A Multiple Time Steppng Algorithm For Efficient Multiscale Modeling of Platelets Flowing in Blood Plasma

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***Abstract*—Numerical simulation of complex biological systems is an immense computational and algorithmic challenge due to modeling complexity and disparate spatiotemporal scales of the mechanisms occur. We develop a parallel multiscale multiple time stepping (MTS) algorithm for exploring the mechanisms at disparate spatiotemporal scales. Specifically, we apply our algorithm on parallel computers to study flow-induced platelet-mediated thrombogenicity. This MTS algorithm improves considerably the computational efficiency without significant loss of accuracy. The numerical experiments demonstrated 3000x reduction in computing time over standard MTS methods for solving the multiscale model. We present mathematical models and multiscale methods for study of dynamic properties of flowing platelets, multiscale parallel algorithms for reducing the computing time, implementation, and quantitative analysis of performance metrics versus accuracy metrics. This MTS algorithm establishes a computationally feasible approach for performing efficient multiscale simulations.**

Keywords—multiple time stepping, multiscale modeling, coarse-grained molecular dynamics

I. INTRODUCTION

Quantitatively determining the illusive dynamics and mechanics of platelets in pathological cases can facilitate developing effective treatments and elucidating the platelet initiate processes such as thrombus formation [1]. 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. A useful model must encapsulate sufficient spatial and temporal details. While a complete all-atom molecular dynamics simulation of a biological system can capture the dynamics of platelets at molecular scales, this is not practical due to the prohibitive computational resources required [2].

A multiscale particle-based model is proposed to combine the Dissipative Particle Dynamics (DPD)–Coarse Grained Molecular Dynamics (CGMD) methods for modeling the dynamics of platelets flowing in response to extracellular flow-induced stresses [3]. The model adapts DPD method for describing macroscopic transport of blood plasma in vessels and CGMD method for handling individual platelets. A hybrid force field formulated for establishing a functional interface between the platelet membrane and the surrounding fluid, in which the microstructural changes of platelets may respond to extracellular flow-induced stresses transferred to them.

The research work is sponsored by grants from National Institute of Health: NHLBI R21 HL096930 (DB) and NIBIB Quantum Award Implementation Phase II-U01 EB012487 (DB). The research utilized computing resources at the National Supercomputing Center in Jinan, China, under National Key Technology Research and Development Program of China (Grant No. 2012BAH09B03).

Extending our previous efforts on a multiscale model of platelets flowing in viscous blood plasma flows [3, 4], we develop an integrated MTS algorithm for performing multiscale simulations [5]. We present the force fields and describe the formulation and properties of MTS algorithms for coupling the DPD and CGMD. In this integrated MTS algorithm various parameters are introduced to guide the selection of step sizes for achieving performance optimization. To estimate the quality of the MTS algorithms, we introduce the accuracy vs. speed relationships as functions of step sizes. Extensive numerical experiments were conducted using performance metrics, to measure the relative performances of standard single-scaled time stepping (STS) algorithm vs. ours.

II. MULTOPLE TIME STEPPING ALGORITHM FOR MULTISCALE SIMULATIONS

The temporal scales for CGMD and DPD require nanoseconds and microseconds respectively. Standard timesteping (STS) algorithm requires a timestep small enough to resolve fastest motions. Thus, the nanoscale integrator should be applied to both top-scale and bottom-scale methods for capturing the dynamics of platelets flowing in viscous blood plasma. However, this significantly increases the unnecessary computation for DPD with fine-grained integrators. Moreover, even for the CGMD, a long-range and low-frequency force can be calculated with a larger time step than a short-range and high-frequency one. To improve the computing efficiency within error boundaries, we must design MTS algorithms for handling the disparity in temporal scales between DPD and CGMD. MTS algorithms have been widely used in each of CGMD and DPD independently and have been extended with the velocity Verlet integrator. Therefore, in our proposed integration of MTS algorithms for the DPD-CGMD model, we decompose the whole integrator process into four levels (Fig. 1).

III. ACCURACY VERSUS SPEED FOR MULTISCALE SIMULATIONS

MTS algorithm is usually a matter of trade-offs between speed and accuracy for efficient multiscale simulations. Energy conservation and maintenance of adequate precisions of other measures must be verified while accelerating the computations. We aim to investigate the microscopic shape changes of platelets in response to macroscopic flow-induced stresses. Thus, in measuring numerical solutions we focus on the accuracy of characterizing the hybrid system and the flowing platelets, as well as the accuracy of calculating the dynamic flow-induced stresses on the surface membrane. For measures of speed, we

consider several indictors 1) computing speed, which measures the length of simulated time per core-hour; 2) speedup of a MTS algorithm, which measures the ratio of the speed of a MTS algorithm over that of a STS algorithm so it refers to how much MTS is faster than STS using the same resources; 3) Parallel efficiency measures strong scalability of MTS simulations.

IV. RESULTS AND DISCUSSION

For comparative purposes we benchmark all algorithms against the standard time-stepping (STS) algorithm at smallest $\Delta t = 10^{-7}$ in its integrator. The largest stepsize for the DPD flow regime is $\Delta t = 10^{-3}$. By varying parametersK_1, K_2 and K_3, we produce four representative MTS configurations as shown in Table 1. Fig 3. shows that MTS-M1, MTS-M2 and MTS-S are roughly 10-fold faster than STS and MTS-L, achieving about 2000~3000 reduction in computation time. The timing records indicate that for the computational challenge of simulating one millisecond multiscale phenomena of platelets flowing in viscous fluid flow, STS requires 26 years using 600 cores, where using the same resources MTS requires only ~3.5 days. MTS algorithms offered an opportunity of simulating the molecular-scale mechanisms of deformable platelets flowing in the viscous fluid flows within affordable computing demands with bounded errors.

V. SUMMARY

This paper presents an integrated multiple time stepping (MTS) algorithm to solve a multiscale model of the dynamics of platelets flowing in viscous blood flow. The MTS algorithm proposes a multi-level integration scheme, allowing an optimization procedure for seeking a faster performer within certain error boundaries. This work establishes a computationally feasible approach for solving large-scale particle-based systems at multiple scales for performing efficient multiscale simulations. Integrated MTS algorithms such as the one presented in the current work are essential for achieving full multiscale particle-based modeling of complex physiological flows, e.g., flow-induced platelet-mediated thrombosis, etc. Using MTS, we have achieved a dramatic reduction of the modeling time for system sizes and simulation times that are relevant to multiscale phenomena such as thrombosis formation. By developing computationally feasible and efficient approaches, such challenging simulations of molecular biomechanics at multiple scales are brought within the reach of current high-performance computing resources.

Table 1 The time steps and configurations for different MTS cases

Case Name	Time steps for each scale				Configurations		
	DPD	DPD-CGMD	CGMD -NB	CGMD Boned	K_1	K_2	K_3
MTS-L	10^{-3}	2×10^{-4}	2×10^{-4}	2×10^{-4}	5	1	1
MTS-M1	10^{-3}	10^{-5}	10^{-6}	10^{-7}	100	10	10
MTS-M2	10^{-3}	10^{-4}	10^{-5}	10^{-7}	10	10	100
MTS-S	10^{-4}	10^{-4}	10^{-6}	10^{-7}	1	100	10
STS	10^{-7}	10^{-7}	10^{-7}	10^{-7}	1	1	1

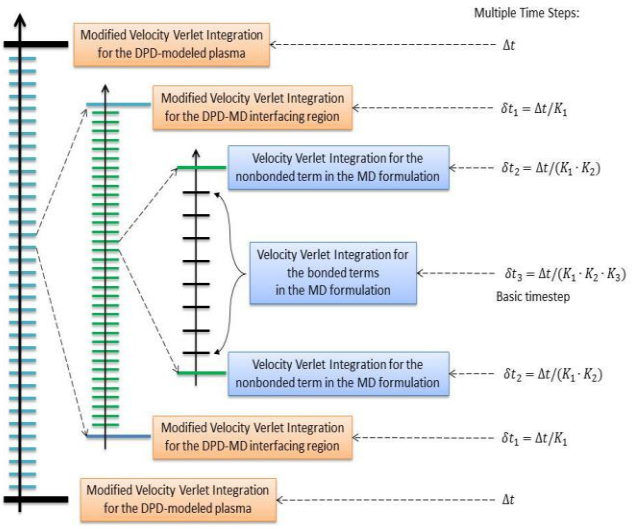

Fig. 1 Overview of the multiple time-stepping algorithms for the multiscale model

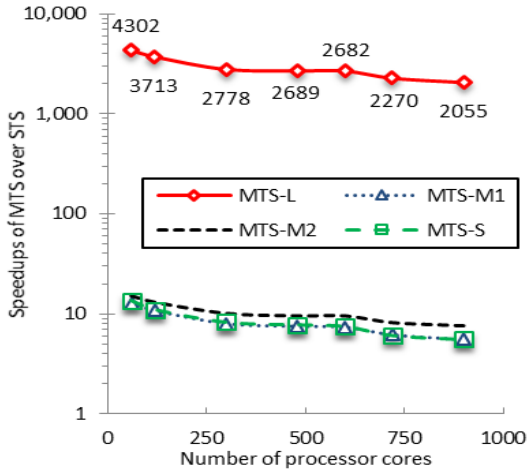

Fig 2. Speedups of MTS algorithms over the STS algorithm (A base 10 logarithmic scale for the vertical axis)

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