A Predictive Multiscale Model for Simulating Platelets Activation in Shear Flows

Peng Zhang[1], Chao Gao[1], Na Zhang[2], Marvin J. Splepian[1,3], Yuefan Deng[2], Danny Bluestein[1]

[1]Stony Brook University, Stony Brook, NY, [2]University of Arizona, Tucson, AZ, USA

Stony Brook University

NIH National Heart, Lung, and Blood Institute

NIH National Institute of Biomedical Imaging and Bioengineering

IMAG

2015 IMAG Multiscale Modeling (MSM) Consortium Meeting

Integrated MSM on HPC

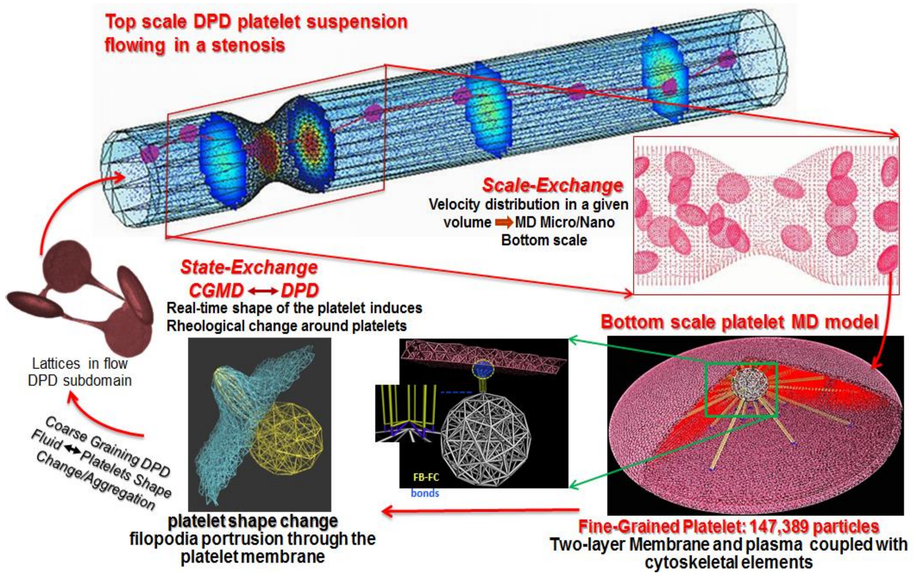
Biomedical Multiscale Model (MSM)

High Performance Computing (HPC)

Top Supercomputers

Project Summary

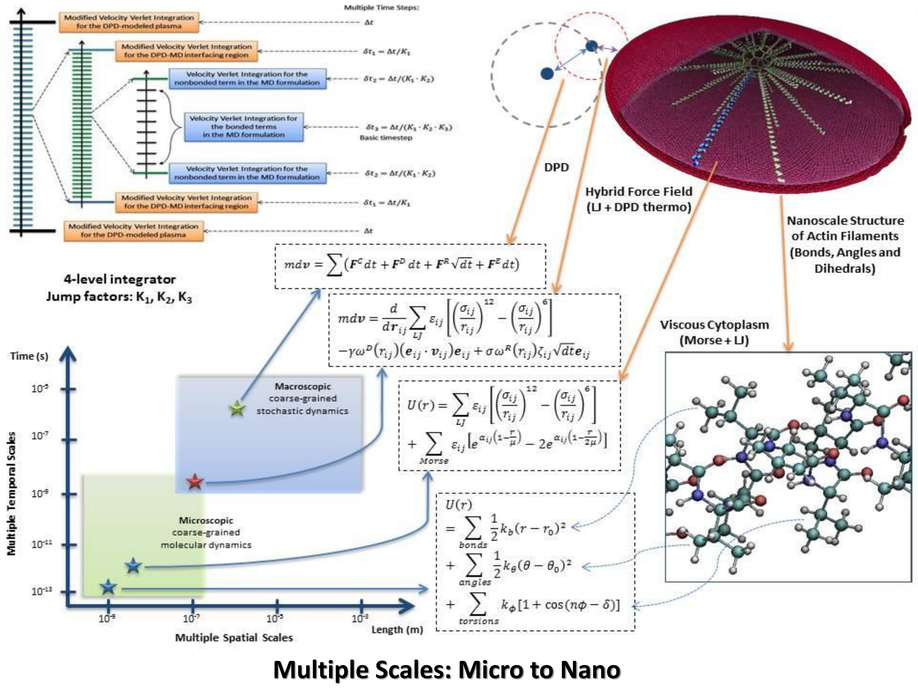
INTRODUCTION: The coagulation cascade of blood may be initiated by flow-induced platelet activation, which prompts clot formation in prosthetic cardiovascular devices and arterial disease processes. Upon activation, platelets undergo complex morphological changes of filopodial formation that play a major 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 interface *nanoscale microstructures* of human platelets and *microscale transport* of blood flows, for providing a more accurate flow-induced dynamic stress mapping on platelets and predict their activation [1-5].



MULTISCALE MODEL: Two spatiotemporal scale methods:

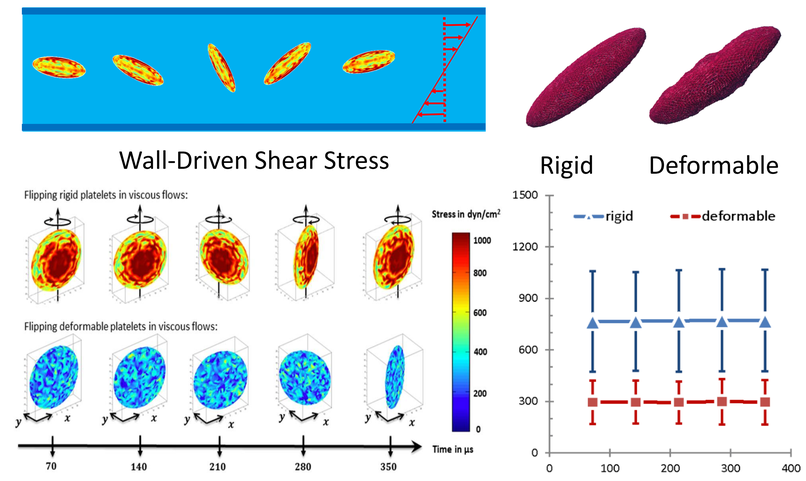
(1) Top/microscale using dissipative particle dynamics (**DPD**) to describe viscous blood fluid flows (viscosity, compressibility);

(2) Bottom/nanoscale using coarse-grained molecular dynamics (**CGMD**) to describe the platelet membrane, cytoplasm and the cytoskeleton.

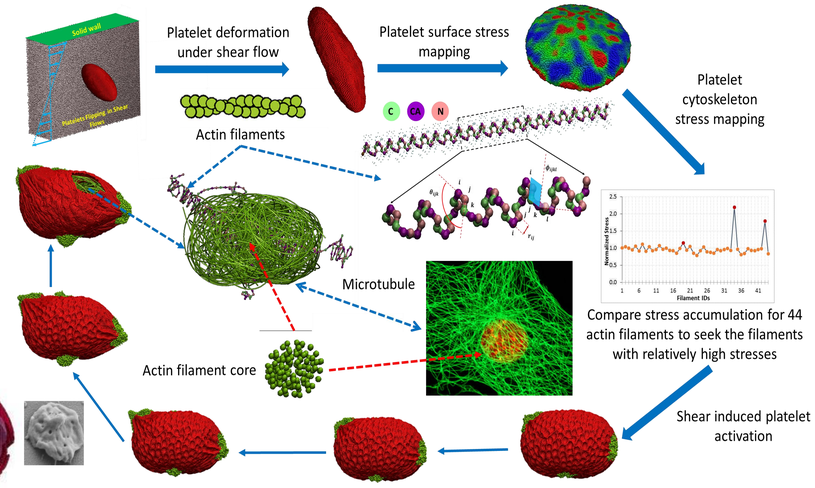


Progress and Milestones

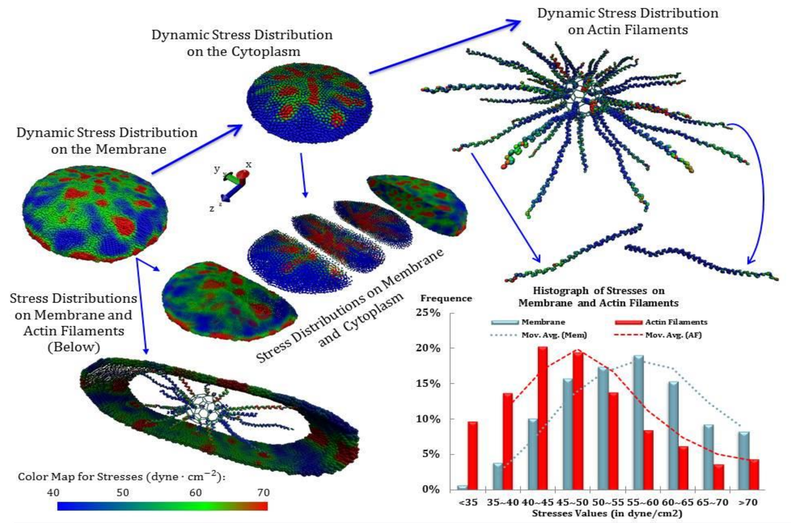
➢ **Platelet Flipping:** Fluid-platelet dynamic interaction allows the platelets to **continuously** change their morphology while reflecting the microstructural changes of the platelets in response to these extracellular stresses that are transferred to them.



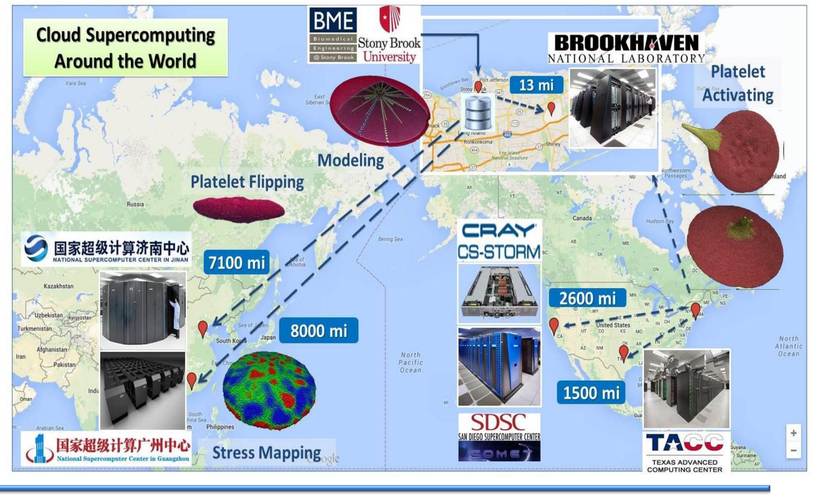
➢ **Platelet Activation:** The hemodynamic stresses are computed and accumulated on actin filaments. Filopodial formation is stimulated for filaments which are exposed to highest stresses. The filopodia formation compared favorably with *in vitro* measurements.



➢ **Mechanotransduction Process:** The hemodynamic stresses that may lead to activation and filopodial formation mapped on the deforming membrane and **dynamically** transferred to the platelet cytoskeleton **while platelets flowing and flipping**.



➢ **High Performance Computing (HPC) and Efficient Algorithms for Multiscale Modeling:** We perform the multiscale simulations on **top supercomputers** including the Tianhe-2, Sunway (China), and the Stampede, CS-Storm, Comet (US). For the system of **10.89-million** particles and **16** platelets, the simulation time is reduced **from 3 years to 37 days**, using 512 cores and 16 GPUs.



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* microchannel 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.

BioFluids Lab @ Stony Brook U

ACKNOWLEDGEMENT:

- **NIH** (NHLBI R21 HL096930-01, DB)
- **NIH** (NIBIB Quantum U01EB012487, DB)
- **XSEDE** (DMS140019 on TACC Stampede, PZ)
- **XSEDE** (DMS150011 on SDSC Comet, PZ)

NIH National Institutes of Health

Open Science Grid

XSEDE Extreme Science and Engineering Discovery Environment

PUBLICATION:

[1] Zhang, P., et al, *Cellular and Molecular Bioengineering*, 7:552-574, 2014.
[2] Zhang, P., et al, *Journal of Computational Physics*, 284:668-686, 2015.
[3] Pothapragada, S., et al, *Int J Numer Meth Biomed Engng*, 31:1-16, 2015.
[4] Zhang, N. et al, *Journal of Computational Physics*, 257:726-736, 2014.
[5] Zhang, N., et al, *Proceedings of XSEDE15*, July, 2015.