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Evaluation of trapping performance of fluid microcapsules to the parameter variation in acoustic radiation

照射超音波のパラメータ変化に対する流路内マイクロカプセルの捕捉性能評価

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1. Introduction

Making use of the phenomena that microcapsules or microbubble of μm order collapse themselves after ultrasound emission near their resonant frequency, physical DDS (Drug Delivery System) has been proposed[1]. To minimize the side effect of medication, drug should affect to the target area, not to other parts inside human body. Though recent mainstream of DDS is focused on the gene transduction by using gene vector, it takes time and cost to develop for each object. The microcapsules, which can contain the specified drug inside the shell, have the possibility to correspond to various kinds of medications. However, because of the diffusion of capsules after injection, it was difficult to enhance the efficiency of medication. If the density of capsules inside human body can be controlled, the amount of drug would be minimum. Then we have noticed the acoustic radiation force [2], which is a physical phenomenon where an acoustic wave pushes an obstacle along its direction of propagation. When a microcapsule receives the acoustic radiation force against flow, it is trapped or propelled to the opposite direction of the flow. In this paper, we introduce our research to investigate local density of microcapsules in the straight artificial blood vessel according to the acoustic condition.

2. Principle

Fig.1 shows behavior of fluid microcapsules under acoustic emission. Considering the shape of a microcapsule as sphere, the acoustic radiation force F_{ac} acts to push the microcapsules to the direction of acoustic propagation[3]. On the other hand, when the microcapsules are put in flow, a capsule receives the flow resistant F_d. Thus, if F_d and F_{acx} in Fig.1 are similar, the acoustic radiation force balances with the flow resistant to trap fluid microcapsules.

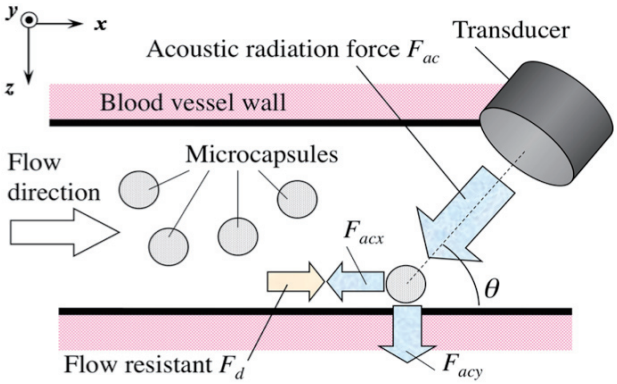

Fig.1 Behavior of fluid microcapsules under ultrasound emission.

3. Experiment

We used microcapsule F-04E (Matsumoto Oil, Japan) which shell is made of PVC (polyvinyl chloride) with specific gravity as 0.0225 and average of diameter as 3.5 [μm]. We sieved it as the range of diameter is 20 [μm] or less and the size is to be applied to use *in vivo*. Also we have prepared the artificial blood vessel, which is made of PEG (polyethylene glycol), including the straight vessel as **Fig.2**.

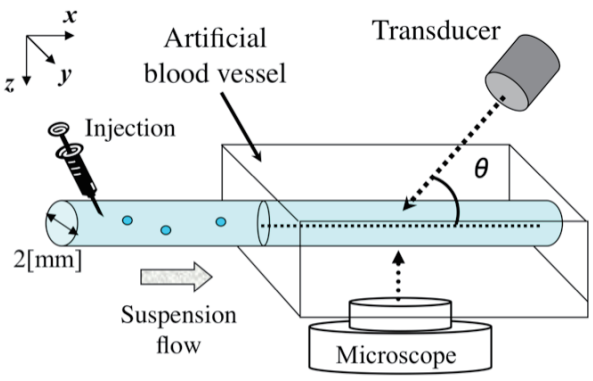

Fig.2 Schematic view of the experiment to trap fluid microcapsules

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The external size is 50x80x10 [mm] and inner diameter of the path is 2 [mm]. The transducer is set a direction of acoustic propagation to be opposite flow direction and θ = 45 [deg] to *x-y* plane as shown in **Fig.2**. We used a focal type transducer with center frequency of 1 [MHz] to emit ultrasound. We injected suspension of microcapsules with water of 0.3 [g/l] from upstream of the observed area, where focal point of ultrasound is included in the center. By using an optical microscope (KH-7700, Omron, Japan), behavior of microcapsules is observed and recorded.

4. Results

We produced several kinds of ultrasound waveform by varying PRF (pulse repetition frequency) and duty ratio, which ranged 10, 20 and 50 [kHz], and 40, 60, 80 and 100 [%], respectively. We adjusted maximum sound pressure at the focal point to be 300 [kPa]. **Fig.3** shows time series images of the observed area, when the suspension was injected by 20 [mm/s]. Injection was finished within 10 [sec]. In 20 [sec] after injection 100 [μm] order size aggregations of microcapsules were confirmed through thick suspension. The size of the aggregation saturated before 90 [sec]. As long as the behaviors of microcapsules were observed through the experiments, the reproducibility in shape, number and motion of the aggregation was poor. However, total occupied area of microcapsules was seemed to increase with the duty ratio, which indicates the amount of microcapsules increases in proportion to the duration of ultrasound emission.

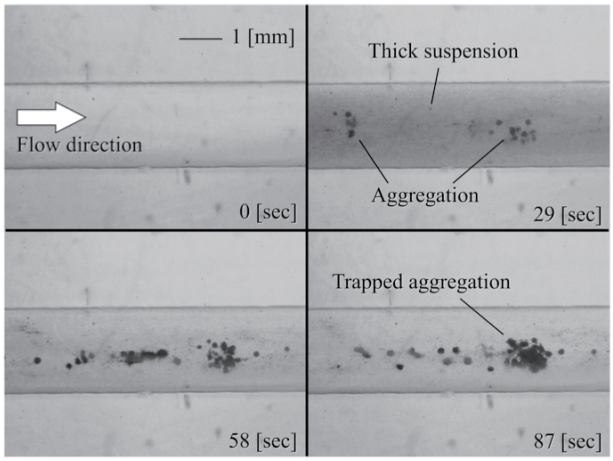

Fig.3 Time series images of the observed area after injection of the suspension with ultrasound emission.

To evaluate quantitative amount of trapped microcapsules, we measured the occupied area of microcapsules by labeling method. **Fig.4** shows the total occupied area of trapped microcapsules in 0~87 [sec] after ultrasound emission versus the duty ratio with PRF as a parameter. We confirmed the area increases according to duty ratio, where there was no significant difference in PRF variation. Therefore duration of ultrasound emission is important to trap microcapsules in flow. In many cases, aggregations of microcapsules were seen upstream before they were trapped, which should be caused by Bjerknes forces [1] produced by an ultrasound pressure gradient and oscillation of the diameter of the microcapsules. We consider that an aggregation of capsules makes equivalently a larger diameter capsule to receive more acoustic radiation force, which is proportional to the cube of the size of a microcapsule.

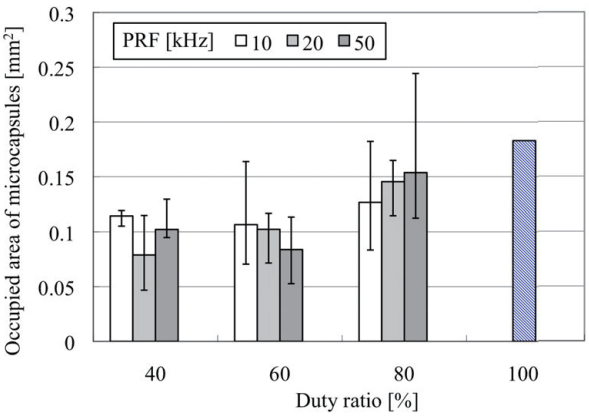

Fig.4 Occupied area of trapped microcapsules versus duty ratio of ultrasound

5. Conclusions

In this study, we have experimented to trap fluid microcapsules in artificial blood vessel. We confirmed the capsules with diameter of 3.5 [μm] were trapped in the middle of the path and by ultrasound of sinusoidal signal of 1 [MHz]. To trap capsules in flow, duration of ultrasound emission was important to make aggregation of capsules. We are going to apply the experiment by varying other parameters and to investigate the mechanism of the phenomena.

Acknowledgement

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References

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