Micro bubble trapping by ultrasonic wave fields
Yoshiki Yamakoshi
Faculty of Engineering, Gunma University
Japan
yamakosi@el.gunma-u.ac.jp

Abstract

The ultrasonic wave assisted micro bubble trapping at the desired position inside the tissue may be a promising technology in future drug delivery system. In constructing the micro bubble trapping, several techniques are required in order to control the dynamics of micro bubbles. However, the dynamics of the bubbles is often too complicated due to the mutual interaction between bubbles and due to the bubble nonlinear oscillation.[1] In this paper, an ultrasonic wave assisted micro bubble trapping is discussed both theoretically and experimentally. The Bjerknes force between the aligned bubbles and a single oscillating bubble, which is a typical situation in the micro bubble trapping system, is derived. The experiments are carried out for bubbles which are designed for an ultrasonic wave contrast agent and for bubbles which have PVC shell. Some in vitro experiments using ultrasonic wave contrast agent bubbles in human blood are shown. Novel methods in order to characterize the bubble oscillation parameters in situ are also proposed.

1. Introduction

It is considered that three key technologies are required in constructing the future drug delivery system. These technologies are, targeting of drug carrying bubbles at the desired position, controlled release of carrying drug and the dose improvement to the tissue. For these applications, it may be considered that the ultrasonic wave assisted methods may be a useful means.

In this paper, micro bubble trapping by ultrasonic wave is discussed both theoretically and experimentally. The Bjerknes force, which is an acoustic radiation force applied to the oscillating bubble under the ultrasonic wave radiation, is formulated for 2n+1 aligned bubbles which oscillate independently. It is derived that relative phase between secondary wave radiation and the radial oscillation of surrounding single oscillating bubble is an important parameter in order to characterize the micro bubble trapping pattern (micro bubble aggregation pattern). Several experiments are demonstrated as well as the results for human blood.[2] Two characterization methods of bubble oscillation under the ultrasonic waves in situ are also proposed.

2. Examples of the experimental results

Figure 1 shows the experimental set-up.[3] The micro bubbles flow into the water channel, whose size is 3mm width, 1mm depth. The bubbles are trapped by an acoustic radiation force (Bjerknes force) inside the ultrasonic wave field. This ultrasonic wave field is produced by two concave ultrasonic wave transducers. The dynamics of the bubbles inside the flow channel is observed by microscope with CCD camera.

Figure 2 shows examples of the trapped micro bubbles. Figure 2 (a) is the image acquired for an ultrasonic wave contrast agent (Mean radius of the bubbles is 1.3

Fig.1 Schematic diagram of the experimental set-up.

(a) (b)

Fig.2 Examples of the trapped micro bubbles.
(a): ultrasonic wave contrast agent (b): bubbles with PVC shell. Incident ultrasonic wave frequency is 2.5 MHz for both cases.
µm). Figure 2 (b) is the image for the bubbles with PVC shell. (Mean radius of the bubble is about 10 µm) The applied ultrasonic wave frequency is 2.5 MHz and the sound pressure is 150 kPa for both cases. We found that the micro bubbles are trapped as aggregated bubbles showing completely different patterns for two bubbles.

3. In situ characterization of bubble oscillation [4,5]

Different bubbles produce different aggregation pattern (micro bubble trapping pattern). This result suggests that the bubbles oscillate in different way producing different interference forces between the neighboring bubbles. In order to evaluate the secondary ultrasonic wave, which produce interference force (Bjerknes force), we have proposed two methods. First method is based on holographic secondary wave source mapping by holographic image reconstruction.[5] Though this method evaluates both relative amplitude and the relative phase of the secondary wave, it is applied to the bubbles which produce trapping pattern with concentric circles around center bubble, as is shown in figure 2 (a).

Second method is based on aggregated bubble pattern analyses. This method is applied to the bubbles with circular aggregation pattern as is shown in figure 2 (b). Figure 3 shows the equations of the system under consideration. We assume that 2n+1 independent oscillating bubbles are aligned over x axis. The plane incident ultrasonic wave is introduced from –x direction. If the width of the aligned bubbles is much shorter than the wave length, the Bjerknes force which is applied to the bubble be at the position (x,z0) is derived as follows:

\[
F_B = \frac{3\varepsilon_0 R_{b0} P_P (2n+1)^2}{2x} \left[ k \sin(k(x-z_0)+\theta_0) + \frac{1}{x} \cos(k(x-z_0)+\theta_0) \right]
\]

where \(V_0, R_{b0}, P_0, P_0\) are the equilibrium bubble volume, bubble radial oscillation amplitude, secondary wave amplitude and the incident wave amplitude, respectively. The parameter \(\theta_0\) is the relative phase between the secondary wave radiation of the aligned bubbles and the radial oscillation of the bubble \(b_c\). If the aggregated bubbles are full filled with the micro bubbles, the radius of the aggregated bubbles is derived from eq.(1) by setting \(F_B = 0\) and \(\partial F_B/\partial x > 0\) for x>0. Hence, the relative phase of oscillating bubble is estimated from the radius measurement of the aggregated bubbles. Using the proposed method, we estimate the relative phases for the bubbles with PVC shell. The radius of the aggregated bubbles are measured by changing the ultrasonic wave frequency, sound pressure, flow velocity, concentration of the bubble, we found that most sensitive parameter to fix the radius is the ultrasonic wave frequency for this bubble. The relative phase is 82 degrees for 5MHz ultrasonic wave frequency and it is 85 degrees for 2.5 MHz ultrasonic wave frequency. These values are consistent with the values derived by pulsator model.[6]

4. Conclusion

The ultrasonic wave assisted micro bubble trapping is discussed both theoretically and experimentally. The parameter to characterize the micro bubble trapping pattern is discussed by deriving the Bjerknes force between bubbles. The experiments are carried out for an ultrasonic wave contrast agent and for the bubble with PVC shell. It is shown that the bubbles are trapped as aggregated bubbles and the different bubbles show different bubble trapping patterns inside the ultrasonic wave field. In order to evaluate the secondary wave radiation from the bubble, which is an important in discussing the micro bubble trapping pattern, two novel characterization methods are proposed.

5. References