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Numerical simulation of red blood cell distributions in three-dimensional microvascular bifurcations

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ABSTRACT

We constructed three-dimensional microvascular bifurcation models using a parent vessel of diameter 10 μm and investigated the flow behavior of the red blood cells (RBCs) through bifurcations. We considered symmetric and asymmetric model types. Two cases of equal daughter vessel diameter were employed for the asymmetric models, where the first was 10 μm, which is the same as the parent vessel and the second was 7.94 μm, which satisfies Murray's law. Simulated blood flow was computed using the lattice Boltzmann method in conjunction with the immersed boundary method for incorporating fluid–membrane interactions between the flow field and deformable RBCs. First, we investigated the flow behavior of a single RBC through microvascular bifurcations. In the case of the symmetric bifurcation, the turning point of the fractional plasma flow wherein the RBC flow changed from one daughter vessel to the other was 0.50. This turning point was however different for asymmetric bifurcations. Additionally, we varied the initial offset of RBCs from the centerline of the parent vessel. The simulation results indicated that the RBCs preferentially flow through the branch of a larger flow ratio. Next, we investigated the distribution characteristics of multiple RBCs. Simulations indicated that the results of the symmetric model were similar to those predicted by a previously published empirical model. On the other hand, results of asymmetric models deviated from those of the symmetric and empirical models. These results suggest that the distribution of RBCs varies according to the bifurcation angle and daughter vessel diameter in a microvascular bifurcation of the size considered.

Introduction

Red blood cells (RBCs) occupy approximately 40–45% of the total blood volume and are therefore the principal component of blood. Hence, the rheological properties of RBCs have significant influence on the microvascular flow when diameters of RBCs and vessels are of the same order of magnitude (Goldsmith, 1986; Fung, 1997; Popel, 2005). RBCs are biconcave disc-shaped and contain hemoglobin, which is an oxygen-transporting protein, and exhibit a deformability that depends on the enveloping of the cell membrane. A characteristic of deformable RBCs is their axial concentration. The RBCs near the vessel wall migrate to the axial center with deformation. As a result, a plasma layer forms near the wall where no RBCs exist. The formation of a plasma layer decreases the flow resistance and increases the flow velocity. Consequently, the hematocrit of microcirculation, which is the volume fraction of RBCs, decreases with decreasing vessel diameter, a phenomenon called the Fåhræus effect. Moreover, the formation of the plasma layer leads to a nonproportional distribution of RBCs and plasma at the bifurcation, which can result in a complete absence of RBC flow passing through the bifurcation. This phenomenon is called plasma skimming. As a result, heterogeneity of oxygen in microvascular networks occurs. Therefore, it is very important to investigate the flow behavior of RBCs in microvascular flows.

Several recent numerical studies have focused on the behaviors of deformable RBCs in microvascular flows (Boryczko et al., 2003; Dupin et al., 2007; Sugiyama et al., 2010; Zhao et al., 2010; Tsubota and Wada, 2010; Imai et al., 2010; Alizadehred et al., 2012). Numerical studies on RBC aggregation (Liu et al., 2004; Liu and Liu, 2006; Zhang et al., 2008, 2009) and low deformability (Zhang et al., 2009) in abnormal RBC states have also been reported. RBC behaviors indicated in these studies are well described by existing numerical techniques.

Other studies have investigated the distribution of cells at microvascular bifurcation. Chien et al. (1985) experimentally investigated the distribution of spherical and disk-shaped particles at a symmetric T-bifurcation at low Reynolds number. Pries et al. (1990) examined the plasma separation effect in vivo and proposed an empirical relationship describing the distribution of RBC flows at microvascular bifurcations. Several studies numerically investigated RBC motion, trajectories, and partitioning through two-dimensional (2D) microvascular bifurcation. (Hyakutake et al., 2006; Barber et al., 2008; Chesnutt and Marshall, 2009; Xiong and Zhang, 2012; Xu et al., 2012; Yin et al., 2013).

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Hyakutake et al. (2008) investigated flow behaviors of RBCs and liposome-encapsulated hemoglobin at 2D microvascular bifurcations using the lattice Boltzmann method (LBM) and clarified that the partial replacement of RBCs by liposome-encapsulated hemoglobin reduces the bias of oxygen flux. Moreover, an extension to a deformable RBC model was conducted (Hyakutake et al., 2010). However, these studies conducted simulations using 2D models, but there are no studies employing a three-dimensional (3D) microvascular bifurcation model. In this study, in order to demonstrate behaviors of flowing RBCs at a microvascular bifurcation in more detail, we constructed 3D microvascular bifurcation models using a parent vessel of diameter 10 μm and investigated the effect of the bifurcation angle and shape on the distributions of RBCs. These results provide valuable insights into the mechanism of RBC behavior through microvascular bifurcations.

Numerical model and methods

Numerical model

For the present simulation, we constructed 3D microvascular bifurcation models and investigated flow behaviors of RBCs, especially the distributions of RBCs. Fig. 1 shows schematics of microvascular bifurcation models employed. We considered two types of models, that is, a symmetric model (Model A) and asymmetric models (Models B and C). In the case of Models A and B, diameters of the parent vessel (D_p) and daughter vessels (D_1 and D_2) are 10 μm whereas, in the case of Model C, D_p is 10 μm and D_1 and D_2 are both 7.94 μm, which satisfy Murray's law. Figs. 1(a) and (b) illustrate Models A and C, respectively. Table 1 lists the geometrical characteristics of Models A, B, and C. First, a single RBC was placed in the center of the parent vessel, and we investigated distribution characteristics in the bifurcation. Next, we investigated the case of multiple RBC flow. Single RBCs were arranged one by one as time passed, and we investigated the relationship between the flow and particle fluxes. The blood flow was computed using LBM in conjunction with the immersed boundary method (IBM) for incorporating fluid–membrane interactions between the flow field and deformable RBCs. The RBC model used in the present 3D simulations is the one based on our previous 2D study (Hyakutake et al., 2010).

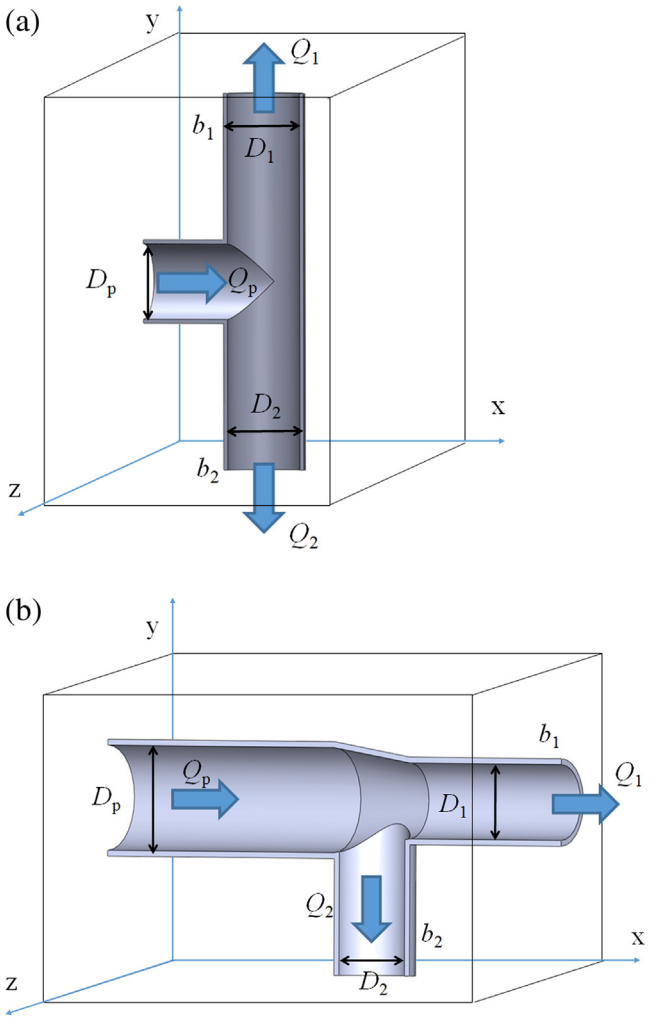

Fig. 1. We considered two types of models: a symmetric model, Model A (shown in (a)), and asymmetric models, Model B and Model C (shown in (b)). In the case of Models A and B, diameters of the parent vessel (D_p) and daughter vessels (D_1 and D_2) are 10 μm whereas, in the case of Model C, D_p is 10 μm and D_1 and D_2 are both 7.94 μm, which satisfy Murray's law. The total volumetric flow from the parent vessel (Q_p) is divided into flows Q_1 and Q_2 in the two daughter vessels b_1 and b_2, respectively.

Governing equation

In the present simulations, flows are computed by LBM (McNamara and Zanetti, 1998; Succi, 2001). LBM is a relatively new and promising numerical scheme for simulating complex flows and has attracted much attention as an alternative approach to conventional Navier–Stokes equations in computational fluid dynamics. Since LBM enables simple handling of complex moving geometries, it is an effective tool for analyzing multiphase fluid flows, such as those occurring in this study.

The fluid modeled by LBM is composed of fictitious particles whose velocities are restricted to a finite set of vectors. Since our study involves a 3D issue, a 15-velocity model (Qian et al., 1992) is used in the following calculations. The velocity vectors are defined as follows.

$$[\mathbf{c}_1,\mathbf{c}_2,\mathbf{c}_3,\mathbf{c}_4,\mathbf{c}_5,\mathbf{c}_6,\mathbf{c}_7,\mathbf{c}_8,\mathbf{c}_9,\mathbf{c}_{10},\mathbf{c}_{11},\mathbf{c}_{12},\mathbf{c}_{13},\mathbf{c}_{14},\mathbf{c}_{15}] = \begin{bmatrix} 0 & 1 & 0 & 0 & -1 & 0 & 0 & 1 & -1 & 1 & 1 & -1 & 1 & -1 & -1 \\ 0 & 0 & 1 & 0 & 0 & -1 & 0 & 1 & 1 & -1 & 1 & -1 & -1 & 1 & -1 \\ 0 & 0 & 0 & 1 & 0 & 0 & -1 & 1 & 1 & 1 & -1 & -1 & -1 & -1 & 1 \end{bmatrix} \quad (1)$$

The particle distribution function $f_i(\mathbf{x}, t)$, whose velocity at point $\mathbf{x}$ and time t, given by $\mathbf{c}_i$, evolves as

$$f_i(\mathbf{x}+\mathbf{c}\Delta x, t+\Delta t) - f_i(\mathbf{x},t) = -\frac{1}{\tau}\left[f_i(\mathbf{x},t) - f_i^{eq}(\mathbf{x},t)\right] \quad \text{for } i = 1,2,\ldots,15, \quad (2)$$

where $f_i^{eq}(\mathbf{x}, t)$ is the equilibrium distribution function, τ is a single relaxation time, Δx is the lattice spacing, and Δt is the time step. The Bhatnagar–Gross–Krook model (Bhatnagar et al., 1954) is used for the collision term on the right hand side of Eq. (2). The following is a suitable equilibrium distribution function (Qian et al., 1992):

$$f_i^{eq} = E_i\rho\left[1 + 3\mathbf{c}_i\cdot\mathbf{u} + \frac{9}{2}(\mathbf{c}_i\cdot\mathbf{u})^2 - \frac{3}{2}\mathbf{u}\cdot\mathbf{u}\right] \quad (3)$$

where $E_1 = 2/9$, $E_i = 1/9$ (for $i = 2, 3, \ldots, 7$) and $E_i = 1/72$ (for $i = 8, 9, \ldots, 15$). The fluid density ρ and fluid velocity $\mathbf{u}$ given in Eq. (3) are calculated in terms of the particle distribution function as

$$\rho = \sum_{i=1}^{15} f_i, \quad \mathbf{u} = \frac{1}{\rho}\sum_{i=1}^{15} f_i\mathbf{c}_i, \quad (4)$$

Table 1
Bifurcation geometries and turning points for Models A, B, and C.

Model	Bifurcation geometry	D_p [μm]	D_1, D_2 [μm]	Turning point Q_1/Q_p
A	Symmetric	10	10	0.50
B	Asymmetric	10	10	0.57
C	Asymmetric	10	7.94	0.61