Fully-Implicit Finite-Volume Methods for Clot Formation Modelling

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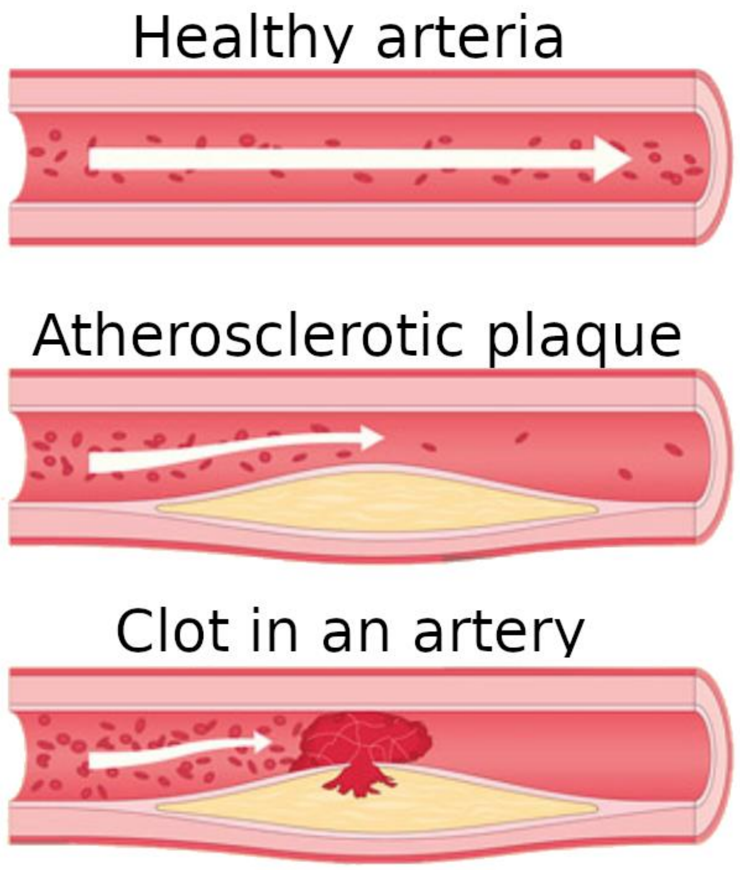
BIOMATH, November 2, 2021

Problem

actuality and complexity

Problem:

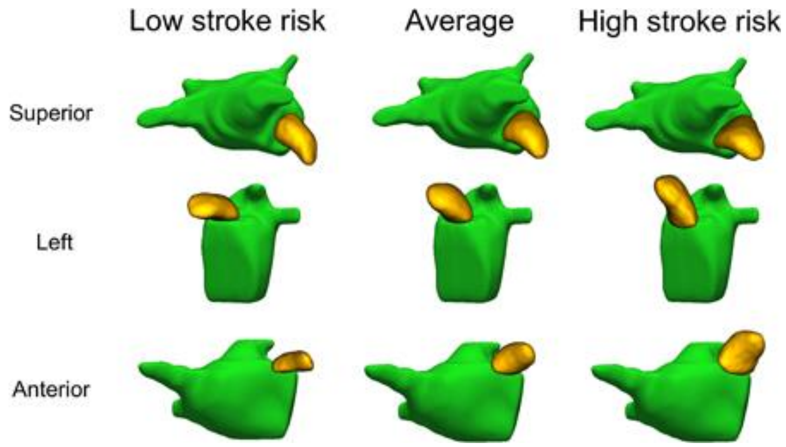
- Construction of **three-dimensional** model of blood flow and coagulation, clot formation after damage of blood vessel

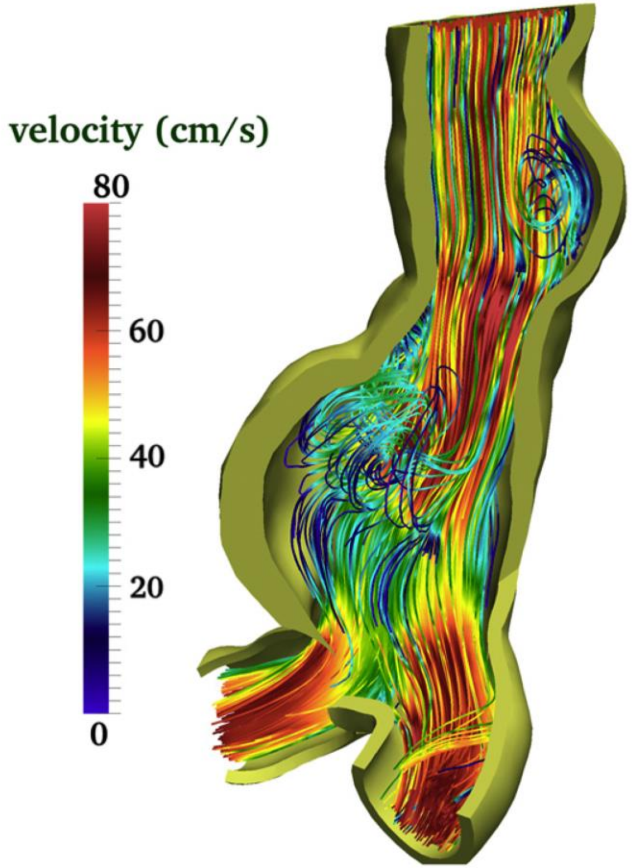


Clot formulation
(illustration from internet)

What for?

- **Three-dimensional** model is needed for decision making in case of complex patient-oriented geometry of blood vessel or arteria.

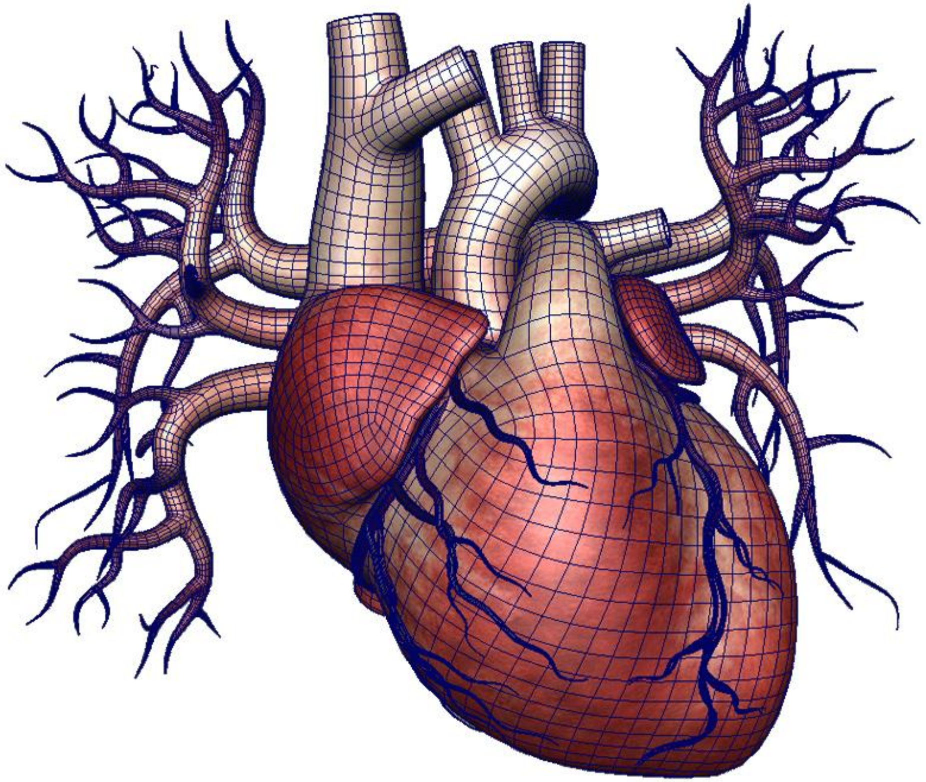




Modeling of aneurysm (from Quarteroni)

What for?

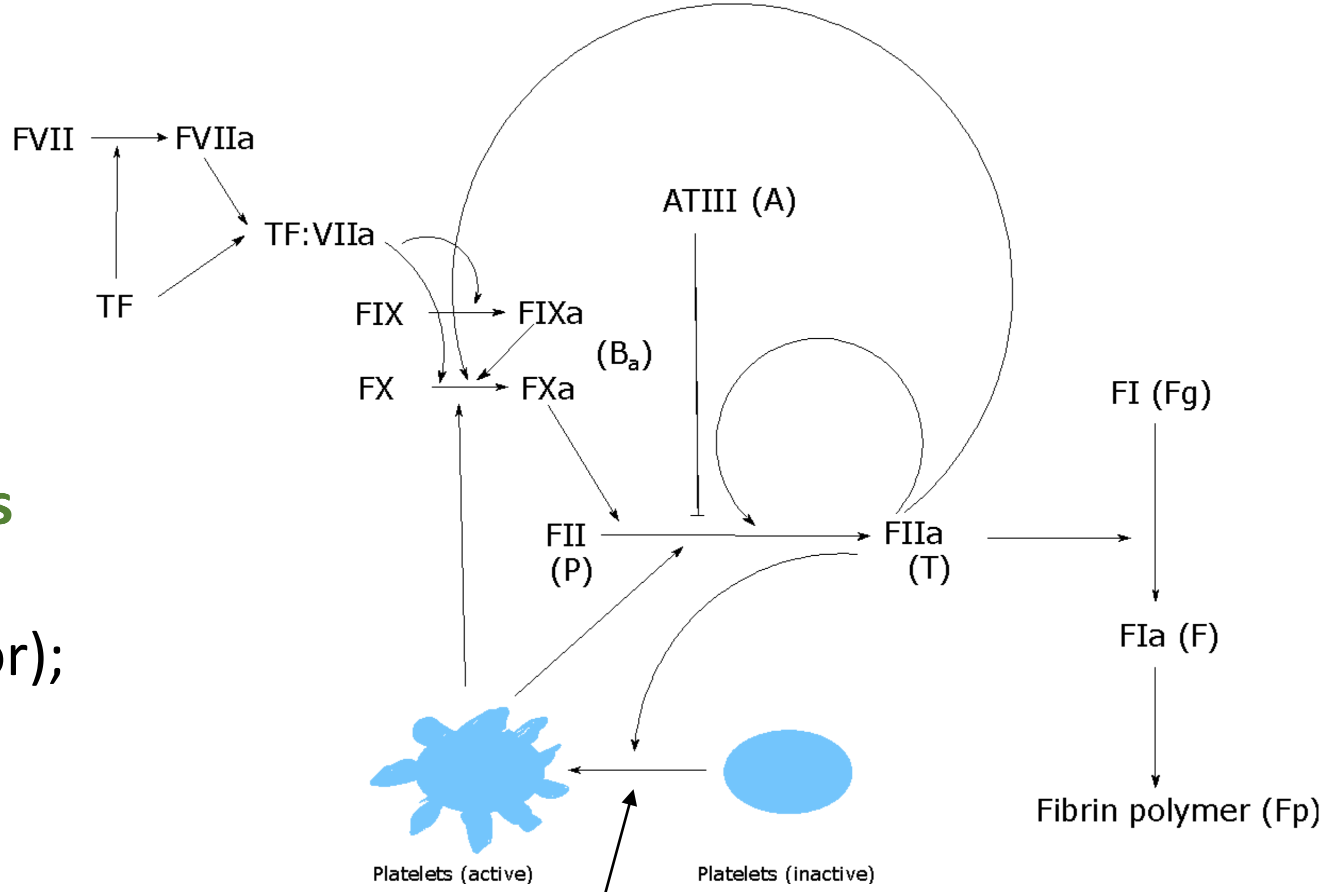
- Diseases of the heart and blood vessels is the **primary** cause o death
  - thromboembolic complications
- **Three-dimensional** model allows to assess the risk of
  - vessel occlusion
  - myocardial infarction



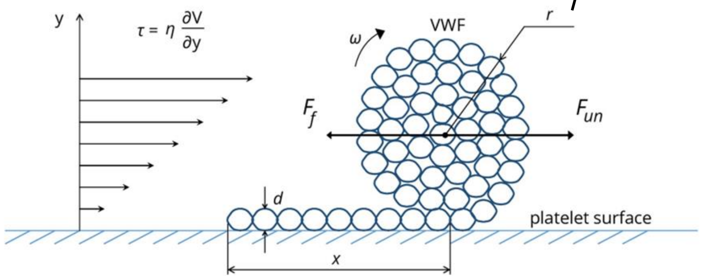
Heart model

Complexity

- Model coupling:
  - **Hemodynamics** model with account for fibrin-polymer permeability .
  - Model of **biochemical reactions** for blood plasma coagulation:
    - Due to damage (tissue factor);
    - Due to shear (vWF factor).
  - Model of **platelets.**
- **Reaction cascade** and model fo **platelets** are **stiff**: very small time step.
- **Fully implicit** model.



Reaction cascade (simplified)



von Willebrand factor (from Guria)

Assumptions

- Blood is considered as an **incompressible Newton's** fluid: no account for **complex nonlinear rheology** of blood
- Blood vessels/arteria are **rigid**: no account for **wall motion**
- Fibrin-polymer is **immoble**: no account for clot **detachment**

Complete system

- Navier-Stokes system:

$$\frac{\partial \rho \boldsymbol{u}}{\partial t} + \mathrm{div}\left(\rho \boldsymbol{u}\boldsymbol{u}^T - \boldsymbol{\tau} + p\mathbb{I}\right) = -\frac{\mu}{K_f}\boldsymbol{u},$$

$$\mathrm{div}(\rho \boldsymbol{u}) = 0,$$

$$\boldsymbol{\tau} = 2\mu\boldsymbol{\epsilon}, \qquad \boldsymbol{\epsilon} = \frac{\mathbf{1}}{\mathbf{2}}\left(\boldsymbol{u}\nabla^T + \nabla\boldsymbol{u}^{\mathrm{T}}\right), \qquad \dot{\gamma} = ||\boldsymbol{\epsilon}||_{\boldsymbol{F}},$$

- Prothrombin (II): $\frac{\partial P}{\partial t} + \mathrm{div}(P\boldsymbol{u} - D\nabla P) = -(k_1\phi_c + k_2B_a + t(T))P,$
- Thrombin (IIa): $\frac{\partial T}{\partial t} + \mathrm{div}(T\boldsymbol{u} - D\nabla T) = (k_1\phi_c + k_2B_a + t(T))P - k_6 g(A,T),$
- Clot factors (IXa, Xa): $\frac{\partial B_a}{\partial t} + \mathrm{div}(B_a\boldsymbol{u} - D\nabla B_a) = (k_7\phi_c + k_8T)(B_0 - B_a) - k_9AB_a,$
- Antithrombin (ATIII): $\frac{\partial A}{\partial t} + \mathrm{div}(A\boldsymbol{u} - D\nabla A) = -k_6 g(A,T) - k_9AB_a,$
- Fibrinogen (I): $\frac{\partial F_g}{\partial t} + \mathrm{div}\left(F_g\boldsymbol{u} - D\nabla F_g\right) = -\frac{k_{10}TF_g}{K_{10}+F_g},$

To be continued…

Complete system

- Fibrin (Ia): $\frac{\partial F}{\partial t} + \mathrm{div}(F\boldsymbol{u} - D\nabla F) = \frac{k_{10} T F_g}{K_{10} + F_g} - k_{11} F,$
- Fibrin-polymer: $\frac{\partial F_p}{\partial t} = k_{11} F,$
- Inactivated platelets: $\frac{\partial \phi_f}{\partial t} + \mathrm{div}\left(k(\phi_c, \phi_f)(\phi_f \boldsymbol{u} - D_{\mathrm{p}} \nabla \phi_f)\right) = (k_{12} T - k_{13}\phi_c - K\gamma^n)\phi_f,$
- Activated platelets: $\frac{\partial \phi_c}{\partial t} + \mathrm{div}\left(k(\phi_c, \phi_f)(\phi_c \boldsymbol{u} - D_{\mathrm{p}} \nabla \phi_c)\right) = -(k_{12} T - k_{13}\phi_c - K\gamma^n)\phi_f,$
- Platelets mobility: $k(\phi_c, \phi_f) = \tanh\left(\pi\left(1 - \frac{\phi_c + \phi_f}{\phi_{max}}\right)\right),$
- Anitcoagulation: $g(A, T) = \frac{ATH}{\alpha k_{AT} k_T + \alpha k_{AT} T + \alpha k_T A + AT},$ Thrombin generation: $t(T) = k_3 T + k_4 T^2 + k_5 T^3.$
- Permeability: $\frac{1}{K_f} = \frac{16}{\alpha^2} \phi_p^{\frac{3}{2}} (1 + 56\phi_p) \frac{\phi_{max} + \phi_c}{\phi_{max} - \phi_c}, \quad \phi_p = \min\left(\frac{7}{10}, \frac{F_p}{7000}\right)$
- Bouchnita, A., Terekhov, K., Nony, P., Vassilevski, Y., & Volpert, V.: ***A mathematical model to quantify the effects of platelet count, shear rate, and injury size on the initiation of blood coagulation under venous flow conditions*. PloS one,** 15(7), e0235392, 2020

Complete system

- Fibrin (Ia): $\frac{\partial F}{\partial t} + \mathrm{div}(F\boldsymbol{u} - D\nabla F) = \frac{k_{10} T F_g}{K_{10}+F_g} - k_{11} F,$
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Immobile fibrin polymer

vWF factor (Hellums, Goodman)

Non-monotone function (Leiderman et al)

Griffith model for Heparin

For platelets-rich plasma (Wufsus et al)

Boundary Conditions

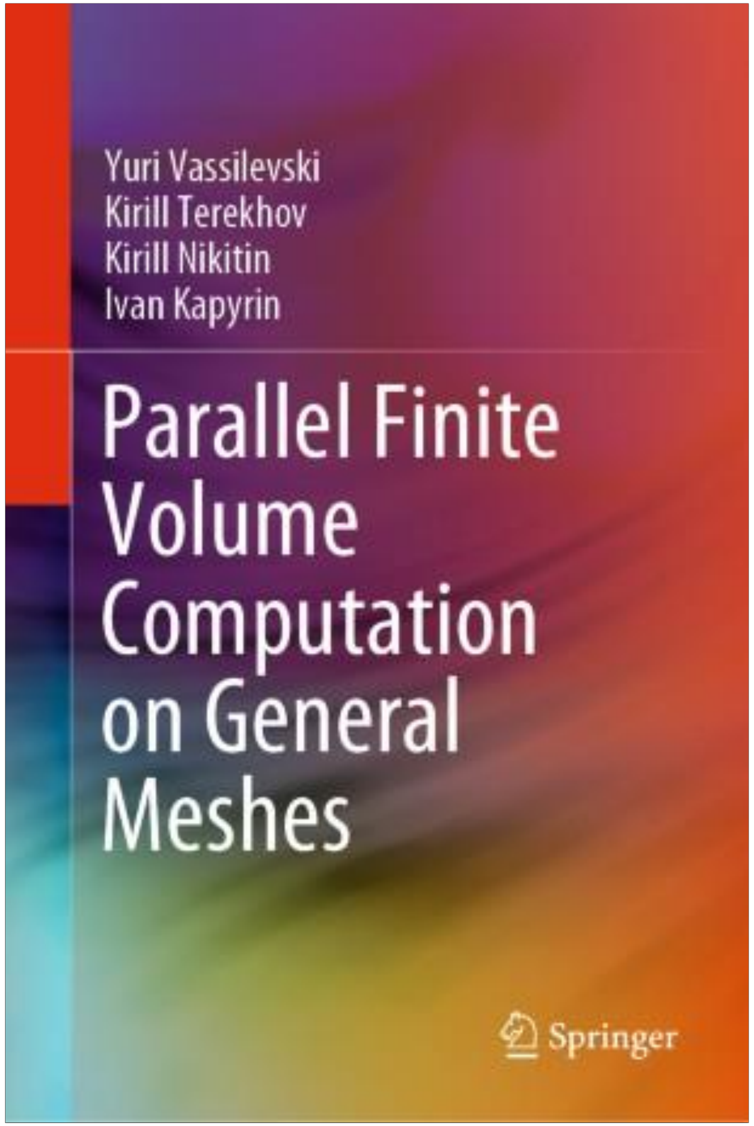
- BC on blood vessel damage:

$$\frac{\partial B_a}{\partial \boldsymbol{n}} = \frac{\alpha(B^0 - B_a)}{1 + \beta(B^0 - B_a)}$$

- BC for Navier-Stokes:
  - no-slip condition on walls
  - pressure drop between inflow and outflow
- BC of Dirichlet/Neumann type for blood components.
- Model parameters:
  - from literature (Griffith, Goodman, Hokin et al, Kuharsky, Leiderman, Fogelson, Wiebe et al, Tsian et al, …),
  - from 0D thrombin generation model,
  - fitted by Anass.

Numerical Methods

for model construction



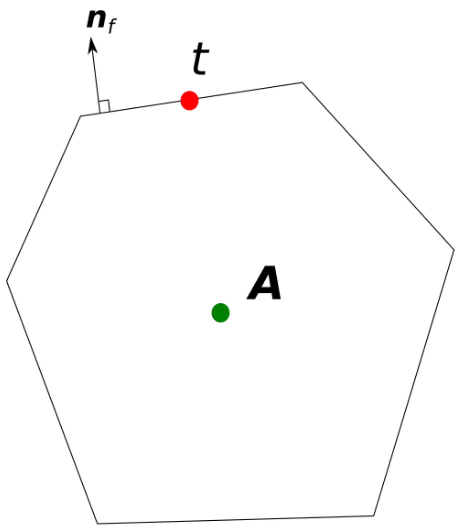
- Vassilevski, Y., Terekhov, K., Nikitin, K., & Kapyrin, I. (2020). **Parallel Finite Volume Computation on General Meshes.** Springer Nature.
- Terekhov, K. (2020). **Collocated Finite-Volume Method for the Incompressible Navier-Stokes Problem.** Journal of Numerical Mathematics.
- Terekhov K. (2021) **Fully-Implicit Collocated Finite-Volume Method for the Unsteady Incompressible Navier–Stokes Problem**, Numerical Geometry, Grid Generation and Scientific Computing

Finite-Volume Method

- Ostrogradsky-Gauss theorem:

$$-\mathrm{div}(\boldsymbol{A}) = \boldsymbol{g} \implies -\oint\limits_{\partial V} \boldsymbol{A} \mathrm{d}\boldsymbol{S} = \int\limits_{V} \boldsymbol{g} \mathrm{d}\boldsymbol{V}$$

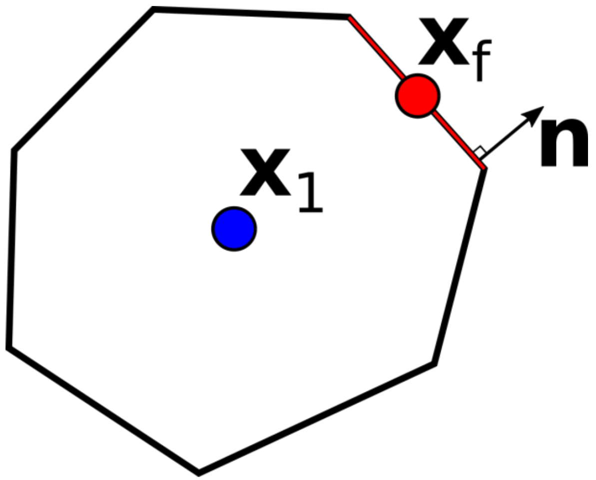
$$\implies -\sum_{f \in \mathcal{F}(\boldsymbol{V})} |f| \, \boldsymbol{A}\boldsymbol{n}|_{\mathbf{x}_f} = |V| \, \boldsymbol{g}|_{\mathbf{x}_V}$$



- Requires the **flux approximation**:

$$\boldsymbol{t} = \boldsymbol{A}\boldsymbol{n}|_{\mathbf{x}_f}$$

FVM for Navier-Stokes



- Flux:

$$\boldsymbol{t} = \begin{cases} \rho \boldsymbol{u}\boldsymbol{u}^T\boldsymbol{n} - \mu(\nabla \boldsymbol{u}^T + \boldsymbol{u}\nabla^T)\boldsymbol{n} + p\boldsymbol{n} \\ \boldsymbol{n}^T\boldsymbol{u} \end{cases}$$

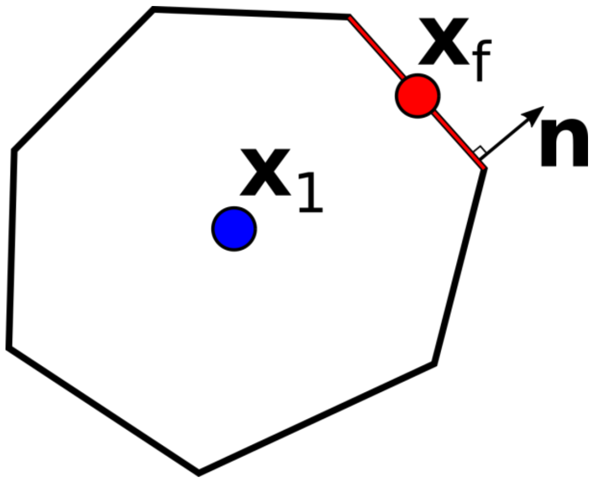
- Second-order Taylor series for advective term:

$$\rho \boldsymbol{u}\boldsymbol{u}^T\boldsymbol{n}\Big|_{\boldsymbol{x}_f} \approx \rho \boldsymbol{u}\boldsymbol{u}^T\boldsymbol{n}\Big|_{\boldsymbol{x}_1} + \rho \frac{\partial \boldsymbol{u}\boldsymbol{u}^T\boldsymbol{n}}{\partial \boldsymbol{u}}\Big|_{\boldsymbol{x}_1} \nabla \boldsymbol{u}(\boldsymbol{x}_f - \boldsymbol{x}_1)$$

$$\approx \frac{\rho}{2}\left(\boldsymbol{u}_1\boldsymbol{n}^T + \boldsymbol{u}_1 \cdot \boldsymbol{n}\mathbb{I}\right)\left(2\boldsymbol{u}_f - \boldsymbol{u}_1\right)$$

- K.M. Terekhov. *Fully-Implicit Collocated Finite-Volume Method for the Unsteady Incompressible Navier-Stokes Problem*, Lecture Notes in Computational Science and Engineering, 2021

FVM for Navier-Stokes



- Flux:

$$\boldsymbol{t} = \begin{cases} \rho \boldsymbol{u}\boldsymbol{u}^T\boldsymbol{n} - \mu(\nabla \boldsymbol{u}^T + \boldsymbol{u}\nabla^T)\boldsymbol{n} + p\boldsymbol{n} \\ \boldsymbol{n}^T\boldsymbol{u} \end{cases}$$

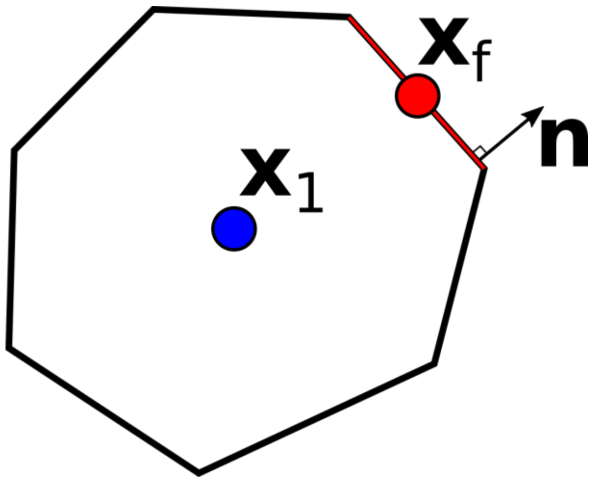
- Second-order decomposition of viscous term:

$$-\mu(\nabla \boldsymbol{u}^T + \boldsymbol{u}\nabla^T)\boldsymbol{n}\Big|_{\boldsymbol{x}_f} \approx \frac{\mu}{r_1}(\mathbb{I} + \boldsymbol{n}\boldsymbol{n}^T)(\boldsymbol{u}_1 - \boldsymbol{u}_f)$$

$$-\mu\left(\mathbb{I} \otimes \boldsymbol{n}^T + \boldsymbol{n} \otimes \mathbb{I} - \frac{1}{r_1}(\mathbb{I} + \boldsymbol{n}\boldsymbol{n}^T) \otimes (\boldsymbol{x}_f - \boldsymbol{x}_1)^T\right)(\boldsymbol{u}_1 \otimes \nabla)$$

- Two-point yields positive matrix coefficients.
- Transversal correction **do not vanish** on orthogonal grids.

FVM for Navier-Stokes



- Flux:

$$\boldsymbol{t} = \begin{cases} \rho \boldsymbol{u}\boldsymbol{u}^T\boldsymbol{n} - \mu(\nabla \boldsymbol{u}^T + \boldsymbol{u}\nabla^T)\boldsymbol{n} + p\boldsymbol{n} \\ \boldsymbol{n}^T\boldsymbol{u} \end{cases}$$

- Decomposition of **indefinite** matrix coefficient:

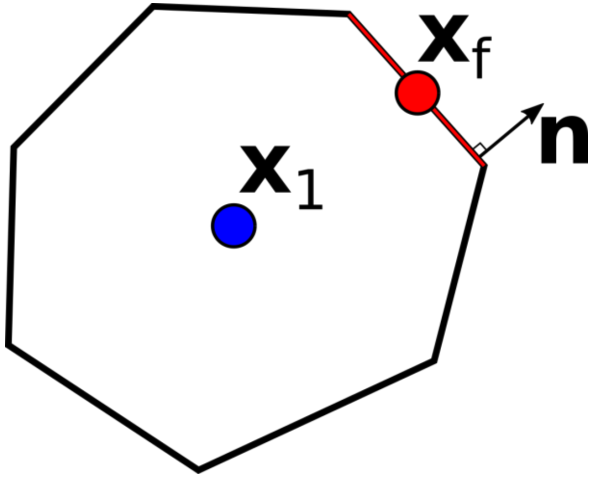
$$\begin{Bmatrix} p\boldsymbol{n} \\ \boldsymbol{n}^T\boldsymbol{u} \end{Bmatrix}\Bigg|_{\boldsymbol{x}_f} = \begin{bmatrix} & \boldsymbol{n} \\ \boldsymbol{n}^T & \end{bmatrix}\begin{bmatrix} \boldsymbol{u}_f \\ p_f \end{bmatrix}$$

$$\approx \begin{bmatrix} a(\mathbb{I} + \boldsymbol{n}\boldsymbol{n}^T) & c\boldsymbol{n} \\ c\boldsymbol{n}^T & b \end{bmatrix}\begin{bmatrix} \boldsymbol{u}_1 \\ p_1 \end{bmatrix} - \begin{bmatrix} a(\mathbb{I} + \boldsymbol{n}\boldsymbol{n}^T) & (c-1)\boldsymbol{n} \\ (c-1)\,\boldsymbol{n}^T & b \end{bmatrix}\begin{bmatrix} \boldsymbol{u}_f \\ p_f \end{bmatrix}$$

$$+ \begin{bmatrix} a(\mathbb{I} + \boldsymbol{n}\boldsymbol{n}^T) & c\boldsymbol{n} \\ c\boldsymbol{n}^T & b \end{bmatrix} \otimes (\boldsymbol{x}_f - \boldsymbol{x}_1)^T \left(\begin{bmatrix} \boldsymbol{u}_1 \\ p_1 \end{bmatrix} \otimes \nabla\right)$$

- Coefficients are tuned for LBB-**stability**.

FVM for Navier-Stokes



- Flux:

$$\boldsymbol{t} = \begin{cases} \rho \boldsymbol{u}\boldsymbol{u}^T\boldsymbol{n} - \mu(\nabla \boldsymbol{u}^T + \boldsymbol{u}\nabla^T)\boldsymbol{n} + p\boldsymbol{n} \\ \boldsymbol{n}^T\boldsymbol{u} \end{cases}$$

- Combining the approximations:

$$\boldsymbol{t} \approx (T_1 - Q_1)\begin{bmatrix} \boldsymbol{u}_1 \\ p_1 \end{bmatrix} - (T_1 - S_1 - 2Q_1)\begin{bmatrix} \boldsymbol{u}_f \\ p_f \end{bmatrix} + \left(T_1 \otimes (\boldsymbol{x}_f - \boldsymbol{x}_1)^T - W_1\right)\left(\begin{bmatrix} \boldsymbol{u}_1 \\ p_1 \end{bmatrix} \otimes \nabla\right),$$

- Matrix coefficients are:

$$T_1 = \begin{bmatrix} \left(a + \frac{\mu}{r_1}\right)(\mathbb{I} + \boldsymbol{n}\boldsymbol{n}^T) & c\boldsymbol{n} \\ c\boldsymbol{n}^T & b \end{bmatrix}, \qquad Q_1 = \begin{bmatrix} \frac{\rho}{2}(\boldsymbol{u}_1\boldsymbol{n}^T + \boldsymbol{u}_1 \cdot \boldsymbol{n}\mathbb{I}) & \\ & \end{bmatrix},$$

$$S_1 = \begin{bmatrix} & \boldsymbol{n} \\ \boldsymbol{n}^T & \end{bmatrix}, \qquad W_1 = \begin{bmatrix} \mu(\mathbb{I} \otimes \boldsymbol{n}^T + \boldsymbol{n} \otimes \mathbb{I}) & \\ & \end{bmatrix}.$$

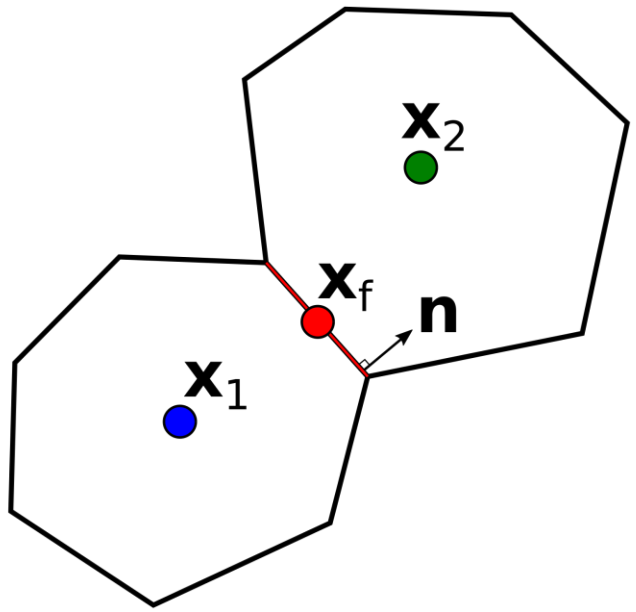
FVM for Navier-Stokes

- Flux:

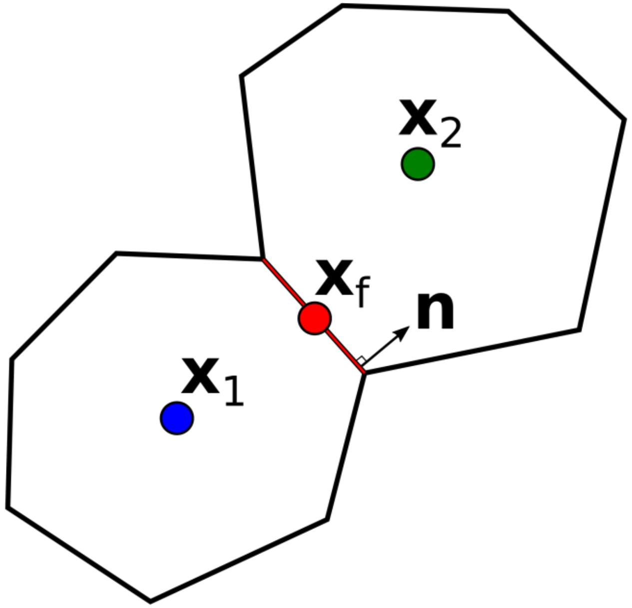
$$\boldsymbol{t} = \begin{cases} \rho \boldsymbol{u}\boldsymbol{u}^T\boldsymbol{n} - \mu(\nabla\boldsymbol{u}^T + \boldsymbol{u}\nabla^T)\boldsymbol{n} + p\boldsymbol{n} \\ \boldsymbol{n}^T\boldsymbol{u} \end{cases}$$

- From the flux continuity:

$$\begin{bmatrix} \boldsymbol{u}_f \\ p_f \end{bmatrix} \approx (T_1 + T_2 - S_1 - S_2 - 2Q_1 - 2Q_2)^{-1}$$
$$\times \begin{pmatrix} (T_1 - Q_1)\begin{bmatrix} \boldsymbol{u}_1 \\ p_1 \end{bmatrix} + (T_1 \otimes (\boldsymbol{x}_f - \boldsymbol{x}_1)^T - W_1)\left(\begin{bmatrix} \boldsymbol{u}_1 \\ p_1 \end{bmatrix} \otimes \nabla\right) \\ +(T_2 - Q_2)\begin{bmatrix} \boldsymbol{u}_1 \\ p_1 \end{bmatrix} + (T_2 \otimes (\boldsymbol{x}_f - \boldsymbol{x}_2)^T - W_2)\left(\begin{bmatrix} \boldsymbol{u}_1 \\ p_1 \end{bmatrix} \otimes \nabla\right) \end{pmatrix}$$



FVM for Navier-Stokes



- Flux:

$$\boldsymbol{t} = \begin{cases} \rho \boldsymbol{u}\boldsymbol{u}^T\boldsymbol{n} - \mu(\nabla\boldsymbol{u}^T + \boldsymbol{u}\nabla^T)\boldsymbol{n} + p\boldsymbol{n} \\ \boldsymbol{n}^T\boldsymbol{u} \end{cases}$$

- From the flux continuity:

$$\begin{aligned} \boldsymbol{t} \approx\ & (T_2 - S_2 - 2Q_2)(T_1 + T_2 - S_1 - S_2 - 2Q_1 - 2Q_2)^{-1} \\ & \times (T_1 - Q_1)\begin{bmatrix}\boldsymbol{u}_1 \\ p_1\end{bmatrix} + \left(T_1 \otimes \left(\boldsymbol{x}_f - \boldsymbol{x}_1\right)^T - W_1\right)\left(\begin{bmatrix}\boldsymbol{u}_1 \\ p_1\end{bmatrix} \otimes \nabla\right) \\ & -(T_1 - S_1 - 2Q_1)(T_1 + T_2 - S_1 - S_2 - 2Q_1 - 2Q_2)^{-1} \\ & \times (T_2 - Q_2)\begin{bmatrix}\boldsymbol{u}_1 \\ p_1\end{bmatrix} + (T_2 \otimes \left(\boldsymbol{x}_f - \boldsymbol{x}_2\right)^T - W_2)\left(\begin{bmatrix}\boldsymbol{u}_1 \\ p_1\end{bmatrix} \otimes \nabla\right) \end{aligned}$$

- Computation of the gradients is based on the Green’s formula.

Eigenvalues in Matrix Coefficients

- Single-sided flux expression:

$$\mathbf{t} \approx (T_1 - Q_1)\begin{bmatrix} \mathbf{u}_1 \\ p_1 \end{bmatrix} - (T_1 - S_1 - 2Q_1)\begin{bmatrix} \mathbf{u}_f \\ p_f \end{bmatrix} + \left(T_1 \otimes (\mathbf{x}_f - \mathbf{x}_1)^T - W_1\right)\nabla \otimes \begin{bmatrix} \mathbf{u}_1 \\ p_1 \end{bmatrix}$$

- **Eigenvalues** for $T_1 - Q_1$:

$$\lambda_{1,2} = a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1/2 + b/2 \pm \sqrt{\left(a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1/2 - b/2\right)^2 + c^2},$$

$$\lambda_{3,4} = a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1/2.$$

- **Eigenvalues** for $T_1 - S_1 - 2Q_1$:

$$\lambda_{1,2} = a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1 + b/2 \pm \sqrt{\left(a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1 - b/2\right)^2 + (c-1)^2},$$

$$\lambda_{3,4} = a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1.$$

Eigenvalues in Matrix Coefficients

- Find **minimal possible** values with constraints:

$$a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1 \geq 0, \quad a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1/2 \geq 0,$$

$$2b\left(a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1\right) \geq (c-1)^2, \quad 2b\left(a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1/2\right) \geq c^2.$$

- Results in:

$$a = \max\left(\rho \mathbf{n} \cdot \mathbf{u}_1 - \mu r_1^{-1}, 0\right) + \theta > 0$$

$$b \geq \frac{1}{2} \max\left(\frac{(1-c)^2}{a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1}, \frac{c^2}{a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1/2}\right)$$

- If **a** is too **small**, **b** has to be **big**!
- To control this, use $\theta = \rho\sqrt{\mathbf{u}_1\left(\mathbb{I} - \mathbf{n}\mathbf{n}^T\right)\mathbf{u}_1} + \varepsilon$

Eigenvalues in Matrix Coefficients

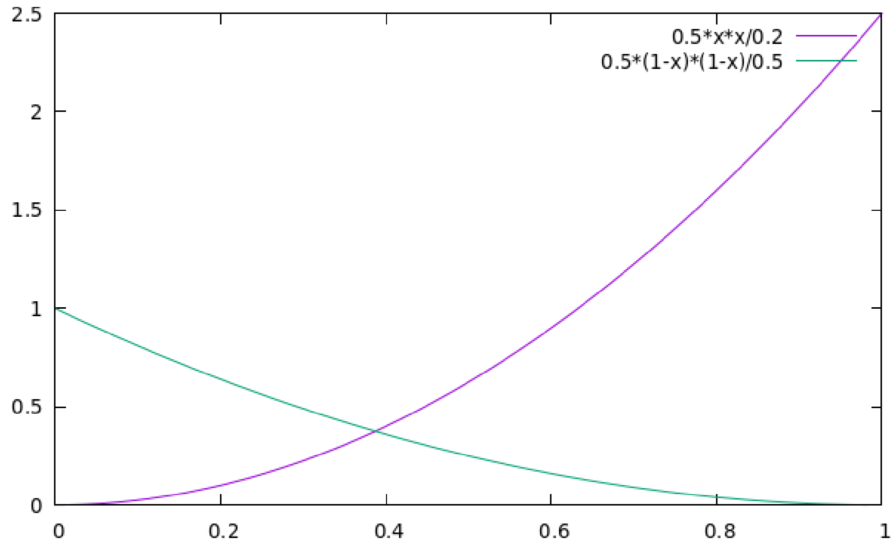
- Find **minimal possible** values with constraints:

$$b \geq \frac{1}{2} \max \left(\frac{(1-c)^2}{a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1}, \frac{c^2}{a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1 / 2} \right)$$

- Solution

$$c = \begin{cases} 1 + t - \sqrt{t + t^2}, & \rho \mathbf{n} \cdot \mathbf{u}_1 > 0, \\ 1/2, & \rho \mathbf{n} \cdot \mathbf{u}_1 = 0, \\ 1 + t + \sqrt{t + t^2}, & \rho \mathbf{n} \cdot \mathbf{u}_1 < 0, \end{cases}$$

- Where $t = 2 \left(\frac{a + \mu r_1^{-1}}{\rho \mathbf{n} \cdot \mathbf{u}_1} - 1 \right)$



Intersection of two parabolas for **c**

Eigenvalues in Matrix Coefficients

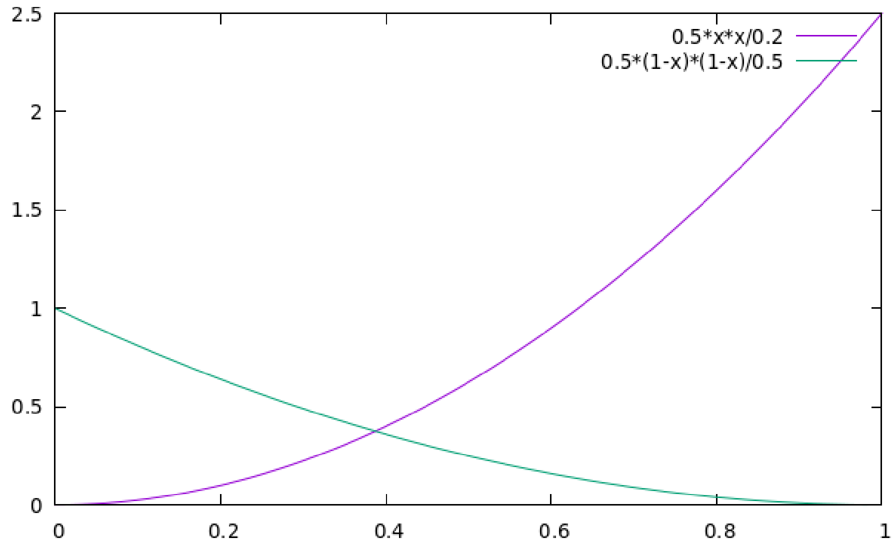
- Find **minimal possible** values with constraints:

$$b \geq \frac{1}{2} \max \left(\frac{(1-c)^2}{a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1}, \frac{c^2}{a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1 / 2} \right)$$

- Solution $b \left(a + \mu r_1^{-1} - \rho \mathbf{n} \cdot \mathbf{u}_1 \right) =$

$$\begin{cases} t \left(1/2 + t - \sqrt{t + t^2} \right), & \rho \mathbf{n} \cdot \mathbf{u}_1 > 0, \\ 1/8, & \rho \mathbf{n} \cdot \mathbf{u}_1 = 0, \\ t \left(1/2 + t + \sqrt{t + t^2} \right), & \rho \mathbf{n} \cdot \mathbf{u}_1 < 0, \end{cases}$$

- Where $t = 2 \left(\frac{a + \mu r_1^{-1}}{\rho \mathbf{n} \cdot \mathbf{u}_1} - 1 \right)$



Intersection of two parabolas for **c**

FVM for Blood Components

- Flux expression: $\boldsymbol{n}^T(C\boldsymbol{u} - D\nabla C)$
- Advection: **first-order** upstream:

$$C\boldsymbol{n}^T\boldsymbol{u} \approx \frac{1}{2}\left(C_1(\boldsymbol{n}^T\boldsymbol{u} + |\boldsymbol{n}^T\boldsymbol{u}|) + C_2(\boldsymbol{n}^T\boldsymbol{u} - |\boldsymbol{n}^T\boldsymbol{u}|)\right)$$

- Diffusion: **second-order** nonlinear two-point approximation:
-

$$D\boldsymbol{n}^T\nabla C \approx D\frac{(C_1 - C_2)}{|\boldsymbol{x}_1 - \boldsymbol{x}_2|} - D(\mu_1\nabla C_1 + \mu_2\nabla C_2)\cdot\left(\boldsymbol{n} - \frac{(\boldsymbol{x}_1 - \boldsymbol{x}_2)}{|\boldsymbol{x}_1 - \boldsymbol{x}_2|}\right) = D(T_1 C_1 - T_2 C_2)$$

- Solution is **nonnegative** – very important for reactions!

FVM for Traffic Flow

- Flux expression: $\lambda(C)\boldsymbol{n}^T\boldsymbol{u}$
  - advection: $\lambda(C) = C$
  - traffic: $\lambda(C) = C(1 - C)$
  - our case: $\lambda(C) = C\tanh(1 - C)$
- **First-order** upstream approximation:

$\lambda'(C_1)\boldsymbol{n}^T\boldsymbol{u}$	$\lambda'(C_1)\boldsymbol{n}^T\boldsymbol{u}$	$\boldsymbol{t}$
+	+	$\lambda(C_1)\boldsymbol{n}^T\boldsymbol{u}$
-	-	$\lambda(C_2)\boldsymbol{n}^T\boldsymbol{u}$
+	-	$\mathrm{minmod}(\lambda(C_1), \lambda(C_2))\boldsymbol{n}^T\boldsymbol{u}$
-	+	$\lambda(C)\boldsymbol{n}^T\boldsymbol{u},\ \lambda'(C) = 0$

Moscow traffic
(image from internet)

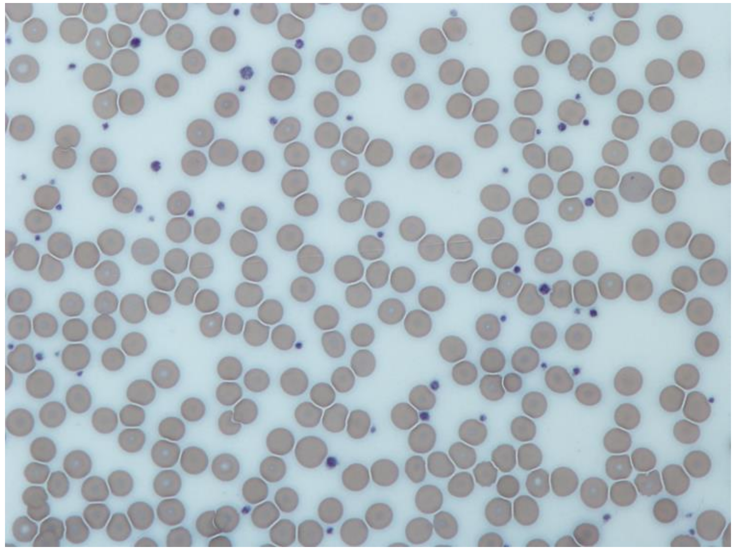
FVM for Platelets

- Flux expression: $\boldsymbol{t}(\phi_c, \phi_f) = \tanh\left(\pi\left(1 - \frac{\phi_c + \phi_f}{\phi_{max}}\right)\right)\boldsymbol{n}^T(\boldsymbol{u} - D_p\nabla)\begin{pmatrix}\phi_c \\ \phi_f\end{pmatrix}$
- Jacobian contribution:

$$J(\phi_c, \phi_f) = \begin{pmatrix} \frac{\partial \boldsymbol{t}_1(\phi_c, \phi_f)}{\partial \phi_c} & \frac{\partial \boldsymbol{t}_1(\phi_c, \phi_f)}{\partial \phi_f} \\ \frac{\partial \boldsymbol{t}_2(\phi_c, \phi_f)}{\partial \phi_c} & \frac{\partial \boldsymbol{t}_2(\phi_c, \phi_f)}{\partial \phi_f} \end{pmatrix}\begin{pmatrix} d\phi_c \\ d\phi_f \end{pmatrix} = Q(\phi_c, \phi_f)\begin{pmatrix} d\phi_c \\ d\phi_f \end{pmatrix}$$

- Matrix-weighted combination for two cells:

$$\Phi = M_1\begin{pmatrix}\phi_{c,1} \\ \phi_{f,1}\end{pmatrix} + M_2\begin{pmatrix}\phi_{c,2} \\ \phi_{f,2}\end{pmatrix}$$



Platelets
(image from internet)

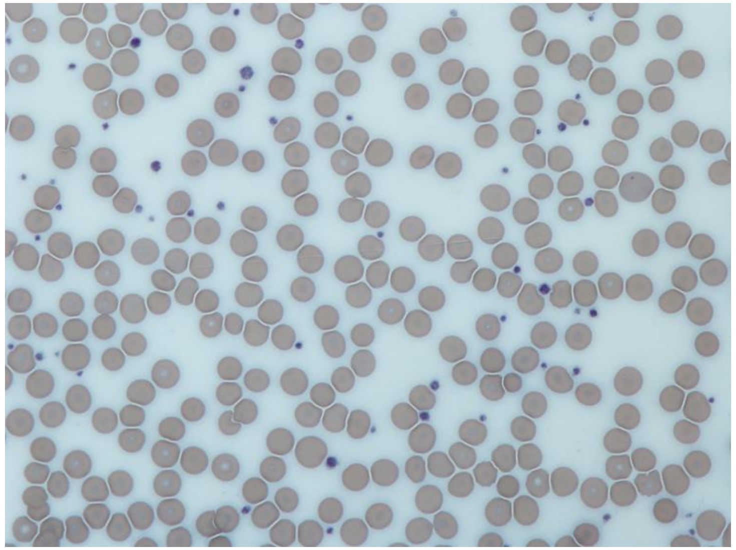
FVM for Platelets

- Flux expression: $\boldsymbol{t}(\phi_c, \phi_f) = \tanh\left(\pi\left(1 - \frac{\phi_c + \phi_f}{\phi_{max}}\right)\right)\boldsymbol{n}^T(\boldsymbol{u} - D_p\nabla)\begin{pmatrix}\phi_c \\ \phi_f\end{pmatrix}$
- Iterative search:

$$J(\Phi) = Q(\Phi)M_1\begin{pmatrix}d\phi_{c,1} \\ d\phi_{f,1}\end{pmatrix} + Q(\Phi)M_2\begin{pmatrix}d\phi_{c,2} \\ d\phi_{f,2}\end{pmatrix}$$

- Matrices are obtained using eigendecomposition:

$$Q(\Phi) = L\Lambda L^T,$$
$$M_1 = \frac{1}{2}L(\mathrm{sgn}(\Lambda) + |\mathrm{sgn}(\Lambda)|)L^T$$
$$M_2 = \frac{1}{2}L(\mathrm{sgn}(\Lambda) - |\mathrm{sgn}(\Lambda)|)L^T$$



Platelets
(image from internet)

Approximation for Reactions

- Reactions lead to very **small time step** even with fully implicit integration.
- Problem – **bad contribution** to off-diagonal terms of Jacobian matrix.

➢ **Automatic approach in the talk by Ivan Butakov, Moscow Institute of Physics and Technology.**

Approximation for Reactions

- Red terms are extrapolated from previous time steps:

$$R(\Theta^{n+1}) \approx \begin{pmatrix} -\left(k_1\hat{\phi}_c + k_2 B_\alpha^{n+1} + k_3\hat{T} + k_4\hat{T}^2 + k_5\hat{T}^3\right) P^{n+1} \\ \left(k_1\hat{\phi}_c + k_2 B_\alpha^{n+1} + k_3\hat{T} + k_4\hat{T}^2 + k_5\hat{T}^3\right) P - k_6 A^{n+1} T^{n+1} \\ \left(k_7\phi_c^{n+1} + k_8 T^{n+1}\right)\left(B^0 - B_\alpha^{n+1}\right) - k_9 A^{n+1} B_\alpha^{n+1} \\ -\left(k_6 T^{n+1} + k_9 B_\alpha^{n+1}\right) A^{n+1} \\ -\frac{k_{10}\hat{T} F_g^{n+1}}{K_{10}+F_g^{n+1}} \\ \frac{k_{10}\hat{T} F_g^{n+1}}{K_{10}+F_g^{n+1}} - k_{11} F^{n+1} \\ k_{11} F^{n+1} \\ -\left(k_{12}\hat{T} - k_{13}\phi_c^{n+1}\right)\phi_f^{n+1} \\ \left(k_{12}\hat{T} - k_{13}\phi_c^{n+1}\right)\phi_f^{n+1} \end{pmatrix} \begin{matrix} P \\ T \\ B_a \\ A \\ F_g \\ F \\ \phi_f \\ \phi_c \end{matrix}$$

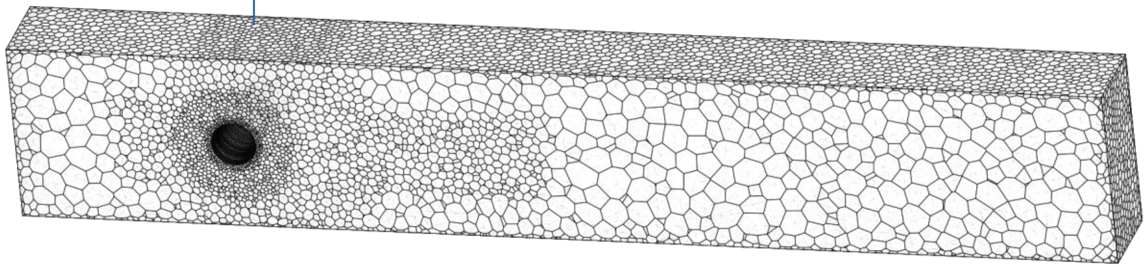
- Fully implicit model with 13 unknowns.

Verification

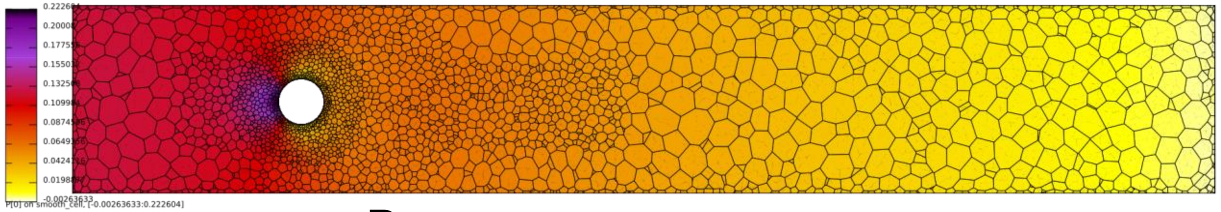
of the methods and model

Viscous Flow Past a Cylinder

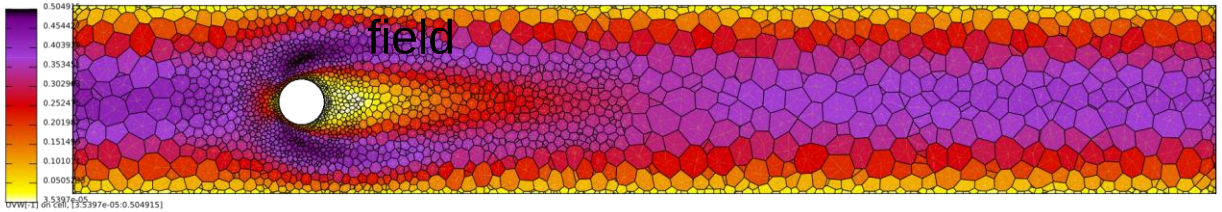
Refinement	Cells	Drag	Lift	Pressure drop
1	910	3.862	-0.08556	0.1481
2	4328	4.964	-0.02525	0.1854
3	24687	5.515	0.07256	0.1672
4	164806	5.876	0.00803	0.1890
$3^{\dagger}$	53211	6.064	0.01015	0.1801
$3^{\ddagger}$	98517	6.155	0.01006	0.1792
Schäfer & Turek [23]	-	6.05-6.25	0.008-0.01	0.165-0.175
Braack & Richter [7]	-	6.185331	0.00940	0.1713



Locally refined polyhedral mesh



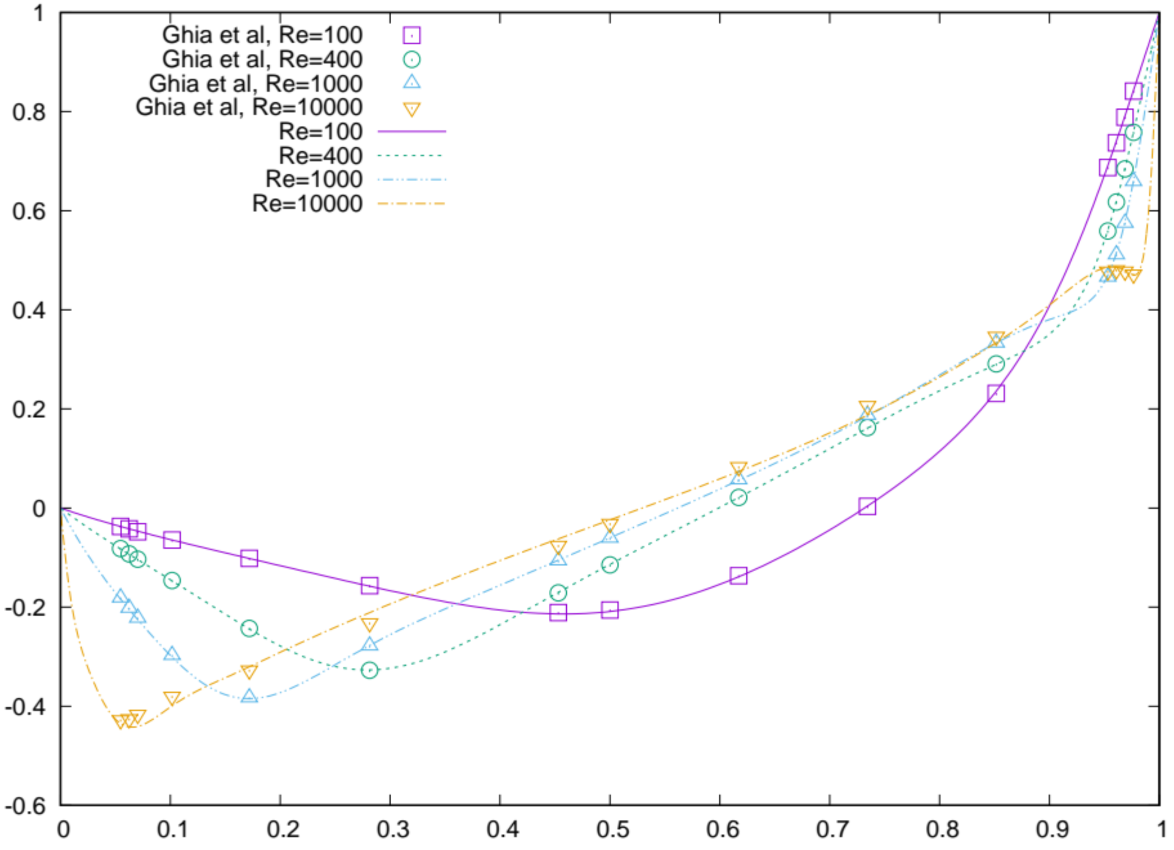
Pressure field

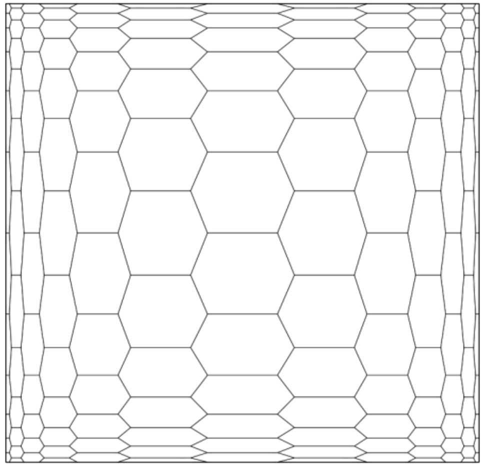


Velocity magnetude

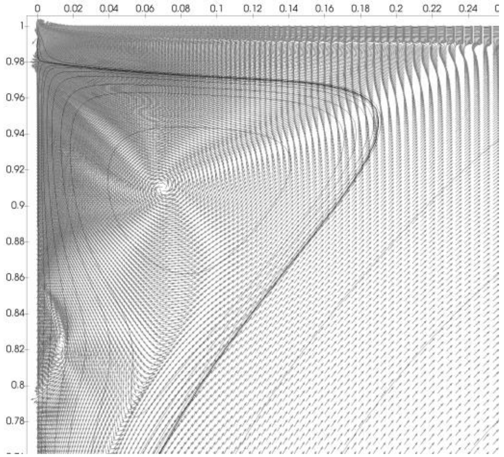
Cavity Flow at High Reynolds Numbers

- Comparison to reference data of Ghia et al.

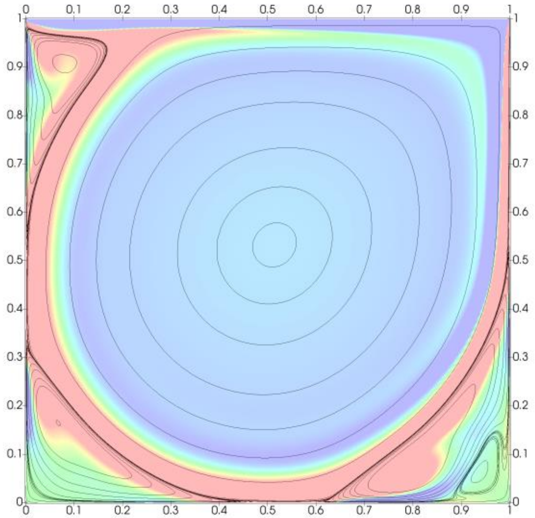




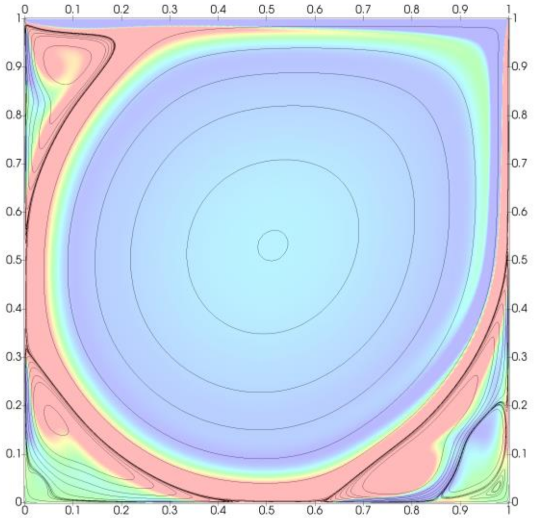
Hexagonal mesh



Tertiary vortex, Re = 16000



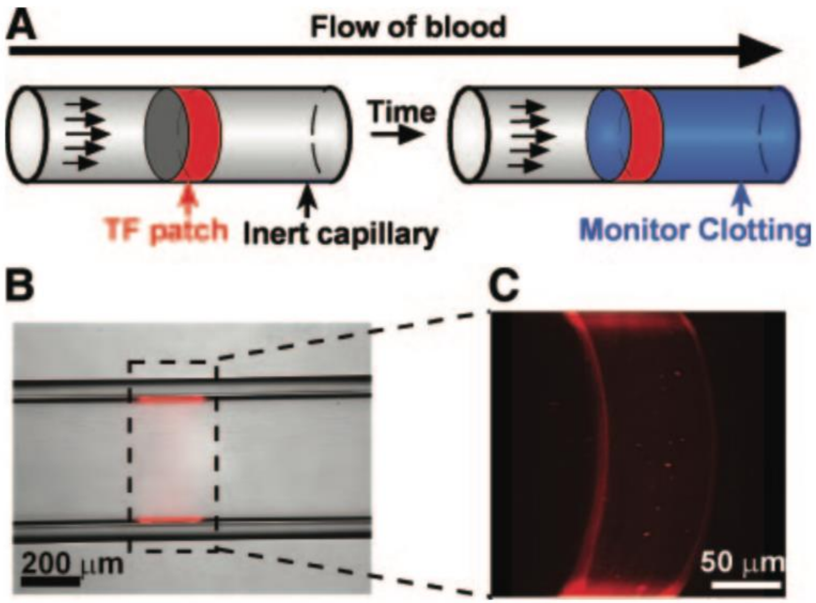
Re = 10000



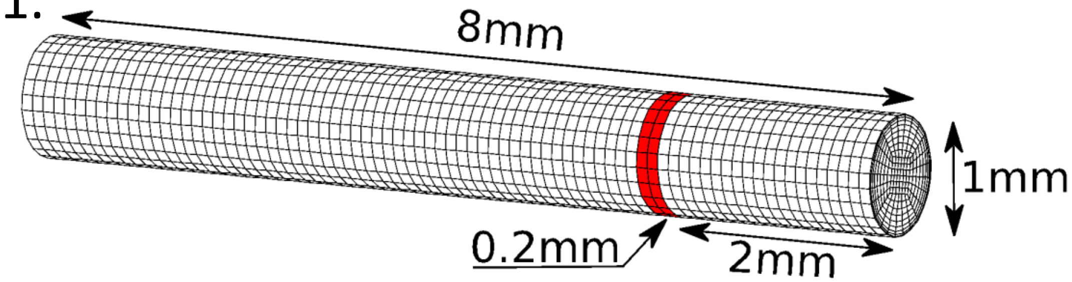
Re = 16000

Comparison to the Experimental Data

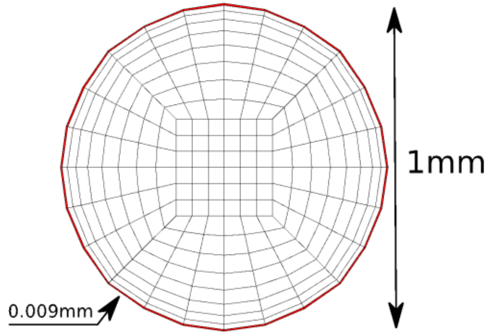
- Based on the **experimental research**: Shen F., Kastrup C.J., Liu Y., Ismagilov R.F.: ***Threshold response of initiation of blood coagulation by tissue factor in patterned microfluidic capillaries is controlled by shear rate.*** **Arteriosclerosis, thrombosis, and vascular biology.** 2008, 28(11): 2035–2041.



Experiment illustration



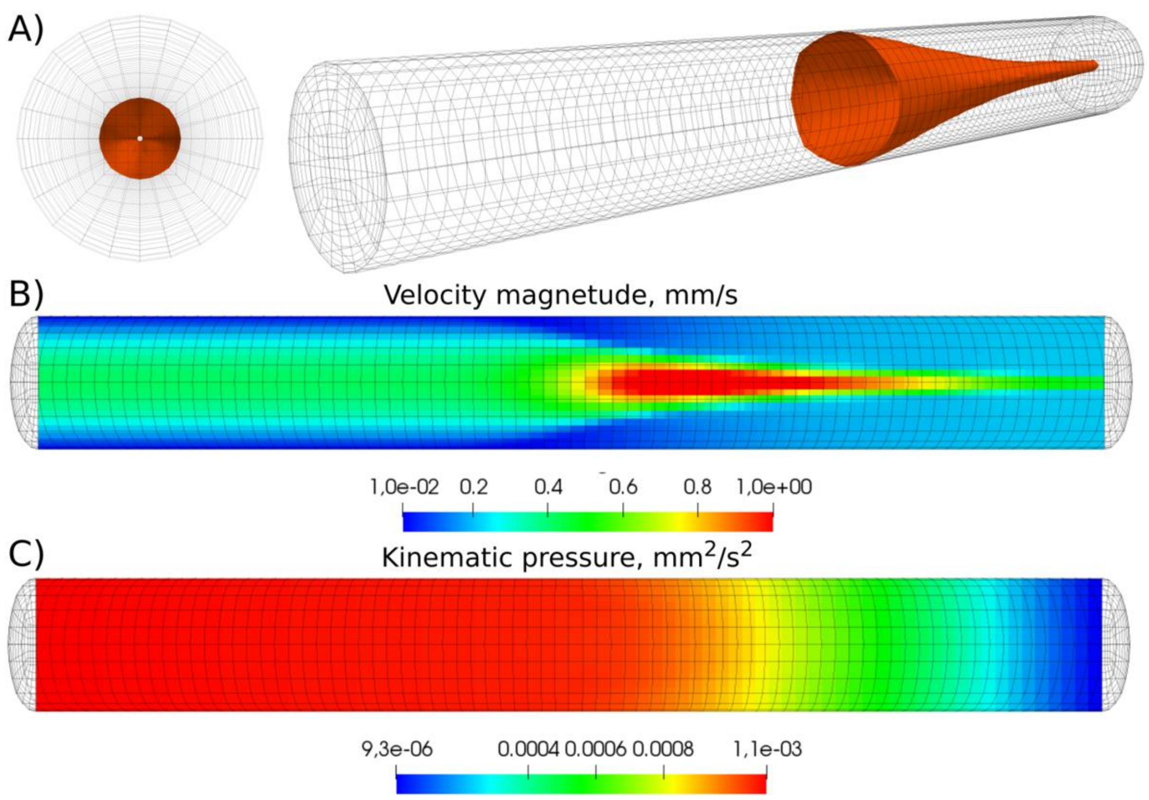
Computational domain



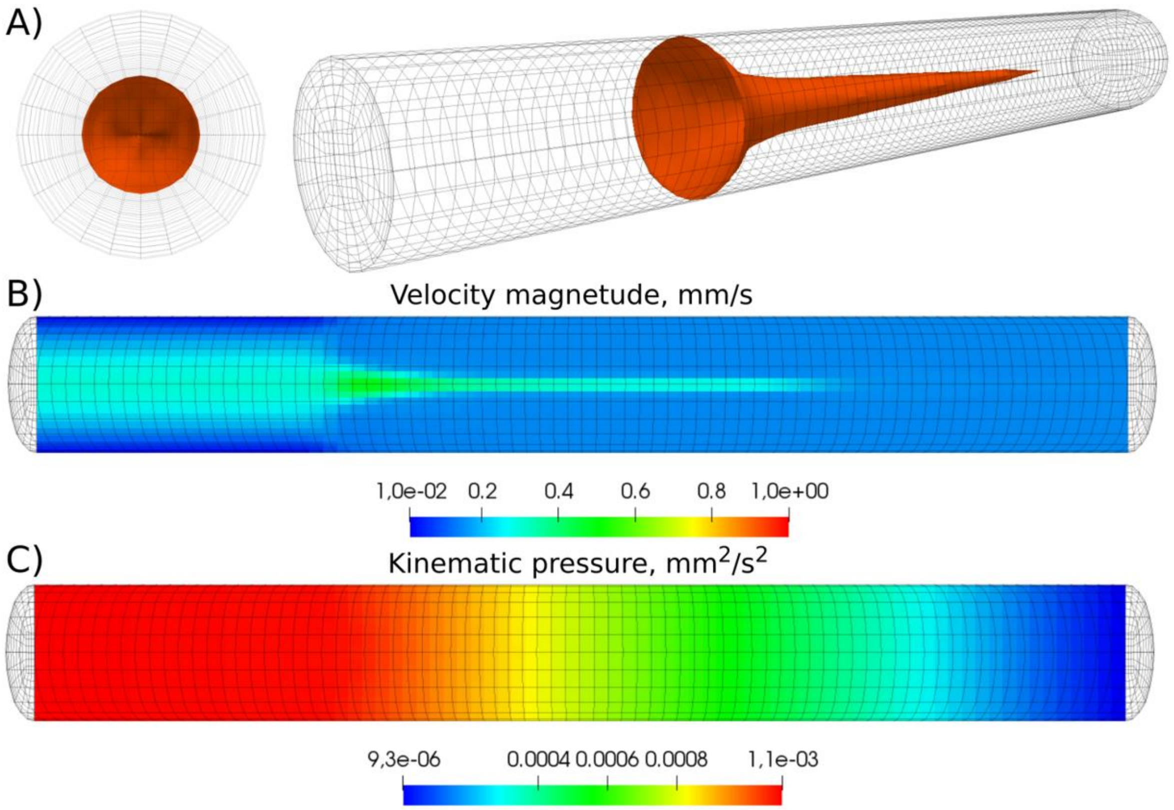
Section of the cylinder

Comparison to the Experimental Data

T=60s



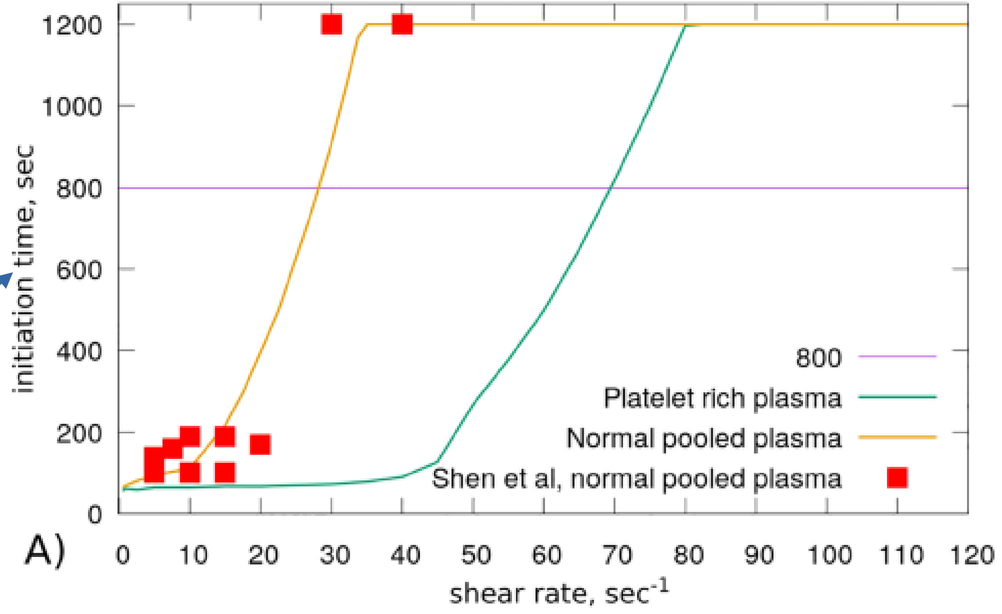
T=70s



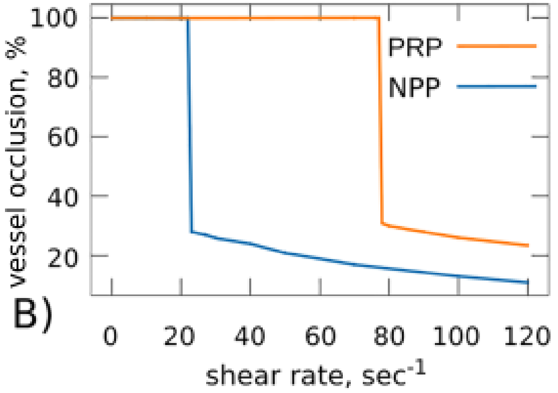
Reproduction of qualitative characteristics of the experiment

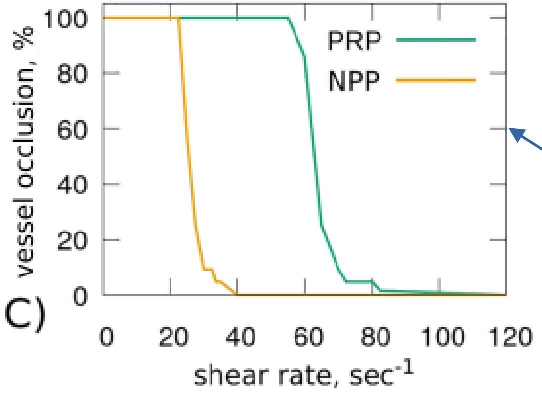
Comparison to the Experimental Data

A) Validation of 3D model
on experimental data



B) Simplified 1D
clot formation model

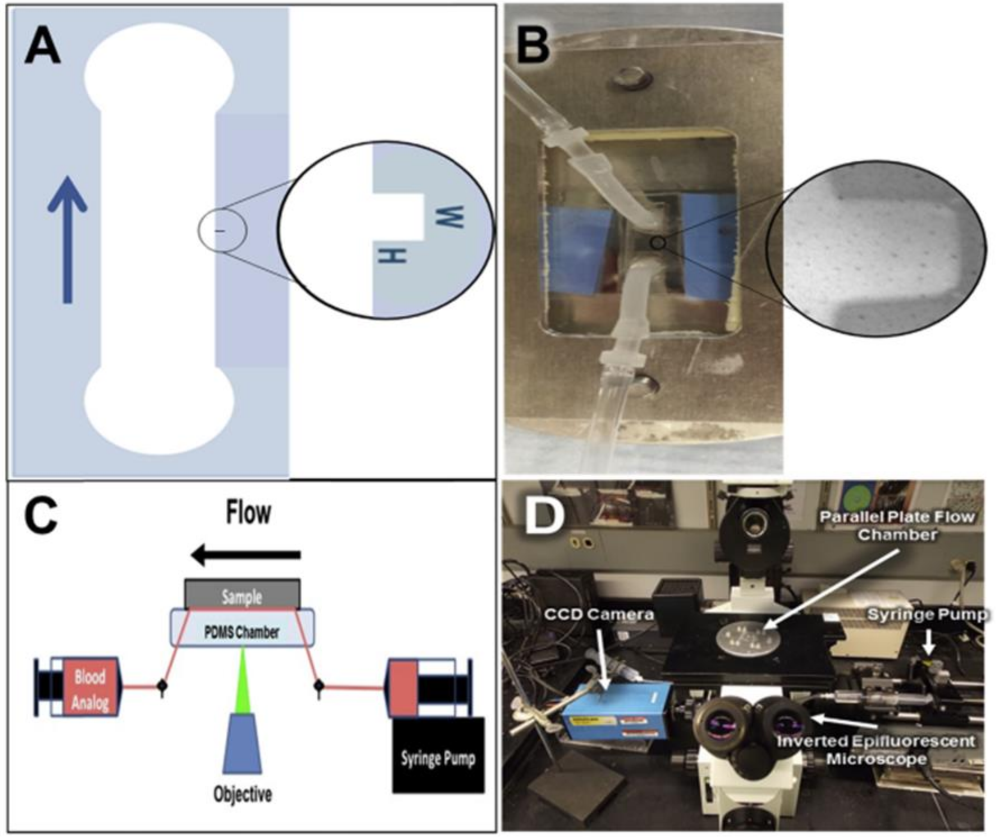




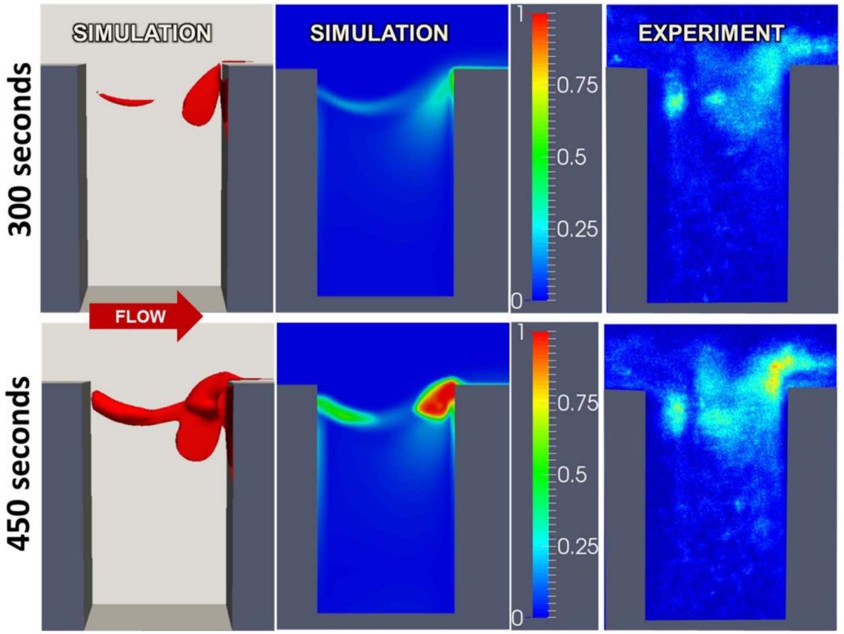
C) Full 3D simulation of
clot flormation

Bouchnita, A., Terekhov, K., Nony, P., Vassilevski, Y., & Volpert, V.: ***A mathematical model to quantify the effects of platelet count, shear rate, and injury size on the initiation of blood coagulation under venous flow conditions*****. PloS one,** 15(7), e0235392, 2020

Comparison to the Experimental Data



Jamiolkowski et al. (2016). Visualization and analysis of biomaterial-centered thrombus formation within a defined crevice under flow. *Biomaterials*, *96*, 72-83.

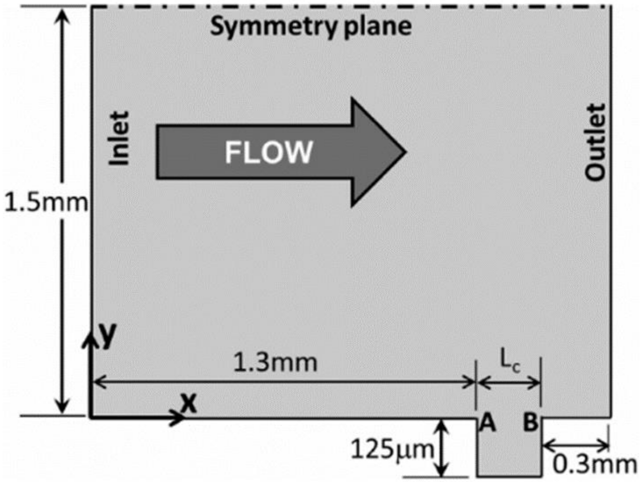


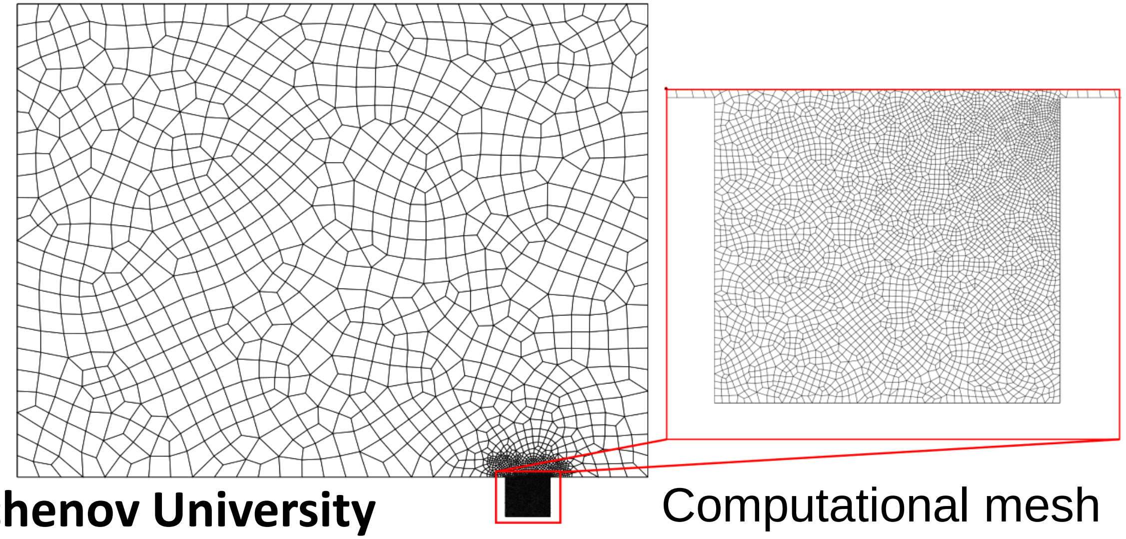
Wei-Tai Wu et al, (2017). Multi-constituent simulation of thrombus deposition. *Scientific reports*, *7*(1), 1-16.

Comparison to the Experimental Data

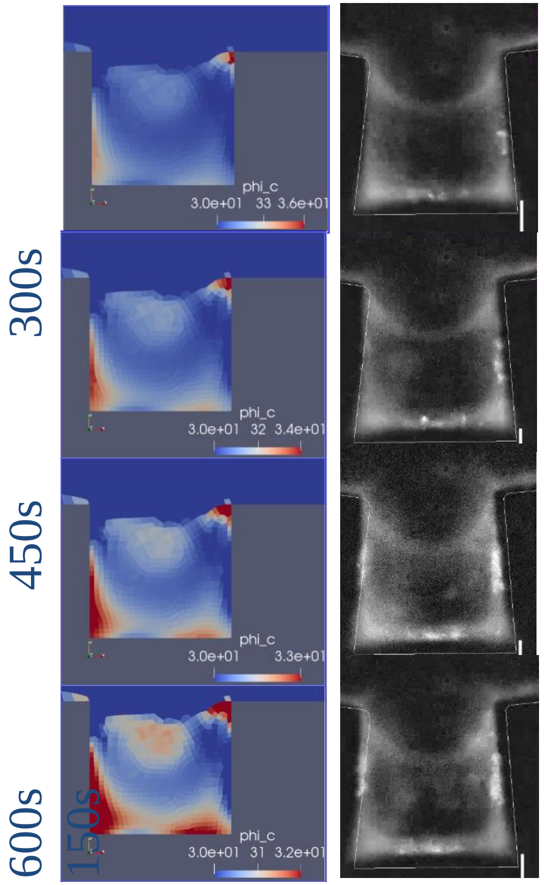
Difference from previous test:

- No tissue factor due to damage.
- Large role of anticoagulation agent.
- Reduced role of Fibrin polymer (**red clot**).
- Larger contribution of platelets (**white clot**).
- Current model poorly capture white clot dynamics.





Computational mesh

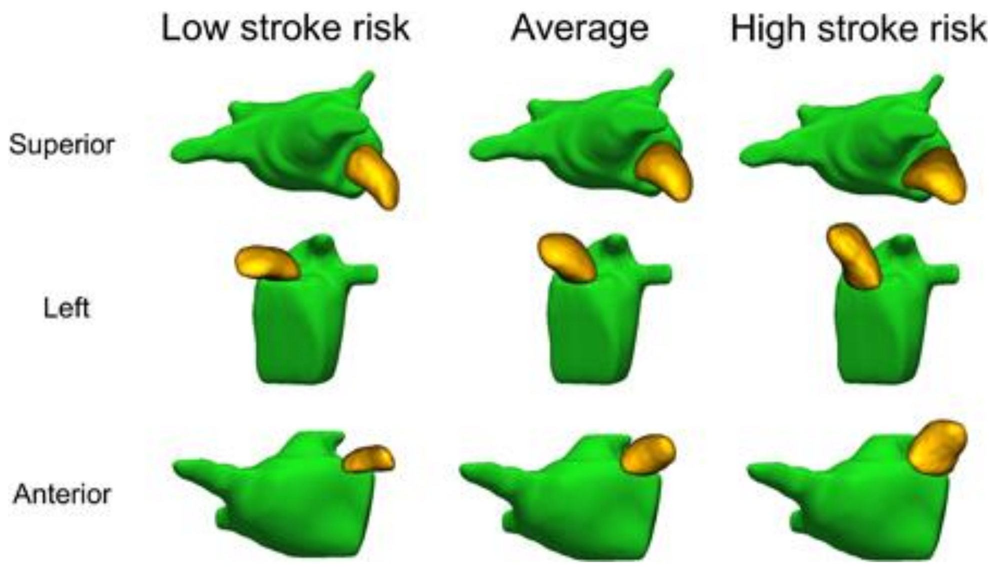


Simulated and real platelets distribution

by Nadezhda Suslova, Sechenov University

Future Directions

- Integration of automatic stabilization of chemical reactions (Ivan Butakov)
- Improve model for white clots.
- Tuning of coefficient in dependence of von Willebrant length and concentration.
- Modelling of clot formation in left ventrical appendage.



Thank you for your attention!

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Links

- WWW.INMOST.ORG

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