Published in final edited form as:

J Comput Appl Math. 2020 October ; 376: . doi:10.1016/j.cam.2020.112856.

Simulation of blood flow in a sudden expansion channel and a coronary artery

Wei-Tao Wu¹, Nadine Aubry², James F. Antaki³, Mehrdad Massoudi⁴

¹School of Mechanical Engineering, Nanjing University of Science and Technology, Nanjing, J.S., 210094, China

²Department of Mechanical Engineering, Tufts University, Medford, MA, 02155, USA

³Nancy E. and Peter C. Meinig School of Biomedical Engineering, Cornell University, Ithaca, NY 14853, USA

⁴U. S. Department of Energy, National Energy Technology Laboratory (NETL), Pittsburgh, PA, 15236, USA

Abstract

In this paper, we numerically simulate the flow of blood in two benchmark problems: the flow in a sudden expansion channel and the flow through an idealized curved coronary artery with pulsatile inlet velocity. Blood is modeled as a suspension (a non-linear complex fluid) and the movement of the red blood cell (RBCs) is modeled by using a concentration flux equation. The viscosity of blood is obtained from experimental data. In the sudden expansion flow, the predicted velocity profiles for two different Reynolds numbers (based on the inlet velocity) agree well with the available experiments; furthermore, the numerical results also show that after the sudden expansion there exists a RBCs depletion region. For the second problem, the idealized curved coronary artery, it is found that the RBCs move towards and concentrate near the inner surface where the viscosity is higher and the shear stress lower; this phenomenon may be related to the atherosclerotic plaque formation which usually occurs on the inside surface of the arteries.

Keywords

Blood flow; Shear-thinning fluid; Non-linear fluid; Coronary artery; Suspension

1. Introduction

Blood is composed of red blood cells (RBCs), white blood cells (WBCs) and platelets suspended in plasma, constituting 55% of whole blood [1]. A understanding of the pathogenesis of blood-related diseases and improving of the design of blood-wetted medical

Address for correspondence: Mehrdad Massoudi, PhD, U. S. Department of Energy, National Energy Technology Laboratory (NETL), 626 Cochran Mill Road, P.O. Box 10940, Pittsburgh, PA. 15236. Mehrdad.Massoudi@NETL.DOE.GOV.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

devices have been the driving force for the development of mathematical and computational models to the properties of quantitatively analyze and predict the behavior of blood *in vivo* or *in vitro* [2,3]. Similar to many concentrated solid-fluid suspensions, the rheological properties of blood are complex. In large vessels, blood usually behaves as a Newtonian fluid [4]; while in small vessels (20 to 500 microns) or at low shear rate (about 100 s^{-1}), blood shows some non-Newtonian and multi-component features, such as shear-thinning behavior, the Fahraeus effect, stress relaxation, etc. [5]. Due to the RBCs aggregation, blood shows shear-thinning behavior [1,6,7]; at high shear rates the deformability of the RBCs contributes to the shear-dependent property of the blood viscosity [8]; furthermore, attributed to high hematocrit of the RBCs, the variation of the hematocrit greatly changes the magnitude of the blood viscosity significantly [9–11].

In general, blood can be considered to behave as a multi-component fluid composed of red blood cells (RBCs) suspended in plasma. In the past several decades, several mathematical or computational models for blood have been developed, including mesoscale simulations, CFD-DEM models, and continuous multi-component Eulerian models (Fenech, Garcia, Meiselman, & Cloutier, 2009; Wu et al., 2016; Wu, Aubry, Massoudi, Kim, & Antaki, 2014; Wu, Yang, Antaki, Aubry, & Massoudi, 2015; Yin, Thomas, & Zhang, 2013; Zhang, Johnson, & Popel, 2008). The mesoscale simulations, such as the Lattice Boltzmann Method - Immersed Boundary Method (LBM-IBM) (Dupin, Halliday, Care, Alboul, & Munn, 2007; Zhang et al., 2008), Moving particle semi-implicit method (MPS) (Tsubota, Wada, & Yamaguchi, 2006), Dissipative particle dynamics (DPD) (Fedosov, Caswell, & Karniadakis, 2010; Li, Popel, & Karniadakis, 2012), are able to reveal the detail behavior of blood flow; however the computational cost of mesoscale simulations is usually much higher than the other methods. This limits its application for many engineering-scale problems (van der Hoef et al., 2006). The CFD-DEM approach instead considers the blood cells as soft-sphere particles and the motion of blood is calculated by integrating Newton's second law where the multiple cell-cell, cell-wall and cell-plasma interactions are considered. The CFD-DEM model is a reasonable alternative to mesoscale simulations when the computational cost is expensive or prohibitive." Using the basic ideas of continuum mechanics, blood can be mathematically modeled by at least three different ways: (1) a single component suspension approach, (2) a non-homogeneous suspension model, and (3) a two-fluid (mixture theory) approach. In large vessels with shear rates larger than 100 s^{-1} , the single component approach is usually applied, where (whole) blood is treated as either a Newtonian or a non-Newtonian fluid [4,22–24] Chabannes et. al, (2013) [25], Janela et al., (2010) [26]. In small/micro size vessels, where the multi-phase features of blood are important, distinguishing the RBCs and plasma distributions, the non-homogeneous suspension model or the two-fluid model should be used. In the two-fluid approach, plasma and RBCs are modeled as two interacting continua, where they are coupled through interaction forces, such as drag force, shear lift force, etc. [2,13,27], Kim et al., (2016) [28]. In the non-homogeneous approach, the movement of RBCs is described by concentration fluxes. The single component non-homogeneous approach has been shown to be useful in certain problems including flow of fluid-solid suspensions (Phillips, Armstrong, Brown, Graham, & Abbott, 1992; Wu, Zhou, Aubry, Antaki, & Massoudi, 2017). With lower computational cost, this approach can retain some of the important features of the Eulerian-Eulerian model (mixture theory approach).

For the multi-component case, one can use the averaging method or the mixture theory approach [31–33]. Based on the averaging method, Jung et. al (2006) [27] developed a multiphase transient non-Newtonian three-dimensional model for blood. Numerical simulations were performed for an idealized curved coronary artery with pulsatile hemodynamics; the authors observed that there are RBCs buildup on the inside curvature. Their numerical results also show that the shear-thinning effect is more significant in the multi-phase non-Newtonian viscosity model than the single-phase non-Newtonian model. Zhao et. al (2008) [34] studied the distribution of the RBCs and the platelets in a sudden expansion channel; they noticed that there is a clear RBCs depletion region and platelets enrichment in the flow circulation zone after the sudden expansion. Karino and Goldsmith (1979) [35] also found similar patterns for platelets adhesion in a sudden expansion pipe. Based on Mixture Theory and the shear induced diffusion method, Wu et. al (2017) [36] developed a multiphase model for the blood and platelet transport; using the model the authors numerically showed the RBCs depletion and the platelets accumulation in the flow circulation region. Recently, Wu et. al (2018) [37] developed a non-homogeneous suspension model for blood, where the viscosity depends on the local volume fraction and the shear rate. The motion of the RBCs is governed by a concentration (flux) equation, where the effects of gravity and the non-uniform distribution of the viscosity and the shear rate on particles migration are considered. To better understand the model, they non-dimensionalized the equations and performed parametric studies for a simple shear flow and a pressure driven flow (between two plates), where the effects of shear-thinning viscosity and RBCs flux terms on the RBCs distribution and velocity were investigated.

In this paper, we use the model developed by Wu et. al (2018) [37] and study two benchmark problems: the blood flow in a sudden expansion pipe and in an idealized curved coronary artery with an inlet pulsating velocity. The numerical results will be compared with available experimental observations. In section 2, the governing equations will be presented. In section 3, we introduce the constitutive equations for the stress tensor and the RBCs fluxes, where a new correlation for the blood viscosity is proposed by fitting the experiments of Brooks et al. [11]. In Sections 4, the geometries and kinematics of the problems are presented, and our numerical results discussed in section 5.

2. Governing Equations

In the absence of any thermo-chemical and electro-magnetic effects, the governing equations of motion for the flow of a non-linear fluid suspension are the conservation equations for mass, linear momentum, and angular momentum [38,39]. A convection-diffusion type equation is also needed for the flow of the RBCs. As we are only considering a purely mechanical system, the energy equation and the entropy inequality are not considered.

2.1. Conservation of mass

The conservation of mass is:

$$\frac{\partial \rho}{\partial t} + \text{div}(\rho \mathbf{v}) = 0 \quad (1)$$

where $\mathbf{v}$ is the velocity vector (of the blood), $\rho = (1 - \phi)\rho_{f0} + \phi\rho_{s0} = \alpha\rho_{f0} + \phi\rho_{s0}$ is the density of the (whole) blood, ϕ is the volume fraction (concentration) of the RBCs, ρ_{f0} and ρ_{s0} are the pure density of plasma and RBCs in the reference configuration (before mixing), $\partial/\partial t$ is the derivative with respect to time, and div is the divergence operator. For an isochoric motion, $\text{div } \mathbf{v} = 0$.

2.2. Conservation of linear momentum

With $\mathbf{T}$ representing the Cauchy stress tensor, the balance of the linear momentum reads:

$$\rho \frac{d\mathbf{v}}{dt} = \text{div} \mathbf{T} + \rho \mathbf{b} \quad (2)$$

where $\frac{d\mathbf{v}}{dt} = \frac{\partial \mathbf{v}}{\partial t} + (\text{grad} \mathbf{v})\mathbf{v}$ and $\mathbf{b}$ stands for the body force. The conservation of angular momentum implies that in the absence of couple stresses the Cauchy stress tensor is symmetric, that is $\mathbf{T} = \mathbf{T}^T$.

2.3. Conservation of RBCs concentration

The convection-diffusion equation governing the motion of the RBCs is [29,40],

$$\frac{\partial \phi}{\partial t} + \mathbf{v} \cdot \text{grad} \phi = -\text{div} \mathbf{N} \quad (3)$$

where the first term on the left hand side denotes the rate of accumulation of the RBCs, the second term represents the convected RBCs flux (where $\frac{\partial \phi}{\partial x}$ denotes the gradient of the concentration), and the term on the right hand side denotes the diffusive RBCs flux. The diffusive RBCs flux $\mathbf{N}$ is composed of fluxes related to the Brownian motion, the variation of the interaction frequency and the viscosity [29,40]. Constitutive relations are needed for the stress tensor and for the RBC flux. In the next section, we discuss this issue.

3. Constitutive Equations

3.1. Stress tensor

Based on numerous experimental observations, the viscosity of blood depends on the shear rate and volume fraction [11,41,42]. In our previous paper, Wu et. al (2018) [37], we suggested that (the whole) blood is a suspension which can be modeled as a non-linear viscous fluid,

$$\mathbf{T} = -p\mathbf{I} + \mu(\phi, \dot{\gamma})\mathbf{D} \quad (4)$$

where μ is the viscosity of the (whole) blood, which depends on the volume fraction and the shear rate ($\dot{\gamma} = \sqrt{2\text{tr}(\mathbf{D}^2)}$), $\mathbf{I}$ is the identity tensor, p is the pressure (or more accurately the mean value of the stress), and $\mathbf{D} = 1/2(\text{grad} \mathbf{v} + (\text{grad} \mathbf{v})^T)$ is the symmetric part of the velocity gradient. We assume that the viscosity is given by a Carreau-type viscosity. When the shear rate is close to zero, the viscosity approaches a lower limit, μ_0 , and when the shear rate is

close to infinity, the viscosity approaches an upper limit, μ_∞ . As suggested by Yeleswarapu (1994) [43], we assume μ is given by,

$$\mu = \mu_\infty(\phi) + (\mu_0(\phi) - \mu_\infty(\phi)) \frac{1 + \ln(1 + k\dot{\gamma})}{1 + k\dot{\gamma}} \quad (5)$$

where $\mu_0(\phi)$ and $\mu_\infty(\phi)$ are the viscosities when the shear rate approaches zero and infinity, respectively, and k is the shear-thinning parameter. The values or the correlations for $\mu_0(\phi)$, $\mu_\infty(\phi)$ and k are obtained by using the experimental measurements of Brooks et al., over a range of hematocrit from 8.6%–70.2% [11] :

$$\mu_0 = 566.912\phi^3 + 17.740\phi^2 + 10.285\phi + 1.0 \quad (6a)$$

$$\mu_\infty = 7.695\phi^2 + 6.445\phi + 1.0 \quad (6b)$$

$$k = 11 \quad (6c)$$

The above equations account for the low volume fraction of RBCs that occurs in blood flows at micro-scale [2]. Also equations (6a) and (6b) imply that the viscosity of the whole blood approaches the plasma viscosity, which is considered to be 1.0cP, when the haematocrit approaches zero, and the whole blood behaves as a Newtonian fluid in that case. Figure 1 displays the comparison between the viscosities measured by experiments and obtained by the correlations used here, showing good agreement.

3.2. RBCs flux

In suspensions composed of solid particles and a fluid, the particles flux can be due to the Brownian motion, turbulent diffusivity, particles interactions, gravity, etc. [29,30,40]. We ignore the Brownian motion, due to the large size of RBCs, and we also assume that the flow is laminar. For more information, see Wu et. al (2018) [37]. We assume that the flux term N is given by:

$$N = N_c + N_\mu + N_g \quad (7)$$

where N_c , N_μ and N_g are the contributions to the flux due to particles collision, spatial variations in the viscosity and gravity respectively. As suggested by Phillips et al. [29], we assume that N_c and N_μ are given by:

$$N_c = -a^2\phi K_c \nabla(\dot{\gamma}\phi) \quad (8)$$

$$N_\mu = -a^2\phi^2 \dot{\gamma} K_\mu \nabla(\ln\mu) \quad (9)$$

$$\dot{\gamma} = (2\mathbf{D}_{ij}\mathbf{D}_{ij})^{1/2} = (\Pi)^2 \quad (10)$$

where a is the characteristic particle length (e.g. radius), and K_c and K_μ are empirically-determined coefficients. Following Phillips et al. and Subia et al. [29,44], we assume that $K_c = 0.43$, $K_\mu = 0.62$.

For the effect of gravity, Hsu et al. [45] proposed,

$$\mathbf{N}_g = \phi(1 - \phi)t_p \left(1 - \frac{\rho_{f0}}{\rho_{s0}}\right) \mathbf{g} \quad (11)$$

$$t_p = \frac{\rho_{s0}}{\beta_D} \quad (12)$$

$$\beta_D = \frac{18\rho_{f0}\nu_{f0}}{d^2(1 - \phi)^q} \quad (13)$$

where t_p is the particle response time suggested by Drew [46], β_D is calculated by Stokes' law for a sphere of diameter d setting in a fluid of kinematic viscosity ν_{f0} , and q is a correction factor from Stokes' Law [47]. According to Hsu et al. [45], the value of q is chosen as 3.0. Based on the work of Acrivos et al. [48], we assume that the particle flux due to the gravity is given by,

$$\mathbf{N}_g = \frac{2}{9}\phi f(\phi) \frac{a^2(\rho_{s0} - \rho_{f0})}{\mu_{f0}} \mathbf{g} \quad (14)$$

$$f(\phi) = \frac{(1 - \phi)\mu_{f0}}{\mu(\phi, \dot{\gamma})} \quad (15)$$

Note that the above equations have been used in various problems, such as the falling flow of a thin film [49]. It is worth mentioning that Abedi et al. [50] assumed that the gravity flux can be given by,

$$N_g = \frac{\phi(1 - \phi_m\phi)}{\phi_m\Gamma\mu(\phi, \dot{\gamma})} \quad (16)$$

$$\Gamma = \frac{9\mu_{f0}U}{2g(\rho_{s0} - \rho_{f0})H^2} = \frac{9}{2} \frac{a}{H} Sh \quad (17)$$

where ϕ_m is the value of the maximum packing of the solid particles and Sh is the Shields number, which is the ratio of the fluid force on the particle to the weight of the particle. Abedi et al. [50] suggested a value of 1.134 for the Shields number. In our work, we choose the equations proposed by Acrivos et al. [48], (equations (14) and (15)). For a more detailed

discussion of our modelling approach, we refer the readers to Wu, et. al (2018) [37]. In the next section, we consider the two geometries and flow conditions that we study in this paper.

4. Geometry and kinematics of the flow

In this paper, we consider two benchmark problems: (1) the flow in sudden expansion channels, see Figure 2 (a); (2) the flow through an idealized curved coronary artery [27,51], Figure 2 (b). The first geometry is common for many blood-wetted medical devices. Near the sudden expansion channel, flow separation usually occurs. This is believed to be the cause of platelets enrichment or thrombosis [36]. The second geometry is a simplified or an idealization representation of a human coronary artery. The later, especially when considering its multi-phase features, may provide useful information for revealing the mechanism of cardiovascular diseases, such as atherogenesis [27].

The vectorial (expanded) forms of the governing equations for the conservation of linear momentum are:

$$\begin{aligned} & \rho \left[\frac{\partial \mathbf{v}}{\partial t} + (\text{grad } \mathbf{v}) \mathbf{v} \right] \\ &= - \text{grad } p + \text{div} \left(\left(\mu_{\infty}(\phi) + (\mu_0(\phi) - \mu_{\infty}(\phi)) \frac{1 + \ln(1 + k(2\text{tr} \mathbf{D}^2)^{1/2})}{1 + k(2\text{tr} \mathbf{D}^2)^{1/2}} \right) \mathbf{D} \right) \\ &+ \rho \mathbf{b} \end{aligned} \quad (18)$$

while the RBCs concentration equation reads:

$$\begin{aligned} & \frac{\partial \phi}{\partial t} + \mathbf{v} \text{grad} \phi \\ &= \text{div} \left(a^2 \phi K_c \nabla(\dot{\gamma} \phi) + a^2 \phi^2 \dot{\gamma} K_{\mu} \nabla(\ln \mu(\phi, \dot{\gamma})) - \frac{2}{9} \phi \frac{(1 - \phi)}{\mu(\phi, \dot{\gamma})} a^2 (\rho_{s0} - \rho_{f0}) \mathbf{g} \right) \end{aligned} \quad (19)$$

We define the Reynolds number as:

$$Re = \frac{\rho_r v_r H_r}{\mu_r} \quad (20)$$

where ρ_r , v_r , H_r and μ_r are the density, velocity, length and viscosity in reference, respectively. Numerically we use the finite volume method to solve the above equations; a CFD solver is developed using the solvers and the libraries of OpenFOAM®, a C++ toolbox for the development of customized numerical solvers, and the pre-/post-processing operations for the solution of the governing equations [52]. The PIMPLE algorithm is used for imposing the incompressibility condition. The details of how the governing equations are discretized in OpenFOAM, the PIMPLE algorithm, the numerical schemes, etc., are given in [2,52–55]. The boundary conditions are provided in Table 1, for more detail see [53]. For alternative numerical schemes in solving fluid-particle systems, see Gorb et al., (2014) [56],

Koeune and Ponthot (2010) [57]. For each geometry, the domain is discretized as hexahedral meshes using ICEM [58]. In each case, mesh-dependence studies are performed.

5. Results and Discussion

5.1. Flow in sudden expansion channels

In this section, the first problem is based on the classic experiments of Karino and Goldsmith (1977) [59] with water ($\mu = 1\text{cP}$) and 1% hardened RBCs through a tubular sudden expansion channel. The diameters of the sudden expansion pipe are $77.5\mu\text{m}$ and $252\mu\text{m}$ (the expansion ratio is 3.25), and the lengths of the pipe before and after the expansion are 1mm and 5mm respectively. Two flow rates are simulated, corresponding to the inlet velocities of $v_i = 0.0757\text{ m/s}$ ($Re = \rho v_i D_1 / \mu_\infty = 10.7$) and $v_i = 0.233\text{ m/s}$ ($Re = 33.1$). According to Karino and Goldsmith (1977) [59], the sudden expansion pipe is vertically positioned on a mechanically movable platform [59], therefore, we can consider the gravity to be $\mathbf{g} = (9.8, 0, 0)\text{m/s}^2$, see Figure 2 (a) for the definition of the coordinate system. All the numerical results below are simulated sufficiently long times to ensure that the flow reaches a steady-state or semi steady-state condition. Figure 3 (b) shows a comparison of experimental and the numerical results for the velocity profiles along the A-B line (see the definition of A-B line see Figure 3 (a)). We observe that the numerical simulations accurately predict the velocity distribution measured by the experiments. As Figure 3 (a) indicates, for both cases, after the sudden expansion, flow separation occurs immediately, and blood begins to circulate in this region. As the Reynolds number increases, the circulation region becomes larger. Blood cells and platelets entering this region may be trapped by the vortices and stay there for a long time; this increases the possibility of deposition. Figure 3 (c) shows the velocity profiles along the radial direction at different dimensionless axial (X) positions. After the sudden expansion, we can see that the flow separation (negative velocity) occurs; and as X increases, the velocity gradually develops to be parabolic. At the axial location $X=15$, the flow is almost fully developed.

Figure 4 shows the effect of inlet velocities (Reynolds number) on the velocity field (streamlines) and the RBCs concentration distribution, when the hematocrit is 20%. When the hematocrit (concentration) is 1%, the size of the flow circulation zone is smaller. As the hematocrit increases, the overall blood viscosity increases, and therefore the Reynolds number decreases for the same flow rate. From Figure 4, we can also observe that in the circulation region, there is a RBC depletion region. According to many experimental and computational studies [36,60–62], in such a RBCs depletion region, platelets tend to concentrate, and this can be the source for cascade thrombosis.

Here, we compare our simulations with the experiments of blood flow through a sudden expansion channel performed by Zhao et. al (2008) [63]. The hematocrit is 20%, the heights of the sudden expansion channel are $100\mu\text{m}$ and $200\mu\text{m}$ (the expansion ratio is 2), and the lengths of the pipe before and after the expansion are 1mm and 2mm, respectively. Two flow rates are simulated, corresponding to the inlet velocities of $v_i = 0.167\text{m/s}$ ($Re = 30.5$) and $v_i = 0.833\text{ m/s}$ ($Re = 152$). In Figure 5, we compare the RBCs concentration with the

experimental results. There is reasonable agreement between the two observations where the captured RBCs (in the depletion region) after sudden expansion are shown.

5.2. Flow in an ideal curved coronary artery

Next, we study flow in an ideal curved coronary artery, [see Figure 2 (b)], where gravity is $g = (0, -9.8, 0)\text{m/s}^2$. A pulsatile inlet velocity is applied for mimicking the flow condition in the right coronary artery [27,64], see Figure 6 (a); the corresponding mean velocity is $v_0 = 0.22\text{ m/s}$ and the mean Reynolds number is $Re = \rho v_0 D / \mu_\infty = 10.7$. Flow in an ideal curved coronary artery is a classical problem [27], which can be used to study the newly proposed particle flux model.

Figure 6 (b) shows the streamlines at the fourth systolic phase (2.34s) and diastolic phase (2.94s), when the value of the velocity reaches the peak and the trough, respectively. We can see that the streamlines are a bit distorted for the systolic case (the peak velocity), [see the red dash circles in Figure 6 (b)].

Figure 6 (c) indicates that in both systolic and diastolic phases, the position of the maximum velocity is closer to the outer walls of the vessel. (See Figure 2 (b) for the definition of the inner and the outer curvature of the vessel.) The 2-D slice fields are the cross sections at the position indicated by S-S (see Figure 6 (b)), and all the velocity and concentration profiles are plotted along the M-N line (see Figure 6 (c)). At the systolic phase, the velocity profile deviates from the parabolic case.

Figure 6 (d) indicates that under the effect of gravity, the RBCs move towards and concentrate near the inner curved part of the vessel. RBCs concentration at the diastolic phase (the trough velocity) is lower than the systolic phase (peak velocity); that is, for high flow rates, more RBCs are convected (washed away) by the flow. From the RBCs concentration curves in Figure 6 (d), it can be observed that the concentration gradients are the strongest near the walls of the vessel, and the variations are negligible in the main flow.

Figure 7 shows the profiles of the velocity, shear rate, volume fraction of the RBCs, and the blood viscosity at different axial positions, at the time $t=2.34\text{s}$. The axial positions, a-e, are indicated in Figure 2 (b). For velocity fields, near the inlet (position a) the field is uniform in the main flow region; before entering the curved portion of the pipe (position b) the velocity is fully developed; in the middle of and before leaving the curved vessel (positions c and d) the high velocity region has shifted towards the outer curvature; near the outlet (position e) the velocity field begins to take the parabolic shape. As far as the shear rate is concerned, before entering the curved vessel, the field is symmetric along the angular direction (similar to the flow in a straight pipe); in the curved section, the shear rate is non-uniform with its magnitude being much higher near the outer walls. For the RBCs concentration, due to the effect of gravity, after entering the curved section of the pipe the RBCs concentrate near the inner surface; downstream the accumulation of the RBCs is reduced. The behavior of the viscosity distribution is basically opposite to the shear rate; indeed, it can be seen that at positions c, d and e, viscosity is higher in the regions where the RBCs accumulate.

Figure 8 shows the velocity, shear rate, volume fraction of the RBCs, and viscosity fields at different times. The 2-D fields are the cross sections at position c. For the velocity, the variation as a function of the pulsatile (inlet) flow rate is clear, and it seems that the deviation of the higher velocity region near the outer curvature is stronger at point B (where the velocity is at its peak). Overall, the shear rate keeps the same pattern: higher rates are present near the outer surface than near the inner surface. For the concentration of the RBCs, it is interesting to note that the high concentration region near the inner surface experiences increasing and decreasing values as time (the inlet velocity) changes. Due to the synergistic effect of the shear rate and the RBCs concentration, except in the main flow region, the viscosity is significantly higher near the inner surface. Figure 9 shows the shear rate, viscosity, and wall shear stress variations as a function of time at positions M (the outer surface) and N (the inner surface). See Figure 6 (c) for the details of points, M and N. We can see that for most part, the shear rate and the shear stress at the inner surface are much lower than at the outer surface, while the viscosity is always higher at the inner surface; furthermore, due to the accumulation effect of the RBCs, the viscosity near the inner surface changes more significantly during the pulsation period, which leads to a larger relative variation of the shear stress in this region. According to clinical studies, despite the influence of many important clinical or biological factors, the plaques only develop in arteries, especially where there are branches, curvatures and bifurcations; furthermore, the portion of the artery exposed to high shear stress usually remains plaque-free [65]. The patterns of the shear rate, viscosity and wall shear stress variation during the pulsatile period may be related to the development of the atherosclerotic plaque formation, which usually occurs on the inside surface of the arteries [27]. Furthermore, it will be interesting to study the effect of RBCs accumulation on the plaque formation near the inner surface.

6. Conclusions

In this paper, we have used a recently proposed non-linear rheological model of blood [Wu et. al (2018) [37]] to study two problems. The (whole) blood is modeled as a complex fluid, and the motion of the RBCs is modeled by a concentration flux equation. A correlation for the shear-thinning behavior of blood is proposed and fitted with the available experiments [11]. The hematocrit range of the experimental data is 8.6%–70.2%. In the first problem, the flow in a sudden expansion channel, the model accurately predicts the velocity profiles in the circulation regions after the sudden expansion, for two different Reynolds numbers (inlet). The numerical results also show that after the sudden expansion there exists a RBCs depletion region, which may favor platelets accumulation. In the second problem, the flow in an ideal curved coronary artery with a pulsatile inlet velocity is studied, and the results show that the RBCs move towards and concentrate near the inner surface, which is consistent with the results predicted by the two-fluid approach. The high viscosity, low shear stress and large variation of the shear stress near the inner surface of the arteries may be related to the atherosclerotic plaque formation observed clinically in those regions. It may be worthwhile to study the mechanical and chemical effects due to the high RBCs concentration, and their relationship with plaque formation. Based on these two studies, we believe that the non-linear fluid model with the RBC flux equation can capture many of the multi-phase

features of (whole) blood. It is hoped that this model can be a useful tool for studying more complex blood flow problems *in vivo* and *in vitro* in the future.

Acknowledgment

This work was jointly supported by Natural Science Foundation of China (11802135) and NIH grant 1 R01 HL089456.

References

- [1]. Robertson AM, Sequeira A, V Kameneva M, Hemorheology, in: Hemodynamical Flows, Springer, 2008: pp. 63–120.
- [2]. Wu W-T, Yang F, Antaki JF, Aubry N, Massoudi M, Study of blood flow in several benchmark micro-channels using a two-fluid approach., *Int. J. Eng. Sci* 95 (2015) 49–59. [PubMed: 26240438]
- [3]. Wu W-T, Jamiolkowski MA, Wagner WR, Aubry N, Massoudi M, Antaki JF, Multi-Constituent Simulation of Thrombus Deposition, *Sci. Rep* 7 (2017) 42720. doi:10.1038/srep42720. [PubMed: 28218279]
- [4]. Fung YC, Biomechanics: Mechanical Properties of Living Tissues, 2nd ed., Springer, New York, 1993.
- [5]. Bagchi P, Mesoscale simulation of blood flow in small vessels, *Biophys. J* 92 (2007) 1858–1877. [PubMed: 17208982]
- [6]. Popel AS, Johnson PC, Microcirculation and hemorheology, *Annu. Rev. Fluid Mech* 37 (2005) 43. [PubMed: 21151769]
- [7]. Bäuml H, Neu B, Donath E, Kieseewetter H, Basic phenomena of red blood cell rouleaux formation, *Biorheology*. 36 (1999) 439–442. [PubMed: 10818642]
- [8]. Chien S, Shear dependence of effective cell volume as a determinant of blood viscosity, *Science* (80-.). 168 (1970) 977–979.
- [9]. Chien S, Usami S, Dellenback RJ, Bryant CA, Comparative hemorheology--hematological implications of species differences in blood viscosity., *Biorheology*. 8 (1971) 35–57. [PubMed: 4103884]
- [10]. Chien S, Usami S, Taylor HM, Lundberg JL, Gregersen MI, Effects of hematocrit and plasma proteins on human blood rheology at low shear rates., *J. Appl. Physiol* 21 (1966) 81–87. [PubMed: 5903948]
- [11]. Brooks DE, Goodwin JW, V Seaman G, Interactions among erythrocytes under shear., *J. Appl. Physiol* 28 (1970) 172–7. [PubMed: 5413303]
- [12]. Fenech M, Garcia D, Meiselman HJ, Cloutier G, A particle dynamic model of red blood cell aggregation kinetics, *Ann. Biomed. Eng* 37 (2009) 2299–2309. doi:10.1007/s10439-009-9775-1. [PubMed: 19669883]
- [13]. Wu W-T, Aubry N, Massoudi M, Kim J, Antaki JF, A numerical study of blood flow using mixture theory, *Int. J. Eng. Sci* 76 (2014) 56–72. [PubMed: 24791016]
- [14]. Yin X, Thomas T, Zhang J, Multiple red blood cell flows through microvascular bifurcations: cell free layer, cell trajectory, and hematocrit separation, *Microvasc. Res* 89 (2013) 47–56. [PubMed: 23727384]
- [15]. Zhang J, Johnson PC, Popel AS, Red blood cell aggregation and dissociation in shear flows simulated by lattice Boltzmann method, *J. Biomech* 41 (2008) 47–55. [PubMed: 17888442]
- [16]. Wu W-T, Martin AB, Gandini A, Aubry N, Massoudi M, Antaki JF, Design of microfluidic channels for magnetic separation of malaria-infected red blood cells, *Microfluid. Nanofluidics* 20 (2016) 41. doi:10.1007/s10404-016-1707-4. [PubMed: 27761107]
- [17]. Dupin MM, Halliday I, Care CM, Alboul L, Munn LL, Modeling the flow of dense suspensions of deformable particles in three dimensions, *Phys. Rev. E* 75 (2007) 66707.

- [18]. Tsubota K, Wada S, Yamaguchi T, Particle method for computer simulation of red blood cell motion in blood flow, *Comput. Methods Programs Biomed* 83 (2006) 139–146. [PubMed: 16879895]
- [19]. Li X, Popel AS, Karniadakis GE, Blood–plasma separation in Y-shaped bifurcating microfluidic channels: a dissipative particle dynamics simulation study, *Phys. Biol* 9 (2012) 26010.
- [20]. Fedosov DA, Caswell B, Karniadakis GE, A multiscale red blood cell model with accurate mechanics, rheology, and dynamics, *Biophys. J* 98 (2010) 2215–2225. [PubMed: 20483330]
- [21]. van der Hoef MA, Ye M, van Sint Annaland M, Andrews AT, Sundaresan S, Kuipers JAM, *Computational Fluid Dynamics*, Elsevier, 2006. doi:10.1016/S0065-2377(06)31002-2.
- [22]. Oshima M, Torii R, Kobayashi T, Taniguchi N, Takagi K, Finite element simulation of blood flow in the cerebral artery, *Comput. Methods Appl. Mech. Eng* 191 (2001) 661–671.
- [23]. Byun HS, Rhee K, CFD modeling of blood flow following coil embolization of aneurysms, *Med. Eng. Phys* 26 (2004) 755–761. [PubMed: 15564112]
- [24]. Wu W-T, Yang F, Wu J, Aubry N, Massoudi M, Antaki JF, High fidelity computational simulation of thrombus formation in Thoratec HeartMate II continuous flow ventricular assist device, *Sci. Rep* 6, 38025 (2016). [PubMed: 27905492]
- [25]. Chabannes V, Pena G, Prud'Homme C, High-order fluid–structure interaction in 2D and 3D application to blood flow in arteries, *J. Comput. Appl. Math* 246 (2013) 1–9.
- [26]. Janela J, Moura A, Sequeira A, A 3D non-Newtonian fluid–structure interaction model for blood flow in arteries, *J. Comput. Appl. Math* 234 (2010) 2783–2791.
- [27]. Jung J, Lyczkowski RW, Panchal CB, Hassanein A, Multiphase hemodynamic simulation of pulsatile flow in a coronary artery., *J. Biomech* 39 (2006) 2064–73. [PubMed: 16111686]
- [28]. Kim J, Antaki JF, Massoudi M, Computational study of blood flow in microchannels, *J. Comput. Appl. Math* 292 (2016) 174–187.
- [29]. Phillips RJ, Armstrong RC, Brown RA, Graham AL, Abbott JR, A constitutive equation for concentrated suspensions that accounts for shear- induced particle migration, *Phys. Fluids A Fluid Dyn* 4 (1992) 30–40.
- [30]. Wu W-T, Zhou Z-F, Aubry N, Antaki JF, Massoudi M, Heat transfer and flow of a dense suspension between two cylinders, *Int. J. Heat Mass Transf* 112 (2017) 597–606. doi:10.1016/j.ijheatmasstransfer.2017.05.017.
- [31]. Rajagopal KR, Tao L, *Mechanics of mixtures*, Series on Advances in Mathematics for Applied Sciences, vol. 35, World Scientific, Singapore, 1995.
- [32]. Massoudi M, Antaki JF, An Anisotropic Constitutive Equation for the Stress Tensor of Blood Based on Mixture Theory, *Math. Probl. Eng* 2008 (2008) 1–30.
- [33]. V Papalexandris M, A two-phase model for compressible granular flows based on the theory of irreversible processes, *J. Fluid Mech* 517 (2004) 103–112.
- [34]. Zhao R, Marhefka JN, Shu F, Hund SJ, Kameneva MV, Antaki JF, Micro-flow visualization of red blood cell-enhanced platelet concentration at sudden expansion, *Ann. Biomed. Eng* 36 (2008) 1130–1141. [PubMed: 18418710]
- [35]. Karino T, Goldsmith HL, Adhesion of human platelets to collagen on the walls distal to a tubular expansion, *Microvasc. Res* 17 (1979) 238–262. [PubMed: 459938]
- [36]. Wu W-T, Aubry N, Massoudi M, Antaki JF, Transport of platelets induced by red blood cells based on mixture theory, *Int. J. Eng. Sci* 118 (2017) 16–27. doi:10.1016/j.ijengsci.2017.05.002.
- [37]. Wu WT, Aubry N, Antaki JF, Massoudi M, A non-linear fluid suspension model for blood flow, *Int. J. Non. Linear. Mech* 109 (2019) 32–39. doi:10.1016/j.ijnonlinmec.2018.11.002. [PubMed: 31447489]
- [38]. Slatery JC, *Advanced transport phenomena*, Cambridge University Press: Cambridge, UK, 1999.
- [39]. Liu I-S, *Continuum mechanics*, Springer Science & Business Media, Berlin, Germany, 2002.
- [40]. Wu W-T, Massoudi M, Heat Transfer and Dissipation Effects in the Flow of a Drilling Fluid, *Fluids*. 1 (2016) 4. <http://www.mdpi.com/2311-5521/1/1/4/html> (accessed April 4, 2016).
- [41]. Thurston GB, Viscoelasticity of human blood., *Biophys. J* 12 (1972) 1205–17. doi:10.1016/S0006-3495(72)86156-3. [PubMed: 5056964]

- [42]. Thurston GB, Frequency and shear rate dependence of viscoelasticity of human blood., *Biorheology*. 10 (1973) 375–381. [PubMed: 4772010]
- [43]. Yeleswarapu KK, Antaki JF, V Kameneva M, Rajagopal KR, A generalized Oldroyd-B model as constitutive equation for blood, *Ann. Biomed. Eng* 22 (1994) 16.
- [44]. Subia SR, Ingber MS, Mondy LA, Altobelli SA, Graham AL, Modelling of concentrated suspensions using a continuum constitutive equation, *J. Fluid Mech* 373 (1998) 193–219.
- [45]. Hsu T, Traykovski PA, Kineke GC, On modeling boundary layer and gravity-driven fluid mud transport, *J. Geophys. Res. Ocean* 112 (2007).
- [46]. Drew DA, Production and dissipation of energy in the turbulent flow of a particle-fluid mixture, with some results on drag reduction, *J. Appl. Mech* 43 (1976) 543–547.
- [47]. Richardson JF, Zaki WN, The sedimentation of a suspension of uniform spheres under conditions of viscous flow, *Chem. Eng. Sci* 3 (1954) 65–73.
- [48]. Acrivos A, Mauri R, Fan X, Shear-induced resuspension in a Couette device, *Int. J. Multiph. Flow* 19 (1993) 797–802.
- [49]. Mavromoustaki A, Bertozzi AL, Hyperbolic systems of conservation laws in gravity-driven, particle-laden thin-film flows, *J. Eng. Math* 88 (2014) 29–48.
- [50]. Abedi M, Jalali MA, Maleki M, Interfacial instabilities in sediment suspension flows, *J. Fluid Mech* 758 (2014) 312–326.
- [51]. Berthier B, Bouzerar R, Legallais C, Blood flow patterns in an anatomically realistic coronary vessel: influence of three different reconstruction methods, *J. Biomech* 35 (2002) 1347–1356. [PubMed: 12231280]
- [52]. OpenCFD, OpenFOAM Programmer's Guide Version 2.1.0, Free Software Foundation, Inc.: Boston, MA, USA, 2011.
- [53]. Rusche H, Computational Fluid Dynamics of Dispersed Two-Phase Flows at High Phase Fractions, Imperial College London (University of London): London, UK, 2002. doi:10.1145/1806799.1806850.
- [54]. Ubbink O, Numerical prediction of two fluid systems with sharp interfaces, University of London PhD Thesis, 1997.
- [55]. Kim J, Multiphase CFD Analysis and Shape-Optimization of Blood-Contacting Medical Devices, Carnegie Mellon University, 2012.
- [56]. Gorb Y, Mierka O, Rivkind L, Kuzmin D, Finite element simulation of three-dimensional particulate flows using mixture models, *J. Comput. Appl. Math* 270 (2014) 443–450.
- [57]. Koeune R, Ponthot J-P, An improved constitutive model for the numerical simulation of semi-solid thixotforming, *J. Comput. Appl. Math* 234 (2010) 2287–2296.
- [58]. C.F.D. ICEM, ver. 14.0, ANSYS Inc., Southpointe. 275 (2012).
- [59]. Karino T, Goldsmith HL, Flow Behaviour of Blood Cells and Rigid Spheres in an Annular Vortex, *Philos. Trans. R. Soc. B Biol. Sci* 279 (1977) 413–445. doi:10.1098/rstb.1977.0095.
- [60]. Wu W-T, Li Y, Aubry N, Massoudi M, Antaki JF, Numerical Simulation of Red Blood Cell-Induced Platelet Transport in Saccular Aneurysms, *Appl. Sci* 7 (2017) 484.
- [61]. AlMomani T, Udaykumar HS, Marshall JS, Chandran KB, Micro-scale dynamic simulation of erythrocyte-platelet interaction in blood flow, *Ann. Biomed. Eng* 36 (2008) 905–920. [PubMed: 18330703]
- [62]. Skorczewski T, Erickson LC, Fogelson AL, Platelet motion near a vessel wall or thrombus surface in two-dimensional whole blood simulations, *Biophys J*. 104 (2013) 1764–1772. [PubMed: 23601323]
- [63]. Zhao R, Experimental and theoretical investigation of blood flow dynamics associated with blood contacting devices, ProQuest, 2008.
- [64]. Nichols W, O'Rourke M, Vlachopoulos C, McDonald's blood flow in arteries: theoretical, experimental and clinical principles, CRC press, 2011.
- [65]. Lehoux S, Jones EA, Shear stress, arterial identity and atherosclerosis, *Thromb. Haemost* 115 (2016) 467–473. [PubMed: 26676959]

Figure 1.
RBCs viscosity as a function of shear rate. Experimental data are taken from Brooks et al. (1970) [11].

Figure 2.

Schematic of the problems. (a) Sudden expansion channel. (b) Idealized curved coronary artery [27,51]. Along the y-direction, positions a and e are located at a distance of 1mm from the inlet and the outlet, and positions b and d are located at a distance of 20 mm from the inlet and the outlet for 20mm.

Figure 3.

(a) Velocity distribution and streamlines near the sudden expansion, when the Reynolds number is $Re=12.2$ (left) and $Re=37.8$ (right). The reattachment points measured by experiments are $230\mu m$ and $715\mu m$, respectively. (b) Velocity profiles along the line (A-B) crossing the circulation center, when $Re=12.2$ (left) and $Re=37.8$ (right). (c) Velocity profiles along radial direction at different dimensionless axial (X) positions, when $Re=37.8$. $X = x/r_1$, where r_1 is the radius of the pipe before expansion.

Figure 4. Velocity, streamlines and RBC concentrations, for inlet velocities of (a) 75.7 mm/s ($Re = \rho v_i D_1 / \mu_\infty = 4.48$), (b) 151 mm/s ($Re = 8.94$), and (c) 233 mm/s ($Re = 13.79$). The inlet hematocrit is 20%.

Figure 5. RBC concentrations by experiments [34] and simulations for inlet velocities of (a) $v_i = 0.167$ m/s ($Re = 30.5$) and (b) $v_i = 0.833$ m/s ($Re = 152$). The inlet hematocrit is 20%. The experimental figures [34] are reused by permission.

Figure 6.

(a) The pulsatile inlet velocity for mimicking the flow condition in a right coronary artery [27,64]. (b) The streamlines at the fourth systolic phase (2.34s) and diastolic phase (2.94s). (c) The 2-D slice fields and profiles of the velocity at the fourth systolic and diastolic phases. (d) The 2-D slice fields and profiles of the RBCs concentration at the fourth systolic and diastolic phases. The 2-D slice fields are the cross section at the position indicated by S-S (see Figure (b)), and all velocity and concentration profiles are plotted along line M-N (see Figure (c)).

Figure 7.
The velocity, shear rate, volume fraction of the RBCs, and the viscosity distributions at different axial positions, at time $t=2.34s$. The axial positions, a-e, are indicated in Figure 2 (b).

Figure 8.

The velocity, shear rate, volume fraction of the RBCs, and the blood viscosity at the axial position c at different times. The points, A-F, are shown in Figure 6 (a). B is where the peak velocity occurs, E is the location of the second peak velocity, D and F correspond to the trough velocity, A is the accelerating phase and C is the decelerating phase of the pulsatile period.

Figure 9.

(a) Shear rate, (b) viscosity, (c) and wall shear stress variations as a function of time at positions M (outer surface) and N (inner surface). See Figure 6 (c) for details.

Table 1

Boundary conditions. For more discussion on the boundary condition, see [53].

Boundary type	Pressure (p)	Velocity (v)	Volume Fraction (ϕ)
Wall	Fixed flux(0)	Fixed value	Fixed flux(0)
Inlet	Fixed value (0)	Fixed value	Fixed value (0)
Outlet	Fixed value (0)	Fixed flux(0)	Fixed flux(0)