Particle Modeling for Complex Multi-Phase System with Internal Structures using DEM

Project Representative
Hide Sakaguchi Institute for Research on Earth Evolution, Japan Agency for Marine-Earth Science and Technology

Authors
Hide Sakaguchi Institute for Research on Earth Evolution, Japan Agency for Marine-Earth Science and Technology
Shigeo Wada Department of Mechanical Science and Bioengineering, Osaka University
Masanori Nakamura The Center for Advanced Medical Engineering and Informatics, Osaka University
Yosuke Imai Department of Biomechanics and Robotics, Tohoku University
Kenichi Tsubota Graduate School of Engineering, Chiba University

In 2008, we ran the simulation of red blood cells' (RBC) flow for a prolonged period and at more physiological hematocrit using an RBC model established in 2007. A multi-scale simulation of blood flow was also carried out in order for analyzing mesoscopic phenomena of blood flow and investigating the effects of hematocrit on the axial velocity profile.

Keywords: Red blood cell (BRC), Particle, Fluid, Multi-phase system, Internal structure, Discrete Element Method

1. Introduction

Physics of the mixture of solid and liquid is of major interest to scientists. It exhibits significantly complex rheology in relation to a bulk proportion of solid. The nature becomes much more complex as the solid particles form an internal micro-structure within a mixture. Even with a low percentage of solid, the material shows more or less solid-like behavior.

The main objective of this project is to establish a particle-continuum-coupled model based on a discrete element method, which is capable of expressing the multiphasic nature consisting of solid, liquid or perhaps gas that shows complex behaviors with forming an internal structure such as clustering.

The blood is a concentrated suspension of cells (solid) in plasma (fluid), an aqueous solution that generally follows Newtonian dynamics. The blood cells are mainly red blood cells (RBCs) which constitute for about a half of the total blood volume. Approximately 5 million RBCs are present in 1 mm^3 of blood. Thus, blood flow is essentially multiphasic. Under a low shear flow, RBCs stack up, forming rouleaux and aggregations which are internal structures. The particulate nature of RBCs, their inclining and deformabilities, and physical interactions such as collisions and contacts significantly contribute to behaving as a multiphase suspension and resulting in non-Newtoninan dynamics.

It is generally accepted that hemodynamics is related to cardiovascular and cerebrovascular disorders including arterial sclerosis. For instance, prolonged disturbances of blood flow triggers a formation of thrombus, thereby leading to stroke, which can cause permanent neurologic and myocardial damage or even death. With westernization of the Japanese-style, it has been obvious that death from coronary heart disease and cerebral infarction stemmed from atherosclerosis is increasing. Atherosclerosis is characterized by accumulation of lipids and macrophages under the inner wall of arteries. It causes stenosis that narrows the vessels and impedes normal blood flow. It is therefore of central importance to analyze hemodynamics at micro and mesoscopic levels based on the discipline of multi-phase system with internal structures.

In 2007, we studied collective behaviors of RBCs flowing in a stenosed artery. From the results, we found that stenosis jeopardizes a man not only because it obstructs blood flow but also because it may seed thrombus formations by enhancing agglomeration of RBCs. We also found that stiffening of RBCs may contribute to causing hypertension. In 2007, we also implemented a multi-scale simulation of blood flow in order for analyzing mesoscopic phenomena of blood flow. Since this method is very time-consuming, we had not obtained a converged-state yet by the end of 2007, which was a remaining problem to this year.

In 2008, we continued a multi-scale simulation of blood flow in which blood flow is modeled in two different scales; a macroscopic blood flow was represented by a continuum model, and a microscopic blood flow was modeled by par-

ticulate RBCs' flow. By means of this simulation, we investigated the influence of hematocrit (RBC volume fraction) on macroscopic blood rheology. In addition, we ran the simulation of red blood cells' (RBC) flow for a prolonged period and at more physiological hematocrit.

2. Prolonged calculation of RBC flow

This year, we ran a simulation of RBCs flow for a period much longer than before. The model of an RBC was the same as used in 2007 [1]. In brief, the RBC was modeled as a closed shell membrane consisting of triangular meshes. Neighboring meshes were connected with bending springs to prevent folding of membrane. Nodal points were linked by spring elements to resist to stretching. Fluid forces exerted by blood flow were estimated based on the momentum conservation and Newton's friction law. In order to maintain the volume and surface area of RBC, constraint functions of those were imposed. A mechanical interaction between two RBCs is expressed by a potential function with respect to a distance between these two. A dynamic behavior of RBC in the given flow field was determined toward the minimum energy state. RBCs were distributed uniformly within a cylindrical blood vessel at hematocrit of 15%. Assuming that each RBC motion does not affect velocity field of blood flow, we prescribed a macroscopic velocity of Poiseuille flow. Flowing behaviors of RBCs were simulated using 256 processors on ES for 72 hrs.

RBC showed various flowing behaviors, depending on their radial position; RBCs concentrate around the center of the vessel, forming a cluster, while those near the wall were relatively sparse. Figure 1 plots the ratio of the axial velocity of each RBC to that of Poiseuille flow against its radial position. Here, a radial position is normalized with a channel radius. As seen in Fig. 1, the ratio was more diverse towards the wall. The diversity of the ratio was quantified as the standard deviation for the data of normalized radius 0-0.1, 0.1-0.2, 0.2-0.3 and so forth as shown in Fig. 2. The standard deviation increased significantly from the center to the wall. Due to a fluid shear, RBCs flowing near the wall are more prone to moving towards the center of a flow channel, causing frequent collision and contact between RBCs and thereby enhancing fluctuation of the axial velocity near the wall. On the other hand, as RBCs flowing around the center of a channel do not undergo such a radial displacement, they did not collide each other and therefore variation of the ratio was not comparatively large.

3. Calculation of RBCs' flow under more physiological condition

In general, hematocrit, RBC volume concentration, is 40%. By 2007, most of RBC flow calculations we made was conditioned at hematocrit of less than 25%, since a higher

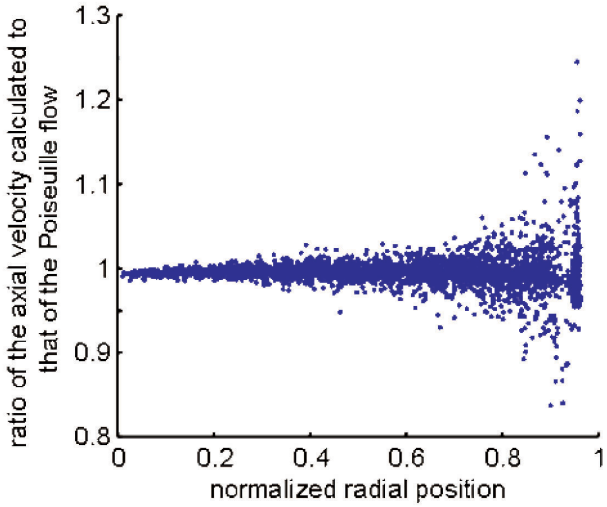

Fig. 1 Plot of the ratio of the axial velocity of each RBC to that of Poiseuille flow against its radial position.

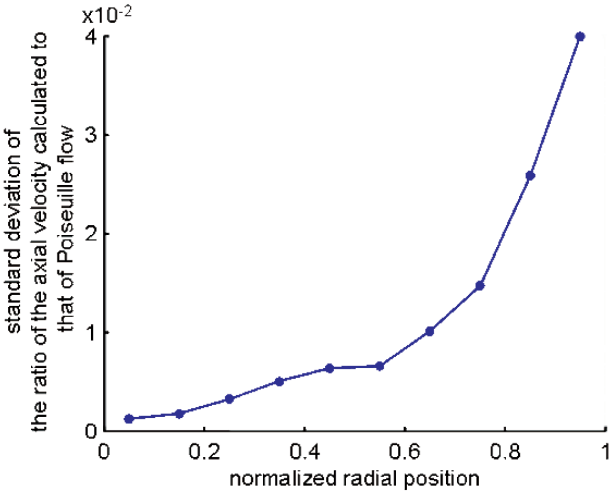

Fig. 2 Change in standard deviation of the ratio of the axial velocity calculated to that of Poiseuille flow against the normalized radial position.

hematocrit condition is computationally expensive and it was quite difficult to pack RBCs within a limited room of blood vessel at a high hematocrit. Actually, it was necessary to align RBCs orderly within a blood vessel in order to achieve hematocrit of 35%. In 2006, we calculated RBCs flow at this hematocrit, however, the results were not fluid-mechanically interesting since the initial alignment of RBCs was not disturbed because it was too crowded for RBCs to move in a radial direction.

We here attempted to break the initial alignment of RBCs with randomly providing virtual velocity in a radial direction. Figure 3 shows snapshots of RBCs at the initial alignment and after the disturbing treatment. As seen, the initial arrangement of RBCs totally disappeared, showing a randomized alignment of RBCs within the flow channel. Using this RBC alignment as the initial condition, we calculated

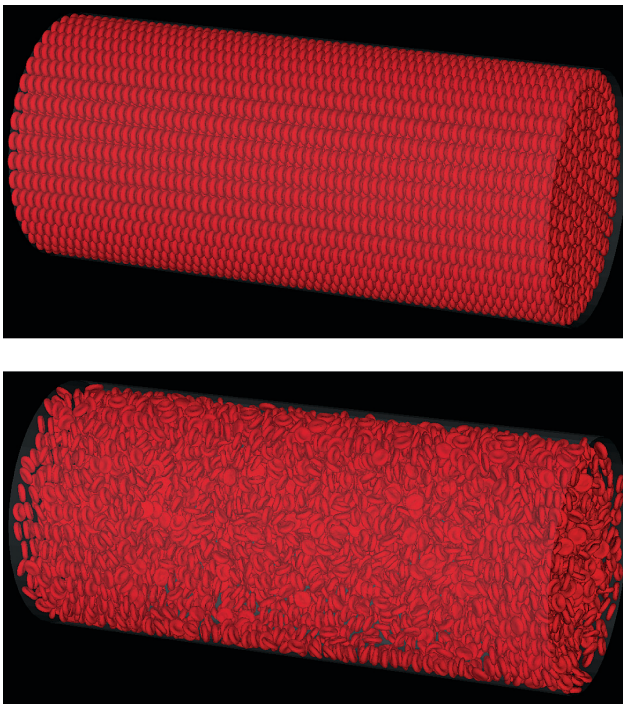

Fig. 3 Snapshots of RBCs at hematocrit of 35% at the initial alignment (upper) and after disturbing treatment (lower).

RBCs' flow in Poiseuille flow. A series of snapshots showed that RBCs near the central axis flow as agglomerate and often show tank-treading motions. On the other hand, those near the vessel wall behave more individually, inclining against a flow direction and showing axial migrations. Such a difference in RBC motions may contribute to enhancement of RBC flow and oxygen transports.

4. Mesoscopic blood flow simulation by multi-scale modeling

Approximately half volume of blood is composed of RBCs which are believed to strongly influence blood flow properties. Non-Newtonian properties of blood are basically derived by the collective behaviors of RBCs. We therefore investigated the rheological properties of blood at a meso-scale by interactively carrying out the micro-scale simulation of RBCs' flow and the macro-scale simulation of the blood flow.

A micro-scale flow was simulated by solving multiple RBCs flow which are the same as the one in section 2 and 3. The macroscopic flow was modeled by a continuum described by the equations of continuity and Navier-Stokes. In order to take into account a local variation of blood viscosity due to a spatial distribution of RBCs within a blood vessel, we expressed a viscous coefficient in the Navier-Stokes equation as an exponential unction of the local hematocrit. Based on the empirical formula of the relationship between Casson viscosity and hematocrit [2]. The macroscopic flow and the microscopic flow were calculated interactively to simulate the mesoscopic flow. Assuming Poiseuille flow as the initial macroscopic flow, the microscale flow for a period of 0.1 s was calculated. From gained RBC distributions, local viscosity in each subdivided flow regime within a cross-section was estimated. Using local viscosity in the Navier-Stokes equation, the macroscale flow was calculated. The resultant velocity profile was then sent back to the microscale simulation. This process was repeated until no substantial change in the axial velocity profile.

The results showed a drastic change in the distribution of RBCs with progress of the simulation. The spatial distributions of RBCs at the initial state and the converged state are shown in Fig. 4 as a contour plot of hematocrit. At the initial state, RBCs were randomly distributed within the flow channel. As RBCs were carried downstream by a fluid flow, they inclined and migrated to the center of the flow channel. As a result, RBCs were concentrated around the center and barely found near the wall, forming a plasma layer. A series of the axial velocity profile from the initial to the converged state are depicted in Fig. 5. At the initial state, the velocity profile was parabolic as given. With progress of the simulation, there was a tendency that velocity at the center of the flow channel decreased.

Figure 6 plots a change in the axial velocity at the center of channel with progress of mesoscopic simulation for hematocrit of 15, 25 35%. Here, the axial velocity at each step is normalized with that at the first step or Poiseuille flow. Comparison of the results at different hematocrit showed that the axial velocity at hematocrit of 35 % decreased more drastically than others, but at the converged state, the normalized velocity at hematocrit of 35 % is

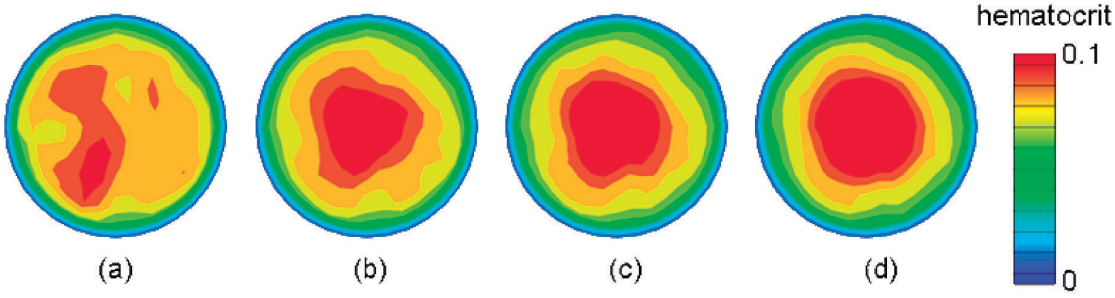

Fig. 4 Contour plots of hematocrit at (a) 1st step, (b) 6th step, (c) 11th step and 16th step.

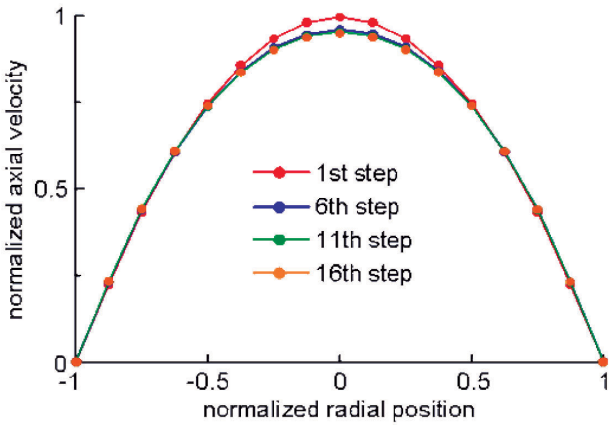

Fig. 5 Change in an axial velocity profile during the mesoscopic blood flow simulation at hematocrit of 0.15.

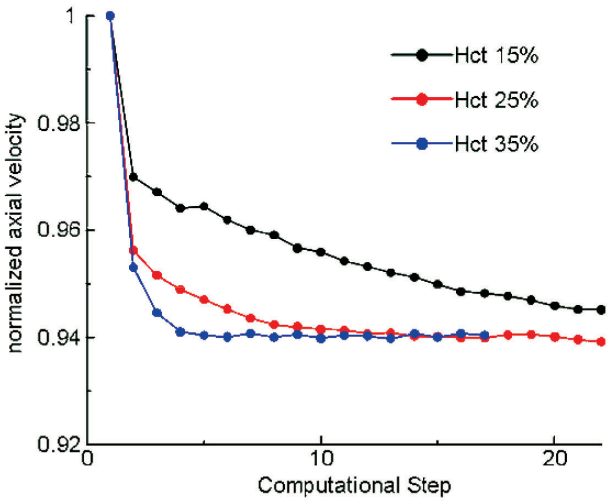

Fig. 6 Change in the normalized maximum velocity during the mesoscopic blood flow simulation at hematocrit of 0.15, 0.25 and 0.35.

almost the same as that of 25%. The velocity at 15% was larger than that of 25% and 35% at the final step, however, declining tendency may last until the normalized velocity becomes equal to the one at hematocrit of 25 and 35%. This would be due to the limited number of RBCs that can exist at the central part.

It is quite obvious that RBC behavior induced a change in a macroscopic velocity profile and *vice versa*. With an axial migration of RBCs, the RBC concentration became higher around the center of the channel while that near the wall became less, bringing about an increase in blood viscosity around the center and the decrease near the wall, respectively. As a consequence, the flow velocity around the center of the channel decreased and that near the wall increased, developing into a flat velocity profile. These results addressed the potential of the present computational approach to the analysis of the rheology of blood in small vasculatures where non-Newtonian property of blood is not negligible.

5. Conclusion

This year, we studied performed a prolonged calculation of RBC's flow, simulation of RBC flow at more physiological condition and mesoscopic blood flow simulation by multi-scale modeling in order to gain better understanding of blood rheology in microcirculation. The former two works provide useful information to understand not only an RBC behavior but also collective behaviors of RBCs. Comparison of snapshots of RBCs flow with other physical data such as velocity provides indispensable information that is not directly measured. The multi-scale simulation of blood flow was quite time-consuming. Nonetheless, this method provides valuable information to understand the mechanism to induce non-Newtonian nature of blood flow.

Toward the year 2010, we will perform some experiments to corroborate our simulations results that have been obtained. At the same time, we fill focus more on RBCs flowing in a high-shear flow. In-depth analysis of RBC deformation and strain distributions over the RBC membrane will contribute to exploring the mechanism of hemolysis.

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DEMによる内部構造を持つ複雑多相系の粒子モデル

プロジェクト責任者
阪口　秀　海洋研究開発機構　地球内部変動研究センター
著者
阪口　秀　海洋研究開発機構　地球内部変動研究センター
和田　成生　大阪大学　大学院基礎工学研究科
中村　匡徳　大阪大学　臨床医工学融合研究教育センター
今井　陽介　東北大学　大学院工学研究科
坪田　健一　千葉大学　大学院工学研究科

本プロジェクトは粒子系離散モデルに基づいて、液相（血漿）と固相（赤血球）が混在する血液の複雑な流動現象を解明することを目的としている。2008年度は①赤血球流動の長時間計算、②生理学的な条件まで赤血球容積率をあげた場合における赤血球流動計算、③血流のマルチスケールシミュレーションの3項目について研究を行った。まず、①であるが、これまで実時間スケールにおいて1秒以下でしか検討できなかった赤血球流動がより長い時間スケールではどのように変化していくのかを検討するために、一つの赤血球容積率において長時間に渡って計算し、血球流動パターンの変化していく様子について検討した。これにより、ランダムに配置された赤血球が、ポアズイユ流が発達した直円管内で、流れに沿ってどのように振舞うのかについて明らかにした。②についてであるが、昨年まで赤血球の容積率は最大で20%程度で生理学的な条件のほぼ半分であった。今年度は、これを生理学的な35%まで上げて赤血球流動の計算を行い、ヘマトクリットが赤血球流動に与える影響について検討した。③は，昨年度において試みた血流のマルチスケールシミュレーション手法を今年度は完成させて、異なる赤血球容積条件下でメゾスコピックスケールでの血液流動の解析を行ったものである。ここでは血流を赤血球集合と連続体という2つの異なるスケールにてモデル化し、それらのモデルを局所赤血球体積濃度に基づく局所血液粘度および血管軸流速度という物理的要素を通じて、相互に関連づけて計算を繰り返した。個々の赤血球が流動することで赤血球濃度の空間的な分布の変化し、計算収束時に得られた血流速度分布は、初期に与えた放物線状の速度分布とは異なる流速分布となった。血管内全体に対する赤血球容積濃度（ヘマトクリット）を15、25、35%の3通りに変えて、計算を行ったところ、ヘマトクリットが大きくなるにつれて、中心軸付近での速度低下が大きくなり、より生体内での流れ場に近いものとなった。

キーワード：赤血球, クラスタ形成, 流体, 多相系, 離散要素法