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A Particle Method for Blood Flow Simulation, – Application to Flowing Red Blood Cells and Platelets –

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Abstract A new computer simulation using a particle method was proposed to analyze the microscopic behavior of blood flow. A simulation region, including plasma, red blood cells (RBCs) and platelets, was modeled by an assembly of discrete particles. The proposed method was applied to the motions and deformations of a single RBC and multiple RBCs, and the thrombogenesis caused by platelet aggregation. It is expected that, combined with a sophisticated large-scale computational technique, the simulation method will be useful for understanding the overall properties of blood flow from blood cellular level (microscopic) to the resulting rheological properties of blood as a mass (macroscopic).

Keywords: Computational Biomechanics, Blood Flow, Red Blood Cell, Platelet, Rheology

1. INTRODUCTION

Presently, cardiovascular disease is one of the most frequent causes of death in industrialized countries [1]. There is considerable indication that complex hemodynamics (blood fluid mechanics) plays an important role in the development of artherosclerosis and other kinds of vascular diseases [2, 3]. Although extensive experimental, theoretical and numerical studies have been conducted in this area, to the best of our knowledge, there is as yet no study that has revealed a direct relationship between blood fluid dynamics and the development of atherosclerosis [3]. In this regard, some unresolved questions need to be clarified, one of which is the property of blood flow from blood cellular level.

Because human blood can be regarded as a homogenous fluid from a macroscopic viewpoint, established numerical techniques based on continuum mechanics, such as finite difference method (FDM), finite volume method (FVM) and finite element method (FEM), have been used to analyze blood flow as homogeneous fluid. At the microscopic level, however, blood is regarded as a suspension in which solid blood cells, such as red blood cells (RBCs), white blood cells (WBCs) and platelets, are suspended in fluid plasma. Consequently, the particle method is a natural choice for simulating blood flow on a blood cellular scale, in which each component of blood is modeled by an assembly of discrete particles [4, 5].

The purpose of this paper is to propose a computer simulation method of blood flow using a particle method, in which blood cells and plasma are directly modeled to investigate blood flow behavior at the microscopic level. The motion of a single deformable RBC [6] and the thrombogenesis caused by platelet aggregation [7] are analyzed as problems at the capillary level. Moreover, this particle method is useful for investigating the micro-macro relationships of blood flow from a viewpoint of computational biomechanics, in which mechanical interaction among multiple blood cells is important. To realize this kind of multiscale simulation by direct modeling using a particle method, which is computationally more expensive compared with FDM, FVM and FEM, parallel-vector computation using the Earth Simulator (ES) system [8] is employed in the proposed particle method. This is one of the methods among the current computational environments that can overcome the difficulty in computing the collective behavior of a large number of RBCs (on the order of 100 μm to cm) directly from blood cellular scale (μm).

2. PARTICLE METHODS

FDM, FVM and FEM are very powerful and most popularly and widely used methods for solving engineering

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problems. In these methods, continuum domain is discretized into fixed discrete grids (nodes) or meshes (elements), which are connected together in a predefined manner with a suitable interpolation function. This strategy with fixed grids or meshes assures both robustness and accuracy when obtaining the solution of a differential equation using the discrete system. However, this strategy also gives several limitations in analyzing complex geometries and multiphysics problems, which consequently limits the application of these methods to biomechanical problems.

The limitations of the fixed grid- and mesh-based methods have triggered the development of a mesh free method which uses only a set of distributed nodes to express the mechanical system in a discretized form [9]. Each node is called "particle" in a particle method, and it moves in Lagrangean coordinates driven by interaction forces determined by the discretized form of governing equations for the particles. This makes it easy to trace the solid-fluid interface for a large deformation. In a blood flow simulation using a particle method, every particle can represent one discrete physical object (e.g., a small blood cell such as a platelet) or can be generated as a set of particles to represent a part of the physical domain (e.g., a large blood cell such as an RBC, and fluid plasma) [10], as shown in Fig. 1.

In this paper, the moving particle semi-implicit (MPS) method [11] is used to analyze blood plasma flow. This method is a particle method developed for incompressible flow analysis based on Navier-Stokes (N-S) equations. The number density of particles is maintained as its reference value to express incompressibility. The gradient and Laplacian of physical quantity ϕ, used in Navier-Stokes equations, on particle i are expressed by the summation of physical quantities ϕ over neighboring particles j with a kernel function w (weighing function of distance) as

$$\langle \nabla \phi \rangle_i = \frac{d}{n^0} \sum_{j \neq i} \left[\frac{\phi_j - \phi_i}{|\mathbf{r}_j - \mathbf{r}_i|^2} (\mathbf{r}_j - \mathbf{r}_i) w(|\mathbf{r}_j - \mathbf{r}_i|) \right] \quad (1)$$

and

$$\langle \nabla^2 \phi \rangle_i = \frac{2d}{n^0 \lambda_i} \sum_{j \neq i} \left[(\phi_j - \phi_i) w(|\mathbf{r}_j - \mathbf{r}_i|) \right],$$
$$\lambda_i = \frac{\sum_{j \neq i} \left[|\mathbf{r}_j - \mathbf{r}_i|^2 w(|\mathbf{r}_j - \mathbf{r}_i|) \right]}{\sum_{j \neq i} w(|\mathbf{r}_j - \mathbf{r}_i|)}, \quad (2)$$

where $\mathbf{r}$ is the position vector, d is the number of space dimensions and n^0 is the reference value of the particle number density [11]. With this discretization using particles, fluid flow is solved using an algorithm similar to a simplified marker and cell method.

3. BLOOD FLOW SIMULATION USING PARTICLE METHOD

Two-dimensional numerical examples are briefly summarized as follows: (1) motion and deformation of a single RBC [6], (2) primary thrombogenesis caused by platelet aggregation [7], and (3) collective behavior of multiple RBCs.

3.1 Motion and Deformation of Single RBC [6]

Simulation model of blood flow between parallel plates

Blood flow on a capillary scale was analyzed to examine the basic characteristics of the proposed particle method. A two-dimensional particle model was constructed for the blood flow between parallel rigid plates, as shown in Fig. 2 (a). The model consisted of fluid particles for blood plasma, elastic particles for the RBC membrane, and rigid particles for the rigid plates. The sizes of the model were L = 80 μm in regard to axial flow length and D = 10 μm in regard to the distance between the plates. Particle distance was set to 0.5 μm, and the total number of particles was 4919. The physical property of plasma was assumed to be the same as that of water. As a boundary condition, constant and uniform velocity in the axial direction was applied to the fluid particles placed at the inlet. The Reynolds number with respect to the dis-

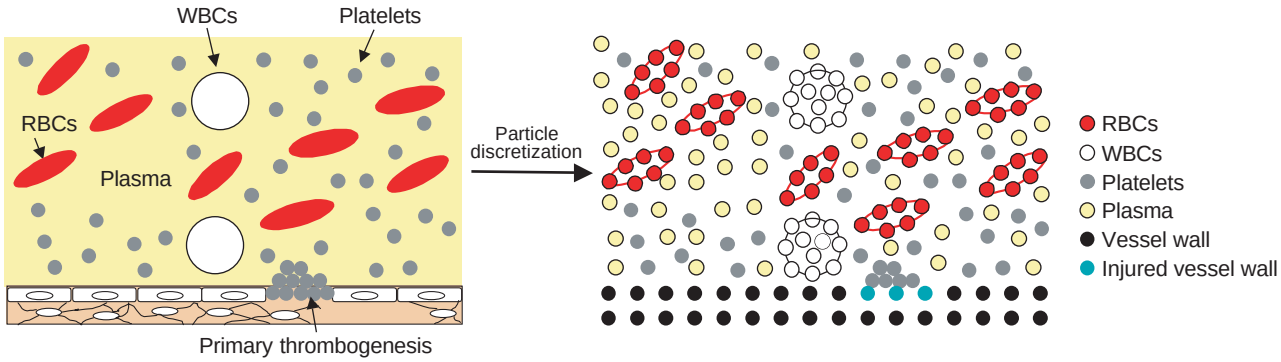
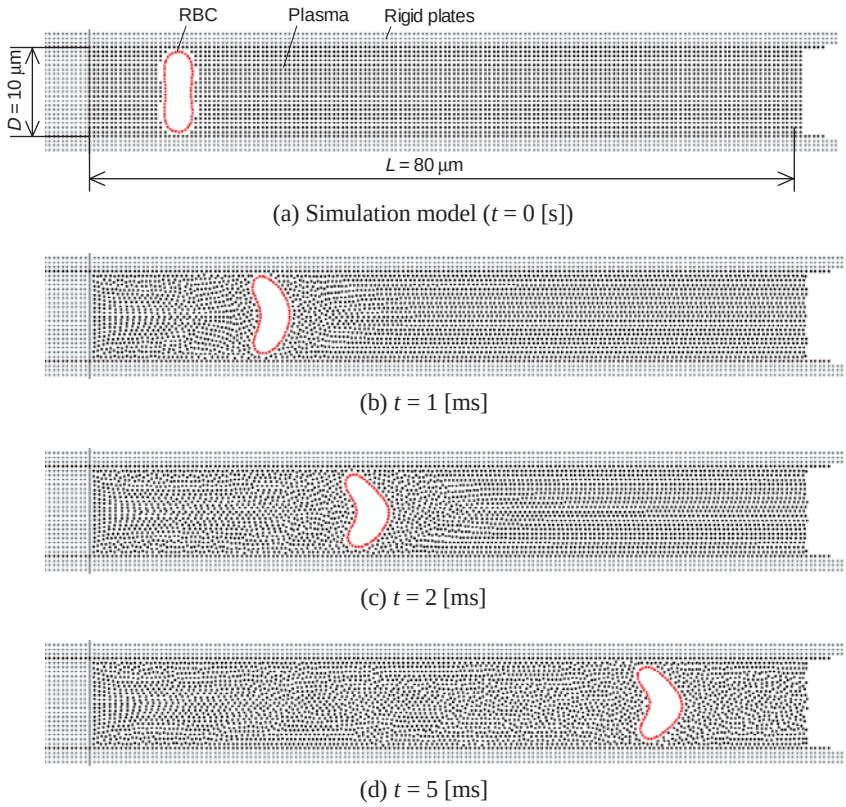


Fig. 1 Particle modeling of blood at blood cellular level



(a) Simulation model (t = 0 [s])

(b) t = 1 [ms]

(c) t = 2 [ms]

(d) t = 5 [ms]

Fig. 2 Particle method simulation of motion and deformation of single red blood cell (RBC) in blood flow

tance between the plates D was 0.1. Zero pressure was applied at the outlet, and a nonslip condition at the inner vessel wall.

Motion of deformable RBC

RBC was modeled by 59 particles configuring an RBC membrane. These particles configured the same number of line elements to express the mechanical behavior of an RBC membrane with a small number of particles. The elastic energy of the RBC membrane was considered for changes in the length of the element and the angle between the neighboring elements [12]. Moreover, areal constraint was introduced to express internal pressure within an RBC [12]. An initial biconcave shape, as shown in Fig. 2 (a), was obtained by the shape change simulation of a swollen RBC based on a minimum energy principle for a decrease in the RBC area by 70% from a circular shape.

Results

The simulation result revealed changes in RBC shape and position in blood flow. Because fluid pressure was higher upstream than downstream, the RBC was accelerated to move downstream at the beginning of the simulation, as shown in Figs. 2 (a) and (b). The fluid pressure caused the deformation of RBC into a concave shape on the upstream and a convex shape on the downstream. These shapes correspond to an experimental observation, the so-called parachute shape. After the initial acceleration, pressure force became proportional to viscous force, and the RBC moved at a constant velocity maintaining its deformed shape, as shown in Figs. 2 (c) and (d).

3.2 Primary Thrombogenesis Caused by Platelet Aggregation [7]

Model of platelet aggregation and adhesion

The particle method simulation is applied to primary thrombogenesis caused by platelet aggregation to an injured vascular wall, in which fluid mechanical factors play an important role. Each platelet was modeled by a single particle. Because the size of each platelet is considered to be very small compared with the characteristic size of a blood vessel, the platelets were assumed to move along with blood plasma flow when they were far from the injured wall. In the region near the injured wall within distance d_{ag}, the aggregation of the platelets was assumed to be stochastic and the probability of aggregation is higher for the platelets closer to the injured wall. This probability was expressed by introducing an attractive force acting between the aggregating platelet and the injured wall. When the aggregating platelets were within the distance d_{ad} ($< d_{ag}$), the platelets were assumed to adhere on the injured wall and neighboring adhered platelets, and to behave as a solid material. The deforma-

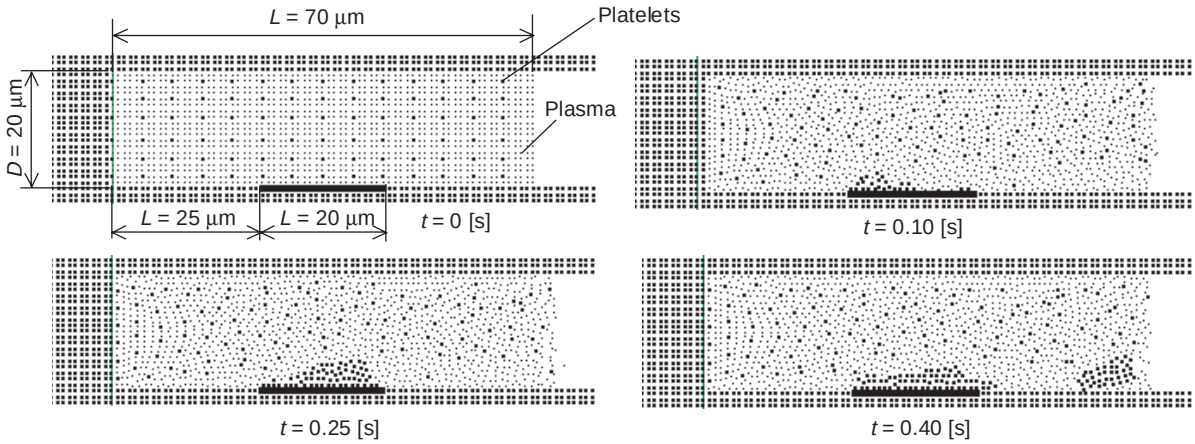


Fig. 3 Particle method simulation of primary thrombogenesis caused by platelet aggregation

tion of the adhered platelets as a solid material was expressed by introducing normal and tangential spring forces acting among the adhered platelets and the injured wall.

Results

A two-dimensional blood flow simulation between parallel plates was conducted in the case of the Reynolds number of 0.02, as shown in Fig. 3. The sizes of the model were L = 70 μm in regard to axial flow length and D = 20 μm in regard to the distance between the plates. Particle distance was set to 1.0 μm and the total number of particles was 3044.

An injured wall was placed on the center of the lower plates. At t = 0.10 [s], the platelets started to aggregate to the injured wall because of an attractive force acting between the platelets and the injured wall. After the first aggregation, the number of platelets attached to the injured wall increased with time and the size of the aggregated platelets grew until t = 0.25 [s]. Thereafter, the platelets were detached because of the fluid force of the plasma flow at t = 0.40 [s]. These results suggest that the proposed particle method can simulate the generation, growth and destruction of a primary thrombus.

3.3 Collective Behavior of Multiple RBCs

Flow model of multiple RBCs [13]

In blood vessels larger than an RBC, collective behavior under the influence of mechanical interaction between RBCs is increasingly important to determine the rheological properties of blood as a mass. In this section, a simulation method for multiple RBCs is proposed for understanding the rheological properties of blood from a viewpoint of multiscale mechanics. Assuming that macroscopic flow field is not affected by each RBC motion, macroscopic flow field was determined by theoretical/numerical analysis. The momentum and viscous fluid forces acting on RBC were evaluated from the difference in the velocities between the RBC and the prescribed flow field. Moreover, the mechanical interaction among the multiple RBCs was expressed by an attraction-repulsive potential function assigned at each nodal point on the RBC membrane.

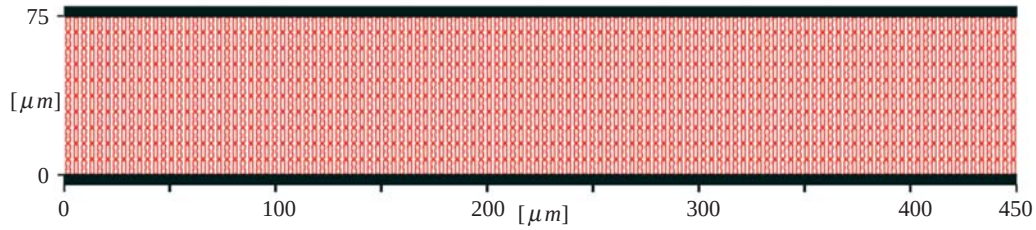
Simulation model and parallel computing technique

A two-dimensional blood flow model between parallel plates was constructed using 10 × 120 = 1200 RBCs as shown in Fig. 4 (a). Each RBC was modeled by 100 particles. The size of the model was 200 μm in regard to axial flow length and 75 μm in regard to the distance between the plates. The Poiseuille flow was assumed as the prescribed flow field. The ES system [8], a vector/parallel super computer system, was used to simulate the problem, in which we used 80 processors and 12 hours in real time (960 hours in CPU time). The parallel computation using a standard MPI library was employed, and the simulation region was divided into 80 regions similar to the number of the processors. Preliminary numerical experiments showed that data communication time greatly affected computing time in the simulation. Therefore, communication was performed per 1000 calculation steps, which did not change the essential result from that obtained in the case of a full communication.

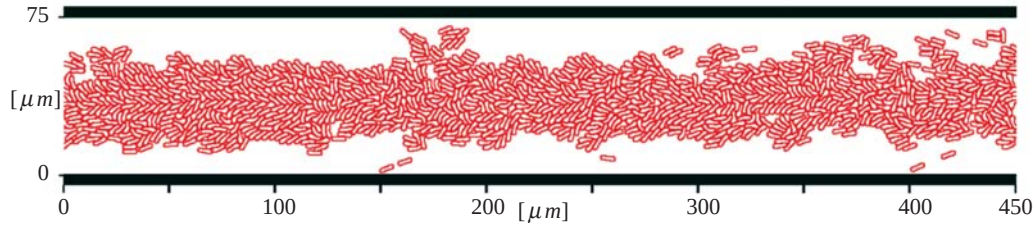
Results

As for the simulation codes developed for the 80 processors on the ES system, the vector operation ratio, average vector length and parallel efficiency were 99.30%, 203.19 and 98.69%, respectively. These specs were acceptable when using 1024 processors in the ES system. The code enabled us to calculate blood flow in 98.9 [s] of simulation time, in which RBCs could travel from the inlet to the outlet.

The simulation result demonstrated that RBCs flowed downstream because of fluid force and concentrated to



(a) Simulation model



(b) Multiple RBCs flow obtained by simulation

Fig. 4 Large-scale simulation of flow of multiple RBCs using parallel computing technique

the flow axis as shown in Fig. 4 (b). This axial concentration, corresponding to experimental observation, would play an important role in the distribution of the RBCs into daughter vessels at bifurcations [13]. To understand this kind of collective behavior in RBC flow, further studies are necessary to clarify the characteristics of the model parameters introduced into the RBC model [12,13], and to investigate the effects of assumptions on the prescribed flow field in the simulation results.

4. DISCUSSION AND CONCLUSION

Three applications of a particle method for studying blood flow were briefly analyzed. The simulation results demonstrate that the proposed method enables the analyses of a single RBC motion and deformation, initial thrombogenesis, growth and destruction of a thrombus, and the collective behavior of multiple RBCs. This indicates that this particle method is potentially an important and useful approach for investigating the mechanical behavior of blood cells in blood flow at the microscopic level.

Although the proposed method seems to be very useful in evaluating the microscopic mechanical behavior of blood flow, the results obtained by the computer simulation need to be validated by comparing these simulation results with experimental results. Thus, we are currently developing a parallel plate flow chamber to obtain some experimental results using a confocal micro particle image velocimetry (μPIV) [14]. Moreover, another very important ongoing work is the performance of a large-scale calculation using a parallel computing technique, which will be an extended work under Sec. 3.3. Sophisticated computing techniques using a powerful hardware, such as the ES system [8], will increase significantly the number of particles used in the proposed particle method. Furthermore, we intend to extend our simulations from a two-dimensional analysis to a three-dimensional analysis. With these developments, the proposed simulation method would express blood flow from the viewpoints of both multiphysics and multiscale, contributing to the understanding of the overall properties of blood flow from blood cellular level (microscopic) to the resulting rheological properties of blood as a mass (macroscopic).

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