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Optical observation of biodegradable microcapsules under ultrasound irradiation
生分解性マイクロカプセルの超音波駆動下における挙動の光学的観測

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1. Introduction

Microcapsules are used as contrast agents [1] to image blood flow vessels. In this application, microcapsule vibration under ultrasound irradiation is used. Therefore, clarification of capsule behavior is necessary. Recently, several methods to observe capsule vibration and destruction phenomena were reported[2]. However, there are only few reports that clarify the detail of the behavior in real time. Also, the effect of the shell material and thickness of the shell on capsule behavior is not clarified.

In this report, investigation of the capsule behavior was conducted. Capsules with biodegradable shell were fabricated and capsule behavior was observed by a high-speed camera. Moreover, to clarify the detail of capsule vibration and destruction mechanism, observation technique using a laser Doppler vibrometer (LDV) was introduced.

2. Fabrication of microcapsules

In this experiment, capsules were fabricated by evaporation method. The shell material was poly-DL-lactic acid (PDLLA) which is biodegradable. Fabrication procedure and the experimental condition are indicated below.

1)Fabricate 100 ml of 10 % polyvinyl aqueous solution as dispersion aqueous solution of the bubble.
2) Dissolve 0.05 g of PDLLA by 4 ml of methylene chloride.
3) Mix two of the solution above and generate bubbles by a syringe. Generated bubbles are surrounded by polymer solution and methylene chloride in the polymer solution evaporates. In this process, the bubble is surrounded by only shell material.

3. Experimental method

The capsule behavior under ultrasound irradiation was observed by a high-speed camera (SHIMADZU, HPV-1). Experimental system is shown in **Fig. 1**. Xenon light was concentrated by lens and the camera was focused to the concentrated area of the light to observe the capsule behavior. A Capsule was attached to a glass substrate via an adhesive tape immersed in the cell filled with degassed water and ultrasound was driven by the transducer beneath the cell. Also, LDV (NLV-2500, Polytec) with an objective lens (M Plan Apo 20×, Mitutoyo) was set up above the cell. The focus point of the laser which is emitted by LDV was controlled to be at the surface of capsule. The focal distance of objective lens is 20 mm. The laser spot size concentrated by the objective lens was 1.5 μm which is small enough to capture local vibration of capsules. Sinusoidal burst electrical signal at frequency of 28 kHz with 10 cycles was input to the transducer.

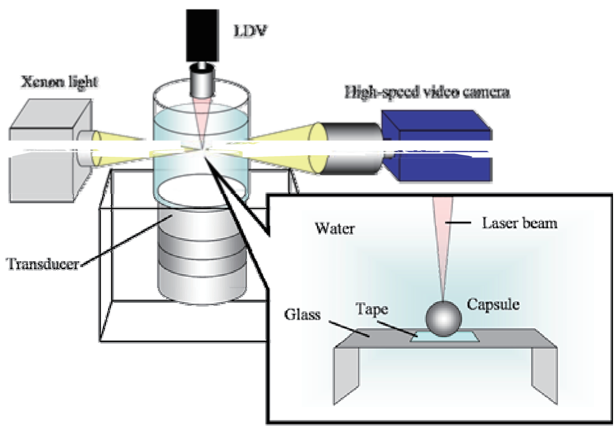


Fig. 1 Measurement system

4. Result

4.1 Observation by high speed camera

In case of low sound pressure, vibration of the microcapsule was not confirmed by high speed camera image. When the sound pressure was increased, the capsule vibrated locally and emitted the internal gas. **Fig. 2** shows an example of observation result by the high-speed camera. The capsule repeated the local vibration (92 μs) and internal gas was emitted from the place where vibration was observed (224 μs).

4.2 Observation by LDV

To clarify the detail of the capsule behavior when it vibrates and gets destructed, LDV was introduced. When sound pressure was 6 kPa, emission of the internal gas wasn't confirmed from the high speed camera. However, the LDV captured the vibration waveform. The waveform obtained from LDV is shown in **Fig. 3(a)** while $t=0$ is the commencement time when ultrasound was irradiated. This waveform shows the velocity variation of the capsule. However, there is a possibility that LDV captured a flexural oscillation of the glass substrate which capsule was attached to. Therefore, capsule behavior cannot be evaluated precisely from this observation result. On the other hand, when the sound pressure was 73 kPa, the emission of the internal gas was observed by high speed camera. This emission of internal gas is the premonitory phenomenon before destruction[3], but the capsule vibration cannot be confirmed from the picture observed by high speed camera. **Fig. 3(b)** shows the observation result obtained from LDV. The wave distortion is distinctive in **Fig. 3(b)** and it is presumable that this distortion attributes to the nonlinear vibration of the capsule. This result shows the possibility of LDV obtaining the small amplitude vibration at the capsule surface before destruction phenomenon.

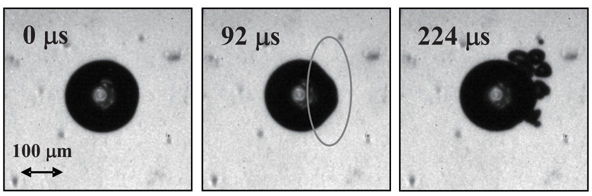
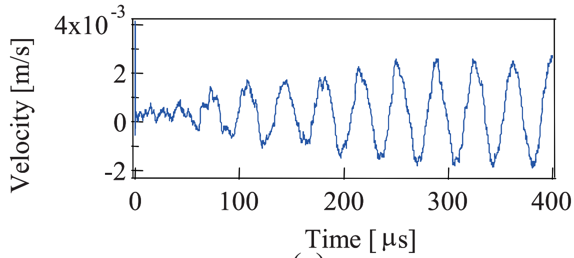
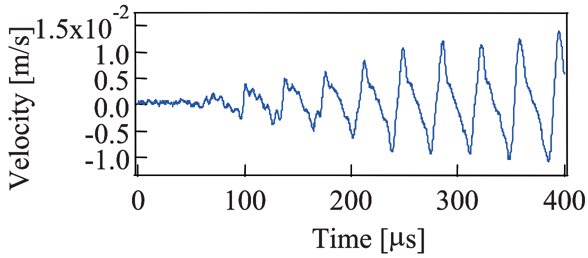


Fig. 2 Capsule behavior of PDLLA capsule at the pressure amplitude of 20 kPa.



(a)



(b)

Fig. 3 Vibration velocity waveforms measured by the LDV with the sound pressure amplitude of (a) 6 kPa and (b) 73 kPa.

5. Conclusions

Observation of capsule which possesses biodegradable shell (PDLLA) was conducted by using a high-speed camera and an LDV. From the results, possibility of obtaining the small amplitude vibration before the destruction phenomenon was indicated. To eliminate the undesirable vibration of the glass substrate superimposed on the capsule vibration, there is necessity of improvement on fixation method of capsule.

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