# Математические модели тромбообразования в потоке крови в движущейся области

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# Two basic mechanisms of coagulation

Basic mechanisms:

- primarily fibrin polymerization (e.g. due to tissue injury) $\rightarrow$ red clot
- primarily platelet adhesion (due to increased shear stress) $\rightarrow$ white clot

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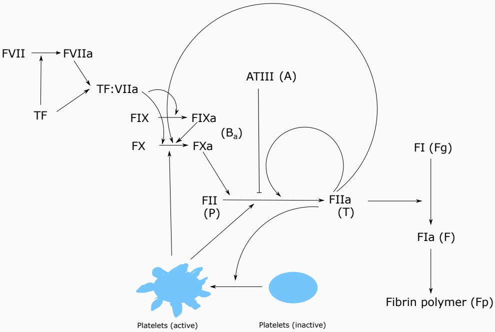
Tissue factor (TF) exposed in vessel injury of

- arteries: platelets adhere to subendothelium $\rightarrow$ white clot
- veins: fibrin propagates earlier and prevents platelets from aggregating $\rightarrow$ red clot (platelets accelerate production of fibrin mesh)

# Blood coagulation caused by injury of vein




prothrombin $P$ (factor FII)

thrombin $T$ (factor FIIa)

antithrombin $A$ (factor ATIII)

fibrinogen $G$ (factor FI)

fibrin $F$ (factor FIa)

fibrin polymer $M$

inactive platelets $\phi_f$

active platelets $\phi_a$

tissue factor $TF$

# Equation of the model for blood coagulation

Navier–Stokes equations & Brinkman term: $\operatorname{div}(\mathbf{u}) = 0$

$$\partial_t \mathbf{u} + \operatorname{div}\left(\mathbf{u}\mathbf{u}^T - \nu_b\left(\nabla\mathbf{u} + \nabla\mathbf{u}^T\right) + p\mathbb{I}\right) + \frac{\nu_b}{K}\mathbf{u} = \mathbf{0}$$

Coagulation eqs. for blood factors **(prothrombin $P$, thrombin $T$, tissue factors $B$, antithrombin $A$, fibrinogen $G$, fibrin $F$, fibrin polymer $M$, platelets $\phi_f$, $\phi_a$)**

$$\partial_t P + \operatorname{div}(\mathbf{u}P - D\nabla P) = -\left(k_1\phi_a + k_2 B + k_3 T + k_4 T^2 + k_5 T^3\right) P$$

$$\partial_t T + \operatorname{div}(\mathbf{u}T - D\nabla T) = \left(k_1\phi_a + k_2 B + k_3 T + k_4 T^2 + k_5 T^3\right) P - k_6 AT$$

$$\partial_t B + \operatorname{div}(\mathbf{u}B - D\nabla B) = (k_7\phi_a + k_8 T)(B^0 - B) - k_9 AB$$

$$\partial_t A + \operatorname{div}(\mathbf{u}A - D\nabla A) = -k_6 AT - k_9 AB$$

$$\partial_t G + \operatorname{div}(\mathbf{u}G - D\nabla G) = -k_{10} TG\,(k_{11} + G)^{-1}$$

$$\partial_t F + \operatorname{div}(\mathbf{u}F - D\nabla F) = k_{10} TG\,(k_{11} + G)^{-1} - k_{12} F$$

$$\partial \phi_f + \operatorname{div}(k(\phi_f, \phi_a)(\mathbf{u}\phi_f - D_p\nabla\phi_f)) = -(k_{13} T + k_{14}\phi_a)\phi_f$$

$$\partial \phi_a + \operatorname{div}(k(\phi_f, \phi_a)(\mathbf{u}\phi_a - D_p\nabla\phi_a)) = (k_{13} T + k_{14}\phi_a)\phi_f$$

$$\partial_t M = k_{12} F$$

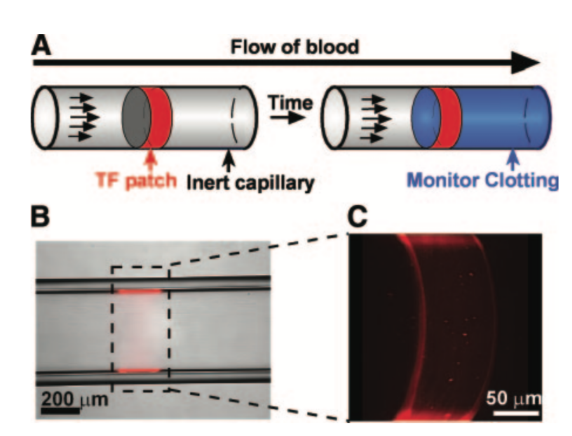
$$\frac{1}{K} = \frac{16}{r^2} S^{3/2}\left(1 + 56 S^3\right)\frac{\phi_f + \phi_a}{\phi_f - \phi_a}$$

$$k(\phi_f, \phi_a) = \tanh\left(\pi\frac{\phi_{\max} - \phi_f - \phi_a}{\phi_{\max}}\right), \qquad S = \min\{0.7; M/7000\}$$

+ initial and boundary conditions

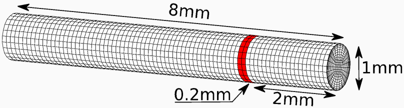
**Bouchnita, A., Terekhov, K., Nony, P., Vassilevski, Y., Volpert, V.: A mathematical model to quantify the effects of platelet count, shear rate, and injury size on the initiation of blood coagulation under venous flow conditions. PloS one, 15(7), e0235392, 2020**

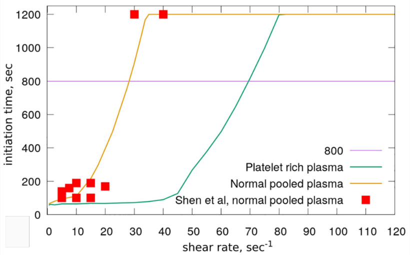
# Experiment in microfluidic capillaries




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.

# Numerical experiment in microfluidic capillaries




For shear rate $< 30\mathrm{s}^{-1}$ the flow of the normal pooled plasma is occluded at $t \sim 180\mathrm{s}$.

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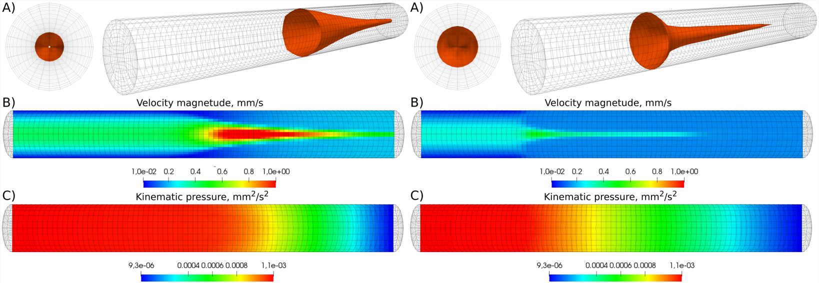
# Numerical experiment in microfluidic capillaries

60 s

70 s

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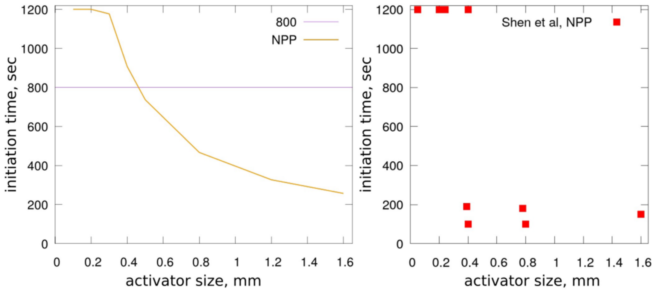


Clotting initiation time for normal pooled plasma and platelates rich plasma as a function of TF patch size for shear rate $40\mathrm{s}^{-1}$


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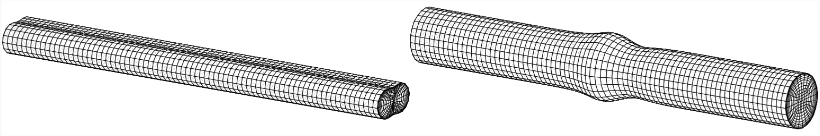
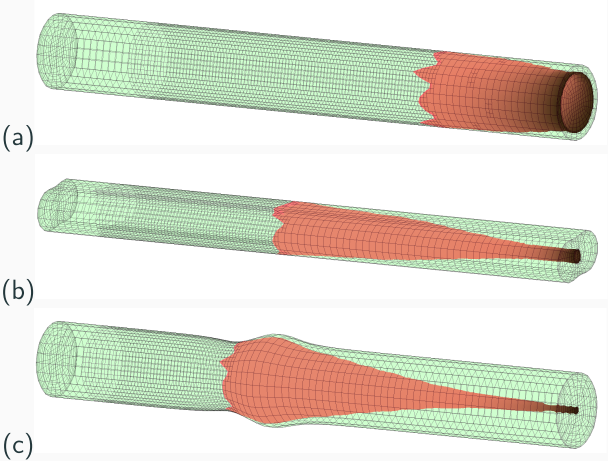
# Blood coagulation in pulsating capillaries



Dumbbell-shaped deformation and pulse-wave deformation at $t = 8\mathrm{s}$. The outflow is to the left; the deformation is periodic with period $16\mathrm{s}$.

**K.Terekhov, I.Butakov, A.Danilov, Yu.Vassilevski. Dynamic adaptive moving mesh finite-volume method for the blood flow and coagulation modeling. Int J Numer Meth Biomed Engng. 2023; e3731. doi:10.1002/cnm.3731**

# Blood coagulation in pulsating capillaries




Normal pooled plasma, $K^{-1}$-isosurface 100 ($mm^{-2}$) at t = 87 s for (A) static capillary, (B) dumbbell-shaped deformation and (C) pulse-wave deformation. The outflow is to the right

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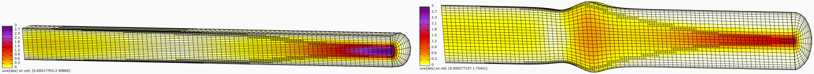

Velocity magnitude $|\mathbf{u}| \in [0, 3]$ $\mathrm{m/s}$ at $t = 87$ $\mathrm{s}$ for dumbbell-shaped and pulse-wave deformations. The outflow is to the right.

**At $K^{-1} = 100$ mm$^{-2}$ the fluid flow is obstructed by the clot: $|\mathbf{u}|$ drops in region with $K^{-1} \geq 100$ mm$^{-2}$**

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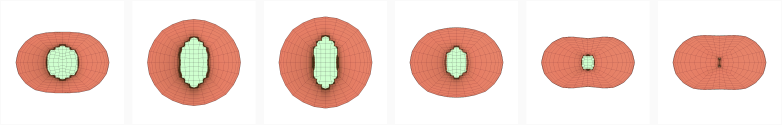

Front view of $K^{-1}$-isosurface 100 mm$^{-2}$ at $t = \{75, 78, 81, 84, 87, 90\}$ s for dumbbell-shaped deformation

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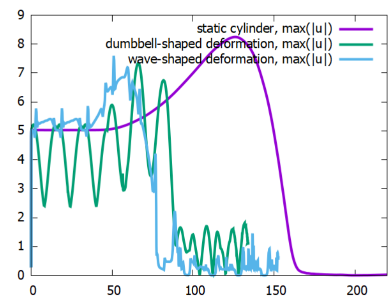


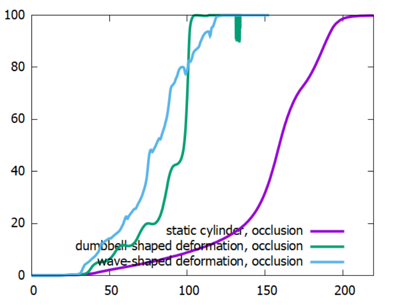


Maximal velocity

Volumetric occlusion

$$V_{occ} = \frac{1}{|\Omega|} \sum_{\omega_i} |\omega_i| \max\left(0.01 K^{-1}, 1\right) \cdot 100$$

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# Conclusion

- The proposed model for fibrin (“red”) clot formation relates platelets, blood flow, tissue factors, and other elements of hemostasis
- The model fits coagulation experiments with PRR and NPP in microfluidic capillaries
- Pulsating capillaries accelarate clotting