Figure 5.



Figure 6.



Figure 7.

Table I

The relationships between the driving conditions of SBAT in experiments, calculated wavelength, calculated beam width and targeted particle size

| Excitation frequency (MHz) | Excitation Voltage (V) | The calculated Wavelength (µm) | The calculated Beam width (µm) | Particle size (µm) |
|-------------------------------|------------------------|-----------------------------------|-----------------------------------|--------------------|
| 380 | 1.8 | 3.94 | 5.12 | 3 |
| 300 | 2.7 | 5.00 | 6.50 | 5 |
| 200 | 4.2 | 7.50 | 9.75 | 6.3 |
| 150 | 15 | 10.00 | 13.00 | 10 |
| 150 | 27 | 10.00 | 13.00 | 50 |
| 180 | 30 | 8.33 | 10.83 | 100 |

Table II

Success (\checkmark) and failures (×) in trapping microparticles of different sizes by using different excitation frequencies, the corresponding wavelengths and beam widths. The number in the bracket is the number of trapped particles in the experiment.

| Particle size>Excitation frequency /wavelength/beam width | | 5μm | 6.3µm | 10µm |
|---|--------------|--------------|--------------|--------------|
| 400MHz /3.75µm /4.87µm | √ (1) | × | × | × |
| 350MHz/4.28µm /5.57µm | √ (1) | × | × | × |
| 300MHz/5.00µm /6.50µm | √ (2) | √ (1) | × | × |
| 250MHz/6.00μm /7.80μm | √ (2) | √ (1) | √ (1) | × |
| 200MHz/7.50µm /9.75µm | √ (2) | √ (2) | √ (2) | × |
| 150MHz/10.0µm /13.00µm | √ (2) | √ (2) | √ (2) | √ (1) |