Modelling and simulation of interactions of reactive flow with a solid structure leading to volume changes

Application to plaque formations in arteries

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Outline

Motivation

- The interaction of reactive flow with a solid structure is an important aspect in various applications.

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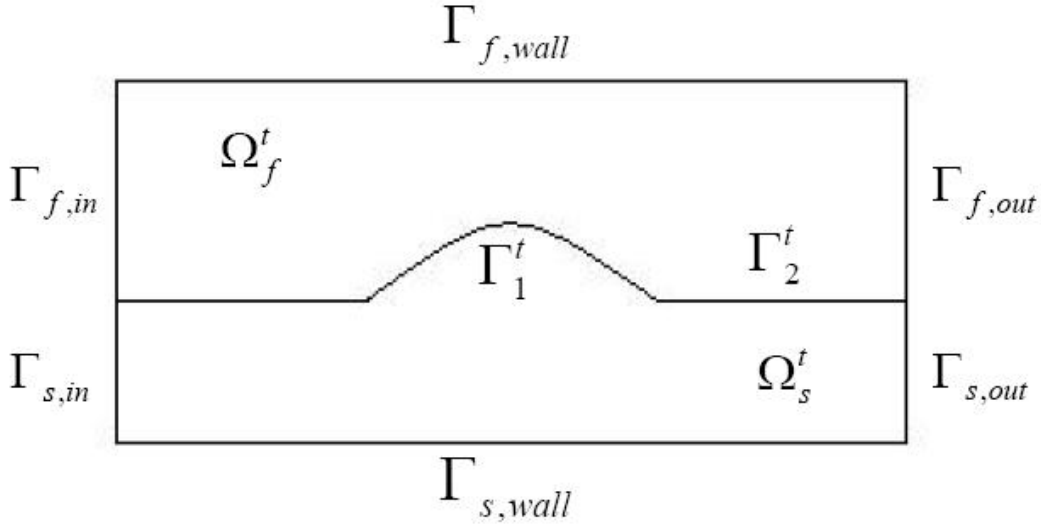
- Penetration of chemical substances from the flow into the solid phase leads to changes in volume of the solid.

Motivation

Volume Changes



- Ω_f^t: the fluid domain; Ω_s^t: the solid domain.
- $\Gamma_1^t \cup \Gamma_2^t$: the interface between Ω_f^t and Ω_s^t. Γ_1^t is permeable to chemical substances.
- Chemical substances migrate through Γ_1^t from Ω_f^t into Ω_s^t. Their accumulation and chemical reactions lead to volume growth of Ω_s^t.

Motivation

- The interaction of reactive flow with a solid structure is an important aspect in various applications.
- Penetration of chemical substances from the flow into the solid phase leads to changes in volume of the solid.
- This type of processes occurs e.g. in plaque formation in arteries.

Outline

Processes to be modeled

- Main processes of such interaction can be categorized as either biomechanical or biochemical.
  - Biomechanical processes: fluid-structure interaction between reactive flow and solid structure.
  - Biochemical processes: transport and reactions of chemical substances.
- The problems of biomechanical and biochemical processes are coupled with growth modeling.

Processes to be modeled

- Main variables:
  - p: pressure (both in Ω_f^t and Ω_s^t) ρ: density (in Ω_s^t)
  - v: velocity (both in Ω_f^t and Ω_s^t) u: displacement (in Ω_s^t)
  - $c_{1,f}, c_{2,f}, ..., c_{n,f}$: concentrations of chemical substances (in Ω_f^t)
  - $c_{1,s}, c_{2,s}, ..., c_{m,s}$: concentrations of chemical substances (in Ω_s^t)
  - g: metric of growth(in Ω_s^t)

- All the variables are distinguished by lower indexes "f" and "s" in Ω_f^t and Ω_s^t.
- All the equations are derived in Eulerian coordinate.

Outline

Derivation of the Equations

Fluid-Structure Interaction Problem

- The fluid dynamics (incompressible fluid):

$$div v_f = 0 \quad \text{in} \quad \Omega_f^t$$
$$\rho_f \partial_t v_f + \rho_f v_f \cdot \nabla v_f = div \sigma_f \quad \text{in} \quad \Omega_f^t$$

- The structural mechanics (elastic material):

$$\partial_t \rho_s + div(\rho_s v_s) = f_s^g \quad \text{in} \quad \Omega_s^t$$
$$\rho_s \partial_t v_s + \rho_s v_s \cdot \nabla v_s = div \sigma_s \quad \text{in} \quad \Omega_s^t$$
$$\partial_t u_s + v_s \cdot \nabla u_s = v_s \quad \text{in} \quad \Omega_s^t$$

Derivation of the Equations

Reactive Transport Problem

- Motion of chemical substances in Ω_f^t:

$$\partial_t c_{i,f} + div(c_{i,f} v_f) - D_{i,f} \triangle c_{i,f} = 0 \quad \text{in} \quad \Omega_f^t, \quad i = 1, 2, ..., n$$

- Motion of chemical substances in Ω_s^t:

$$\partial_t c_{j,s} + div(c_{j,s} v_f) - div(D_{j,s} \nabla c_{j,s}) = f_{j,s}^r \quad \text{in} \quad \Omega_s^t, \quad j = 1, 2, ..., m$$

  - Reaction functions:

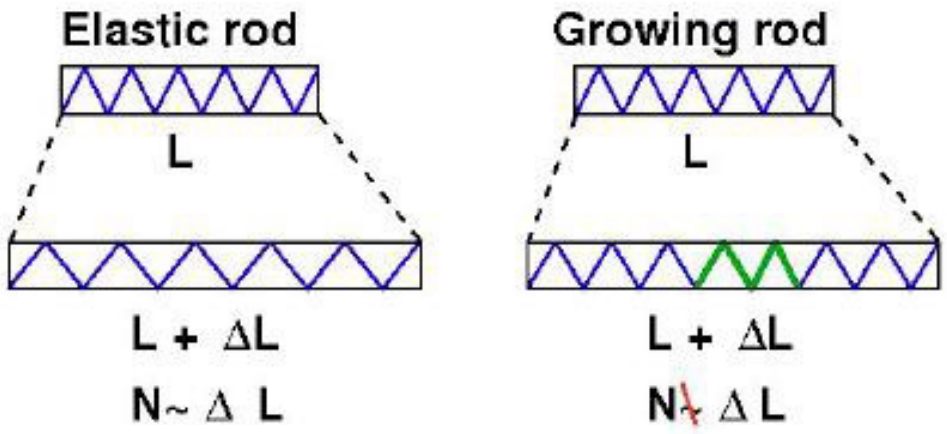
$$f_{j,s}^r = f_{j,s}^r(c_{1,s}, c_{2,s}, ..., c_{m,s}) \quad j = 1, 2, ..., m$$

Derivation of the Equations

The stress tensor σ_s

- σ_s is determined by the deformation gradient F_s:

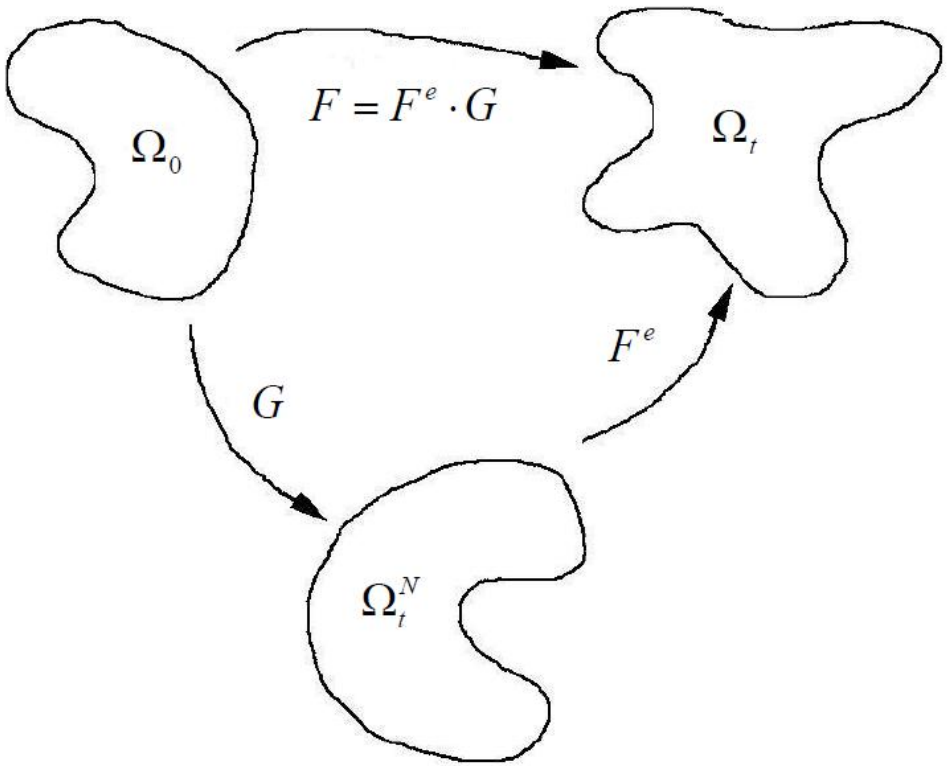
$$\sigma_s = \sigma_s(F_s), \quad F_s = ?$$



- Growth may falsify the usual way of quantifying the deformation.

Derivation of the Equations

The decomposition of deformation gradient



- Ω_t^N: the natural configuration of the domain at time t
- F_s is decomposed in a product of corresponding tensors G_s and F_s^e.

Derivation of the Equations

Growth modeling

- The growth matrix:

$$F_s = F_s^e \cdot G_s, G_s = g_s I$$

$$\sigma_s = \sigma_s(F_s^e)$$

- The metric of growth:

$$d\partial_t g_s + dv_s \cdot \nabla g_s = \frac{f_s^g}{\rho_s} g_s \quad \text{in} \quad \Omega_s^0$$

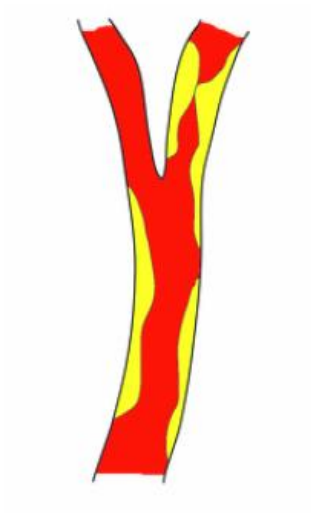
  - Growth function:

$$f_s^g = f_s^g(f_{1,s}^r, f_{2,s}^r, ..., f_{m,s}^r)$$

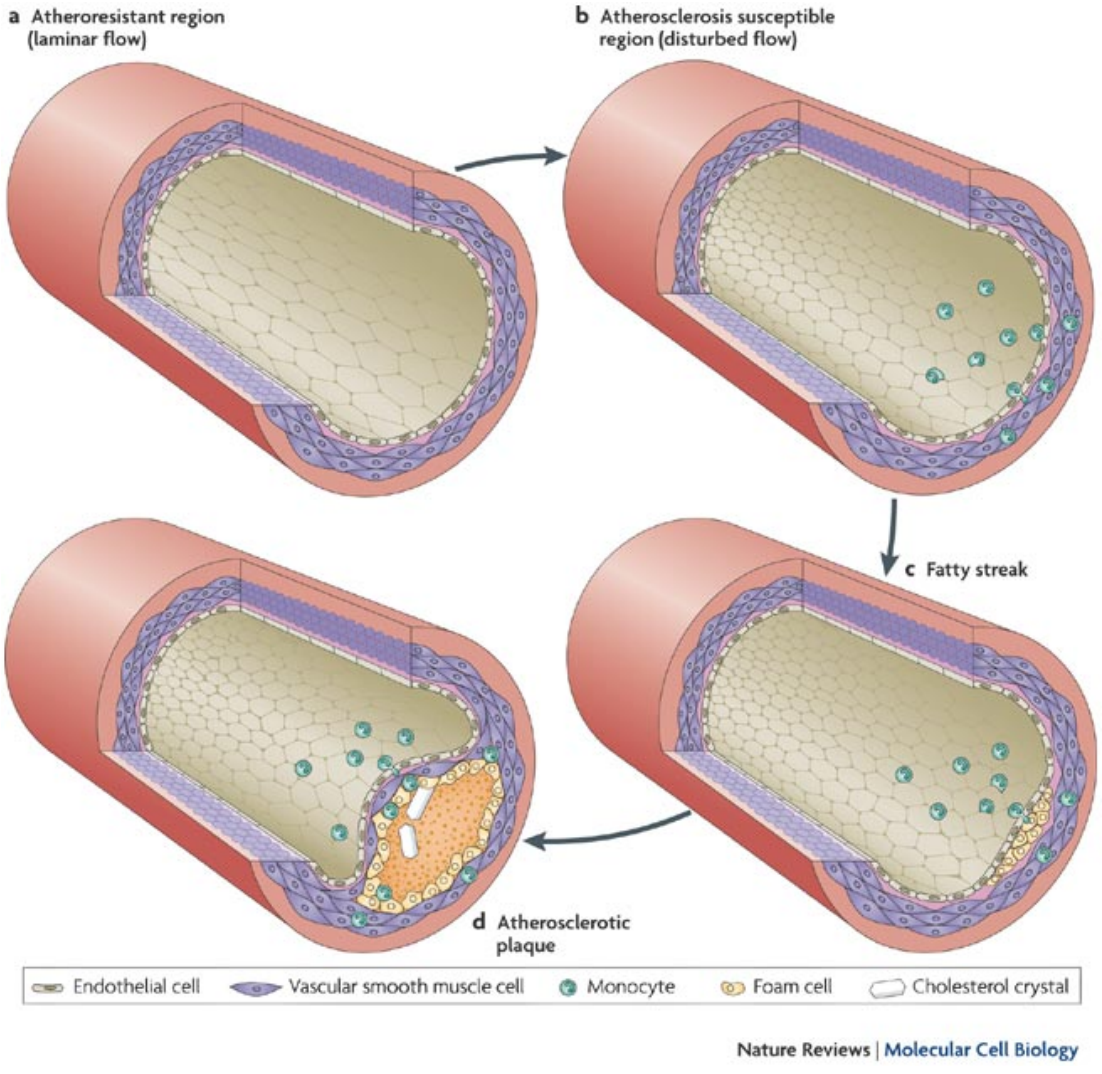
Outline

Atherosclerotic Plaque Formation

- Plaque formation is induced by penetration of monocytes. The growth and rupture of plaque is one of the main causes for blockage of a main artery which can lead to ischaemic brain infarct, heart attack and some other cardiovascular diseases.

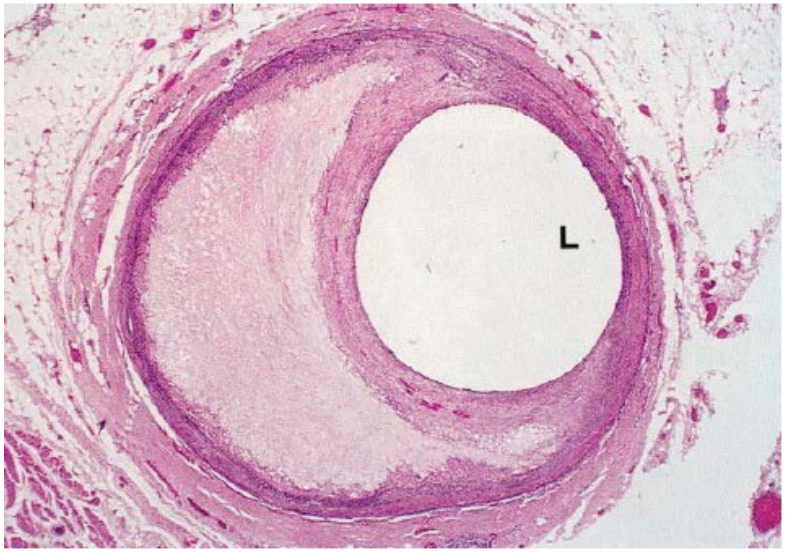


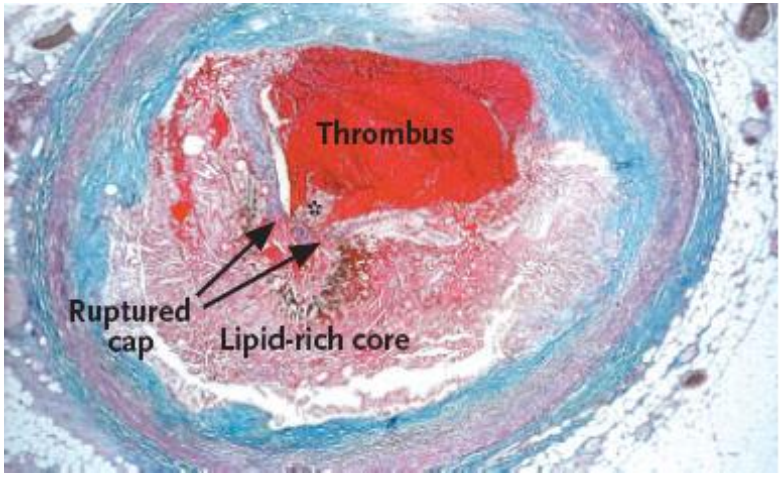
Atherosclerotic Plaque Formation



Hahn and Schwartz, Nature Reviews 10:53-62, 2009

Atherosclerotic Plaque Formation





- Foam cells form a lipid core surrounded by a fibrous cap formed by smooth muscle cells, narrowing the vessel lumen and making the plaque be vulnerable.
- If plaque rupture happens on the fibrous cap, an occlusive thrombus will be superimposed on the plaque to block the vessel.

Outline

Mathematical Model

- Ω_f^t is occupied by blood flow.
- Ω_s^t is occupied by vessel wall.
- Chemical substances:
  - c_f: concentration of monocytes (in Ω_f^t)
  - c_s: concentration of macrophages (in Ω_s^t)
  - c_s^*: concentration of foam cells (in Ω_s^t)
- All the equations are derived in Eulerian coordinate in Ω_f^t and in Lagrangian coordinate in Ω_s^0.

Mathematical Model

- Fluid-structure interaction problem:

$$
\begin{aligned}
div v_f &= 0 \quad \text{in} \quad \Omega_f^t \\
\rho_f \partial_t v_f + \rho_f v_f \cdot \nabla v_f &= div \sigma_f \quad \text{in} \quad \Omega_f^t \\
\hat{J}_s \hat{\rho}_s \partial_t \hat{v}_s &= \widehat{div}(\hat{J}_s \hat{\sigma}_s \hat{F}_s^{-T}) \quad \text{in} \quad \Omega_s^0 \\
\partial_t \hat{u}_s &= \hat{v}_s \quad \text{in} \quad \Omega_s^0
\end{aligned}
$$

- Reactive transport problem:

$$
\begin{aligned}
\partial_t c_f + v_f \cdot \nabla c_f - D_f \triangle c_f &= 0 \quad \text{in} \quad \Omega_f^t \\
\partial_t(\hat{J}_s \hat{c}_s) - \widehat{div}(\hat{J}_s \hat{F}_s^{-1} \hat{D}_s \hat{F}_s^{-T} \hat{\nabla} \hat{c}_s) &= -\hat{J}_s \hat{f}_s^r \quad \text{in} \quad \Omega_s^0 \\
\partial_t(\hat{J}_s \hat{c}_s^*) &= \hat{J}_s \hat{f}_s^r \quad \text{in} \quad \Omega_s^0.
\end{aligned}
$$

Mathematical Model

- The metric of growth:

$$d\partial_t \hat{g}_s = \frac{\hat{f}_s^g}{\hat{\rho}_s} \hat{g}_s \quad \text{in} \quad \Omega_s^0$$

- Growth function:

$$\hat{f}_s^g = \hat{f}_s^g(\hat{f}_s^r)$$

- Reaction functions:

$$\hat{f}_s^r = \hat{f}_s^r(\hat{c}_s)$$

Mathematical Model

- Constitutive equations:

$$\sigma_f = -p_f I + \rho_f \nu(\nabla v_f + \nabla v_f^T) \quad \text{(Navier-Stokes)} \quad \text{in} \quad \Omega_f^t$$

$$\hat{\sigma}_s = -\hat{p}_s I + \hat{\mu}_s(\hat{F}_s^e \hat{F}_s^{eT} - I) \quad \text{(incompressible neo-Hookean)} \quad \text{in} \quad \Omega_s^0$$

$$\hat{F}_s^e = \hat{F}_s \hat{G}_s^{-1} = \frac{1}{\hat{g}_s} \hat{F}_s \quad \text{in} \quad \Omega_s^0$$

- Transmission conditions on the interface:

$$\sigma_f \cdot n_f + \sigma_s \cdot n_s = 0, \quad v_f = v_s \quad \text{on} \quad \Gamma_1^t \cup \Gamma_2^t$$

$$D_f \nabla c_f \cdot n_f + D_s \nabla c_s \cdot n_s = 0 \quad \text{on} \quad \Gamma_1^t \cup \Gamma_2^t$$

$$D_f \nabla c_f \cdot n_f + \zeta(c_f - c_s) = 0 \quad \text{on} \quad \Gamma_1^t \cup \Gamma_2^t$$

Outline

Numerical Simulation

- Main difficulty of Numerics:
  - The equations are formulated in different coordinates (Eulerian coordinate in Ω_f^t and Lagrangian coordinate in Ω_s^0).
  - Some of the equations are formulated in the moving domain Ω_f^t, so we need different meshes at each time step.

- The clue to treat this problem is to formulate the systems in one common coordinate: Arbitrary Lagrangian Eulerian(ALE) Coordinate.
  - All the equations are rewritten in the fixed domain Ω_f^0 or Ω_s^0.
  - The construction of the ALE mapping in Ω_f^0 is obtained in terms of the artificial variable $\hat{u}_f$, which is defined by harmonic extension.

Numerical Simulation

Variational formulation in ALE Coordinate

- Fluid-structure interaction problem:

$$(\hat{J}\hat{\rho}_f(\partial_t\hat{v} + \hat{F}^{-1}(\hat{v} - \partial_t\hat{u})\cdot\hat{\nabla}\hat{v}), \hat{\phi}^v)_{\Omega_f^0} + (\hat{J}\hat{\rho}_s\partial_t\hat{v}, \hat{\phi}^v)_{\Omega_s^0}$$

$$+ (\hat{J}\hat{\sigma}_f\hat{F}^{-T}, \hat{\nabla}\hat{\phi}^v)_{\Omega_f^0} + (\hat{J}\hat{\sigma}_s\hat{F}^{-T}, \hat{\nabla}\hat{\phi}^v)_{\Omega_s^0} = \langle \hat{g}_f^{out}, \hat{\phi}^v\rangle_{\Gamma_{f,out}}$$

$$(\hat{div}(\hat{J}\hat{F}^{-1}\hat{v}), \hat{\phi}^p)_{\Omega_f^0} + (\hat{J}_s^e - 1, \hat{\phi}^p)_{\Omega_s^0} = 0$$

$$\alpha(\hat{\nabla}\hat{u}, \hat{\nabla}\hat{\phi}^u)_{\Omega_f^0} + (\partial_t\hat{u} - \hat{v}, \hat{\phi}^u)_{\Omega_s^0} = 0$$

$$\begin{aligned}
\hat{\sigma}_f &= -\hat{p}I + \hat{\rho}_f\nu(\hat{\nabla}\hat{v}\hat{F}^{-1} + \hat{F}^{-T}\hat{\nabla}\hat{v}^T)\\
\hat{\sigma}_s &= -\hat{p}_sI + \hat{\mu}_s(\hat{F}_s^e\hat{F}_s^{eT} - I)\\
\hat{g}_f^{out} &= \hat{J}\hat{\rho}_f\nu\hat{F}^{-T}\hat{\nabla}\hat{v}^T\hat{F}^{-T}
\end{aligned}$$

Numerical Simulation

- Reactive transport problem:

$$(\hat{J}\partial_t\hat{c}_f, \hat{\phi}_f^c)_{\Omega_f^0} + (\hat{J}\hat{F}^{-1}(\hat{v} - \partial_t\hat{u}) \cdot \hat{\nabla}\hat{c}_f, \hat{\phi}_f^c)_{\Omega_f^0} + (\hat{J}D_f\hat{F}^{-T}\hat{\nabla}\hat{c}_f, \hat{F}^{-T}\hat{\nabla}\hat{\phi}_f^c)_{\Omega_f^0}$$
$$= \langle\zeta(\hat{c}_f - \hat{c}_s)\hat{J}|\hat{F}^{-T} \cdot N_f|, \hat{\phi}_f^c\rangle_{\Gamma_1^0\cup\Gamma_2^0}$$

$$(\partial_t(\hat{J}\hat{c}_s), \hat{\phi}_s^c)_{\Omega_s^0} + (\hat{J}\hat{D}_s\hat{F}^{-T}\hat{\nabla}\hat{c}_s, \hat{F}^{-T}\hat{\nabla}\hat{\phi}_s^c)_{\Omega_s^0} + (\hat{J}\hat{f}_s^r, \hat{\phi}_s^c)_{\Omega_s^0}$$
$$= \langle\zeta(\hat{c}_s - \hat{c}_f)\hat{J}|\hat{F}^{-T} \cdot N_s|, \hat{\phi}_s^c\rangle_{\Gamma_1^0\cup\Gamma_2^0}$$

$$(\partial_t(\hat{J}\hat{c}_s^*), \hat{\phi}_s^{c*})_{\Omega_s^0} - (\hat{J}\hat{f}_s^r, \hat{\phi}_s^{c*})_{\Omega_s^0} = 0$$

- Metric of growth:

$$(d\hat{\rho}_s\partial_t\hat{g}_s, \hat{\phi}_s^g)_{\Omega_s^0} - (\hat{f}_s^g\hat{g}_s, \hat{\phi}_s^g)_{\Omega_s^0} = 0$$

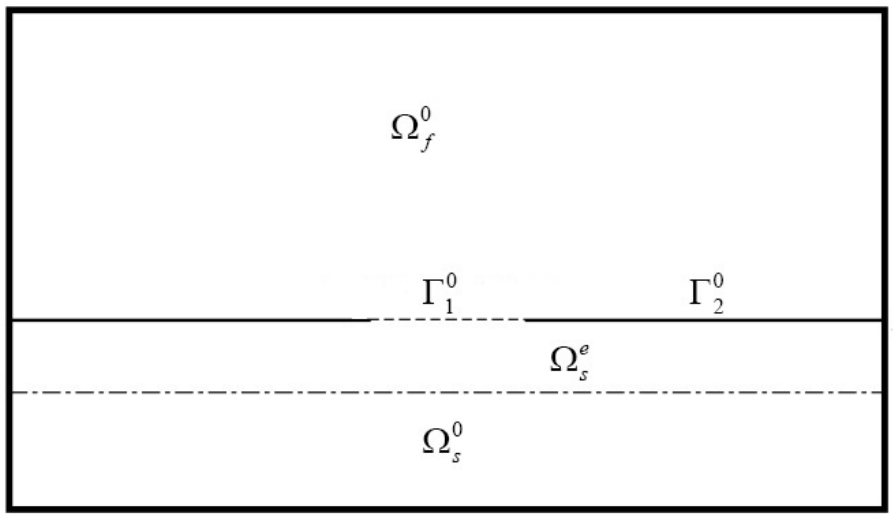
Numerical Methods

- Numerical simulations are performed by using Gascoigne, the software developed by the Numerical Methods Group in IWR, Heidelberg University.

- The time discretization is achieved with implicit backward Euler scheme.
- The spatial discretization is based on the Galerkin finite element method.
- The nonlinear problems are linearized and solved by Newton method.

Numerical Results

Initial Computational Domain



- The upper dashed line Γ_1^0 denotes the interface permeable for monocytes.
- The layer Ω_s^e between two dashed lines represents the endothelial cells and smooth muscle cells, where chemical reactions rarely take place.

Numerical Results

- Distribution of velocity in $x-$direction and motion of the interface

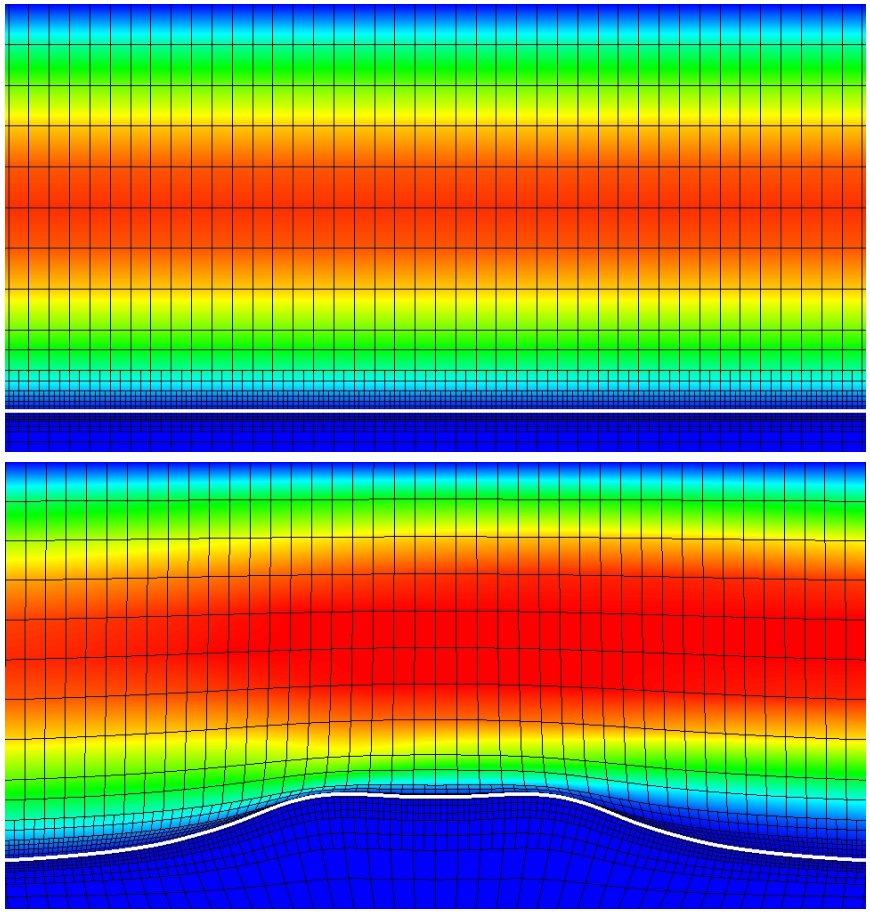
$t = 0$

$max\ v_x = 300mm/s$

$t = 4.5 \times 10^7$seconds

≈ 521days

$max\ v_x = 334.51mm/s$



Numerical Results

- Distribution of displacement in $y-$direction in Ω_s^t

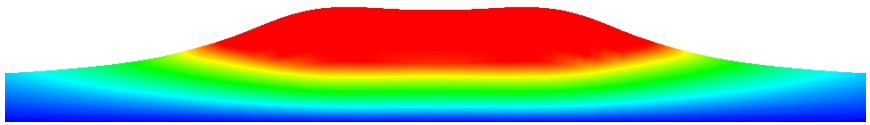
$t = 0$

$max\ u_{s,y} = 0mm$

$t = 4.5 \times 10^7$seconds

≈ 521days

$max\ u_{s,y} = 0.92mm$

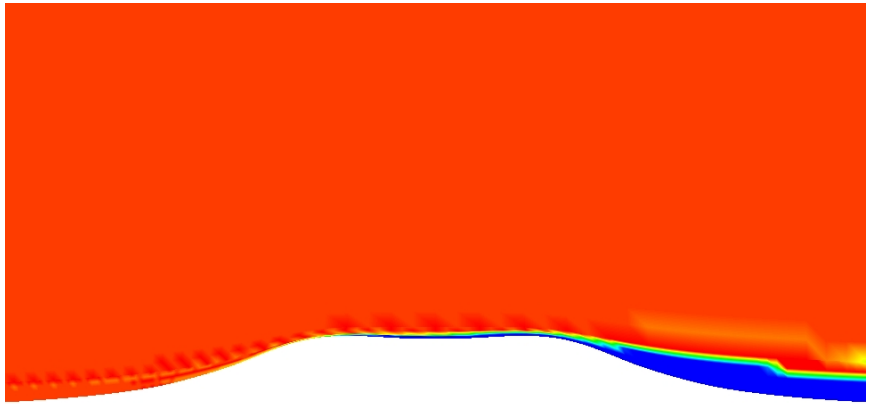


Numerical Results

- Distribution of concentration of monocytes in Ω_f^t

$t = 0$

$t = 4.5 \times 10^7$ seconds
≈ 521 days

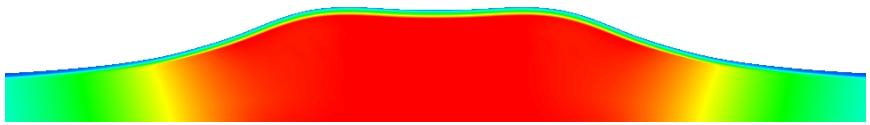


Numerical Results

- Distribution of concentration of foam cells in Ω_s^t

$t = 0$
$max\ c_s^* = 0/mm^3$

$t = 4.5 \times 10^7$seconds
≈ 521days
$max\ c_s^* = 1393/mm^3$



Numerical Results

- Distribution of principal stress in Ω_s^t

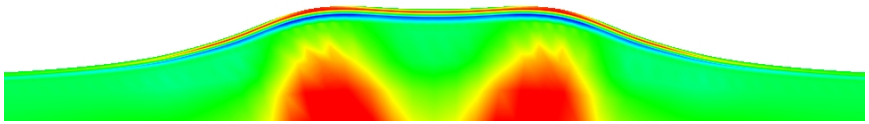
$t = 0$

$max\ \sigma_{s,p} = 0 g/mm \cdot s^2$

$t = 4.5 \times 10^7$ seconds

≈ 521 days

$max\ \sigma_{s,p} = 2662.98 g/mm \cdot s^2$



Outline

Conclusion and Outlook

- We treat a mathematical model consisting of a fluid-structure interaction problem coupled with a reactive transport problem.
- This model is used to describe plaque formation, and the numerical results are in good agreement with observations.
  - The penetration of monocytes and accumulation of foam cells lead to the formation and growth of plaques.
  - The formation and evolution of plaques induces the increase of stresses in the vessel wall, which is an indicator of plaque rupture.
- More realistic description of the vessel wall including the oscillation of blood flow and parameter estimation from real data will be considered.

Thank You!