Finite Element Method Analysis of the Deformation of Human Red Blood Cells

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An erythrocyte and a spherocyte are subjected to aspiration pressure with a micropipette and analyzed by the finite element method (FEM). The comparison of the erythrocyte and the spherocyte indicates that the $y$-direction displacement of the erythrocyte was larger than that of the spherocyte under the same aspiration pressure. The $x$-direction stress distributions show that it is easier to change the shape of the erythrocyte model than that of the spherocyte model because a force in the opposite direction appears in the erythrocyte. This force seems to move the erythrocyte membrane to its center. The results indicate that the shape of the erythrocyte membrane changes partially under aspiration pressure at the point of contact with the micropipette and aspiration pressure. The results also indicate that the shape of the spherocyte membrane changes under aspiration pressure, but not only at a point of contact with the micropipette and the area subject to aspiration pressure; the entire spherocyte membrane seems to change the shape.

Key Words: Biomechanics, Finite Element Method, Visco Elasticity, Deformability, Human Red Blood Cells, Erythrocyte Type, Spherocyte Type

1. Introduction

A blood clot in a narrow artery brings about vascular blockage, the rupture of a blood vessel and other detrimental effects. One of the causes of this type of sickness is an increase in the viscosity of the blood that is linked to the decrease in the deformability of human red blood cells. There is a direct connection between the progression of a certain inherited disease and the mechanical deformation characteristics of red blood cells; sickle erythrocytes are a typical example of an inherited disease of red blood membranes. As the cause of the sickle erythrocyte, the structure of the cell cytoplasm, the shape of the cell, and the molecular constitution of its membrane are altered during the maturation of a parasite (considering the case of malaria) in the cell so that the red blood cell progressively loses its ability to undergo a large deformation. The hereditary spherocytosis is also the diseases of the red blood cell and tend to get trapped in narrow blood passages. Thus, in this study, an erythrocyte and an spherocyte subjected to aspiration pressure with a micropipette are analyzed by the finite element method (FEM) and the deviation between erythrocyte and spherocyte types is shown. Figure 1 shows the forms of the erythrocyte-type and spherocyte-type models used.

2. Red Blood Cell Model

A human red blood cell with a biconcave shape and an average diameter of about 8 µm has a typical life span of 120 days during which time it circulates through the human body nearly half a million times. During the course of its circulation, it undergoes severe elastic deformation as it passes through narrow arteries whose inner diameter is smaller than 3 µm. Figure 2 shows the human red blood cell membrane structure, which is made up of comprises the phospholipid bilayer, the spectrin network and transmembrane proteins, and the inside of the membrane, which consists of hemoglobin and other units. To determine the mechanical properties of cells, the micropipette aspiration technique has been widely used in previous studies(1)–(3). In this method, a stepwise increase in suction pressure causes a cell to be drawn into a glass tube, whose inner diameter, in conjunction with the aspiration pressure, can be appropriately chosen so as to control the extent of deformation. In an analysis of the deformation
of a human red cell, the large deformation response of the red blood cell has been analyzed using continuum constitutive models and other approaches. One such approach is based on the use of a hyperelastic elective material to model the membrane of red blood cells\(^4\). Evans\(^5\) suggested that the relationship between the membrane shear stress \(T_s\) and the deformation is expressed as

\[
T_s = 2\mu \gamma_s = \frac{\mu}{2} (\lambda_1^2 - \lambda_2^2) = \frac{1}{2} (T_1 - T_2) \quad (1.a)
\]

\[
\gamma_s \equiv \frac{1}{2} (\epsilon_1 - \epsilon_2) = \frac{1}{4} (\lambda_1^2 - \lambda_2^2) \quad (1.b)
\]

\[
\lambda_1 \lambda_2 = 1 \quad (1.c)
\]

where \(T_1\) and \(T_2\) are the in-plane principal membrane stresses, \(\epsilon_1\) and \(\epsilon_2\) are the in-plane principal Green’s strains of the membrane, \(\lambda_1\) and \(\lambda_2\) are the principal stretch ratios, \(\mu\) is the membrane shear modulus and \(\gamma_s\) is the shear strain. From the micropipette aspiration of a human red blood cell, the measured value of initial shear modulus of the membrane is given in the report of Evans and Skalak\(^6\) as \(\mu_0 = 6.3 \times 10 \mu\text{N/m}\) and \(\mu_0 = 0.75 G_0 h_0\), where \(G_0\) is the initial bulk shear modulus and \(h_0\) is the initial membrane thickness. The incompressible hyperelastic elective material model with the arruda-boyce form of strain energy potential is given by

\[
W = \mu \left[ \frac{1}{2} (l_1 - 3) + \frac{1}{20} A_L (l_1^2 - 9) + \frac{11}{1050} A_L (l_1^3 - 27) \right]
\]
where $W$ is the strain energy, $l_1$ is the first deviatoric strain invariant, $J$ is a determinant of the elastic deformation gradient $F$, $\mu$ is the initial shear modulus of the material, $\lambda_L$ is the limiting network stretch, and $d$ is a material incompressibility parameter.

Evans and Fung \cite{7} estimated the shape of the erythrocyte, and average biconcave shape function was given as

$$y = \pm 0.5R_0 \left[ 1 - \frac{x^2 + z^2}{R_0^2} \right] \left[ C_0 + C_1 \frac{x^2 + z^2}{R_0^2} + C_2 \left( \frac{x^2 + z^2}{R_0^2} \right)^2 \right]$$

(3)

$R_0 = 3.91 \mu m,$

$C_0 = 0.207 \ 161,$  $C_1 = 2.002 \ 558,$  $C_2 = -1.122 \ 762,$

where $2R_0$ is the average erythrocyte diameter in the axial direction. The diameters of the spherocyte and erythrocyte were chosen to be 7.82 $\mu m$. Figure 3 shows the dimensions of the human red blood cells with the tip of the micropipette. Taking into account the axial symmetry of the model, two dimensions of the human red blood cells are analyzed. The membrane of the human red blood cell is modeled using the hyperelastic model and the inside of the red blood cell is modeled using the viscoelastic model. The calculations have been performed using the finite element package, ANSYS. Figure 4 shows the boundary conditions used in the FEM calculations. In analysis, the contact condition is used between the human red blood cell and the tip of the micropipette. Figure 5 shows an example of mesh divisions in the FEM analysis.

3. Results of FEM Calculations

Figure 6 shows the coordinates used in the analysis. The stress distribution and displacement of lines A and B were obtained in the calculation. Figures 7–12 show the calculation results for the human erythrocyte and spherocyte. Figures 7 and 8 show the $x$-direction stress. The ordinate is the $x$-direction stress $S_{X}$ on lines A and B; the abscissa is the distance $x$ from the center of the red blood cell. The aspiration pressure is $-0.1 \text{ Pa}$, and the material properties of the erythrocyte and spherocyte are the same. A solid line represents the erythrocyte and a dashed line represents the spherocyte. Figure 7 shows that the line-A $x$-direction stress distribution of the erythrocyte exhibits a
negative value near the region of $x=0.7$ and it is assumed that the shape of the erythrocyte is easier to change than that of the spherocyte because the negative force moves the erythrocyte to its center. The spherocyte shows a positive force and moves in the direction away from its center. Figure 8 shows the stress distributions of the erythrocyte and spherocyte on line-B. A solid line represents the erythrocyte and the dashed line represents the spherocyte.

The spherocyte shows a positive $x$-direction stress distribution and the erythrocyte shows a negative $x$-direction stress distribution. It is assumed that the shape of the erythrocyte is easier to change than that of the spherocyte.

Figures 9 and 10 show the $x$-direction displacement. Figure 9 shows the $x$-direction displacement on line-A, where a solid line is the erythrocyte and a dashed line represents the spherocyte. The $x$-direction displacement of the erythrocyte increases as membrane position approaches $x=0.75$ and the $x$-direction displacement of the spherocyte decreases from $x=0.6$ to $x=0.75$. The $x$-direction displacement of the spherocyte is larger than that of the erythrocyte in the range from $x=0$ to $x=0.6$. Comparing the $x$-direction displacements of the erythrocyte and the spherocyte, the erythrocyte shows a large $x$-direction displacement when $x$ comes close to 0.75 and
the spherocyte displacement decreases gradually after the peak of $x$-direction displacement ($x = 0.48$). The spherocyte shows a smaller displacement than the erythrocyte when $x$ comes close to 0.75. Figure 10 shows the $x$-direction displacement on line-B; a solid line represents the erythrocyte and a dashed line represents the spherocyte. The erythrocyte shows a large displacement compared with the spherocyte. The $x$-direction displacement of the spherocyte is almost zero whereas the erythrocyte shows a large $x$-direction displacement when $x$ comes close to 0.75.

Figure 11 shows the $y$-direction displacement on line-A; a solid line represents the erythrocyte and a dashed line represents the spherocyte. The $y$-direction displacement of the erythrocyte is larger than that of the spherocyte in the range from $x = 0$ to $x = 0.5$, and a maximum $y$-direction displacement is shown in the erythrocyte. It is assumed that the shape of the erythrocyte model is easier to change than that of the spherocyte one. From the point of $x = 0.5$, the spherocyte $y$-direction displacement is larger than the erythrocyte one. The erythrocyte shows a large $y$-direction displacement as $x$ comes close to the center of the cell. Figure 12 shows the $y$-direction displacement on line-B. The $y$-direction displacement of the spherocyte is larger than that of the erythrocyte. When $x = 1$, the erythrocyte and spherocyte show maximum $y$-direction displacement. It is considered that the erythrocyte shows a large displacement when its membrane comes close to the point of contact with the micropipette, and the spherocyte shows a positive $y$-direction displacement over the entire length of B.

4. Discussion

The three topics were discussed to evaluate the calculations performed in this paper.

(1) Human red blood cells flow in blood vessels and their form can easily change under pressure. To know the deformability of human red blood cells in blood, the influence of the fluid cannot be disregarded. However, taking into the account the fact that the shape of red blood cells changes within a very short time, the analysis focused on nano-order deformation is an important problem. In subjecting cells to pressure within a very short time, FEM analysis shows that there is a difference between the erythrocyte red blood cell and the spherocyte one.

(2) The cytosol is assumed to be a fluid which acts to preserve the interior volume of a red blood cell during deformation as well as to maintain the even distribution of the internal fluid pressure on the inner membrane surface. A previous study clearly indicates that the viscous energy...
dissipation of the cytoplasm within a red cell filled with concentrated hemoglobin solution is known to be two orders of magnitude smaller than that of the membrane\(^9\). In this paper, we discussed the effect of the inside of the red blood cell, but accurate values of the material properties are not used in this analysis, supposing that the material properties of the viscosity of the cytosol are negligible. To obtain an accurate stress value, the exact physical properties of the cytosol are needed.

\(3\) It is well known that the deformability of the spherocyte is lower than that of the erythrocyte\(^10\). This phenomenon well corresponds with the calculated results by us. However, the observation of nano-order deformation of the human red blood cells by the micropipette method is not established yet, and the difference of the deformation method between the erythrocyte and spherocyte is not clarified by the experiment. The micropipette method has a difficulty in managing the red blood cell, and also demands a lot of experience to treat the micropipette. There are several experimental methods other than micropipette method\(^11\)–\(^14\). However, any methods have no ability to evaluate the nano-order deformation of the human red blood cells.

There are a lot of correlations between the deformability of the red blood cell and the blood vessel decease. The measurement of the deformability of red blood cell is needed to obtain the information about the blood vessel decease. Now, we are planning to establish a new method to observe the deformability using the micropipette and microscope.

5. Conclusions

This paper has dealt with the FEM analysis of the human red blood cell subject to aspiration pressure with a micropipette. The stress distribution and displacement were obtained by the finite element method. The following results were established.

The \(x\)-direction stress distributions of the erythrocyte and spherocyte were obtained by the FEM calculation. It was found that the shape of the erythrocyte model is easier to change than that of the spherocyte one because a negative force appears in the case of the erythrocyte, and this force seems to move the erythrocyte to its center. The \(x\)-direction displacement was obtained from the calculation. The erythrocyte shows a large displacement compared with the spherocyte as comes close to the point of contact with the micropipette.

The \(y\)-direction displacement was obtained from the calculation and the line-A \(y\)-direction displacement of the erythrocyte was larger than that of the spherocyte in case of \(x\) coming close to the center of the cell. The results indicate that the shape of the erythrocyte membrane under aspiration pressure changes at the point of contact with the micropipette and that of the area subject to the aspiration pressure partially, whereas the spherocyte membrane subject to the aspiration pressure changes in shape, not only at the point of contact with the micropipette and the area subject to the aspiration pressure but also over the cell’s entire membrane.

References

\(1\) Hochmuth, R.M. and Waugh, R.E., Erythrocyte Membrane Elasticity and Viscosity, Ann. Rev. Physiol., Vol.49 (1987), pp.209–219.

\(2\) Hochmuth, R.M., Mohandas, N. and Blackshear, P.L., Measurement of the Elastic Modulus for Red Cell Membrane Using a Fluid Mechanical Technique, Biophys. J., Vol.13, No.8 (1973), pp.747–762.

\(3\) Hochmuth, R.M., Worthy, P.R. and Evans, E.A., Red Cell Extensional Recovery and the Determination of Membrane Viscosity, Biophys. J., Vol.26, No.1 (1979), pp.101–114.

\(4\) Mills, J.P., Qie, L., Dao, M., Lim, C.T. and Suresh, S., Nonlinear Elastic and Viscoelastic Deformation of the Human Red Blood Cell with Optical Tweezers, Mech. Chem. Biosystems, Vol.1, No.3 (2004), pp.169–180.

\(5\) Evans, E.A., New Membrane Concept Applied to the Analysis of Fluid Shear and Micropipette Deformed Red Blood Cells, Biophys. J., Vol.13, No.9 (1973), pp.941–954.

\(6\) Evans, E.A. and Skalak, R., Mechanics and Thermal Dynamics of Biomembranes, (1980), CRC Press, Boca Raton, FL.

\(7\) Evans, E.A. and Fung, Y.C., Improved Measurements of the Erythrocyte Geometry, Microvasc. Res., Vol.4, No.4 (1972), pp.335–347.

\(8\) Evans, E.A., Bending Elastic-Modulus of Red-Blood-Cell Membrane Derived from Buckling Instability in Micropipette Aspiration Tests, Biophys. J., Vol.43, No.1 (1983), pp.27–30.

\(9\) Evans, E.A. and Hochmuth, R.M., Membrane Viscoelasticity, Biophys. J., Vol.16, No.1 (1976), pp.1–11.

\(10\) Oka, S., Biorheology, (in Japanese), (1984), pp.99–100, Syokabo, Tokyo.

\(11\) Hénon, S., Lenormand, G., Richert, A. and Gallet, F., A New Determination of the Shear Modulus of the Human Erythrocyte Membrane Using Optical Tweezers, Biophys. J., Vol.76, No.2 (1999), pp.1145–1151.

\(12\) Lenormand, G., Hénon, S., Richert, A., Siméon, S. and Gallet, F., Direct Measurement of the Area Expansion and Shear Moduli of the Human Red Blood Cell Membrane Skeleton, Biophys. J., Vol.81, No.1 (2001), pp.43–56.

\(13\) Lim, C.T., Dao, M., Suresh, S., Sow, C.H. and Chew, K.T., Large Deformation of Living Cells Using Laser Traps, Acta Materialia, Vol.52, No.7 (2004), pp.1837–1845.

\(14\) Bassis, M. and Mohandas, N., A Diffractometric Method for the Measurement of Cellular Deformability, Blood Cells, Vol.1 (1975), pp.307–313.