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Observation of aggregation forming of microcapsules under various conditions of ultrasound emission

超音波照射条件に対するマイクロカプセルの凝集体形成挙動の観測

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1. Introduction

Microcapsules are known to form aggregation when they are put into an ultrasound field because secondary Bjerknes force, which acts attractive or repulsive between neighboring capsules, is produced [1] by local condition of oscillation. Multiple capsules form aggregation where they are oscillated in the same phase locally. The applications of this phenomenon are reported to sonoporation [2] and capillary embolization [3]. Meanwhile, we have previously reported our attempt to propel microcapsules in flow [4,5] owing to a primary Bjerknes force [6,7], which is a physical phenomenon where an acoustic wave pushes an obstacle along its direction of propagation. However, because the primary Bjerknes force is proportional to square of the radius of a capsule, there was a limitation in efficiency to propel capsules in blood flow when the size of a capsule is as small as red blood cell.

Thus we consider that forming aggregations of capsules is effective to be propelled before entering into an ultrasound field to receive more primary Bjerknes force. In this study, we have investigated the phenomenon of forming aggregations of capsules and observed variation of diameter and density of aggregations under various conditions of ultrasound exposure.

2. Theory

Assuming spherical capsules, a primary Bjerknes force [8] acts to propel the capsules in the direction of acoustic propagation as per the following equation,

$$F_r = \pi r^2 Y_p P\,, \qquad (1)$$

where P is the mean energy density of the incident wave, Y_p is a dimensionless factor called the radiation force function that depends on the scattering and absorption properties of the capsule, and r is the radius of the capsule.

Also if two capsules are located in an even ultrasound field and oscillated, secondary Bjerknes force between the neighboring capsules [9] is given as per the following equation,

$$\langle F \rangle = -\frac{2\pi\rho R_{10}^3 R_{20}^3 \omega^2}{D^2} \varepsilon_{10}\varepsilon_{20} \cos(\varphi_1 - \varphi_2)\,, \qquad (2)$$

where symbol of < > means time integration of the driven ultrasound emission in one period, ρ is the density of the liquid, R_{10} and R_{20} are initial radius of the capsule 1 and 2, ε_{10} and ε_{20} are oscillation amplitude of the capsule 1 and 2, ω is angular frequency, D is the distance between capsules, and ϕ_1 - ϕ_2 is the phase difference of the oscillation between capsules. Fig.1 shows transition to form aggregations of capsules under ultrasound emission.

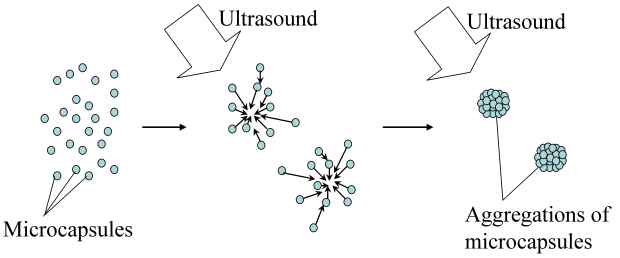

Fig.1. Transition to form aggregations of microcapsules under ultrasound emission.

Here if an aggregations of capsules can be regarded as a larger capsule, it would be easily propelled by less primary Bjerknes force. When the radius became 10 times greater than original size of a capsule, the primary Bjerknes force becames 100 times greater than a single capsule. Thus it is very important to investigate reproducibity of the aggregations with conditions of ultrasound.

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3. Experiment

We used the F-04E microcapsule (Matsumoto Oil, Co. Ltd), which has a shell made of polyvinyl chloride (PVC), a specific gravity of 0.0225, and an average diameter of 4 μm. It contains isobutene inside and is stable in room temperature. We selected only those microcapsules with a diameter less than 20 μm. We also prepared a small channel made of polyethylene glycol (PEG), which is placed in the bottom of a tank filled with water. Suspension of capsules is enclosed in the channel, which size is approximated 4×0.7 mm in cross-section as shown in Fig.2. The angle of the axis of the transducer, which includes a flat ceramic disc with a diameter of 25 mm to emit plane wave of ultrasound, is set 60 degrees to the *xy*-plane. The focal point of ultrasound field is set to be in center of the observation area, where behavior of capsules was recorded optically using an inverted microscope (Leica, DMRIB).

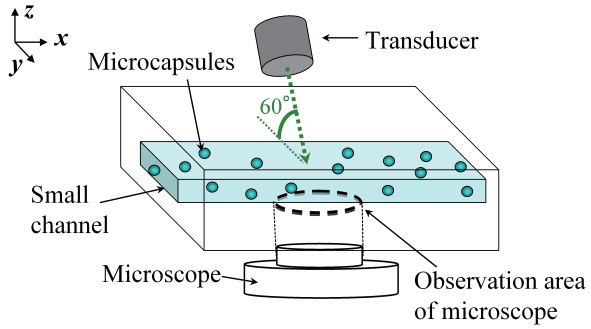

Fig.2. Position relationship between the transducer and observation area in the small channel.

4. Results

We recorded behavior of microcapsules in the observation area by 15 frames/s upon emission of sinusoidal ultrasound with central frequencies of 1, 2, 3, 5, 7 and 10 MHz with the maximum sound pressure of 300 kPa. Fig.3 shows the observation areas when aggregations of capsules were formed 1.2 sec after starting ultrasound emission of 2 and 7 MHz, respectively.

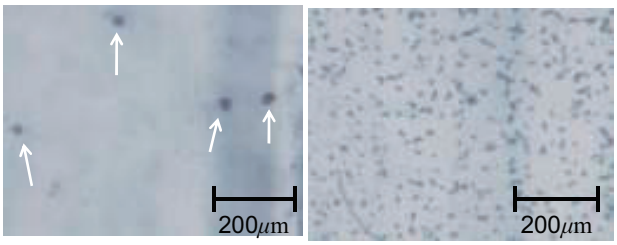

Fig.3. Aggregation of microcapsules under ultrasound emission of 2 MHz (left) and 7 MHz (right).

We have measured average diameter of the aggregations appeared in the frames by an image analysis software of Image-Pro Plus (Media Cybernetics Co. Ltd). Fig.4 shows the time variations of the average diameter in various central frequencies. According to the result, greater aggregations were confirmed with lower frequency but the size of aggregations was reached more quickly to its saturation with higher frequency. Thus for active path selection of capsules in our previous attempt [8], appropriate combination of both conditions to form aggregations of capsules and to propel the aggregations should be selected.

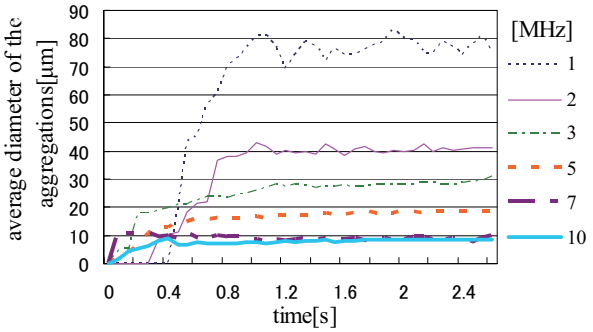

Fig.4. Time variation of average diameter of aggregations with various central frequencies.

5. Conclusion

In this study, we observed aggregation formation of microcapsules using continuous wave with central frequencies between 1 and 10 MHz. We confirmed that the size and the saturation time of the aggregations depend on the central frequency. For further analysis, appropriate conditions of ultrasound emission to realize active control the aggregations of capsules should be elucidated. Also we are going to apply to *in vivo* experiment.

Acknowledgment

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