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Rheology of red blood cell aggregation by computer simulation

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Abstract

The aggregation of red blood cells (RBC) induced by the interactions between RBCs is a dominant factor of the in vitro rheological properties of blood, and existing models of blood do not contain full cellular information. In this work, we introduce a new three-dimensional model that couples Navier–Stokes equations with cell interactions to investigate RBC aggregation and its effect on blood rheology. It consists of a depletion mediated aggregation model to describe the interactions of RBCs and an immersed continuum model to track the deformation/motion of RBCs in blood plasma. To overcome the large deformation of RBCs, the meshfree method is used to model the RBCs. Three important phenomena in blood rheology are successfully captured and studied via this approach: the shear rate dependence of blood viscosity, the influence of cell rigidity on blood viscosity, and the Fahraeus–Lindqvist effect. As a microscopic illustration of the shear-rate dependence of the blood's viscoelasticity, the disaggregation of an RBC rouleau at shear rates varying between 0.125 and 24 s^{-1} is modeled. Lower RBC deformability and higher shear rates above 0.5 s^{-1} are found to facilitate disaggregation. The effective viscosities at different shear rates and for cells with different deformabilities are simulated. The numerical results are shown to agree with the reported experimental measurements. The Fahraeus–Lindqvist effect is, for the first time, studied through three-dimensional numerical simulations of blood flow through tubes with different diameters and is shown to be directly linked to axial-migration of deformable cells. This study shows that cell–cell interaction and cell deformability have significant effects on blood rheology in capillaries.

Keywords: Immersed finite element method; Navier–Stokes equations; Cell interaction; Red blood cell; Aggregation; Hemorheology; Capillary

1. Introduction

The aggregation of human red blood cells (RBC) is a dominant factor of the in vitro rheological properties of blood. Past studies on RBC aggregation [1–3] have confirmed the effects of fibrinogen (a cross-linking protein) concentration on RBC aggregation. Due to the presence of fibrinogen on cell membranes and globulin in the plasma, RBCs tend to form aggregates called rouleaus, in which RBCs adhere loosely like a stack of coins. The presence of massive rouleaus can impair the blood flow through micro- and capillary vessels and cause

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fatigue and shortness of breath. The difference in the percentage of aggregated RBCs may be an indication of a thrombotic disease. Recently, Neu and Meiselman [4] proposed a theory for depletion mediated RBC aggregation. However, the direct link between RBC aggregation and the rheological properties of blood has not been established yet. It is therefore of significant clinical relevance to understand blood composition and its rheological behavior in the context of multiscale and multiphysics hemodynamics. In this paper, the macroscopic rheological properties of the blood will be shown to be determined by the cellular scale nature of blood cells.

Human blood is a biological fluid composed of deformable cells, proteins, platelets, and plasma. In the study of the heart, arteries, and veins, blood is usually simplified as a homogeneous Newtonian fluid. However, the rheological behavior of blood flows in micro- and capillary vessel strongly depends on the flow condition, cell deformability, vessel size, and many other biochemical factors [5,6]. Biological phenomena such as blood coagulation, sickle cell disease, involve the cellular and molecular nature of blood. Eggleton and Popel [7] have studied deformation of one or two cells under shear flow. Wagner et al. [8,9] have modeled the shear flow with rigid particles with continuum enrichment methods. However, no method is yet available to study blood rheology in micro-vessels from the underlying cellular mechanism. Currently, there are three critical challenges in direct numerical simulation of the blood flow with deformable RBCs: the coupling between complex nonlinear solid motions and fluid flow, handling very large deformation of solids, and computational expense.

In [10], we have presented a two-dimensional model of blood cell interactions. Due to the difficulties in handling large RBC deformations and the limitations of 2D simulation, only simple illustrative examples of cell–cell interactions were given there. In this work, we concentrate on the rheological aspects of three-dimensional flow systems of micro- and capillary vessels which involve deformable cells, cell–cell interactions, and complex flow conditions. In particular, we propose a new modeling technique which combines the newly developed immersed finite element method (IFEM) [11,33] with RBC–RBC interaction mechanisms. It consists of a depletion mediated aggregation model introduced by Neu and Meiselman [4] to describe the interactions of RBCs and an immersed continuum model to track the deformation/motion of RBCs in plasma. We have used a meshfree formulation [28] to handle the large deformation of RBCs. Our results suggest that cell interaction and cell deformability are critical factors that influence the hemorheology in capillaries.

We first describe the discrete RBC model and aggregation model, and illustrate the key ingredients of the proposed combination of the IFEM and cell interactions. The results are then presented in Section 3, where the shear rate dependent blood viscosity, the influence of cell rigidity, and the Fahraeus–Lindqvist effect are studied. The conclusions are presented in Section 4.

2. Method

2.1. Discrete RBC model

In suspension culture, RBC assumes a biconcave disc shape which permits its passage through capillaries and enables its surface to volume ratio to be significantly higher than that of a sphere. In addition, the biconcave disc shape suggests that the membrane cytoskeleton has both bending and membrane rigidities. The RBC membrane is modeled as a flexible three-dimensional thin structure enclosing an incompressible fluid, using a Lagrangian description. Both the cytoplasm inside the RBC and the blood plasma outside the RBC have a viscosity of around 0.01 dyn s/cm, thus are treated as the same fluid.

The static shape of a normal RBC is a biconcave discoid. The x–y coordinates of the cross-sectional profile of a RBC are described by

$$\bar{y} = 0.5[1 - \bar{x}^2]^{1/2}(a_0 + a_1\bar{x}^2 + a_2\bar{x}^4), \quad -1 \leqslant \bar{x} \leqslant 1 \tag{1}$$

with $a_0 = 0.207$, $a_1 = 2.002$, and $a_2 = 1.122$, and the non-dimensional coordinates $\bar{x}$ and $\bar{y}$ are scaled as $x/5$ μm and $y/5$ μm, respectively.

A Mooney–Rivlin strain energy function is used to depict the material behavior of the RBC membrane

$$W = C_1(I_1 - 3) + C_2(I_2 - 3) \tag{2}$$