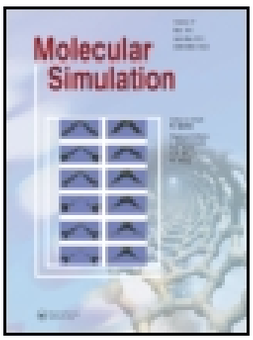

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Simulation of RBC dynamics using combined low dimension, immersed boundary and lattice Boltzmann methods

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ABSTRACT

A 3-D simulation of red blood cells (RBCs) described as deformable cells in plasma flow is an indispensable element of blood flow analysis in the human vessels. To numerically investigate RBC motion in shear and Poiseuille flow, a mesoscale low dimensional-RBC method based on dissipative particle dynamics method has been successfully combined with a hybrid lattice Boltzmann method-immersed boundary method. This new model decreases the computational cost compared to the low dimensional RBC method and models the deformation of red blood cell accurately. To evaluate and validate the present numerical method, the relationship between the RBC diameter and the force value derived by the low dimensional-RBC method is compared with numerical and experimental data. In addition, as a benchmark test, the deformation index as the function of the capillary number of RBC motion through a narrow cylindrical tube has been performed. The behaviour of RBC in a shear flow and Poiseuille flow has been investigated. The present results demonstrated that this model is applied to reduce the computational cost, while maintaining the model precision.

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KEYWORDS
Dissipative particle dynamics; lattice Boltzmann method; red blood cell; immersed boundary

1. Introduction

Erythrocytes, also known as red blood cells (RBCs), are the most numerous cell types in the body and they have a flexible plasma membrane to squeeze through microvessels. The shape of RBC is ideal for oxygen transport and squeeze through small opening in passage ways [1]. Over the past decades, the development of realistic and low computational cost models for the RBC shape and deformation in microvessels has attracted much research. There are various numerical simulations to understand the complex red blood cell dynamics in microvessels. Gross et al. [2] used the immersed boundary (IB) method, and a finite element model for the RBC deformation with the lattice Boltzmann method (LBM) for the hydrodynamics. They simulated suspension of RBCs in wall driven shear flow. So, they showed that cell elasticity and the distance to the jamming point are the most superior factors determining the rheology of RBCs behaviour. Pan et al. [3] developed a new low dimensional RBC (LD-RBC) a model based on the dissipative particle dynamics method (DPD) to simulate the RBC deformation in the microcirculation. They presented that the results are in good agreement with recent experiments. Boryczko et al. [4] used discrete- particle approach to model a 3-D system consisting of RBCs, plasma and capillary walls. Their modelling carried out with sufficient resolution by using 1–10 million particles. Fedosov et al. [5] modelled infected RBCs by malaria by using multiscale RBC model based on the DPD method. Their present results match those obtained by experiments. Chen and Boyle [6] investigated the spring- network mechanics in large deformation for 3-D RBC. They showed the effect of network parameters, i.e. network mesh, spring type and surface constraint.

All of the above methods obtained are very promising results, but still suffer from the high computational cost for 3-D RBC deformation in microvessels. For example, in biological flows for small arteries where explicit modelling of RBCs is often required, DPD and discrete-particle models employ hundreds to ten thousand particles to represent a single RBC [7]. Such multi-particle representations may render a simulation prohibitively expensive. For example, in an arteriole of 50 μm diameter (500 μm length) with 35% of volume occupied by RBCs, it would require millions to hundreds of millions of particles to represent the flow. Furthermore, for LBM, 3-D mesh of RBC should be constructed via harmonic forces with their nearest neighbours by finite element numerical technique. Implementing 3-D unstructured adaptive mesh for modelling red blood cell may be very limited due to the extremely high computational cost [8].

To decrease the number of particles and mesh used in simulating RBCs, LD-RBC model based on the DPD algorithm is employed to obtain the force acting on the discrete particles of the membrane in this paper. In LD-RBC model, a closed tortus-like ring of 10 DPD particles is used [3]. These particles are connected by worm-like chain springs combined with bending resistance. As mentioned recently, millions of particles are used to represent the flow in DPD. Although, an increase of the flow density will give better statistics, but is computationally more expensive. To solve this problem, the combination of the LBM to account for the plasma flow and LD-RBC model for

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the RBC motion is developed in this work. To show the interaction of moving and deformable RBCs with the incompressible plasma flow, IB method is combined with LBM and LD.

The proposed model focuses on the simulation of the 3-D RBC motion in a microvessel by hybrid IB-LB-LD-RBC method. To investigate the possibility for accuracy of hybrid IB-LB-LD, simulation of a single red blood cell deformation is demonstrated in shear and Poiseuille flows. The presented model is examined by comparing the results with the existing numerical and experimental results and very good agreement is obtained. It is shown that the proposed hybrid method (IB-LB-LD-RBC) produces a more accurate and low computational cost results compared to the DPD method mentioned for modelling the 3-D RBC motion.

2. Numerical method

2.1. Computational domain

Based on physiological values [1], laminar, Newtonian and incompressible plasma flow is considered in microvessels. For modelling of RBC deformation in Couette shear flows, the shear rate is defined as [9]:

$$\dot{\gamma} = V/H \tag{1}$$

where V is the velocity of the moving plate and H is the distance between two plates.

The blood flow is modelled as a suspension of a red blood cell in plasma. A ring of 10 colloidal particles connected by a wormlike chain (WLC) spring is considered to simulate RBC by LD-RBC and LBM is used for modelling plasma flow.

2.2. Low dimensional-DPD

Dissipative particle dynamics is a stochastic mesoscopic simulation approach [3], bridging the gap between atomistic and continuum fluid descriptions. Hoogerbrugge and Koelman [10] introduced this scheme for the first time and its basis in statistical mechanics becomes well known by Español, Warren [11] and Marsh [12]. DPD appears as a successful approach in the simulation of complex fluids, such as suspensions of polymers, DNA, colloids and cells in blood [7]. This method includes particles representing coarse-grained molecules which move together in the Lagrangian method.

It should be mentioned that the LD method is a generalised version of DPD based on this new formulation [7], it resolves the DPD deficiency. This approach can be used with confidence to study the properties of suspended particles in a fluid phase, including the transport of macromolecules, colloids, biomolecules such as DNA, and blood cells such as RBC.

To construct the cell in addition to DPD forces [7], the WLC spring and bending force should be defined. The WLC spring force interconnecting the colloidal particles in each cell is taken as [3]:

$$F^{U}_{WLC} = k_B T/\lambda_p \times \left[1/4(1-\frac{r_{ij}}{L_{\max}})^2 - 1/4 + r_{ij}/L_{\max}\right] \tag{2}$$

where λ_p is the persistence length which measures the chain's stiffness, r_{ij} is the distance between two neighbour particles, $L_{\max}$ is the maximum allowed length for each spring, $k_B$is the Boltzmann constant and T is the equilibrium temperature of the system for DPD. The bending resistance is modelled in the form of angle bending force dependent on the angle between two springs. This force is given by [3]:

$$\begin{aligned} F_b &= -\partial U_{ijk}/\partial r_j \\ U_{ijk} &= E_b \times [1 - \cos\theta_{ijk}] \end{aligned} \tag{3}$$

where θ_{ijk} is the angle between two springs.

For the RBC with an average radius of 9μm the adopted length scaling is shown in Table 1.

The mechanical properties of the RBC membrane are the important factors which have an effect on the cell motion. So, defining two dimensionless groups as follows is helpful [9]:

$$\begin{aligned} E_B &= E_b/E_s a^2 \\ G &= \mu U_m/E_s \end{aligned} \tag{4}$$

where a is the radius of RBC, U_m is the mean velocity of the flow, μ is the fluid viscosity, E_s is the elastic coefficient (it is equal to $k_B T/\lambda_P$) and E_b is the membrane bending resistance. E_B is the ratio of membrane stretching resistance to its bending resistance. The second dimensionless group is the ratio between viscose fluid forces and the membrane elasticity.

2.3. Lattice Boltzmann method

As mentioned previously, LBM is suitable for modelling plasma flow in microvessels. LBM is a particle-based mesoscopic method for simulating fluid flow which has been applied successfully in 3-D tube like microvessels. The density distribution function $f_\alpha(x, t)$ is the fundamental quantity in LBM. Generally, the discretized Boltzmann equation with external force is expressed as [13]:

$$\begin{aligned} &f_\alpha(x + e_\alpha \delta t, t + \delta t) - f_\alpha(x, t) \\ &= \frac{f^{(eq)}_\alpha(x, t) - f_\alpha(x, t)}{\tau} + F_\alpha \Delta t \end{aligned} \tag{5}$$

where τ is the single relaxation time, e_α is the lattice velocity [13], δt is time step, α shows the discrete speed directions and F_α as the force distribution function for D_3Q_{19} can be defined as [13]:

$$\begin{aligned} F_\alpha &= (1 - \frac{1}{2\tau})\omega_\alpha(\frac{e_\alpha - \vec{u}}{c_s^2} + \frac{e_\alpha.\vec{u}}{c_s^4}.e_\alpha).g \\ \omega_0 &= 1/3 \\ \omega_\alpha &= 1/18 \quad for \alpha = 1 - 6 \\ \omega_\alpha &= 1/36 \quad for \alpha = 7 - 18 \end{aligned} \tag{6}$$

where g is the force density acting on the fluid (in this paper can be defined as the function of RBC elasticity and bending) and

Table 1. Parameters used in DPD simulation [7].

A	$L_{\max}$	λ_p	k_b	r_c	k_BT
500	1.3	0.0005	50	1.2	0.1

the corresponding equilibrium distribution function is taken as [13]:

$$f_\alpha^{eq} = \rho\omega_\alpha\left[1 + \frac{e_\alpha.\vec{u}}{c_s^2} + \frac{(e_\alpha.\vec{u})^2}{2c_s^4} - \frac{\vec{u}^2}{2c_s^2}\right] \tag{7}$$

where c_s is the sound speed. Moreover, the density, velocity and kinetic viscosity of fluid are calculated as [13]:

$$\begin{aligned} \rho &= \sum_\alpha f_\alpha \\ \rho\vec{u} &= \sum_\alpha e_\alpha f_\alpha + 1/2g\Delta t \\ \nu &= \frac{2\tau - 1}{6}\Delta t \end{aligned} \tag{8}$$

2.4. IB method

The IB method was developed [9] to model the coupling between fluid and solid. In this method, there are two coordinate systems: Lagrangian grid for the solid boundary and Eulerian mesh for the fluid. Interpolation is used to communicate between both coordinate systems in IBM. Details of the IBM formulation may be found in refs. [14,15]. Briefly, the discretized IBM equations are defined as [14]:

$$\begin{aligned} g(x,\,t) &= \int_\Gamma G(s,\,t)\delta(x - X(s,\,t))ds \\ \frac{\partial X(s,\,t)}{\partial t} &= \vec{u}(X(s,\,t),\,t) = \int_\Omega \vec{u}(x,\,t)\delta(x - X(s,\,t))dx \end{aligned} \tag{9}$$

where $\vec{u}$ is the fluid velocity, x and X are Eulerian and Lagrangian coordinate, G is force density acting on the boundary, Γ and Ω are the solid and fluid domains and $\delta(x - X(s,\,t))$ is a Dirac delta function. Fluid forces, $g(x,t)$, are computed by spreading the solid forces, while the solid velocity is obtained by interpolating velocity from fluid nodes.

2.5. Hybrid method

As mentioned previously, the large time for simulation of red blood cell motion in microvessels, necessitates the use of a hybrid method (LB-LD) which shows the benefit of everyone. This allows for the use of a larger simulation time step.

Given a LBM for the fluid and low dimensional method (the model based on dissipative particle dynamics) for the red blood cell, a method to couple the two techniques together is required. Incorporating a moving boundary (such as the surface of the red blood cell) into the LBM is done by the IB. In the following, the hybrid algorithm is shown as:

1 Compute the force on particles based on the membrane deformation by LD method [7]
2 Spread the force from particles to the fluid by IB [14,15]
3 Obtain the flow velocity by LBM [13]
4 Interpolate the velocity back to the particles by IB [14,15]
5 Update all particles position according to new velocity

3. Results

To show the accuracy of the LD-RBC model used to simulate red blood cell, different stretching force is applied in the opposite direction to two particles of RBC separated by the diameter of the ring. The parameter used in this simulation is indicated in Table 1.

Figure 1 shows the RBC shape evolution from equilibrium to 200 pN stretching force at different Nc (the number of particles) in compare with experimental data [3]. It should be noticed that an increase in the number of particles results in a smoother RBC surface. For simulating the flow in microvessels, the number of particles could be chosen between 6 and 10 particles to get accurate results in accordance with Figure 1.

To validate the described proposed model, the deformation index (DI) which determines the deformation and behaviour of RBC in the flow, is investigated and compared with the previous numerical results in [16]. DI is defined as [17]:

$$DI = \frac{l}{d} \tag{10}$$

where l is the RBC length and d is the diameter of the cell. These parameters are shown in Figure 2.

In this paper, the motion of a single RBC in a tube with diameter of 20μm and 180μm in length is considered. The no-slip boundary condition is employed on the tube wall and the periodic condition is imposed in the horizontal x-direction as expected, the RBC deforms along the tube length and it will be obtained a parachute shape. In Figure 3 DI is shown as the function of capillary number (Ca). Ca is defined as:

$$Ca = \frac{\mu\dot{\gamma}r_{RBC}}{k_s} \tag{11}$$

where k_s is shear elasticity and r_{RBC} is RBC radius.

G can be linked to the capillary number in drop dynamics [18]. As it is indicated in Figure 3 DI increases as Ca increases and this figure demonstrates that the present results are in good

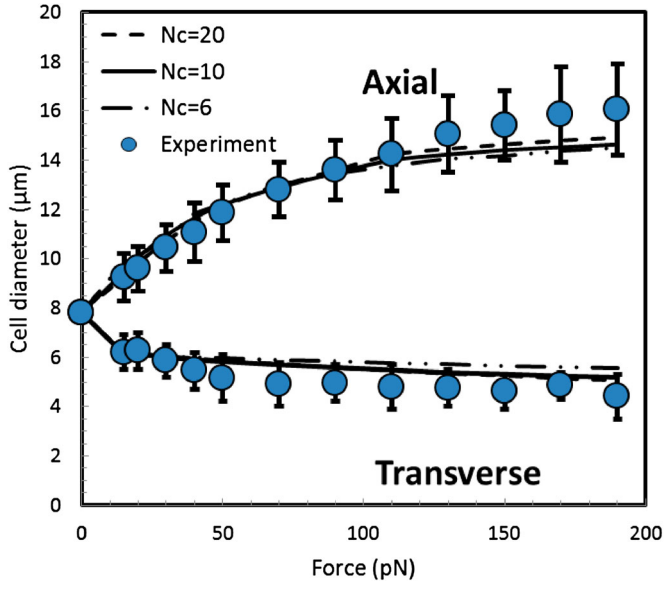

Figure 1. (Colour online) Cell diameter as the function of RBC stretching force.

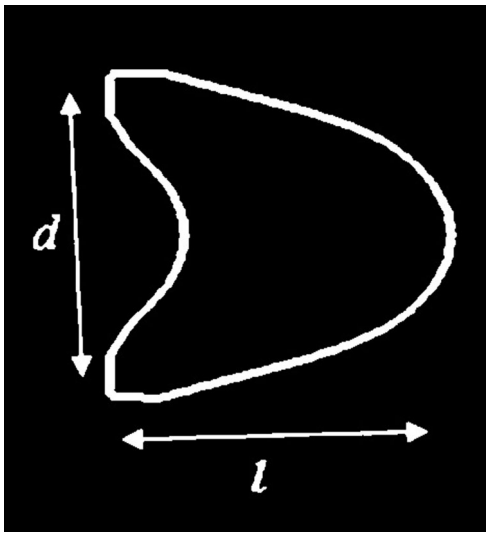

Figure 2. Schematic of red blood cell in blood flow.

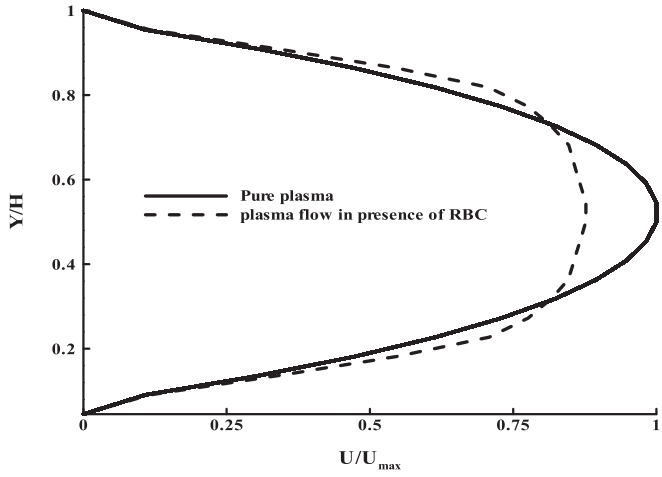

Figure 4. Flow velocity profile with and without the present of RBC ($G = 0.22$, $E_B = 0.7$).

agreement with the numerical results presented by Zhao et al. [16] compared with 2-D LBM model.

Moreover, the fluid velocity in a microvessel is investigated. The parabolic profile in the flow of whole blood through 3-D microvessel is observed as shown in Figure 4. When RBC moves along the tube, the flattened velocity profile is found in the microvessel as depicted in Figure 4.

The variation of the streamwise (U_x) is shown as the function of z axis in Figure 4. As can be seen, the velocity of the fluid is smaller in the vicinity of the RBC. It should be noted that the plasma velocity profile is closely related to the RBC deformation and haematocrit. When the flow approaches an RBC, the velocity profile becomes more blunted. The image of the steady shape of RBC on the x–y plate (horizontal plate) is demonstrated in Figure 5. As expected RBC deforms along the microvessel and the parachute-like shape of RBC in poiseuille flow can be observed. The central part of the cell bulges forward due to the higher values of flow velocity close to the microvessel centreline. Moreover, the formation of a parachute-like steady cell shape is closely related to fluid viscous forces which can affect the natural curvature of RBC

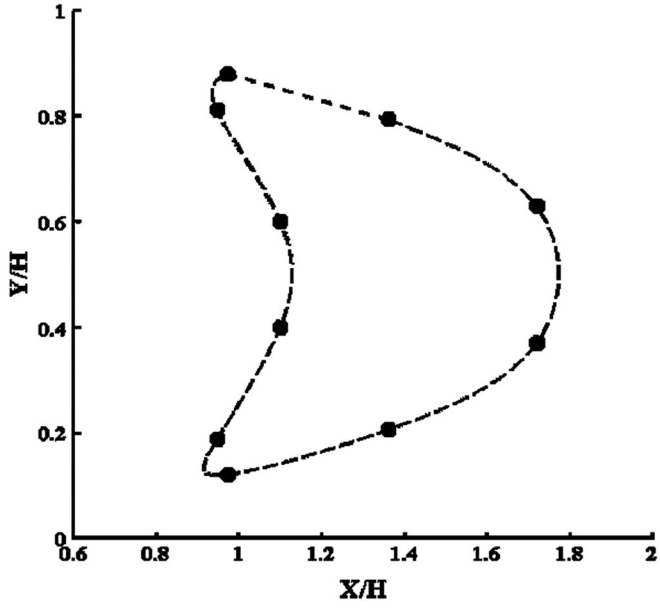

Figure 5. Parachute shape of RBC in Poiseuille flow ($G = 0.22$, $E_B = 0.7$).

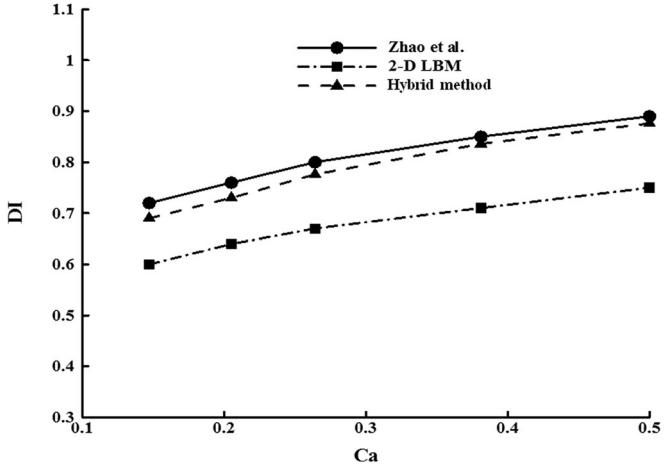

Figure 3. DI as a function of capillary number.

membrane. In addition, the variation of velocity around the centre area is smaller for higher rigidity.

All of the present computations are done using a core-i7/2.4 GHz computer. As demonstrated in Table 2, the computational time is 24 h for the present hybrid model and 720 h for the DPD method. As a result, the proposed method reduces the computational time and is significantly 30 times faster than the DPD method.

As illustrated, the main innovation of the proposed model when compared with other common computational fluid dynamics solvers such as 3-D LBM and DPD, is that, in

Table 2. Comparing computational time.

2-D LBM	DPD method	Hybrid method	Method
0.25	720	24	Time (hour)

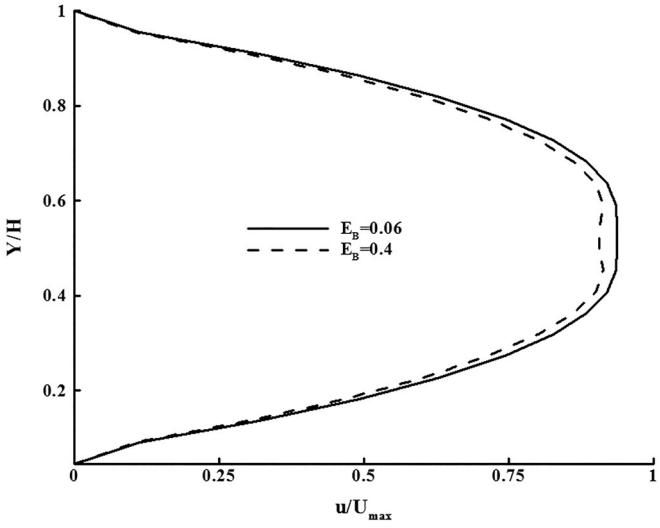

Figure 6. Velocity profile for different RBC deformabilities at constant ($G = 0.43$).

addition to solving the problem with high accuracy, it decreases the computational time.

Furthermore, increasing the membrane elastic modulus and/or bending resistance leads to the more rigidity. In Figure 6 variation of vertical velocity profile is indicated as the function of cell rigidity. For this purpose, the deformability decreases with increasing bending resistance and constant elastic module. As it is shown in this figure, the cell deformability is imposed by decreasing the membrane bending resistance and it increases the flow velocity.

In the following, the effect of two values of shear rate on RBC deformation is considered in the steady shear flow. For this purpose, a ring of 8 particles is embedded horizontally in the centre of a $50\mu m \times 10\mu m \times 10\mu m$ fluid channel (between two plates) with the same velocities prescribed on the top and bottom surface.

There is a direct relation between the value of shear rate and RBC deformation. In fact, under simple shear flow only two RBC motions: tumbling and tank-treading have been demonstrated and related to the RBC mechanics. For very low stress, the RBC rotates in a solid-like fashion [19] and has been reported to tumble. This behaviour happens when the cell axis of symmetry rotates in the shear plane. At high shear stress, the red blood cell deforms into an ellipsoid and it has a 'fluid-like' tank-treading movement in which the membrane rotates around an otherwise steady cell shape. Figure 7 demonstrates the RBC motions at different shear rates. A rigid-body-like behaviour of the RBC can be seen in this figure. It is shown

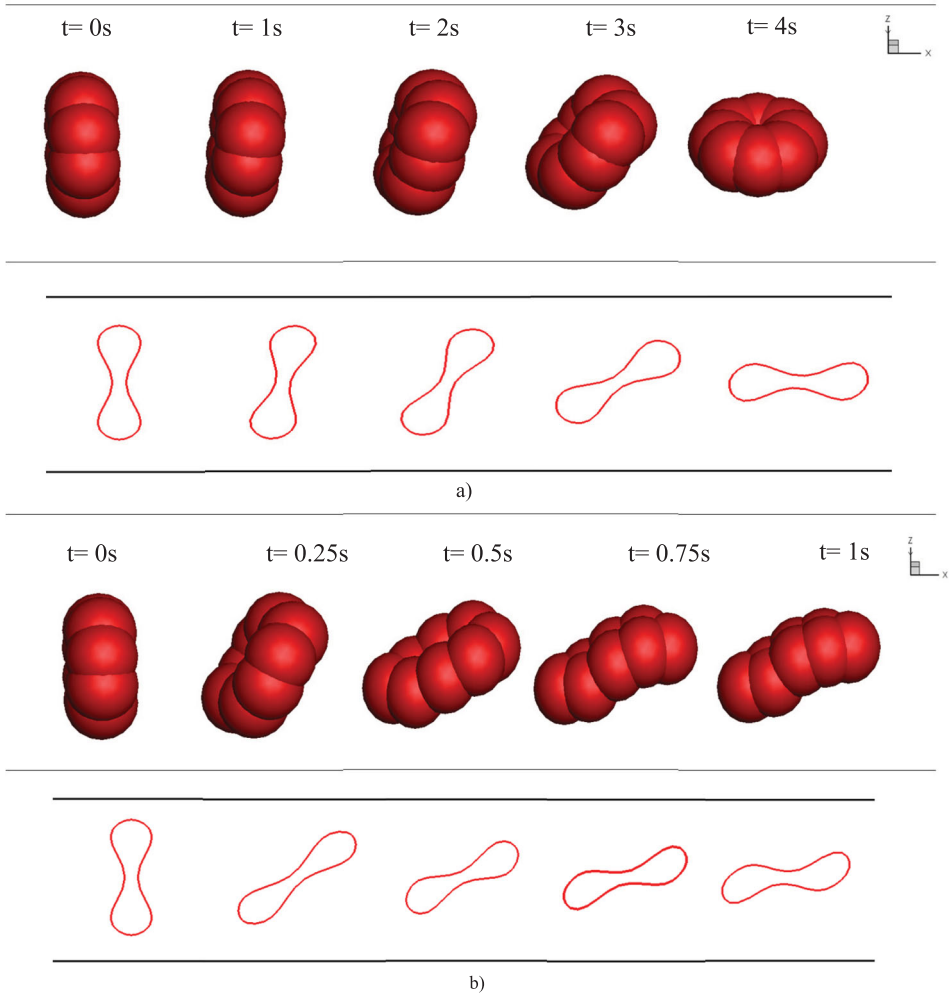

Figure 7. (Colour online) (a) Deformation of RBC in slow shear flow with shear rate $\dot{\gamma} = 0.05s^{-1}$ (b) Deformation of RBC in slow shear flow with shear rate $\dot{\gamma} = 1.5s^{-1}$.

that the shape of the cell stays unchanged during the rotation which is called tumbling in a low shear rate.

To investigate the response of RBC to high shear stress, the shear rate of $\dot{\gamma} = 1.5s^{-1}$ is considered in Figure 7(b). When the shear rate increases, tank-treading occurs and the streamlines around the RBC change from circular spinning to a back-and-forth motion along the flow direction. In this behaviour the RBC rotates around its centre mass and has a quasi-stable inclination. It is shown that the RBC elongates and orients to an ellipsoidal-like shape while tank-treading occurs due to strong shear flow. The results show that the RBC orientation in flow changes when $\dot{\gamma}$ increases. Furthermore, the present results demonstrate that the proposed model recovers the tumbling and tank-treading behaviour.

4. Concluding remarks

In this paper, hybrid IB-LBM has been successfully combined with an LD-RBC based on DPD to simulate the motion and deformation of RBC in microvessels and shear flow. As mentioned the proposed numerical model was created by using the LD-RBC for modelling of RBC and LBM for the plasma flow. IB condition is used to present the interaction of RBC with plasma. The results show that our mesoscale method has an advantage in dealing with the dynamics of RBCs in shear and Poiseuille flow. The present results show that the deformation and mechanical behaviour of RBCs are the important factors to affect the flow velocity profile. Furthermore, the effect of shear rate on RBC deformation is investigated in this paper. The results demonstrate that high shear stress exchanges the behaviour of RBC from tumbling to tank-treading. In tumbling, the RBC rotates around the centre of mass without change, whereas in tank-treading, the RBC elongates to an ellipsoidal like shape. It should be noted that either tank-treading or fluid tumbling, depending on the viscosity ratio. Based on the present results, the proposed numerical model was able to predict all motions and deformations of human RBC as accurate as Zhao method compared with the 2-D model with significant reduced computational time. The computational cost using the hybrid numerical method was reduced by a factor of 30.

Disclosure statement

No potential conflict of interest was reported by the authors.

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