Usage Report for Fiscal Year 2022

Project Title:

The numerical analysis of oxygen transport in the microcapillary

Name:

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1. Background and purpose of the project, relationship of the project with other projects

Red blood cells (RBCs) are the most abundant cells in human blood and are essential for tissue oxygenation. Their ability to deform and pass through narrow capillaries is crucial for their function. Multiple equilibrium states, such as tumbling, parachute, and slipper, have been observed in experimental and numerical studies. However, the effects of local hydrodynamics and RBC deformability on equilibrium states and transformations over a wide range of Capillary numbers are unclear.

RBC deformability is determined by various factors, including viscosity ratio and membrane shear modulus. Viscosity ratio is the ratio of the viscosity of the fluid inside the cell to that of the fluid outside the cell, which is usually five times higher than the viscosity of plasma outside the cell. Studies have shown that as the viscosity ratio increases, the deformability of RBCs decreases. The membrane's shear modulus, which refers to its resistance to shear deformation, also plays a crucial role in RBC deformation. The stiffer the membrane (higher the shear modulus), the more difficult it is for RBCs to deform.

It is important to understand how deformability affects the phase transition of erythrocytes in microchannels to understand blood rheology in pathological conditions in diseases[1-3] such as sickle cell anemia, diabetes, and others in which the deformability of cells are impaired because of stiffened cell membranes or viscosity-increased cytoplasm. In this report, we investigate the different roles of viscosity ratio and shear modulus of RBC membrane on phase diagrams and equilibrium positions.

2. Specific usage status of the system and calculation method

In FY2022, our Quick Use project utilized approximately 2,300,000 core*hours to simulate the motion and deformation of red blood cells in a microchannel using a parallel code based on hybrid OpenMP and MPI.

Figure 1 shows a cross-section of the simulation area, where the microchannel has a length of L, a diameter of D, and a radius of R. A pressure difference Δp drives the fluid flow, and the unperturbed velocity profile is given by equation (1), where $r(r \in [0, R])$ is the distance from the channel's centerline, and μ_{out} is the viscosity of the extracellular fluid.

$$u(r) = \frac{1}{8\mu_{out}} \frac{\Delta p}{L} (R^2 - r^2), \quad (1)$$

The average velocity $\bar{U}$ is given by equation

$$\bar{U} = \frac{\int_0^R u(r)\mathrm{d}r}{\pi R^2} = \frac{D^2}{32\mu_{out}} \frac{\Delta p}{L}, \quad (2)$$

and the average shear rate of the flow field is defined as

$$\bar{\dot{\gamma}} = \frac{\bar{U}}{D}. \quad (3)$$

To explore the influence of the initial position on the equilibrium state and position, we placed the RBCs at various positions r_{int}, defined as the

initial position of the cell's center of mass from the channel's axis. To maximize the range of r_{int}, we initially arranged the cells with the axis of symmetry perpendicular to the flow direction, as shown in Figure 1.

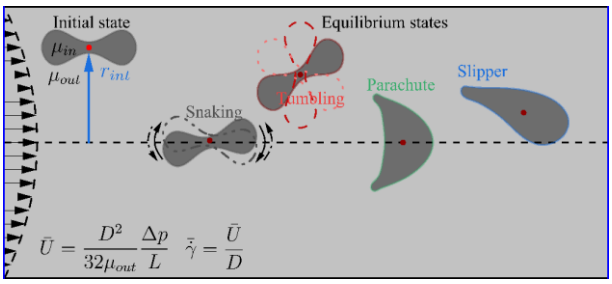

Fig. 1. Schematic diagram of the computational domain of the present simulation. The fluid viscosity inside and outside the cell is μ_{in} and μ_{out}, respectively. RBCs are initially placed at a distance r_{int} from the tube center and then released, and the cells of varying colors represent potential equilibrium states when the flow is fully developed.

The fluid-structure interaction(FSI) problems are solved by the immersed boundary method(IBM). The Navier-Stokes equations are solved with the Simplified Marker and Cell(SMAC) Method. The second-order central difference scheme is used for the spatial discretization and the implicit Euler scheme is used for the viscous term to loosen timestep constraints.

3. Result

In Fig. 2, we show the equilibrium states and positions of red blood cells with a threefold greater shear modulus than normal cells. The solid and hollow dots represent the results for normal erythrocytes and those with hardened cell membranes, respectively. Our findings suggest that increasing the shear modulus has little effect on the distribution of equilibrium states in the phase diagram. This supports the results of Fedosov's previous research[4] and further clarifies that the Capillary number, represented by $\dot{\gamma}^* = Ca * \chi$, is the critical parameter that controls the distribution of RBC equilibrium states under the combined influence of initial positions and shear rates. Although changes in the cell's shear modulus have little effect on the phase diagrams of the equilibrium state along the horizontal axis of $\dot{\gamma}^*$, our simulations provide valuable insights into the complex interplay between local hydrodynamics and cell deformability in microchannels.

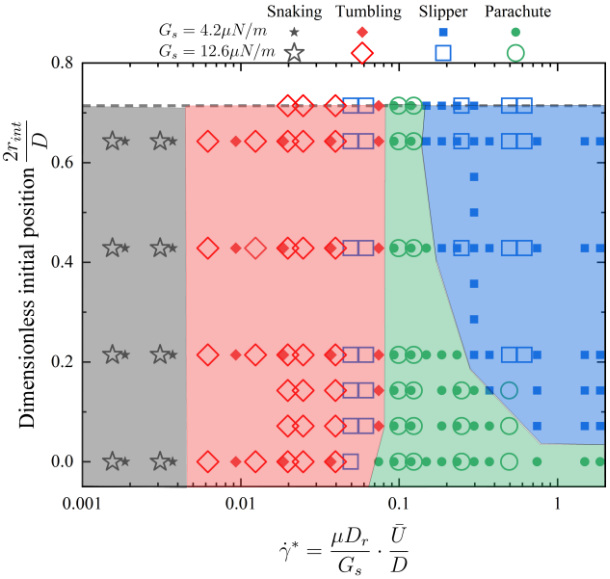

Fig 2. The effect of the shear modulus of the cell membrane on the distribution of equilibrium states.

Fig. 3 illustrates how the shear modulus affects the equilibrium position of cells originally positioned near the wall. In the present study, we demonstrate that varying the shear modulus had little effect on the profiles of the equilibrium position of RBCs with the same $\dot{\gamma}^*$ or Ca number.

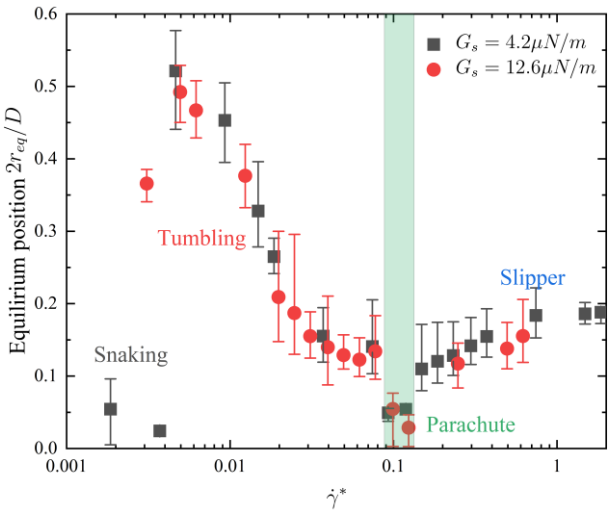

Fig 3. The effect of the shear modulus of the cell membrane on the distribution of equilibrium positions.

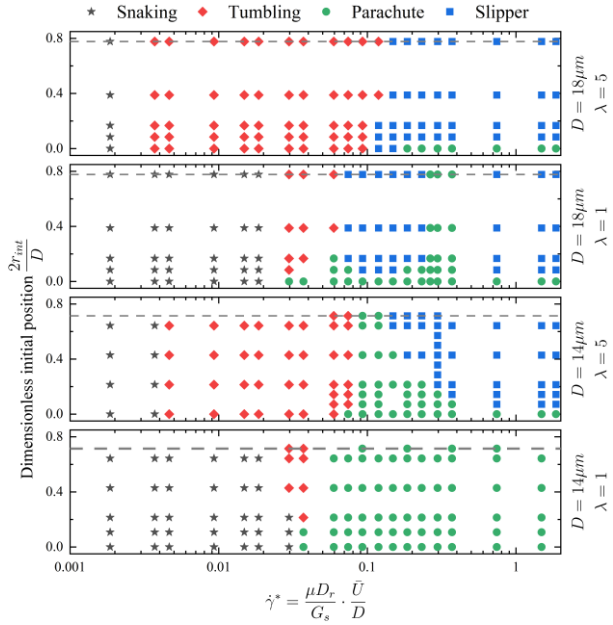

Fig 4. Effect of internal and external viscosity ratio on the distributions of cell equilibrium states.

In addition to the shear modulus of the cell membrane, the viscosity ratio λ is another crucial factor that affects the deformability of red blood cells. Fig. 4 illustrates the phase diagrams of the equilibrium states with viscosity ratios $\lambda = 5$ and 1 in microchannels with diameters of $D = 18\mu m$ or $14\mu m$, respectively. For a shear rate $\dot{\gamma}^* < 0.1$, the equilibrium state with $\lambda = 5$ exhibits a larger tumbling zone than RBCs with $\lambda = 1$, which is consistent with Dasanna's findings[5]. However, when the shear rate $\dot{\gamma}^* > 0.1$, the effect of internal and external viscosity ratio becomes more complex. The bistability phenomenon disappears at $\lambda = 1$, and cells exhibit a parachute equilibrium state in the $D = 14\mu m$ channel, while the cell equilibrium state changes from a slipper to a parachute shape with increasing shear rate, which is consistent with Agarwal et al.'s study[6].

Fig. 5 illustrates how the viscosity ratio λ affects the equilibrium position of RBCs in different motions. As λ decreases, the equilibrium positions of RBCs get closer to the tube center.

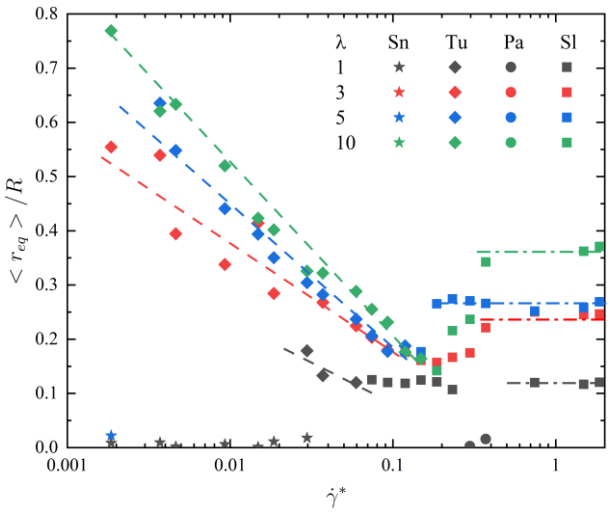

Fig 5. Effect of internal and external viscosity ratio on the distributions of cell equilibrium position.

4. Conclusion

As two critical characteristics impacting a cell's deformability, the cell membrane shear modulus G_s and the internal-external viscosity ratio λ play distinct roles in determining a cell's dynamic behavior. Based on the results, it can be concluded

that the shear modulus G_s had little effect on the phase diagram of the equilibrium state and position of the cells with $\dot{\gamma}^*$ as the horizontal axis, however increasing λ not only increased the slipper area in the phase diagram, but also contributed to the equilibrium position, which inclined toward the tube wall. The differential effect can be used to construct microfluidic devices for the high-throughput measurement of the internal and exterior viscosity ratios of red blood cells, and may be employed to the diagnosis of diseases such as diabetes.

5. Schedule and prospect for the future

In response to the fact that viscosity ratio and cell membrane stiffness have different effects on the equilibrium position of cells, it is possible to develop microfluidic chips for high-throughput measurement of intracellular viscosity for early diagnosis of diseases such as diabetes and evaluation of dialysis effects.

6. If no job was executed, specify the reason.

Ref:

[1] Hosseini, S. M., & Feng, J. J. (2012). How malaria parasites reduce the deformability of infected red blood cells. Biophysical journal, 103(1), 1-10.

[2]Byun, H., Hillman, T. R., Higgins, J. M., Diez-Silva, M., Peng, Z., Dao, M., ... & Park, Y. (2012). Optical measurement of biomechanical properties of individual erythrocytes from a sickle cell patient. Acta biomaterialia, 8(11), 4130-4138.

[3] Tomaiuolo, G. (2014). Biomechanical properties of red blood cells in health and disease towards microfluidics. Biomicrofluidics, 8(5), 051501.

[4] Fedosov, D. A., Peltomäki, M., & Gompper, G. (2014). Deformation and dynamics of red blood cells in flow through cylindrical microchannels. Soft matter, 10(24), 4258-4267.

[5] Dasanna, A. K., Mauer, J., Gompper, G., & Fedosov, D. A. (2021). Importance of viscosity contrast for the motion of erythrocytes in microcapillaries. Frontiers in Physics, 9, 666913.

[6] Agarwal, D., & Biros, G. (2020). Stable shapes of three-dimensional vesicles in unconfined and confined Poiseuille flow. Physical Review Fluids, 5(1), 013603.

Fiscal Year 2022 List of Publications Resulting from the Use of the supercomputer

[Paper accepted by a journal]

Peng Jing, Satoshi Ii, Xiaolong Wang, Kazuyasu Sugiyama, Shigeho Noda, Xiaobo Gong, Effects of fluid–cell–vessel interactions on the membrane tensions of circulating tumor cells in capillary blood flows, Physics of Fluids 34.3 (2022): 031904.

[Conference Proceedings]

[Oral presentation]

Xiaolong Wang, Satoshi Ii, Kazuyasu Sugiyama, Shigeho Noda, Peng Jing, Deyun Liu, Xiaobo Gong, Numerical analysis of equilibrium state and lateral migration of erythrocytes in 3D cylindrical microchannel, 15th World Congress on Computational Mechanics (WCCM-XV) & 8th Asian Pacific Congress on Computational Mechanics (APCOM-VIII),31 July – 5 August 2022, Yokohama, Japan

Peng Jing, Satoshi Ii, Xiaolong Wang, Kazuyasu Sugiyama, Shigeho Noda, and Xiaobo Gong, Numerical Investigation of the Membrane Tensions and Motional Behaviors of Circulating Tumor Cells in Microvessels, 15th World Congress on Computational Mechanics (WCCM-XV) & 8th Asian Pacific Congress on Computational Mechanics (APCOM-VIII),31 July – 5 August 2022, Yokohama, Japan

[Poster presentation]

[Others (Book, Press release, etc.)]