

Deformation of a single red blood cell in a microvessel

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Abstract

Red blood cells (RBCs) are the most common type of cells in human blood and they exhibit different types of motions and deformed shapes in capillary flows. The behaviour of the RBCs should be studied in order to explain the RBC motion and deformation mechanism. This article presents a numerical simulation method for RBC deformation in microvessels. A two dimensional spring network model is used to represent the RBC membrane, where the elastic stretch/compression energy and the bending energy are considered with the constraint of constant RBC surface area. The forces acting on the RBC membrane are obtained from the principle of virtual work. The whole fluid domain is discretized into a finite number of particles using smoothed particle

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hydrodynamics concepts and the motions of all the particles are solved using Navier–Stokes equations. Minimum energy concepts are used to simulate the deformed shape of the RBC model. To verify the model, the motion of a single RBC is simulated in a Poiseuille flow and the characteristic parachute shape of the RBC is observed. Further simulations reveal that the RBC shows a tank treading motion when it flows in a linear shear flow.

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1 Introduction

The microcirculation of blood plays an important role in the human body by bringing oxygen from the lungs to the tissues and nutrients to the organs, while removing wastes and carbon dioxides from organs and tissues, respectively. These processes are greatly affected by the rheological properties of the red blood cells (RBCs), such as deformability. Healthy RBCs have a biconcave disk

shape. Human RBCs are non-nucleated deformable liquid capsules enclosed by a thin viscoelastic membrane, which consists of a lipid bilayer supported by a mesh-like cytoskeleton, formed by a network of spectrin proteins linked by short filaments of actins [1]. This biological membrane contains a large amount of haemoglobin which is highly efficient in binding oxygen.

Blood continuously flows within the cardiovascular network, as blood flows from heart to arteries, capillaries, veins and then flows back to the heart. In the capillary vessels, RBCs reveal a number of interesting shapes and dynamics in response to the flow conditions and which are crucial for optimal mass transfer. The importance of understanding the mass transfer, such as oxygen and carbon dioxide exchange between the RBCs and tissues through capillaries, motivated a number of experimental (in vivo and in vitro), theoretical and numerical studies [5].

In this study, we present an advanced numerical modelling technique using smoothed particle hydrodynamics (SPH) to analyse the behaviour of RBCs. SPH is advantageous in the direct modelling of blood components, such as RBC membranes, RBC exterior fluid (plasma) and RBC interior fluid (cytoplasm). The RBC membrane is modelled by a spring network and the forces acting on the RBC membrane are determined based on the minimum energy principal [14]. In the first step of this study, a mathematical model based on the conservation of mass and momentum is developed to describe the RBC motion in plasma flow, using both SPH concepts [9, 8, 6] and the spring network model for the RBC [10, 13]. Then the model is converted into a discretized meshfree framework in a Fortran program to analyse the motion and deformation mechanism of RBCs. To verify the model, the motion of a single RBC is simulated in a Poiseuille flow and in a linear shear flow.

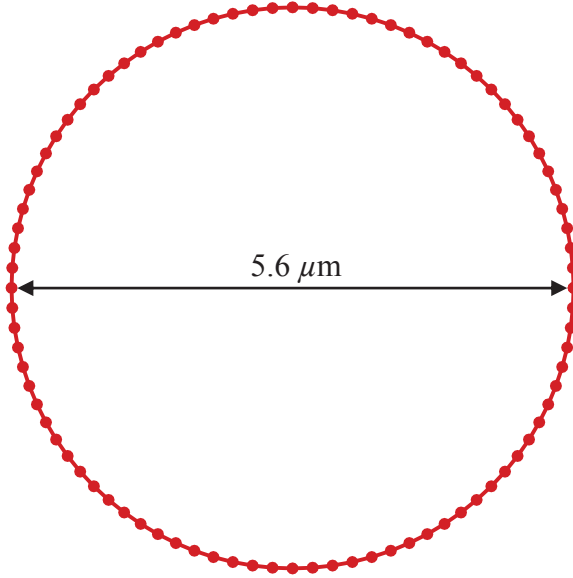


Figure 1: Particle location for the RBC membrane.

2 Model and method

2.1 Spring network model of RBC

A two dimensional spring network model is used to represent the RBC membrane, as used in previous studies [13, 10]. In this model, the initial RBC membrane shape is assumed to be a circle. Then the circular RBC membrane is discretized into a finite number of point masses as shown in Figure 1. The radius of the initial circle should be chosen such that the diameter of the final shape of the RBC gives the average diameter of RBCs, about $7.6 \mu\text{m}$. Further, the number of particles in the RBC membrane should be chosen ensuring that the minimum distance between two neighbouring particles is equal to the particle minimum spacing in the fluid (plasma) domain, for effective and efficient simulation by SPH. Therefore, **88** particles are used and they are in-

terconnected by 88 elastic springs (see Figure 2) and this number is chosen so that the distance between two neighbouring particles is approximately $0.2 \mu\text{m}$. The radius of the initial circle is assumed to be $2.8 \mu\text{m}$ [10]. The elastic energy stored in the springs due to stretching/compression is

$$E_l = \frac{1}{2} K_l \sum_{i=1}^N \left(\frac{l_i - l_0}{l_0} \right)^2, \quad (1)$$

and the elastic bending energy stored in the springs due to the bending is

$$E_b = \frac{1}{2} K_b \sum_{i=1}^N \tan^2 \left(\frac{\theta_i}{2} \right). \quad (2)$$

In the above, l_i , θ_i and l_0 are the length of the springs, the angle between a pair of consecutive springs, and the reference length (the length with no deformation) between a pair of consecutive RBC particles, i and $i + 1$, respectively. In addition, K_l and K_b are the spring constants. We set $K_l = K_b = 3 \times 10^{-12} \text{ N m}$.

In order to maintain a constant membrane area, an energy penalty function is introduced:

$$E_s = \frac{1}{2} K_s \left(\frac{s - s_e}{s_e} \right)^2, \quad (3)$$

where s and s_e are the cross-sectional area of the RBC and the equivalent cross-sectional area of the RBC membrane, respectively, and K_s is the penalty coefficient. Here $s_e = \pi (2.8 \times 10^{-6})^2 \times 0.55 \text{ m}^2$ is chosen as it is the physiological area of a healthy RBC [10]; it corresponds to a 55% reduction of total cross-sectional area from the initial area of the circle. We set $K_s = 3 \times 10^{-8} \text{ N m}$.

The total energy of the RBC membrane is the sum of all the three types of energies:

$$E = E_l + E_b + E_s. \quad (4)$$

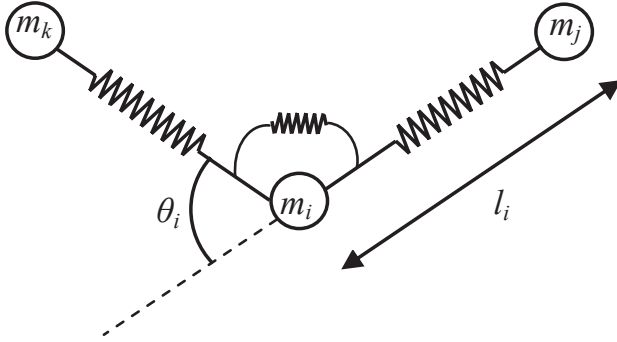


Figure 2: Spring network model of the RBC.

The forces acting on the i th membrane particle are calculated using the principal of virtual work:

$$\mathbf{F}_i = -\frac{\partial E}{\partial \mathbf{r}_i}, \quad (5)$$

where \mathbf{r}_i is the position vector of the i th membrane particle and \mathbf{F}_i is the vectorial force acting on the i th membrane particle. After about 0.15 s, the typical shape of the RBC membrane is obtained. Further simulations do not show any change in the RBC membrane and the energy curve shown in Figure 3 proves that the total elastic energy in the RBC membrane does not change after about 0.15 s. Since there is no change in total elastic energy and since the total energy obtains a minimum value, after 0.15 s the forces acting on the RBC membrane particles are minimized and no further change in RBC membrane shape will occur.

2.2 Governing equations for the flow field

Navier–Stokes equations in Lagrangian form are used to model the whole flow field, with the assumption that all the fluids are incompressible and the system is isothermal. Neglecting gravitational effect, the conservation of mass

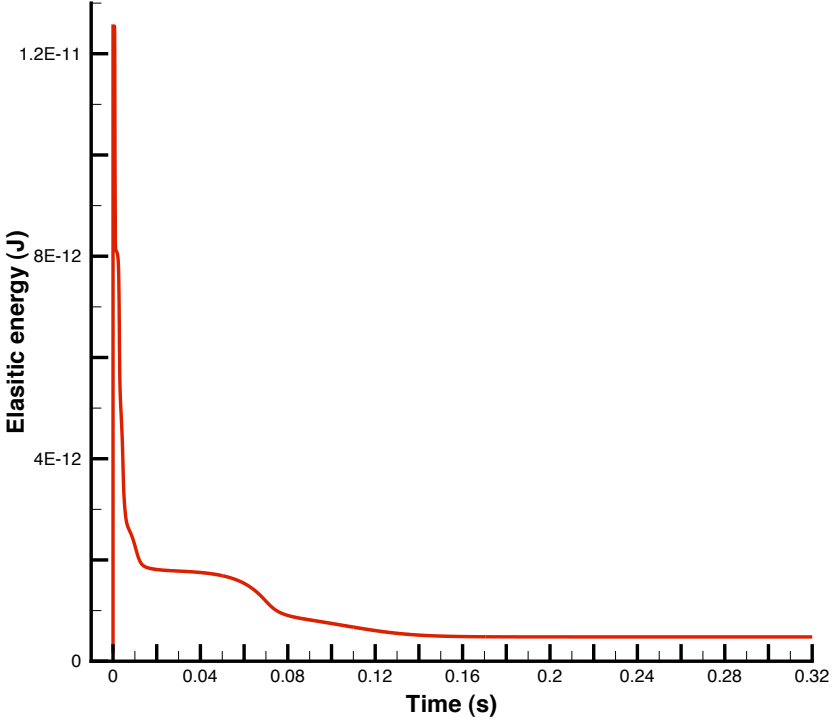


Figure 3: Change in elastic energy of RBC membrane.

and conservation of momentum equations are

$$\frac{d\rho}{dt} = -\rho \nabla \cdot \mathbf{v}, \quad (6)$$

$$\frac{d\mathbf{v}}{dt} = -\frac{1}{\rho} \nabla p + \frac{\mu}{\rho} \nabla^2 \mathbf{v} + \mathbf{f}, \quad (7)$$

where ρ and μ are the density and the dynamic viscosity of the fluid, respectively, \mathbf{v} is the velocity vector, p is the pressure, and \mathbf{f} is the external force acting on the fluid and RBC particles (the latter obtained from equation (5)).

The full flow field including the RBC exterior fluid (plasma) and interior fluid (cytoplasm), is discretized into a set containing a finite number of particles.

Each particle represents a finite mass, associated with density and pressure. The system evolves due to the interaction between discretized particles and externally exerted forces. In the SPH method, any field function value of the i th particle is approximated from the same field function value of the neighboring j th particles using a smoothing or kernel function W . Using the SPH concepts, equations (6) and (7) are rewritten as

$$\frac{d\rho_i}{dt} = \sum_{j=1}^N m_j (\mathbf{v}_i - \mathbf{v}_j) \cdot \nabla_i W_{ij}, \quad (8)$$

$$\begin{aligned} \frac{d\mathbf{v}_i}{dt} = & - \sum_{j=1}^N m_j \left(\frac{\mathbf{p}_j}{\rho_j^2} + \frac{\mathbf{p}_i}{\rho_i^2} \right) \cdot \nabla_i W_{ij} \\ & + \sum_{j=1}^N m_j \frac{(\mu_j + \mu_i) (\mathbf{r}_i - \mathbf{r}_j) \cdot \nabla_i W_{ij}}{\rho_i \rho_j |\mathbf{r}_i - \mathbf{r}_j|^2} (\mathbf{v}_i - \mathbf{v}_j) + \mathbf{f}_i, \end{aligned} \quad (9)$$

where N is the number of neighbouring particles of the i th particle and m is the mass. For the kernel W , a cubic spline smoothing function is used [9].

3 Results

3.1 RBC motion in Poiseuille flow

The obtained shape of the RBC membrane (see Section 2.1) is rotated, such that the major axis of the RBC membrane is vertical. Finally, the RBC membrane is put into a plasma domain. To represent the plasma component, the fluid particles are arranged outside the RBC membrane such that the particle spacing is equal to $0.2 \mu\text{m}$ (see Figure 4). The cytoplasm particles in the RBC interior are arranged in the same manner.

To validate the model, pressure driven Poiseuille flow is applied to the fluid domain and the behaviour of the RBC shape is investigated. Lennard-Jones

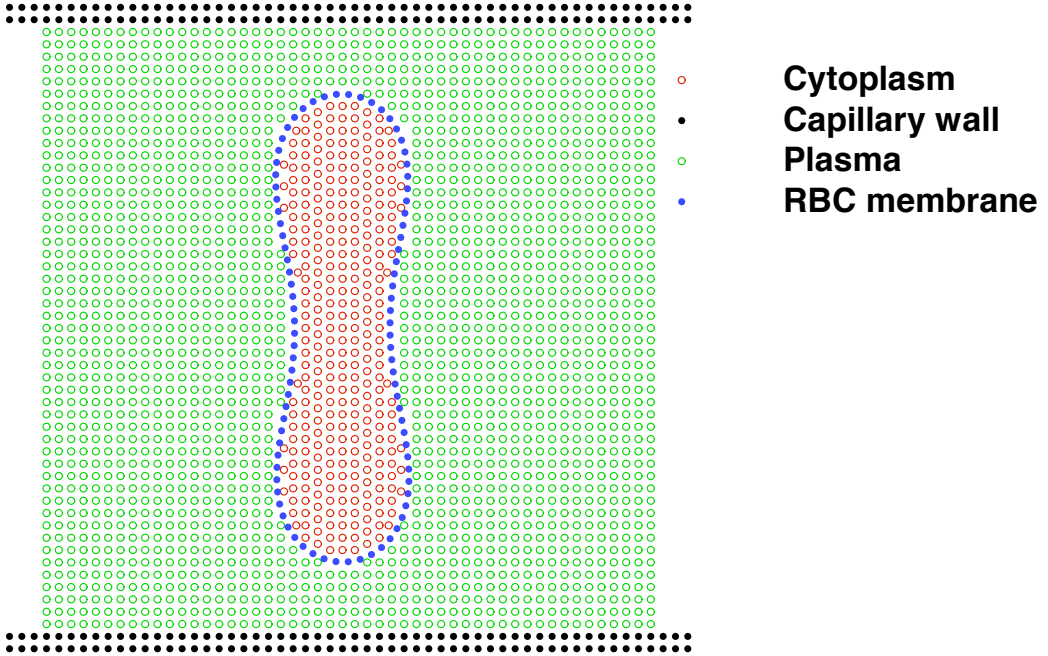


Figure 4: Initial particle configuration.

type repulsive forces [9] are applied pair-wise to the plasma and cytoplasm particles to avoid the penetration of fluid particles through capillary walls and RBC membrane [4]. Pressure is applied to all the plasma particles, with a uniform pressure gradient along the length of the capillary to create the Poiseuille flow. Periodic boundary conditions are applied to the inlet and the outlet. The time step is 1×10^{-9} s over a temporal domain of 1×10^{-2} s. The dynamic viscosity of plasma, cytoplasm and RBC membrane particles is assumed to be 1×10^{-3} Pa·s and other parameters are given in Table 1.

In contrast to the Poiseuille flow, the velocity of neither the RBC nor the plasma flow can be accurately calculated in terms of analytical functions. The RBC acts as a barrier to plasma flow and distorts the Poiseuille velocity profile. If there are no objects within the plasma domain, then a pure Poiseuille

Table 1: Simulation parameters

Parameter	Definition	Value	References
K_l	Spring constant for stretching	$5 \times 10^{-8} \text{ N m}$	[10]
K_b	Spring constant for bending	$5 \times 10^{-10} \text{ N m}$	[10]
K_s	Penalty coefficient	$5 \times 10^{-5} \text{ N m}$	[10]
ρ_{RBC}	Density of RBC membrane	1098 kg/m^3	[12]
ρ_{plasma}	Density of plasma	1025 kg/m^3	[3]
$\rho_{\text{cytoplasm}}$	Density of cytoplasm	1050 kg/m^3	[7]

velocity profile is seen. However, due to the existence of the RBC, parabolic shaped velocity profiles are not observed.

The RBC shape gradually deforms from its initial biconcave shape to a parachute shape, as the RBC advances in the Poiseuille flow (see Figure 5). Initially, RBC membrane particles follow a parabolic velocity profile, similar to the velocity profile of the Poiseuille flow. Gradually, all the RBC membrane particles reach an equilibrium velocity, which implies there is a relative motion of the RBC with respect to the plasma flow. The velocity profile of the system reveals that the plasma particles next to the capillary wall boundary have zero velocity, while the plasma particles at the centreline of the fluid flow reach the maximum velocity. Shi et al. [11] reported similar behaviour. At the steady state, the RBC obtains a parachute shape which allows it to move even through capillaries which have smaller diameters than the diameter of the RBC at rest. The steady state shape obtained by this study is comparable the shapes reported by Tsubota et al. [14]. This phenomenon is important for effective capillary mass transfer in microcirculation [15].

3.2 RBC behaviour in a linear shear flow

Fischer et al. [2] experimentally observed that the RBCs gradually deform and elongate from their initial biconcave shape to an ellipsoidal shape when

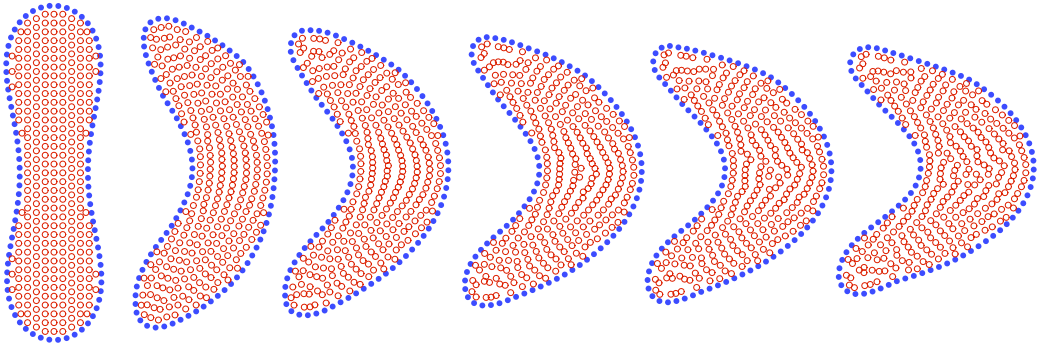


Figure 5: RBC's shape in Poiseuille flow at time 0 s, 0.002 s, 0.004 s, 0.006 s, 0.008 s and 0.01 s.

they are subjected to a shear flow. At the steady state, the deformed shape of the RBCs do not change and the RBCs make a constant inclination angle with the flow direction. Meanwhile, the RBC membrane circulates around the cytoplasm, known as tank treading motion. To verify the developed SPH model, the RBC membrane (see Section 2.1) is rotated, such that the major axis of the RBC membrane is horizontal and is put into a plasma domain. The initial particle distribution of plasma and cytoplasm is the same as in the previous section. The height and the length of the microchannel were $7\ \mu\text{m}$ and $12\ \mu\text{m}$, respectively. Shear flow is generated by the sudden motion of the upper and lower plates in opposite directions at a constant velocity of $2 \times 10^{-3}\ \text{m/s}$ and with a time step of $1 \times 10^{-9}\ \text{s}$.

Simulation results reveal that, when the RBC is subjected to a shear flow, the membrane rotates around the cytoplasm, while the RBC makes a constant angle with the vertical direction (see Figure 6). In Figure 6, the black dot represents the first particle of the RBC membrane. With time that particle rotates in a clockwise direction along the RBC membrane. Further, the velocity distribution of the whole flow field confirms the tank treading behaviour of the RBC membrane. The inside fluid of the RBC (cytoplasm) also circulates inside the membrane, due to the tank treading motion of the RBC membrane

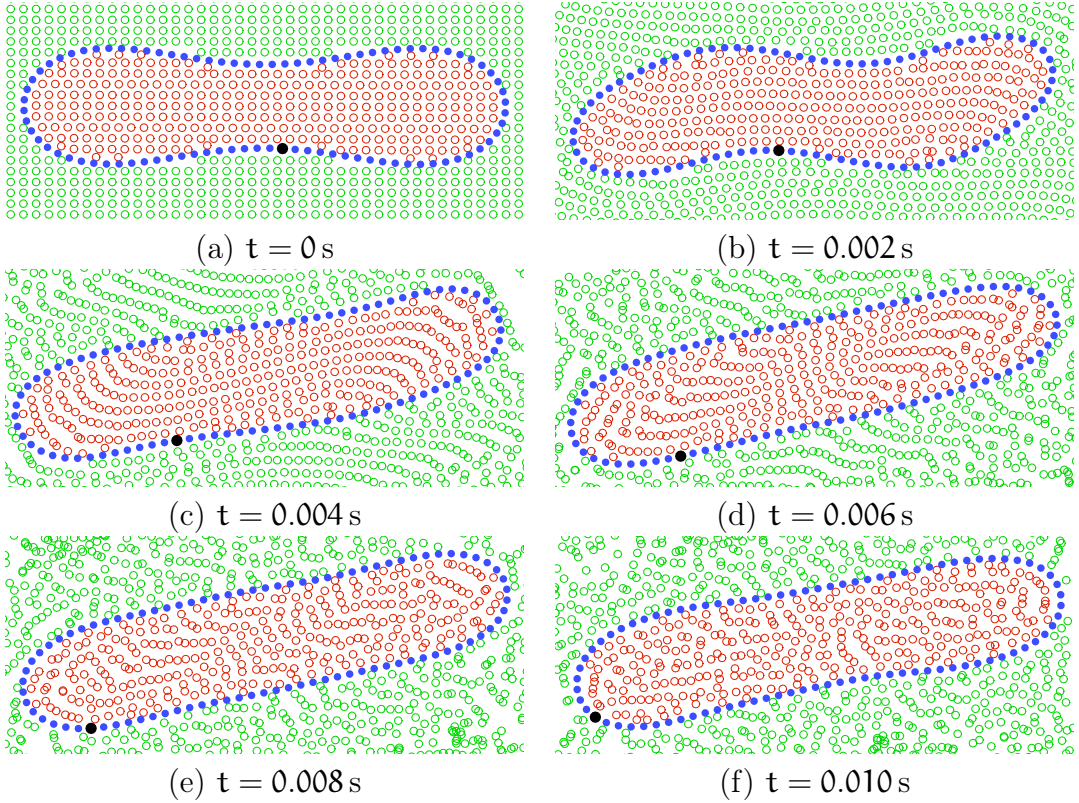


Figure 6: Tank treading motion of the RBC membrane.

(see Figure 7).

4 Conclusions

In summary, the deformation of a single RBC was simulated using the SPH method and with the aid of an existing two dimensional spring network model. The RBC membrane shape was determined using the minimum energy principal. Initially, a modified SPH code simulated the plasma flow in microchannels. For

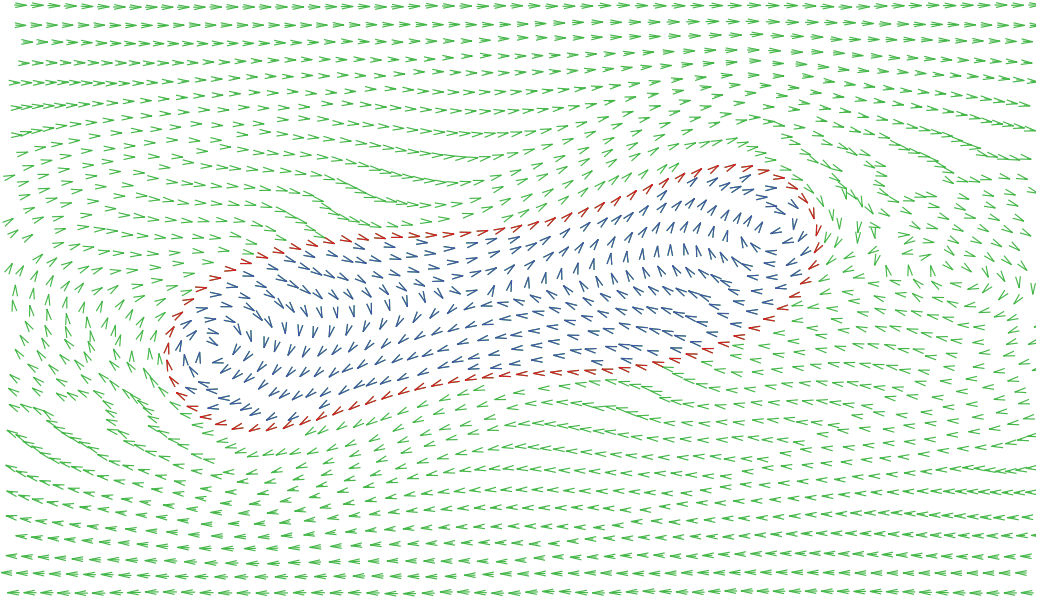


Figure 7: Velocity distribution of flow field at time 0.003 s.

the first time, the minimum energy concept was applied with SPH concepts to simulate the motion and the deformation of the RBC. The deformation of a RBC was simulated under both Poiseuille flow and linear shear flow. Results revealed that the RBC obtains a parachute shape when within a Poiseuille flow. Further, the RBC showed a tank treading motion in linear shear flow while the cytoplasm particles showed a rotational-like motion. Using the minimum energy principal with SPH concepts was successful, as the simulation results showed good agreement with previously reported results. We conclude that using the SPH method, RBC membrane fluid interactions are easily simulated. However, this model assumes that the plasma and cytoplasm have the same viscosity as water. For a more precise study, the interaction of multiple RBCs should be considered. This methodology will be extended to investigate an accurate deformation mechanism of a three dimensional RBC.

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