Efficient Multiscale Platelets Modeling Using Supercomputers

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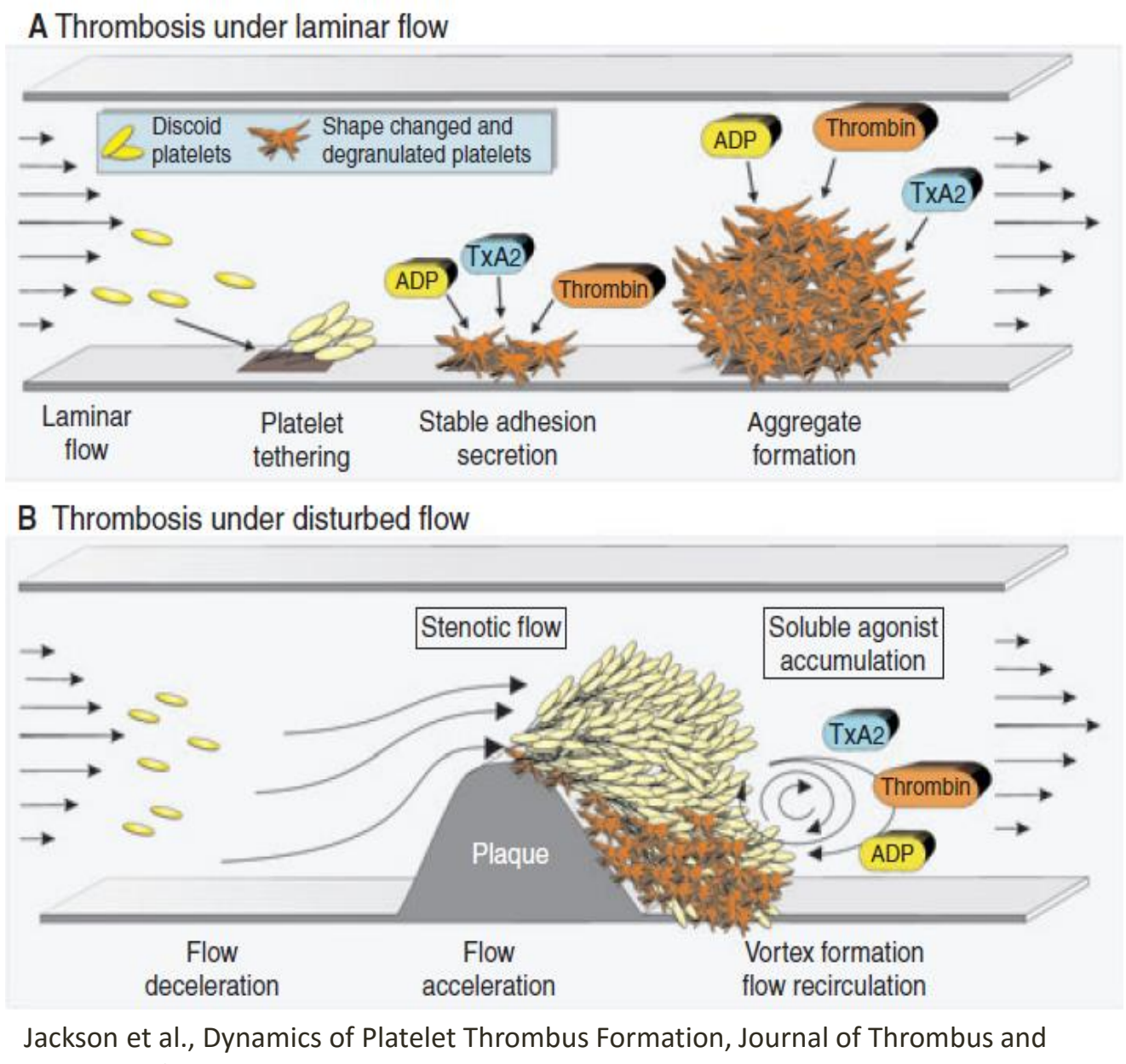
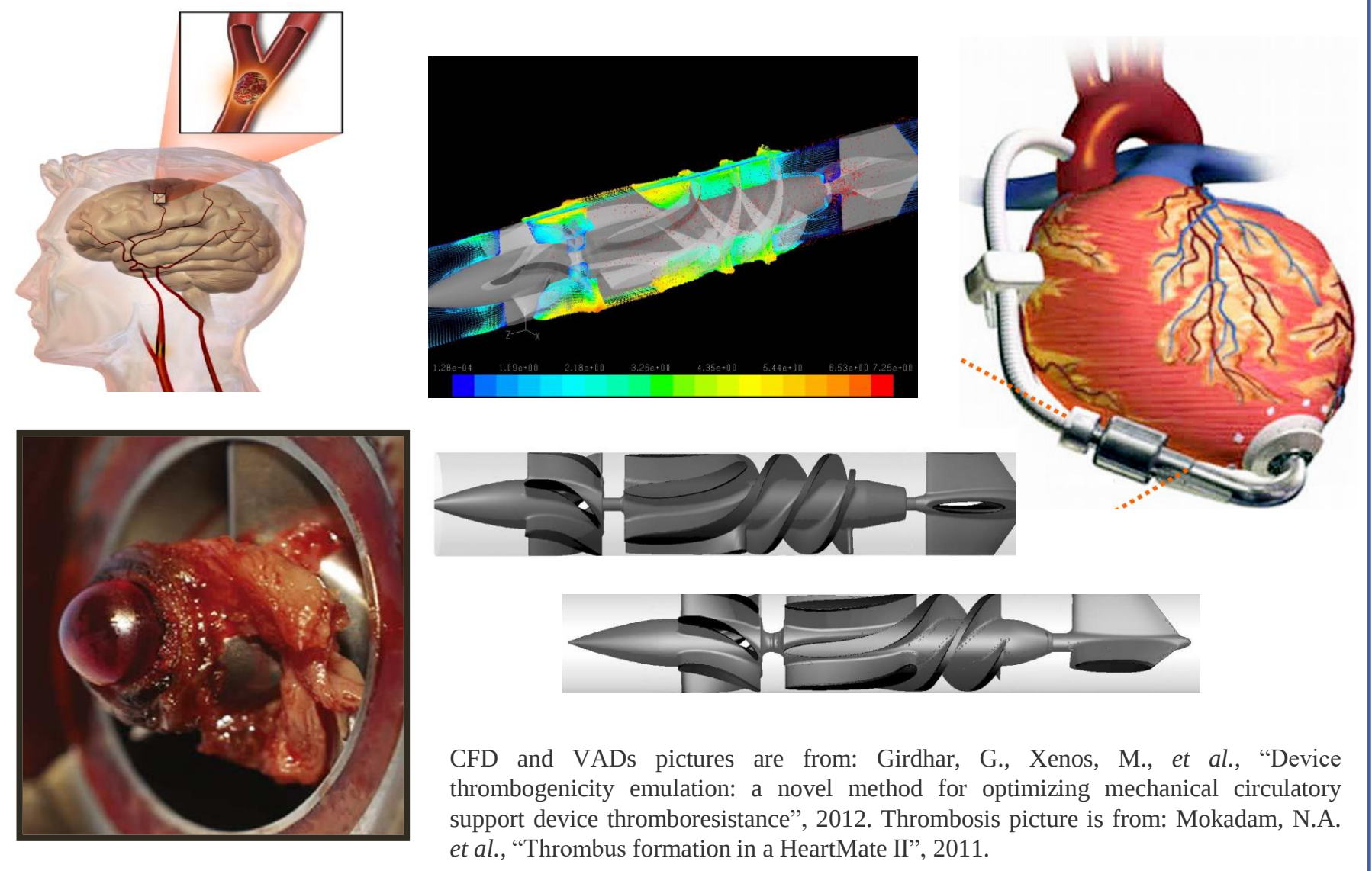
Motivation



Jackson et al., Dynamics of Platelet Thrombus Formation, Journal of Thrombus and Haemostasis, 2009

Thrombosis Burden!

Activation of Platelets in Cardiovascular Devices

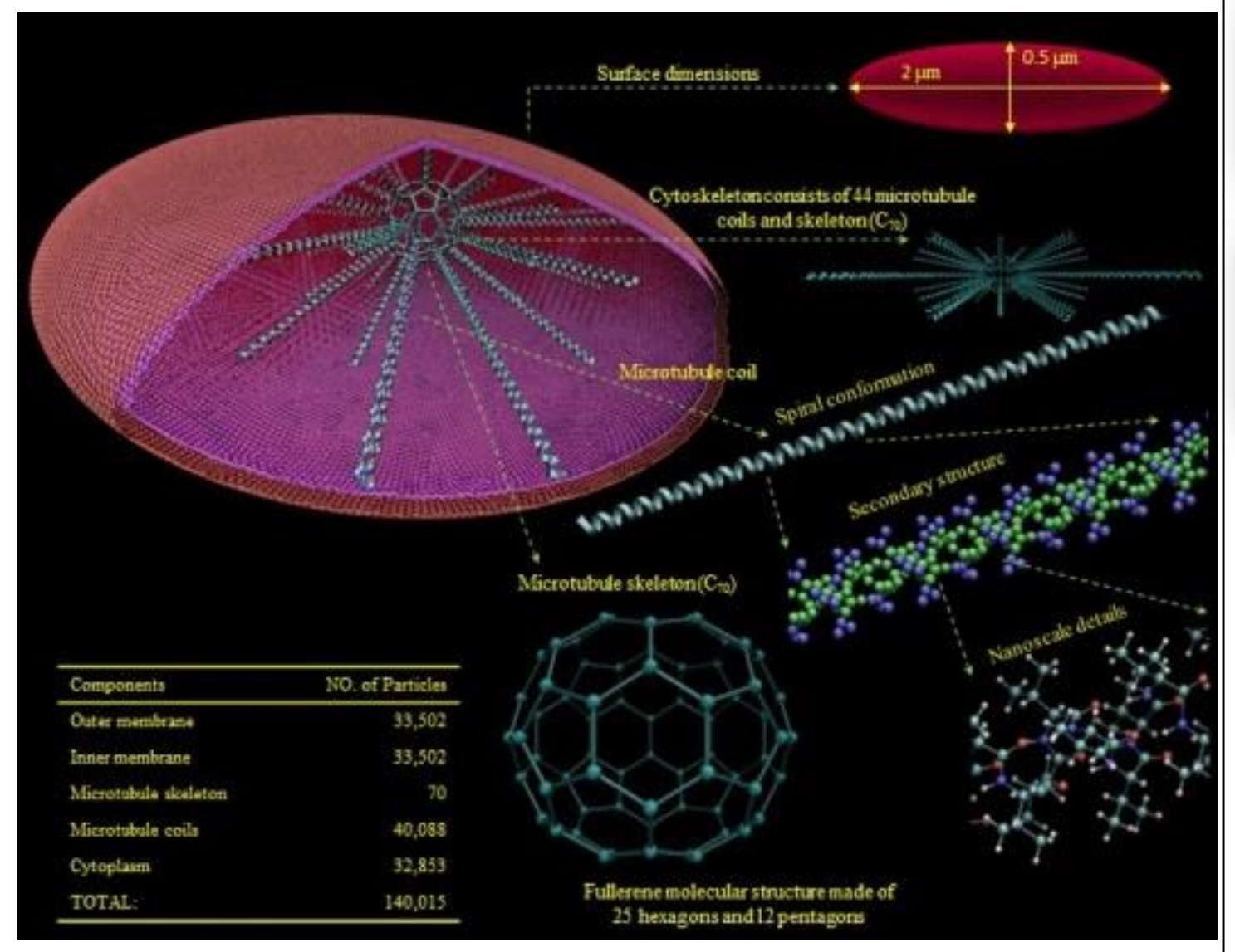
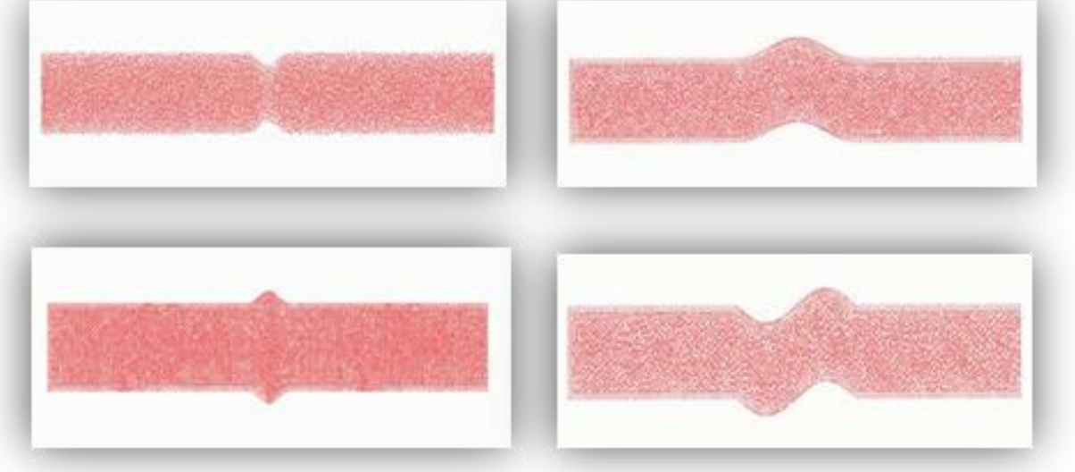
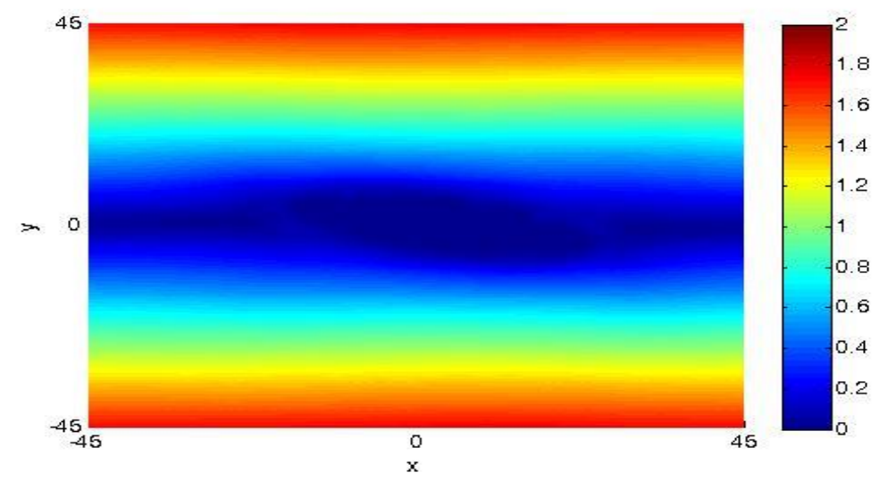
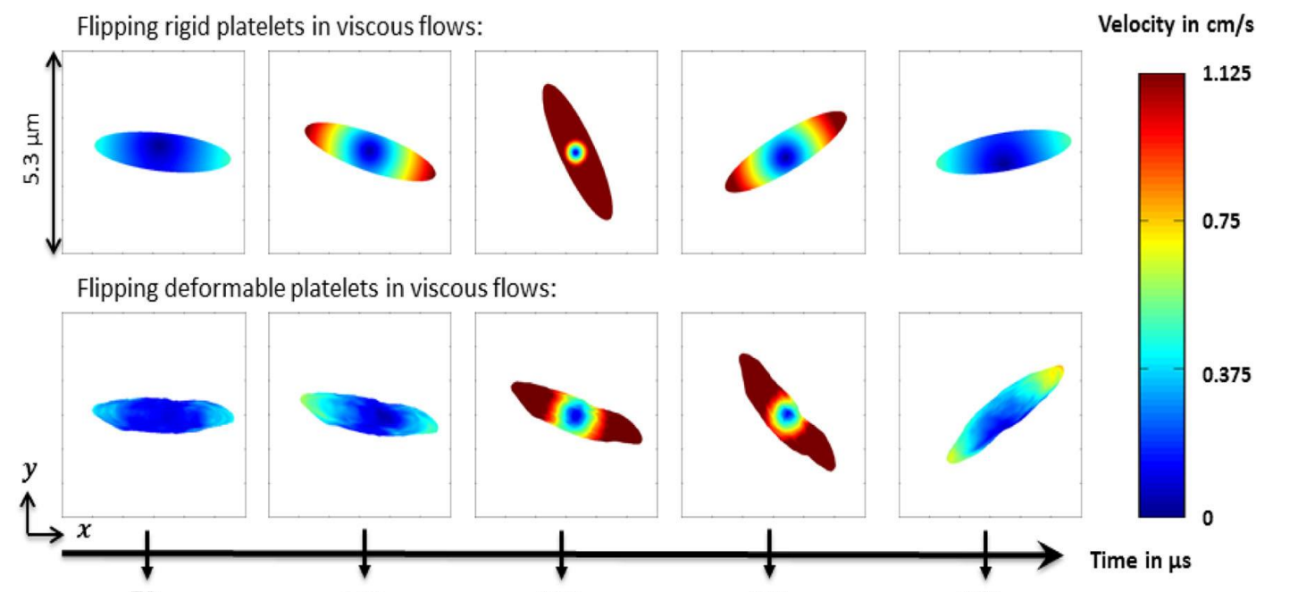


CFD and VADs pictures are from: Girdhar, G., Xenos, M., *et al.*, "Device thrombogenicity emulation: a novel method for optimizing mechanical circulatory support device thromboresistance", 2012. Thrombosis picture is from: Mokadam, N.A. *et al.*, "Thrombus formation in a HeartMate II", 2011.

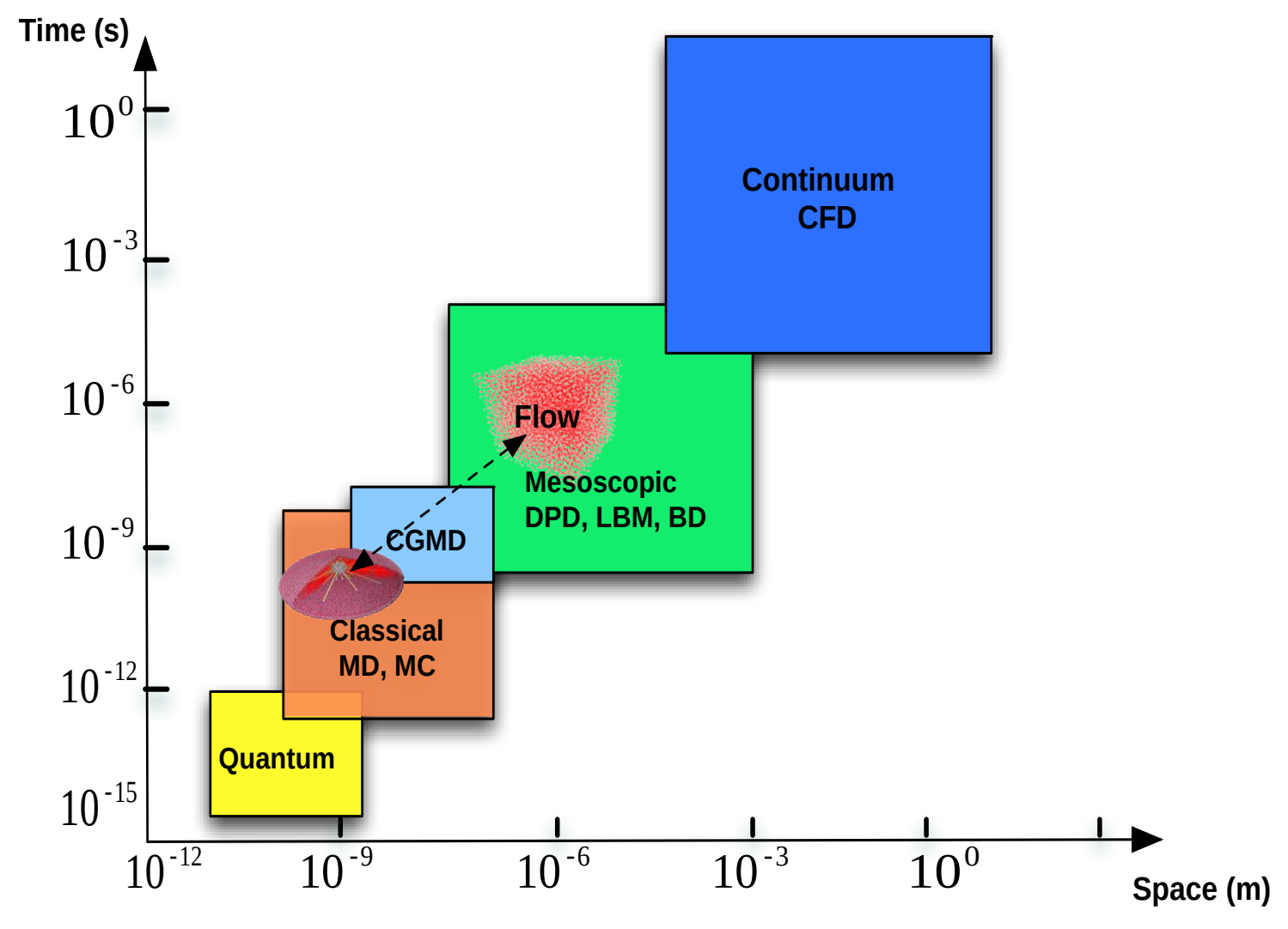
This objective of this project is to efficiently simulate flow-induced platelet activation in order to better understand thrombosis formation mechanisms. The methodologies include:

- **Mathematical modeling of viscous blood flows and human platelet cell**
- **Multiscale coupling methods**
- **Data analysis of thermodynamic properties**
- **Algorithmic acceleration**
- **Heterogeneous computing**
- **Visualization**

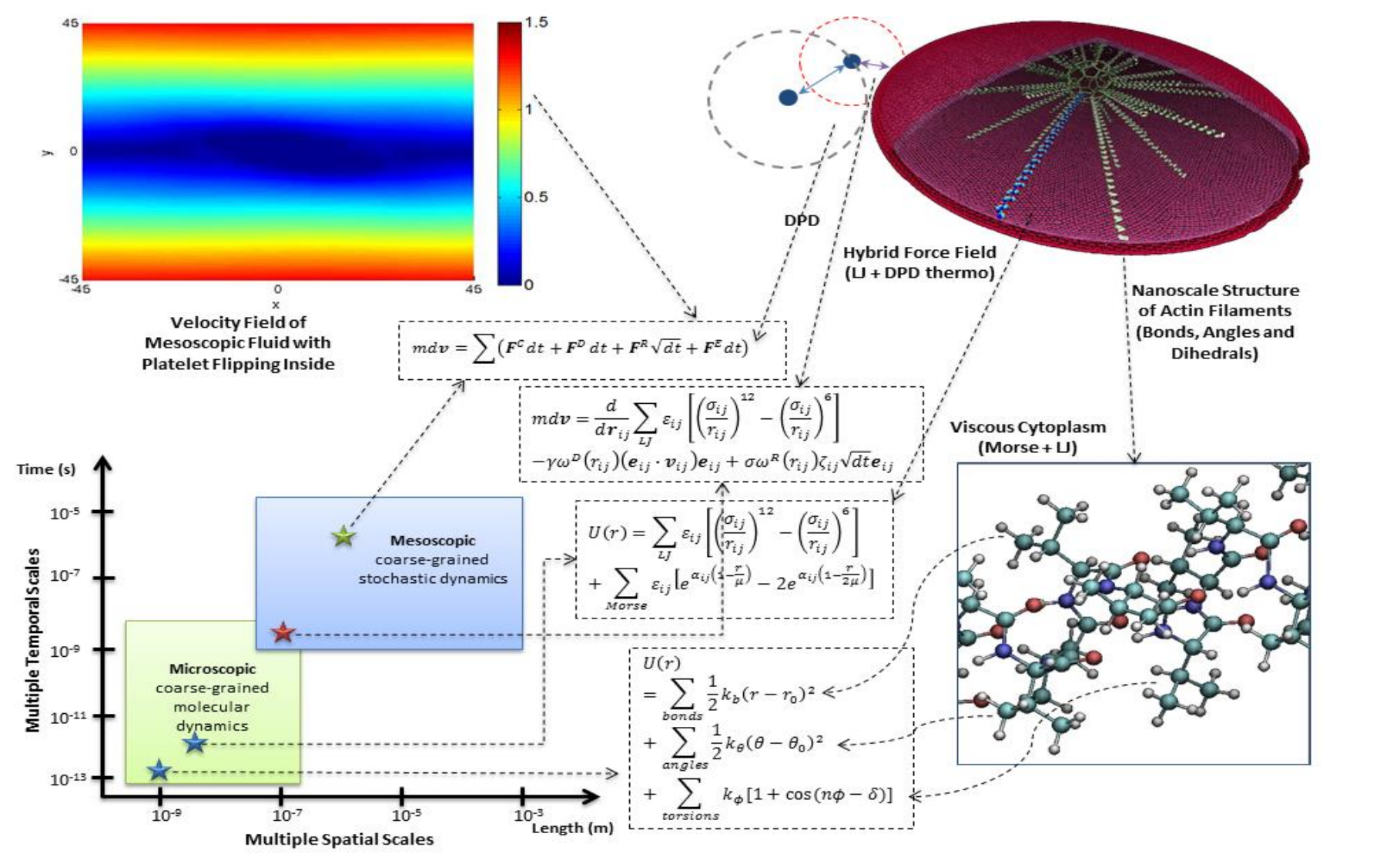
Multiscale Fluid-Platelet Models

Scales	Nanoscale	Mesoscale
Simulation Domains	Platelet Cell	Blood Plasma
Methods	Coarse-Grained Molecular Dynamics (CGMD)	Dissipative Particle Dynamics (DPD)
Temporal Scales	10~100 fs	0.01~1 μs
Spatial Scales	1~20 A	0.1 ~ 1 μm
Model Abstraction	 Physical structures and constitutes of Multiscale model of human platelets	 Various vascular geometries simulated by Dissipative Particle Dynamics method  Couette flow
Force Fields	$V(r)=\sum k_b(r-r_0)^2+\sum k_\theta(\theta-\theta_0)^2$ Bond and Angle Terms $+\sum k_\phi[1+\cos(n\phi-\delta)]+\sum\frac{q_iq_j}{4\pi\varepsilon_0 r}$ Dihedral and Electrostatic $+\sum 4\varepsilon\left[\left(\frac{\sigma}{r}\right)^{12}-\left(\frac{\sigma}{r}\right)^{6}\right]$ Van Der Waals (L-J) $+\sum\epsilon\left[\alpha\left(1-\frac{r}{R(\mu)}\right)-2\exp\left(\frac{\alpha}{2}\left(1-\frac{r}{R(\mu)}\right)\right)\right]$ Modified Morse V is the total energy on each particle composed of platelet. It includes a classical MD potential for describing the actin filament structure, a modified Morse potential for describing the viscous cytoplasm structures, and a CGMD for describing the filamentous core and the membrane structures	$\boldsymbol{F_{ij}}=\boldsymbol{F_{ij}^C}+\boldsymbol{F_{ij}^D}+\boldsymbol{F_{ij}^R}$ (Groot and Warren 1997) $\boldsymbol{F_{ij}^C}=\alpha\omega(r_{ij})\boldsymbol{e}_{ij}$ Conservative Term $\boldsymbol{F^D}=-\gamma\omega^2(r_{ij})(\boldsymbol{e}_{ij}\cdot\boldsymbol{v}_{ij})\boldsymbol{e}_{ij}$ Dissipative Term $\boldsymbol{F^R}=\sigma\omega(r_{ij})\zeta_{ij}\boldsymbol{e}_{ij}\Delta t^{-\frac{1}{2}}$ Random Term Where $\boldsymbol{r_{ij}}=\boldsymbol{r_i}-\boldsymbol{r_j}$, $r_{ij}=\lvert\boldsymbol{r_{ij}}\rvert$, $\boldsymbol{e_{ij}}=\frac{\boldsymbol{r_{ij}}}{\lvert\boldsymbol{r_{ij}}\rvert}$ $\omega(r_{ij})=1-\frac{r_{ij}}{r_C}\ for\ r_{ij}\le r_c; o.w.\ \omega(r_{ij})=0$ The ξ_{ij} are symmetric random variables with zero mean and unit variance, uncorrelated for different pairs of particles and different times.
Properties Considerations	Parameterize the undetermined parameters to match physical properties: ▪ Platelet Cell Size ▪ Membrane Young's Modulus ▪ Membrane Shear Modulus ▪ Stretching Response ▪ Cell Plasma Compressibility ▪ Cell Plasma Viscosity ▪ Cell Plasma Pressure ▪ Cell Plasma Density Besides, we also need to consider computational feasibility and the ability of platelet model to become activated.	Parameterize the undetermined parameters and modify boundary conditions to match the physical properties: ▪ Viscosity ▪ Compressibility ▪ Reynolds Number ▪ Density ▪ Viscous Boundary Layers
Spatial Interfacing	Hybrid force filed containing the dissipative and random terms from DPD and Lenard-Jones potential from MD. It's exploited to mimic friction between platelet membranes and surrounding blood flows. $\boldsymbol{F_{ij}}=\boldsymbol{F_{ij}^{LJ}}+\boldsymbol{F_{ij}^D}+\boldsymbol{F_{ij}^R}$ Parameterize the undetermined parameters to match: ▪ platelets flipping trajectory with analytical solution (Jeffery's orbit) in Couette flow ▪ Rotation angle: $\phi=\phi(\dot{\gamma}t)=\operatorname{atan}\left(\frac{1}{r_e}\tan\left[-\dot{\gamma}t\frac{r_e}{r_e^2+1}+\tan^{-1}(r_e\tan\phi_0)\right]\right)$	 Membrane velocity distribution of platelet during it flips in Couette flow

Computational Complexities

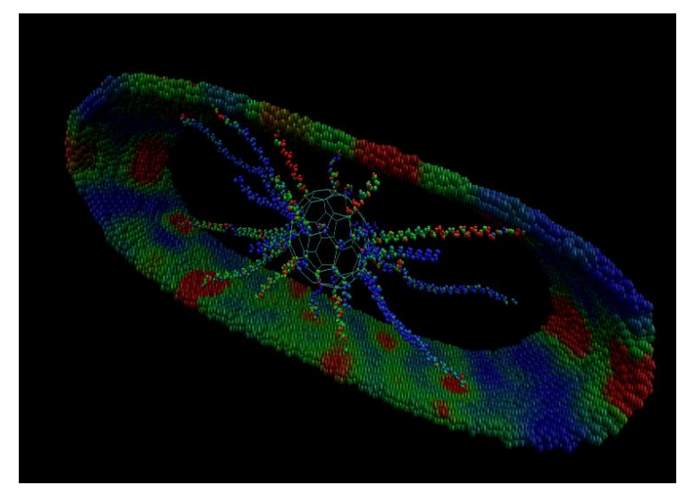


Complexity I: Disparate Temporal and Spatial Scales



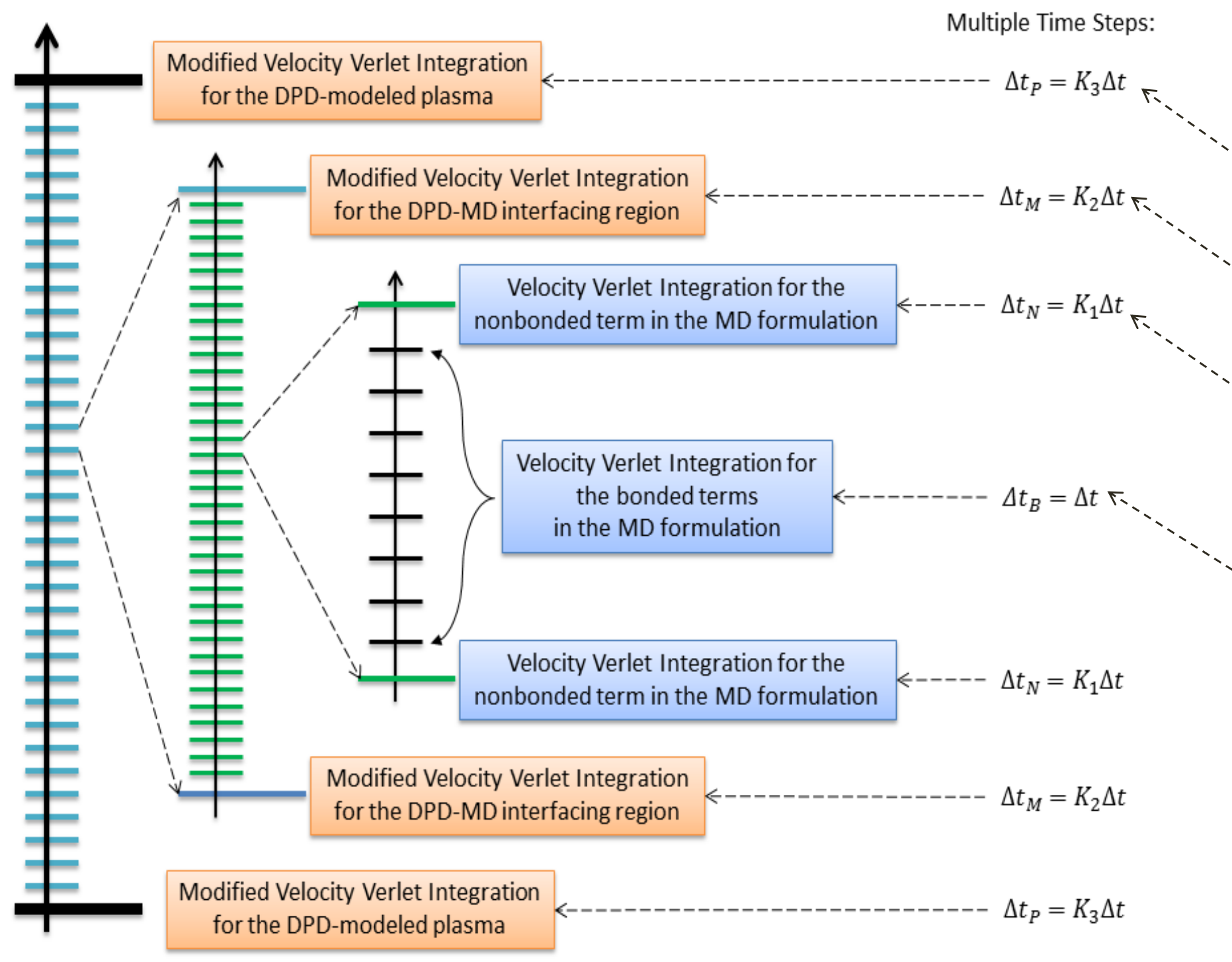
Complexity II: Complicated Model and Force Fields

Categories	Single Platelet	Multiple Platelets
In Vacuum	~0.14 million particles	Complex interactions among platelets
In Blood Plasma	~0.6 million particles	~2.7 million particles for 4 platelets flipping in blood plasm ~10.9 million particles for 16 platelets flipping in blood plasma > 50 million particles for 100 platelets in blood plasma
In Blood Vessels	Many types of blood cells and complex interactions among those cells	
With Shear Stresses & Thermo Conditions	Much more complex inputs and outputs control; On-the-fly analysis of large datasets	

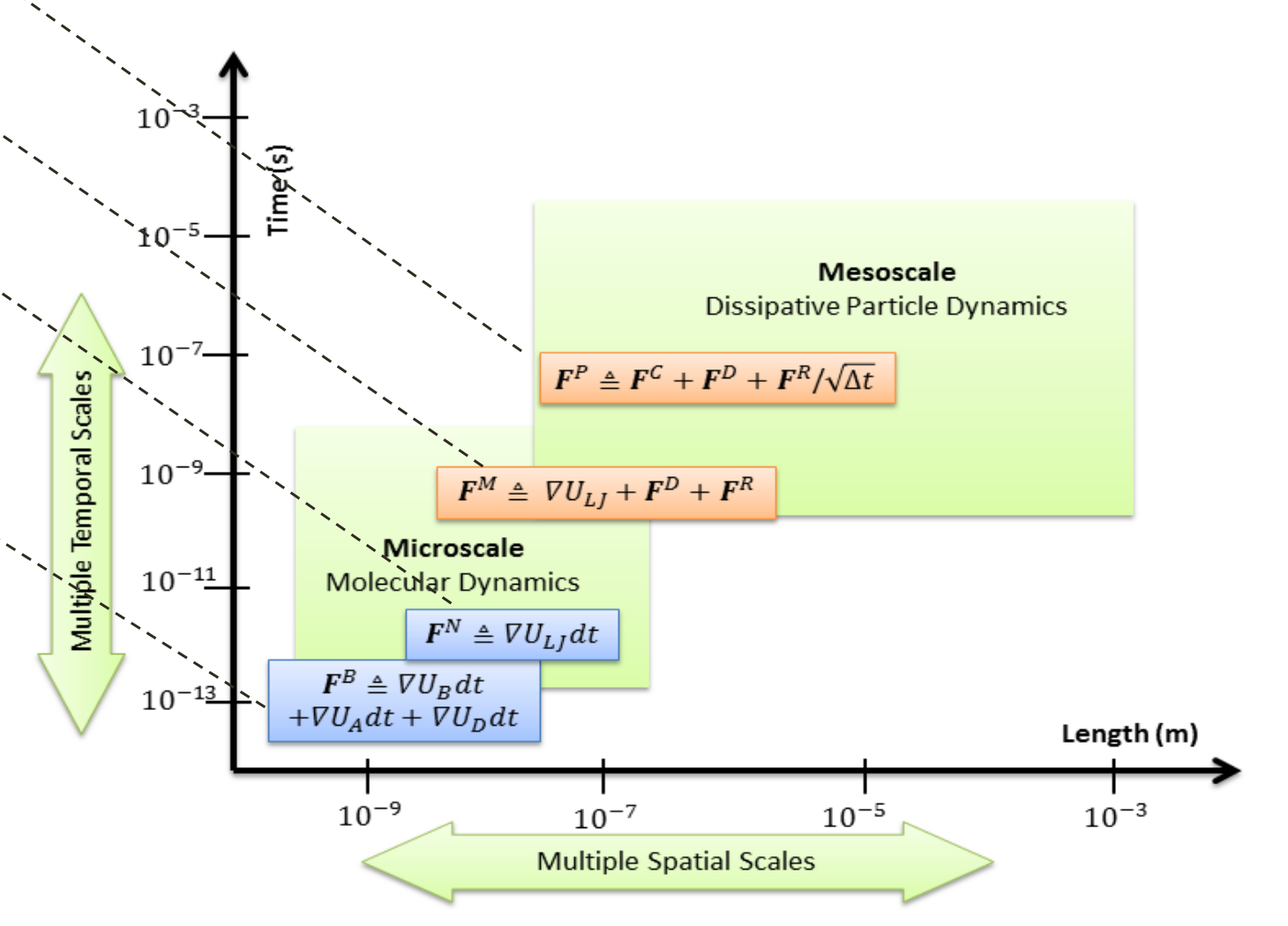


Complexity III: Large Demand of On-the-fly Analysis

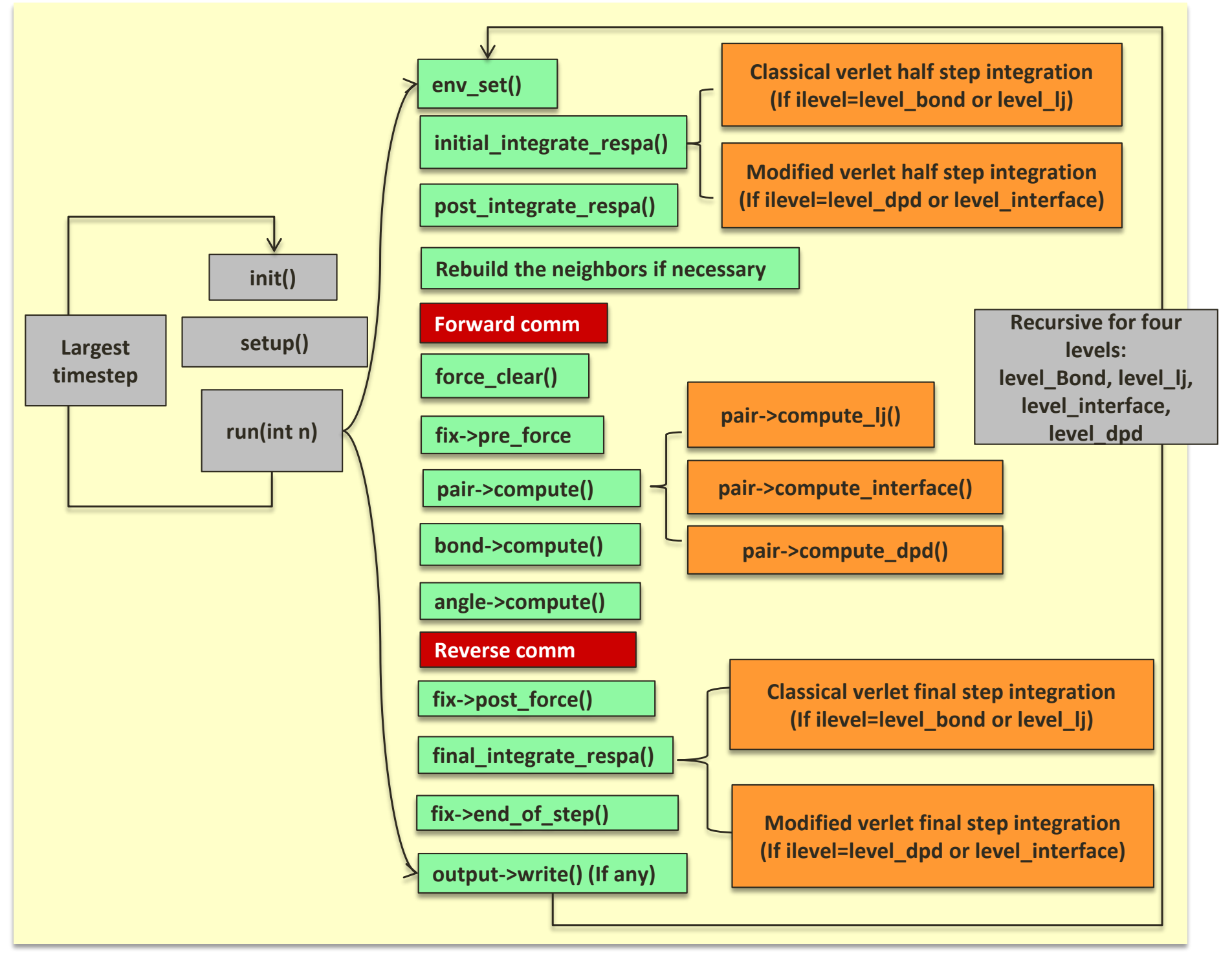
Speedup Strategy I-Multiscale Multiple Time Stepping Algorithm



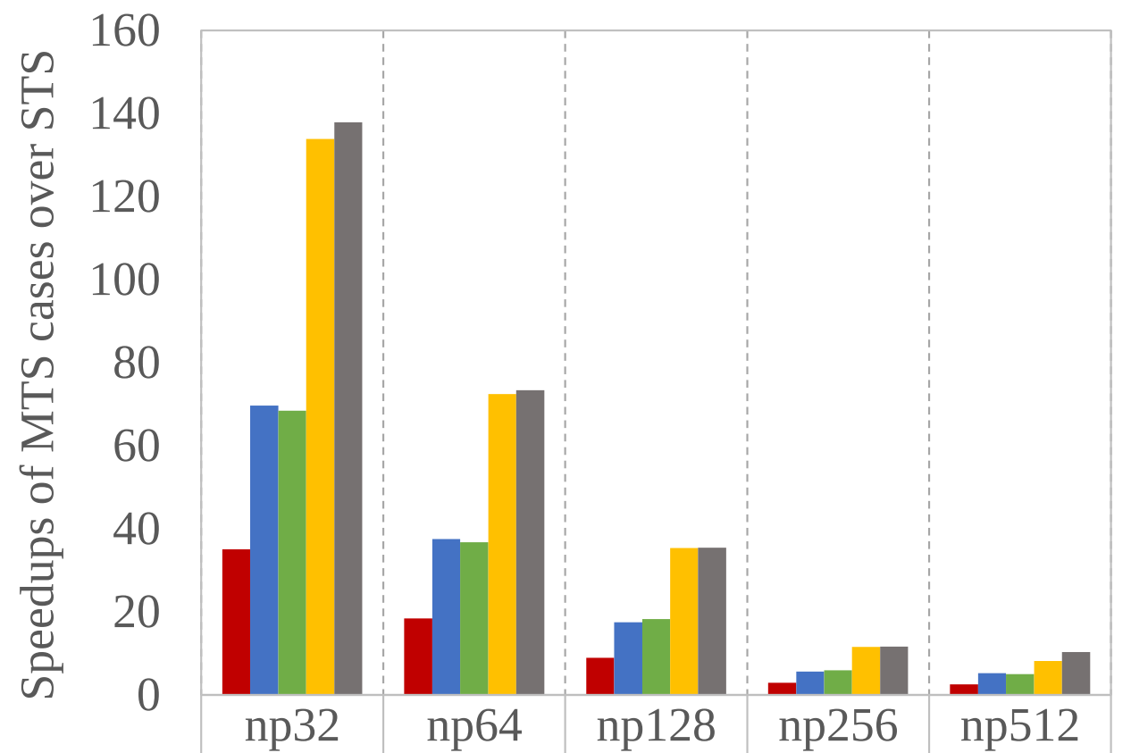
$\mathrm{K}_1, \mathrm{K}_2, \mathrm{K}_3$ are "Jump Factors"



Multiple Scales in the Model



Recursive 4-level Multiple Time Stepping Algorithm
(Code modifications based on LAMMPS framework)



	np32	np64	np128	np256	np512
🟥 CaseA	35.04	18.46	8.94	2.96	2.55
🟦 CaseB	69.68	37.54	17.47	5.67	5.24
🟩 CaseC	68.48	36.75	18.30	5.92	5.05
🟨 CaseD	133.86	72.45	35.42	11.54	8.19
⬛ CaseE	137.90	73.39	35.48	11.67	10.34

Times faster of MTS algorithms over the STS algorithm

Platform: Stampede

Usage: 32 ~ 512 Procs (2 ~ 32 CPU nodes)

Problem Size: 2.7 million particles (4 platelets flipping in blood plasma)

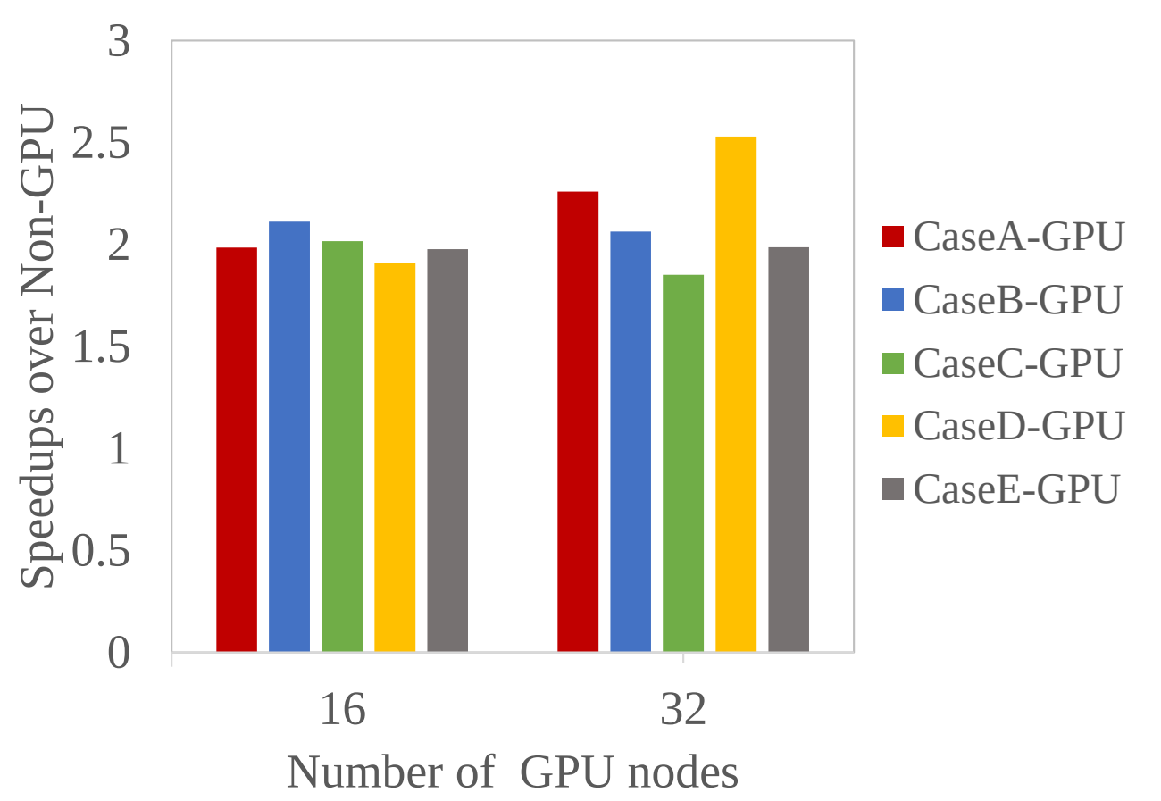
Speedup Strategy II-GPGPU Acceleration

LAMMPS (S. Plimpton et al.) and LAMMPS GPU Package (M. Brown et al.)

- Based on existing spatial decomposition of MPI processes
- Particle data is exchanged between host and device every step.
- Force evaluations and neighbor list build can be accelerated.
- Three precision options: single, mix, and double

Tailored Modifications:

- No-slip boundary condition for DPD flows
- Above 4-level multiscale MTS algorithm
- DPD predictor-and-corrector time integration

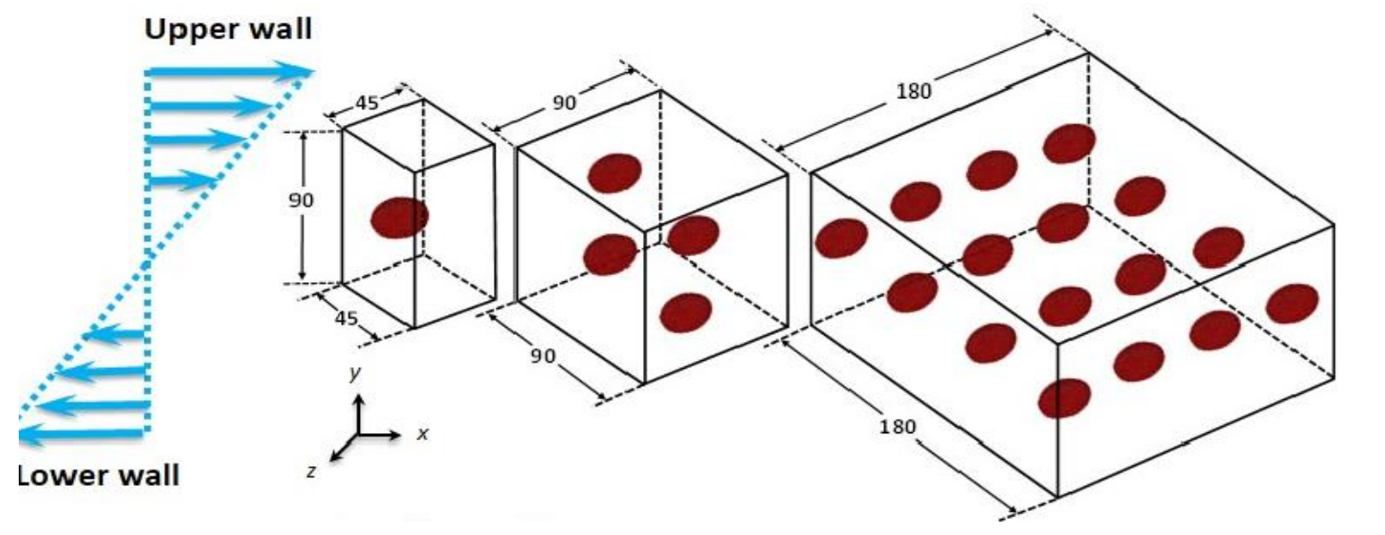


Times faster GPU solutions over CPU-only solutions for different MTS cases

Performance Results on Supercomputers

- Varying Problem Sizes:

Experiments	# of Platelets	# of Particles	Dimensions
Exp-S	1	680,718	45 × 90 × 45
Exp-M	4	2,722,872	90 × 90 × 90
Exp-L	16	10,891,488	180 × 90 × 180

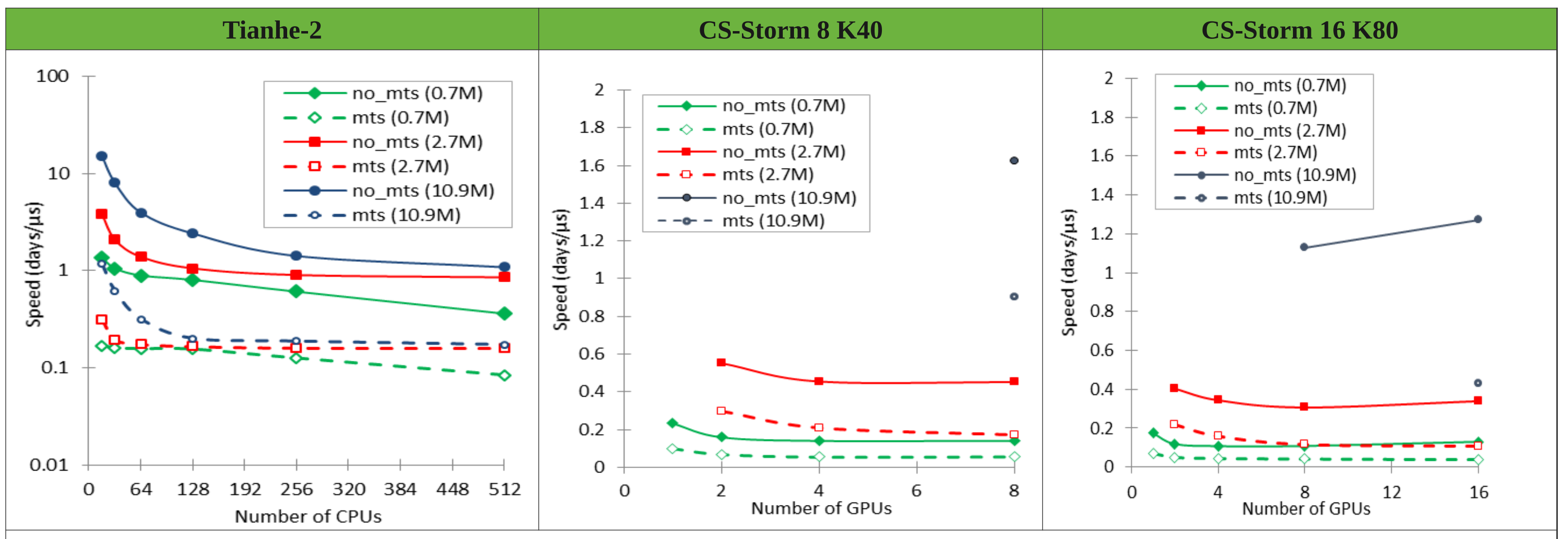


- Varying MTS Jump Factors:

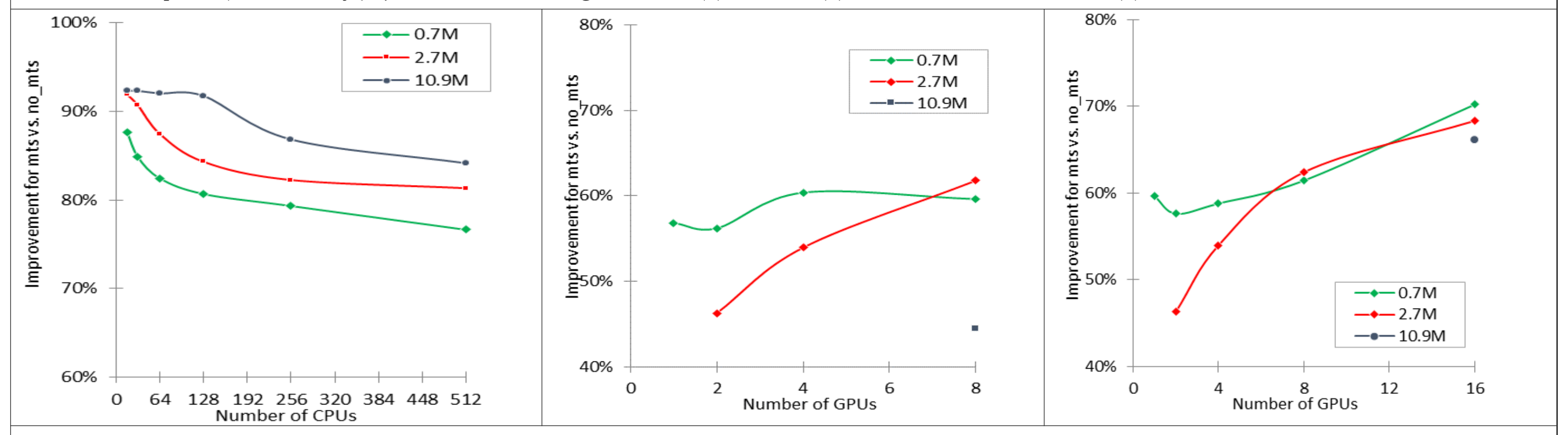
Case	Time steps for each scale				Configurations			
	CGMD-BD ($\Delta t_1\times10^{-6}$)	CGMD-NB ($\Delta t_2\times10^{-6}$)	DPD-CGMD ($\Delta t_3\times10^{-6}$)	DPD ($\Delta t_4\times10^{-6}$)	$\Delta t\times10^{-6}$	K_1	K_2	K_3
CaseA	2.5	2.5	25.0	500.0	500.0	1	10	20
CaseB	5.0	5.0	50.0	1000.0	1000.0	1	10	20
CaseC	5.0	5.0	50.0	500.0	500.0	1	10	10
CaseD	10.0	10.0	100.0	500.0	500.0	1	10	5
CaseE	10.0	10.0	100.0	1000.0	1000.0	1	10	10
STS	1.0	1.0	1.0	1.0	1.0	1	1	1

- Varying Test Systems (Tianhe-2 versus High-Density GPGPU Server):

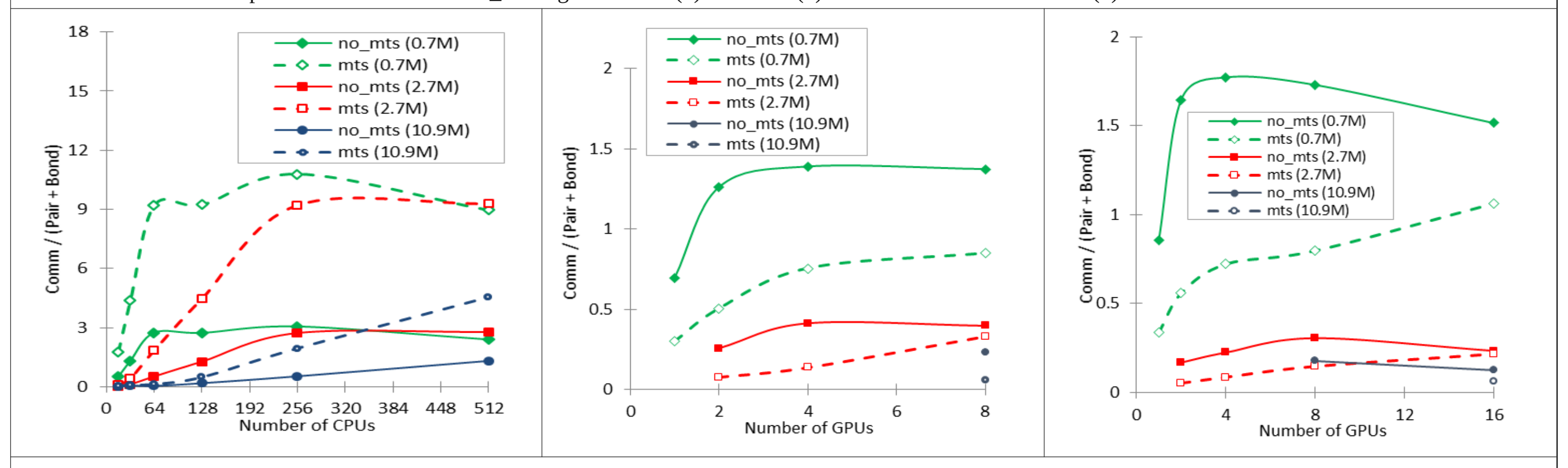
Tianhe-2 | **CS-Storm 8 K40** | **CS-Storm 16 K80**



Speeds (in unit of day/μs) of no_mts or mts algorithms on (1) Tianhe-2 (2) CS-Storm with 8 K40 cards (3) CS-Storm with 16 K80 cards



Perf. Improvement of mts over no_mts algorithms on (1) Tianhe-2 (2) CS-Storm with 8 K40 cards (3) CS-Storm with 16 K80 cards



Ratios of communication over computation(1) Tianhe-2 (2) CS-Storm with 8 K40 cards (3) CS-Storm with 16 K80 cards

Summary and Future Work

- **With combined algorithmic and hardware accelerations, we can efficiently simulate 1-ms the millisecond-scale hematology at resolutions of nanoscale platelets and mesoscale bio-flows using millions of particles.**
- **The rule of thumb is to consider the balance of speed and accuracy for an optimal MTS scheme and the balance of computation and communication for an optimal load-balancing scheme between accelerators and CPUs.**
- **Future work involves with the efforts to reduce communication overheads and simulate more complicated multiscale phenomena**.

References and Related Published Work

- N. Zhang, P. Zhang, L. Zhang, X. Zhu, L. Huang, and Y. Deng, "Performance Examinations of Multiple Time-Stepping Algorithms on Stampede Supercomputer", XSEDE15 Technical Paper Program, St. Louis, MO, 07/2015.
- P. Zhang, N. Zhang, Y. Deng, and D. Bluestein, "A Multiple Time Stepping Algorithm for Efficient Multiscale Modeling of Platelets Flowing in Blood Plasma", Journal of Computational Physics, vol. 284, pp. 668-686, 01/2015.
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- N. Zhang, P. Zhang, W. Kang, D. Bluestein, and Y. Deng, "Parameterizing the Morse potential for coarse-grained modeling of blood plasma", Journal of Computational Physics, vol. 257, pp. 726-736, 01/2014.

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