

Comparison between the discrete erythrocyte method and constitutive equations for blood

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There are a number of methods for analyzing blood flow; however, their applicability and advantages are not sufficiently clear. In this research, the characteristics of a discrete erythrocyte method (DEM), which is proposed by the present authors, are compared with constitutive equations for blood. The Casson model and a pseudo-Casson model are chosen and compared with the DEM. By discussing the advantages and disadvantages of DEM, its applicability to blood flow simulation is clarified. The results show that the DEM is an appropriate method for simulating the blood flow in small vessels. Moreover, the DEM can express certain rheological properties that are not expressed by the constitutive equations.

Key words: blood flow, discrete erythrocyte method, constitutive equations for blood

1. Introduction

The blood flow in an artery is widely investigated because fluid dynamical factors play an important role in the development of arterial diseases. The blood flow in large arteries is commonly analyzed by means of constitutive equations for blood [1]–[4]. The Casson model [5], often used as a constitutive equation for blood, is known as an appropriate model for large vessels; however, it cannot express the elasticity of blood. Besides, it is not suitable for blood plasticity either, because shear rate and shear stress do not correspond one-to-one when the shear stress is lower than the plasticity. Therefore, the pseudo-Casson model [2], [6] should be used in order to compute complex flow fields.

Constitutive equations suffer from another disadvantage – they are not appropriate for small arteries. In a small artery, the distribution of erythrocytes in the flow field affects their rheological properties; however, the constitutive equations assume homogeneity of the fluid. It is, therefore, hard to explain basic phenomena of blood flow such as the Fahreus–Lindqvist effect [7], etc. In order to simulate blood flow in a small artery, it is necessary to compute simultaneously both the erythrocyte motions and the flow field.

There are several ways to compute both the erythrocyte motions and the flow field simultaneously. One way is to assume an erythrocyte as a rigid elliptic body. With this method, it is possible to compute erythrocyte distributions in a flow field without a high computational load. However, the erythrocyte deformation cannot be expressed in such a way. Therefore, this method cannot be applied in the description of the shear-thinning property and the elasticity induced by the deformation of an erythrocyte. Another way is to treat the blood as a liquid–liquid two-phase fluid [8]–[11]. This method allows us to compute the droplet deformation if we accept the high computational load. This method, however, cannot model the stress tensor on the membrane of an erythrocyte, which results in neglecting basic properties of blood.

The behaviour of a single erythrocyte with a membrane was simulated in detail by POZRIKIDIS [12]–[15]. Although his method consistently expresses blood rheology, it requires a high computational load for computing practical blood flows, in which five million of erythrocytes exist per 1 mm^3 . It is, therefore, necessary to simplify the erythrocyte model so that the stress tensor on the membrane is appropriately expressed avoiding a high computational load. In order to express the basic properties of blood such as the shear-thinning property, elasticity and so on, an erythrocyte model is required to express the deformation of an erythrocyte and its membrane.

Keeping this in mind, the authors proposed a new erythrocyte model as an alternative way to simulate blood flow [16], [17]. The model is called *the discrete erythrocyte method* (DEM), in which an erythrocyte is modelled by using beads and springs. Then the DEM is modified in such a way that drag points are used instead of beads [18], [19]. The drag points represent the fluid dynamical drag force acting on the membrane of an erythrocyte, while the springs represent the elasticity of the membrane. This method can approximate the deformation of an erythrocyte with its membrane and the distribution of erythrocytes in the flow field without a high computational load, therefore, it can express the rheological properties of blood sufficiently well.

There are a number of methods for analyzing the blood flow; however, their applicability and advantages are not quite clear. In this research, the characteristics of the DEM are compared with the constitutive equations for blood, and the advantages and disadvantages are discussed. Then the applicability of the DEM to blood flow simulation is clarified.

2. Constitutive equations

2.1. Casson model [5]

The Casson model is often used to derive the constitutive equation for blood. It is expressed in one dimension as follows:

$$\begin{aligned} \sqrt{\tau} &= \sqrt{p_y} + \sqrt{\mu\dot{\gamma}} & : \quad \tau \geq p_y, \\ \dot{\gamma} &= 0 & : \quad \tau < p_y, \end{aligned} \quad (1)$$

where: τ – the shear stress, p_y – the yield stress, μ – the viscosity and $\dot{\gamma}$ – the shear rate.

2.2. Pseudo-Casson model [2], [6]

Although the Casson model is often used as the constitutive equation for blood, it is very troublesome in a numerical simulation. In the Casson model, the shear rate falls to zero, while the shear stress is below the yield stress. Therefore, shear stress and shear rate do not correspond one-to-one in this shear stress range. To avoid this difficulty, one of the authors proposed the pseudo-Casson model. The dimensionless constitutive equation for the pseudo-Casson model is

$$\tau_{ij} = 2 \left[1 + \sqrt{\frac{2He}{Re\sqrt{2|\Pi|} + 2\beta He}} \right]^2 \cdot e_{ij}, \quad (2)$$

where: Re is the Reynolds number $\left(\equiv \frac{\rho U d}{\mu} \right)$, He – the Hedstrom number $\left(\equiv \frac{\rho p_y d^2}{4\mu^2} \right)$, ρ – the density, U – the characteristic velocity, d – the characteristic length, e_{ij} – the (i, j) component of the deformation rate tensor and Π is defined as $\Pi = e_{ij} \cdot e_{ji}$.

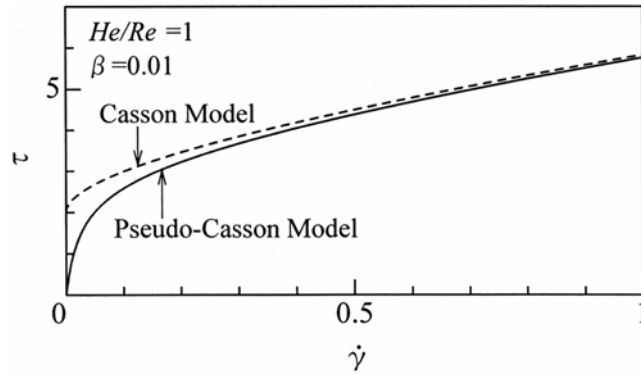


Fig. 1. $\tau - \dot{\gamma}$ correlation of constitutive equations

In this equation, only β is a model constant. The value $1/\beta$ adjusts the viscosity in the low-shear rate region, i.e. the plug region. If β is small enough, the viscosity in the plug region is so large that the results obtained based on the pseudo-Casson model and based on the Casson model are not very different from each other. However, for very small β , the

viscosity changes drastically at the boundary of the plug region, which may cause the instability in the numerical analysis. According to former research [6], the optimum value of β is approximately 0.01. The one-dimensional $\tau - \dot{\gamma}$ correlation of the constitutive equations is shown in figure 1.

3. Discrete erythrocyte method [16]–[19]

3.1. Erythrocyte model

Most of the blood cells consist of erythrocytes, therefore, in the present model the blood is assumed be a suspension of erythrocytes and plasma. An erythrocyte is modelled by using six drag points and fifteen springs as shown in figure 2. This kind of modelling is similar to the modelling of polymer chains in polymer solutions. In order to derive a constitutive equation for polymer solutions, many researchers assume a bead–spring model for a polymer chain.

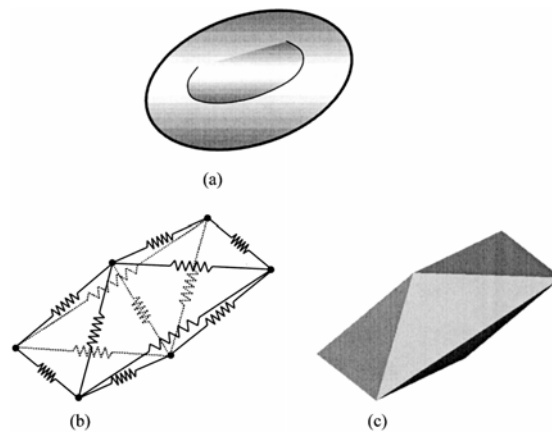


Fig. 2. Modelling an erythrocyte: erythrocyte (a), schema of erythrocyte model (b), imaginary appearance of the model (c)

The drag points in figure 2 express the fluid dynamical drag force acting on the membrane of an erythrocyte, and the springs express the elasticity of the membrane. It is considered that these two forces dominate the stress tensor of an erythrocyte. In this model, the following three points are assumed: (1) the drag force acting at the drag point is calculated from the drag coefficients based on Stokes's law, (2) the inertia of a drag point is neglected, (3) a dilute suspension of erythrocytes and plasma is assumed, therefore the interaction between erythrocyte models is neglected.

If the number of drag points is increased, it is possible to imitate the biconcave shape of an actual erythrocyte. However, a large number of drag points has a high computational load, which we want to avoid. The DEM ought to express the stress tensor generated by

an erythrocyte avoiding a high computational load. The DEM is supposed to be applied to a practical flow field in which the computational mesh size is larger than half of the erythrocyte diameter. Therefore, the erythrocyte model does not need to express higher mode deformations by increasing the number of drag points.

In figure 2, the length of the major axis is set to $1.3D$ and that of minor axis is set to one third of it. D is the length of the major axis of an erythrocyte, which is given as $8 \mu\text{m}$. The equilibrium length of each spring is given so that the springs generate no force under natural conditions shown in figure 2. The drag force acting at the drag point is calculated as the sum of the force acting at the drag point and one sixth of the force acting at the center of gravity of the erythrocyte model by assuming Stokes's law.

The drag coefficients at the drag point are given as $K_n = K_h = 1.13 \mu D \text{ Pa}\cdot\text{s}\cdot\text{m}$, and the drag coefficients at the center of the gravity are given as $K_n = 1.5 \mu D$, $K_h = 0$, where K_h is the drag coefficient against uniform flow in the direction of the major axis, K_n – for the minor axis direction, and μ the viscosity of the plasma. The total drag coefficients of the erythrocyte model are derived to be: $K_n = 8.28 \mu D$, $K_h = 6.78 \mu D$, $L_n = 1.91 \mu D^3$ and $L_h = 1.06 \mu D^3 \text{ Pa}\cdot\text{s}\cdot\text{m}$. L_h is the drag coefficient against the rotation about the major axis, and L_n for that about the minor axis. These values are similar to the drag coefficients of an elliptic body ($K_n = 8.28 \mu D$, $K_h = 6.78 \mu D$, $L_n = 1.91 \mu D^3$ and $L_h = 1.38 \mu D^3$), whose major and minor axes are D and $D/3$, respectively. Therefore, the erythrocyte model generates drag forces against a uniform flow and a rotational flow similar to that of an actual erythrocyte.

The spring constant of an erythrocyte model is given as $5.0 \times 10^{-6} \text{ N/m}$. The plot in figure 8 confirms that the deformation of an erythrocyte model with this spring constant subject to constant shear fields corresponds well to experimental results obtained by BESSIS and MOHANDAS [20].

3.2. Governing equations

Since in the DEM, the blood is assumed to be a dilute suspension of erythrocytes and plasma, the interactions between erythrocyte models are neglected. A governing equation for a drag point i in an erythrocyte model is given by equation (3) that shows the balance of the drag force and the spring force:

$$1.13\mu D(\mathbf{u}_i - \mathbf{v}_i) + \frac{1.5\mu D}{6} \{(\mathbf{u}_g \cdot \mathbf{n} - \mathbf{v}_g \cdot \mathbf{n})\mathbf{n}\} = - \sum_j^m \left\{ \frac{\mathbf{r}_i - \mathbf{r}_j}{|\mathbf{r}_i - \mathbf{r}_j|} k(l - l_0) \right\}, \quad (3)$$

where \mathbf{u} is the velocity of plasma, \mathbf{v} – the velocity of an erythrocyte model, \mathbf{r} – the position of the drag point, \mathbf{n} – the unit vector in the minor axis direction, l – the length of a spring, l_0 – the equilibrium length of a spring. The subscript i indicates the position at a drag point i , and the subscript g indicates the position at the center of gravity of an erythrocyte model. The left side expresses the drag force that is the sum of the force

acting at the drag point and one sixth of the force acting at the center of gravity of the erythrocyte model. The drag force is calculated from the drag coefficients by assuming Stokes's law. The right side of equation (3) represents the spring force, where the subscript j stands for the drag point connected with the point i by the spring.

The governing equation for the plasma is given as follows:

$$\rho \frac{\partial \mathbf{u}}{\partial t} + \rho(\mathbf{u} \cdot \nabla) \mathbf{u} = -\nabla p + \mu \nabla^2 \mathbf{u} - \frac{1}{\Delta V} \sum_{m=1}^{\Delta N} \left[1.13 \mu D (\mathbf{u}_i - \mathbf{v}_i) + \frac{1.5 \mu D}{6} \{ (\mathbf{u}_g \cdot \mathbf{n} - \mathbf{v}_g \cdot \mathbf{n}) \mathbf{n} \} \right], \quad (4)$$

where p is the pressure, ΔV – the volume of a computational cell of a flow field and ΔN – the number of the drag points in ΔV . The last term in equation (4) denotes the reaction from the erythrocyte models in ΔV . By solving equations (3) and (4) simultaneously, it is possible to simulate a blood flow without using a constitutive equation.

3.3. Numerical methods

In order to simulate a blood flow, initially thousands of erythrocyte models are randomly put in the flow field with random attitudes. Then the motion of the erythrocyte models and the flow field are computed simultaneously. The motion of the erythrocyte models and the flow field are calculated three dimensionally. Equation (3) is solved by the Runge–Kutta scheme of a fourth-order accuracy, and equation (4) is solved by an implicit Euler scheme. At the wall boundary, complete inelastic collision is assumed for a drag point. The rebounding and the friction between the drag point and the wall are neglected, because the value of the Reynolds number of erythrocyte is very small and the collision is mainly dominated by the viscous force of the plasma. After a certain period of simulation, the velocity distribution of the flow field converges. The computation is continued until this convergence is obtained.

4. Applicability to the flow field

The applicability of the constitutive equations and the DEM to flow field modelling is listed in table 1.

Table 1. Applicability to flow field

Flow Field	Casson	Pseudo-Casson	DEM
Complex geometry	no	yes	Yes
Large vessel	yes	yes	high load
Small vessel	no	no	Yes
Capillary	no	no	no

High hematocrit	yes	yes	no
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4.1. Complex geometry

In the Casson model, the shear stress and the shear rate do not correspond one-to-one when the shear stress is below the yield stress, therefore, the stress tensor in the momentum equation cannot be replaced by the deformation rate tensor. In this case, the number of unknown variables, including the stress tensor, is higher than the number of equations, which are the continuity equation and the momentum equation. Generally it is impossible to solve such simultaneous partial differential equations. However, this becomes possible for sufficiently simple flow fields, for example, a developed steady flow in a straight pipe. In this flow field, the stress tensor can be calculated before knowing the velocity, which makes it possible to divide the flow region into a plug region and a non-plug region. Once we divide the flow region, it is not so hard to solve the velocity. It is said that the normal flow field is too complex to allow us to calculate the stress tensor in advance and that it is impossible to solve it by using the Casson model.

Bearing this in mind, one of the authors proposed a pseudo-Casson model [2], [6]. The concept of this model is similar to that of the bi-viscosity model [21] used instead of the Bingham model. In the pseudo-Casson model, the shear stress and the shear rate always correspond one-to-one, and the number of unknown variables is the same as the number of equations. In this case, we can solve a flow field in the same way as for other non-Newtonian fluids. It is said that even complex flow fields can be simulated by using the pseudo-Casson model.

The concept of the DEM is similar to that of the Euler–Lagrange method used for dispersed two-phase flows. It commonly deals with three-dimensional flow fields with or without wall boundaries.

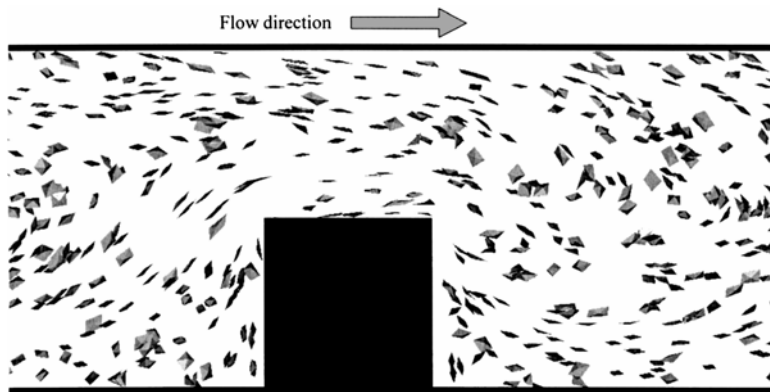


Fig. 3. Blood flow in a small vessel with stenosis by means of the DEM [19]

Figure 3 [19] is an example that shows a blood flow in a small vessel with stenosis by using the DEM. We think that complex flow fields can be simulated by using the DEM.

4.2. Vessel size

Constitutive equations are appropriate for large vessels, where blood can be assumed to be a continuous fluid. On the other hand, blood is no longer assumed to be a continuous fluid in a small vessel or a capillary, where the erythrocyte size is not negligibly small compared with the computational mesh size of a flow field. The constitutive equations always assume blood to be a continuous fluid, therefore they are not appropriate for small vessels and capillaries.

The DEM assumes that blood is a suspension of erythrocytes and plasma. This method can be used for calculating each erythrocyte motion, therefore it is appropriate even for small vessels where the erythrocyte size is not negligibly small compared to the computational mesh size for flow field. The DEM can also allow us to compute the flow in a large vessel; however, it then has a high computational load. In order to avoid high computational load, it seems necessary to employ stochastic simulation techniques for huge numbers of erythrocytes. Constitutive equations are, therefore, more appropriate for large vessels than the DEM.

Since the present erythrocyte model has only six drag points, it is impossible to express higher mode deformations smaller than half the size of an erythrocyte. The computational mesh for a flow field should therefore have a size of at least from 4 to 8 μm . The diameter of capillaries ranges approximately from 5 to 10 μm . Because of the resulting mesh size limitations, it is impossible to apply the DEM to a capillary flow.

4.3. Blood with high hematocrit

In the blood with high hematocrit, a lot of erythrocytes being suspended in plasma interfere with each other. This interference plays an important role in the rheological properties of the blood with high hematocrit. The Casson model and the pseudo-Casson model were proposed so as to express the rheological properties of the blood with rather high hematocrit, which were experimentally investigated. In order to adjust the constitutive equations to a certain hematocrit level, one just needs to adjust the viscosity and the plasticity in equations (1) and (2). Since these constitutive equations do suppose the blood with high hematocrit, they are not appropriate for the blood with very low hematocrit.

The present DEM assumes a dilute suspension of erythrocytes and plasma, therefore, the pair interaction between erythrocyte models is neglected. In order to treat the blood with high hematocrit, it is necessary to consider the interaction between

erythrocyte models and to express the reulaux structure for the low shear-rate range. This is essential for modelling normal blood with hematocrit of approximately 45%. We expect to improve the present DEM taking this interaction.

5. Rheological properties of the models

The rheological properties of the constitutive equations and the DEM are listed in table 2.

Table 2. Rheological property of the models

Rheological property	Casson	Pseudo-Casson	DEM
Shear-thinning	yes	yes	yes
Plasticity	yes	pseudoplasticity	no
Elasticity	no	no	yes
Erythrocyte deformation	no	no	yes
Plasma layer	no	no	yes

5.1. Shear-thinning property

The Casson and the pseudo-Casson models have a shear-thinning properties as shown in figure 1.

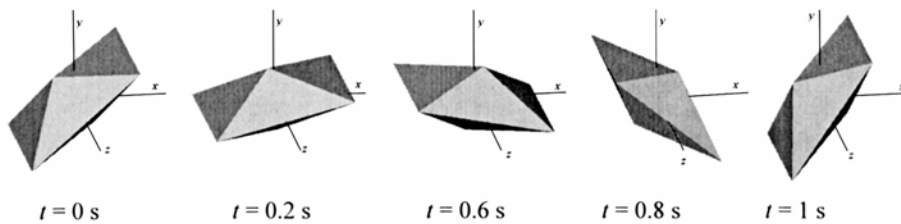


Fig. 4. Motion of an erythrocyte model subject to $\dot{\gamma} = 10 \text{ s}^{-1}$

The DEM also has a shear-thinning property, and its mechanism can be explained by the deformation of an erythrocyte model. Figures 4, 5 and 6 show the behaviour of an erythrocyte model under the constant shear rates of $\dot{\gamma} = 10, 1000$ and 10000 s^{-1} , respectively. There x is the coordinate axis in the flow direction, y the coordinate axis in the direction of the velocity change and z the coordinate axis perpendicular to the x - and y -axes. For $\dot{\gamma} = 10$, the erythrocyte model rotates without deformation like a solid body. For $\dot{\gamma} = 1000$, the model starts to deform and to be stretched in the x direction.

For $\dot{\gamma} = 1000$, the model is always flattened in the x - z plane during the rotation. This behaviour shows the characteristics similar to the tank tread motion [22], [23] of an erythrocyte.

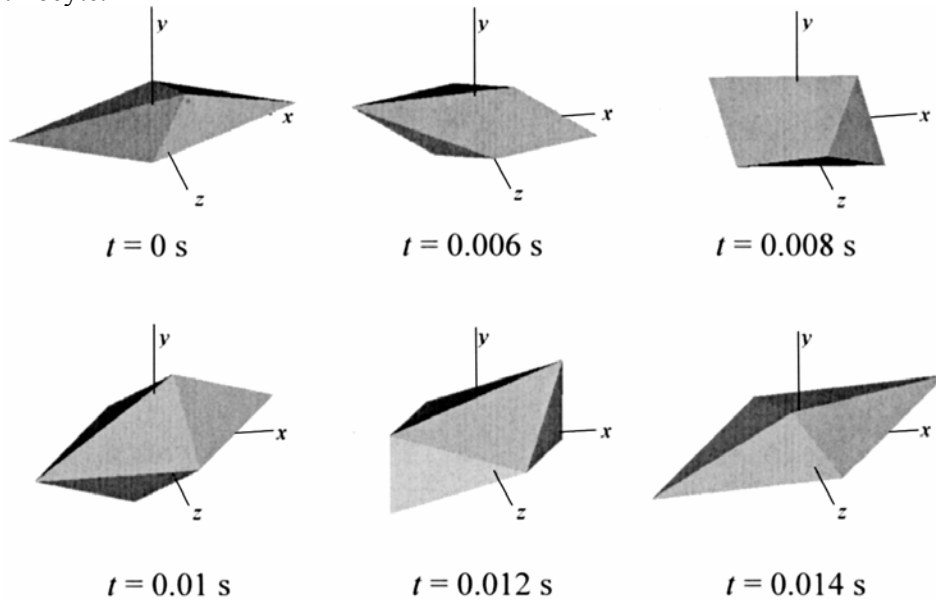


Fig. 5. Motion of an erythrocyte model subject to $\dot{\gamma} = 1000 \text{ s}^{-1}$

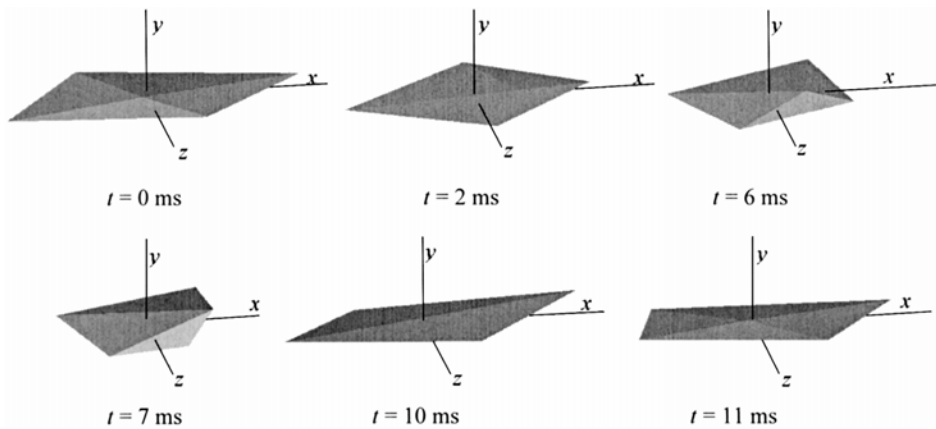


Fig. 6. Motion of an erythrocyte model subject to $\dot{\gamma} = 10\,000 \text{ s}^{-1}$

Figure 7 shows the change in a relative viscosity of the DEM, with the plasma viscosity subtracted. In this figure, η stands for an apparent viscosity and η_0 is that at the zero shear rate. It is found that the DEM also has a shear-thinning property,

which can be explained as follows. The thickness of the erythrocyte model in the y -direction decreases with increasing deformation. The decrease of the thickness induces a decrease of the force acting on a drag point and a de-

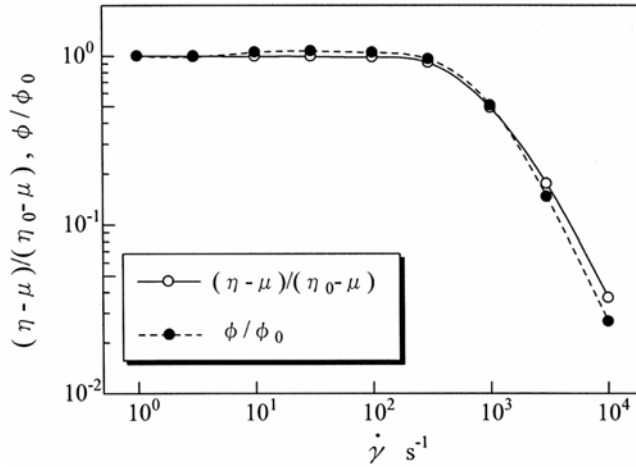


Fig. 7. Change of relative viscosity and the first normal stress difference coefficient with shear rate (DEM)

crease of the momentum transport in the y -direction, which results in a decrease of the stress components.

5.2. Plasticity and elasticity

The Casson model can rigorously express the plasticity of the blood, while the pseudo-Casson model cannot express the plasticity sufficiently well. It can only express the pseudo-plasticity. Both constitutive equations cannot express the elasticity of blood.

The DEM cannot express plasticity. In the low shear-rate range, the plasticity of blood is generated by the reulaux structure, therefore it becomes necessary to model the interaction between erythrocyte models in order to express the plasticity. But the DEM can express elasticity, because the erythrocyte model is stretched in the x -direction in figures 5 and 6, which generates the normal stress difference. In figure 7, the change of the relative first normal stress difference coefficient ϕ/ϕ_0 is also shown, where ϕ_0 is the first normal stress difference coefficient at the zero shear rate. It is found that the first normal stress difference coefficient also shows the shear-thinning property. It is well known that the viscosity of blood shows a shear-thinning property; however, not much is known about the shear-thinning property of the first normal stress difference coefficient. Since viscoelastic fluids typically show the shear-thinning property of the first normal stress difference

coefficient, it is to be supposed that blood, which is a viscoelastic fluid, also shows this property.

5.3. Erythrocyte deformation and plasma layers

Constitutive equations assume that blood is a continuous fluid, therefore, they cannot express either the deformation or the distribution of erythrocytes.

The DEM can express the deformation of erythrocytes as shown in figures 4–6. The deformation is large in the high shear-rate range, and small in the low shear-rate range. The aspect ratio of the projection chart of the erythrocyte model in the x - z plane is compared with the experimental results obtained by BESSIS and MOHANDAS [20] under the same shear-stress condition, and is shown in figure 8. It is confirmed that the present spring constant can consistently express the deformation of an erythrocyte.

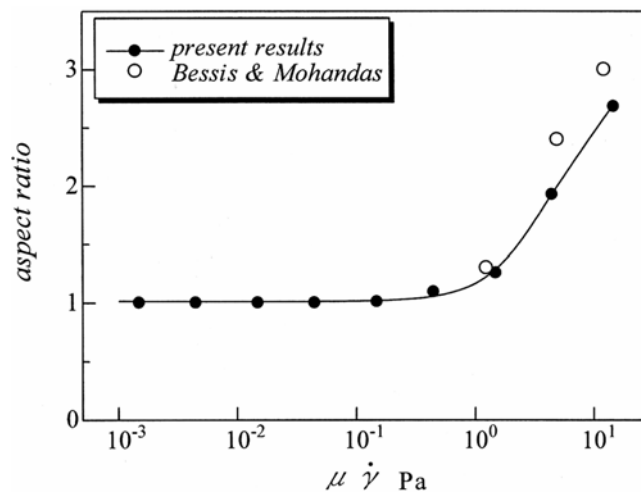


Fig. 8. Comparison of aspects ratio obtained by the DEM with that reported by BESSIS and MOHANDAS [20]

The DEM can also express the distribution of erythrocytes. Since the size of an erythrocyte model approaches $8 \mu\text{m}$, its center of gravity cannot get closer to the wall boundary than $4 \mu\text{m}$. In the present DEM, the plasma layer appears near the wall with a thickness of approximately $5 \mu\text{m}$. In a study dealing with the Poiseuille flow between flat plates [18], it was found that the DEM showed the Fahreus–Lindqvist effect for sufficiently narrow flow fields.

6. Conclusions and future projects

By comparing the DEM with the constitutive equations, it becomes clear that the DEM is an appropriate method for simulating the blood flow in small vessels. Moreover, the DEM can express elasticity, erythrocyte deformation and plasma layers, which are not well expressed by the constitutive equations.

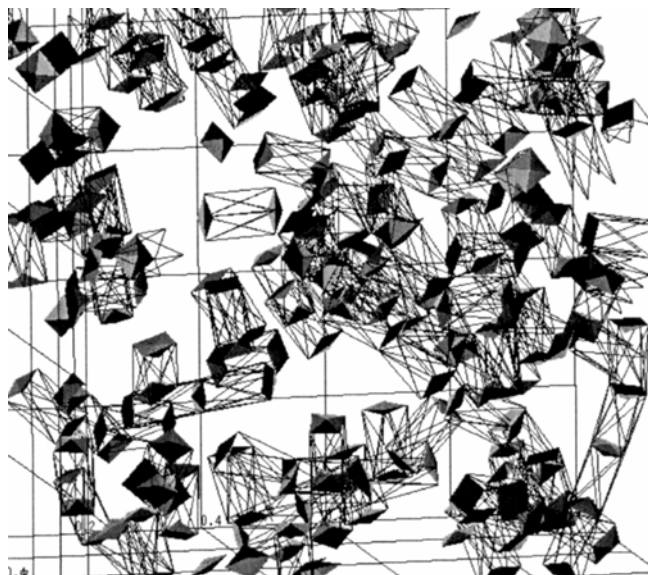


Fig. 9. Improved DEM that represents the interaction between erythrocyte models [24]

Yet the DEM still has some disadvantages compared with the constitutive equations. In order to improve the DEM, it is necessary to consider the interaction between erythrocyte models and to express the reulaux structure. One example for an improved DEM that considers the interaction between erythrocyte models is shown in figure 9 [24]. In order to expand DEM applicability, we intend to improve continuously the model in the future.

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