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

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Following the development of thee-dimensional model of an elastic red blood cell (RBC) and establishment of a simulation scheme of RBCs flowing up to the end of 2005, we developed a visualization tool of RBCs flow and investigated the influence of hematocrit and stenotic geometry on collective behavior of RBCs. We also performed an experimental study to verify computational results and study chaotic fluctuations of velocities of RBCs flowing.

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

1. Introduction

Mixtures of solid and liquid are of major interest in many physical applications. Generally, those materials exhibit significantly complex rheology as related to a fraction of solid. The phenomenon becomes much more complex when the solid forms an internal micro-structure composed of particles. In this case, 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 discrete element method, for the system where particulate materials exist as a mixture of solid, liquid and perhaps gas phases and show complex behaviors with forming an internal structure such as clustering.

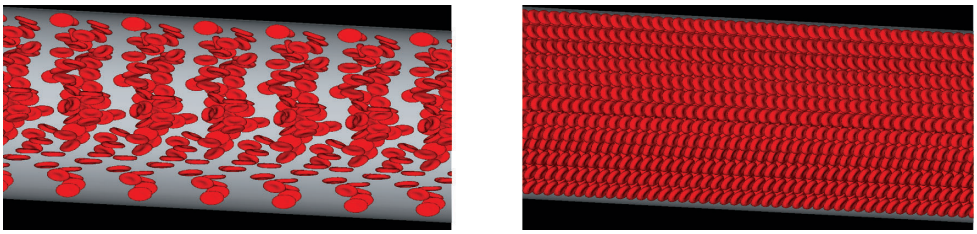
The blood is a concentrated suspension of cells (solid) in plasma (fluid), an aqueous solution that generally follows Newtonian dynamics. The blood cells are mainly red blood cells (RBCs) which constitute for about a half of the total blood volume. Approximately 5 million RBCs are present in 1 mm^3 of blood. Thus, blood flow is essentially multiphasic phenomenon. Under a low shear flow, RBCs begin to 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.

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.

2. Influence of hematocrit on RBC flow

Blood is composed with approximately half volume of red blood cells (RBCs) which is believed to strongly influence its flow properties. Hematocrit (RBC concentration) of the simulation results we presented in 2005 was 17.5%, which was much smaller than reality. This year, we ran a simulation of RBCs flow under a much more concentrated condition. The model of an RBC was the same as used in 2005. In brief, an RBC was expressed with a spring network that gives elastic resistances to bending and stretching. The interaction between multiple RBCs was expressed by a potential function. RBCs were distributed uniformly within a cylindrical blood vessel at desired hematocrit. For instance, 16256 RBCs were placed for hematocrit of 35%. Assuming macroscopic flow field is not affected by each RBC motion, the macroscopic flow field was prescribed. Fluid forces acting on RBCs due to the difference in the velocities between the RBC and the macroscopic flow were estimated based on the



(a) hematocrit 5% at t = 2.0 s (b) hematocrit 35% at t = 0.24 s

Fig. 1 Snapshots of RBC flowing through a cylindrical blood vessel.

momentum conservation and the Newton's law. Here, we adopted Poiseuille flow as the macroscopic flow field. Flowing behaviors of RBCs were simulated using 256 processors on ES for 12 hrs [1].

Figure 1 shows snapshots of RBCs flowing at hematocrit of 5 and 35%. Note that the time when those snapshots were taken was not the same: t = 2.0 s for 5% and t = 0.24 s for 35%. As seen in Fig. 1 (a), the initial arrangement of RBCs was totally broken in the case of 5% hematocrit. RBCs show 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. On the other hand, in the case of 35% hematocrit the initial arrangement was rarely disturbed, not showing fluid-mechanically interesting flowing behaviors due to insufficient length of a computation time.

In 2006, we made efforts in effectively parallelizing a computational code to deal with a high-hematocrit RBC flow. In fact, this contributes to enlarging a simulation scale and actually allows us to implement much dense RBC flow as described above. However, because not only the number of RBCs to be calculated but also physical interactions between RBCs increase as hematocrit became larger, a computational cost increases drastically. These results addressed the importance of improvement in RBC models and vectorization of the computational code for analyzing a real blood flow.

3. Visualization of RBC flow at the inside of a blood vessel

In order to investigate collective and individual behaviors of RBCs flowing though a micro vessel, it was necessary to develop a visualization tool. The tool must be easy to handle, and can be run on a normal PC.

We developed the visualization method using OPEN-GL and POV-Ray. Figure 2 shows a snapshot of RBCs flowing through a circular blood vessel, in which a part of the vessel is removed such that behavior of the RBCs flowing even near the central axis of the vessel can be visualized[2]. A series of snapshots revealed 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 the RBCs behavior is a quite new finding in biorheology. Detailed study to confirm the reality of these numerical observations is currently under way.

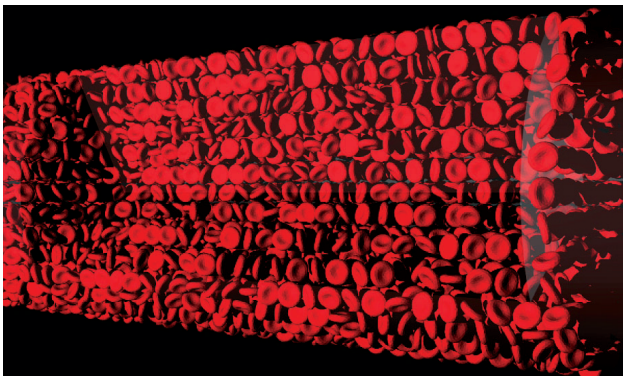


Fig. 2 A part of the vessel is removed such that behavior of the RBCs flowing even near the central axis of the vessel can be visualized.

4. Experimental study of fluctuations in RBC flow velocity by a confocal micro-PIV

The computer simulations have shown that flowing velocity of an RBC is not constant even at a stable state as illustrated in Fig. 3 where radial and axial velocities are plotted against a radial position of each RBC. These velocity variations were expected to be derived from physical interactions of RBCs.

An experimental study of investigating velocity fluctuations of RBCs' flowing was performed using a confocal mico-PIV system[3]. This technique combines the conventional PIV system with a spinning disk confocal microscope (SDCM). Due to its outstanding spatial filtering technique together with the multiple point light illumination system, this technique has the ability to obtain in-focus images with optical thickness less than 1 μm.

The RBCs were labeled with a fluorescent cell tracker (CM-Dil, C-7000, Molecular Probes) and then diluted with dextran 40 to make up the desired RBCs concentration by volume. The microchannel used was a PDMS circular microchannel (75 μm in diameter) fabricated by a wire casting technique.

The confocal micro-PIV system used consists of an inverted microscope (IX71, Olympus, Japan) combined with a confocal scanning unit (CSU22, Yokogawa) and a diode-

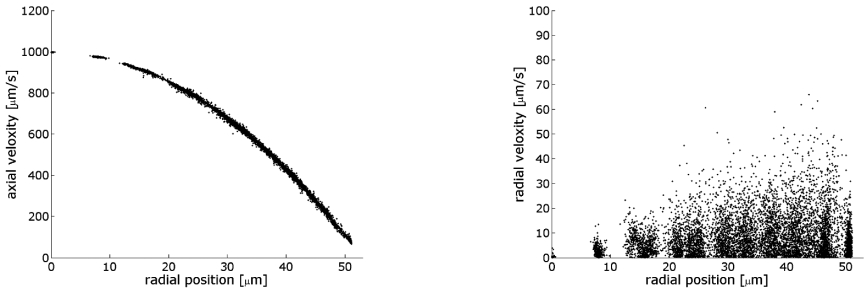
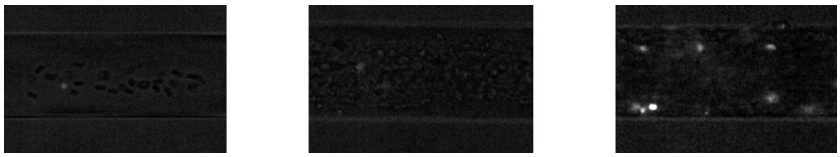


Fig. 3 Axial and radial flow velocities of RBCs obtained from computer simulations are plotted against their radial positions to show their variations.



(a) hematocrit 3% (b) hematocrit 14% (c) hematocrit 37%

Fig. 4 Snapshots of RBCs flowing through a microchannel (20×, 1.6 zoom objective lens).

pumped solid state (DPSS) laser (Laser Quantum Ltd) with an excitation wavelength of 532 nm. The flow rate of the working fluids was kept constant (Re = 0.004). A thermo plate controller (Tokai Hit) was set to 37°C. All the confocal images were captured in the middle of the microchannels with a resolution of 640 × 480 pixels, 12-bit grayscale, at a rate of 100 frames/s with an exposure time of 9.4 ms.

Figure 4 shows labeled RBCs flowing in the microchannel at different Hcts. RBC paths are strongly dependent on the Hct and as a result the radial RBC displacement increases with the hematocrit. The results also indicate that the interactions of RBCs are more predominant around the plasma layer.

Fluctuation of the RBC velocities was assessed by the root mean square (RMS) of the axial velocities. An RMS of the experimental results is shown in Fig. 5. The RMS was almost constant except near the wall. In addition, RMS increased with an increment of hematocrit. A similar tendency, but more profound increase in RMS towards the wall was found in our computer simulation as depicted in Fig. 6. Contrary to the experimental results, the computer simulations have shown that the RMS became smaller as hematocrit increased. The reason to account for this discrepancy is currently unclear. Ongoing detailed simulations as well as experiments will provide an opportunity to uncover it.

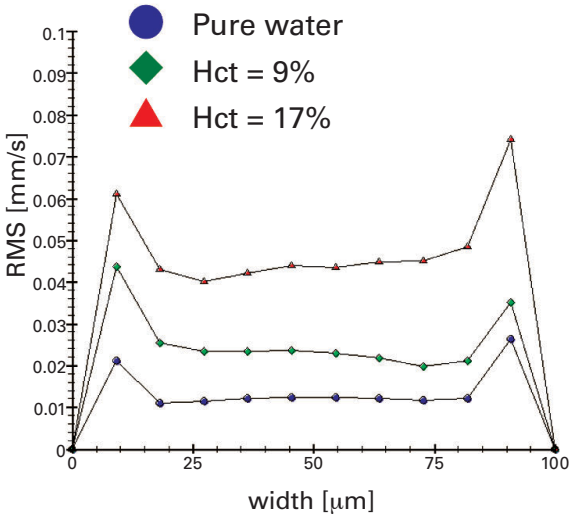


Fig. 5 RMS of RBC velocities obtained by experiments.

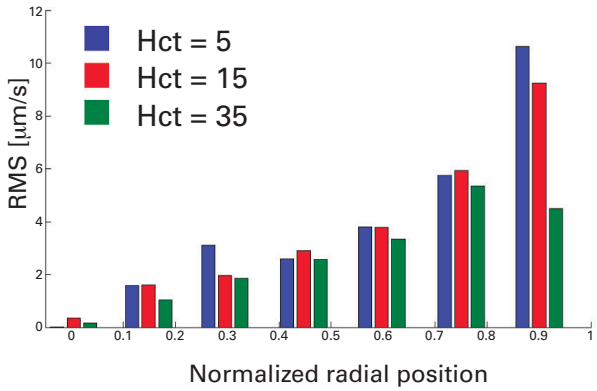


Fig. 6 RMS of RBC velocities obtained by computer simulations.

5. Computer simulation of stenotic RBC flow

In diseased arteries, a fatty material called plaque accumulates in the inner lining of blood vessels and results in narrowing and stenosis. To investigate behavior of RBCs flowing through a stenotic blood vessel, simulations were performed. Vessel models with being differently stenosed were prepared. RBCs were distributed evenly within the vessel at the hematocrit of 15%. Simulations were run with 256

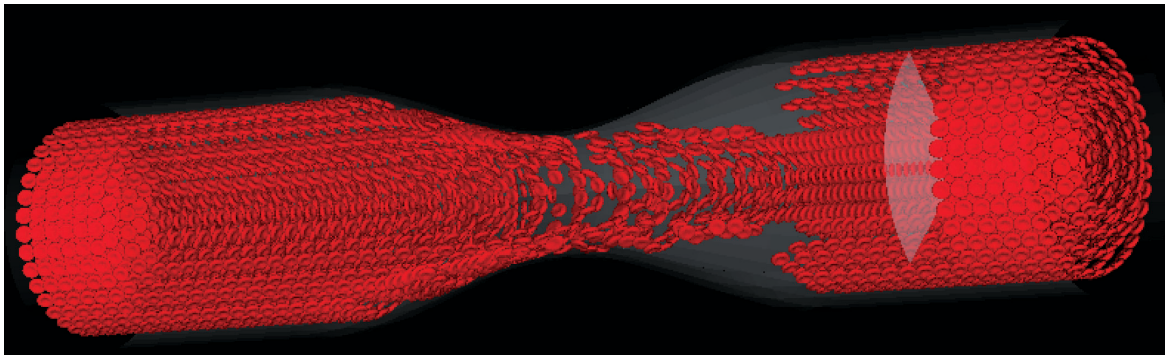


Fig. 7 Snapshot of RBCs flowing through an artery with 50% stenosis.

processors on ES for 12 hrs.

Figure 7 is a snapshot of RBCs flowing through a 50% stenosed blood vessel at t = 0.1 s after the simulation was commenced. When RBCs were passing through stenosis, they were forced to concentrate and developed into a cluster due to tapering of the vessel. In other words, even though hematocrit is normal, the stenosis can cause an abnormal hematocrit condition instantaneously. Moreover, once the cluster was formed, it had not been disassembled even after RBCs have passed the stenosis. If such a cluster persists and grows, it becomes a large thrombus that causes of stroke and acute myocardial infarction. Therefore, the stenosis is risky not only from a viewpoint of vessel narrowing but also from a viewpoint of a seed of thrombus formation.

6. Conclusion

This year, we developed a visualization tool of RBCs flow and investigated the influence of hematocrit and stenotic geometry on collective behavior of RBCs. We also performed an experimental study to verify computational results and study chaotic fluctuations of velocities of RBCs flowing. Toward the year 2008, we will continue to investigate blood flow dynamics. Multi-scale modeling will break through in more detailed analysis of mesoscopic blood rheology. By calculating deformation and stresses acting on RBCs when they flow and collide with others, the mechanism of hemolysis will be explored.

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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

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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。2006年度は①赤血球流動に及ぼすヘマトクリット（赤血球体積分率）の影響に関する検討、②赤血球流動の可視化手法の開発、③赤血球流動速度のゆらぎに関する検討、④血管狭窄部の血球流動計算を行った。①ヘマトクリットが5, 15, 25, 35%の場合における赤血球流動を計算し、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。結果として、いずれのヘマトクリット条件においても赤血球が物理的に相互干渉しながらクラスタを形成するが、ヘマトクリットによりクラスタの大きさや形状が変化し、それが全体の赤血球流動に影響を及ぼすことがわかった。しかしながら、ヘマトクリットが上昇するにつれて、1CPUが計算する赤血球量が増えると共に赤血球同士の干渉頻度が大きくなるため、計算コストが劇的に増大し、高ヘマトクリットの条件では定常な流れ場の結果を得ることができなかった。このことから、今後、計算コードのベクトル化の強化を図ると共に赤血球モデルの節点数を削減する必要があることが示された。②赤血球流動の様子を可視化するための手法を開発した。これにより血管壁に近い位置では赤血球は流れに沿って配向しつつ、離散的に流れているのに対し、中心部では配向せず、赤血球同士が密着して集団的に流れることがわかった。③これまでの計算結果より、赤血球間の干渉により赤血球が流動する速度は一定ではなく、揺らいでいることが示されてきた。これを検証するためにマイクロ流路中に実際に血液を流し、共焦点レーザー顕微鏡にPIVにて赤血球速度を計測した。実験においても赤血球速度の揺らぎが観察され、その程度は壁に近づくにつれて増加した。この結果は計算結果と定性的に一致しており、計算結果の妥当性が示された。④中央付近に狭窄を有する血管内における赤血球流動について検討した。結果より狭窄部にて赤血球が合流することにより、瞬間的に高ヘマトクリット状態になることがわかった。このことから血管の狭窄は急性心筋梗塞を引き起す塞栓の形成に関与している可能性が示された。

キーワード：赤血球, クラスタ形成, 流体, 多相系, 離散要素法