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Journal of Biomechanics 41 (2008) 47–55

JOURNAL OF BIOMECHANICS

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Red blood cell aggregation and dissociation in shear flows simulated by lattice Boltzmann method

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Accepted 25 July 2007

Abstract

In this paper we develop a lattice Boltzmann algorithm to simulate red blood cell (RBC) behavior in shear flows. The immersed boundary method is employed to incorporate the fluid–membrane interaction between the flow field and deformable cells. The cell membrane is treated as a neo-Hookean viscoelastic material and a Morse potential is adopted to model the intercellular interaction. Utilizing the available mechanical properties of RBCs, multiple cells have been studied in shear flows using a two-dimensional approximation. These cells aggregate and form a rouleau under the action of intercellular interaction. The equilibrium configuration is related to the interaction strength. The end cells exhibit concave shapes under weak interaction and convex shapes under strong interaction. In shear flows, such a rouleau-like aggregate will rotate or be separated, depending on the relative strengths of the intercellular interaction and hydrodynamic viscous forces. These behaviors are qualitatively similar to experimental observations and show the potential of this numerical scheme for future studies of blood flow in microvessels.

Keywords: Microscopic blood flows; Aggregation; Hemodynamics; Hemorheology; Lattice Boltzmann method

1. Introduction

Red blood cells (RBCs) are an important component in blood because of their large number density ($\sim 5 \times 10^6/\text{mm}^3$) and their crucial role in oxygen transport. Typically, a human RBC has a biconcave shape of $\sim 8\,\mu\text{m}$ in diameter and $\sim 2\,\mu\text{m}$ in thickness. The interior fluid (cytoplasm) has a viscosity of 6 cP, which is about 5 times of that of the suspending plasma (~ 1.2 cP). The cell membrane is highly deformable so that RBCs can pass through capillaries of as small as $4\,\mu\text{m}$ inner diameter with large deformation (Popel and Johnson, 2005; Mchedlishvili and Maeda, 2001). RBCs can also aggregate and form one-dimensional stacks-of-coins-like rouleaux or three-dimensional aggregates (Popel and Johnson, 2005; Stoltz et al., 1999; Baumler et al., 1999). The process is reversible and the rouleaux and aggregates can be broken by, for example, increasing the flow shear rate. This phenomenon is particularly important in microcirculation, since such rouleaux or aggregates can dramatically influence blood flow in microvessels. However, the underlying mechanism of RBC aggregation is not yet clear. Currently, there exist two theoretical descriptions of this process: the bridging model and the depletion model (Popel and Johnson, 2005; Baumler et al., 1999). The former assumes that macromolecules, such as fibrinogen or dextran, can adhere onto the adjacent RBC surfaces and bridge them together (Merill et al., 1966; Brooks, 1973; Chien and Jan, 1973a). The depletion model attributes the RBC aggregation to a polymer depletion layer between RBC surfaces, which is accompanied by a decrease of the osmotic pressure (Baumler and Donath, 1987; Evans and Needham, 1988). Detailed discussions of these two models can be found elsewhere (see, for example, a review by Baumler et al., 1999).

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0021-9290/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jbiomech.2007.07.020

The nature of blood flow changes greatly with the vessel diameter. In vessels larger than 200 μm, the blood flow can be accurately modeled as a homogeneous fluid. However, in arterioles and venules smaller than 25 μm, and also in capillaries with diameter of 4–10 μm, the RBCs have to be treated as discrete fluid capsules suspended in the plasma. Significant efforts have been devoted to numerically study the RBC behaviors in various flow situations. For example, Pozrikidis and coworkers (1995,2001,2003) have employed the boundary integral method for Stokes flows to investigate RBC deformation and motion in shear and channel flows; Eggleton and Popel (1998) have combined the immersed boundary method (IBM) (Peskin, 1977) with a finite element treatment of the RBC membrane to simulate large three-dimensional RBC deformations in shear flow. Recently, a lattice Boltzmann approach has also been adopted for RBC flows in microvessels, where the RBCs were represented as rigid rods in two dimensions (Migliorini et al., 2002; Sun et al., 2003; Sun and Munn, 2005). Bagchi (2007) has simulated a large RBC population in vessels of size 20–300 μm. However, RBC aggregation was not considered in these studies. Liu et al. (2004) modeled the intercellular interaction through a Morse potential, thus accounting for RBC aggregation. The cell membrane was represented by elastic elements. Bagchi et al. (2005) have extended the IBM approach of Eggleton and Popel (1998) to two-cell systems and introduced the intercellular interaction according to a ligand–receptor binding model. Chung et al. (2006) have utilized the theoretical formulation of depletion energy proposed by Neu and Meiselman (2002) to study two rigid elliptical particles in a channel flow. Sun and Munn (2006) have also improved their lattice Boltzmann model by including an interaction force between rigid RBCs.

In this paper, we develop a two-dimensional lattice Boltzmann scheme to simulate multiple deformable RBCs in shear flow. The lattice Boltzmann method (LBM) was chosen to solve the incompressible fluid field for its ability to deal with complex boundary conditions and its advantage for parallel computation (Succi, 2001), both of which could be valuable in our future studies. Different from previous LBM studies of RBC flows (Migliorini et al., 2002; Sun et al., 2003; Sun and Munn, 2005), here we modeled the cells as deformable fluid capsules and hence the membrane mechanics and cytoplasm viscosity could be considered. IBM was also utilized to incorporate the fluid–membrane interaction, and a Morse potential to describe the intercellular interaction. Detailed theory and formulations will be given in the next section. The algorithm and program have been validated by comparing simulation results with theoretical predictions, and excellent agreement was found. Finally, simulations of multiple deformable RBCs were conducted and the results demonstrated the effects of intercellular interactions and shear rate on the RBC rheological behaviors, which are also in qualitative agreement with experimental observations.

2. Theory and methods

Here we employ the LBM (Zhang and Kwok, 2005; Zhang et al., 2004) to solve the flow field and the IBM (Peskin, 1977) to incorporate the fluid–membrane interaction. The LBM approach is advantageous for parallel computations due to its local dynamics and can be relatively easily applied to systems with complex boundaries (Succi, 2001). Detailed descriptions of these methods are available elsewhere (also see the Supplemental Materials).

2.1. RBC membrane mechanics

Experiments have shown that the RBC membrane is a neo-Hookean, highly deformable viscoelastic material (Hochmuth and Waugh, 1987). Also it exhibits finite bending resistance that becomes more profound in regions with large curvature (Evans, 1983). For the two-dimensional RBC model in this work, according to Bagchi et al. (2005), the neo-Hookean elastic component of membrane stress can be expressed as

$$T_e = \frac{E_s}{\varepsilon^{3/2}}(\varepsilon^3 - 1), \tag{1}$$

where E_s is the membrane shear modulus and ε is the stretch ratio. To incorporate the membrane viscous effect, an extra term should be added to the stress expression as (Evans and Hochmuth, 1976; Mills et al., 2004; Bagchi et al., 2005)

$$T_v = \frac{\mu_m}{\varepsilon}\frac{d\varepsilon}{dt}, \tag{2}$$

where μ_m is the membrane viscosity. In addition, the bending resistance can also be represented by relating the membrane curvature change to the membrane stress with (Pozrikidis, 2001; Bagchi et al., 2005)

$$T_b = \frac{d}{dl}[E_b(\kappa - \kappa_0)], \tag{3}$$

where E_b is the bending modulus and κ and κ_0 are, respectively, the instantaneous and initial stress-free membrane curvatures. l is a measure of the arc length along the membrane surface. Therefore, the total membrane stress $\mathbf{T}$ induced due to the cell deformation is a sum of the three terms discussed above:

$$\mathbf{T} = (T_e + T_v)\mathbf{t} + T_b\mathbf{n}. \tag{4}$$

Here, $\mathbf{t}$ and $\mathbf{n}$ are the local tangential and normal directions on the membrane.

2.2. Intercellular interactions

The physiological and pathological importance of RBC aggregation has been realized and extensive experimental investigations have been performed (Popel and Johnson, 2005; Stoltz et al., 1999; Baumler et al., 1999; Kim et al., 2006; Kounov and Petrov, 1999; Chien et al., 1977); however, the underlying mechanisms of the RBC aggregation are still subjects of investigation. Both the bridging and the depletion models can describe certain aggregation phenomena; however, they fail to explain some specific observations (Baumler et al., 1999; Armstrong et al., 1999). In general, it can be assumed that the attractive interaction between RBC surfaces would occur when they are close, and repulsive interaction would occur when the separation distance is sufficiently small. The repulsive interaction includes the steric forces due to the glycocalyx and electrostatic repulsion from the negative charges on RBC surfaces (Liu et al., 2004). In previous studies, to model such intercellular interactions, Bagchi et al. (2005) adopted the formalism of a ligand–receptor dynamics according to the bridging model. However, this description involves a number of parameters whose values are not available from experiments. On the other hand, Chung et al. (2006) employed a mathematical description of the depletion model proposed by Neu and Meiselman (2002). It was noticed that such a description results in a constant (instead of a decaying) attractive force at large separation, which is not physically realistic.