

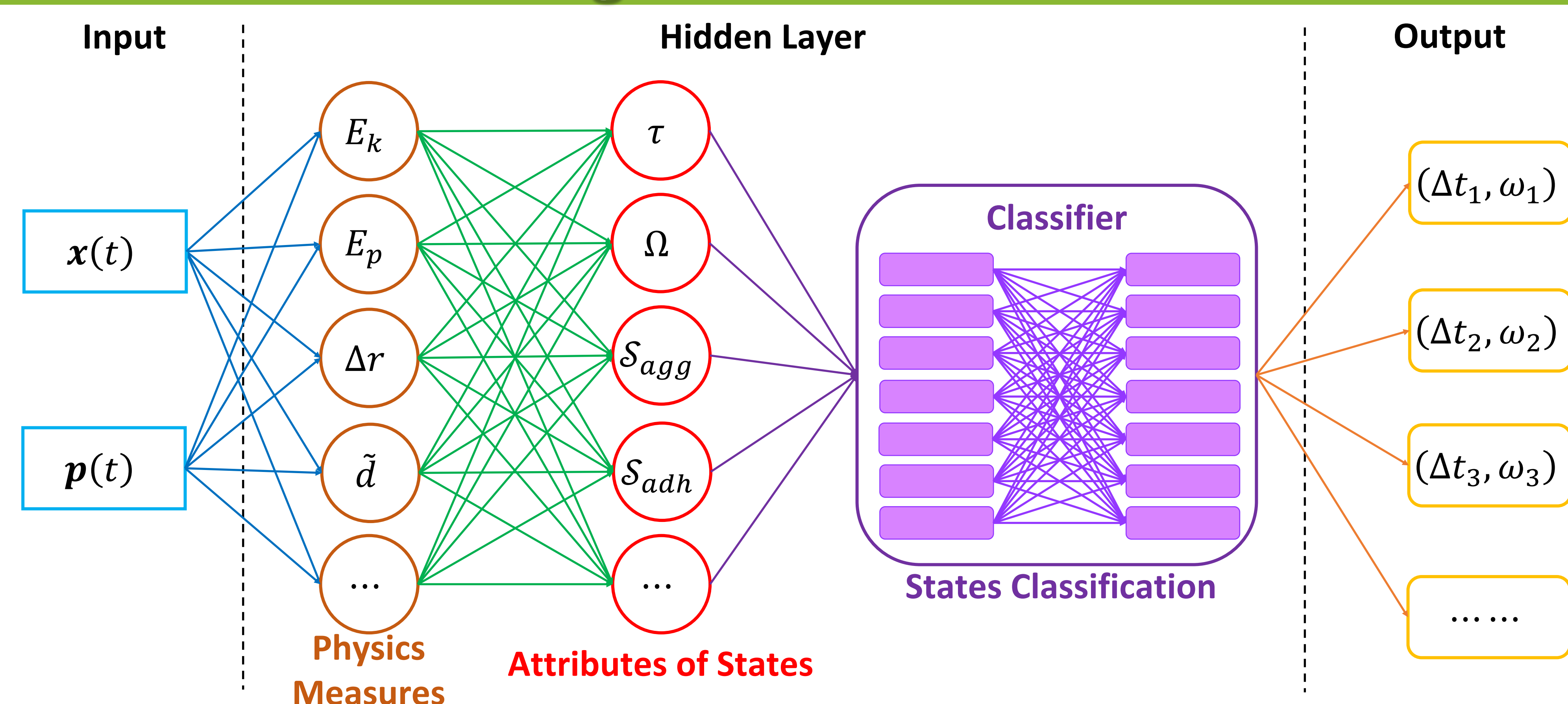
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Introduction

We developed a particle-based multiscale model (MSM) employing dissipative particle dynamics (DPD) and coarse-grained molecular dynamics (CGMD) methods to characterize initial formation of thrombosis in blood flow via flow-induced platelet activation under pathological shear rate [1-3]. To study the two-platelet recruitment aggregation occurring at multiple spatial and temporal scales, we designed, and implemented, a novel adaptive time stepping (ATS) algorithm to automatically adapt time stepsizes to the underlying biophysical phenomena. We utilized the physiological states across DPD and CGMD scales, and designed the corresponding trigger mechanisms using machine learning, to regulate the time stepsizes. Comparing with the traditional methods using the smallest stepsize for all spatial and temporal scales involved in the two-platelet modeling, our ATS algorithm significantly improves the efficiency, while maintaining the accuracy, of the modeling. Our ATS algorithm will establish a framework for simulation of various biomedical phenomena at multiscale, efficiently and accurately.

ATS Algorithm Framework

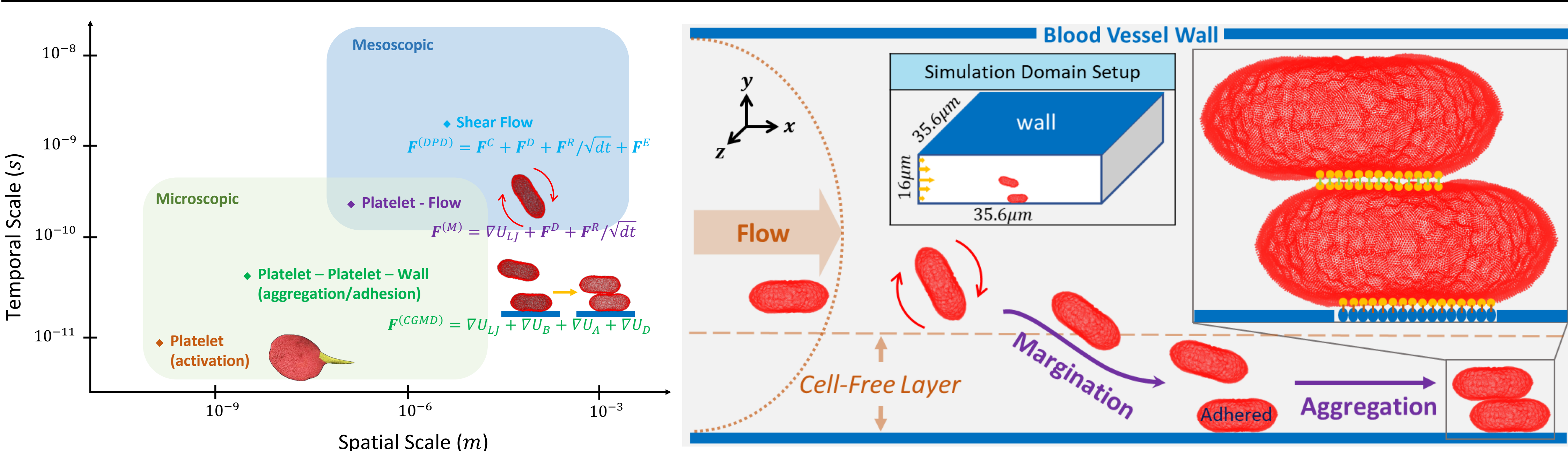


Framework	Symbol	Meaning
Input	$x(t), p(t)$	Position and momentum at time t
Hidden Layer	E_k, E_p	Kinetic and potential energy (pJ)
	Δr	Platelet trajectory difference (μm)
	$\tilde{d}$	Shortest inter-platelet distance approximation (μm)
	τ	Shear stress (dyne/cm ²)
	Ω	Contact area (μm^2)
Output	$\mathcal{S}_{adh}, \mathcal{S}_{agg}$	States of adhesion and aggregation
	$\Delta t_i, \omega_i$	Time stepsize and state checking frequency for component i

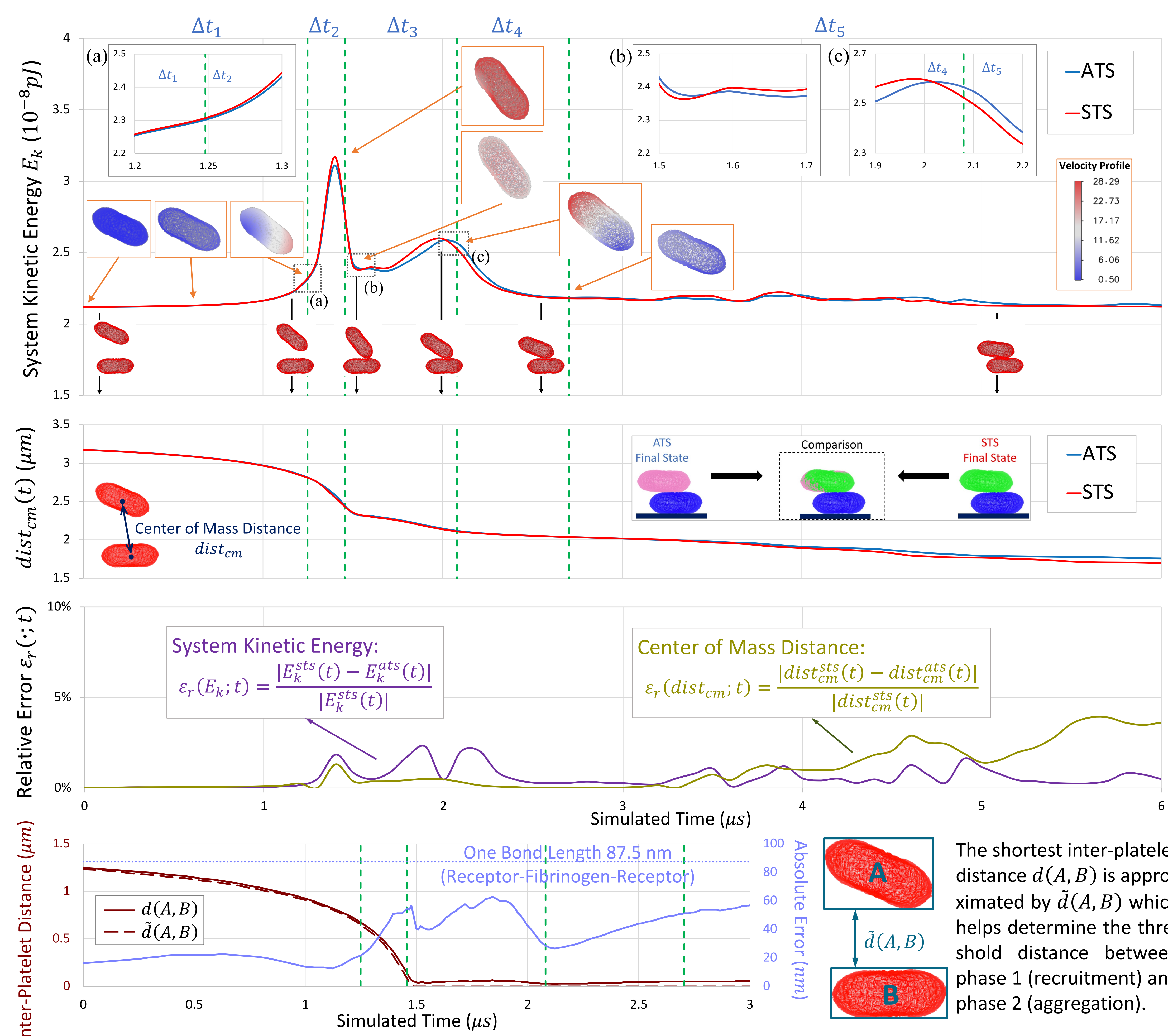
Multiscale Modeling of Platelets

Two spatial-temporal scale methods [2]:

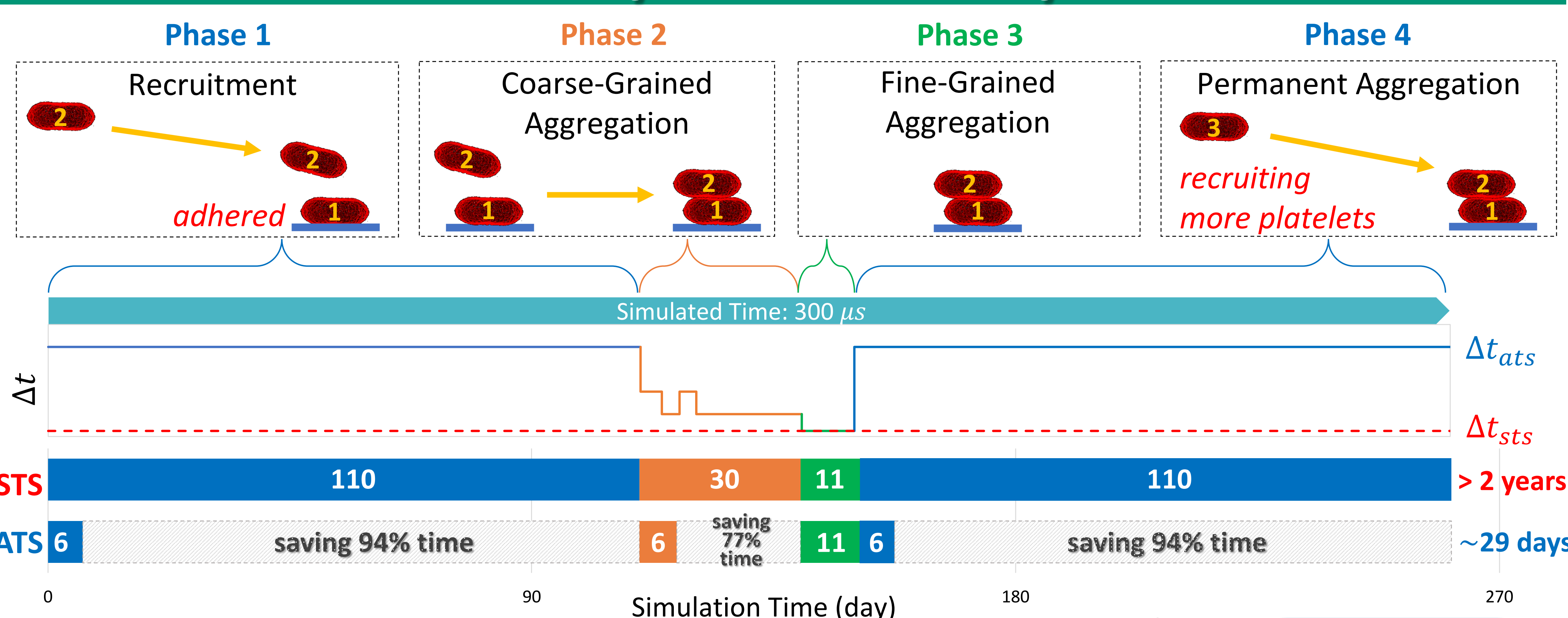
Scale	Component	Method
Mesoscopic (top-scale)	Viscous Blood Fluid Flows 10,787,776 particles, $\rho = 532/\mu m^3$	Dissipative Particle Dynamics (DPD) $\mathbf{F}^{(DPD)} = \sum_{j \neq i}^N (\mathbf{F}^C + \mathbf{F}^D + \mathbf{F}^R/\sqrt{dt} + \mathbf{F}^E)$ $\mathbf{F}^C = \alpha \omega^C(r_{ij}) \mathbf{e}_{ij}, \mathbf{F}^D = -\gamma \omega^D(r_{ij}) (\mathbf{e}_{ij} \cdot \mathbf{v}_{ij}) \mathbf{e}_{ij}, \mathbf{F}^R = \sigma \omega^R(r_{ij}) \zeta_{ij} \sqrt{dt} \mathbf{e}_{ij}$
Microscopic (bottom-scale)	Platelet (membrane, cytoplasm, cytoskeleton) 140,303 particles, $\rho = 16708/\mu m^3$	Coarse-Grained Molecular Dynamics (CGMD) $V(r) = \sum_{bonds} k_b (r - r_0)^2 + \sum_{angles} k_\theta (\theta - \theta_0)^2 + \sum_{nonbonded\ pairs} U_{LJ}(r)$
Total: Flow 10.8M (97%) + 2× Platelets 280K (3%) = 11 Million Particles		



Analysis of Accuracy



Analysis of Efficiency



Modified LAMMPS ♦ SBU Seawulf Cluster ♦ 192 Computing Cores

ATS algorithm significantly reduces simulation time by 89% with 9x speedup over STS algorithm for two-platelet recruitment aggregation while no significant loss of accuracy. Our ATS algorithm is novel at making more efficient use of these computing powers and offered a promising insight for solving massive particle-based multiscale problems efficiently.

References & Acknowledgement

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- [1] Zhang, P., et al., *Cellular and Molecular Bioengineering* **7**(4): 552-574, 2014.
- [2] Zhang, P., et al., *Journal of Computational Physics* **284**: 668-686, 2015.
- [3] Zhang, P., et al., *Journal of Biomechanics* **50**: 26-33, 2017.