Intensely oscillating cavitation bubble in microfluidics

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Abstract. This study reports the technical breakthrough in generating intense ultrasonic cavitation in the confinement of a microfluidics channel [1], and applications that has been developed on this platform for the past few years [2,3,4,5]. Our system consists of circular disc transducers (10-20 mm in diameter), the microfluidics channels on PDMS (polydimethylsiloxane), and a driving circuitry. The cavitation bubbles are created at the gas-water interface due to strong capillary waves which are generated when the system is driven at its natural frequency (around 100 kHz) [1]. These bubbles oscillate and collapse within the channel. The bubbles are useful for sonochemistry and the generation of sonoluminescence [2]. When we add bacteria (Escherichia coli), and yeast cells (Pichia pastoris) into the microfluidics channels, the oscillating and collapsing bubbles stretch and lyse these cells [3]. Furthermore, the system is effective (DNA of the harvested intracellular content remains largely intact), and efficient (yield reaches saturation in less than 1 second). In another application, human red blood cells are added to a microchamber. Cell stretching and rapture are observed when a laser generated cavitation bubble expands and collapses next to the cell [4]. A numerical model of a liquid pocket surrounded by a membrane with surface tension which was placed next to an oscillating bubble was developed using the Boundary Element Method. The simulation results showed that the stretching of the liquid pocket occurs only when the surface tension is within a certain range.

1. Introduction: bubbles in microfluidics channel

1.1. Bubble dynamics in confinement

Ultrasonic cavitation is created by ultrasound in water. These bubbles oscillate and collapse creating high energy concentration (up to 1000 bar and 5000 K). They are used in industrial and bioprocessing applications such as mixing, emulsification, rupturing of cell membrane, and catalyzing chemical reactions. However, in microfluidics, the use of ultrasonic cavitation has been mainly restricted to mixing and pumping. The ultrasound is used to cause pre-existing air pockets in a microfluidics channel to oscillate so as to facilitate liquid flow. In our study, strongly oscillating cavitation bubbles are created instead. They do not oscillate spherically but collapse violently with high speed jets.
2. Cavitation bubbles in microfluidics

Figure 1 shows the experimental setup to generate intense ultrasonic cavitation in our microfluidics channels. The microfluidics channel is made with polydimethylsiloxane (PDMS). It is then attached to a microscope glass slide. A Lead Zirconium Titanate (PZT) transducer is placed next to the microfluidics channel. It is driven by a linear amplifier and a function generator. The experimental observation is recorded by a high speed camera via microscope lens. Details about the setup are found in [1].

![Experimental Setup](image)

Fig. 1 The experimental setup to generate intensely oscillating ultrasonic bubbles in microfluidics channels. The microfluidics channel has two inlets (one for liquid and one for gas), and one outlet. This creates a liquid with gas pockets in the microfluidics channel. The ultrasound is transmitted from the oscillating transducer through the glass slide into the microfluidics channel.

2.1. Generation of intensely oscillating bubble by surface waves

The volume of liquid in a microfluidics channel is small. Thus to create cavitation bubbles in the microfluidics liquid is difficult even with high acoustic pressure. Thus air pockets which act as bubble nuclei are introduced into the microfluidics channel. The acoustic energy is transmitted to the PDMS via the glass slide. It causes surface waves to form at the air-water interface inside the channel. Figure 2 shows the process at which the cavitation bubble is formed [2]. The first frame (time = 0) shows two crests coalescing and then forming a gas pocket (as indicated by white arrows). Subsequently the gas pocket oscillates and moves away from the interface. More oscillating bubbles are formed this way and eventually fill up the whole channel.

![Cavitation Process](image)

Fig. 2 The entrapment of a gas bubble at the air-water interface (air on top, water below). The surface wave generated by the ultrasound causes two crests to coalesce (time = 0) and a gas bubble is formed as indicated by the white arrows. Driving voltage and frequency is 50 V and 100 kHz, respectively. The video was recorded at 250,000 frames per second with an exposure time 1µs. Width of each frame is 100 µm.

2.2. Sonochemistry and sonoluminescence

The ultrasonic bubble in our microfluidics channel collapses and heats up the liquid locally. This process generates an intense concentration of energy which is able to trigger chemical reactions (sonochemistry) and to emit light (sonoluminescence) [3]. Figure 3 shows the oxidation of luminal in a
sodium carbonate base solution. Radicals H and OH are produced and they trigger the formation of an amino phthalate derivative with electrons in an excited state. When these electrons relax to lower energy states, excess energy is emitted as visible bluish light (Fig. 3). It is noted that the luminal emission only occurs in the liquid, and close to the gas-liquid interface where the cavitation occurs.

![Fig. 3 Luminol chemiluminescence from cavitation bubbles in microfluidics channels as captured by an intensified Electron Multiplying Charge Coupled Device (EMCCD) camera. The overlaid green lines indicate the microfluidics channels. The blue light is emitted from the chemical reaction of luminal oxidation.](image)

2.3. Applications in biotechnology
Cavitation bubbles in microfluidics channels are useful for the harvesting of inter-cellular contents, and for the study of rheology of the red blood cell [5]. Often in biotechnology, bacteria or yeast cells with modified DNA are utilized. Their intracellular contents need to be extracted for analysis. We report the use of ultrasonic cavitation in a microfluidics channel for this purpose [3].

2.3.1. Lysis of cells: Yeast cells and E. Coli. The intensely oscillating bubbles are capable of lysing *Escherichia coli* (*E. Coli*), and *Pichia pastoris* (yeast cell) when they are placed in the microfluidics channel [3]. As seen in Fig. 4, the rod-shaped bacteria (*E. Coli*) is broken down into small fragments after being sonicated at 128.7 kHz, 200 V for 389 ms. The more robust yeast cells are completely lysed within 1 s. Fluorescence intensity measurements of the green fluorescence protein (GFP) expressing bacteria and cells show that the functionality of GFP is maintained after the treatment. Real-time polymerase chain reaction (qRT-PCR) analysis confirms that the genomic DNA of the bacteria and cells remain intact after sonication. This technique provides a gentle yet efficient way for the lysis of *E. Coli* and yeast cells in microfluidic channels.

![Fig. 4 The lysis of *E. Coli* in a microfluidics channel as viewed under a microscope. The rod-shaped bacteria are broken into pieces after sonication (389 ms at 128.7 kHz).](image)

2.3.2. Stretching of red blood cell. The phenomenon of stretched cells in the vicinity of a single cavitation bubble in a micro-chamber is studied [4]. The bubble is generated by heating up the liquid using a pulsed laser. Figure 5 shows the bubble-cell interaction. In the experiment, the bubble is generated at a distance of 84 µm from the cell (Fig. 4A). It expands to its maximum size of 100 µm in radius at frame 4. The cell is pushed up and is slightly flattened. The bubble then collapses. The liquid flow around the cell generated by the collapsing bubble causes the cell to be strongly elongated.

Figure 4B shows a numerical simulation of an oscillating bubble next to an elastic liquid vesicle (mimicking a cell) using the Boundary Element Method. In this method only the boundaries of the bubble and cell are meshed. The cell surface has elasticity as it is modeled with membrane tension. It is found from parametric study of the membrane tension and stand-off distance (the separation between the bubble and cell centers) that cell stretching can only if the cell elasticity is within certain
threshold. Also the maximum elongation occurs when the bubble oscillates at half of the oscillation time of the cell.

Fig. 5 (A) The expansion of a large bubble (only part of the interface is captured within the frame) near a human red blood cell. The bubble expands to its maximum size (frame 4) and then collapses. The cell is stretched as the bubble collapses. The initial cell radius is 4 µm, and the maximum bubble radius is 100 µm. The width of each frame is 16 µm. The framing rate is 360,000 frames per second. (B) Numerical simulation of an oscillating bubble near an elastic liquid pocket (cell-like object). The ‘cell’ stretches a lot as the bubble collapses.

3. Conclusion
We present a series of studies involving the use of cavitation bubbles in microfluidics. We have developed a technique to generate strongly oscillating bubble in a microfluidics system. These bubbles are capable of inducing sonochemistry and sonoluminescenc. The strong shear flow generated by the collapsing bubbles could be utilized to lyse E. Coli and yeast cells effectively and efficiently. The intracellular contents remain intact after the brief sonication. The same flow created by a collapsing laser-generated cavitation bubble is seen to stretch a human red blood cell. The phenomenon is modeled successfully using the Boundary Element Method. The numerical study indicates that elastic object with certain elastic properties is much elongated next to a collapsing bubble. In conclusion, our ultrasonic microfluidics system is versatile and useful for many biotechnology applications. We are currently investigating the use of the system for emulsification, gene transfection, and lysis of endospores.

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