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Three-dimensional behavior reproduction of microbubbles in flow under local ultrasound exposure
局所的超音波照射下における流体中の微小気泡動態の 3 次元再現シミュレーション

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1. Introduction

We have researched to control microbubbles in blood vessel by use of the acoustic radiation force [1-3] (primary Bjerknes force). Moreover, we have also reported that the acoustic radiation force increases by making aggregate of microbubbles by use of secondary Bjerknes force [3, 4]. However, behavior of microbubbles under the ultrasound exposure is complicated because of many kinds of parameters. In addition blood vessel network in human body is complicated. From these reasons, it is difficult to decide optimal ultrasound exposure condition, such as location of the transducer, sound pressure, and frequency. Therefore, numerical simulation models of microbubbles in human body are required. We have reported two-dimensional simulation of behavior of microbubbles by numerical simulation using finite element method (FEM) [5], but there was a limitation to reproduce three-dimensional behavior of them in flow under ultrasound exposure. In this study, we expanded the simulation study to three-dimension to compare with the results obtained from our experiments.

2. Theory

Fig. 1 shows boundary setting in flow velocity field. The calculated domain is defined as following incompressible Navier-Stokes equations,

$$\rho(\boldsymbol{u}\cdot\nabla)\boldsymbol{u} = \nabla\left[-p_0\,\mathbf{E} + \mu\left\{\nabla\boldsymbol{u} + (\nabla\boldsymbol{u})^{\mathrm{T}}\right\}\right], \quad (1)$$

$$\rho\nabla\boldsymbol{u} = 0\,, \quad (2)$$

where ρ is density, $\boldsymbol{u}$ is flow velocity, p_0 is fluid pressure, $\mathbf{E}$ is unit diagonal matrix, and μ is viscosity. In inlet of flow, boundary i, initial flow velocity is defined as $\boldsymbol{u} = u_0$. Alternatively, in the actual vessel wall, boundary ii, flow velocity is defined as $\boldsymbol{u} = 0$. Here because of the mesh size of FEM, to prevent a microbubble trapped at the boundary ii, whose flow velocity is 0. We also have defined the imaginary wall, boundary iii, in the distance w inside from boundary ii. Since the distance w is set to be more than the radius of a microbubble, there is no contact between a microbubble and the vessel wall.

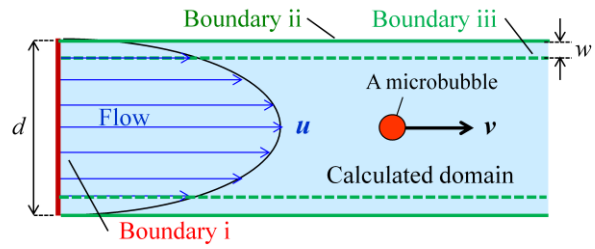

Fig. 1 Boundary setting of flow.

Under ultrasound exposure, a microbubble receive above-mentioned acoustic radiation force $\boldsymbol{F}_{ac}$, which acts to propel the microbubble along the direction of propagation and is defined as

$$\boldsymbol{F}_{ac} = \pi a^2\left(\frac{\boldsymbol{I}}{c}\right)Y_p\,, \quad (3)$$

where a is radius of the microbubble, $\boldsymbol{I}$ is acoustic intensity, c is sound velocity, ρ is density, and Y_p is acoustic radiation function. Here Y_p is very complicated function because of many kinds of parameters. I is proportional to the square of sound pressure p, which is calculated as following,

$$p = \left|\frac{2J_1(kr\sin\theta_x)}{kr\sin\theta_x}\cdot\frac{2J_1(kr\sin\theta_z)}{kr\sin\theta_z}\right|P \quad (4)$$

Here three-dimensional distribution of sound pressure was approximated to be independent to the distance from the sound source, if the interested area is near the focal point, using Bessel function, where P is the peak value of sound pressure, k is wave number, r is radius of transducer, θ_x and θ_z are angle from beam axis of x and z, respectively.

As shown in **Fig. 2**, when a microbubble is propelled by acoustic radiation force, it receives the flow residence $\boldsymbol{F}_d$, which is derived from Stoke's low as the following,

$$\boldsymbol{F}_d = 6\pi a\mu(\boldsymbol{u}-\boldsymbol{v}), \quad (5)$$

where $\boldsymbol{v}$ is relative velocity of a microbubble.

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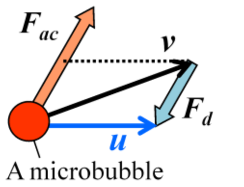

Fig. 2 Directions of forces on a microbubble.

3. Simulation method

Fig. 3 shows a three-dimensional analytical model of flow in Y-form bifurcation, where suspension of microbubbles comes from left to the bifurcation. Acoustic field was set as shown to propel more microbubbles to be induced to path A than B.

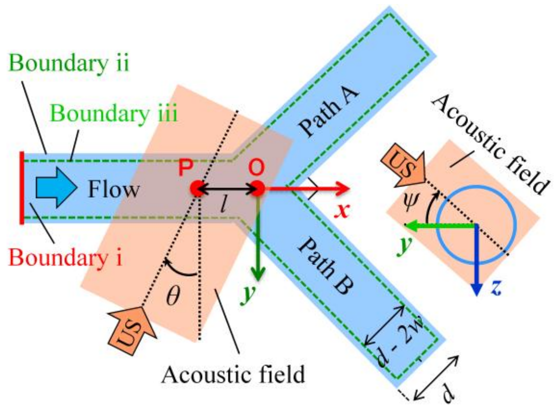

Fig. 3 Simulation model of microbubbles induction.

We set the diameter of paths d = 2.0 mm and the distance w = 0.05 mm. The initial flow velocity in boundary i was set u_0 = 20 mm/s. The number of microbubbles was 600. The elevation axis of ultrasound exposure, which was plane wave, was set at ψ = 40° from the $-y$ direction around x-axis. And the azimuth axis was set at θ = 30°. The axis of the ultrasound exposure was directed to point P, as shown in **Fig. 3**, which was set to be l = 2 mm from the bifurcation point O to the upstream course.

4. Results

We have set the acoustic field to be a plane wave with the central frequency of 3 MHz and the sound pressure P of 300 kPa. Moreover, in simulation, parameters were set as ρ = 1000 kg/m^3, c = 1500 m/s, μ = 1 mPa･s, and a = 2 μm, respectively. **Fig. 4** shows the simulated behavior of microbubbles in the bifurcation shown in **Fig. 3**. Time interval of each images is 600 ms.

Fig. 5 shows the comparison of the simulation with the experiment [2] under the same condition of the central frequency of 2 MHz and the sound pressure P of 400 kPa, θ = 45° and flow velocity of 20 mm/s. From this result this simulation can reproduce the behavior of microbubbles.

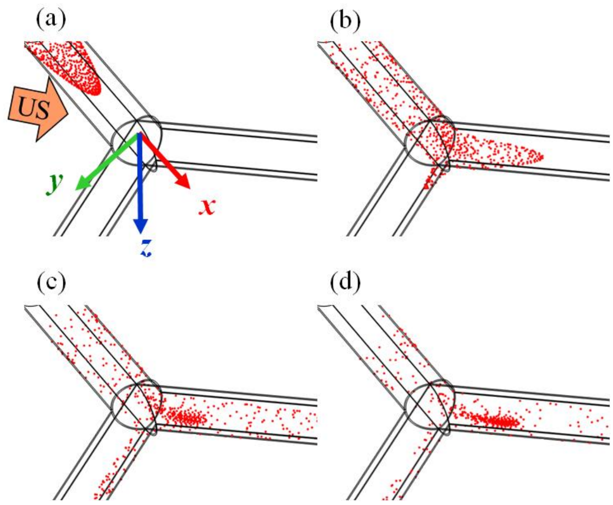

Fig. 4 Three-dimensional simulation results of behavior of microbubbles.

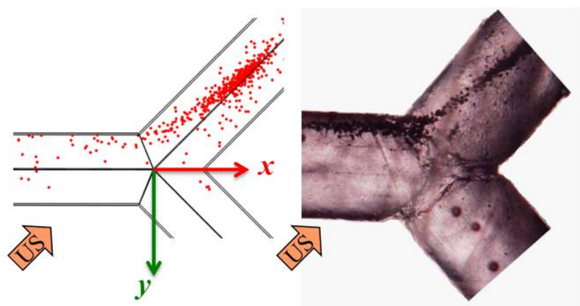

Fig. 5 Comparison of simulation and experiment.

5. Conclusions

We have expanded our simulation method to three-dimension to reproduce behavior of microbubbles in flow under ultrasound exposure. We have confirmed the correspondence in results between the simulation and our previous experiments through a Y-form bifurcation flow.

Acknowledgment

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