An immersed boundary-lattice Boltzmann model for simulation of malaria-infected red blood cell in micro-channel

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Abstract

The mechanical properties of Red Blood Cells (RBCs) are influenced by invasion and occupation of Plasmodium falciparum (Pf). The corresponding variation results from the stiffening of RBCs and their ability to adhere to endothelial cells. In this study, the transient deformation of Plasmodium falciparum-parasitized red blood cell (Pf-RBC) has been studied numerically. The cell is modeled as deformable liquid capsule enclosed by neo-Hookean elastic membrane. The effect of shear elasticity is included, but bending stiffness is neglected. The numerical model is based on the immersed boundary-lattice Boltzmann method (IB-LBM). The LBM is used to simulate fixed grid while the IBM is utilized to incorporate the fluid-membrane interaction in a Lagrangian manner by a set of moving grids for membrane. The results investigate the significance of elastic shear modulus and initial shape on hematocrit ratio and deformation of Pf-RBC at different stages. The Pf-RBC at trophozoite and schizont stages obtain the lower hematocrit ratio, as they become near-circular. The results are in good agreement with experiments and previous studies. It appears, therefore, that the IB-LBM can be used to predict in vitro and in vivo studies of malaria.

1. Introduction

Red Blood Cells (RBCs) are an important component in blood because of their large number density (~5 × 10^6/mm^3). Being highly deformable particle, RBCs (approximately 40% of blood volume) are primary cell species influencing rheological properties of blood. RBC may exhibit reduced deformability and stronger aggregation in many pathological situations, such as heart disease, hypertension, diabetes, sickle cell anemia and malaria [1]. Malaria is one of the most severe infection diseases on earth. There are about five hundred million clinical cases worldwide with more than two million deaths each year [2]. The rheological properties and hemodynamic of blood are changed by malaria infection. When a malaria parasite invades and grows within a red blood cell, the structure and biophysical characteristics of Pf-RBC are changed. The elastic shear modulus of Pf-RBC membrane may increase about ten-fold due to molecular and structural changes in the cell membrane at the late stage of schizont [3]. These changes can lead to blood vessel blockage and altered blood circulation. Understanding of hemodynamic changes is an essential step to develop new methods for identification and treatment of this disease. To design clinical therapies, it is needed to understand how the deformation of the cells is affected by fluid flow.

A major problem in microcirculation is the small dimension of vessels. The current experimental techniques are sometimes tedious or too difficult to carry out. Therefore, several mathematical and computational models with various degrees of physical relevance and idealization have been proposed to describe the motion of RBCs in microvessels and its dependence on the mechanical properties. In vessels larger than 200 µm, blood flow may be treated homogenously because the cells are much smaller than the vessel size. In vessels smaller than 200 µm, such as arterioles and venules and especially capillaries (4–10 µm), blood behaves as a multiphase suspension of deformable particles. Significant efforts have been conducted with the focus on the behavior of RBCs in various flow situations or conditions to predict their deformation and approximate apparent viscosity of RBC suspension. For example, Pozrikidis et al. [4–6] have used the boundary integral method to study RBC deformation and...
motion in shear and channel flow. Eggelton and Poppel [7] have combined Immersed Boundary Method (IBM) [8] with a finite element treatment of the RBC membrane to simulate large three-dimensional RBC deformation in shear flow. Dupin et al. [9] have improved the lattice-spring model to simulate a number of situations including elastic membrane in flow. An LBM algorithm has been also applied for RBC flow in 20–40 μm channel, where RBCs were represented as rigid particles in two dimensions [10,11]. Bagchi [12] has simulated a large cell population comprising of as high as 2500 RBCs in the range of vessel size 20–30 μm and discharge hematocrit 10%–60%. Recently, Zhang et al. [13,14] have developed an integrated IB-LBM to study RBC behavior in both shear and channel flow. They have also investigated the effect of different kinds of deformability and aggregation strengths on cell-free layer structure and flow resistance in microscopic blood flow [15]. Ma et al. [16] have combined the finite volume method with front tracking technique to study motion of two-dimensional capsule in microchannel with different initial shapes and positions. Sun and Munn [17] have also developed their lattice Boltzmann model by including an interaction force between rigid RBCs. Xiong and Zhang [18] have utilized an IB-LBM to analyze the included wall shear variation for RBC flowing in microvessel.

The numerical analysis for the stretching of a Pf-RBC by optical tweezers has been conducted by Suresh et al. [19]. Although their model can be useful for understanding malaria pathology quantitatively, the Pf-RBC membrane model is not coupled with flow. More recently, a remarkable step in simulation of Malaria-infected red blood cell has been achieved. For example, a two-dimensional model for malaria infection between parallel plates is proposed by Kondo et al. [20]. Their model has demonstrated that the deformability and adherent property of Pf-RBC affect the blood flow. Imai et al. [21] have used a particle method to analyze the three-dimensional hemodynamic arising in malaria infection. They have also investigated the effect of Pf-RBC on the rheological property of blood in microchannels. There have not been many mesoscopic simulations performed for Pf-RBC in small vessels.

The numerical method used in this paper combines the LBM for solving the fluid problem with IBM proposed by Peskin [8] for capturing and tracking the cell membrane. As compared to traditional computational fluid dynamics, the major advantage of LBM is its simplicity, easy for implementation, algebraic operation and intrinsic parallel nature. LBM is a particle-based numerical technique, which has been proven to be an efficient approach for simulation of flow field. Based on kinetic theory, for the particle distribution function, the macroscopic quantities are obtained through moment integration of distribution function. In the early 1990, Ladd [22,23] well applied LBM to simulate particle fluid suspensions. As an alternative technique to Navier–Stokes solver, LBM has achieved great success in simulating particulate fluid in the past decade. When the boundaries are geometrically irregular or undergoing large deformation, some fluctuations in the resulting computation of forces and velocities of the particle are observed.

The concepts of IBM first have been proposed by Peskin [8] in the 1970s in order to model flow in the heart. IBM uses a fixed Eulerian mesh for flow field, which is in fact the fixed Cartesian mesh points, and a set of Lagrangian points to represent the physical boundaries.

The results have been validated by comparing results with other simulations. The main goal of the present article is computational simulation of the motion of Pf-RBC flowing through a two-dimensional channel of size 20 μm as closely as possible subject to the constraints of two-dimensionality. The flow field is solved by LBM, and the fluid-membrane interaction is explicitly tracked by IBM. This article presents a short time simulation of the dynamic behaviors of deformable healthy RBC and Pf-RBC at different parasitemia levels in flow fields by using IB-LBM. The numerical results are demonstrated with other experimental and numerical observations.

2. Materials and methods

2.1. Lattice Boltzmann method

LBM is a kinetic theory-based method for simulating flow fluid and transport phenomena. It decomposes the continuous
flow fluid into pseudo-particle which can move or stay at rest over lattice domain. The composition of lattice node depends on the lattice model which is used. The D2Q9 model using a square Cartesian mesh with nine possible velocities (see Figure 1) is one of the most popular models in two dimensions, in which the discrete lattice Boltzmann equation in classical statistical physics has the form of [24]:

\[
f_i(x + e_i \Delta t, t + \Delta t) - f_i(x, t) = -\frac{1}{\tau} \left[ f_i(x, t) - f_{eq}^i(x, t) \right], \quad (1)
\]

where \( f_i(x, t) \) is the density distribution function, indicating the particle amount moving in the \( i \)th lattice direction with velocity \( e_i \) at position \( x \) and time \( t \). \( \Delta t \) is the time step. \( f_{eq}^i(x, t) \) is the equilibrium distribution function and \( \tau \) is the relaxation time. For the D2Q9 model, the discrete velocities of the fluid particles are given by:

\[
e_i = \begin{cases} 0 & \text{for } i = 0 \\ \left( \cos \left[ \pi (i - 1)/2 \right], \sin \left[ \pi (i - 1)/2 \right] \right) c & \text{for } i = 1, 2, 3, 4 \\ \sqrt{2} \left( \cos \left[ \pi (9 - 2i)/2 \right], \sin \left[ \pi (9 - 2i)/2 \right] \right) c & \text{for } i = 5, 6, 7, 8 \end{cases}, \quad (2)
\]

where \( c = \Delta x/\Delta t \) is the particle streaming speed, \( \Delta x \) and \( \Delta t \) are lattice spacing and time step. For the case of \( \Delta x = \Delta t \), \( c \) is taken as 1. The corresponding equilibrium distribution \( f_{eq}^i \) can be expressed as:

\[
f_{eq}^i = E_i(\rho, u), \quad (3)
\]

\[
E_i(\rho, u) = w_i \rho \left[ 1 + \frac{u_i \cdot e_i}{c_s^2} + \frac{9}{2} \left( \frac{u_i \cdot e_i}{c_s^2} \right)^2 - \frac{3}{2} \frac{u^2}{c_s^2} \right], \quad (4)
\]

where \( c_s = c/\sqrt{3} \) is the sound speed and \( w_i \) is the weighting factor for the various lattice links as follow.

\[
\begin{align*}
& w_0 = 4/9 \\
& w_i = 1/36 \quad \text{for } i = 1, 2, 3, 4 \\
& w_i = 1/9 \quad \text{for } i = 5, 6, 7, 8.
\end{align*} \quad (5)
\]

In the discrete velocity space, the macroscopic density and momentum can be calculated by:

\[
\rho = \sum_i f_i, \quad (6)
\]

\[
\rho u = \sum_i e_i f_i, \quad (7)
\]

The kinematic viscosity of the fluid in Navier–Stokes is related to the relaxation time by the following equation:

\[
v = \left( \tau - \frac{1}{2} \right) c_s^2 \Delta t, \quad (8)
\]

and the pressure \( p \) is expressed as:

\[
p = c_s^2 \rho. \quad (9)
\]

The standard LBM is an explicit-time-step solver for isothermal compressible flows within the continuum and incompressible limit. In the computation, the temporal step can be split in a streaming step, which accounts for advection and in a collision step, to represent inter-particle interaction. Thus Eq. (1) is computed by the following sequence:

\[
\tilde{f}_i(x, t + \Delta t) = f_i(x, t) - \frac{1}{\tau} \left[ f_i(x, t) - f_{eq}^i(x, t) \right], \quad (10a)
\]

\[
f_i(x + e_i \Delta t, t + \Delta t) = \tilde{f}_i(x, t + \Delta t), \quad (10b)
\]

where \( \sim \) denote post-collision state of the distribution function. It is noted that the collision step is local, that is, it does not require any spatial temporal derivatives. The streaming step following the collision simply moves the updates distribution functions from one lattice to neighboring nodes. Each time step of the LBM scheme consists of the following sub-steps:

1. Initialize \( \rho, u \).
2. Initialize \( f = f_{eq} \).
4. Calculate \( u \) and \( \rho \) by using Eqs. (6) and (7).
5. Calculate \( f_{eq} \) from \( u \) and \( \rho \) by using Eqs. (3) and (4).

### 2.2. Immersed boundary method

Peskin [8] developed the novel Immersed Boundary Method (IBM) to simulate deformable membranes in flow field. The interaction between incompressible viscous fluid and elastic membrane (fluid–membrane interaction) is achieved by distributing membrane forces and updating membrane configuration according to local flow velocity.

A two-dimensional segment of the membrane and nearby fluid domain is shown in Figure 2. The fluid domain is denoted by \( \Lambda \) containing a mass less elastic filament with boundary \( \Psi \). The boundary configuration is represented by Lagrangian
coordinate s, the fluid domain is represented by Eulerian coordinate x and any position on the membrane is denoted by \( X(s,t) \). The no-slip boundary condition is satisfied by enforcing the velocity at boundary nodes to be equal to the velocity of its adjacent fluid as follow:

\[
\frac{\partial X(s,t)}{\partial t} = u(X(s,t),t),
\]

where \( u \) is the fluid velocity. The fluid–structure interaction is modeled by adding a force term to the right-hand side of the Navier–Stokes equation which governs the fluid motion. The force density of fluid \( f(x,t) \), may be obtained from the membrane force density \( F(s,t) \) induced by membrane deformation and obtained from its constitutive law.

\[
f(x,t) = \int_\nu F(s,t) \delta(x-X(s,t)) \, ds,
\]

where:

\[
\delta(r) = \begin{cases} 
\frac{1}{4} + \cos \left( \frac{\pi |r|}{2} \right) & r \leq 2 \\
0 & r > 2.
\end{cases}
\]

In which \( r \) is the distance between Eulerian and Lagrangian nodes divided by the Eulerian grid space. For two-dimensional cases the discrete delta function can be written as follow:

\[\delta(x-x_0) = \delta(y-y_0).\]

The velocity of Lagrangian points on moving boundary is obtained from velocities of Eulerian points as follows:

\[
\frac{\partial X(s,t)}{\partial t} = \int_\Lambda u(x,t) \delta(x-X(s,t)) \, dx.
\]

### 2.3. Immersed boundary-lattice Boltzmann method

In order to solve problems with a body force, the common lattice Boltzmann equation must be modified. In practical application, Guo et al. [25] have modified lattice Boltzmann equation in the following form:

\[
f_i(x+t, t + \Delta t) - f_i(x,t) = -\frac{1}{\tau} [f_i(x,t) - f_i^{eq}(x,t)] + \Delta t F_i
\]

\[
f_i^{eq} = E_i(\rho, u^*),
\]

\[
\rho u = \sum_i e_i f_i + \frac{1}{2} J'' \Delta t,
\]

\[
F_i = \left( 1 - \frac{1}{2 \tau} \right) \omega_i + \left[ \frac{e_i - u}{c_i^2} + \frac{(x^* - u)}{c_i^2} \right] \cdot J'.
\]

\( J' \) is in fact, the force density of the fluid, \( f(x,t) \), which may be obtained from the immersed boundary force density \( F(s,t) \) through the integration over the immersed boundary by Eq. (12).

### 2.4. RBC membrane mechanics

Following equation suggested by Evans and Fung [26], is used to describe biconcave shape of RBC:

\[
\bar{y} = 0.5 (1 - \bar{x}^2) \left( c_0 + c_1 \bar{x}^2 + c_2 \bar{x}^4 \right) - 1 < \bar{x} < 1.
\]

In which \( c_0 = 0.207 \), \( c_1 = 2.002 \), and \( c_2 = 1.122 \), and the non-dimensional coordinates \( \bar{x} \) and \( \bar{y} \) are scaled as \( x/3.91 \) and \( y/3.91 \), respectively. As the profile is symmetric with respect to x and y axes, thus the center of \((x,y)\) coordinate is on the intersection of symmetric axes.

The RBC membrane mechanics is described by Neo–Hookean model, in which the membrane material is assumed incompressible and isotropic. RBC membrane is strongly resistant to area dilatation, but this modeling does allow area dilatation. For the two-dimensional RBC membrane in the present study, following Bagchi [12], the neo–hookean elastic component of membrane stress is given by:

\[T_e = \frac{E_s h}{\varepsilon^{3/2}} (\varepsilon^3 - 1),\]

where \( E_s \) is elastic shear modulus of the membrane, \( h \) is the thickness and \( \varepsilon \) is the stretch ratio. Furthermore, the bending resistance is neglected. For the 2D simulations considered here, the membrane is a closed curve. The 2D cell is then equivalent to an actual 3D cell subject to a stretching in one direction only. That is, \( T_1 \neq 0, T_2 = 0, \) where \( T_1 \) indicates the “in plane” direction along the membrane, and \( T_2 \) indicates the “out of plane” direction normal to Figure 2.

For a discretized cell, \( T_i \) is the tension along a line segment connecting two adjacent Lagrangian grid points on the membrane, and \( \varepsilon_i \) is the stretch ratio (undeformed length by deformed length) of the line segment. At any Lagrangian grid point on the membrane two line segments meet.

The membrane elastic force \( F_i \) at the Lagrangian point is then the resultant vector of the tensions in the two adjacent segments:

\[F_i = T_i n_i - T_j n_j,\]

where \( i \) and \( j \) denotes two adjacent line segments, and \( n_i \) and \( n_j \) are the unit tangent vectors along them.

### 2.5. Immersed boundary-lattice Boltzmann algorithm

Each time step of the combined IB-LBM scheme consists of the following sub-steps:

1. Impose the fluid velocity on the boundary and update the boundary points’ positions to \( X(s,t) \) by using Eq. (11).
2. Calculate the force density \( F(s,t) \) at the boundary points from membrane stress by using Eq. (21).
3. Spread the boundary point force \( F(s,t) \) to the fluid external force \( f(x,t) \) by using Eq. (12).
4. Calculate the LBMs’ external forcing terms \( F_i \) by using Eq. (19).
5. Perform Lattice Boltzmann equation evolution (Eq. (16)) to obtain the distribution functions \( f_i \).
6. Calculate the fluid flow variables \( \rho \) and \( u \) by Eqs. (6) and (18).

### 3. Numerical results and discussion

Simulations are carried out over a \( 100 \times 300 \) rectangle in lattice units \((20 \mu m \times 60 \mu m)\) per lattice unit: \( \Delta x = 0.2 \mu m \) with a single RBC. The simulation parameters based on experimentally determined data, are listed in Table 1. The bounce-back and periodic boundary conditions are applied on the channel walls and inlet/outlet, respectively [24].

The IBM algorithm ensures that there will be no relative velocity between membrane and fluid, therefore no mass transport across the membrane can occur and the volume of RBC is naturally conserved. The results show that the change in the enclosed RBC area is less than 1%.

Flow is generated by a pressure-gradient along the channel, using the modified periodic boundary condition [27]. The pressure gradient, according to the Poiseuille law, will generate a mean velocity of 7.5 mm/s for pure plasma flow without RBCs.
The present model is applied to simulate the deformation of healthy RBC and Pf-RBC at different stages of parasite development in Poiseuille flow in a rectangular microchannel of 20 μm. Under diseased condition, progression through the parasite development stages (ring → trophozoite → schizont), Pf-RBC lose their deformability compared to the healthy one [3,28]. Moreover, the shape of Pf-RBC at each stage is determined experimentally. During the ring stage, RBC maintains its biconcavity. Thus, the initial resting shape of the healthy and ring stage RBC are considered biconcave. In the next two stages trophozoite and schizont, the RBC shape becomes near spherical. The IBS2 (Iran Baluchistan Sye 2) strain of *Plasmodium falciparum* is used in this study. Ring stage parasites are synchronized by using d-sorbitol 18% in Phosphate-Buffered Saline (PBS) for treatment. The synchronized parasites are further cultured to trophozoite and schizont stages. Furthermore, the optical microscope (Olympus BX41, Olysysa software) images for stages of RBCs which were infected by *Plasmodium falciparum* parasites are given from thin blood film. New mathematical shape equations for RBCs in all three stages of *Plasmodium* growth (ring, trophozoite and schizont) are defined; these equations can be helpful for blood simulation in vessels and can give a good concept for simulation and treatment of this dangerous disease. Consequently, the curves for trophozoite and schizont stages are obtained experimentally. The experimental process is being published in another paper. The simulation results are obtained with elastic shear modulus $E = 6.3 \times 10^{-6}$ N/m for healthy RBC, 14 for ring stage, 29 for trophozoite and 60 μN/m for schizonte; these values are in agreement with the experiment [28].

Evolution of positions and shapes of healthy and Pf-RBCs in different stages are illustrated in Figure 3. At time $t = 0$, the initial $y$ coordinate of the cell center position is 10 μm, meaning that the cell flows along the centerline of the channel. The initial $x$ coordinate of the capsule center in this study is chosen 5 μm. The simulations correspond to 1.94 ms in real time.

As shown in Figure 3, the cell shape gets more convex at the front and becomes more concave at the rear, in agreement with shapes predicted in vivo and vitro experiments [16,18] in which the front/downstream end of capsule bulges or gets less concave, and the rear/upstream end becomes less convex or more concave, showing more or less similar parachute shapes predicted for capsules and red blood cells. The cell shape undergoes deformation due to hydrodynamic stresses imposed by the background Poiseuille flow on the RBC membrane. It can be seen from Figure 3(a) and (b) that in the ring stage, no significant difference is observed [29]. For trophozoite and Schizont stages, upper membrane elastic shear modulus together with less biconcave shape renders the cell with more resistance to flow force and less obvious deformation.

### Table 1: Simulation parameters.

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Delta x$</td>
<td>Lattice unit</td>
<td>0.2 μm</td>
</tr>
<tr>
<td>$\Delta t$</td>
<td>Time step</td>
<td>$2.77 \times 10^{-3}$ s</td>
</tr>
<tr>
<td>$\mu_p$</td>
<td>Plasma viscosity</td>
<td>1.2 cP</td>
</tr>
<tr>
<td>$\rho_s$</td>
<td>Plasma density</td>
<td>1000 kg/m$^3$</td>
</tr>
<tr>
<td>$E_s$</td>
<td>Membrane elastic modulus</td>
<td>6.3 × 10$^{-6}$ N/m</td>
</tr>
<tr>
<td>$H$</td>
<td>Channel height</td>
<td>20 μm</td>
</tr>
<tr>
<td>$L$</td>
<td>Channel length</td>
<td>60 μm</td>
</tr>
<tr>
<td>$\Delta P$</td>
<td>Axial pressure gradient</td>
<td>270 kPa/m</td>
</tr>
</tbody>
</table>

![Figure 3: Evolutions of positions and shapes of the (a) healthy RBC, (b) ring stage, (c) trophozoite stage, and (d) schizont stage.](image-url)
also the long axes of their equimomental ellipses are along perpendicular direction to the flow, similar to Ref. [16] in which the dispersion of biconcave and circular centerline capsules increases with time and the long axes of their equimomental ellipses are along \( y \) direction in the whole simulation time range.

The Fahraeus effect [30] indicates that tube hematocrit in microvessels \( (H_T) \) of less than 200 \( \mu \)m is lower than supply hematocrit \( (H_D) \). This is due to the fact that RBC mean velocity is higher than mean fluid velocity. The velocity difference originates from RBCs concentration in the center of the vessel. A simple mass balance predicts the relation between hematocrit ratio \( H_T/H_D \) and velocity ratio as:

\[
\frac{H_T}{H_D} = \frac{U_{avg}}{U_c}, \tag{22}
\]

where \( U_{avg} \) is the mean velocity of the whole suspension and \( U_c \) is the cell velocity. The lower bound of \( H_T/H_D \) can be derived by setting the cell velocity equal to the centerline velocity of 2D Poiseuille flow, \( U_c = 3/2U_{avg} \) where upon \( H_T/H_D = 2/3 \). The initial cell velocity is near to centerline velocity of Poiseuille flow, because cell with zero speed is suddenly inserted in the background flow and the cell membrane velocities are obtained according to local flow field. Consequently, the initial value of \( H_T/H_D \) is near to its minimum value, 2/3. The evolution of the hematocrit ratio for healthy and Pf-RBC in different stages are shown in Figure 6. After a rapid increase from lower value at the beginning, the hematocrit ratio for all cases increases with time and shows some similar behavior. Hematocrit ratio for healthy and ring stage RBC almost coincide, while changes in membrane mechanical and geometrical properties lead to significant differences in hematocrit ratio for the trophozoite and schizont stages with healthy and ring stages. The hematocrit ratio is even lower at trophozoite and schizont stages where the Pf-RBC shape becomes near-circular, i.e., the higher translational velocity. The healthy and ring stage RBC have higher hematocrit ratios, i.e., the lower translational velocity. Ma et al. [16] also found that the biconcave capsule has higher hematocrit ratio with respect to circular capsule. For schizont stage, the hematocrit ratio in comparison with trophozoite stage, increases with elastic shear modulus, i.e. the capsule translational velocity decreases with increasing elastic shear modulus, showing similar trend to the centerline circular capsule in [16,18].

4. Conclusion

The transient motion and deformation of healthy and Pf-RBC at different stages are studied in a two-dimensional microchannel. The numerical simulation method is based on
where $A_i = 0.5(x_iy_{i+1} + x_{i+1}y_i - x_{i+1}y_{i+1} - x_{i+1}y_{i-1})$. From the zero- and first-order moments, the centroid of the 2D shape is calculated by the following equations:

\[
\begin{align*}
X_c &= m_{10}/m_{00} \\
Y_c &= m_{01}/m_{00},
\end{align*}
\] (A.2)

Three second-order central moments are calculated as:

\[
\begin{align*}
\mu_{20} &= m_{20} - (m_{10}^2/m_{00}) \\
\mu_{11} &= m_{11} - (m_{10}m_{01}/m_{00}) \\
\mu_{02} &= m_{02} - (m_{01}^2/m_{00}).
\end{align*}
\] (A.3)

Based on the above variables, three normalized central moments, which are invariant to change in size of the 2D shape, are given as follows:

\[
\begin{align*}
\eta_{20} &= \mu_{20}/m_{00}^2 \\
\eta_{11} &= \mu_{11}/m_{00} \\
\eta_{02} &= \mu_{02}/m_{00}. \\
\end{align*}
\] (A.4)

Two second-order measures of shape that are invariant to rotation are expressed as:

\[
\begin{align*}
\phi_1 &= \eta_{20} + \eta_{02} \\
\phi_2 &= (\eta_{20} - \eta_{02})^2 + 4\eta_{11}.
\end{align*}
\] (A.5)

The two rotational invariants can be calculated:

\[
\begin{align*}
\lambda_1 &= 2\pi \left( \phi_1 + \sqrt{\phi_2} \right) \\
\lambda_2 &= 2\pi \left( \phi_1 - \sqrt{\phi_2} \right).
\end{align*}
\] (A.6)

The morphological measures, extension, dispersion of 2D shape can be determined by:

\[
\begin{align*}
m_{ex} &= \log(\lambda_1) \\
m_{dy} &= \log_2 (\sqrt{\lambda_1\lambda_2}).
\end{align*}
\] (A.7)

References


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Marzieh Rezazadeh received her M.Sc. degree from Mashhad University, Iran, and is now a Ph.D. degree student of Mechanical Engineering at Iran University of Science and Technology, Iran. Her main research interest includes work on the numerical simulation of red blood cell in microchannel flow, numerical methods such as control volume, lattice Boltzmann method, and immersed boundary method.