INTEGRATING MACHINE LEARNING IN MULTISCALE MODELING FOR BLOOD FLOW AND PLATELET-MEDIATED THROMBOSIS INITIATION

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BACKGROUND: Our multiscale modeling (MSM) incorporated a coarse grained molecular dynamics model (CGMD) model of platelets and a dissipative particle dynamics (DPD) model of flow, to describe platelet mechanotransduction events induced by blood flow in cardiovascular pathologies which may initiate thrombosis via platelet activation, aggregation and adhesion [1-2]. We integrated two Machine Learning (ML) pipeline approaches to our MSM methodology for synthesizing in vitro data to in silico models (ML-1), and for significantly reducing computing time without losing accuracy (ML-2). [3]

METHODS: (ML-1) ML pipeline was developed for synthesizing sparse in vitro data and is comprised of two learning systems: a semi-unsupervised learning (SULS), implementing active learning, is developed for segmentation with a focus on platelets morphologies. High-speed streaming images in vitro at 1000 FPS are processed by the SULS at submicron resolutions. The segmented data, combined with physical conditions, input into the second FCN-based models to predict (*a*) inter-platelet contact areas during recruitment aggregation and (b) the platelet adhesion events: flipping and reattachment periods. (ML-2) ML pipeline was developed for coarsening predictive in silico data in temporal scales and is developed as state-driven adaptive time-stepping (ATS) algorithm that adapts time stepsizes to the underlying biophysical phenomena.

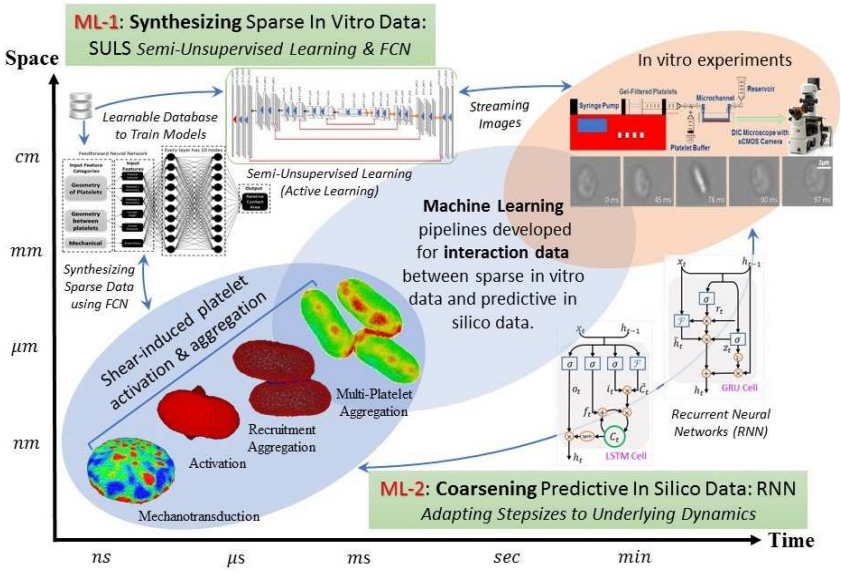

Figure 1: Two machine learning pipelines for bridging the gaps, in multiscale modeling, between in vitro experiments and in silico models.

RESULTS: Our MSM model describes biophysical properties of platelets down to nanoscales [1-2], with membrane Young's modulus of 31.2 μN/m and cytoplasm viscosity of 4.1 mPa·s. Mean normalized contact area model predictions and in vitro data (0.094±0.021 and 0.092±0.021, respectively) suggest that our ML model can accurately predict the contact area for aggregated platelets and was used for determining parameters in our MSM of platelet aggregation via αIIbβ3-Fibrinogen-αIIbβ3 bonds. Simultaneously, our MSM was extended to simulate the mechanism of platelet membrane GPIbα receptors and arterial wall von Willebrand factor (vWF) binding under shear stress. The SULS used to segment platelet boundaries as a time series, and for analyzing the major and minor platelet axes and angular flipping velocity for each adhesion event. ATS algorithm was compared with the single time-stepping (STS) algorithm. The results in both algorithms are consistent with each other. Computing time using ATS for different phases were cut by 20~75% on supercomputers [3].

CONCLUSIONS: Two machine learning pipelines were developed for synthesizing sparse in vitro data (ML-1) and for adaptive discretization in massive multiscale simulations (ML-2). Conceptually, our ML methods enable interactions across the vast different spatial and temporal scales. These ML models are serving as the "interaction data" between sparse in vitro data and predictive in silico data, and will be used to further improve our MSM model credibility and accelerate the model construction process from the in vitro data.

REFERENCES:

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3. Zhang, P., et al, *J Comput Phys*, 284:668-686, 2015.

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