A Multiple Time Stepping Algorithm for Efficient Multiscale Modeling of Platelets Flowing in Blood Plasma

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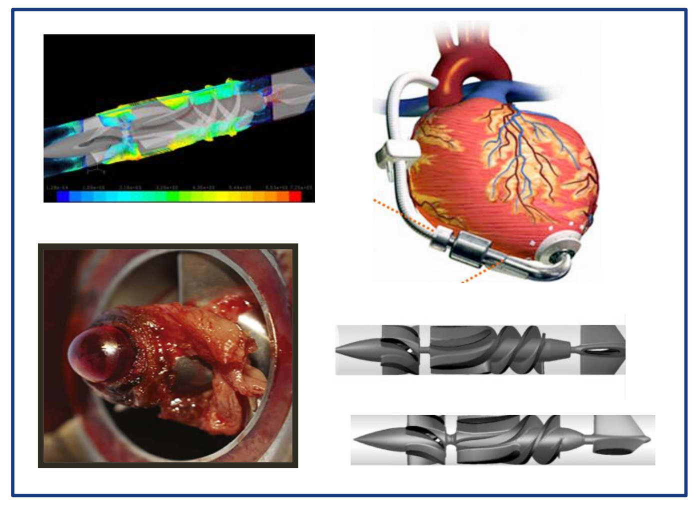
Motivations



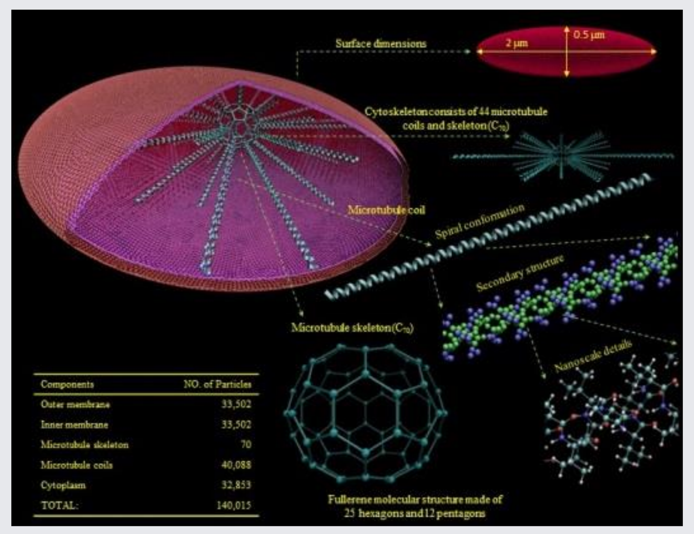
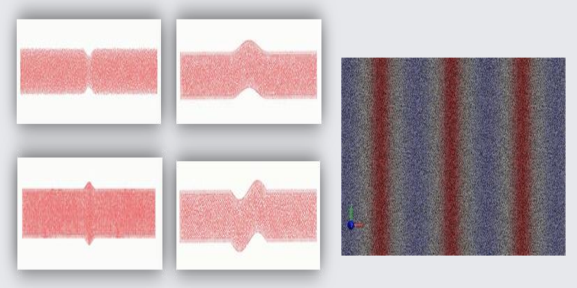
Source: Thrombogenicity Potential of Mechanical Heart Valves Simulations, Bio fluids Laboratory, Department of Biomedical Engineering, Stony Brook University

Cardiovascular diseases and thrombosis burden in implantable blood recirculating devices account for near 30% of all deaths globally and 35% in the US annually. Thrombosis in vascular diseases and implants is potentiated by an interaction of platelets with an injured wall or foreign surface. However, numerical simulations of flow-induced platelet-mediated thrombogenicity is an immense computational and algorithmic challenge due to the modeling complexity and disparate spatiotemporal scales of the mechanisms occur.

Methodologies

- Mathematical Models – Study mechanical and dynamics properties of blood flow and platelets;
- Coupling Method – Interface disparate spatial scales of blood flow and platelets and simulate flow-induced platelet-mediated thrombogenicity under viscous flows;
- **Multiscale Multiple Time Stepping (MTS) Algorithm – 3000x reduction in computing time over standard MTS for solving multiscale models**

Multiscale Models

Scales	Nanoscale	Mesoscale
Simulation Domain	Platelet Cell	Blood Plasma
Methods	Coarse Grained Molecular Dynamics (CGMD)	Dissipative Particle Dynamics (DPD)
Time step	10~100 fs	0.01~1 us
Length	1~20 A	0.1 ~ 1 um
Model Abstraction	 Figure 1 Physical structures and constitutes of Multiscale model of human platelets	 Figure 2(a) Various vascular geometries simulated by Dissipative Particle Dynamics method Figure 2(b) Periodic Poisefuille flow by applying two counter body forces on all fluid particle; in such case, its viscosity can be determined and desired blood viscosity is matched by selecting the model parameters.
Force Fields	$V(r) = \sum_{\text{bonds}} k_b(r-r_0)^2 + \sum_{\text{angles}} k_\theta(\theta-\theta_0)^2 + \sum_{\text{torsion}} k_\phi[1+\cos(n\phi-\delta)] + \sum_{\text{electrostatics}} \frac{q_i q_j}{4\pi\varepsilon_0 r} + \sum_{\text{L-J}} 4\varepsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^6\right] + \sum_{Modfied\ Morse} \epsilon\left[\alpha\left(1-\frac{r}{R(\mu)}\right) - 2\exp\left(\frac{\alpha}{2}\left(1-\frac{r}{R(\mu)}\right)\right)\right]$ 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	$\dot{\boldsymbol{p}}_i = \sum_{j\neq i}\left(\boldsymbol{F}^C dt + \boldsymbol{F}^D dt + \boldsymbol{F}^R\sqrt{dt} + \boldsymbol{F}^E dt\right)$ $\boldsymbol{F}^C = \alpha_b \omega(r)\boldsymbol{e}_{ij}$ $\boldsymbol{F}^D = -\gamma_b\omega^2(r)(\boldsymbol{e}_{ij}\cdot\boldsymbol{v}_{ij})\boldsymbol{e}_{ij}$ $\boldsymbol{F}^R = \sigma_b\omega(r)\xi_{ij}\sqrt{dt}\boldsymbol{e}_{ij}$ F^C, F^D *and* F^C are the conserveative, dissipative, and random forces acting on fluid F^E is the force exerted to lead to blood fluid flow.
Description	Our group has developed a multiscale particle based model of human platelet, to systematically study how mechanical stimuli from surrounding fluid induces blood coagulation and thrombosis.	

A Multiple Time Stepping Algorithm

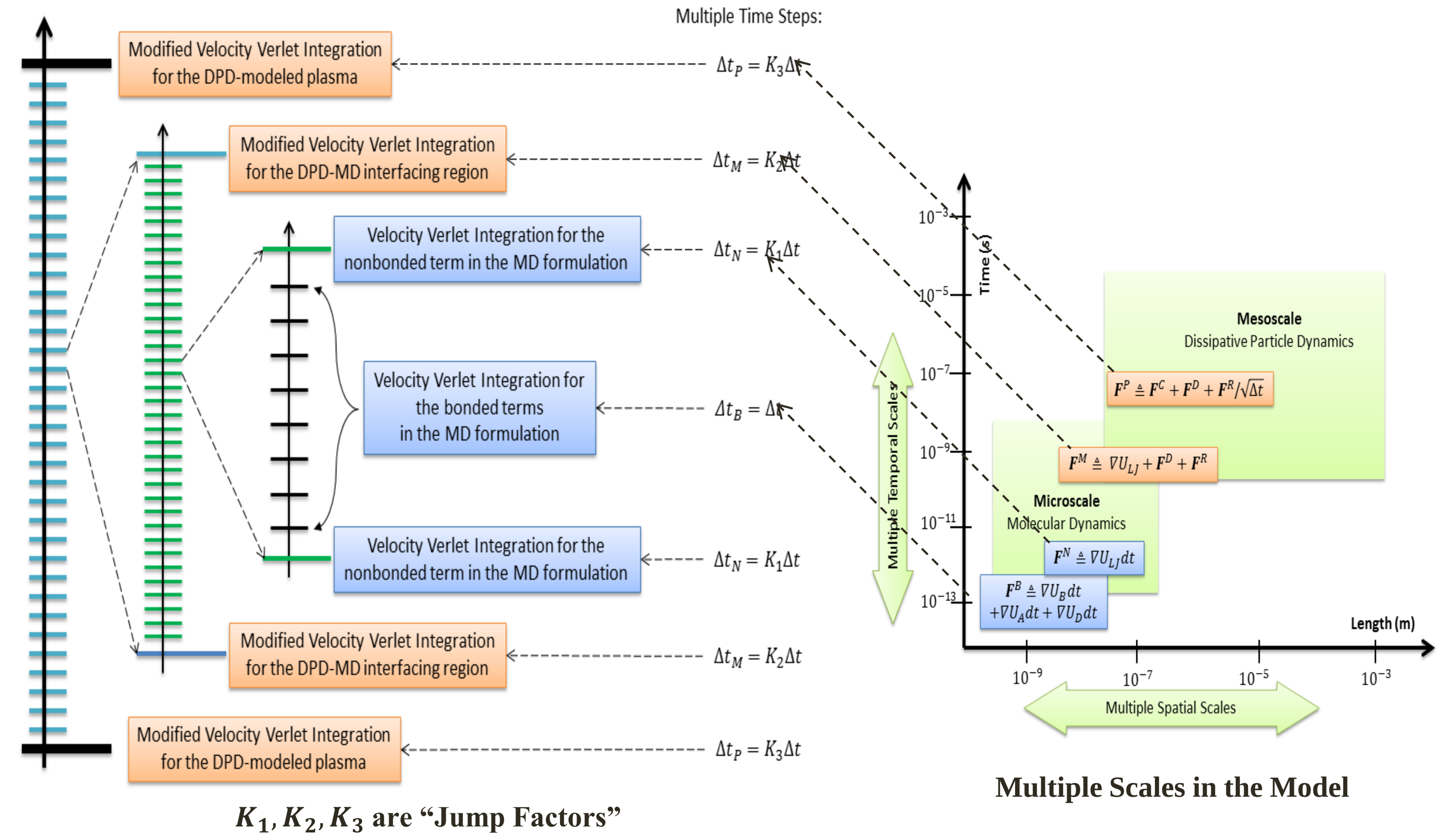


Figure 3 Integrated multiscale multiple time stepping algorithm for particle-based platelets flowing in blood plasma model. We decompose the whole integrator process into four levels: (1) DPD-modeled blood plasma (which has the largest time step $\Delta t\sim10^{-3}$); (2) DPD-CGMD modeled deformable platelet membrane at contact region of two scales; (3) GGMD modeled platelet of non-bonded component; (4) GGMD modeled platelet of bonded component (which needs the most frequent update, $\Delta t\sim10^{-7}$). Jump factors are introduced to make trade-off between speed and accuracy.

Overview of the multiple time stepping algorithms for the multiscale model

► $\boldsymbol{v}_p \leftarrow \boldsymbol{v}_p + \lambda_p\cdot(\Delta t/m)\cdot\boldsymbol{F}^P$	DPD
► For $l_1 = 0 \dots K_1 - 1$	DPD-CGMD
► set $\delta t_1 \equiv \Delta t/K_1$	DPD-CGMD
► $\boldsymbol{v}_m \leftarrow \boldsymbol{v}_m + \lambda_m\cdot(\delta t_1/m)\cdot\boldsymbol{F}^M$	DPD-CGMD
► For $l_2 = 0 \dots K_2 - 1$	CGMD-NB
► set $\delta t_2 \equiv \delta t_1/K_2 = \Delta t/(K_1\cdot K_2)$	CGMD-NB
► $\boldsymbol{v}_n \leftarrow \boldsymbol{v}_n + (\delta t_2/2m)\cdot\boldsymbol{F}^N$	CGMD-NB
► For $l_3 = 0 \dots K_3 - 1$	CGMD-BD
► set $\delta t \equiv \delta t_3 = \delta t_2/K_3 = \Delta t/(K_1\cdot K_2\cdot K_3)$	CGMD-BD
► $\boldsymbol{v}_b \leftarrow \boldsymbol{v}_b + (\delta t/2m)\cdot\boldsymbol{F}^B$	CGMD-BD
► $\boldsymbol{r} \leftarrow \boldsymbol{r} + \delta t\cdot\boldsymbol{v}$	All Particles
► Communication of positions and velocities.	
► compute $\boldsymbol{F}^B(\boldsymbol{r})$	CGMD-BD
► Communication of forces.	
► $\boldsymbol{v}_b \leftarrow \boldsymbol{v}_b + (\delta t/2m)\cdot\boldsymbol{F}^B$	CGMD-BD
► compute $\boldsymbol{F}^N(\boldsymbol{r})$	CGMD-NB
► Communication of forces.	
► $\boldsymbol{v}_n \leftarrow \boldsymbol{v}_n + (\delta t_2/2m)\cdot\boldsymbol{F}^N$	CGMD-NB
► compute $\widetilde{\boldsymbol{F}}^M(\boldsymbol{r},\boldsymbol{v})$	DPD-CGMD
► *Communication of forces.*	
► $\boldsymbol{v}_m \leftarrow \boldsymbol{v}_m + (\delta t_1/2m)\cdot(\boldsymbol{F}^M + \widetilde{\boldsymbol{F}}^M)$	DPD-CGMD
► $\boldsymbol{F}^M \leftarrow \widetilde{\boldsymbol{F}}^M$	DPD-CGMD
► compute $\widetilde{\boldsymbol{F}}^P(\boldsymbol{r},\boldsymbol{v})$	DPD
► Communication of forces.	
► Add external forces to the viscous flow if any.	Add Forces to flow
► $\boldsymbol{v}_p \leftarrow \boldsymbol{v}_p + (\Delta t/2m)\cdot(\boldsymbol{F}^P + \widetilde{\boldsymbol{F}}^P)$	DPD
► $\boldsymbol{F}^P \leftarrow \widetilde{\boldsymbol{F}}^P$	DPD

Accuracy vs. Computing Speed for Multiscale Simulations

Schemes	Timestep Sizes for Each Scale				Jump Factors			
	DPD	DPD-CGMD	CGMD-NB	CGMD-BD	Δt	K_1	K_2	K_3
MTS-L	10^{-3}	2×10^{-4}	2×10^{-4}	2×10^{-4}	10^{-3}	5	1	1
MTS-M1	10^{-3}	10^{-5}	10^{-6}	10^{-7}	10^{-3}	100	10	10
MTS-M2	10^{-3}	10^{-4}	10^{-5}	10^{-7}	10^{-3}	10	10	100
MTS-S	10^{-4}	10^{-4}	10^{-6}	10^{-7}	10^{-4}	1	100	10
STS	10^{-7}	10^{-7}	10^{-7}	10^{-7}	10^{-7}	1	1	1

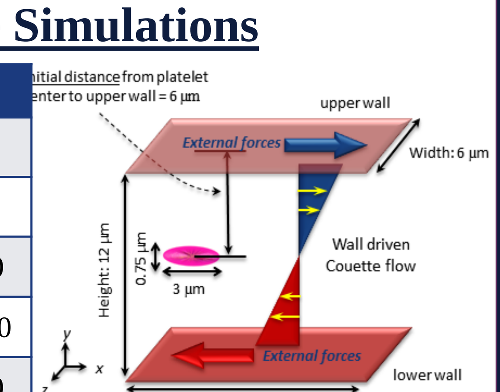


Figure 4: Wall Driven Couette Flow

Performance Metrics Versus Accuracy Metrics

Computing Speed	$S(np) = \frac{ts}{np\cdot T(ts,np)}$ ts: simulation time; np: number of processes; $T(ts,np)$: wall clock time given the number of	Physics Observables' Deviation from Equilibrium	$\varepsilon(v;t) = \frac{\lVert v(t) - v_0\rVert}{\lVert v_0\rVert}$ Time-dependent function $\varepsilon(v;t)$ measures the normalized deviation for variable $v(t)$ (system's total energy, temperature, fluid induced stresses) from the equilibrium over time
Parallel Efficiency	$E(np_1,np_2) \triangleq \frac{np_1\cdot\frac{T(ts_1,np_1)}{ts_1}}{np_2\cdot\frac{T(ts_2,np_2)}{ts_2}} = \frac{S(np_2)}{S(np_1)}$ for $np_1 < np_2$	Root Mean Square Deviation (RMSD)	$\mathrm{RMSD}(\hat{\tau},t) = \sqrt{\frac{1}{N_m}\sum_{p=1}^{N_m}\lVert\hat{\tau}_m(p,t) - \hat{\tau}_0(p,t)\rVert^2}$ N_m is the total number of the system particles. $\hat{\tau}_m(p,t)$ is the physics observables of per particle p at time t through using the MTS algorithm

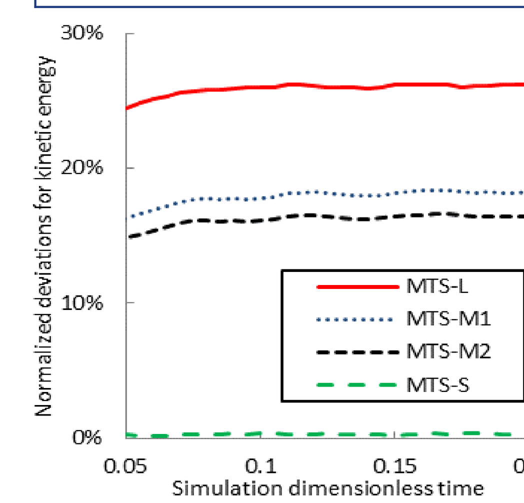


Figure 5 (a) Normalized deviations for the kinetic energy of single platelet over time

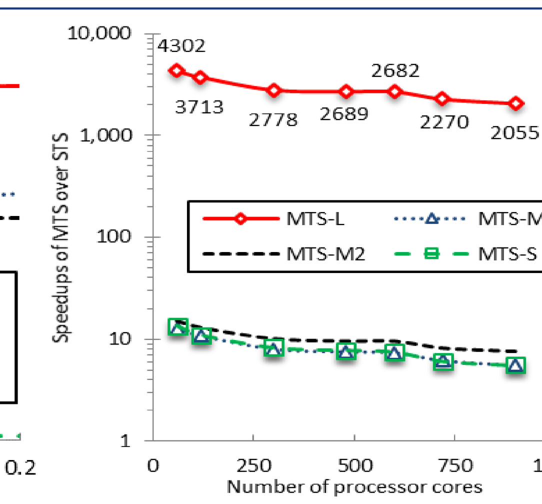


Figure 5 (b) Speedups of MTS algorithms over the STS algorithm

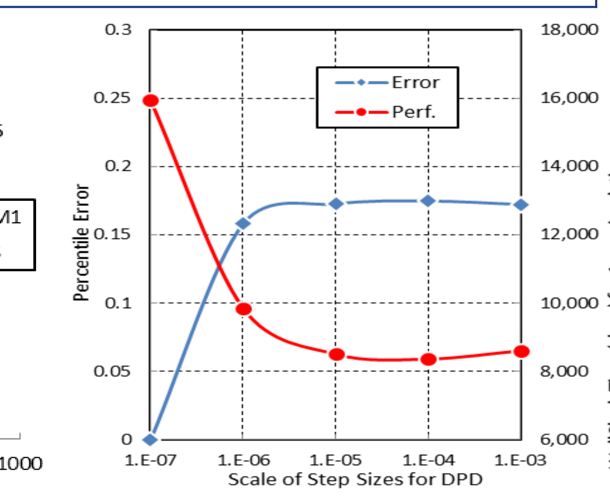
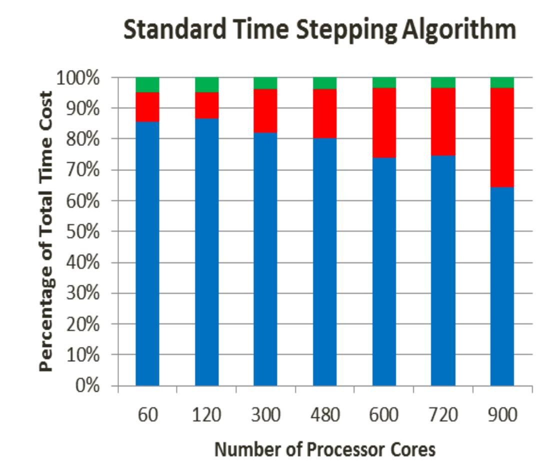
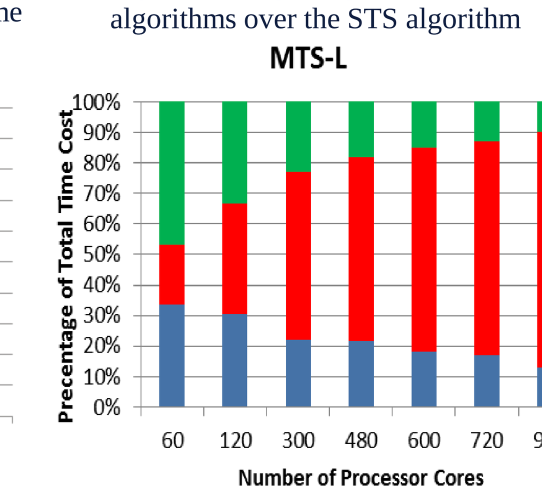


Figure 5 (c) Percentile error and wallclock time (in days) for 1-ms simulation with 300 cores





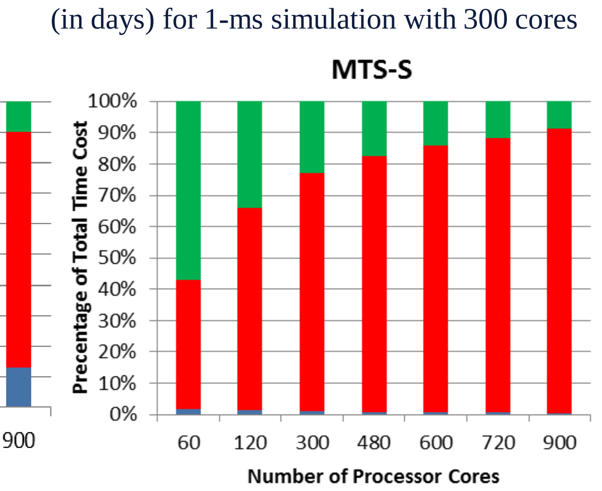
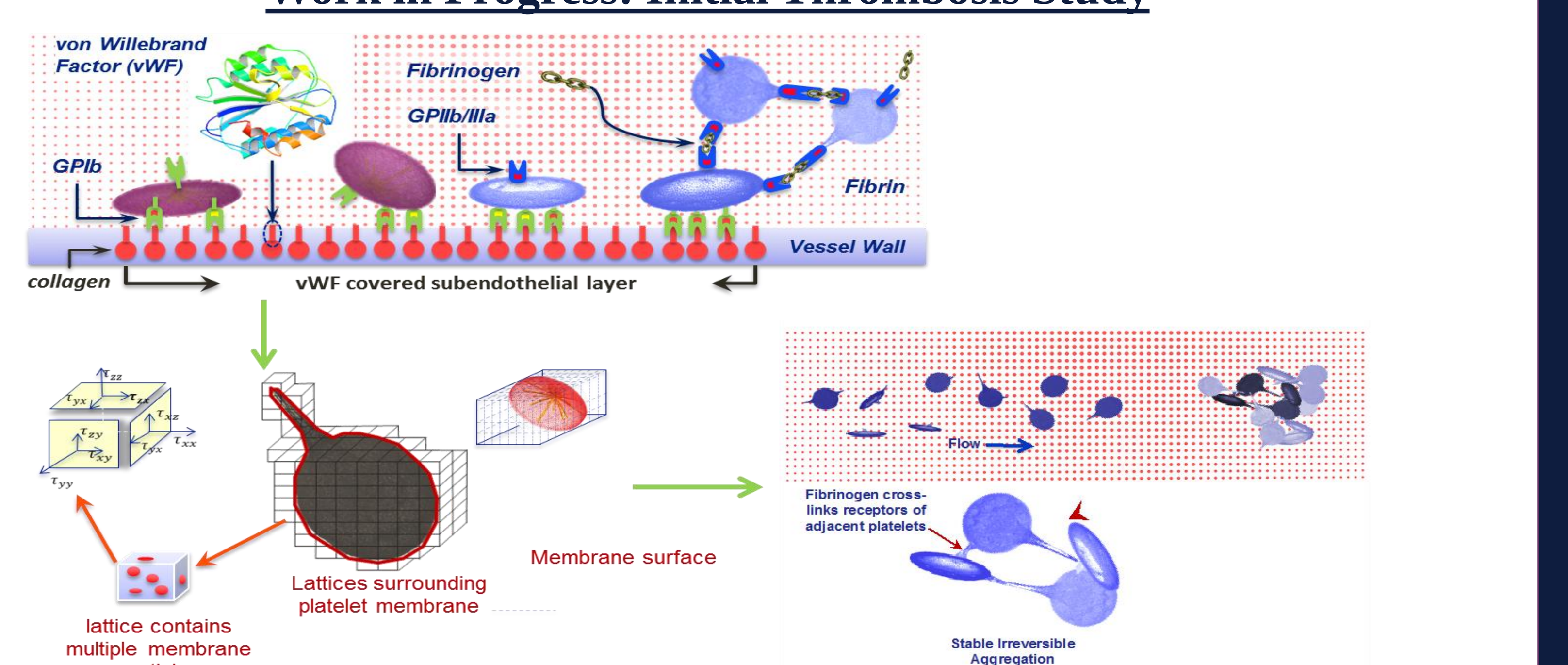


Figure 6 Percentage of loop time spent on computation (blue), communication(red) , and others (green) over processor cores

Work in Progress: Initial Thrombosis Study



References

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[2] Zhang, P., **Zhang, N.**, Deng, Y., *A Multiple Time Stepping Algorithm for Multiscale Modeling of Platelets Flowing in Blood Plasma*, Journal of computational Physics, 2014. *(Under Revision)*

[3] Zhang, P., Gao, C., **Zhang, N.**, Slepian, M.J., Deng, Y., Bluestein, D., "Multiscale Particle-Based Modeling of Flowing Platelets in Blood Plasma Using Dissipative Particle Dynamics and Coarse Grained Molecular Dynamics", Cellular and Molecular Bioengineering, pp. 1-23, 2014. DOI: 10.1007/s12195-014-0356-5

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