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3D Particle Simulations of Deformation of Red Blood Cells in Micro-Capillary Vessel

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1. Introduction

With the increase in arteriosclerosis, thrombosis, etc., in order to find out the cause, research of the flow characteristic of blood attracts attention. As for the analysis of the flow phenomenon of the RBC (Red Blood Cell or Erythrocyte), the numerical simulation (Wada et al., 2000, Tanaka et al., 2004) as well as experiment observation (Gaehtgens et al., 1980) is becoming a strong tool. Particle methods, such as SPH method (Monaghan J., 1992) and the MPS method (Koshizuka, 1997), treats both solid and liquid as particles, and can be applied to complicated flow analysis. When applying a particle method to the flow analysis of RBC, RBC is divided into the elastic film and internal liquid, and its deformation was analyzed in detail (Tanaka et al., 2004, Tsubota et al., 2006).

The RBC which is actually flowing in our body occupies 40-60% by volume ratio of blood (hematocrit), and is numerous. The objective of our research is clarifying the flow characteristic of the blood flow containing many RBCs. We reported preliminarily simulation of 2D blood flow (Nagayama et al., 2004), where many RBCs were simply treated as a lump of an elastic particle, the flow was analyzed qualitatively. Moreover, three dimensional RBC was modelled with double structure, and the RBC shape in flow was more realistic (Nagayama et al., 2005). The relation of the blood vessel diameter and the blood-flow with many RBCs was studied by 2D model (Nagayama, 2006) and by 3D model (Nagayama et al., 2008a). The model was also applied to 3D blood flow in capillary bend tube (Nagayama et al., 2008b).

The objective is to understand the fundamental flow phenomenon in a blood vessel. In this paper, 3 dimensional blood flows with RBCs in capillary tube were simulated.

In Section 2, simulation model was described. And the shape of single red blood cell in static fluid was shown.

In Section 3, blood flows with RBCs in capillary straight tube were simulated. And the relations of the blood vessel diameter and the hematocrit were investigated. Furthermore, transient phenomena of interacting red blood cells and their shape were investigated.

In Section 4, the model is applied to the capillary vessel flow at finger tip edge. The capillary vessel is modelled as two cases. One case is bent tube and another is bent and twisted tube, and RBC deformation were investigated.

2. Model descriptions

The particle model used for simulation is described. Then calculation conditions will be explained.

2.1 Mathematical descriptions

Particle method considers the interaction between particles and pursues motions of particles in Lagrangian way. Instead of NS equation, a momentum equation in particle model (1) consists of inertial force, inter-particle force, viscous diffusion and external force. Inter-particle force is attracting force or repulsing force between particles using particle pressure as shown in equation (2), so that to keep the density uniform in the domain.

Spring model is also considered for the elastic RBC surface. For the viscous diffusion term, MPS method (Koshizuka, 1997) is used. As for the external force, pressure difference between both ends of blood vessel was taken into consideration. The symbols are, u: velocity vector, t: time, ω: weighting function, n: number density, r: position, d and λ: constants. In addition i: particle number, j: surrounding particle number, 0: basic condition. RBC film particle is tied by surrounding particles using springs. In addition, resistance against bending is modelled as the force to the center of mass of surrounding particles. In addition, damping force is treated as viscous force in Eq. 1. The size of RBC is about 8 μm in diameter and 3 μm in thickness.

$$\frac{\partial \mathbf{u}_i}{\partial t} = -\frac{1}{\rho}\frac{d}{n^0}\sum_{j\neq i}\left[\left(P_j - P_i\right)\omega_{ij}\frac{\mathbf{r}_{ij}}{\left|\mathbf{r}_{ij}\right|^2}\right] + \nu\frac{2d}{n^0\lambda}\sum_{j\neq i}\left[\omega_{ij}\left(\mathbf{u}_j - \mathbf{u}_i\right)\right] + \mathbf{F} \tag{1}$$

$$P_i = \frac{1}{\kappa}\left(1 - \frac{n_0}{n_i}\right) \tag{2}$$

2.2 RBC shape in static fluid

RBC is double structure: surface film and plasma liquid inside. RBC film particle is tied by surrounding film particles by springs with coefficient of 7.52×10^{-2}N/m as shown in Fig. 1. In addition, resistance against bending with coefficient of 3.76×10^{-4}N/m, is modelled as the force to the center of mass of surrounding particles. Surface area is 140μm^2 and volume is 90μm^3. In the simulation, starting from sphere shape and removing 42% of plasma particle inside, the shape of RBC is formed. Fig.2 is the simulated RBC shape in static fluid. The size of RBC is about 8 μm in diameter and 3 μm in thickness. RBC shape will change with flow in blood vessel.

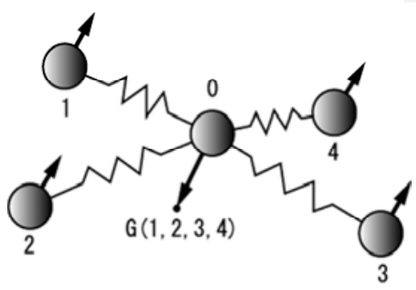


Fig. 1. Elastic film model

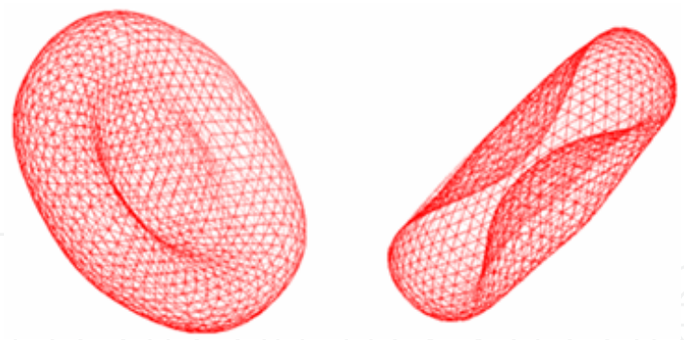


Fig. 2. Simulated RBC shape in static fluid

3. Deformation of RBCs in various inner diameter capillaries and hematocrit

Deformation of RBCs in various inner diameter capillaries and hematocrit was studied. Next, transition from single-file to multi-file flow as a function of hematocrit in capillaries of various diameters was discussed.

3.1 Simulation conditions

Simulation conditions are shown in Table 1. Simulations were carried out using normalized value. The velocity is normalized by 1 mm/s and the length is normalized using 10 μm. Physical properties are also shown in Table 1. Total simulation time is 0.3 s (300000 iterations with time step1 μs), which is enough to reach stable flow.

Cases for simulation with various inner diameter (ID) capillaries and hematocrit are shown in Table 2. To study transition phenomena from single-file to multi-file flow, hematocrit 0.24-0.54 and capillaries of various inner diameters 5.5-8.7 μm were chosen for simulation.

Velocity of normalization	1	[mm/s]
Length of normalization	10	[μm]
Viscosity	0.001	[Pa s]
Density	1000	[kg m3]
Simulation time	0.3	[s]
Elasity of stretching	7.52 E-04	[N/m]
Elasity for bending	2.63 E-05	[N/m]

Table 1. Simulation conditions

Case	ID [μm]	Ht
(a)	5.5	0.31
(b)	7.37	0.24
(c)	7.37	0.49
(d)	8.5	0.21
(e)	8.7	0.54

Table 2. Cases for simulation

3.2 Results for cases in various inner diameter capillaries and hematocrit

In this section, first of all, results of deformation of RBCs in various ID and hematocrit will be shown. Next, transition from single-file to multi-file flow will be discussed. The deviation of RBC distribution in a capillary blood vessel will also be shown.

3.2.1 Deformation of RBCs in various inner diameter capillaries and hematocrit

Simulation conditions are shown in Table1. Simulations were carried out for 5 cases with various inner diameter capillaries and hematocrit. Results are shown in Fig. 3 and the RBC shape was studied for each cases.

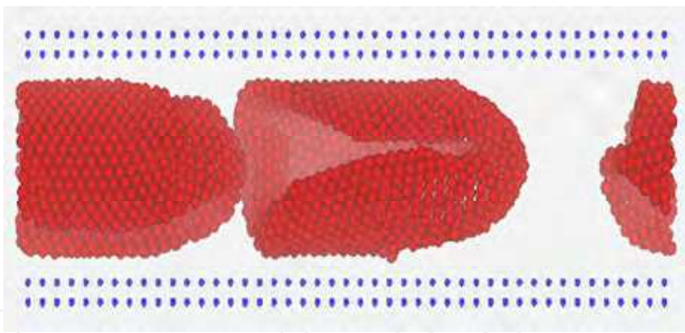
In case of (a) ID=5.5 μm Ht=0.31 (narrowest capillary), RBC flows in lines (single-file flow). RBC contacts with wall and deforms to consistently non-axisymmetric rocket shape 'torpedo' exhibiting a membrane-fold which extends from the open rear-end along one side toward the leading end (Gaehtgens et al., 1980).

In case of (b) ID=8.5 μm Ht =0.2, RBC flows in lines (single-file flow), rarely contact with the wall. RBCs flow at center of the blood vessel, parachute type deformation appeared.

In case of (c) ID=7.37 μm Ht =024, RBC flows basically in lines (single-file flow). RBCs do not flow at center of blood vessel. RBC interact each other, and sometimes contact with another RBC.

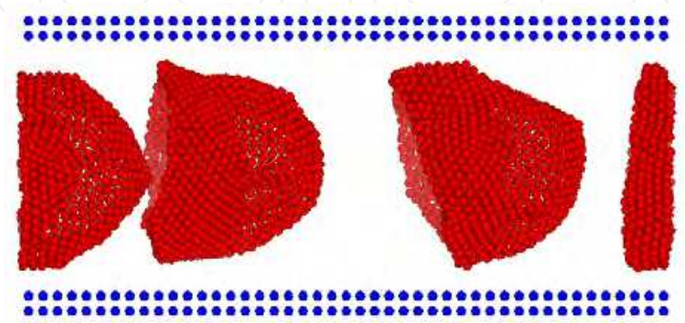
In case of (d) ID=7.37 μm Ht=0.49, RBC interacts (multi-file flow) with each other and contact with the wall, forming zipper shape.

In case of (e) ID=8.7 μm Ht=0.54, RBC interacts (multi-file flow) strongly with each other and contact with the wall, forming strong and complex deformation.

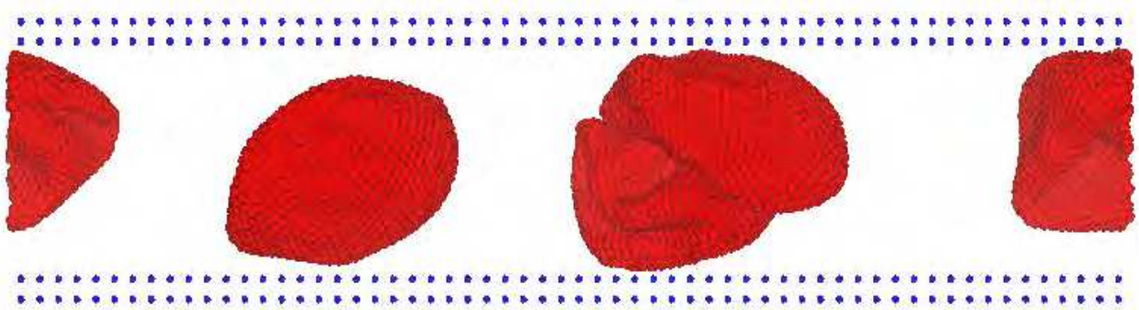


Inlet outlet

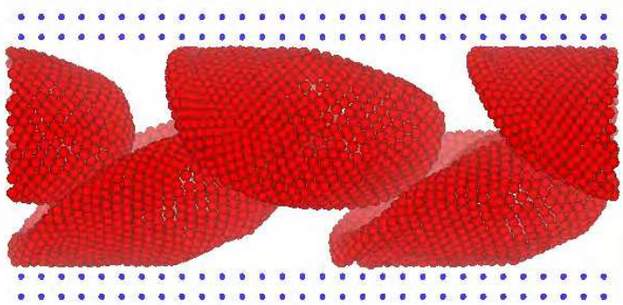
(a) ID=5.5 μm Ht=0.31



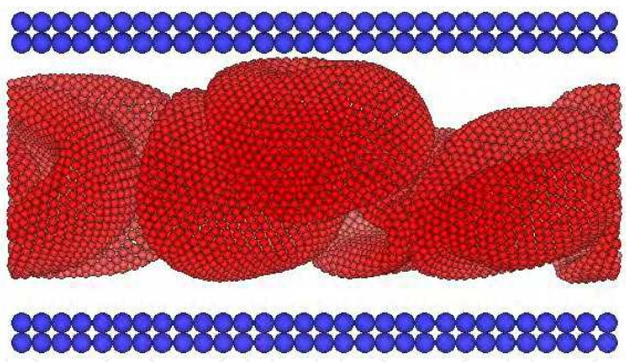
(b) ID=8.5 μm Ht=0.2



(c) ID=7.37 μm Ht=0.24



(d) ID=7.37 μm Ht=0.49



(e) ID= 8.7 μm Ht=0.54

Fig. 3. Deformations of RBCs in various inner diameter capillaries and hematocrit

3.2.2 Transition from single-file to multi-file flow

Transition from single-file to multi-file flow as a function of hematocrit in capillaries of various diameters is shown in Fig.4. Overall tendency in the experiment (Gaehtgens et al., 1980) and simulation are similar qualitatively. RBCs are single-file in narrow tube and at low hematocrit, while they are multi-file as the tube diameter increases or hematocrit increases. A line in Fig.2 is Ht = 2.8/ID. By a rough classification, RBCs are single-file when Ht < 2.8/ID, while they are multi-file when Ht >2.8/ID.

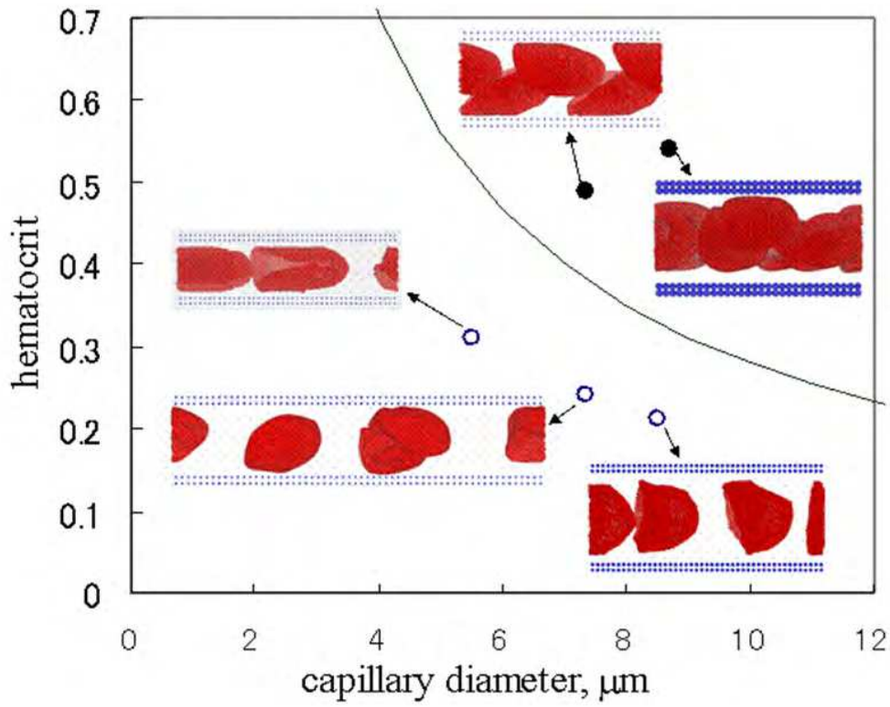


Fig. 4. Transition from single-file to multi-file flow as a function of hematocrit in capillaries of various diameters

3.2.3 Particle simulation about the deviation of RBC distribution in a capillary blood vessel

In Case (d), although RBCs were placed in line initially, they interacted and flows like zipper shape finally. This transition will be described in detail here. In Fig.5, RBC shape are shown for Case (d) ID=7.37 μm Ht =0.49, at 0 ms, 40 ms, 80 ms, 140 ms, 200 ms and 260 ms.

At 40 ms, RBCs are at the center of the blood vessel, parachute type shape, and flows in line. The back of the erythrocyte is dented, and it can also be said the bowl type.

In addition, plasma flow without the RBCs was calculated, the flow was Hagen-Poiseuille flow and velocity distribution at the cross section in pipe was parabola-shaped. When there were RBCs, RBC particles flows together due to the elastic film, and the velocity distribution was near in a trapezoid.

In 80 ms, the inclination occurs to arrangement of RBCs, and intervention happened. Uniformity in the axis center of the parachute-shaped collapsed, and intervention with a face of wall and the surrounding erythrocyte happened.

In time 140 ms, more mutual intervention of an erythrocyte was seen, and the shape is being changed complicatedly while having contact and rallying. A back RBC enters into the indent of the previous RBC, and the transfer state to the zipper type was seen.

Moreover its tendency was strengthened in time 200 ms. Back erythrocyte was entering into the indent of the previous erythrocyte, and 4 erythrocytes have ranged. At 260 ms, RBCs flow in the zipper shape, and it became stable.

As shown, RBCs flow with intervention of a tube wall and between the erythrocytes mutually. Initially RBCs flows with the parachute shape at early stage, but they begun to fluctuate and became unstable state. Mutual intervention of an erythrocyte was seen, and

the shape is being changed complicatedly while having contact and rallying. Finally RBCs flow in the zipper shape, and it became stable.
It is thought that the placement of the red blood cell changes when the condition changes. It is expected that the stable state changes by pipe diameter, a red count, the properties of matter of the red blood cell.

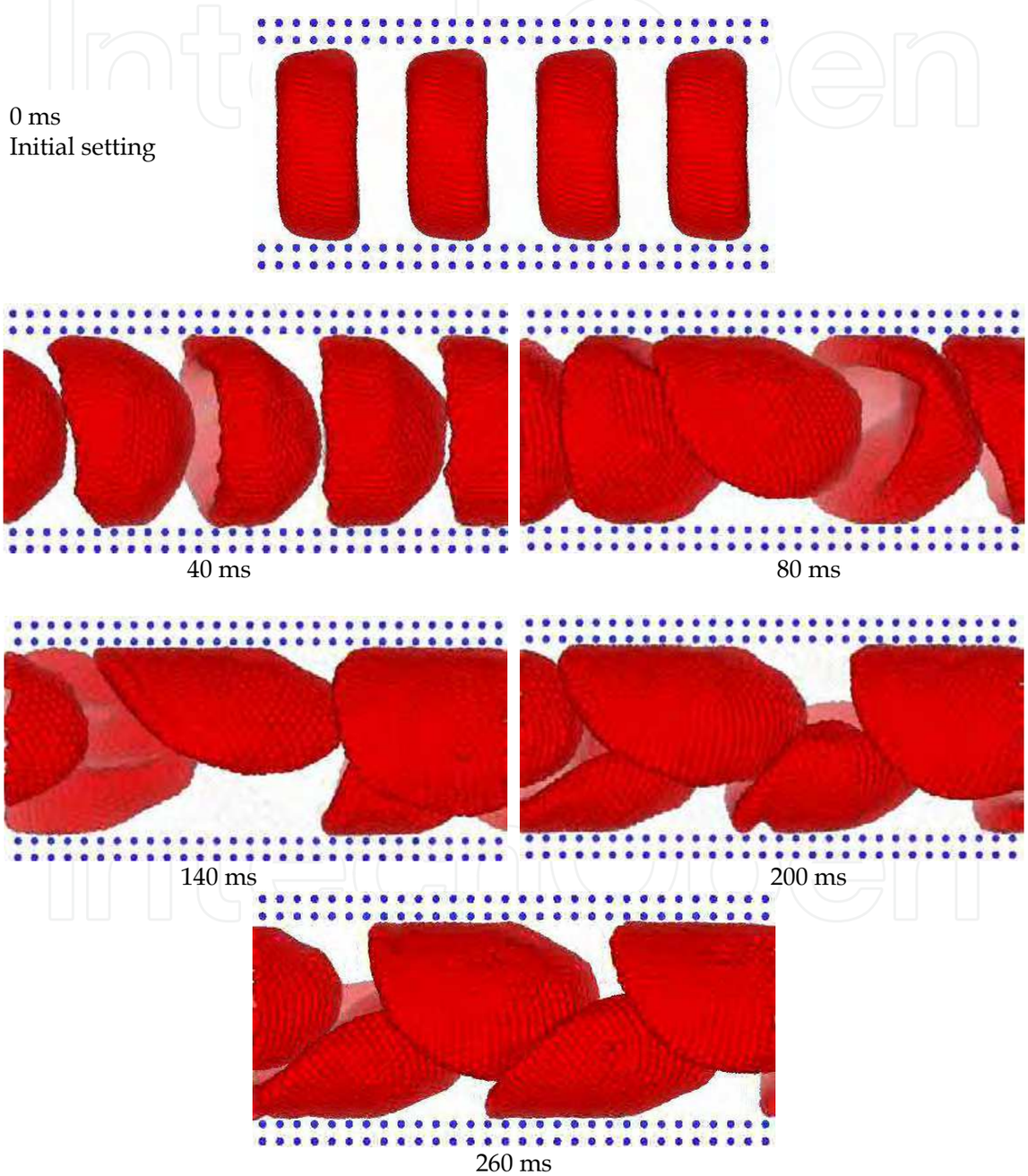


Fig. 5. RBC shape change for ID=7.37 μm Ht =0.49

4. Particle simulations of blood flow in bent and twisted capillary vessel with red blood cells

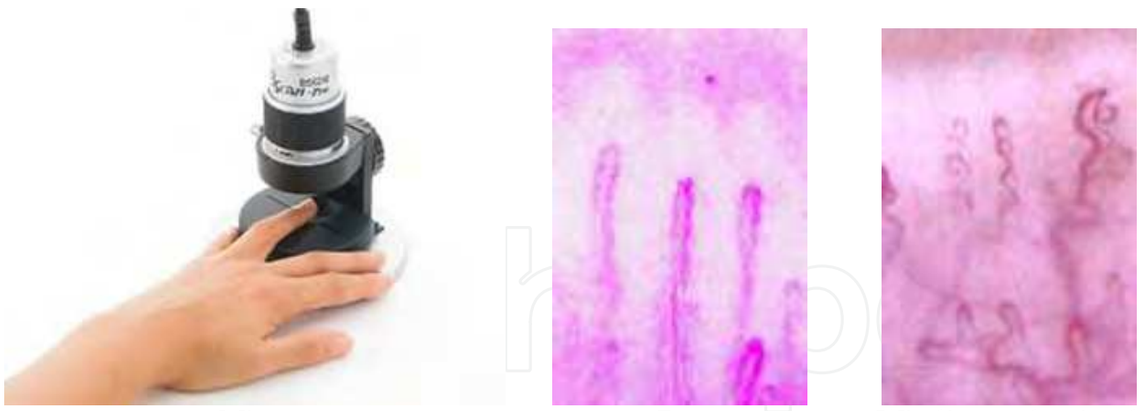
In this section, particle model is applied to simulate the capillary vessel flow in the turning point of blood vessel at finger tip. The capillary vessel is modelled as two cases: one is bent tube and another is bent and twisted tube.

4.1 Simulation conditions

Using microscope, capillary blood vessels can be observed at the finger tip as shown in Fig. 6. They change their shape depending on the health. To supply nutrition and to remove wastes, bent shape is usual and in good health. Winding and twisted shape tend to be observed in unhealthy condition such as high viscosity, although the reason is not clear. Blood flow analysis is important to study blood circulation. Here, particle model is applied to the capillary vessel flow to clarify the flow characteristics and mechanism of shape change.

Physical properties of plasma are density 1030 kg/m^3, and viscosity 1.2 mPa･s. Pressure gradient of 100 kPa/m is applied which cause blood velocity about 1 mm/s. (Note pressure gradient is fixed and the velocity depends on the tube shape and RBC number). Reynolds number is 0.86×10^{-2} and flow field is laminar. Periodic boundary condition is used at inlet and outlet, exit particles are supplied from inlet again.

Two type of basic shape of the capillary vessel is modelled as shown in Fig.7. One is bent tube and another is bent and twisted tube. All the RBC, blood vessel and plasma fluid are modelled as particles and Fig.2 is the initial setting of particles (plasma particles are not shown). Bent tube is inner diameter 6.82μm, length of straight portion 37.2μm. Twisted tube is inner diameter 7.37μm, height 90μm.



Microscope Bent Winding and twisted

Fig. 6. Observed blood vessel at the finger tip

Particles are set every 0.62 μm in bent tube and 0.67 μm in twisted tube. At the surface of RBC, particle density is high to increase the accuracy of RBC shape. Cases for simulation with various RBC number for bent tube and twisted tube are shown in Table 3. To study the effect of RBC on flow field, cases with different number of RBC are simulated. Volume ratio (Hematocrit) of one RBC is 2.23% in bent tube and 1.57% in twisted tube. Hematocrit is 31% in bent tube and 38 % in twist tube, which is close to the typical range of 40-50%. Total particle number including plasma, wall and RBC is minimum 29490 in plasma flow in bent

tube, maximum 85304 in 24 RBC flow in twisted tube. Total simulation time is 100 ms (100000 iterations with time step1 s).

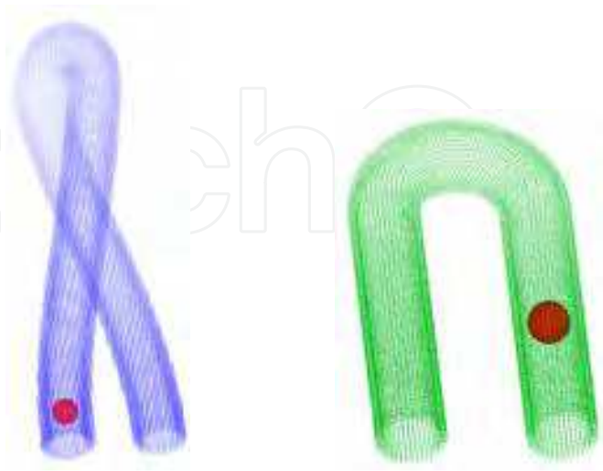


Fig. 7. Model for bent tube and twisted tube (with 1RBC)

Tube type	Number of RBC	Particle number for simulation
Bent tube	0	29490
	1	30742
	14	46995
Twisted tube	0	54446
	1	55728
	24	85304

Table 3. Cases for simulation

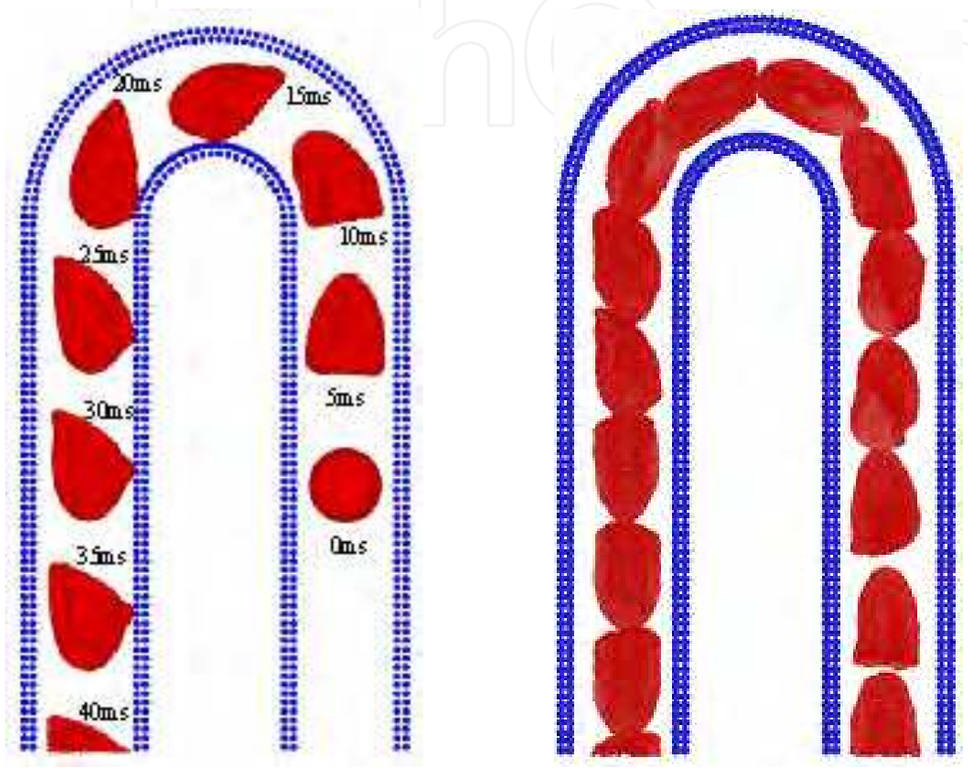
4.2 Results for blood flow in bent and twisted capillary vessel

In this section, results of RBC deformation for two cases: one is bent tube and another is bent and twisted tube will be shown for one RBC and many RBCs.

4.2.1 RBC deformation in bent tube

Simulated RBC shape in bent tube is shown in Fig.8. Fig.8 (a) is the result of one RBC case, and RBC shape is shown every 5 ms up to 40 ms. At 5 ms in the straight portion, RBC is parachute shape due to the fast flow at the tube center and slow flow close to the wall, which is typical in capillary tube. Velocity field around RBC is trapezoid, while parabolic Poiseuille flow in plasma flow far from RBC. At 10 ms to 20 ms, RBC is passing through the bent portion, starts to deform to asymmetric parachute shape. RBC particle tends to pass quickly inside the bent and slowly outside the bent, due to the flow length difference. After 25 ms, RBS shape tends to recover to symmetric parachute shape.

Fig.8 (b) is the snapshot of 14 RBC case at t=80 ms. RBCs tend to flow at the tube center, and the shape is between rocket and parachute. RBCs interact each other and tend to go in the back end of another RBC. When passing through the bent, RBC tends to keep the dent inside the bent.



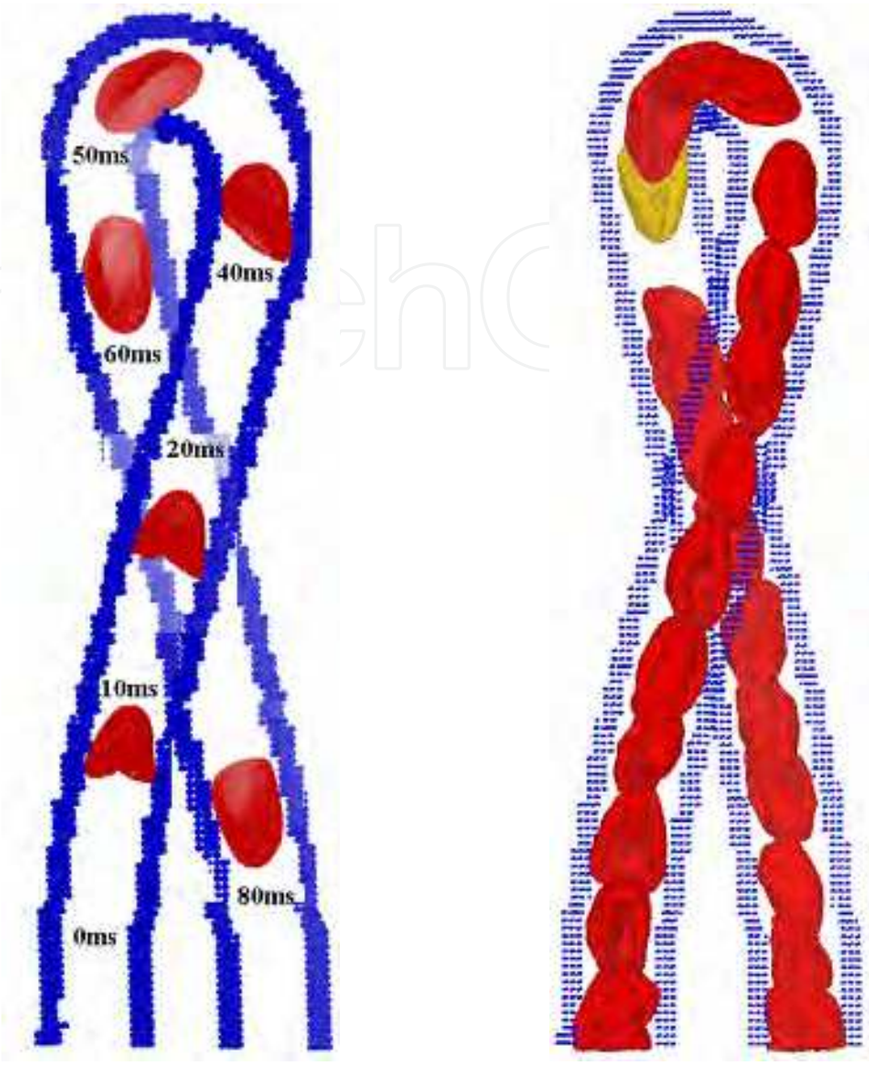
(a) 1 RBC (b) 14 RBCs

Fig. 8. Simulated RBC shape in bent tube

4.2.2 RBC deformation in twisted tube

Simulated RBC shape in twisted tube is shown in Fig.9 Fig.9 (a) is the result of one RBC case, and RBC shape is shown at 20, 40, 50, 60, 80 ms. RBC is parachute shape slightly asymmetric before the bent at 20 ms. At 40 ms to 60 ms, RBC is passing through the bent portion and deforms to asymmetric shape (between flat and parachute shape) due to the twist and bend flow. RBC particle tends to pass quickly inside the bend and slowly outside the bend, due to the flow length difference. After 60 ms, RBS shape tends to recover to symmetric parachute shape.

Fig.9 (b) is the snapshot of 24 RBC case at t=90 ms. RBC shapes are quite uneven by the strong interaction due to the twist and bent.



a) 1 RBC (b) 24 RBCs

Fig. 9. Simulated RBC shape in twisted tube

5. Conclusion

3 dimensional particle model is applied to the capillary straight tube flow.

1. Deformations of RBCs in various ID (inner diameter) capillaries and hematocrit were studied. In case of ID=5.5μm Ht=0.31, RBC flows in lines contacting with the wall and deforms to consistently non-axisymmetric rocket shape. In case of ID=8.5μm Ht =0.2, RBCs flow at center of the blood vessel, parachute type deformation appeared. In case of ID= 7.37μm Ht = 0.49, RBC interacts (multi-file flow) with each other and contact with the wall, forming zipper shape. In case of ID=8.7μm Ht =0.54, RBC interacts (multi-file flow) strongly with each other and contact with the wall, forming strong and complex deformation.

2. Transition from single-file to multi-file flow as a function of hematocrit in capillaries of various diameters is studied. RBCs are single-file in narrow tube and at low hematocrit, while they are multi-file as the tube diameter increases or hematocrit increases.
3. RBC shape change in time was studied for a case of ID= 7.37μm Ht = 0.49 in details. At first, RBCs were flowing in line like a parachute. But after that the shape fluctuated gradually, and it became stable in this case in the zipper state finally. A stable state is expected that it also changes by the pipe diameter, the number of erythrocytes and the physical properties of the RBCs.
4. Particle simulations were applied to the capillary vessel flow at finger tip. In case of bent tube, the RBCs is initially parachute shape at straight tube and then deforms to asymmetric parachute shape. In case of bent and twisted tube, initially RBC is parachute shape and then deforms to asymmetric shape (between flat and parachute shape) due to the twist and bend flow.

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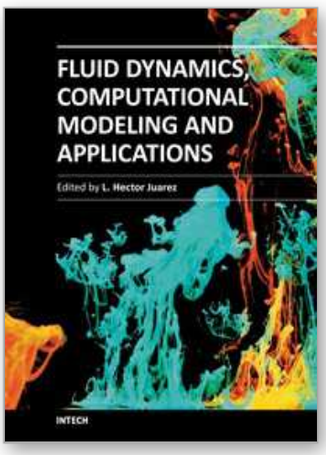

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