Reducing the effects of compressibility in DPD-based blood flow simulations through severe stenotic microchannels

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\textbf{A B S T R A C T}

Viscous fluid flow simulations based on dissipative particle dynamics (DPD) may bear compressible flow effects when flowing through severe stenotic geometries. This is caused by the soft repulsive potential employed in the DPD force field, which limits the particle-based fluid system ability to sustain a large degree of compression. To mitigate this problem, a Morse potential was added to the DPD force field. We studied the fluid properties of the modified fluid model (DPD–Morse) and compared it with a previously published conventional DPD based fluid model. Our DPD–Morse model demonstrated reduced compressibility while preserving other fluid properties such as the fluid density and viscosity. We further investigated the fluid flow properties for a severe 3D stenotic microchannel with a 67\% stenosis, using the two models. The DPD fluid model presented a significant density gradient along the flow direction, where the fluid density increased upstream towards the stenosis and decreased downstream from the stenosis before regaining its initial value. In contrast, the DPD–Morse model demonstrated a far better uniform fluid density distribution along the flow direction. We compared both solutions with CFD simulations. The DPD–Morse fluid resembled the behavior of the continuum fluid model whereas DPD fluid deviated from it. To estimate the effect that the difference between the two DPD formulations may have on the platelet activation potential, we have further embedded a platelet model within the flow field and investigated the shear stress accumulation along the platelet transport trajectory. In the stenotic section, the DPD fluid demonstrated a larger stress gradient than the DPD–Morse fluid. The platelet transport period was shorter for the DPD fluid as it generated a larger fluid density gradient that overestimated the acceleration of the platelet through the stenosis. With reduced fluid compressibility, our modified DPD–Morse fluid model was more accurate than the DPD fluid model when computing the platelet activation potential in a severe stenosis.

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1. Introduction

Platelet-mediated thrombus formation is a major culprit in progression of cardiovascular diseases such as coronary artery disease, by occluding blood vessels and creating stenotic flow conditions [1]. The elevated shear stresses through a coronary stenosis may activate blood platelets and induce progressive atherothrombotic events that can lead to unstable angina.

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myocardial infarction, and sudden ischemic death. Similarly, in mechanical circulatory support devices such as ventricular assist devices (VAD), and in mechanical heart valves (MHV), the flow through the small crevices in the devices is a major culprit in high incidence of thromboembolic complications, requiring lifelong anticoagulant therapy for the device recipients [2,3].

The progress of thrombosis is initiated by platelet activation, which can be induced by pathological flow patterns characterizing the flow conditions in stenosed coronary arteries and in prosthetic devices. Multiple activated platelets then interact and aggregate via GPIIb/IIIa-fibrinogen/vWF bridging, followed by the phase change of the coagulated material [4,5]. These processes involve complex phenomena on multiple length scales: the hemodynamics including fluid shear stress, vortices, and recirculation zones are described on the 10 to 100 μm scale; platelet transport dynamics and platelet–platelet interactions are addressed on the 1 to 10 μm scale; the pseudopodia formation, and receptor–ligand binding are on the nm scale [5,6]. Computer simulations with the aid of enhanced computing power have become an essential tool to study hemodynamics and ensuing responses of platelets and thrombosis [5,7,8]. Given the multiscale nature of shear-induced thrombosis particle-based models are better equipped than continuum-based methods such as CFD for coupling the blood flow phenomena across disparate length and time scales. Dissipative particle dynamics (DPD) is a coarse-grained particle-based approach that represents blood flow by directly modeling blood plasma and individual cellular and molecular components as ensembles of discrete particles. It can bridge the gap ranging from 10 nm to 100 μm between the continuum-based blood flow representation and the microscopic molecular events of platelet activation and thrombus formation [9,10]. With the aid of no-slip [11–13] and inflow/outflow [14,15] boundary conditions, it has been successfully employed to simulate the complex rheological properties of blood flow, including blood-plasma separation [15,16], Fahraeus–Lindqvist effect, cell free layer, margination of white blood cells and platelets [17], platelets transport and interactions through stenosis [13,18], and platelet–mediated thrombosis [6]. Through the coupling with platelet model based on coarse grained molecular dynamics (CGMD), DPD can further simulate the mechanotransduction process of shear-induced platelet activation, by providing highly resolved mapping of the surface stress distribution on the platelet membrane under dynamic flow conditions [7,8,19]. DPD has demonstrated the hallmarks of viscous fluid flow properties that were verified by continuum-based simulation approach such as computational fluid dynamics (CFD) [12–14]. However, most of the DPD simulations were conducted in straight and mild stenotic cylindrical or rectangular shaped geometries. In human vasculatures, platelet aggregation and thrombosis can be triggered by arterial stenosis, and the maximum rate of platelet accumulation is increased with increasing stenosis severity [20]. Oclusions greater than 75% in coronary artery can induce occlusive thrombi and generate symptoms of angina [1,21]. A current limitation of DPD-based approaches is their constrained ability to approximate the incompressibility of viscous fluids while flowing through a severe stenosis. In DPD fluid, the fluid particles may accumulate upstream of the stenosis, and a density gradient may appear along flow direction [22,23]. The compressibility effects emerge as a result of the soft interaction potential employed in conventional DPD formulations [24,25].

The compressibility effects of DPD raised intensive interest in the community and tremendous efforts have been taken to address this issue in recent years [22,24,26]. Pan et al. investigated the DPD fluid compressibility either without considering the conservative force, reducing the particle mass, increasing system temperature, or increasing the strength of the repulsion parameter. They suggested that incompressibility can be promoted by a sensible choice of parameters. Mai-Duy et al. investigated the problem in the overdamped limit of DPD system where the particles approach zero mass limit [26]. Both works suggested to reduce the particle mass to promote incompressibility. However, as particle mass is continuously reduced, the corresponding DPD systems become stiff and require different integration scheme to ensure an accurate solution with efficient computation [27]. Yazdani et al. explored the possibility of guiding DPD particles in complex geometries [22]. They suggested that the performance of DPD simulations can be enhanced by including a proper body force in the equation of motion of the DPD particles. In their work, they applied the pressure gradient of the Navier–Stokes (N–S) flow as the body force for DPD simulation. They also noted that there may be restriction for using their proposed method in unsteady flows, in which the finite compressibility effects of DPD fluid will set an upper limit for the frequency of the transient dynamics. The unsteady flows also require to solve N–S equation at every timestep in order to derive the tailored body force. This would increase the computational cost. Other works applied smoothed DPD (SDPD) approach to approximate the incompressible DPD fluid flow by choosing an equation of state and adjusted corresponding parameters [28]. However, the conventional DPD approach does not allow an arbitrary selection of the equation of state [29,30].

Our work continued to address the compressibility effects. We explored the possibility of incorporating Morse potential into the DPD force field to achieve desired incompressibility. Morse potential has been applied as a coarse-grained force field to model water [31] and blood [32] and was able to closely replicate the fluid properties. It was also applied in simulations such as polymer translocation through microchannel [33], aggregation of red blood cells [34–36], and molecular binding between platelet glycoprotein GPIIb and von Willebrand factor (vWF) [37]. In the first case, the repulsive role of Morse potential was augmented to avoid DPD particle interpenetration problem in polymer chains. In latter cases, the attractive part was employed to simulate cell–cell and molecule–molecule attractions. In the case of stenotic flows, a hard short-range repulsive force makes Morse potential a good candidate to minimize the compressibility effects of conventional DPD fluid. When fluid flow is being largely compressed in stenotic section, Morse potential can provide a hard core for the DPD fluid particles to sustain the compression. Therefore, we introduced a hybrid DPD–Morse fluid model to better preserve the fluid incompressibility, in which the Morse potential is added to the conventional DPD force field. The particle interaction range is divided into two regions, an inner hard-core region where both Morse and DPD force fields are applied, and an outer soft layer where only DPD force field is exerted. We conducted a series of comparative studies to investigate the compressibility
effects of DPD–Morse and DPD fluids. Our DPD–Morse fluid model presents an equation of state of a quadratic form, which is the same as in the conventional DPD fluid [29]. However, the equation of state of the DPD–Morse fluid is steeper than the conventional DPD fluid, which means that the DPD–Morse fluid has a larger speed of sound (square root of the slope). This leads to a smaller Mach number – indicating that the incompressibility was improved. We employed counter-Poiseuille flow to study the viscous fluid flow development with periodic boundary condition (PBC) [13], where the DPD–Morse fluid model was in good agreement with the analytical solution in fluid velocity, density, and shear stress. In addition, we employed a 67% stenotic microchannel to investigate the influence of the compressibility effects in fluid flow properties under large compression. We compared the simulation results with CFD solutions for verification. Our simulation results showed that the DPD–Morse fluid model compared favorably with CFD results and represents much better the physics of the fluid flow.

Furthermore, we investigated how compressibility effects of the fluid models affect the platelet transport dynamics passing through the microchannel and measured the shear stress accumulation along platelet flowing trajectory. The simulation results indicated that the DPD–Morse fluid model was more accurate than the DPD fluid model in computing platelet activation potential in a severe stenosis which is of a significant clinical relevance.

2. Methods

2.1. DPD–Morse fluid model

A new viscous blood plasma model is proposed which combines the Morse potential and conventional DPD force field. The Morse potential is being used in order to reduce the fluid compressibility.

A modified DPD formula is presented as

\[
d\vec{v}_i = \frac{1}{m_i} \sum_{j \neq i}^N (F_M^M dt + F_C^C dt + F_D^D dt + F_R^R \sqrt{dt})
\]

(1)

where \(F_M^M\) is the conservative force derived from Morse potential acting on particle \(i\). \(F_C^C, F_D^D, F_R^R\) are the conservative, dissipative and random forces of DPD force field acting on the particle \(i\). \(\vec{v}_i\) and \(m_i\) are velocity and mass of particle \(i\).

\(F_M^M\) is expressed as

\[
F_M^M = 2D_0 \alpha \left[ e^{2\alpha(r_0 - r_{ij})} - e^{\alpha(r_0 - r_{ij})} \right] \vec{e}_{ij}
\]

(2)

where the first term is a repulsive term related to fluid pressure, and the second term is an attractive term related to fluid viscosity. \(D_0\) is the well depth, \(\alpha\) is a scaling factor, and \(r_0\) is the zero-force length. \(r_{ij} = r_i - r_j\), \(r_{ij} = |r_{ij}|\), \(\vec{e}_{ij} = r_{ij}/r_{ij}\). The repulsive term is dominant when \(r < r_0\) and the attractive term becomes more important when \(r > r_0\) [38].

DPD force field is expressed as

\[
F_C^C = a \left( 1.0 - \frac{r_{ij}}{r_c} \right) \vec{e}_{ij}
\]

(3)

\[
F_D^D = -\gamma w^D (r_{ij}) (\vec{v}_{ij} \cdot \vec{e}_{ij}) \vec{e}_{ij}
\]

(4)

\[
F_R^R = \sigma w^R (r_{ij}) \xi_{ij} \vec{e}_{ij}
\]

(5)

\[
w^D (r_{ij}) = \left[ w^R (r_{ij}) \right]^2 = \left( 1.0 - \frac{r_{ij}}{r_c} \right)^{2k}
\]

(6)

where \(F_C^C\) contributes to fluid pressure, \(F_D^D\) contributes to fluid viscosity, and \(F_R^R\) mitigates the missing degree of freedom after coarse-graining. \(a, \gamma, \sigma\) are the strength of conservative, dissipative and random forces. \(\xi_{ij}\) is a random number with zero mean and unit variance [29].

Two cutoff distances \(r_c^M\) and \(r_c\) are defined, \(r_c^M\) is the cutoff for Morse potential, \(r_c\) is the global cutoff, and \(r_c^M < r_c\). The Morse potential plays a significant role as the inter-particle distance is reduced to less than \(r_c^M\) when fluid is being compressed. DPD force field is valid within \(r_c\). Zero-force length \(r_0\) is set the same as \(r_c^M\) because the repulsive term of the Morse potential is essential to the fluid pressure.

2.2. Parameterization of DPD–Morse potential using counter-Poiseuille flow

Characteristic fluid flow phenomena in straight microchannels have been achieved by DPD fluid model with parameter set \(a = 25.0, \gamma = 67.5, k = 0.25, r_c = 1.7, k_B T = 1.0\), number density \(n = 3.0\). To minimize the compressible effects of DPD fluid flowing through severe stenotic microchannel, given the same DPD parameter set, different parameter sets of Morse potential are explored. Three parameters are present in Morse potential: scaling factor \(\alpha\), well depth \(D_0\), and zero-force length \(r_0\). \(\alpha\) controls the potential width. When \(\alpha\) is increased, both repulsive term and attractive term become steeper.
which lead to a narrower potential well. The parameter space of $\alpha$ can be from 0.5 to 2. Here, $\alpha = 0.5$ and $\alpha = 1.0$ were selected to achieve a gentle change of Morse potential in the repulsive range. $D_0$ is the secondary factor that affects the steepness of repulsive term at a fixed $r_0$. When $\alpha$ is determined, the parameter space of $D_0$ is set as $[10, 100, 200, 400, 600]$. For DPD fluid with number density $n = 3.0$, the average inter-particle distance is determined as 0.69, the cubic root of system number density. The parameter space of $r_0$ is therefore selected as $[0.6, 0.8, 1.0, 1.4, 1.7]$.

In our simulations, counter-Poiseuille flow was employed to perform the parameterization of Morse potential, with the objective of preserving fluid dynamic viscosity and increasing system pressure. The fluid dynamic viscosity of DPD fluid is attributed to the dissipative term of DPD force field, and that of DPD–Morse fluid is resulted from both the dissipative term of DPD force field and the attractive term of Morse potential. The pressure of DPD fluid is provided by the conservative term of DPD force field, and that of DPD–Morse fluid is given by the conservative term of both DPD force field and Morse potential. The simulation domain was $30 \times 30 \times 30$, which was divided into two symmetric sections with a pair of body forces $g = 2.0$ applied to the fluid particle of each section in opposite directions [13,39]. Periodic boundary condition was applied in three orthogonal directions. The integration timestep was $dt = 5e - 4$. We followed [29] in using a velocity–Verlet algorithm which is of second order accuracy. Fully developed parabolic velocity profile was achieved after simulation of 10,000 timesteps. For post-processing, the 3D simulation box was divided into 60 vertical bins along $x$ direction with side length of 0.5, where the physical quantities of each fluid bin were obtained by averaging all particles information in each bin for 5000 timesteps. The dynamic viscosity $\mu$ was acquired by fitting the velocity profile from simulation to the analytical solution. The parameter set was considered ineffective if the fluid velocity profile deviated from the conventional DPD fluid. When the fluid velocity profile was the same, the parameter set was selected depending on the system pressure (Fig. 1). $\alpha$ was first set as 1.0. $r_0$ was selected as 0.6 and 0.8. The fluid velocity and pressure were compared in between different sets of parameters. When $r_0 = 0.6$, the change of $D_0$ does not affect the fluid properties compared to the DPD solution; when $r_0 = 0.8$, by changing $D_0$, the fluid velocity profile of the DPD–Morse fluid deviated from the DPD solution. To maintain the same fluid velocity profile, $\alpha$ was reduced to 0.5. When $r_0 = 0.8$, only $D_0 = 100$ allows the DPD–Morse fluid to maintain the same fluid velocity profile. With $\alpha = 0.5$ and $D_0 = 100$, $r_0$ was further adjusted to increase the system pressure. With $r_0 = 1.4$, the DPD–Morse fluid achieved higher system pressure as compared to the DPD fluid while preserving the fluid velocity. When $r_0$ was further increased to 1.7, the DPD–Morse fluid deviated from the DPD fluid velocity profile.

The final parameters were selected as $\alpha = 0.5$, $D_0 = 100$, $r_0 = 1.4$. The DPD–Morse, DPD, and Morse potentials were plotted which indicates that the contribution of DPD force field cannot be negligible. As $r = 0.2$, the DPD repulsive force contributes to 62.86% of the DPD–Morse force magnitude (Fig. 2).

With this parameter set for DPD–Morse fluid, the fluid flow properties, i.e., velocity, number density, shear stress, pressure, and radial distribution function were demonstrated and compared in between DPD and DPD–Morse fluids (Fig. 4). Furthermore, a compression simulation was conducted where 5% compression was applied along $x$ direction to the original fluid system. Given the same volume change, the isothermal compressibility $\kappa_T$ of the DPD–Morse fluid relative to that of DPD fluid was computed as $\frac{\kappa^{DPD-Morse}}{\kappa^{DPD}} = \frac{(P_2 - P_1)_{DPD}}{(P_2 - P_1)_{DPD-Morse}}$, where $P_1$ was original system pressure, and $P_2$ was pressure of compressed system. The speed of sound was determined by $c = \sqrt{\frac{\kappa_T}{\rho}}$ where $\rho$ is the fluid density [13].

### 2.3. Stenotic microchannel simulations with no-slip boundary condition

A 67% stenotic microchannel was constructed in order to study the compressibility effects of DPD fluid flowing in a stenotic channel through a severe constriction (Fig. 3). The stenosis degree was defined as the ratio between the occluded cross-section area and the full cross-section area. The length $L$, height $H$, and width $W$ of the microchannel was $120 \mu m$, $30 \mu m$, $30 \mu m$, respectively. The microchannel consists of three sections, an upstream section with $L = 44 \mu m$, $H = 30 \mu m$, and $W = 30 \mu m$; a downstream section with same dimensions as the upstream section; and a stenotic section with $L = 32 \mu m$, $H = 10 \mu m$, and $W = 30 \mu m$. The fluid flow was driven along the $x$ direction by a body force $g_x = 2.0$. In our model, we followed [13] to implement no-slip boundary condition on the wall. Briefly, we triangulated the wall element and applied boundary forces on the wall including a repulsive term to mitigate the missing fluid particles beyond the wall boundary, and dissipative and random terms to enforce no-slip condition along wall tangential direction.

The platelet was modeled as a rigid ellipsoid with 444 particles with dimension $4 \times 4 \times 2$ in $\mu m$ [13]. Physical quantities in dimensionless units were further converted into physical units for the interpretation of fluid flow properties, platelet transport dynamics, and the shear stress accumulation (SA) along the platelet trajectory [19]. To visualize fluid number density, velocity and shear stress, the simulation data was spatially averaged over a two-dimensional grid of $dx = 0.5$ and $dy = 0.5$, and temporally over 50,000 timesteps.

To compute SA, the platelet centroid $r(t)$ was identified at a constant time interval, where the starting time point $t_0$ was recorded when the platelet was released into the fluid, and the finished time point $t_f$ was recorded when the platelet passed through the outlet of microchannel. SA was computed as the time integral of a scalar shear stress along the platelet transport trajectory,

$$SA = \int_{t_0}^{t_f} \tau(r(t))dt = \int_{t_0}^{t_f} \tau(x(t), y(t), z(t))dt$$

(7)
Fig. 1. Velocity (left) and pressure (right) distribution of the DPD–Morse fluid under counter-Poiseuille flow.

Fig. 2. The force magnitude derived from Morse + DPD, DPD, and Morse potentials with respect to inter-particle distance r.
where \( t_0 \) and \( t_f \) are the initial and final time points of platelet transport, \( \tau(\mathbf{r}(t)) \) is the scalar shear stress at platelet centroid \( \mathbf{r}(t) \), \( t \in [t_0,t_f] \). The scalar shear stress \( \tau(\mathbf{r}(t)) \) is converted from the stress tensor using the formula [40]:

\[
\tau = \frac{1}{\sqrt{3}} \sqrt{\sigma_{xx} + \sigma_{yy} + \sigma_{zz} - \sigma_{xx}\sigma_{yy} - \sigma_{xx}\sigma_{zz} - \sigma_{yy}\sigma_{zz} + 3(\sigma_{xy}^2 + \sigma_{yz}^2 + \sigma_{zx}^2)}
\]

(8)

Following previous work, the stress tensor \( \tau(\mathbf{r}(t)) \) was computed using spatial–temporal averaged virial stress [19,41,42]. Along the spatial scale, the whole microchannel was discretized into bins in \( xy \)–plane. Each bin has dimension \( 1 \times 1 \times 30 \). The fluid bin was selected which enclosed the platelet centroid \( \mathbf{r}(t) \). Each particle within the bin has a per-particle stress tensor,

\[
\tau_{ab} = -\frac{1}{2} \sum_{n=1}^{N_p} (r_1 F_{1b} + r_2 F_{2b})
\]

(9)

where \( r_1 \), \( r_2 \) and \( F_1 \), \( F_2 \) are the positions and pairwise forces of two interacting fluid particles \( i \) and \( j \). \( a \) and \( b \) take on values \( x \), \( y \) and \( z \). \( N_p \) is the number of neighbors of particle \( i \). \( \tau_{ab} \) is the virial stress with physical unit of stress \( \times \) volume. Along temporal scale, the stress \( \tau_{ab}^t \) for each particle \( i \) is averaged over 2.06 ms. Then the spatial-averaged stress \( \tau_{ab} \) for each bin is computed by averaging the per-particle stress \( \tau_{ab}^t \) for all particles \( i \) within this bin.

2.4. CFD continuum fluid simulation

As a reference case, a computational fluid dynamics (CFD) model was solved and its results were compared to the DPD and DPD–Morse models. As the channel is infinitely wide and there is no influence of the side walls the CFD model was solved as a two-dimensional problem with the fluid assumed as incompressible and Newtonian (\( \rho \) of 1060 kg/m\(^3\), \( \mu \) of 0.00119 Pa.s). The inlet and outlet velocity profiles were based on the inlet velocity profile of the DPD–Morse model and were defined with a parabolic function. Navier–Stokes continuum equations were solved using finite volume method. The domain was discretized using homogeneous–quadratic mesh with cell size of 0.1 \( \mu \)m (100 cells in the narrowest region, 296,000 cells in total). The model was solved in ANSYS Fluent 17.0 with coupled pressure–velocity scheme and second order discretization. The CFD data was plotted on the same post-processing grid as the particle simulations.

2.5. Unit conversion from dimensionless to physical units

The model units are converted from dimensionless to physical units [19]. The reference length \( \sigma_r = \frac{D_p}{D_p^*} \), where \( D_p = 4 \mu \)m and \( D_p^* = 4 \). The reference mass \( m_r = \frac{\rho \sigma_r^3}{\rho^*} \), where the fluid density of blood plasma \( \rho = 1060 \) kg/m\(^3\), and the particle density in the model is \( \rho^* = 3 \). The reference velocity \( v_r = \frac{v}{v^*} \), where \( v = 3.6 \) mm/s corresponds to \( v^* = 0.3 \). The reference time \( t_r = \frac{\sigma_r}{v_r} \).
Fig. 4. Counter-Poiseuille flow of DPD and DPD-Morse fluids. The system dimensions are $30 \times 30 \times 30$, number density $n = 3.0$. A body force $g_y = \pm 2.0$ is applied along the $y$ direction. The system is divided into 60 vertical bins along the $x$ direction with side length of 0.5, and fluid particle velocity, number density, shear stress, and pressure are averaged in each bin for 5000 timesteps after the flow is fully developed (all numbers appear in dimensionless units).
3. Results

We first compared the DPD–Morse fluid to the DPD fluid using counter-Poiseuille flow. A series of fluid physical quantities were investigated, including velocity, number density, shear stress and pressure. We also performed the compression simulation to study the isothermal compressibility and speed of sound of the two types of fluids. This was followed by the fluid simulations through the 67% stenotic microchannel, where the compressibility effects were evaluated for the two fluids by examining the fluid number densities in the system. We also compared the velocity and shear stress profiles in the two flow fields. The results were further verified by comparing the results of particle-based simulations with CFD. Furthermore, we embedded a single platelet model into the fluid domain, to compare the platelet transport behavior, including platelet traversing velocities and traversing period. Finally, we computed the shear stress accumulation along the platelet transport trajectory within one period, and examined the difference between the DPD–Morse and DPD fluids in predicting the shear-induced stress accumulation.

3.1. Fluid flow properties in counter-Poiseuille flow

DPD–Morse fluid is shown to have the same fluid flow properties as DPD fluid under counter-Poiseuille flow condition (Fig. 4): parabolic velocity profiles are achieved and are in good agreement with the analytical solution; stable density fluctuations are observed around system average number density; the fluid shear stresses are mapped closely with the analytical solution. Note that the system pressure of DPD–Morse fluid is higher than that of the DPD fluid as a result of stronger repulsive force in between fluid particles in DPD–Morse fluid. The radial distribution function (RDF) of the DPD–Morse fluid closely resembles that of the DPD fluid.

The compression simulation presents a much smaller isothermal compressibility of the DPD–Morse fluid than that of the DPD fluid with \( \frac{kT_{DPD-Morse}}{kT_{DPD}} \approx 0.33 \) which demonstrates that DPD–Morse fluid is more resistant to compression under the same condition. The speed of sound for the DPD–Morse fluid is higher than that of the DPD fluid, where \( c_{DPD-Morse} = 0.23 \) m/s, and \( c_{DPD} = 0.14 \) m/s. This corresponds to Mach number \( Ma_{DPD-Morse} = 0.03 \) and \( Ma_{DPD} = 0.05 \) in the case of the counter-Poiseuille flow correspondingly. Both fluids have a dynamic viscosity \( \mu = 1.197 \) mPa s and Reynolds number of 0.0482. The DPD–Morse fluid reduces the compressibility effects of conventional DPD fluid, while preserving the viscous fluid characteristics.

We plotted the equation of state for DPD–Morse and DPD fluid models. The DPD–Morse fluid demonstrate a quadratic equation of state \( p = 62.953 \rho^2 - 21.000 \) with \( R^2 = 0.9998 \) (Fig. 5), \( p \) is fluid pressure and \( \rho \) is fluid density.

We computed the Schmidt number \( S_c \) of DPD–Morse fluid models. Our simulation results show that \( S_c \) of DPD–Morse is on the order of \( O(10^3) \), compared to \( O(1) \) in previously published conventional DPD model [29]. The Schmidt number is computed by \( S_c = \mu / (\rho D) \), where \( \mu = 280 \), \( \rho = 3.0 \) and \( D = 0.01 \). \( D \) was computed using velocity autocorrelation function (VACF) \( D = \frac{1}{2} \int_0^\infty \langle \mathbf{v}_i(t) \cdot \mathbf{v}_i(0) \rangle \, dt \) [27,43].

3.2. Fluid flow properties in the 67% stenotic microchannel flow

Fluid simulations through the 67% stenotic microchannel were conducted with the two fluid models. The no-slip boundary condition for the DPD–Morse fluid was achieved by creating fictitious fluid particles which interact with real fluid particles near boundaries through DPD forces [13]. No-slip condition was achieved for the fluid particles in the near wall vicinity, but the fluid density was increased close to 1500 kg/m³ (Fig. 6).

We computed the entrance length following the work of [44], where the entrance length is defined as \( L_e = 0.05 \text{Re} D_h \). In our simulation, \( \text{Re} = 0.0482 \), and \( D_h = 30 \). This gives us \( L_e = 0.0723 \). Our channel length \( L = 120 \). This indicates that the fluid flow was fully developed in the microchannel.

The system number density was compared between the DPD–Morse and the DPD fluids (Fig. 7). In the DPD–Morse fluid, a relatively uniform density distribution was observed. In the DPD fluid, a significant difference in fluid density was observed between the upstream and downstream sections of microchannel. The fluid particles accumulated dramatically at
Fig. 6. No-slip boundary condition for the DPD–Morse fluid in a straight channel. Fluid velocities and number densities are shown at five time points: 82.62, 165.24, 247.86, 330.48 and 413.1 μs. The velocity profiles are compared to the analytical solution (blue solid line). The blood plasma density is 1060 kg/m$^3$.

Fig. 7. Fluid density comparison of the DPD and the DPD–Morse fluids in a 67% stenotic microchannel. (a) and (b) show an $xy$ cross-section of the fluid density of the DPD–Morse and the DPD fluids, correspondingly. (c) shows the observations of fluid density gradient along the flow direction at $y=5.5$, where the blue line represents the DPD fluid, and the red line represents the DPD–Morse fluid. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
the upstream. The non-uniform density distribution of the DPD fluid leads to less accurate prediction of fluid quantities, including velocity and shear stress. Fig. 8 shows the velocity field of the stenotic microchannel, simulated by CFD, DPD–Morse, and DPD models. The CFD velocity field was used as a benchmark result. The DPD–Morse fluid resembles the CFD solution. It has a relative uniform velocity distribution in the stenotic section, while the DPD fluid has a large discrepancy in velocity field between upstream and downstream sections. The highest velocity magnitude was found at the exit of stenotic section in the DPD fluid. This is caused by the dramatic decrease of the fluid number density in the downstream section, which provides smaller resistance to the fluid particles exiting the stenosis. The change of fluid density in the microchannel leads to variations in the fluid viscosity within the flow field (Fig. 9). Along the platelet flowing trajectory, the fluid viscosity of the DPD–Morse fluid is more uniform with only gradual changes compared with the more abrupt changes in the DPD fluid, and is closer to the blood plasma viscosity of 1.197 mPa.s. The fluid shear stress distribution was shown in Fig. 10. Symmetric fluid shear stress was observed in the DPD–Morse fluid domain, and is close to the CFD solution. The fluid shear stress was deteriorated in the DPD fluid domain near the exit of the stenotic section.

3.3. Platelet transport dynamics in 67% stenotic microchannel flow

The platelet transport properties in the DPD and the DPD–Morse fluids were compared by tracking the trajectory of a single platelet flowing through the stenotic microchannel (Figs. 11 and 12). The $v_x$ velocity component is shown in Fig. 11(a). The platelet trajectory through the microchannel is shown in Fig. 11(b). In the upstream domain, the platelet flowing in the DPD fluid has a slightly higher $v_x$. When the platelet approached the stenotic section, it started to accelerate with a stronger acceleration in the DPD fluid. The platelet continued to accelerate through the stenotic section, where the DPD fluid reached a maximum $v_x$ at the exit of the stenotic section which twice that achieved with the DPD–Morse fluid.
after which the platelet began to slow down. The $v_y$ component of platelet velocity in both types of fluids is close to zero at upstream, stenotic, and downstream sections (Fig. 11(c)). It becomes evident when platelets approached and exited the stenotic section.

The difference in the platelet transport period through the stenotic microchannel is demonstrated in Fig. 12. The red platelet was immersed in the DPD–Morse fluid, and the yellow one in the DPD fluid. The two platelets are initially positioned at same location at 0 ms (two platelets are overlapped in the first subplot of the figure). The platelet in the DPD fluid moved faster than in the DPD–Morse fluid, and the discrepancy appears gradually as the platelet traveled along the microchannel.

Fig. 9. Fluid viscosity change along a platelet flow trajectory in reference to blood plasma viscosity of 1.197 mPas (the blue and red lines represent the DPD and DPD–Morse fluids, respectively). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 10. Shear stress comparison of the CFD, DPD–Morse and DPD fluids in the 67% stenotic microchannel. (a)-(c) represent xy cross-section of the shear stress of the three fluid models. (c) shows the shear stress change along the flow direction at $y = 5.5$. (green (CFD), red (DPD–Morse), and blue (DPD)). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
At 18 ms, it already passed the outlet and starts a new period for the DPD fluid, whereas the platelet in the DPD–Morse fluid only exited from the stenotic section at that time instant. The platelet transport results are consistent with the significant density and velocity difference between the DPD–Morse and the DPD fluids shown in Figs. 7 and 8.

3.4. Shear stress accumulation along platelet flowing trajectory

The platelet in the DPD fluid took 16.5 ms from release to existing the outlet boundary, and about 30 ms in the DPD–Morse fluid. The resulting stress accumulation was computed and is presented in Fig. 13(b). Before entering the stenotic section, the stress accumulation was close in between the two types of fluids. As the platelets approached the entrance of stenosis, both fluids exhibited a typical sudden increase in the stress accumulation level. Once the platelet entered the stenotic section, the stress accumulation rate began to subside. It was also observed that the stress accumulation in the DPD–Morse fluid exceeded that of the DPD fluid. In the downstream section, the stress accumulation rate became similar between the two types of fluids.

4. Discussion

DPD has been applied successfully in modeling red blood cells and platelets immersed in viscous blood plasma through 3D complex geometries such as human vasculatures and prosthetic cardiovascular devices [9,13,17,19]. It demonstrates
Fig. 12. Snapshots of platelet passing through the stenotic microchannel at different time points. The red platelet is immersed in the DPD–Morse fluid, and the yellow one in the DPD fluid. At 0 ms (the first subplot), the red and yellow platelets overlap. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

The hallmarks of viscous fluid flow characteristics with the imposition of no-slip boundary conditions at the wall [11,13]. However, the compressibility effects limit the application of DPD to straight or mild stenotic microchannels with small fluid compression. The compressibility effects become significant as the degree of stenosis increases, and can lead to a fluid density gradient in the flow direction [22,23]. This prevents DPD methods from correct description of viscous fluid flow in severe stenosis and accurate prediction of platelet dynamics and activation potential in such scenario [45,46].

The compressibility effects of DPD fluid result from the soft interaction potential employed in between fluid particles [12,24]. The soft potential cannot avoid the particle interpenetration and can easily lead to local fluid particle accumulation when a significant constriction such as a stenosis exists. In the current work, the compressibility effects of DPD fluid model are addressed by introducing Morse potential into the DPD force field. This significantly reduces the compressibility effects while preserving the viscous fluid properties. The DPD–Morse fluid exhibits smaller isothermal compressibility and a higher speed of sound resulting in a lower Mach number-indicating that the compressibility effects are less profound than that of conventional DPD fluid, as demonstrated in this work in a severe stenosis channel geometry.

The reduction of compressibility effects in DPD–Morse fluid was confirmed in simulations of a 67% stenotic microchannel flow where large fluid compression is produced. Driven by the same pressure gradient, a discrepancy in the flow field is observed between the two fluid models. The DPD–Morse fluid exhibits more uniform fluid density distribution than the DPD fluid, attributed to the improved conservative force term that favorably preserves the fluid incompressibility. Here we used $\rho = 3.0$ following the work of [13,19,29]. Higher number density performs better suited for the case of a stenosis [22]. A higher number density would also increase the computational cost. The density fluctuations at the walls were discussed in [11,13]. Briefly, this issue can be modulated by modifying forces imposed at the boundary. Also, by applying finer triangulation over large curvature, the boundary force scheme can be implemented more accurately.
Fig. 13. (a) Scalar shear stress along the platelet flow trajectory in the DPD and DPD–Morse fluids. (b) Shear stress accumulation (SA) along the platelet flow trajectory.

Our work provided an alternative solution to address the compressibility issue that appears to be more cost-effective and is applicable to many other DPD flow simulations. Compared to the work of Pan et al. and Mai-Duy et al., our approach improved the incompressibility of DPD fluid with typical DPD parameter sets found in previously published works to model blood flow [13,19]. Compared to the work of Yazdani et al., our model achieved reasonable incompressibility with constant body force. The total force applied on fluid particles is composed of inter-particle force $F_{\text{particle-particle}}$ and body force $F_{\text{body}}$. Yazdani et al. [22] proposed a method to improve DPD performance by using the pressure gradient of the Navier–Stokes (N–S) flow as the tailored driving body force. Here, $F_{\text{body}}$ is modified. In comparison, our work improved the DPD incompressibility by modifying the inter-particle force. Here, $F_{\text{particle-particle}}$ is modified. We employed a constant body force to drive the fluid flow and achieved improved incompressibility for DPD fluid. Our simulation results may be further improved by incorporating a tailored body force of [22]. However, the tailored body force approach may have certain limitations. It may have restriction applying to unsteady flow, where the finite compressibility effects of DPD fluid will set an upper limit for the frequency of the transient dynamics. The unsteady flows also require to solve N–S equation at every timestep to derive the tailored body force. This would increase the computational cost. In addition, $F_{\text{particle-particle}}$ is unchanged in [22]. However, the internal pressure of a fluid system with reduced compressibility should increase. Our approach is capable of reflecting this property.

When using particle dynamics approaches to model blood flow under severe stenosis, special care needs to be taken for the fluid viscosity. In DPD approach, the fluid viscosity is controlled by the friction factor of the DPD force field [47]. A multi-viscosity system can be modeled with DPD by assigning a different friction factor for each fluid. Given the same friction factor, the fluid viscosity can be influenced by the fluid density [48]. For the DPD fluid without compression, the density fluctuates around a constant value. Under severe stenosis as density gradient appears in the DPD fluid, the difference in the fluid viscosity at upstream and downstream becomes apparent. By using the DPD–Morse fluid this problem is mitigated, with the spatial change in fluid viscosity minimized.

The comparison with CFD results indicates that the compressibility effects in the DPD model under severe stenosis dramatically affect the fluid dynamic properties, including velocity and shear stress distribution. In contrast, the DPD–Morse fluid compared favorably with CFD results.

Shear stress accumulation has been shown as an important indicator of shear-induced platelet activation, in which both the shear stress magnitude and the exposure time to it play critical roles [2,40,49]. While a spatial shear stress gradient appeared in both types of fluid models in the stenotic region this gradient in the DPD fluid produced a lower shear stress level at the stenosis exit, resulting in an underestimation of the stress accumulation that translates into underestimation of the platelets activation potential. The capability of the DPD fluid to cope with a severe constriction is also impaired by its significant effect on the platelet transport period across the stenotic channel. The stronger compressibility effects induce a density gradient along the flow direction that accelerates the platelet migration. Considering the combined effect of both the shear stress level and the exposure time (which is determined by the transport time), the DPD fluid model underestimates the shear stress accumulation as compared to the DPD–Morse fluid. As the latter is very close to the CFD, it is clear that
the DPD–Morse fluid model represents much better the physics of such flow field and the quantities derived from it which are of a significant clinical relevance – such as the stress accumulation.

In future work, the proposed DPD–Morse fluid model will be incorporated into a multiscale scheme utilizing our CGMD platelet model that incorporates the platelet subcellular structure to investigate the mechanotransduction process of shear-induced platelet activation [19,50,51]. Platelet activation and aggregation may be promoted when platelets pass through a stenosis or if there is a thrombus on the surface. DPD offers description simulation approach that can bridge the large gap in scales between macro to mesoscopic scales of platelet transport and its potential activation in a heterogeneous blood flow environment. However, the accuracy of DPD in describing stenotic fluid flow and associated platelet transport deteriorates because of the significant compressible effects it generates. Our DPD–Morse fluid model inherits the capability of DPD to simulate complex fluids at mesoscopic scale, and is superior to DPD model in describing viscous fluid phenomena through severe stenotic microchannel by better preserving the fluid incompressibility. Considering the complex constricted geometries such as of a stenosis in the human vasculature or the hinges regions in mechanical heart valves for example, our DPD–Morse model offers a more physically accurate description of the fluid mechanics under such flow conditions relevant to the human vasculature and blood recirculating cardiovascular devices.

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