An investigation on the rheodynamics of human red blood cells using high performance computations

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Keywords: red blood cells, aggregation, immersed boundary method, numerical simulation

Abstract Studies on the haemodynamics of human circulation are clinically and scientifically important. The flow of human blood is extremely complex due to the existence of the highly deformable red blood cells (RBCs), which are able to pass through capillaries smaller than their size. To investigate the effect of deformation and aggregation in blood flow, a computational technique has been developed by coupling the interaction between the fluid and the deformable solids. The flow of 49,512 RBCs at 45% concentration and under the influence of aggregating forces was examined to improve the existing knowledge on how to simulate and study the blood flow and its structural characteristics of blood at a large scale. The simulation was carried out with full parallelization of the coupled fluid-solid code using spatial decomposition and high performance supercomputers. The large scale feature of the simulation has enabled a macroscale verification and investigation of the overall characteristics of RBC aggregations to be carried out. The results are in excellent agreement with experimental studies and, more specifically, both the experimental and the simulation results show uniform RBC distributions under high shear rates (60-100/s) whereas large aggregations were observed under a lower shear rate of 10/s. The statistical analysis of the simulation data also shows that the shear rate has significant influence on both the flow velocity profiles and the frequency distribution of the RBC orientation angles. The flow under the low shear rate also tended to have bi-phasic velocity profile which is mainly due to the formation of large scale aggregation clusters.

Keywords: Red blood cells, Aggregation, Immersed boundary method, Numerical simulation

1. Introduction

The red blood cell (RBC, also referred to as erythrocyte) is the most common type of cell occurring in human blood and occupies approximately 45% of the total blood volume for man and 40% for women. RBCs in a healthy state have a biconcave shape with a diameter of 6-8 μm, a thickness of about 2 μm at the edges and about 1 μm at the centre (Baskurt, 2007). The RBC aggregation, which is the mechanism that greatly influences the non-Newtonian properties of blood (Baskurt *et al*., 2011), occurs when the shear forces are low and cells attract each other to form rouleaux (structures resembling coin piles), larger aggregates and networks of aggregates. RBC aggregation can cause complications in health related issues, therefore, the investigation of deformability and aggregation of RBCs in blood flow can be promising for the better understanding and diagnosis of many diseases in clinical medicine.

Due to the complex mechanism of fluid–structure interaction, the theoretical analysis of RBCs or capsules are difficult and is usually limited to simple geometries and small deformations (Barthes-Biesel, 1980) and an alternative approach - numerical simulation - has attracted much attention. To-date, most simulations have tended to target a relatively small number of cells (Kitano, 2002), due to their complex nature. The intrinsic complexity of biological systems requires a closer

combination between experimental and computational approaches (Doyle, 2001; Kitano, 2002). This requires large scale simulations because experiments usually measure the macroscale effects with large quantities of cells (Doyle, 2001; Dusting et al., 2009; Endy and Brent, 2001; Kaliviotis and Yianneskis, 2008). In this paper, computational research on RBC aggregations is presented in which the large scale nature of the computations have enabled direct comparisons of macro-scale aggregation features with experimental observations.

2. Methodology

To simulate incompressible viscous flow, an in-house Computational Fluid Dynamics (CFD) code, called CgLes (Thomas and Williams, 1997) has been used. CgLes is a three-dimensional fluid solver with second order accuracy in both time and space and is based on a finite volume formulation. The capability of CgLes to simulate both laminar and turbulent flows has been extensively verified (Ji et al., 2012; Xu et al., 2012). The combined finite-discrete element method (FEM-DEM) was used to simulate the movement and deformation of the RBCs under the various forces developed in the fluid (Munjiza and Wiley, 2004; Munjiza et al., 2011). In the present study, the RBC membrane was treated as a thin solid shell with a natural bending stiffness of E_B=1.82 $\times 10^{-11}$ dyn·cm. To couple the fluid motion and solid deformation, an immersed boundary (IB) method (Peskin and Mcqueen, 1980) was used to link the interface between the fluid and the solid, both of which have independent meshes. The adhesive force causing aggregation is short-ranged and originates from molecular forces, such as van der Waals attractions (Kendall and Stainton, 2001). The strength of the adhesion between two cells can usually be described by the adhesion work, σ, which is the work required to separate two adhered cells. The JKR model (Johnson, Kendall & Roberts – 1964-1971, (Johnson et al., 1971) was used in the present study to compute the adhesion forces as this has proved to be applicable to the adhesion of living cells (Chu et al., 2005).

3. Results and discussions

3.1 Simulation of RBC motion in Poiseuille flows

RBCs usually have complex pattern of motions in blood vessels due to the shearing of the background fluid. Widely known motions include tank-trending, tumbling and rotation. To verify the capability of our computational model in reproducing the correct RBC behaviour, simulation was carried for a Poiseuille flow with haematocrit of 20%. Typical computational results are shown in Figure 1. The tube diameter is 22.5 μm and the mean flow velocity is 187.5 μm/s.To make the motion more easily identifiable, two individual RBCs were rendered in different colors.

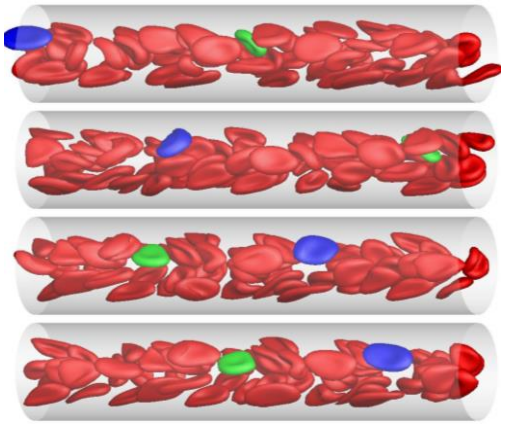

Figure 1 Snapshot of RBC motion (the haematocrit is 20%; Blue – RBC near tube wall; Green- RBC near tube center)

It can be seen that the RBC near the tube wall tends to have a larger stretching ratio and a lower velocity as well. The features of the RBC motions can also be identified by plotting the time history of orientation angle referring to tube axes, see Figure 2. It can be seen that RBC near the tube wall have more regular periodical motion patterns, which is a combination of tank-trending, tumbling and rotation. This kind of motion is also widely reported by other researchers(Liu et al., 2006; Shi et al., 2012; Sui et al., 2008).

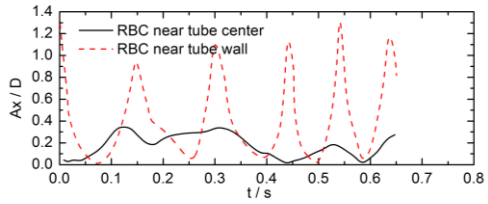

Figure 2 Time history of RBC orientation angle referring to the streamwise direction –Ax (D is the RBC diameter)

3.2 Large scale simulation of RBC aggregation in a shear flow

To investigate the large scale structural characteristics of blood, caused by the formation and development of RBC aggregations, simulations have been carried out with the same configuration as in the experiments performed by Kaliviotis and co-workers (Dusting et al., 2009; Kaliviotis and Yianneskis, 2008). Periodic boundaries were adopted in both streamwise and spanwise directions. As the computational domain is very small compared to the experimental domain and that the viewing window is far from the centre of the rotation, the flow in the computational domain was simplified into a simple shear flow. Such treatment has little influence on the simulation results considering that the domain is large enough to let the largest aggregation structures develop. The fluid was considered to be blood plasma with physical properties set at normal values, see Table 1.

Table 1 Physical properties of the fluid (plasma)

Property	Symbol	Value
Density	ρ_f	1025 kg/m^3
Kinematic viscosity	ν	1.46×106 m^2/s
Shear rate	γ	10 s^{-1}, 60 s^{-1}, 100 s^{-1}
Reynolds number	Re	6.16×10^{-4}-6.16×10^{-2}

During the initialization of the simulation, the 512 RBCs were installed in each block at randomly allocated positions and with random initial velocities. The simulation was then run on 96 cores of a Cray XE6 system.

The numerical simulation provided full information of the position, movement, deformation and aggregation of the RBCs in the shear flow. The shear rate of 100/s showed no major aggregation and the cells tended to move independently under entrainment by the flow and were uniformly distributed in space. However, when the shear rate decreased from 100/s to 10/s, significant aggregation was observed. The RBCs aggregated face-to-face to form coin-stack-like structures (rouleaux), the formation of which can be explained by their unique discoid shape as the flat surfaces provide large surface areas for contact and adhesion. Due to the fact that the haematocrit is quite high (45% in volume), the RBCs tended to form more three-dimensional aggregation structures than linear ones (rouleaux).

The large scale of the simulation has enabled a macroscale verification and investigation into the overall characteristics of RBC aggregations to be carried out, rather than just focusing on several individual cells. The comparisons show apparent similarities of blood micro-structure between the experiment and the simulation. Under the high shear rate (shear rate=100/s), both the experiment and the simulation show no aggregation of RBCs, although to a certain extent, the simulated distribution of gaps among RBCs looks different from the experimental case. This is partly caused by the method of capturing the images and by the optical properties of the RBCs. Furthermore, the similarity between the two is more obvious for the 10/s case when significant aggregation occurs. Qualitatively, both results show large aggregation structures of the RBCs and gaps of similar size. For human blood with a haematocrit of 45%, aggregation characteristics such those simulated in the present study have been widely reported in clinical experiments (Baskurt et al., 2011; Baskurt, 2007).

Spatial correlation curves were computed for the topview of the RBC image from both

experiment (Kaliviotis and Yianneskis, 2008; Dusting et al., 2009) and the present numerical simulation. The simulation results agree well with the experiments under both the high shear rate and the low shear rate, see Figure3. In both the experiment and the simulation, the RBC distribution under the high shear rate shows a correlation coefficient descending much faster than that for the low shear rate case. A correlation coefficient that slowly descends indicates large RBC aggregation blocks.

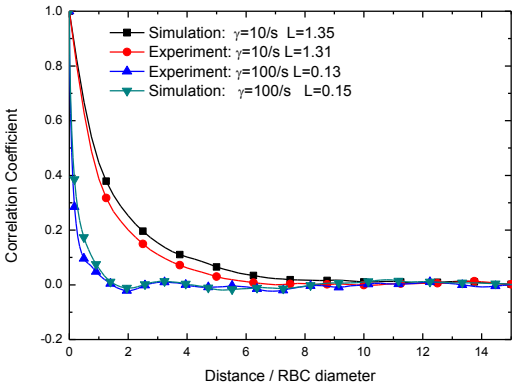

Figure 3 Spatial correlation of topview of the RBCs in shear flows

The results from the simulation show that the shear rates have significant influence on the velocity profiles of the flow (see Figure 4). Owing to the existence of RBCs, all the simulation results show velocity profiles deviating from the linear profile corresponding to a single phase Newtonian flow. This phenomenon has been widely reported for the RBC suspended Poiseuille flows (Fedosov et al., 2011a; Liu and Liu, 2006; Zhang et al., 2008). An interesting tendency here is that under low shear rate (γ=10/s), the middle part of the profile is nearly vertical, which highlights a nearly uniform flow. This phenomenon was also observed in the experimental study of (Kaliviotis et al., 2011). The appearance of large scale aggregation clusters contributed greatly to the bi-phasic velocity profile by forming a plug-flow like status. Although a direct comparison between the simulation and the experiment (Kaliviotis et al., 2011) show quite large deviations, mostly due to the differences in the blood samples used, the tendency of the profile variation against shear rate shown in Figure 3 is quite similar.

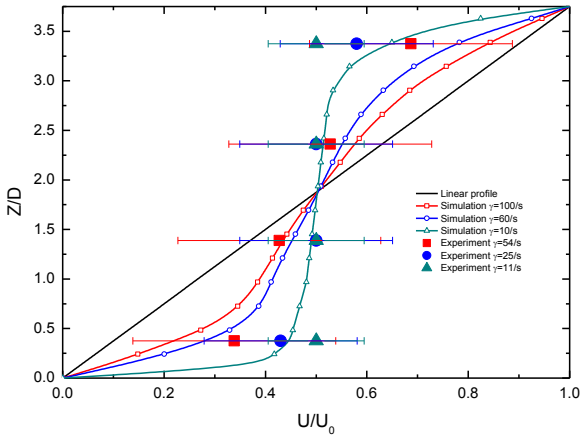

Figure 4 Velocity profiles of the flow between two shearing plates under different shear rates (from Xu et al, 2013, Z is the distance to the bottom, 'D' is the RBC diameter, which is 0.75 μm in the simulations. U is the flow velocity, U_0 is the velocity of the shearing lid)

A statistical analysis was also carried out on the orientation of the RBCs at both high and low shear rates after the simulations reached a statistically steady state. Figure 5 shows that at high shear rates (γ=100/s, γ=60/s), the angle distribution has an obvious peak at around 15-20 ºand the majority of the cells adopt an angle less than 30 ºs, indicating that most of the RBCs are moving with a more-or-less fixed angle to the top plate. Similar behaviour has been observed in studies investigating RBC flow in a tube (Goldsmith and Marlow, 1979) and in a shear flow (Fedosov *et al.*, 2011b). However, for the low shear rate case (γ=10/s), the inclination angles tend to have a more uniform distribution because of the appearance of rouleaux and aggregation network structures.

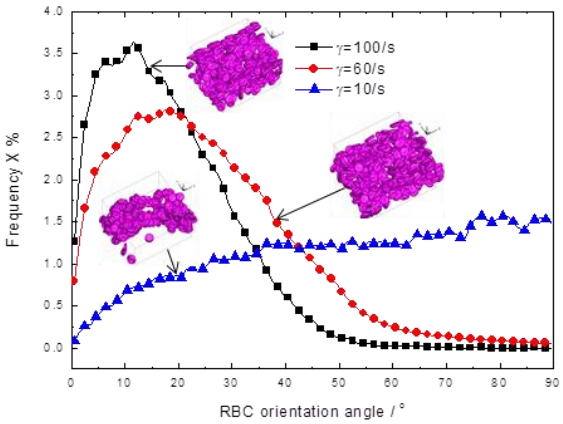

Figure 5 Frequency distribution of the orientation angle of the RBCs under the high and the low shear rates (from Xu et al, 2013)

4. Conclusions

A three-dimensional computational model has been developed to numerically simulate the deformation and aggregation of RBCs by coupling the interaction between the fluid and the deformable solid membrane of the RBC using continuum mechanics. The capability of the proposed model was verified against experimental data and the major contribution of the work reported in this paper is the establishment of a computational framework that can fully resolve the deformation and aggregation of individual RBCs up to a number of 49,152. This was achieved with full parallelization of the fluid-solid coupled solver using spatial decomposition and high performance computers. The large scale feature of the simulation has enabled a macroscale verification and investigation into the overall characteristics of RBC aggregations to be carried out. The results from the simulation have been compared with experimental data with very good agreement. Both the experiment and the simulation show a uniform distribution of RBCs under high shear rates (γ=100/s, γ=60/s) and large aggregation structures under a low shear rate (γ=10/s). Statistical analysis of the simulated results also show that under the high shear rate the inclination angle distribution has an obvious peak at around 15-20º, however, for the low shear rate case the orientation angles tended to have a more uniform distribution. The flow under the low shear rate also tended to have bi-phasic velocity profile which is mainly due to the formation of large scale aggregation clusters.

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