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Numerical Simulations of Destruction of Encapsulated Microbubbles with Bubble-Bubble Interaction
気泡間相互作用を考慮した皮付きマイクロバブルの破壊に関する数値シミュレーション

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1. Introduction

Encapsulated microbubbles have been used as contrast agents in medical ultrasound imaging.[1] There are two types in the shell of an encapsulated microbubble. One is stiff such as polymer or albumin. The other is more flexible such as lipid or phospholipid. In the present study, numerical simulatuions of destruction of encapsulated microbubbles have been performed for Albunex microbubbles which have stiff shells of human albumin. The gas species inside Albunex microbubbles is air. The average radius of an Albunex microbubble is between 1.5 and 2.5 μm. The present numerical simulations have been perfromed under the experimental condition of Chang et al.[2] In the experiment, the Albunex solution was irradiated by 1.1 MHz ultrasound using a HIFU (high intensity focused ultrasound) transducer. The threshold acoustic pressure for destruction of Albunex microbubbles was measured as a function of the Albunex microbubble concentration. It increases as the microbubble concentration increases up to 100 μl/ml.

With regard to theoretical studies on the destruction of an encapsulated microbubble, there are only few papers published. Stride and Saffari[3] calculated the shell stresses during the microbubble pulsation under ultrasound. Postema and Schmitz[4] considered only fragmentation of a microbubble and did not study the rupture of the shell due to surface tension. In the present study, a theoretical model of destruction of encapsulated microbubbles has been constructed taking into account the effect of the bubble-bubble interaction.

2. Model

There are two mechanisms behind the destruction of an encapsulated microbubble such as an Albunex microbubble. One is the rupture of the shell due to surface tension mostly during the bubble expansion. The other is the fragmentation of a microbubble due to its shape instability.

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The rupture of the shell is modeled following the paper by Evans et al.[5] There are three states in a shell: defect-free state, metastable state, and ruptured state. The metastable state is that an annihilable defect is present in the shell. The temporal evolution of the probabilities of being in the defect-free state (S_0), metastable state (S_*), and ruptured state (S_r) is predicted by the statistical master equations.

$$\frac{dS_0}{dt} = -\nu_{0\to*}S_0 + \nu_{*\to 0}S_*$$
$$\frac{dS_*}{dt} = -\left[\nu_{*\to 0} + \nu_{*\to r}\right]S_* + \nu_{0\to*}S_0$$
$$\frac{dS_r}{dt} = \nu_{*\to r}S_* \qquad (1)$$

where $\nu_{0\to*}$ is the rate of the annihilable defect formation, $\nu_{*\to 0}$ is the rate of the defect annihilation, and $\nu_{*\to r}$ is the rate of the unstable-hole formation from an annihilable defect. The equations for each rate have been described in Refs. 5 and 6.

The fragmentation of a microbubble is modeled following the paper by Hilgenfeldt et al.[7] The amplitude of the shape oscillation of a microbubble is calculated as a function of time. When the amplitude of non-spherical oscillation exceeds the mean bubble radius, fragmentation takes place.

The effect of the bubble-bubble interaction on the pulsation of a microbubble has been taken into account following the previous paper by the authors.[8] The equation of the radial dynamics of a microbubble, taking into account the effect of the bubble-bubble interaction, is as follows;

$$\left(1-\frac{\dot{R}}{c_\infty}\right)R\ddot{R} + \frac{3}{2}\dot{R}^2\left(1-\frac{\dot{R}}{3c_\infty}\right)$$
$$= \frac{1}{\rho_{L,\infty}}\left(1+\frac{\dot{R}}{c_\infty}\right)\left[p_B - p_S\left(t+\frac{R}{c_\infty}\right) - p_\infty\right] + \frac{R}{c_\infty\rho_{L,\infty}}\frac{dp_B}{dt} - S\left(R^2\ddot{R} + 2R\dot{R}^2\right) \qquad (2)$$

where R is the bubble radius, the dot denotes the time derivative, c_∞ is the sound velocity in the liquid, $\rho_{L,\infty}$ is the liquid density, p_B is the liquid pressure at the bubble wall, p_S is the instantaneous acoustic pressure, and S is the coupling strength of the bubble-bubble interaction. The last term in Eq.

(2) is the effect of the bubble-bubble interaction. This is the additional local pressure due to the acoustic emissions from surrounding bubbles. The coupling strength is related to the number density (n) of bubbles and the radius of the bubble cloud ($l_{\max}$) as Eq. (3).

$$S=\sum_i \frac{1}{d_i}=\int_{l_{\min}}^{l_{\max}} \frac{4\pi r^2 n}{r}\,dr = 2\pi n\left(l_{\max}^2 - l_{\min}^2\right) \approx 2\pi n l_{\max}^2 \qquad (3)$$

where d_i is the distance between the bubble and another bubble numbered i, the summation is for all the surrounding bubbles, r is the distance from the bubble, and $l_{\min}$ is the distance between the bubble and the nearest bubble. In the last equation, it has been assumed that $l_{\min} << l_{\max}$. The first equation is the definition of S. As the number of surrounding bubbles increases, S increases. As S increases, a bubble expands less during the rarefaction phase of ultrasound due to the bubble-bubble interaction.[8)]

As the physical properties of an Albunex microbubble, the elasticity of the shell and the surface dilatational viscosity of the shell are assumed as 4 N/m and 1.06 x 10^{-7} N s/m, respectively.[6, 9)]

3. Results

An example of the results obtained from the numerical simulations is shown in Fig. 1. The probability of being in defect-free state immediately falls to nearly zero and that of being in metastable state increases to nearly one by the irradiation of ultrasound. The probability of being in ruptured state increases with time especially during the bubble expansion due to the increased surface tension.

4. Conclusion

Numerical simulations of destruction of encapsulated microbubbles have been performed taking into account the bubble-bubble interaction. It has been revealed that the threshold for destruction of an Albunex microbubble increases as the microbubble concentration increases because the bubble pulsation becomes milder due to the stronger bubble-bubble interaction. It qualitatively agrees with the experimental data by Chang et al.[2)]

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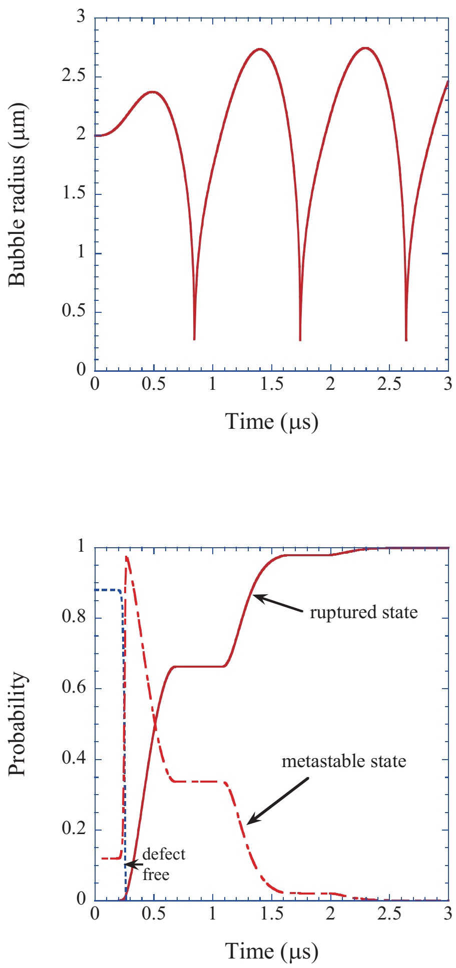

Fig. 1 The result of numerical simulation. Ultrasonic frequency and pressure amplitude are 1.1 MHz and 1.1 MPa, respectively. The ambient bubble radius is 2 μm. S=2.34 x 10^7 (m^{-1}), which corresponds to the microbubble concentration of 0.745 μl/ml. The radius-time curve of an Albunex microbubble (above). The probabilities of being defect-free state, metastable state, and ruptured state as a function of time (below).