Numerical Study of Cell Membrane Trembling

of a Cell Moving through a Bottleneck

of a Channel*

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Abstract

Cell migration and deformation in blood vessels are closely related to cell diseases. Dynamical behaviours of deformation and shear stress variation of cell membrane are effective means for disease diagnosis. This work adopts a planar model for a cylindrical cell and a three-dimensional axi-symmetric model for a spherical cell to numerically study liquid-solid interaction of a cell moving through a bottleneck of a channel filled with plasma. Mooney-Rivlin material is used for cell membrane, and a viscous incompressible fluid is used for cytoplasm and plasma. It is found that the cell experiences considerable shear stress and deformation when passing through the bottleneck with a smaller size than the cell. For numerical stability and convergence, a grid remeshing technique is used in this work to eliminate skewed grids as the cell moves. Dynamic deformation and shear

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stress variation of cell membrane are investigated. A number of peaks of fluctuating shear stress and deformation of cell membrane are found. It implies that cell membrane could tremble when stimulated by a pulse force. Numerical results also indicate that the shear stress fluctuation of the spherical cell is more intense than that of the cylindrical cell in the same environmental condition while the deformation fluctuations are almost the same, mainly depending on the size of the bottleneck.

**Keywords:** Cell membrane, Trembling, Shear stress, Bottleneck, Grid remeshing

**INTRODUCTION**

The mechanical behavior of cells is crucially important for cell physiology and pathology. In order to deliver oxygen to tissues, the red blood cell (RBC) can go through capillaries with smaller diameter than itself[^1^][^2^] due to its high deformability. A good understanding of cell dynamics in the microcirculatory system is needed for blood flow and pathology of related blood diseases, such as sickle cell disease, diabetes, thalassemia and hereditary elliptocytosis[^3^].

Cells are usually sensitive to surface shear stress. The red blood cells can form aggregates in the form of rouleaux[^4^] looking like a stack of coins[^5^][^6^][^7^][^8^], and large aggregates hinder the blood flow[^9^][^10^][^11^]. The cell adhesion mechanism has not yet been fully understood. It is generally believed that surface shear stress plays an important role in the cell adhesion. Schmid-Schonbein[^12^][^13^] found that rouleaux can be dissolved into smaller fractions or even into single cells under a proper shear force. When moving through the bottleneck, a cell experiences large shear stress and deformation. These mechanical stimulations may greatly affect physiological behavior of the cell. Lee[^14^] and Sutera[^15^] performed experiments with a rubber vesica filled with fluid, simulating a blood cell. They found that the cell can enter a tube with smaller size than itself. Zhou et al.[^16^] numerically studied a blood cell moving through a bottleneck with a smaller diameter by using a dissipative particle dynamics (DPD) method, and their numerical result is consistent with Leong's experiment[^17^]. Recent studies[^18^] show that RBC can release a chemical substance, named ATP, which strongly influences the cell's physiological response and blood circulation[^19^]. This implies that the mechanical processes of RBC deformation are closely related to bio-chemical reaction of the cell under mechanical forces. The cell surface shear stress variation can induce cell ATP release[^20^]. The relationship between ATP release and the mechanical forces has not been fully understood. Experiment of a cell moving through a
bottleneck can be one of the useful means for estimating cell bioactivity.

In this work we carried out full fluid-solid interaction computation to study dynamical behaviors of a cell passing through a bottleneck. The numerical results of fluctuating shear stress and deformation of the cell surface indicate cell membrane trembling when experiencing a pulse force.

**DESCRIPTION OF THE PHYSICAL PROBLEM**

We consider a single cell, either spherical or cylindrical, as shown in Fig. (1), in a channel filled with plasma. A bottleneck is located at the middle of the channel. The plasma is driven by a pressure gradient to move through the bottleneck, as shown in Fig. (2).

![Fig. 1 Spherical cell and cylindrical cell](image1)

![Fig. 2 Sketch of a cell moving through a bottleneck in a channel](image2)

Plasma is considered to be a viscous incompressible Newtonian fluid. The liquid flow in the channel in the present study is assumed to be laminar flow with a low Reynolds number. The cell consists of cell membrane and cytoplasm\(^{[21]}\)\(^{[22]}\), which can also be approximated as a viscous incompressible fluid\(^{[23]}\). The cell membrane is a high-deformed, incompressible, elastic material, which can be approximated as a rubber material with the Mooney-Rivin constitutive model\(^{[24]}\), expressed as follows

\[
W_D = C_1(I_1 - 3) + C_2(I_2 - 3)
\]

(1)

Where \(W_D, I_1, I_2\) are strain energy density, and principal invariants, respectively. \(C_1, C_2\) are the constitutive coefficients.
GOVERNING EQUATIONS AND BOUNDARY CONDITIONS OF LIQUID-SOLID INTERACTION

Plasma and cytoplasm are defined as liquid phases, and the cell membrane is defined as a solid phase. The continuity equation and Navier-Stokes equation for viscous incompressible fluids read as follows

\[
\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \mathbf{V}) = 0 \tag{2}
\]

\[
\frac{\partial \mathbf{V}}{\partial t} + (\mathbf{V} \cdot \nabla) \mathbf{V} = -\frac{1}{\rho} \nabla p + \nu \nabla^2 \mathbf{V} \tag{3}
\]

where \( \rho, \nu, p, \mathbf{V} \) are the liquid density, kinetic viscosity, pressure and flow velocity. The constitutive equation, geometrical equation and equilibrium equation for the solid read as follows

\[
\sigma_{ij} = D_{ijkl} \varepsilon_{kl} \tag{4}
\]

\[
\varepsilon_{ij} = \frac{1}{2} (u_{ij,\tau} + u_{ij,\tau}) \tag{5}
\]

\[
\sigma_{ij} + f_i - \rho_s u_{i,t} - \mu u_{i,\tau} = 0 \tag{6}
\]

Where \( \rho_s, \mu \) are the solid density and damping coefficient. \( \sigma_{ij}, \varepsilon_{ij} \) are the stress tensor and strain tensor. \( D_{ijkl} \) is a fourth-order symmetric tensor named elastic constants. \( u_{ij} \) is the displacement vector, and \( u_{i,t}, u_{i,\tau} \) are the second-order and the first-order derivative of \( u_{ij} \).

The liquid flow velocity and stress are equal to those of the solid on the liquid-cell interface when the cell moves. A pressure drop \( \Delta p \) across the channel is specified, and no-slip velocity condition is imposed on walls of the channel. The computational region and boundary conditions are shown in Fig. (3) for the cylindrical cell and Fig. (4) for the spherical cell, respectively.

Fig. 3   The 2-D computational region and boundary conditions for cylindrical cell

Fig. 4   Axi-symmetrical computational region and boundary conditions for spherical cell
NUMERICAL COMPUTATION

Computational software ADINA 8.7 (FSI module with Arbitrary Lagrangian–Eulerian method) is used to perform liquid-solid interaction computation in the present work. A three-dimensional axi-symmetric model is used for the spherical cell, and a two-dimensional planar model is used for the cylindrical cell. Numerical grids near the liquid-solid interface are badly skew as the cell is moving, and a grid remeshing technique is used to eliminate skew grids during computation, as shown in Fig. (5). The grid remeshing technique ensures numerical stability and convergence.

Fig. 5  Sketch of moving grids and remeshed grids as the cell is moving

NUMERICAL EXAMPLES AND DISCUSSION

Computational data are specified as follows: pressure drop $\Delta p = 25 \text{ Pa}$ across the channel, channel length and high $L = 45 \text{ mm}$, $h = 6 \text{ mm}$, the gap of the bottleneck $\delta = 2.4 \text{ mm}$, cell diameter $d = 4 \text{ mm}$, thickness of the cell membrane $b = 0.1 \text{ mm}$, the density of the plasma and cytoplasm $\rho = 1000 \text{ kg/m}^3$, the dynamical viscosity of the plasma $\mu_p = 0.001 \text{ Pa}\cdot\text{s}$, the cytoplasm viscosity $\mu_c = 0.006 \text{ Pa}\cdot\text{s}$, the constitutive coefficients of cell membrane $C_1 = 257 \text{ Pa}$, $C_2 = 25.7 \text{ Pa}$. In general, the real cell dimension is about $10 \text{ mm}$, and cell density is on the same order as the plasma. The objective of this work is to numerically investigate possibility of cell membrane
trembling when stimulated by environmental forces. Cell dimension in the present example is amplified to the (mm) order without losing generality.[25],[26].

Migration and deformation of the cell moving through the bottleneck is shown in Fig. (6) for a spherical cell and Fig. (7) for a cylindrical cell, respectively.

![Fig. 6 Migration and deformation of the spherical cell moving through the bottleneck](image)

![Fig. 7 Migration and deformation of the cylindrical cell moving through the bottleneck](image)

It can be seen that the deformation of the spherical cell at the bottleneck shows an "∞" shape, and the deformation of the cylindrical cell shows a flat ellipse shape, because the spherical cell is compressed in all directions, and the cylindrical cell is compressed only in the plane. The pressure variation inside the cell during its moving through the bottleneck is shown in Fig. (8) for the spherical cell and Fig. (9) for the cylindrical cell, respectively, where the light color denotes low pressure, and the dark color high pressure.

![Fig. 8 The pressure inside the spherical cell during moving through the bottleneck](image)

![Fig. 9 The pressure inside the cylindrical cell during moving through the bottleneck](image)
It can be seen that the internal pressure at the cell tail is greater than that at the cell head when the cell enters the bottleneck, and the cell head is compressed to drive the cytoplasm flow backward, resulting in a pressure increase at the cell tail. When the cell leaves the bottleneck, the cell tail is compressed to drive the cytoplasm flow forward, resulting in a pressure increase at the cell head.

The shear stress and displacement in the y direction at observed points of the cell membrane (Fig. 10) are shown in Fig. (11) - (14) for the cylindrical cell, and in Fig. (15) - (18) for the spherical cell, respectively. It can be seen that the shear stress and deformation of cell membrane rapidly fluctuate when the cell is moving through the bottleneck.
Fig. 12  Y displacement of point 1 of the cylindrical cell

Fig. 13 Shear stress of point 2 of the cylindrical cell

Fig. 14 Y displacement of point 2 of the cylindrical cell
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Fig. 15 Shear stress of point 1 of the spherical cell

Fig. 16 Y displacement of point 1 of the spherical cell

Fig. 17 Shear stress of point 2 of the spherical cell
A number of fluctuating shear stress and deformation of cell membrane can be seen in our numerical solutions. Cell membrane is a kind of high elastic materials like rubber which easily rebounds when experiencing pulse shear stress while passing the bottleneck.

The liquid flow pattern around the moving cell when passing the bottleneck is shown in Fig. (19) where a symmetrical vortex flow can be seen in the channel.

CONCLUSIONS

This work numerically studied dynamical behaviour of a cell moving through a small bottleneck in a channel via fluid-solid interaction computation with Arbitrary Lagrange-Eulerian algorithm. Grid remeshing technique is used to ensure numerical stability and convergence. Numerical results of the spherical and cylindrical cells indicate that the shear stress and deformation of cell membrane fluctuate with a number of digressive peaks when the cell passes through the bottleneck. It implies a possibility that cell membrane could tremble when stimulated by a pulse force. It is also found that the shear stress fluctuation of the spherical cell is more intense than that of the cylindrical cell under the same
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environmental conditions, but the magnitude of deformation fluctuations is the same for two kinds of cells, mainly depending on the gap size of the bottleneck.

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