The behaviour of von Willebrand factor in blood flow

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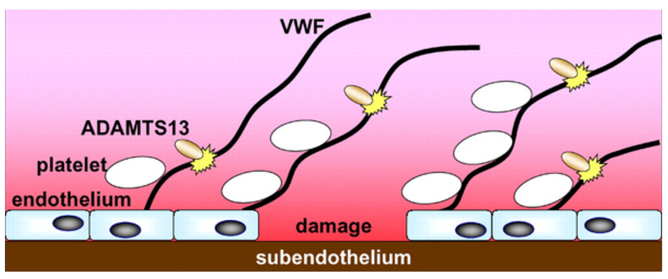
Introduction

The von Willebrand factor (VWF), a large multimeric protein, is essential in haemostasis. Under normal conditions, VWF is present in blood as a globular polymer. In case of an injury, VWF is able to unwrap and bind to the vessel wall and to flowing platelets. Thus, platelets are significantly slowed down and can adhere to the wall and close the lesion. Nevertheless, it is still not clear how the unwrapping of the VWF is triggered [1]. Therefore, the behaviour of VWF in simple shear flow is investigated under different conditions. Additionally, we examine how the migration of VWF to a wall (margination) and the stretching depends on shear rate and volume fraction of red blood cells (RBCs) and compare it to recent results of platelet margination [2].



[3]

Methods

Simulation method

Dissipative Particle Dynamics (DPD) [4]

- Mesoscopic particle-based method
- Full hydrodynamics
- Particles move according to Newton's second law: $\mathbf{F} = m\dot{\mathbf{v}}$, $\dot{\mathbf{r}} = \mathbf{v}$
- Pairwise forces:

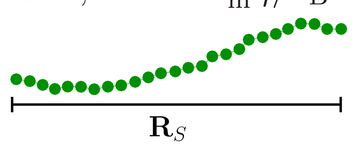
$$\mathbf{F}_i = \sum_{j \neq i} \left(\mathbf{F}_{ij}^{\text{conservative}} + \mathbf{F}_{ij}^{\text{dissipative}} + \mathbf{F}_{ij}^{\text{random}} \right)$$

Particle models

Von Willebrand factor (VWF) [5]
Bead-spring model:

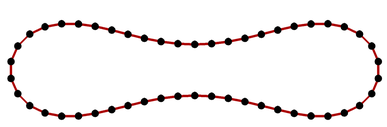
$$\beta U = \kappa \sum_{i=1}^{N-1} (r_{i+1,i} - 2a)^2 + \epsilon \sum_{ij} \left(\left(\frac{2a}{r_{i,j}} \right)^{12} - 2 \left(\frac{2a}{r_{i,j}} \right)^{6} \right) \text{ for } r_{i,j} \leq r_{\text{c}}$$

r_{c}: cut-off radius; $\tau = a_{\text{m}}^2 \eta / k_{\text{B}} T$: time scale



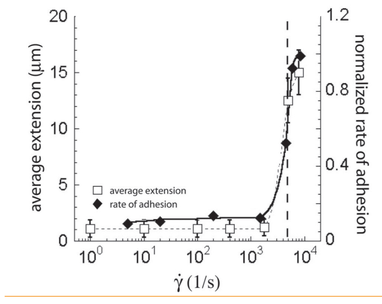
Red blood cell (RBC) [6]
Closed bead-spring model:

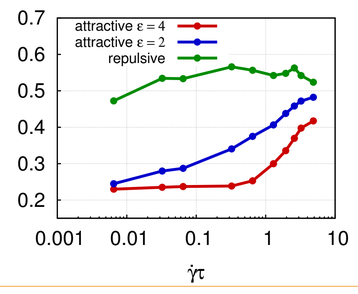
- Vertices connected by springs
- Area conservation constraint
- Bending constraint
- Lennard-Jones repulsion between vertices
- Diameter: $\text{D}_\text{R} = 8\,\mu\text{m}$, height: $\text{h}_\text{R} = 2\,\mu\text{m}$



Simple shear flow

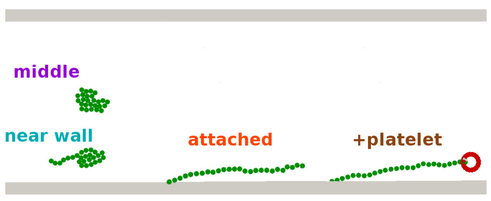
Comparison of experiments and simulations

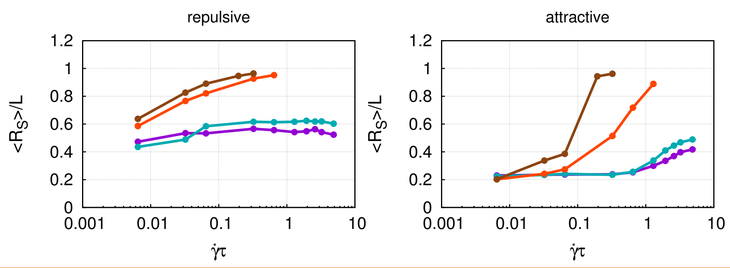




- Polymer in shear flow: periodic stretch-tumble-collapse transition
- Attractive polymer ($r_\text{c} > 2a$) → VWF [5]: stretches for shear rates $\dot{\gamma} > \dot{\gamma}_\text{critical}$
- Repulsive polymer ($r_\text{c} = 2a$): extension is not very sensitive to shear rate

Adhesion to the wall



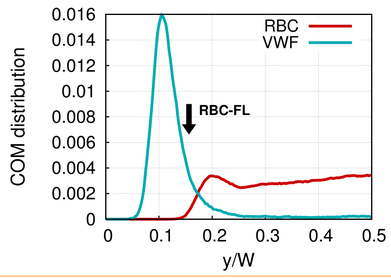


Adhesion reduces critical shear rate by one order of magnitude.

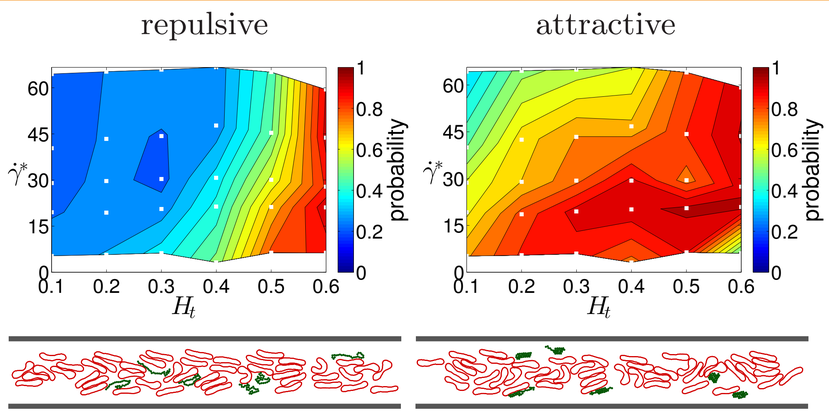
Blood flow

Margination

Center-of-mass (COM) distribution P_COM:



- **Hematocrit $\mathbf{H}_t$**: volume fraction of RBCs
- **Shear rate:** $\dot{\gamma}^* = \bar{\dot{\gamma}} \tau_\text{R}$ with:
  - $\bar{\dot{\gamma}}$ average shear rate
  - τ_R RBC relaxation time
- Margination probability: $p_\delta = 2 \int_0^\delta P_\text{COM}(y) dy$
- $\delta = \Delta_{\text{RBC-FL}}$ RBC-free layer thickness



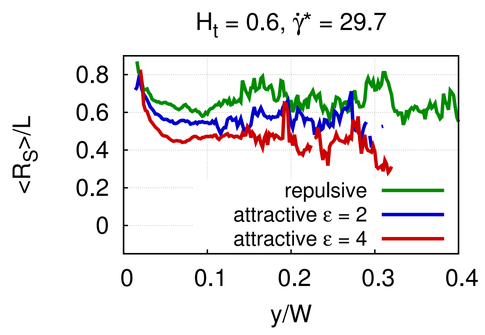
- Attractive polymer is better marginated than repulsive one.
- Margination of attractive polymer depends strongly on shear rate.

Reasons:

- Strong lift force on flexible polymer
- Stretched polymer fits better between RBCs

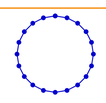
Stretching

Average extension $\langle R_S \rangle$:

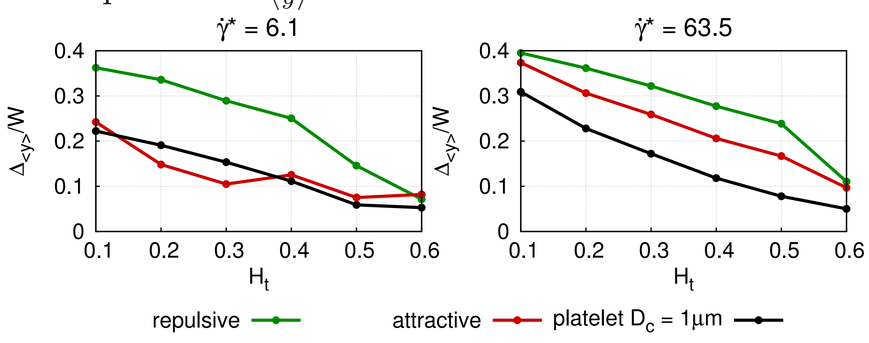


- Bulk: attractive polymer is least extended
- Wall region: similar extensions

Comparison to carriers



Mean position $\Delta_{\langle y \rangle}$:



- Low $\dot{\gamma}^*$: attractive polymer and carrier have similar mean position; repulsive polymer is further away from wall
- High $\dot{\gamma}^*$: also attractive polymer is further away from wall

Summary and Outlook

S: Bead-spring chain with attractive Lennard-Jones interactions is a good VWF model, because stretching in shear flow starts after reaching a critical shear rate.
S: Adhesion of VWF with one end to the wall reduces critical shear rate for stretching.
S: Attractive interactions lead to good margination.
S: Attractive polymer is coiled in the bulk and stretched close to the wall.
S: Polymers marginate worse than rigid carriers.
O: 3D simulations with SDPD [7]
O: Stretching of attached polymer in blood

References

[1] A. J. Reininger, Haemophilia **14**, 11 (2008)
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Acknowledgments

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