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Evaluation of path selection ability of microbubbles in a bifurcated flow based on acoustic field design

音場設計に基づく分岐流路中での微小気泡の経路選択性評価

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1. Introduction

Microbubbles (MBs) are known to form aggregates when they are put into an ultrasound field because of secondary Bjerknes force. The applications of this phenomenon are reported to sonoporation [1] and capillary embolization [2]. We have previously reported our attempt to propel MBs in flow [3-6] by a primary Bjerknes force, which is a physical phenomenon where an acoustic wave pushes an obstacle. Recently, we have demonstrated active path selection of MBs through multi-bifurcations by using a matrix array transducer to produce multiple focal points [4]. However, it was necessary another single element transducer to form aggregates of MBs. If a 2D array transducer can produce the acoustic fields not only to propel MBs in flow but also to form aggregates of MBs, the efficiency of controlling behavior of MBs in flow should be improved. And the probability of reducing the number of sound sources should be expected. In this study, we reported our challenge to design and to produce a continuous acoustic field to improve controlling efficiency of MBs in flow using a 2D array transducer.

2. Method

We used the F-04E microbubble [3-5], which has a shell made of poly (vinyl chloride) and an average diameter of 4 μm. We selected only those MBs with a diameter less than 20 μm.

Fig. 1 shows the position configuration between a 2D array transducer and an artificial blood vessel. We prepared the artificial blood vessel including a Y-form bifurcation with the path widths of w_1 = 1.4 mm, w_2 = 1.0 mm to ensure a constant flow velocity in each part of the model[4,5]. Σc means the capillary coordinate with the x_c-y_c plane corresponding to the capillary plane. The blood vessel was placed in the bottom of a water tank, which was filled with water.

We set the 2D array transducer, which position was adjusted by *xyz*-stage with 0.1 mm precision, to lead stream of MBs to Path B. The transducer has 64 air-backed PZT elements with the aperture of 15.9 x 15.9 mm^2, the size of each element of 1.9 x 1.9 mm^2, and the pitch of the elements of 2.0 mm, respectively. The resonance frequency was 3 MHz. The transducer was driven by a continuous square wave with a frequency of 3 MHz, where the drive unit was required to produce the waves with a minimum delay pitch of 5 ns. The axis and the distance of transducer were set at θ = 40 deg, d = 60 mm from the observation area. We used an optical microscope (Omron KH-7700) to observe four paths originating from consecutive two bifurcations. A 3 mL aliquot of the suspension of MBs was sampled and injected at a flow speed of 40 mm/s.

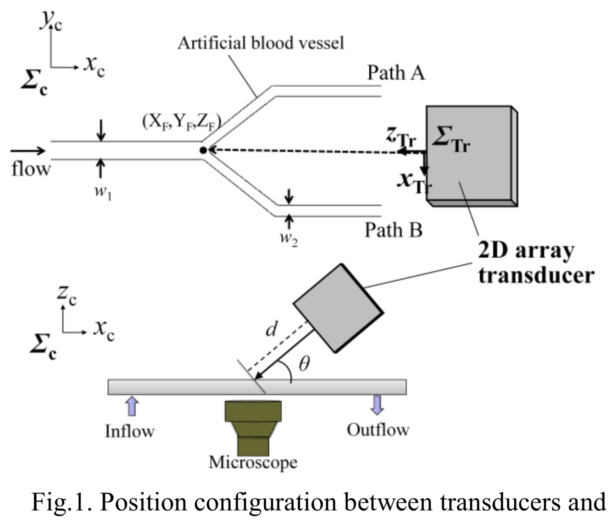

Fig.1. Position configuration between transducers and the artificial blood vessel

Then we prepared two types of acoustic fields, which were produced by setting delay time in 64 elements individually. **Fig. 2** shows the settings of delay times and the sound pressure distributions measured by a hydrophone (ONDA, HNR1000) at a distance of 60 mm from the surface of the 2D array transducer in degassed water. In the Tr coordinate,

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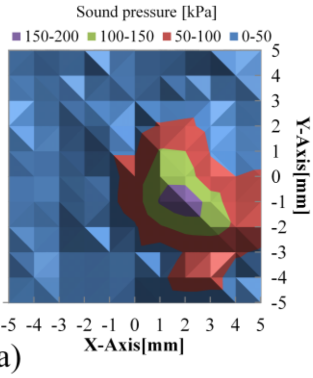
where the z-axis indicates the axis of transducer and the point of z = 0 corresponds to the surface, the position of the focal point was $(x_{Tr}, y_{Tr}, z_{Tr})=(X_F, Y_F, Z_F)$. One of the acoustic field was produced a single focal point of ultrasound at $(x_{Tr}, y_{Tr}, z_{Tr})=(2,-1,60)$ with 64 elements as shown in **Fig. 2 (a)**. On the other hand, we calculated the delay time of the 32 elements divided in two parts as shown in **Fig. 2 (b)**, and the additional focal point pattern of $(x_{Tr}, y_{Tr}, z_{Tr})=(0,4,60)$ was produced by another 32 elements.

unit [μs]

ch	1	2	3	4	5	6	7	8
8	0	0.17	0.30	0.39	0.44	0.44	0.39	0.30
7	0.15	0.32	0.45	0.54	0.59	0.59	0.54	0.45
6	0.26	0.44	0.57	0.65	0.69	0.69	0.65	0.57
5	0.32	0.50	0.63	0.72	0.77	0.77	0.72	0.63
4	0.35	0.53	0.65	0.74	0.78	0.78	0.74	0.65
3	0.32	0.50	0.63	0.72	0.77	0.77	0.72	0.63
2	0.26	0.44	0.57	0.65	0.69	0.69	0.65	0.57
1	0.15	0.32	0.45	0.54	0.59	0.59	0.54	0.45

y_{Tr} Σ_{Tr} x_{Tr}

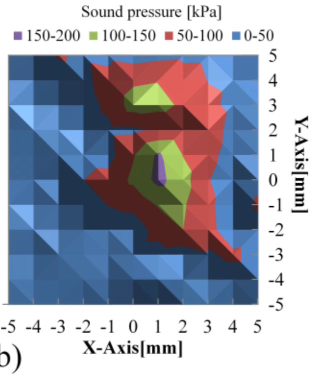


(a)

unit [μs]

ch	1	2	3	4	5	6	7	8
8	0.60	0.74	0.83	0.87	0.87	0.83	0.74	0.44
7	0.65	0.78	0.87	0.92	0.92	0.87	0.68	0.59
6	0.65	0.78	0.87	0.92	0.92	0.83	0.78	0.71
5	0.60	0.74	0.83	0.87	0.90	0.90	0.86	0.77
4	0.51	0.65	0.74	0.78	0.92	0.92	0.87	0.78
3	0.39	0.51	0.60	0.86	0.90	0.90	0.86	0.77
2	0.21	0.35	0.71	0.78	0.83	0.83	0.78	0.71
1	0	0.45	0.59	0.68	0.72	0.72	0.68	0.59

y_{Tr} Σ_{Tr} x_{Tr}



(b)

Fig.2. Delay times and sound pressure distribution: targeted at (a) $(x_{Tr}, y_{Tr}, z_{Tr})=(2,-1,60)$ and (b) $(x_{Tr}, y_{Tr}, z_{Tr})=(0,4,60),(2,-1,60)$.

3. Results

Fig.3 shows the microscopic image of the bifurcation upon emission of sinusoidal ultrasound with 3 MHz and a flow velocity of 40 mm/s. The distributions of sound pressure in the observation area were calculated using the Rayleigh equation and superimposed on the microscopy image of the bifurcation. The maximum sound pressure was about 170 kPa-pp. In **Fig. 3 (a)**, when ultrasound was emitted, MBs affected by ultrasound and were formed the aggregates but were not significantly lead Path B. In **Fig. 3 (b)** additional focal point was produced, the stream of MBs aggregates was smoothly propelled to Path B. This suggests that control was realized because MBs were formed aggregates at upstream of the bifurcation and were easily led to the desired path rather than single MBs. In addition, as the areas of the acoustic field of (b) were widely overlapped with the blood vessel relative to that of (a), the bubbles receive more acoustic force and were controlled well.

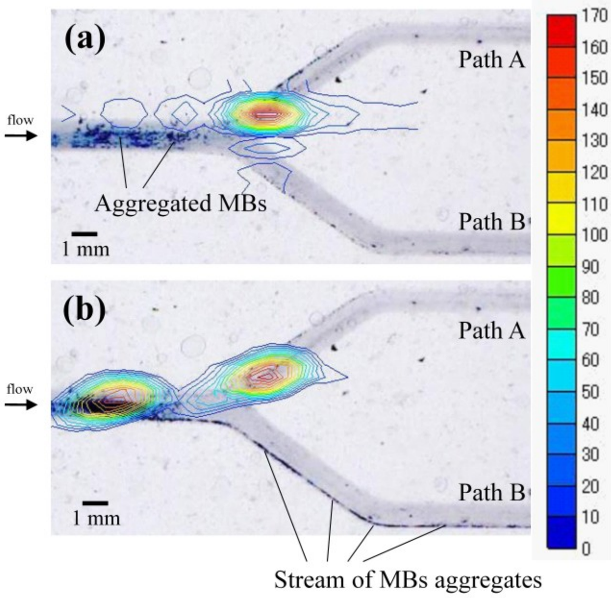


Fig.3 Microscopic images of the bifurcation with the acoustic field of (a) $(x_{Tr}, y_{Tr}, z_{Tr})=(2,-1,60)$ and (b) $(x_{Tr}, y_{Tr}, z_{Tr})=(0,4,60),(2,-1,60)$.

4. Conclusion

In this study, we realized clearly path selection of MBs with multiple focal points of ultrasound. By making use of aggregates formation, the probability of reducing the number of sound sources for controlling bubbles were confirmed. For further analysis, more patterns of acoustic field with various shapes should be applied. In the next step, we are going to measure quantitatively for precise evaluation.

Acknowledgment

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