Multiscale Modeling of Fine-Grained Platelet Suspension in Coarse-Grained Blood Flow using Molecular Dynamics and Dissipative Particle Dynamics

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Multiscale modeling is a cutting edge computational paradigm which couples the dynamic biochemical phenomena at various length and time scales and addresses both scientific and clinical problems in a unified and systematic approach. Our group has been applying multiscale modeling to describe the mechanisms of how shear stress induces blood coagulation and thrombosis. In cardiovascular prosthetic devices, abnormal shear stress arising from pathological blood flow induces platelet activation and aggregation, and makes blood vessels prone to thrombosis. Blood coagulation cascade is inherently a multiscale problem: the biochemical reactions of blood constituents at nanoscale have been observed by microscopic experiments, while the macroscopic properties of blood are modeled through continuum methods like Computational Fluid Dynamics (CFD). A great challenge is to bridge the transitional region from macroscale to nanoscale phenomena in computer simulation. To address this challenge, we developed a multiscale approach based on Dissipative Particle Dynamics (DPD) and Coarse Grained Molecular Dynamics (CGMD) methods. We use DPD, a mesoscopic particle-based simulation method, to model viscous blood flow. Each DPD particle represents a cluster of atoms or molecules which interacts with surrounding particles within a certain cutoff radius. The time evolution of particles is governed by Newton's equation of motion with forces acting between each particle pair. We developed a general boundary condition (BC) that allows the description of any complex 3D wall typical to physiological vasculature enclosing the DPD fluid. We performed fluid simulations in various microfluidic channels of different shapes, with our novel no-slip BC in the radial direction and periodic BC in the flow direction. Our DPD fluid simulations demonstrate adequate viscous fluid characteristics: the velocity profiles are well approximated, shear stresses are transmitted across shear layers, the boundary layers are appropriately developed, density stability is remained near the wall, etc. We use CGMD to model the platelets with detailed cell structures including membrane, cytoplasm, core and filaments at the nm scale. CGMD is able to model platelets related biochemical processes in time and length resolutions better than mesoscopic simulation, while goes faster than all-atom simulation. We integrated DPD fluid and CGMD platelets into a multiscale model by tuning potentials in between fluid and membrane particles, and observed platelets motion close to analytical Jeffery Orbit of an ideal ellipsoid moving in shear flow. This model provides greater resolution for simulating platelets dynamics and kinematics and will be employed to simulate flow induced platelet shape change upon activation. To accelerate our multiscale simulation, we implemented a multiple-time-step algorithm (MTS) by customizing LAMMPS simulation package to reduce both computation and communication time consumption by 20 percent in total. We currently achieve a simulation system size of 10-100 million particles on supercomputers from Texas Advanced Computing Center and National Supercomputing Center at Jinan, China. Our model is promising and offers a significant contribution to the burgeoning field of multiscale modeling utilizing high performance computing for solving complex clinical problems at the interface of engineering and biology.

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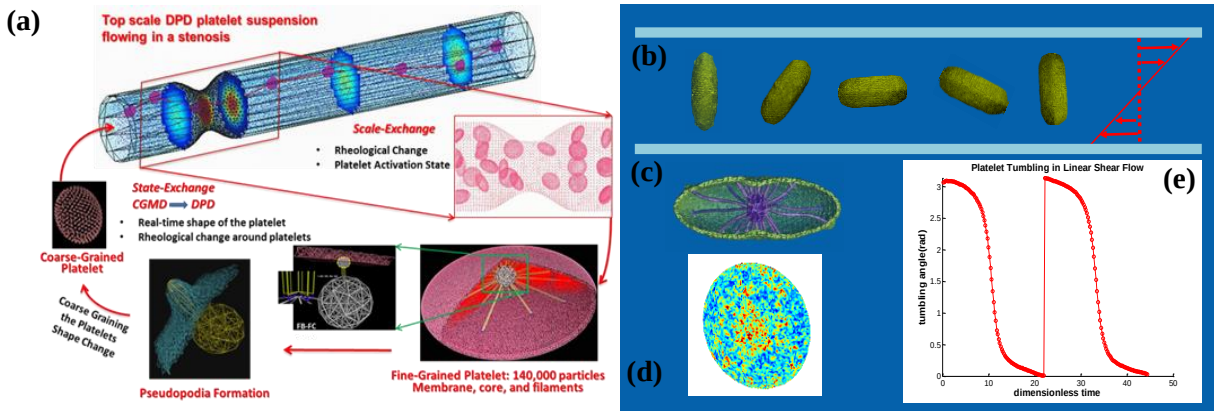

Fig.1 (a) Multiscale modeling of flow-induced platelet activation interfacing DPD and CGMD models. **(b)** CGMD platelet suspended in shear flow- platelets composed of 140,000 particles each, suspended in 9 million particles of fluid. **(c)** The fine-grained platelet structure with supportive elastic membrane and cytoskeletal core connected by filament bundles (140,000 particles). **(d)** Platelet surface velocity distribution. **(e)** Periodic change in orientation angle of platelet;