Modeling of platelet transport in flowing blood using direct numerical simulation of cellular blood flow

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Upon injury to arterial walls, white clots form rapidly to stop bleeding. The rapid formation of white clots is essential for preventing excessive blood loss, but under pathophysiological conditions white clots can rapidly occlude atherosclerotic arteries and cause ischemic cardiac arrest or stroke. Identifying the rate limiting processes in clot formation may guide us in developing more effective treatments for cardiovascular diseases and traumatic injuries.

The growth rate of white clots may depend on the rate of transport of clot components such as platelets and clotting proteins in blood. Whole blood is a complex fluid with red blood cells (RBCs) occupying ∼45% of its volume. RBC interactions in flowing blood can increase the rate of transport of blood cells and solutes by several orders of magnitude compared to transport due to Brownian motion. In addition to the RBC-enhanced transport of platelets and blood solutes, under arterial flow conditions, RBCs migrate away from the walls, and platelets marginate to the RBC-free layer formed near the walls. Platelet margination increases the near-wall platelet concentration compared to the bulk platelet concentration. RBC-enhanced transport and platelet margination may contribute to the rapid formation of white clots.

In this study, we investigate the mechanics of platelet transport in blood and identify important parameters affecting platelet margination. Due to the particulate nature of RBC-enhanced transport and margination processes, numerical study of these phenomena requires a computational model that includes RBC and platelet mechanics and particle-particle and particle-fluid interactions in blood flow. We perform direct numerical simulation (DNS) of cellular blood flow using the XSEDE computing facilities.

For the DNS of blood flow, we use a lattice Boltzmann method (LBM) to solve for the fluid phase (i.e., blood plasma and RBC cytoplasm) coupled to a coarsed-grained spectrin-link (SL) model for RBC membranes and a rigid dynamic solver for rigid particles. The LBM is favorable for simulating suspensions since the computational expense of this method scales linearly with the number of particles. Also, the local nature of the LBM operations makes the LBM optimal for parallel computing. Using a coarse-grained SL approach, the RBC membrane can be modeled efficiently with a small number of nodes while accurately capturing the membrane elastic response both at small and large deformations. The LB-SL solver is parallelized using the message interfacing protocol (MPI) to enabled simulation of $O(10^5)$ particles.

Using the coupled LB-SL method, we model the flow of suspensions of RBCs and marginating particles between parallel plates with heights of H = 40, 80 and 160 μm. We hypothesize that platelet margination in concentrated RBC suspensions is driven by RBC-enhanced shear-induced diffusion of platelets at the RBC-filled region plus a local free-escape effect at the edge of the RBC-free region. Our DNS results show that platelet margination length scales cubically with channel height H (in channels of H = 40, 80 and 160 μm), and is invariant to shear rate $\dot{\gamma}$ (over a range of $\dot{\gamma}$ = 1,000-20,000 s^{-1}). These results are consistent with the hypothesis that RBC-enhanced shear induced diffusion of platelets drives platelet margination. To further test our hypothesis, we developed a continuum diffusion model with free-escape boundary condition at the edge of the RBC-free region. Good agreement between the results of this continuum model and the DNS results supports our proposed mechanism for platelet margination. Our DNS results also indicate that the effect of particle size on margination rate may be more important than particle deformability.