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COMPUTER SIMULATION OF TANK-TREADING AND TUMBLING MOTIONS OF RED BLOOD CELLS UNDER THE INFLUENCE OF THE NATURAL STATE OF AN ELASTIC CELLULAR MEMBRANE

Ken-ichi Tsubota[*], Shigeo Wada[†], and Hao Liu[††]

[*, ††]Department of Mechanical Engineering, Chiba University
1-33 Yayoi, Inage, Chiba 263-8522, Japan
e-mail: {tsubota, hliu}@faculty.chiba-u.jp

[†]Department of Mechanical Science and Bioengineering, Osaka University
1-3 Machikane-yama, Toyonaka 560-8531, Japan
shigeo@me.es.osaka-u.ac.jp

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Abstract. *A two-dimensional computer simulation model was proposed for tank-treading and tumbling motions of an elastic biconcave RBC under viscous shear flow. The RBC model consisted of an outer cellular membrane and an inner fluid; the membrane's elastic properties were modeled by springs for stretch/compression and bending to consider the membrane's natural state in a practical manner. Membrane deformation was coupled with incompressible viscous flow of the inner and outer fluids of the RBC using a particle method. The proposed simulation model was capable of reproducing tank-treading and tumbling motions of an RBC along with rotational oscillation, which is the transition between the two motions. In simulations using the same initial RBC shape with different natural states of the RBC membrane, only tank-treading motion was exhibited in the case of a uniform natural state of the membrane, and a nonuniform natural state was necessary to generate the rotational oscillation and tumbling motion.*

1 INTRODUCTION

A motion of single red blood cell (RBC) under viscous shear flow is characterized by the so-called tank-treading motion, defined as steady membrane rotation with constant shape and inclination angle, and tumbling motion, defined as overall rotation of an RBC. The transition between these two types of motion is observed as a rotational oscillation of the entire RBC accompanied by tank-treading motion [1]. The motion of RBC depends on the shear rate, the viscosity ratio between the inner and outer fluids of RBCs, the material properties of the elastic membrane and other physical constants [2-6]. This dependence is based on the fact that physical parameters determine the mechanical state of RBCs. In this sense, a natural state of the RBC membrane, which is defined as a reference configuration of the membrane at the zero-stress state, plays a key role in the mechanical state of RBCs [3,4,6]. In this study, a two-dimensional computer simulation is carried out to examine the effects of the natural state of an elastic RBC membrane on tank-treading and tumbling motions under steady shear flow [7]. A spring model is used for the elastic membrane to consider the distribution of the membrane's natural state in a practical manner, and a particle method is used to perform a coupled analysis of membrane elastic deformation and incompressible viscous flow of the RBC's inner and outer fluids. The RBC shape is initially set to biconcave with a transmural pressure, and different natural states of the membrane with the same initial shape are examined in numerical simulations of RBC motion.

2 METHODS

2.1 Two-dimensional particle method for motion of deformable RBC

A two-dimensional problem with unit thickness h is considered for an RBC motion under incompressible viscous flow. The RBC is divided into an outer elastic cellular membrane and an inner viscous fluid. The fluids and membrane are discretized by an assembly of computed particles [7-9], in which each particle i has physical quantities such as position $\boldsymbol{r}_i$, velocity $\boldsymbol{u}_i$ and pressure p_i. Particles assigned to the RBC membrane, called membrane particles, have the averaged properties of the membrane and its neighboring fluid under a non-slip condition between them.

The RBC membrane particles are connected with neighboring membrane particles by stretch/compression and bending springs to express the membrane's elastic properties [7-10], as shown in Fig. 1. The elastic energy per unit thickness h stored in the stretch/compression springs due to the change in length l from its reference l_0 is expressed as

$$E_{\mathrm{L}} = \frac{k_{\mathrm{L}}}{2}\sum_{I=1}^{N}\left(\frac{l_I - l_0}{l_0}\right)^2 , \tag{1}$$

where l_I denotes the length of stretch/compression spring element I, N is the total

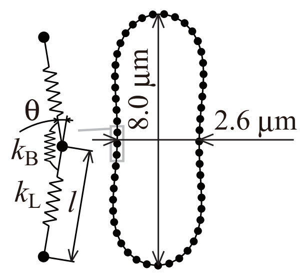

Figure 1: Spring model of RBC.

number of spring elements and k_L is the spring constant. The elastic energy stored in the bending springs is expressed as

$$E_B = \frac{k_B}{2}\sum_{I=1}^{N}\tan^2\left(\frac{\theta_I - \theta_I^0}{2}\right), \qquad (2)$$

where θ_I denotes the angle of bending spring element I, θ_I^0 is the reference angle of the spring I, N is the total number of spring elements and k_B is the spring constant. Spring constants k_L and k_B denote the spring energies per unit strain and angle, respectively. The reference length l_0 of the stretch/compression springs in Eq. (1) and the reference angle θ_I^0 of the bending springs in Eq. (2) are parameters representing a natural state of the elastic membrane. The spring force on each membrane particle i is analytically calculated as

$$\boldsymbol{F}_i = -\frac{\partial W}{\partial \boldsymbol{r}_i}, \qquad \text{where } W = E_L + E_B, \qquad (3)$$

on the basis of the principle of virtual work. In Eqs. (1) and (2), E_L and E_B represent elastic energies $[\mathrm{N}\cdot\mathrm{m}]$ per unit thickness h = 1 m, and thus the units of E_L, E_B, k_L and k_B are Newton [N].

To express an incompressible viscous flow, motions of all particles are determined by the moving particle semi-implicit (MPS) method, a particle method based on an equation of continuity and the Navier-Stokes (NS) equations [11]. For membrane particle i with unit thickness h, the elastic spring force in Eq. (3) is substituted into the particle's NS equation as the external force term [7].

2.2 Simulation model of RBC motion under shear flow

A two-dimensional simulation model is created to investigate an RBC's motion under a steady shear flow, as shown in Fig. 2 [7]. The model consists of an RBC, outer fluid of RBC (i.e. suspending fluid) and the upper and lower walls. The size of the model is D = 20 μm in wall separation distance and L = 20 μm in flow direction. A biconcave RBC, 8 μm in longitudinal length and 2.6 μm in the thickness of the concave part, is placed at the center of the simulation model. As a boundary condition, the upper and lower wall are moved to the left and right, respectively, at a constant velocity u_0 = 1.0×10^{-2} m/s to generate a simple shear flow. A periodic boundary condition is applied to the left and right sides of the model. The viscosity μ_{Out} and density ρ of the RBC's outer fluid are 1.0×10^{-3} $\mathrm{Pa}\cdot\mathrm{s}$ and 1.0×10^{3} kg/m^3, respectively, which are the same as

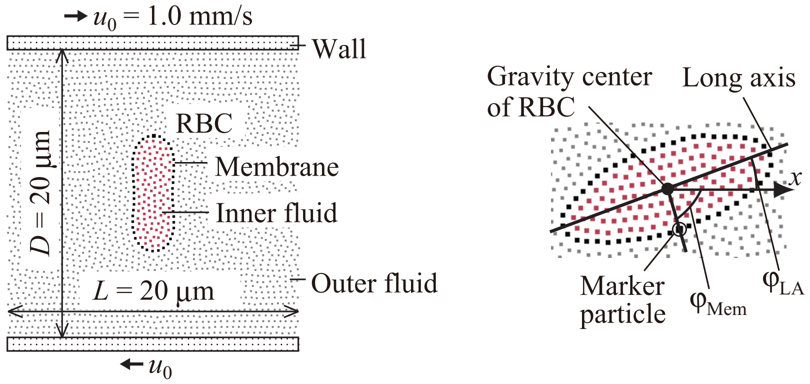

Figure 2: Simulation model of RBC motion under shear flow.

those of water and close to actual blood plasma properties. For the RBC's inner fluid, the viscosity μ_{In} is set to five times the outer value μ_{Out} with the same density ρ, and therefore the viscosity ratio of the inner and outer fluids of RBC, $\mu' = \mu_{\mathrm{In}}/\mu_{\mathrm{Out}}$, is fixed at 5, like that of actual RBCs. With these parameters, the shear rate, $\dot{\gamma} = 2u_0/D$, is 1000, and the Reynolds number, $\mathrm{Re} = u_0 D/\mu_{\mathrm{Out}}$, is 0.2.

An original three-dimensional RBC deformation consisting of planar shear and out-of-plane bending is simplified to bending deformation in the current two-dimensional model. The ratio of the two spring constants, k_{L} and k_{B} in Eqs. (1) and (2), of the RBC membrane is set to be constant, $k_{\mathrm{L}}:k_{\mathrm{B}} = 10:1$, to impose a constraint condition of a constant membrane perimeter that represents incompressibility of the RBC membrane [7]. The area of the inner fluid of the RBC is kept constant to consider a condition of constant RBC volume. The same biconcave shape is maintained under no fluid force, where forces due to membrane stretch/compression and bending springs are balanced by those due to transmural pressure, and residual forces on the membrane of the RBC can be changed according to the spring constants [7].

The relative effect of the fluid viscous force of the outer fluid on the elastic bending force of the RBC membrane is a key parameter in determining the RBC's motion at low Reynolds number Re in the range ~10^1 to ~10^{-2}. This parameter is denoted as bending capillary number $\mathrm{Ca_B} = \mu_{\mathrm{Out}} l_{\mathrm{RBC}}^2 \Phi_{\mathrm{RBC}} \dot{\gamma}/(k_{\mathrm{B}} l_0)$, with $l_{\mathrm{RBC}} = 10$ μm and $\Phi_{\mathrm{RBC}} = 2.5$ μm being the characteristic length and radius of curvature of the RBC, respectively. Simulations of RBC motion are parametrically conducted for different $\mathrm{Ca_B}$ values ranging from 5 to 0.05 by changing k_{B} from 2.0×10^{-11} to 2.0×10^{-9} N. This range of $\mathrm{Ca_B}$ values is equivalent to that of shear rates $\dot{\gamma}$ from 366 to 3.66 with bending spring constant $k_{\mathrm{B}} = 7.3\times10^{-12}$ N, corresponding to a bending modulus of 1.8×10^{-19} $\mathrm{N\cdot m}$ [7].

The mean distance d_0 between computed particles is 0.4 μm, and the number of particles is about 2700. For the elastic membrane model of the RBC, the reference length l_0 in Eq. (1) of all stretch/compression springs is 0.4 μm, the same as the mean particle distance d_0. The reference angle θ_l^0 of the bending spring in Eq. (2) determines a natural state of the two-dimensional membrane and is therefore another key parameter determining the RBC's motion. Therefore, simulations of RBC motion are conducted for different magnitudes and distributions of θ_l^0. The number of springs N in Eqs. (1) and (2) is 48 for both stretch/compression and bending springs.

In the simulation results, RBC motions are characterized as tank-treading and tumbling motions. To quantify these motions, the x axis is set in the flow direction with its origin at the center of gravity of the RBC, and two angles are defined, as shown in the right of Fig. 2. One is angle φ_{Mem} ($-0.5\pi < \varphi_{\mathrm{Mem}} \leq 0.5\pi$) between the x axis and the line connecting the RBC's center of gravity and a certain material point on the membrane. The other is angle φ_{LA} ($-0.5\pi < \varphi_{\mathrm{LA}} \leq 0.5\pi$) between the x axis and the RBC's longitudinal axis. When periodic changes in φ_{Mem} and φ_{LA} are predicted, the periods T_{Mem} and T_{LA} are determined, respectively, by using the time average, and they are normalized by multiplying by the shear rate $\dot{\gamma}$. Time averages of angles φ_{Mem} and φ_{LA} are described as Φ_{Mem} and Φ_{LA}, respectively. For rotational oscillation, the time average of the rotation amplitude in angle is described as Φ_{OA}.

3 RESULTS

RBC motion simulations for different bending capillary numbers $\mathrm{Ca_B}$ from 5 to 0.05 are conducted in the case of the same reference bending angles $\theta_l^0 = 0$ for all bending springs I of the RBC membrane, assuming that a flat membrane shape corresponds to a natural state (zero-stress state) of the RBC membrane. The simulation results show tank-treading motion of the RBC membrane with constant longitudinal angle Φ_{LA} = 0.11π for all Ca_B values considered, following clockwise rotation of the entire RBC in the initial simulation steps, as shown in Fig. 3 [7]. The tank-treading motion is steady, and the nondimensional period of tank-treading is $\dot{\gamma}\, T_{Mem}$ = 66 to 68. Ca_B dependence is observed only for RBC deformation, in that a greater Ca_B results in a more elongated RBC shape, according to the increase in fluid viscous force relative to membrane elastic force. The results are not affected by θ_I^0 values, in terms of steady tank-treading motion with period $\dot{\gamma}\, T_{Mem}$ = 66 to 68 and constant longitudinal angle Φ_{LA} = 0.11π, as long as the same value is set for reference angle θ_I^0 of all bending springs.

Reference bending angles θ_I^0 in Eq. (2) are distributed along the membrane as $-0.01\pi < \theta_I^0 \le 0.11\pi$, as are those in the biconcave RBC shape shown in Fig. 1, and RBC motion simulations for different Ca_B from 5 to 0.05 are conducted. This assumes that a biconcave membrane shape corresponds to a natural state (zero-stress state) of the RBC membrane. In this case, the RBC's motion depends on Ca_B, as shown in Fig. 4 [7]. When Ca_B is greater than 1, a rotational oscillation of the entire RBC occurs, accompanied by a tank-treading membrane motion. The amplitude Φ_{OA} and period T_{LA} of the RBC oscillation increase with decreasing Ca_B, as shown in Fig. 5 [7]. The oscillation period T_{LA} is half the tank-treading period T_{Mem}, reflecting π-rotational symmetry of the RBC shape [4]. Around Ca_B = 1, the RBC's motion transits from rotational oscillation with membrane tank treading to a tumbling motion. In tumbling motion, an RBC is compressed around –0.3π to –0.5π in the longitudinal direction φ_{LA}, as illustrated by snapshots of RBC shapes from $\dot{\gamma}\, t$ = 28 to 31. The period T_{Mem} as a function of Ca_B takes the same values as T_{LA}, illustrating that no tank-treading motion occurs during tumbling motion.

These simulation results demonstrates that an RBC's motion depends on elastic behaviors according to nonuniform distribution of reference bending angle θ_I^0. Here, parameter α is introduced into Eq. (2) to represent the degree of natural state

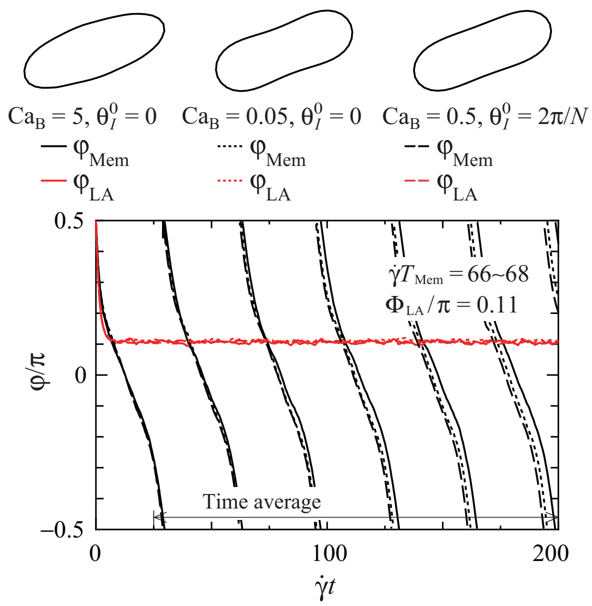

Figure 3: Simulation results of RBC motions in case of uniform natural state of the elastic RBC membrane [7].

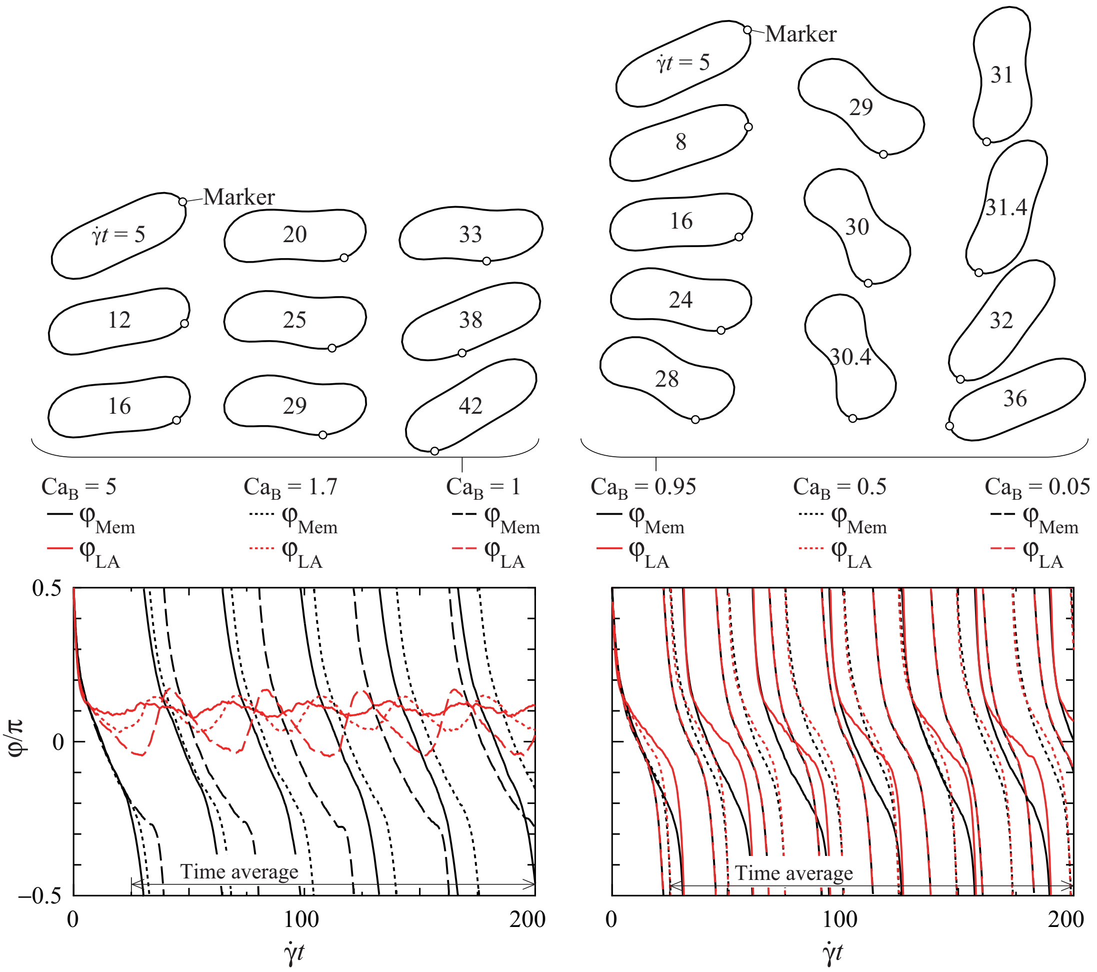

Figure 4: Simulation results of RBC motions in case of nonuniform natural state of the elastic RBC membrane.

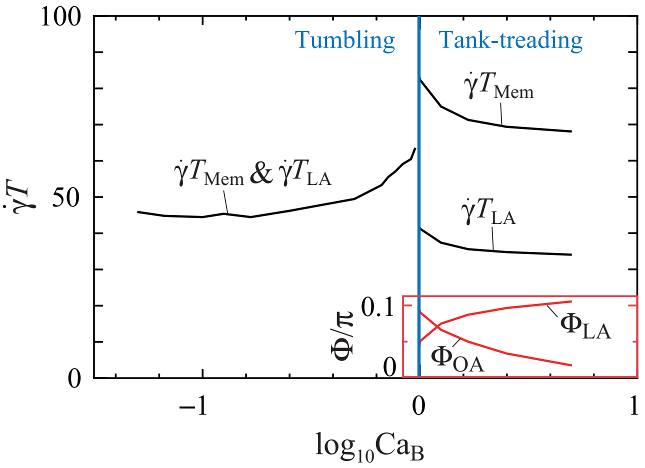

Figure 5: Average periods $\dot{\gamma}\,T$ and angles Φ/π in case of a nonuniform natural state as a function of the logarithm of bending capillary number CaB [7].

nonuniformity,

$$E_b = \frac{k_b}{2} \sum_{I=1}^{N} \tan^2 \left(\frac{\theta_I - \alpha \theta_I^0}{2} \right) \; (0 \le \alpha), \tag{4}$$

and parametric simulations are conducted for different sets of bending capillary number Ca_B and natural state nonuniformity value α. In Eq. (4), $\alpha = 0$ corresponds to a flat membrane in a natural state and $\alpha = 1$ to the biconcave shape shown in Fig. 1. According to bending capillary number Ca_B and natural state nonuniformity α, tank-treading and tumbling motions are exhibited, and the natural state nonuniformity α at which the transition occurs increases with Ca_B. Compiling the results of parametric simulations for seven different Ca_B values, the parameter sets of Ca_B and α at which the transition occurs are plotted in Fig. 6 [7]. This figure provides a phase diagram of an RBC's motion with respect to Ca_B and α.

4 DISCUSSION

Simultaion results demonstrate that elastic deformation plays an important role in overall RBC motions characterised as tank-treading and tumbling motions, in which the natural state of the elastic membrane is an essential consideration. A transition can occur at different bending capillary numbers Ca_B with a certain natural state nonuniformity α, and that the degree of compressive deformation of the RBC increases with Ca_B. Therefore, the natural state and elastic stiffness of an RBC membrane have different roles in determining RBC deformation and motion. The results show good agreement with previously published experimental and computational studies in terms of compressive RBC deformation during tumbling motion, the tank-treading-to-tumbling transition according to the fluid viscous force relative to the membrane elastic force, increase in amplitude Φ_{OA} and period T_{LA} with decreasing Ca_B during overall RBC oscillation, and oscillation periods T_{OA} corresponding to half the values of the tank-treading period T_{Mem} [2-6]. Intermittent behavior of RBC motions in which the two modes occur alternately, predicted by a reduced model [4], is not obtained in this study. This evidence indicates that the tank-treading and tumbling motions are so sensitive to the membrane elastic behavior that under the strong influence of this behavior, the intermittency can be exhibited only in very narrow ranges of parameter space.

The transition behavior between tank-treading and tumbling motions indicated in Fig.

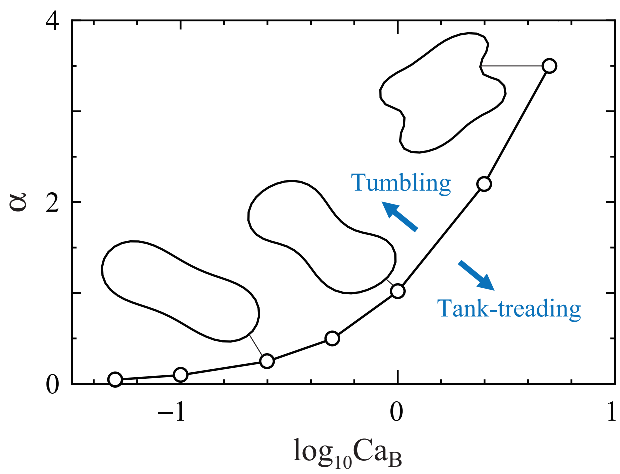

Figure 6: A set of Ca_B and α values at the transitions between tank-treading and tumbling motions.

5 can be explained in terms of the ratio of membrane elastic force to fluid viscous force [7]. In a tank-treading motion, an elastic resistance force is generated in accordance with elastic deformation of the membrane with nonuniform reference angles θ_I^0 of the bending springs. To maintain the tank-treading motion, the elastic force should be less than viscous fluid force applied by RBC's outer fluid.

A blood flow field with multiple blood cells is affected by the motions of a single RBC simulated in this study. The proposed simulation model is applicable to blood flow with multiple RBCs and provides a practical way to examine various conditions for hematocrit, flow velocity and vessel geometry with different diameters and branches. According to the simulation results obtained in this study, the natural state of an RBC membrane would be an essential consideration in understanding multiscale mechanics of blood flow in a micro-vessel network system. In respect to quantitative understanding, three-dimensional simulations are indispensable and now underway [10].

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