# A Parallel Computing Platform for Simulating Platelet Aggregation at Multiple Scales

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## ABSTRACT

Modeling force fields to mimic the complex process of platelet aggregation is a challenge. This paper presents a two platelet multiple scale model for linear shear flow with a modified force field constructed by combining Morse and Hookes force field between platelet membranes. The model uses coarse grained molecular dynamics for describing the internal constituents of the platelets and dissipative particle dynamics for the macroscopic blood flow .The modified force field is parametrized for reproducing platelet collision characteristic such as contact frequency, contact area, contact time and binding efficiency under high shear rate (8000 $s^{-}1$) during the process of platelet aggregation. Predictions for contact frequency, contact area and contact time made using this multiple scale model compare with experimental results. We further investigate platelet aggregation properties using the deformable platelet model and establish the role of membrane stiffness on platelet aggregation. The model demonstrates that such modified force fields can be used to mimic platelet aggregation.

## ROLE OF RECEPTORS IN PLATELET AGGREGATION

There are two types of receptors that play major role in platelet aggregation and adhesion.

- These are GPIb and GPIIb/IIIa. While GPIb is major receptor for platelet adhesion and GPIIb/IIIa is major receptor for platelet aggregation, the process of aggregation is much more complex.
- Aggregation can occurs between activated platelets (with filopodia) as well as between unactivated platelets (without filopodia).
- Receptor involved for activated platelet is GPIIb/IIIa and for unactivated platelet is GPIb.
- Receptors are associated to ligands during the process of aggregation and adhesion.
- Under high shear stress vWF forms a bridge with GPIb (GPIb-vWF-GPIb ) for platelet aggregation.

## MODEL PROPERTIES

We construct a microchannel to study interaction of two platelets in force driven Posieuille flow. The fluid flow is force driven Poiseuille flow in x-direction. Periodic boundary conditions are applied in x- and z-directions. No slip boundary conditions are applied on the top and bottom walls (y-direction). Shear rate considered is $8000s^{1}$.Each platelet has 2000-4000 copies of $\alpha_2\beta_1$ receptors (Platelets, Michelson 2013). The platelet receptor $\alpha_2\beta_1$ and $\alpha_{IIb}\beta_3$ are essential for platelet aggregation. We represent $\alpha_2\beta_1$(GPIb) with particles of the bilayer membrane since we are studying aggregation in unactivated platelets.

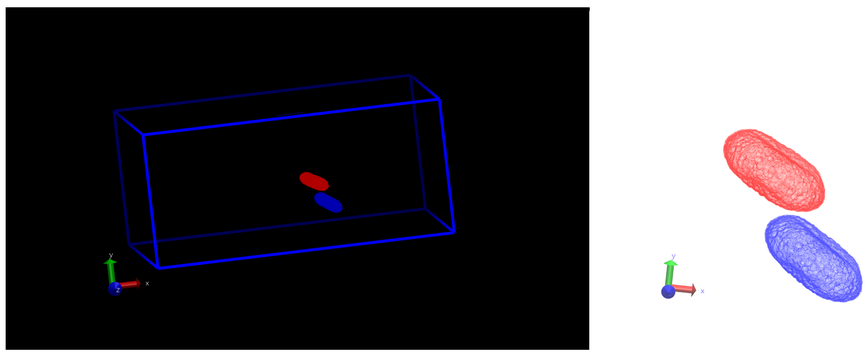


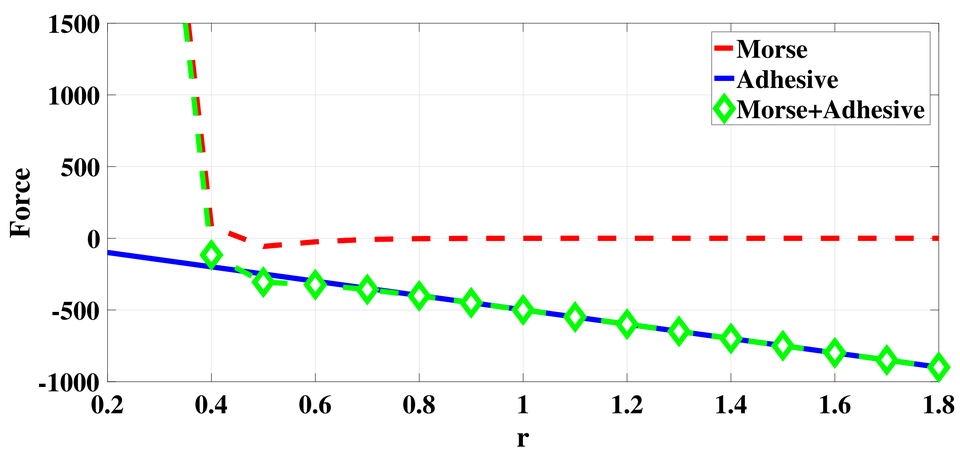
Figure: Microchannel and Platelets

## FORCE FIELDS FOR PLATELET AGGREGATION

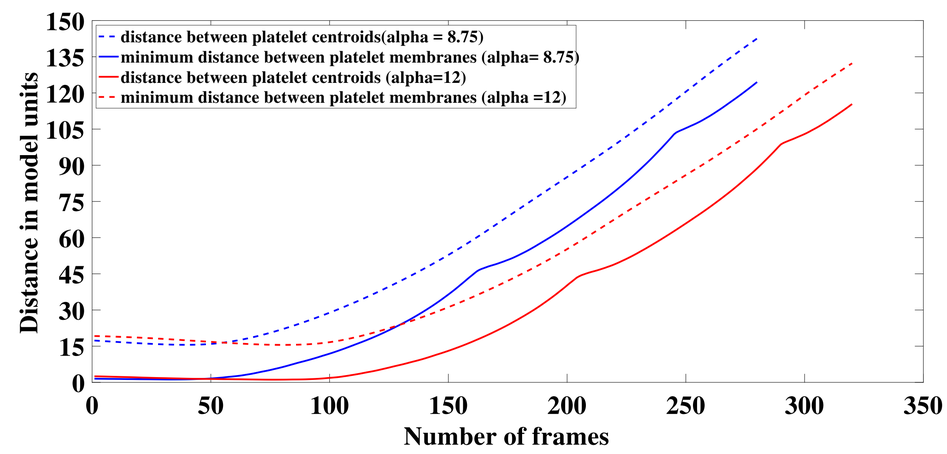
Force field for platelet aggregation is derived by combining force fields from Morse potential and Hooke's force field

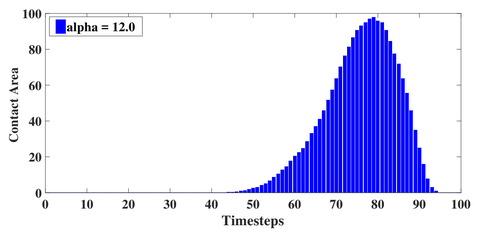
$$\mathbf{F}_{ij}^{rep} = D_0(e^{-2\alpha(r_{ij}-r_0)} - 2e^{-\alpha(r_{ij}-r_0)})\mathbf{e}_{ij} + f^A\left(1 - \frac{r_{ij}}{d_c}\right)\mathbf{e}_{ij}$$

where $D_0$ is the is the well depth $\alpha$ is the scaling factor and $r_0$ is the zero force length $\mathbf{r}_{ij} = \mathbf{r}_i - \mathbf{r}_j$, $r_{ij} = \|\mathbf{r}_{ij}\|$, $\mathbf{e}_{ij} = \frac{\mathbf{r}_{ij}}{\|r_{ij}\|}$, $f^A$ is the force strength coefficient and $d_C$ is the force relaxation distance which is twice the physical radius of the platelets.




## PARAMETER SENSITIVITY RESULTS



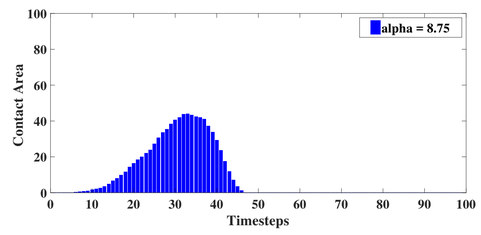
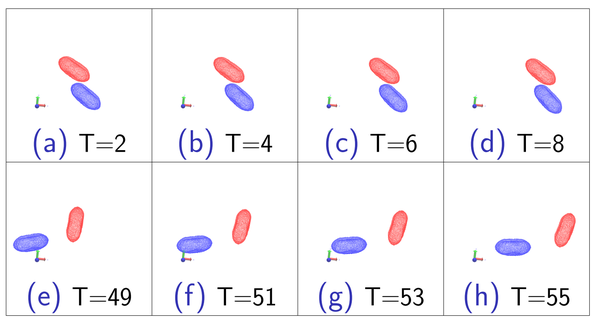




Table: Contact Area

| Alpha | 8.75 | 12.0 |
|---|---|---|
| Contact Area($\mu s$) | 11.96 | 14.04 |

## SIMULATION RESULTS

All simulations were performed with NVE ensemble, using the modified version of LAMMPS (Large-scale of Atomic/Molecular Massively Parallel Simulator) code (30-JUL-2016 version).



(a) T=2 (b) T=4 (c) T=6 (d) T=8
(e) T=49 (f) T=51 (g) T=53 (h) T=55

Figure: Trajectory of Platelets in Flow

## VERIFICATION

- This platelet aggregation model has rigid platelets with repulsive and adhesive force fields between the platelet membranes. We determine collision characteristics and parameter sensitivity to these collision characterstics. Verification with published results.
- In second step we incorporate GPIb-vWF-GPIb in the model by introducing a vWF molecule and calculate the bond formation rate (binding efficiency from step 1 will be used). Verification with experimental results.

For experimental verification a single platelet will be attached to the vessel wall in model. Flowing platelets will be attracted to it. This can be very easily verified through experiments performed in laboratory.

## ACKNOWLEDGEMENTS

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