A mathematical model for blood clot growth based on “advection—diffusion” equations

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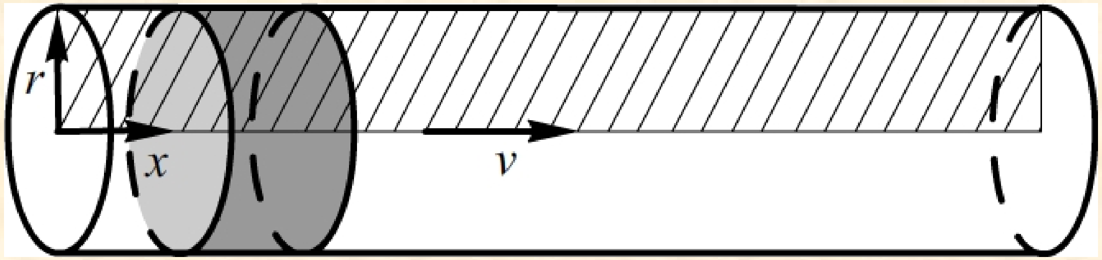
Mathematical model for platelet transport in a shear flow and platelet clot formation

- The goal is to develop an adequate model for platelet clot formation



- Vessel walls are rigid
- Pulse waves are considered as negligible
- Blood → plasma + platelets

Mathematical model for platelet transport in a shear flow

Platelets travel due to

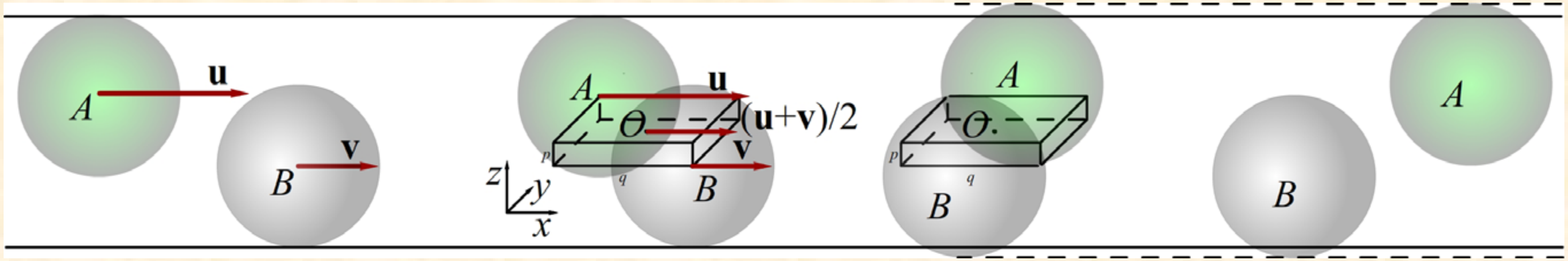
- flow of fluid
- and shear-induced diffusion.

Shear-induced diffusion of platelets

- Particles of radius a in a shear flow of viscous fluid
- Move with parallel velocities, **u** > **v**.
- Reynolds number is small – from 1 to 100.

During the collision

- velocity the center of mass is constant,
- particles don't slip or roll on each other



Evaluation of shear-induced diffusion matrix for platelets

$$D_{xx} = \frac{1}{2}\nu\left\langle \Delta x \right\rangle^2 \qquad \nu = 4a^2\pi c(r)\frac{\partial v}{\partial r}$$

$$\mathbf{D} = \begin{pmatrix} D_{\parallel} & D_{\parallel\perp} \\ D_{\perp\parallel} & D_{\perp} \end{pmatrix} = \frac{va^2}{2}\begin{pmatrix} \frac{2}{9} & \frac{1}{3}\sqrt{4K - \frac{\pi}{2} - \frac{1}{3}} \\ \frac{1}{3}\sqrt{4K - \frac{\pi}{2} - \frac{1}{3}} & 2K - \frac{\pi}{4} - \frac{1}{6} \end{pmatrix}$$

$$\mathbf{D} \approx \frac{va^2}{2}\begin{pmatrix} 0,22 & 0,44 \\ 0,44 & 0,87 \end{pmatrix}$$

Platelets

•"full" — "empty",
•"passive" — "active".

• w — activator concentration,
• c_p, c_f, c — concentrations of "passive", "full" and all "active" platelets,
• k_1, k_2, k_w — reactions rates constants.

- The transformation of "passive" platelets to "active" ones due to interaction with activator is described by a function

$$f(c_p, w) = \frac{k \cdot w^m \cdot c_p}{w^m + w_0^m},$$

where k, w_0, m — constants.

Equations for platelets and activator concentrations balance

$$\frac{\partial w}{\partial t} = -k_w w + k_1 c_f - (\mathbf{V}, \nabla w) + D_w \operatorname{div}(\nabla w)$$

$$\frac{\partial c_p}{\partial t} = -f(c_p, w) - (\mathbf{V}, \nabla c_p) + \operatorname{div}(\mathbf{D} \nabla c_p)$$

$$\frac{\partial c_f}{\partial t} = f(c_p, w) - k_2 c_f - (\mathbf{V}, \nabla c_f) + \operatorname{div}(\mathbf{D} \nabla c_f)$$

$$\frac{\partial c}{\partial t} = f(c_p, w) - (\mathbf{V}, \nabla c) + \operatorname{div}(\mathbf{D} \nabla c)$$

- **D** — diffusion matrix,
- **V** — flow velocity

Boundary conditions

- Full flux of platelets $\mathbf{W} = -\mathbf{D}\nabla u + \mathbf{V}u$
- Vessel axis: symmetry,
- Inlet: constant concentration is given,
- Outlet: non-reflective conditions,
- Vessel wall: normal flux $W_\eta|_{r=R(x)}=0$,
- Active area of the vessel wall:

$$W_\eta|_{r=R(x)} = c\,\mathrm{div}\mathbf{Dn},\ c = c(W_\eta, W_\xi)$$

Calculation algorithm

- Velocity field calculation (Navier—Stokes equation in a complex area)
- Calculation of concentrations (physical processes split)
  - Reaction part by Gear method,
  - Diffusive part by the modified method, proposed by Favorsky,
- If the amount of stuck platelets is enough, then
  - mesh rebuilding,
  - conservative quantities conversion to the new mesh.

Diffusive part of equations calculation method

- Equations for concentrations balance in a flux form:

$$\frac{\partial u}{\partial t} = -\mathrm{div}\mathbf{W}, \qquad (1)$$

$$\mathbf{W} = -\mathbf{D}\nabla u + \mathbf{V}u, \qquad (2)$$

- where *u* is one of concentrations — w, c_p, c_f или c.

- The equation (2) minimizes a functional

$$F(\mathbf{W}) = \int_V \left(\frac{(\mathbf{W},\mathbf{W})}{2} - (\mathbf{V},\mathbf{W})u \right) dV + \boxed{\int_V (\mathbf{D}\nabla u, \mathbf{W}) dV}$$

Calculations

- All platelets considered to be "activated":

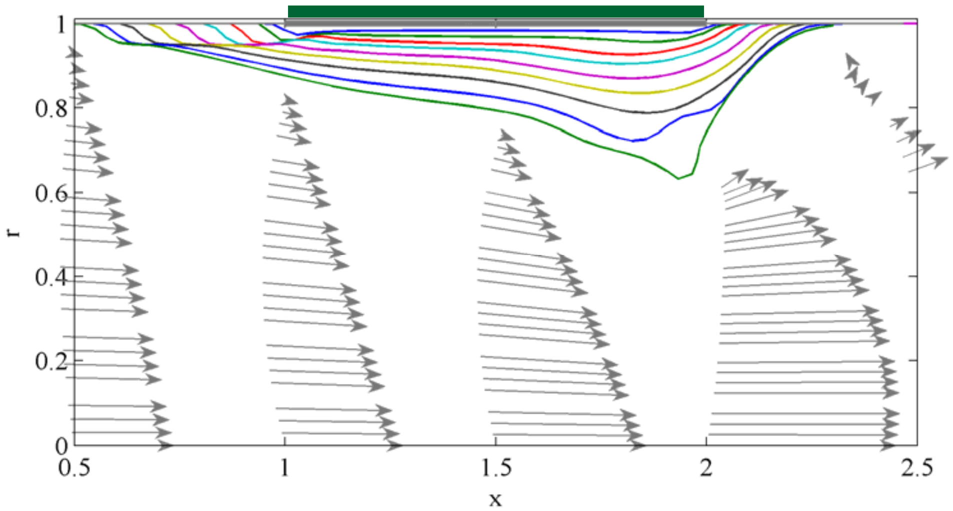
$$\frac{\partial c}{\partial t} = f(c_p, w) - (\mathbf{V}, \nabla c) + \mathrm{div}(\mathbf{D} \nabla c)$$

- Equations were solved in a dimensionless form.

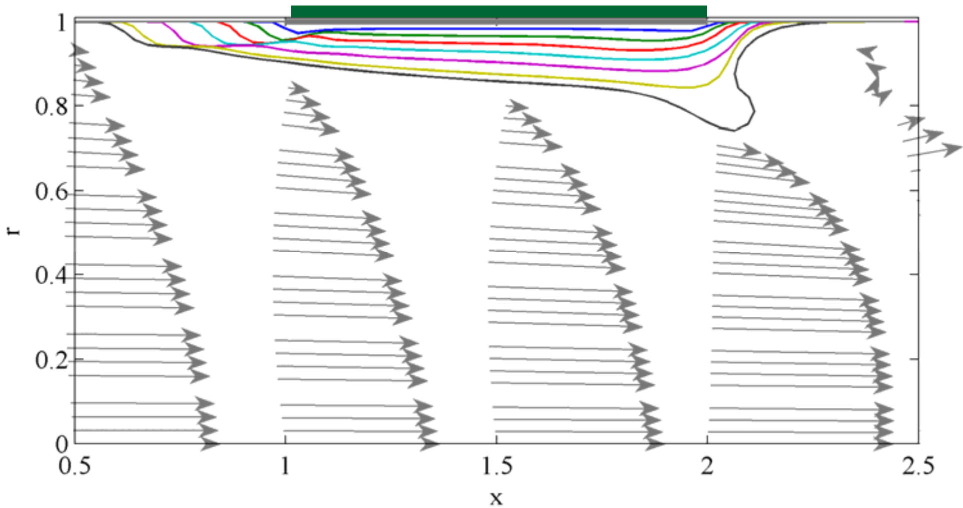
  The characteristic dimension = *R* — vessel radius.

Blood clot's shape depends on Reynolds number

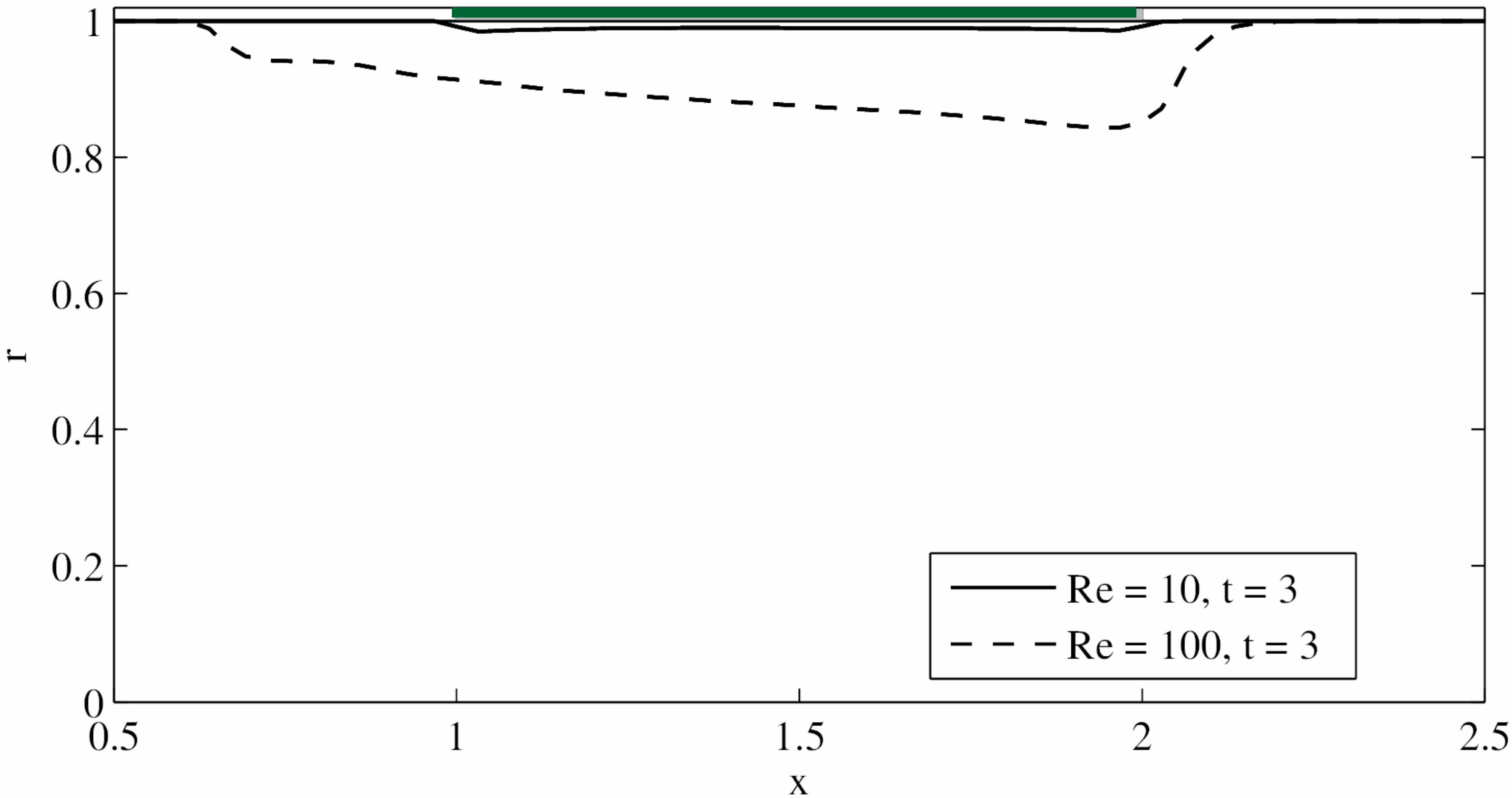
Re~10,
t=5, 10,… 40, 42.76



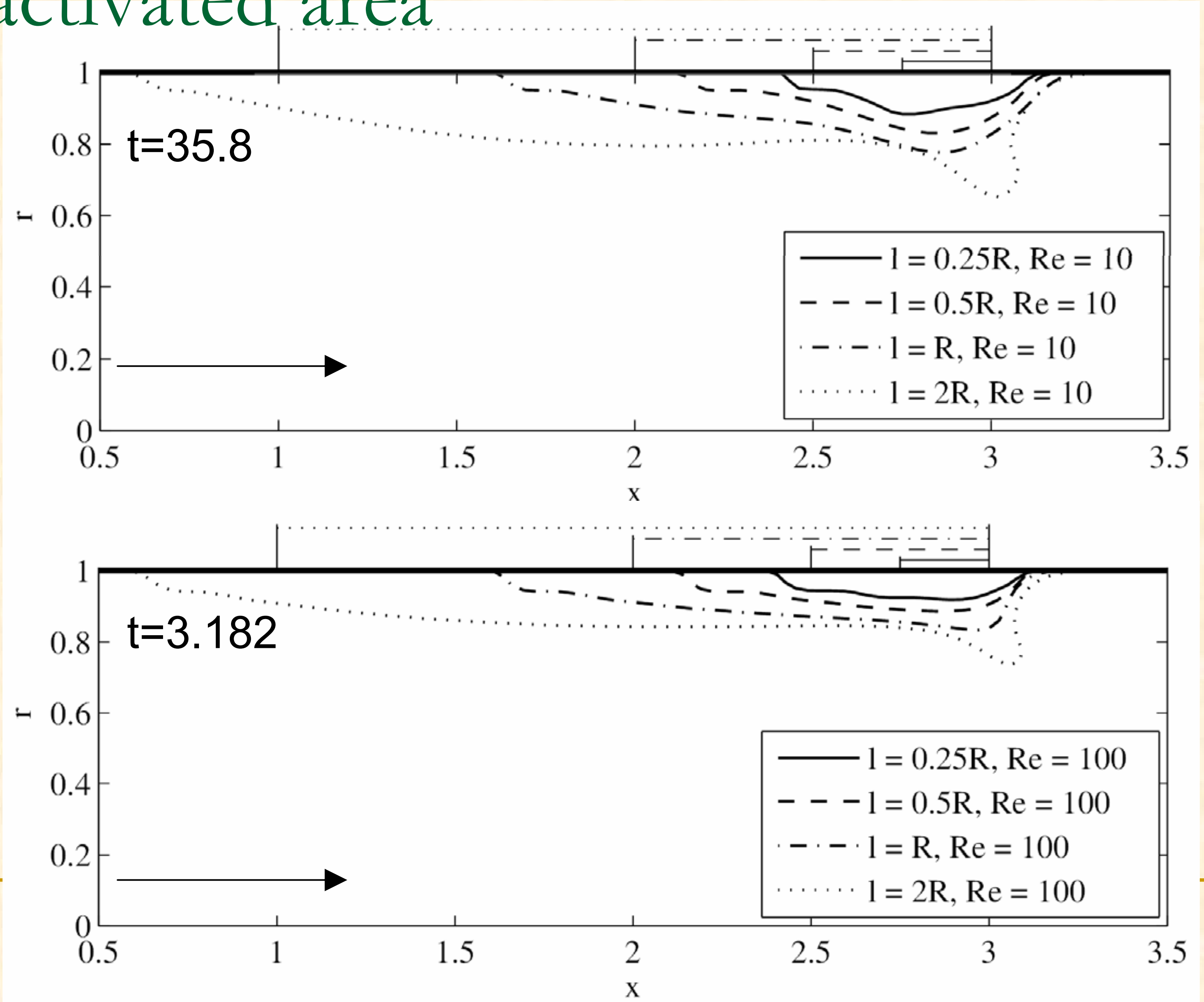
Re~100,
t=0.5, 1,… 3, 3.182



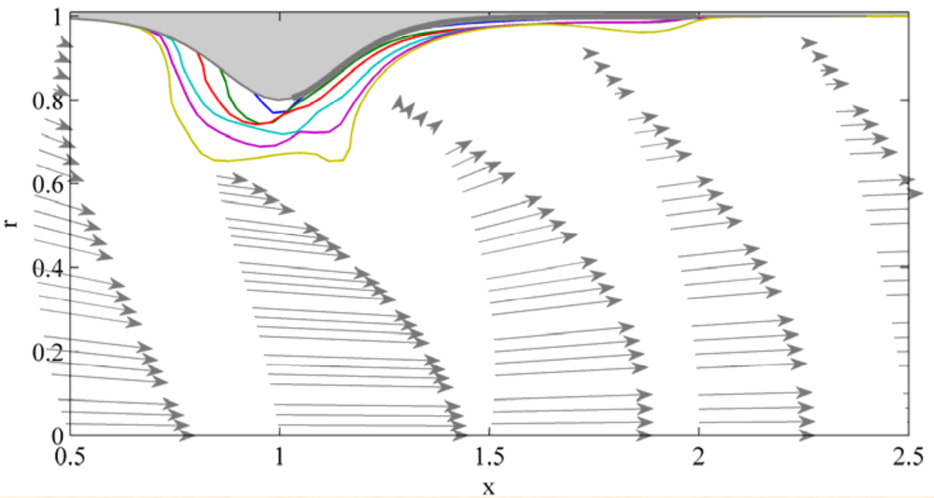
Clot growth rate depends on Re

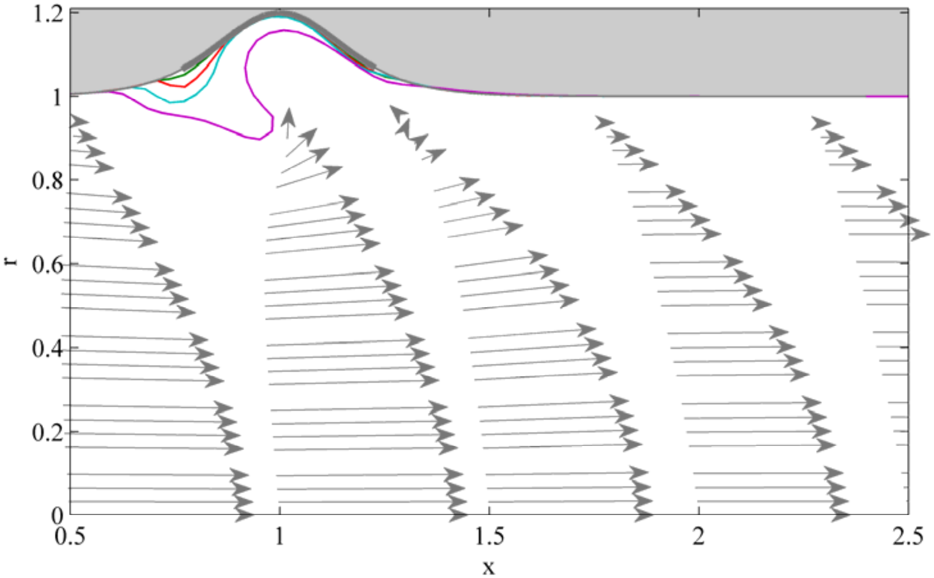


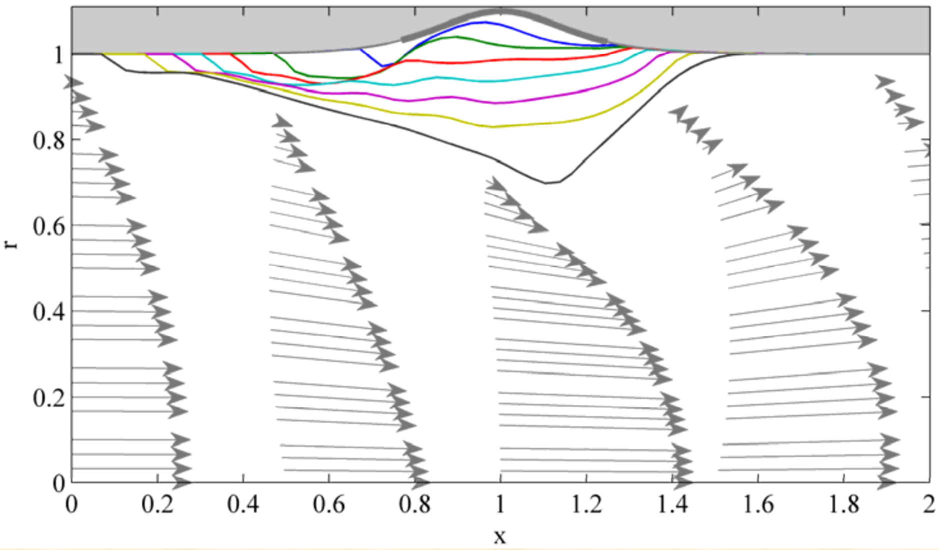
Blood clot's shape depends on the length of activated area



Blood clots on a stenosis and an aneurism, Re=10







Conclusions

- Components of shear-induced diffusion matrix for platelets in the shear flow are estimated.
- The numerical method for calculation of equations, describing platelet transport in a viscous fluid flow is modified and implemented into software. It is taken into account that the shear-induced diffusion matrix for platelets is full.
- On basis of numerical calculations it is showed that the platelet clot shape in viscous fluid flow depends on Reynolds number and on the size of vessel wall activated area.