Sensitivity of Red Blood Cell Dynamics in a Shear Flow

Mariana Ondrušová

Abstract— The computational models of cells have specific parameters that affect their properties in the shear flow. We want to analyze influence of individual parameters on cell behavior when setting simulations. We select the parameters that affect in particular the bending and the frequency of rotation of the cell in the shear flow. For each parameter change, we perform several simulations to improve the visibility of the results. The results indicate that the viscosity of the membrane is the key parameter influencing the rotation frequency of the cells in a shear flow.

Keywords— computational modelling, red blood cell, shear flow, simulations, elastic parameters.

I. Introduction

Behavior of red blood cell (RBC) is closely related to the elastic properties of cell membranes and their interactions. Dynamical properties and morphology of RBC were studied in experimental studies [1, 2].

Nowadays, simulation models are important that help in designing microfluidic devices.[3] A well-designed simulation model helps to verify experimental results. An example of such scenario is the stretching experiment, used in [2]. Here, the RBC is stretched on the opposed sides with optical tweezers. Dependence of deformation index on applied stretching force is used to determine elastic parameters of the model.

Our spring-network based model was described in [4,5]. Here, spring-network based model is defined by triangulation of the membrane of RBC. The static validation of elastic properties was described [8] and the software implementation of the model in [9].

In our article, we focused on analyzing elastic parameters and the sensitivity of RBC behavior during their change. First, we changed the coefficient in the bending modulus. Since this modulus is responsible for the bending of the membrane by prescribing preffered angles between the triangles in discretization of the model, we expect, that changing this parameter will affect the rotation of the cell during simulation. In the next simulation, we changed the set of elastic parameters. We want to verify that a different set of elastic parameters can be suitable for simulation. Finally, we changed the viscoelasticity of the cell membrane. We chose it for its ability to relieve fast changes shape from the original to the stretched and, on the contrary, to remind RBC in the blood.

In Section II we describe our red blood cell model, parameters of RBC and fluid and their interaction. Section III is devoted to basic simulation setup. Sections IV and V describe results with different elastic parameters and visco-elasticity. Finally, in Section VI we summarize the findings and draw conclusions.

II. Model of red blood cell

A detailed description of the model was presented in [6,7]. The red blood cell model is based on membrane deformation and fluid dynamics. Both components are interconnected.

The fluid dynamics: The description of fluid dynamics is based on the lattice-Boltzmann method. It is assumed that the fluid is divided into discrete points evenly located in the cubic lattice (three dimensions with 19 different directions). More details we can found in [10].

M. Ondrušová, Faculty of Management Science and Informatics, University of Zilina, Slovakia (e-mail: mariana.ondrusova@fri.uniza.sk).
This work was supported by the Slovak Research and Development Agency under the contract No. APVV-15-0751, by the Ministry of Education, Science, Research and Sport of the Slovak Republic under the contract No. VEGA 1/0643/17 and by the FVG 2017 grant of Faculty of Management Science and Informatics, University of Žilina.

The cell deformation: RBC is elastic objects whose surface is covered by a spectrin (protein) membrane. Spectrin forms a network of springs that can be stretched and bended to change the shape of the membrane. RBC may significantly deform during the experiments.

Cells are described through points and a triangular network of springs through which these points are linked. By moving the cell, the individual points also move and interact with one another by stretching the springs. The cell model elasticity preserves five basic moduli - the elastic modulus, stretching, bending, local and global area conservation and volume conservation. The following equations for are described in [11].

Stretching - this module affects the stiffness of the object's membrane. It acts on each neighboring pair of points that are interconnected. At higher stretching, the RBC model is stiffer and less flexible. The force between two mesh points is given by

$$F_s = k_s \kappa(L)(L - L_0). \quad (1)$$

Here, k_s is the stretching coefficient denoting the stiffness of the springs, L is the current length of the edge between two points, L_0 is the length of the edge in the relaxed state and a function κ(L) represents the neo-Hookean nonlinearity of the stretching force.

Bending - this module keeps the angles between each pair of adjacent triangles having a common edge and angle θ. Bending is given by

$$F_b = \kappa_b \frac{\theta - \theta_0}{\theta_0} n \quad (2)$$

where κ_b is the bending coefficient modifing modulus, when returning to a relaxed state , θ is the angle between two triangles having a common edge, θ_0 is their relaxed angle, and n is the normal vector to the corresponding triangle.

Fluid-Cell Coupling: The individual forces of fluid and the forces of the cell interact. The fluid develops force on every single particular mesh point of membrane. This force F_d is proportional to the difference between point velocity and fluid velocity at the same location. The magnitude of the force is given

$$F_d = \xi(u - v) \quad (3)$$

The friction coefficient ξ provides the distribution of the resistive force of the object to its individual discrete points. v is the velocity of the mesh point and u is the velocity of the fluid at the position of the mesh point.

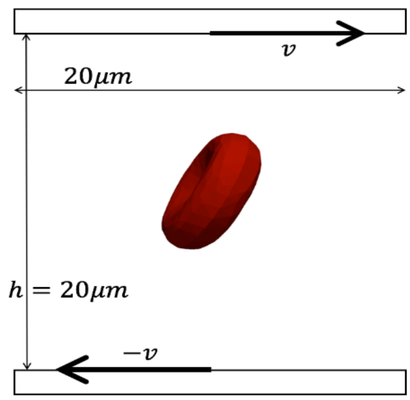

Fig. 1 Simulation setting with velocities of the fluid at the boundaries

III. Simulation setup

Simulations were conducted in cubic box with dimensions $20\ x\ 20\ x\ 20\mu m$. The shear flow is generated by setting the constant velocity v and $-v$ at the top and bottom boundaries of the channel, see Figure 1. In this setting for an empty channel, the velocity field has zero y and z components and the horizontal x component linearly decreases from the value v at the top boundary to value −v at the bottom boundary. This means that the shear rate is constant over the whole channel.

In our simulation, we used one cell in the center of the channel with shear flow. Together we made 3 different sets of simulations, in each set we changed one parameter and we kept other constant. This way we can see how the whole system reacts on the change of one parameter.

To compare the results, we choose 10 different times at the beginning - from 0.0002 µs to 0.002 µs. The following parameters were common in all simulations: density of fluid - 1050 kg. m^{-3} and viscosity 5 mPa. s. These values correspond to biological solutions of dextran that is typically used in experiments as in [4,5]. From a recent study [12], the friction coefficient was taken ξ = 5.0. For discretization of time we use the time step equaling to 0.1µs. To monitor the rotation frequency, we marked a particular point. So we could see a point in Figure 2, which rotated in x-direction around the cell.

During simulations we changed the visco-elasticity and the elastic parameters. Specific values are in the other sections.

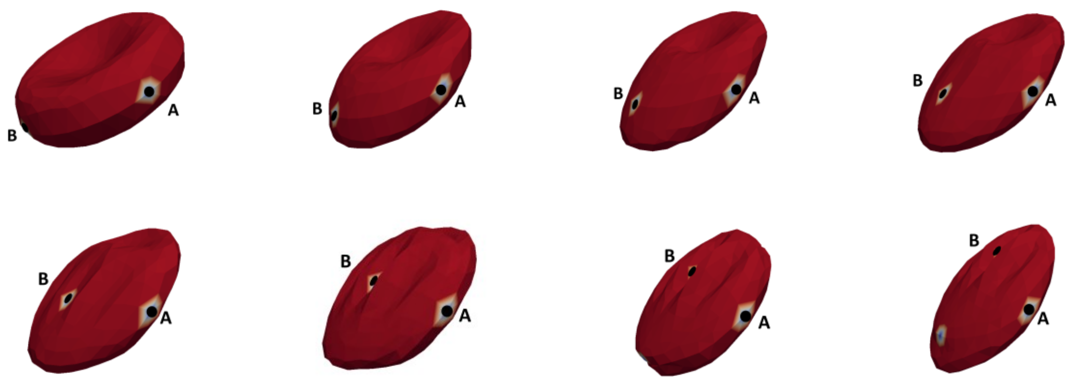

Fig. 2 Two specific mesh points are highlighted. Point A is on the y-axes of rotation. Point B rotates around the cell.

IV. Parameters of the membrane

The biological membrane of a RBC exhibits visco-elastic properties [13]. Viscoelasticity is a property of cells that help to mitigate rapid shape changes. It also influences the rotation frequency. The force is given

$$F_{vis} = k_{visc} \frac{dL}{dt} \qquad (4)$$

Here, k_{visc} is the viscosity coefficient, which complements the visco-elastic properties, dL is the change of the edge length and dt denotes time derivative.

In our previous study [14] we verified the viscoelasticity than closely corresponds to the properties of red blood cells. We also valued k_{visc}, which also correlates with experimental data. [4,5].

By simulations, we find out how different k_{visc} values affect the cell rotation frequency. Results we compared with verified study [14]. We have selected the following values for elastic parameters

$$k_s = 0.008,\ k_b = 0.0003,\ k_{al} = 0.006,\ k_{ag} = 0.9,\ k_v = 0.5,\ k_{visc} = 1.5$$

We started simulations with 5 different values for k_{visc} = 0.0, 0.5, 1.0, 1.5, 2.0. Figure 3 represents the rotation frequency of a point in time for different values of k_{visc}. Results confirmed our assumption, that even a small change in visco-elasticity values affects the rate of rotation. The marked dots indicate the speeds for computation of frequency described in [14].

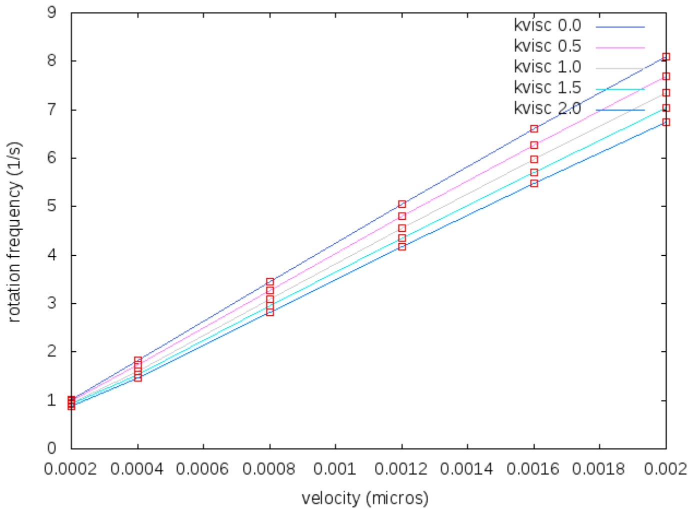

Fig. 3 Frequency of rotation of the cell in shear flow with change of visoelasticity.

V. ELASTIC PARAMETERS

Elastic parameters are an essential part of the model of cell and have an important role in changing shape. We compared results from [14] for which we have elastic parameters like in Section IV.

$$k_s = 0.008,\ k_b = 0.0003,\ k_{al} = 0.006,\ k_{ag} = 0.9,\ k_v = 0.5,\ k_{visc} = 1.5$$

In first part with elastic parameters we focused on change k_b. Bending is main parameter that regulates the cell membrane's flexibility. We chose values - 0.0003, 0.0012, 0.0048. Higher values cause too high resistance to bending, which is atypical behavior of RBC. Simulations were evaluated in the same way as in IV – graph with rotation frequency. We also used the same speeds. In Figure 4 we can see small divergences in line. However, these are negligible and we can conclude that the bending in the range of 0 to 0.0048 does not influence the rotation frequency.

In other simulations, we wanted to find out the rotation behaviour for another set of elastic parameters. From our preliminary simulations we know that elastic behaviour of cell in static case is reproduces also for other value of k_{al}. We have preserved other elastic parameters from (5), but we changed value of k_{al}.

$$k_s = 0.008,\ k_b = 0.0003,\ k_{al} = 0.003,\ k_{ag} = 0.9,\ k_v = 0.5$$

We started simulations with different values for k_{visc} = 1.0, 1.5, 2.0. The results are again reported over the frequency. We can see in Figure 5, that these elastic parameters are very similar to the original results in Figure 3. So they are also suitable for later simulations and we confirmend that k_{visc} influences the dynamical behaviour of cell in the same way as in Figure 3.

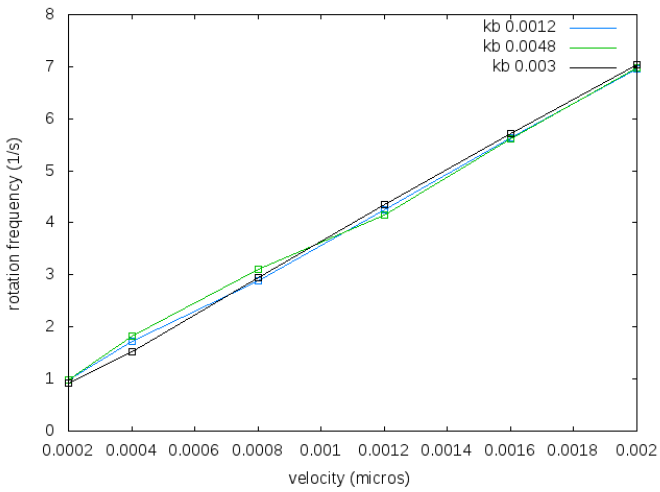

Fig. 4 Frequency with different values of bending. Correct value, which coresponds with RBC is 0.0003.

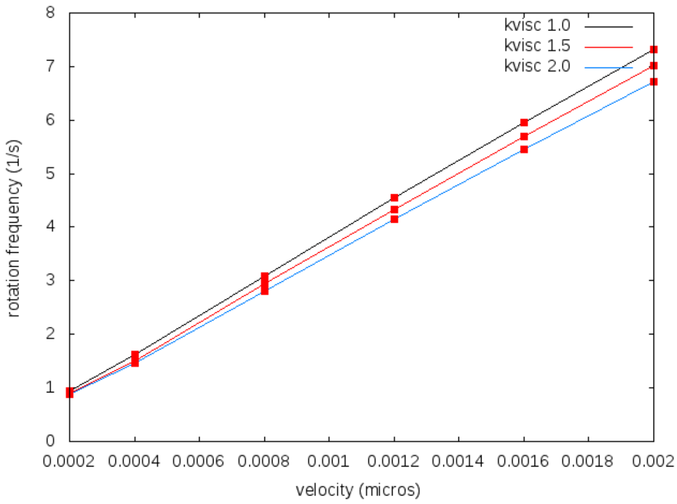

Fig. 5 Frequency using other set of elastic parameters.

VI. Conclusion

The RBC model that has been used, has numerous parameters. The aim of this article was to study the effect of some of these parameters on the behaviour of a red blood cell in a shear flow.

Typically, the RBC starts to rotate in such flow. The speed of rotation, or, the rotation frequency is an important feature of the cells and we decided to analyze how the rotation frequency is influenced by the change in model parameters. In Section 1 we identified two elastic parameters that are likely to affect the rotation frequency: the bending resistance of the membrane, represented by bending coefficient k_b and the membrane viscous coefficient represented by k_{visc}.

A serie of simulations were performed where we tracked how fast the cell rotates for different shear rates. This serie was run numerous times with different k_b and with different k_{visc}. Each of Figures 3-5 shows the results. When k_b was changing (see lines in Figure 4 with different colors), we see no significant changes. When the viscosity coefficient changes, we do see the changes in frequencies in Figures 3 and 5.

Our simulations indicate that the viscous coefficient significantly influences the rotation of the RBC whereas the bending coefficient has only small influence.

ACKNOWLEDGEMENT

We would like to thank prof. M. Klimo that he made it possible to use computational resources from his project ITMS 26210120021.

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