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Platelet aggregation in complex vessel geometries

An in silico study on cellular blood flow mechanics

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Publication date

2024

[Link to publication](#)

Citation for published version (APA):

Spieker, C. J. (2024). *Platelet aggregation in complex vessel geometries: An in silico study on cellular blood flow mechanics*. [Thesis, fully internal, Universiteit van Amsterdam].

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Appendix A

Curved Channel

This appendix contains supplementary material for Chapter 2. Figure A.1 shows the flow profile of a finite element method-based continuum fluid simulation to bridge the scale gap between cellular simulations and microfluidic experiments in the chapter. The results reveal qualitative similarity to the cellular simulations (see Fig. 2.6). Figure A.2 displays preliminary results of anti-GPIIb α blocking agent experiments using the ALMA12 Fab fragment and a control fragment. The results seem to confirm the dependence of increased aggregate sites discovered in Chapter 2 on von Willebrand factor (VWF)-mediated platelet adhesion and aggregation. However, for sufficient fidelity the findings have to be substantiated with additional experiments in the future.

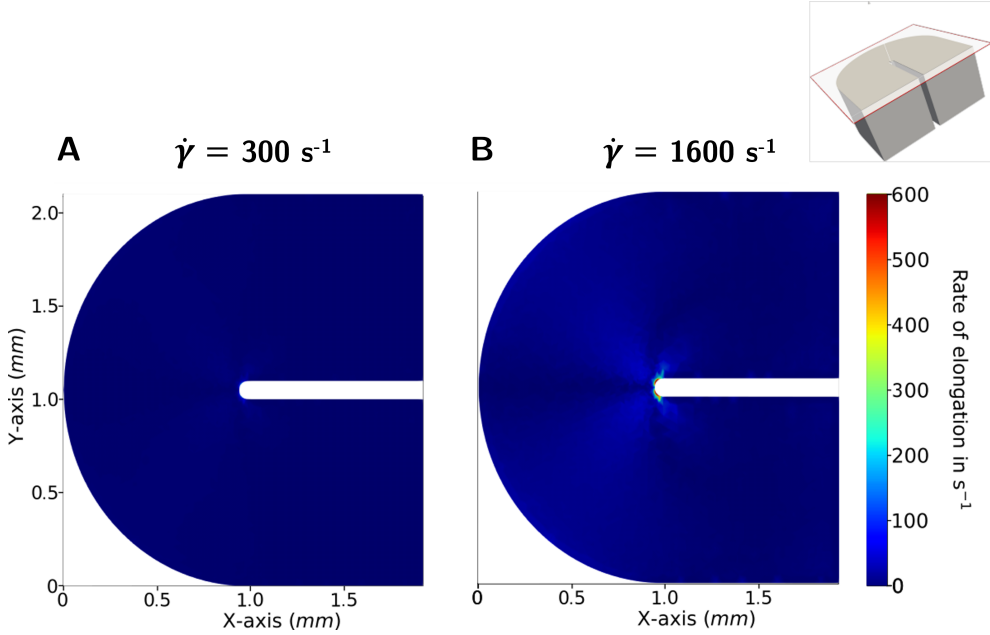


Figure A.1: **Elongational flow magnitude across 1 mm diameter U-channel in continuum simulation.** 3D continuum simulation using the finite element method software FreeFEM (version 4.8, Sorbonne University, Paris, France) resembling a parallel plate flow chamber with Newtonian fluid and a dynamic viscosity $\nu = 3.5 \text{ mPa}\cdot\text{s}$ across a U-channel with 1 mm channel diameter and 100 μm inner arc diameter. Boundary conditions are the same as in the cellular (HemoCell) simulations. The magnitude of the diagonal elements of the rate of strain tensor in flow dimensions produces the 2D elongation profile of the (A): 300 s^{-1} and (B): 1600 s^{-1} initial WSR case. The rate of elongation reaches peak values of $\dot{\epsilon} = 134 \text{ s}^{-1}$ in the $\dot{\gamma} = 300 \text{ s}^{-1}$ case and $\dot{\epsilon} = 715 \text{ s}^{-1}$ in the $\dot{\gamma} = 1600 \text{ s}^{-1}$ case. To allow for better comparison to the results in Fig. 2.6, the same scale is used. The plane is situated 1 μm below the top boundary of the geometry in Z-direction, as depicted in the top right inset panel.

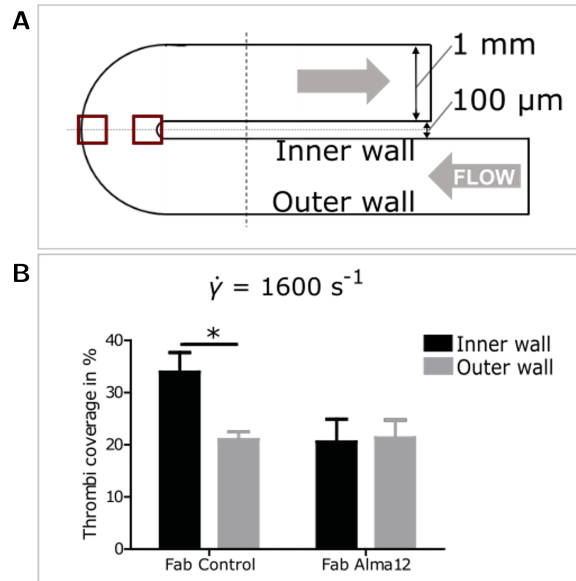


Figure A.2: **Impact of Fab ALMA12 preincubation on platelet aggregation to collagen in curved flow chamber.** Hirudinized human whole blood is preincubated with fragment ALMA12 and subsequently perfused through channels of a microfluidic device coated with a solution of type I fibrillar collagen (200 $\mu\text{g}/\text{mL}$). (A) Schematic and dimensions of the microfluidic “U-shaped” channel. The squares in red indicate the regions of interest observed by video-microscopy. (B) The bar graph represents the quantified surface coverage of platelet aggregates obtained after 4 minutes of perfusion at $\dot{\gamma} = 1600 \text{ s}^{-1}$ with ALMA12 and control fragment. The bars indicate the mean \pm SEM thrombi coverage in the 2 highlighted regions of 5 separate experiments performed with different blood donors.