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Active path selection of microbubbles in an against flow using acoustic radiation force produced by multiple sound sources

音響放射力に対向する流体中の微小気泡に対する複数音源を用いた能動的経路選択

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1. Introduction

Microbubbles are known to form aggregates when they are put into an ultrasound field because secondary Bjerknes force, which acts attractive or repulsive between neighboring bubbles, is produced by local condition of oscillation[1]. The applications of this phenomenon are reported to sonoporation [2] and capillary embolization [3]. We have previously reported our attempt to propel microbubbles in flow [4-6] by a primary Bjerknes force, which is a physical phenomenon where an acoustic wave pushes an obstacle along its direction of propagation. Thus we consider that forming aggregates of bubbles is effective to be propelled before entering into an ultrasound field to receive more primary Bjerknes force because the primary Bjerknes force is proportional to square of the radius of a bubble [7]. We have elucidated the conditions of ultrasound and flow velocity for active path selection of aggregates of bubbles in an artificial blood vessel. However, the direction to the flow of ultrasound propagation was in forward, the ideal direction might not to be ensured *in vivo* because of obstacles such as bones or gases in the body. For another way of induction, we have investigated controlling bubbles in an against flow with making use of aggregates formation. In against flows, propelling aggregates to the direction of ultrasound propagation with a single sound source might be difficult because of increasing of flow resistance. In this study, we introduced multiple sound sources for propelling aggregates of bubbles.

2. Theory

Assuming the shape of the aggregates of bubbles is spherical, a primary Bjerknes force [6] acts to propel an aggregate in the direction of acoustic propagation as per the following equation,

$$F_{ac} = \pi r^2 Y_p P , \qquad (1)$$

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 bubbles, and r is the equivalent radius of the aggregate of bubbles.

When the aggregates of bubbles are placed in flow, a driving force of flow affects an aggregate. Then, the aggregate should receive a resultant force consit of the primary Bjerknes force and the driving force of flow. Fig.1 shows the force direction of the aggregate receiving. If the primary Bjerknes force is greater than the driving force of flow, at smaller value of angle θ in Fig.1, an aggregate should be transferred against the flow.

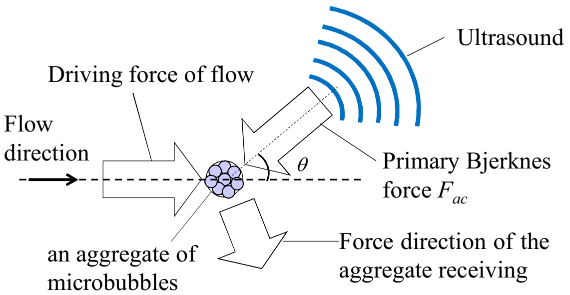

Fig.1 Force direction of the aggregate receiving.

3. Experiment

We used the F-04E microbubble [4], which has a shell made of poly(vinyl chloride) and an average diameter of 4 μm. We selected only those microcapsules with a diameter less than 20 μm. We also have prepared an artificial blood vessel made of polyethylene glycol (PEG), including a Y-form bifurcation with inner diameter of the paths was 2 mm. The blood vessel was placed in the bottom of a

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water tank, which was filled with water. As shown in Fig.2, the observation area was recorded optically using an inverted microscope (Leica, DMRIB).

Fig.2 shows the position configuration between transducers and the artificial blood vessel. We set one transducer Tu for forming aggregates of bubbles at 10 mm upper stream from the bifurcation and the other transducer Tb for inducting the aggregates to path B at 2 mm downstream from the bifurcation in path A. The axis of Tu and Tb were set at 70 and 40 deg from the *x*-axis. Tb1-3 were set at θ=0, 45, 90 deg from the *z*-axis with concentrating their focal points into one point. Tu included a flat ceramic disc to emit plane wave of ultrasound. We prepared same type of transducers Tb1-3 including a concave ceramic disc to emit focused ultrasound. These all transducers central frequencies were 5 MHz. To evaluate the amount of bubbles that passed through each path, we used the induction index [7].

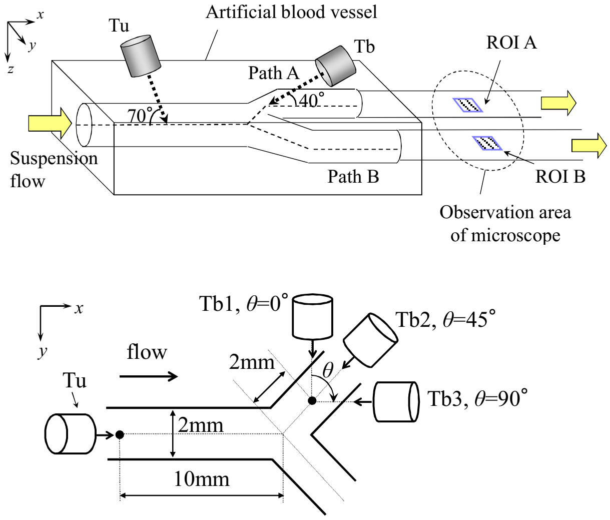

Fig.2. Position configuration between transducers and the artificial blood vessel near the bifurcation

4. Results

Fig.3 shows the microscopic image of the bifurcation upon emission of sinusoidal ultrasound with a Tu maximum sound pressure of 150 kPa, and Tbs of 300 kPa and a flow velocity of 20 mm/s. When ultrasound was emitted from Tu, we confirmed streaming of aggregates of microbubbles was entering to both paths. Additional ultrasound to the bifurcation from Tb2, the aggregates entering to path A were pushed back to the bifurcation and directed to path B. Then, with Tb3, clearly path selection to path B was confirmed. Fig.4 shows the result of the induction index versus several combination of emission. From the result, using multiple sound sources more than 65 % of bubbles were introduced to a desired path. For active path selection of bubbles, larger force against the flow should be required.

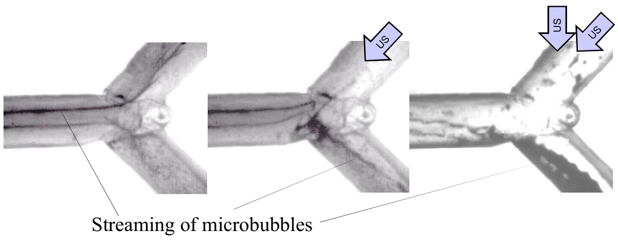

Fig.3 Microscopic images of the bifurcation with Tu emission (left), with Tu+Tb2 (center), with Tu+Tb2+Tb3 (right)

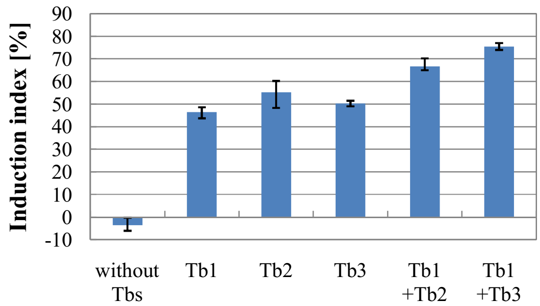

Fig.3. Induction index vs. combinations of ultrasound emission at the bifurcation with Tu

5. Conclusion

In this study, we realized active control of microbubbles in an against flow at a bifurcation with multiple sound sources. We confirmed that bubbles entering the undesired path were pushed back and directed into the desired path. For further analysis, the precise conditions necessary to realize active control of bubbles in a complicated shape of blood vessel should be elucidated. Also we are going to apply to *in vivo* experiment.

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