Title Machine Learning in Multiscale Modeling of Blood Flow and Platelet Mediated Thrombosis

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Abstract Text

Multiscale Problem: We developed MSM approach by incorporating coarse-grained molecular dynamics (CGMD) and dissipative particle dynamics (DPD) to describe platelet mechanotransduction induced by blood flow in cardiovascular pathologies which may initiate thrombosis[1-5].

(1) Machine Learning (ML) for Modeling In Vitro Data

Microscopy images were analyzed to obtain platelet geometric and physical parameters, meshed to determine contact area between aggregated platelets, and input into a neural network ML model to predict inter-platelet contact area (Fig. 1). In the training set, we select shear stresses of 1, 5 and 10 dyne/cm^2. A feed-forward neural network ML model with 2 hidden-layers, each with 10 nodes (Fig. 1a) was trained with 75% of the data, with the remaining 25% as test data. Training loss reaches the minimum gradient when training epochs exceed 3000 (Fig. 1b). Independent in vitro experiments at a shear stress of 6.7 dyne/cm^2 were used to test accuracy. Mean and standard deviation values of normalized contact area model predictions and experimental results (0.094±0.021 and 0.092±0.021, respectively) suggests that our ML model accurately predicts the contact area for aggregated platelets and can be used in our multiscale modeling to validate the in silico results.

(2) Machine Learning for Adaptive Discretization in Massive Multiscale Modeling

While MSM sufficiently describes details at disparate spatial scales, no effective algorithm for adapting temporal scales to these diverse spatial scales exists. We propose a novel state-driven adaptive time-stepping (ATS) algorithm[6,7] that adapts time stepsizes to the underlying biophysical phenomena: mesoscale DPD blood flow is simulated with μs timescale and microscale CGMD platelet is modeled with ns to ps timescales. A ML-based framework trains to adapt the time stepsizes (Fig. 2a). Particle positions and momenta are inputs, and phases are described by the most significant attributes of states from inputs in first two layers– categorized by a neural network and labeled by a two components vector: time stepsize Δt and state examination frequency ω. The simulation proceeds with a new time stepsize in $1/\omega$ steps. The ATS algorithm adjusts time stepsizes at its conclusion. The ATS algorithm was compared with traditional single time-stepping (STS) algorithm with relative errors along time of system kinetic energy, and distance between center of mass of two platelets (Fig 2b). The final states of aggregation in both algorithms are consistent with each other. Computing times using ATS for different simulations phases were cut by 20~75%. Conceptually, ATS ML corresponds to coarse-graining in time.

Acknowledgements: This project was funded by NIH (U01 HL131052, R21 HL096930-01, U01 EB012487, Bluestein, D.) and used the XSEDE computing awards (TACC Stampede, SDSC Comet, DMS140019, DMS150011, Zhang, P.).

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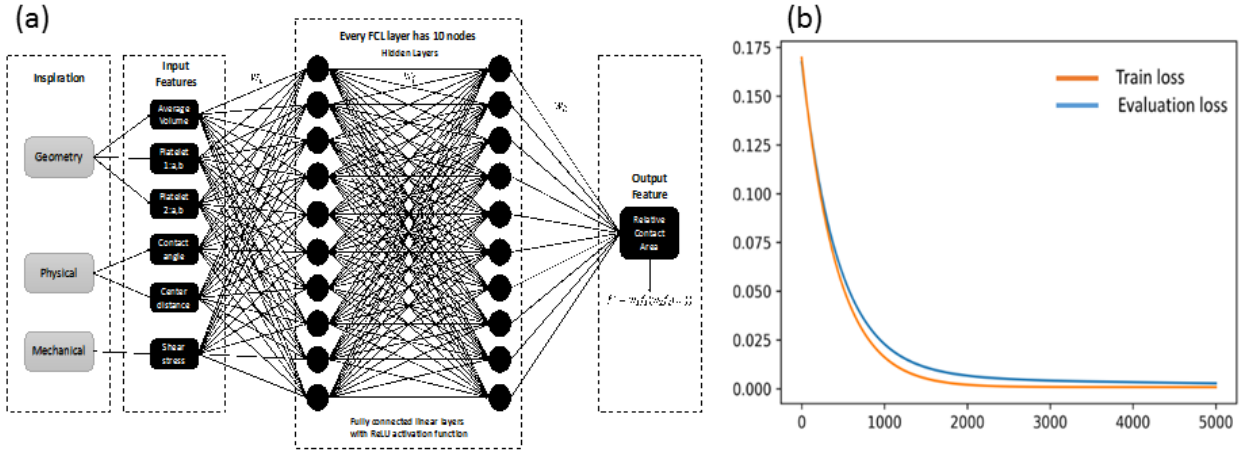

Fig. 1: (a) a NN-based framework for predicting contact area during platelet aggregation. (b) Training loss and evaluation loss (y-axis) trends vs. epochs (x-axis).

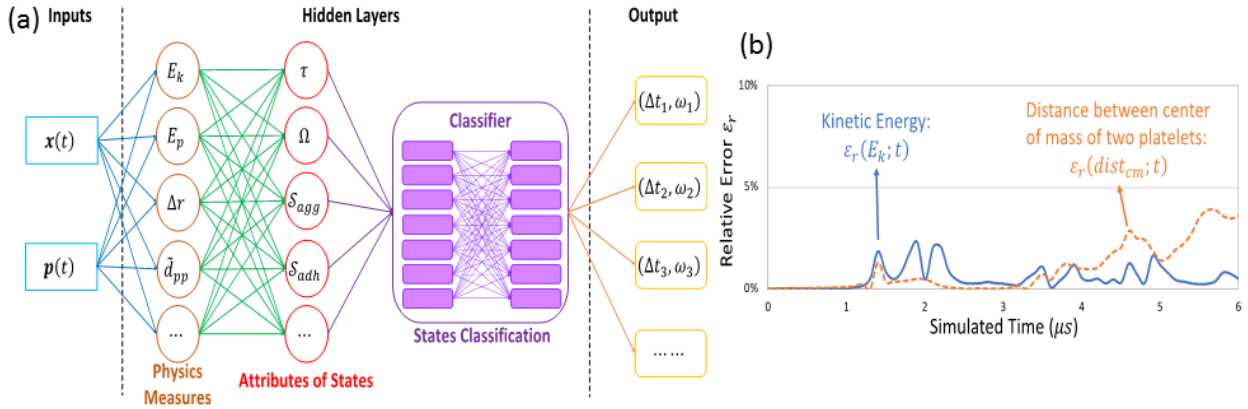

Fig. 2: (a) a NN-based framework for adapting time stepsizes to platelet dynamics under shear stresses. (b) Accuracy analysis in energy and center of mass.