A Predictive Multiscale Model for Simulating Platelets Activation in Shear Flows

Peng Zhang¹, Chao Gao¹, Na Zhang², Marvin J. Splepian¹-³, Yuefan Deng², Danny Bluestein¹
¹Stony Brook University, Stony Brook, NY, ²University of Arizona, Tucson, AZ, USA

Project Summary

INTRODUCTION: The coagulation cascade of blood may be initiated by flow-induced platelet activation, which prompts clot formation in prosthetic cardiovascular devices and arterial disease processes. Upon activation, platelets undergo complex morphological changes that play a major role in aggregation and attachment to surfaces. Continuum methods fail to capture the molecular-scale mechanism such as filopodial formation. Utilizing molecular dynamics (MD) to model this is computationally prohibitive. We developed a multiscale model which can simulate the microstructures of human platelets and microscale transport of blood flows, providing a more accurate flow-induced dynamic stress mapping on platelets and predict their activation [1-5].

MULTISCALE MODEL: Two spatiotemporal scale methods:
(1) Top/microscale using dissipative particle dynamics (DPD) to describe viscous blood fluid flows (viscosity, compressibility);
(2) Bottom/nanoscale using coarse-grained molecular dynamics (CGMD) to describe the platelet membrane, cytoplasm and the cytoskeleton.

Progress and Milestones

- **Platelet Flipping:** Fluid-platelet dynamic interaction allows the platelets to continuously change their morphology while reflecting the microstructural changes of the platelets in response to these extracellular stresses that are transferred to them.
- **Platelet Activation:** The hemodynamic stresses are computed and accumulated on actin filaments. Filopodial formation is stimulated for filaments which are exposed to highest stresses. The filopodia formation compared favorably with *in vitro* measurements.

CONCLUSIONS: Our multiscale numerical approach offers a computationally affordable and highly resolved method for modeling platelet activation in shear flows. Biophysical properties of deformable platelets are accurately described down to the nanoscales. Hemodynamic stress is mapped on membrane and intra-platelet components. The filopodia formation is mimicked and correlate with *in vitro* microrheology experiments. This model can be further employed to simulate other processes involved in platelet activation, aggregation and adhesion, offering a practical multiscale method for solving complex clinical problems at the juncture of biology and engineering.

ACKNOWLEDGEMENT:
- NIH (NHLBI R21 HL096330-01, DB)
- NIH (NIBIB Quantum U01EB012487, DB)
- XSEDE (DMS140019 on TACC Stampede, PZ)
- XSEDE (DMS150011 on SDSC Comet, PZ)

PUBLICATION: