An ALE approach to mechano-chemical processes in fluid-structure interactions

Yifan Yang∗ Thomas Richter† Willi Jäger‡ Maria Neuss-Radu§

Mathematical modeling and simulation of fluid-structure interaction problems are in the focus of research already for a longer period. However, taking into account also chemical reactions, leading to structural changes, including changes of mechanical properties of the solid phase is a rather new, but for many applications highly important area. This paper formulates a model system for reactive flow and transport in a vessel system, the penetration of chemical substances into the solid wall. Inside the wall, reactions take place which lead to changes of volume and of the mechanical properties of the wall. Numerical algorithms are developed and used to simulate the dynamics of such a mechano-chemical fluid-structure interaction problem. As a proof of concept scenario, plaque formation in blood vessels is chosen. A specific model system for this scenario was derived and the simulation results were discussed in [38]. The arbitrary Lagrangian Eulerian approach (ALE) is chosen to solve the systems numerically. Temporal discretization of the fully coupled monolithic model is accomplished by backward Euler scheme, and spatial discretization by stabilized finite elements. The numerical approach is verified by numerical tests and effective methods to maintain mesh qualities under large deformations are described. For realistic system parameters the simulations show that the plaque formation in blood vessel is a long-time effect. The time scale of the formation is in the simulation of comparable order as in reality.

1 Introduction

Modeling reactive flows, diffusion, transport and mechanical interactions in media consisting of multiple phases, e.g. of a fluid and a solid phase in a porous medium or a fluid in a vessel system interacting with the vessel walls, is giving rise to many problems for analysis, numerics and simulation. Besides of the fluid-structure interactions as mechanical systems, it is highly important to include chemical reactions and their effects on the mechanical properties and volume changes in particular of the solid structure. Processes of this kind occur in soil and in porous materials, but also in biological tissues and membranes. In [38], a system of partial differential equations was derived as a reduced model system for the process of plaque formation in blood vessels and simulation results were discussed.

∗Interdisciplinary Center for Scientific Computing, University of Heidelberg
†Institute for Analysis and Numerics, University of Magdeburg
‡Interdisciplinary Center for Scientific Computing, University of Heidelberg
§Department Mathematics, University of Erlangen-Nuremberg
Following this investigation, we are presenting here the scheme for the numerical solution of model systems for fluid-structure interactions including chemical reactions which lead to material changes of the solid structure, in particular changes of volume and in the physical parameters of the mechanical model for the solid structure. The model for the plaque formation is used as a prototypical case for the design of the algorithms and as a test case for evaluation of the simulations. This paper intends to contribute to the numerical methods for multiphase models coupling reactive flow, fluid and solid mechanics in domains moving according to interactions, which go beyond the purely mechanical ones considered usually in fluid-structure interaction, extensively treated in the literature, [4, 6, 10, 11, 13, 14, 20, 23, 28, 34]. In [39], the authors treated one-way coupled processes of reactive transport in a fluid-structure interaction environment. Our setting includes the feedback of the reacting species on the mechanical properties of the fluid and the solid. We will consider a model consisting of the following main steps:

1. The fluid-structure interaction problem coupling the dynamics of an incompressible Navier-Stokes fluid and the elasticity equations for the solid structure.

2. Diffusion, transport and reaction of the chemical or biological species, coupled with the dynamics of the growth of the structure. Here the reaction products induce growth as well as changes in the parameters of the mechanical model.

3. Coupling of the first two steps by combining the deformation due to the elastic effects and due to growth. Using the theory of multiple natural configurations, see [1, 22, 32], the deformation gradient is decomposed into a purely elastic part and a part associated to growth.

In the test case, blood is modelled as Newtonian fluid. The species transported in the blood flow and penetrating into the vessel wall, consists of monocytes. Monocytes are transformed to macrophages and finally to foam cells, increasing the volume and changing parameters in the mechanical model. Two laws for the wall mechanics are considered: the incompressible neo-Hookean model and the Mooney-Rivlin model.

The main aim of this paper is to construct an arbitrary Lagrangian Eulerian approach (ALE) to perform numerical simulations of coupled model systems of the type described above. A fully monolithic approach is chosen to solve the complete set of model equations. In the ALE framework, all the equations are rewritten in a fixed reference domain. The construction of the ALE mapping is obtained using harmonic or biharmonic extensions of solutions variables. Temporal discretization of the fully coupled monolithic model is accomplished by time-stepping schemes, and its spatial discretization is accomplished by stabilized finite elements [3, 5]. The discrete model is realized in the finite element Library GASCOIGNE 3D, see [27]. The discretized problem is highly nonlinear. It is linearized and solved by the Newton iteration. The designed method is applied to the chosen test case, the plaque formation in blood vessels. The obtained results, as far as the developed numerical methods are concerned, can be summarized as follows:

- The convergence of the fully coupled scheme is confirmed by numerical studies with respect to the spatial and temporal discretizations.

- Harmonic and biharmonic extensions in the construction of ALE mappings are compared. Whereas for the harmonic extension the mesh elements become distorted in case of large deformations, mesh elements stay regular for biharmonic extensions during the evolution in time.

- Assuming the incompressible Mooney-Rivlin model, which is widely used in hemodynamics, the plaque formation is simulated. The evolution of the shape of the plaque differs from those
presented in [38] for the incompressible neo-Hookean model. The observed patterns show much more pronounced multiple humps, see Figure 10.

The general model system and the developed numerical methods have a wide application potential in many fields, may be with some adaption to the specific situation. Multi-physics problems of the same structure appear not only in physiology but also in material sciences, geosciences and environmental sciences, where the coupling of fluid dynamics, structural mechanics and chemical reactions becomes relevant. Processes like corrosion of materials and weathering of rocks and solid structure, e.g. made of concrete, are special important examples. Compared to the time scales of the dynamics of the purely mechanical fluid-structure interaction, the changes of the solid structure are in many cases producing observable effects on a far larger time scale. The development of the plaque is in order of months whereas the beating heart creates flow oscillatory in the order of seconds. In this paper the oscillatory heart beat is not taken into account. The problem to link this scales analytically and numerically has to be studied independently. In this paper simulations in 2d for time-constant inflows are presented, which allow to show that the designed model is able to describe observations at least qualitatively. The paper is structured as follows: Section 2 explains modeling procedure and provides the final model. Section 3 introduces the ALE framework and lists the numerical methods. Section 4 presents the plaque formation model and the numerical results of different test cases. Section 5 concludes the paper and provides an outlook for future development.

2 Mathematical modeling of mechano-chemical fluid-structure interactions

In this section, we introduce a mathematical model describing the interaction of an incompressible fluid with an elastic solid subject to material alteration by chemical reactions. As an example, in Section 4, we recapitulate a model derived in [38] describing the biochemical and biomechanical processes leading to formation and growth of plaques in blood vessels. We consider a domain $\Omega \subset \mathbb{R}^2$ which at every time $t$ consists of two subdomains $\Omega^t_f$ and $\Omega^t_s$, separated by an interface $\Gamma^t = \Gamma^t_1 \cup \Gamma^t_2$, see also Figure 1. By $\Omega^t_f$ we denote the fluid domain, by $\Omega^t_s$ the solid domain. Due to the deformation of the solid, both domains will change in time.

![Figure 1: Computational domain](image)

Accepted for publication in *IJNMF*, 2016
2.1 Fluid-structure interaction

We start by describing a simple fluid-structure interaction system, without chemical reaction. In the fluid domain \( \Omega_f^t \), velocity \( v_f \) and pressure \( p_f \) of the incompressible fluid are governed by the Navier-Stokes equations

\[
\begin{align*}
\text{div } v_f &= 0 \quad \text{in } \Omega_f^t \\
\rho_f \left( \frac{\partial v_f}{\partial t} + v_f \cdot \nabla v_f \right) - \text{div } \sigma_f &= 0 \quad \text{in } \Omega_f^t,
\end{align*}
\]

(1)

with the Cauchy stress tensor

\[
\sigma_f = \rho_f \nu_f (\nabla v_f + \nabla v_f^T) - p_f I,
\]

(2)

where by \( \rho_f \) we denote the fluid’s density and by \( \nu_f \) its kinematic viscosity. The boundary of the fluid domain \( \partial \Omega_f^t \) is split into the inflow part \( \Gamma_{f,in} \), where the Dirichlet conditions are given as

\[
v_f = v_f^{in} \quad \text{on } \Gamma_{f,in},
\]

the outflow part \( \Gamma_{f,out} \), where we prescribe the do-nothing outflow condition [19]

\[
\rho_f \nu_f \nabla v_f n_f - p_n = 0 \quad \text{on } \Gamma_{f,out}
\]

with the outward facing unit outer normal vector \( n_f \), a fixed wall \( \Gamma_{f,wall} \) where the no-slip condition is enforced as a Dirichlet boundary

\[
v_f = 0 \quad \text{on } \Gamma_{f,wall}
\]

and the interface \( \Gamma^t \) to the solid problem. This coupling condition will be introduced later in this section. The fluid problem is given in the current configuration in the moving domain \( \Omega_f^t \). This concept is referred to as the Eulerian framework.

In contrast, elastic solids are usually described in the reference configuration \( \Omega_s^0 \), in the Lagrangian framework. By \( \hat{u}_s : \Omega_s^0 \to \mathbb{R}^2 \) we denote the Lagrangian deformation, and by \( \hat{v}_s = dt \hat{u}_s \) we denote the Lagrangian velocity. All quantities in the Lagrangian framework describing actions of material particles will be denoted by a hat “\( \hat{\cdot} \)”. The transformation

\[
\hat{T}_s(\hat{x}, t) = \hat{x} + \hat{u}_s(\hat{x}, t), \quad \hat{T}_s(\cdot, t) : \Omega_s^0 \to \Omega_s^t, \quad t \in I = [0, T]
\]

(3)

is the mapping between the reference configuration and the deformed configuration. For all quantities, scalar, vector or tensor valued, we will always define counterparts in both frameworks, Eulerian and Lagrangian by

\[
\hat{\phi}(\hat{x}, t) = \phi(\hat{T}_s(\hat{x}, t), t) = \phi(x, t), \quad \hat{x} \in \Omega_s^0, x \in \Omega_s^t, t \in I.
\]

(4)

By \( \hat{F}_s := \nabla \hat{T}_s \) we denote the deformation gradient and by \( \hat{J}_s := \det(\hat{F}_s) \) its determinant. We assume that we are in a time interval where the deformation gradient \( \hat{F}_s \) is invertible and its determinant is everywhere strictly positive.

The equations for structural mechanics, describing the displacement \( u_s \) and the velocity \( v_s \) of the vessel wall, are written with respect to Lagrangian variables, because the displacement \( \hat{u}_s = \hat{u}_s(\hat{x}, t) \) is the primary variable in the framework of structural mechanics. We transform the balance equations of mass and momentum to the Lagrangian framework by using the Piola transformation, see e.g. [7]:

\[
\begin{align*}
\hat{J}_s \hat{\rho}_s \frac{\partial \hat{v}_s}{\partial \hat{t}} &= \hat{\text{div}}(\hat{J}_s \hat{\sigma}_s \hat{F}_s^{-T}) \quad \text{in } \Omega_s^0 \\
\frac{\partial \hat{u}_s}{\partial \hat{t}} &= \hat{v}_s \quad \text{in } \Omega_s^0.
\end{align*}
\]

(5)
For the Cauchy stresses, it holds
\[
\dot{\sigma}_s = \frac{1}{\rho_s} \dot{p}_s + \dot{\varepsilon}_s \hat{F}_s^{-T} \hat{F}_s
\]
with the first and second Piola Kirchhoff stress tensors \( \hat{P}_s \) and \( \hat{\Sigma}_s \).

For material modeling, we will consider two types of elastic material, the incompressible neo-Hookean (INH) and the incompressible Mooney-Rivlin (IMR) models:
\[
\hat{\sigma}_s = \begin{cases} 
-\dot{p}_s I + \mu_s (\hat{F}_s^{-T} \hat{F}_s^T - I) & \text{(INH)} \\
-\dot{p}_s I + \tilde{C}_1 \hat{F}_s \hat{F}_s^T - \tilde{C}_2 \hat{F}_s^{-T} \hat{F}_s^{-1} & \text{(IMR)}
\end{cases}
\]
in \( \Omega_s^0 \).

The boundary of the solid domain is split into the outer parts \( \Gamma_{s,in} \cup \Gamma_{s,wall} \cup \Gamma_{s,\text{out}} \) where Dirichlet conditions are given
\[
\mathbf{u}_s = \mathbf{v}_s = 0 \quad \text{on} \quad \Gamma_{s,in} \cup \Gamma_{s,\text{wall}} \cup \Gamma_{s,\text{out}},
\]
and into the interface \( \Gamma^f \) to the fluid, where we finally can formulate the fluid-structure interaction transmission conditions
\[
\mathbf{v}_f = \mathbf{v}_s, \quad \mathbf{\sigma}_f \cdot \mathbf{n}_f + \mathbf{\sigma}_s \cdot \mathbf{n}_s = 0, \quad \text{on} \quad \Gamma^f.
\]

Here \( \mathbf{n}_f \) and \( \mathbf{n}_s \) are the unit outer normal vectors of the interface \( \Gamma^f \) with respect to \( \Omega_f^0 \) and \( \Omega_s^0 \). We have given these coupling conditions in the current coordinate system, i.e. in Eulerian coordinates in the moving domain. This highlights the specific difficulty of fluid-structure interaction problems, where two different coordinate frameworks must be brought together following (4) to derive a monolithically coupled system.

### 2.2 Chemical processes and growth modeling

We assume, that by \( c_{f,i} \) for \( i = 1, \ldots, n_f \) and by \( c_{s,j} \) for \( j = 1, \ldots, n_s \) concentrations of chemical species are given in the fluid and in the solid. Within the two domains, they are governed by transport-diffusion reaction equations
\[
\frac{\partial c_{f,i}}{\partial t} + \text{div}(c_{f,i} \mathbf{v}_f) - \text{div}(D_{f,i} \nabla c_{f,i}) = R_{f,i}(c_{f,1}, \ldots, c_{f,n_f}) \quad \text{in} \quad \Omega_f, \quad \forall i = 1, \ldots, n_f \tag{8}
\]
\[
\frac{\partial c_{s,j}}{\partial t} + \text{div}(c_{s,j} \mathbf{v}_s) - \text{div}(D_{s,j} \nabla c_{s,j}) = R_{s,j}(c_{s,1}, \ldots, c_{s,n_s}) \quad \text{in} \quad \Omega_s, \quad \forall j = 1, \ldots, n_s.
\]

By \( D_{f,i} \) and \( D_{s,j} \) we denote diffusion coefficients (that can depend on the concentrations) and by \( R_{f,i}(\cdot) \) and \( R_{s,j}(\cdot) \) reaction terms. As the chemical system in the solid domain will interact with the elastic structure equations (5), which is formulated in the Lagrangian framework, we will map this system to \( \Omega_s^0 \) with help of the Piola transformation
\[
\frac{\partial}{\partial t}(\hat{J}_s \dot{\mathbf{e}}_{s,j}) - \text{div}(\hat{J}_s \hat{F}_s^{-1} \hat{D}_{s,j} \hat{F}_s^{-T} \nabla \hat{e}_{s,j}) = \dot{R}_{s,j}(\dot{\mathbf{e}}_{s,1}, \ldots, \dot{\mathbf{e}}_{s,n_s}) \quad \text{in} \quad \Omega_s^0, \quad \forall j = 1, \ldots, n_s. \tag{9}
\]

The penetration of chemical species is modeled by transmission conditions for their concentrations on the interface \( \Gamma^f \). Let \( c_{f,i_k} \) and \( c_{s,j_k} \) denote concentrations of chemical species present in both domains \( \Omega_f^0 \) and \( \Omega_s^0 \) (\( i_k \leq n_f, j_k \leq n_s \)). For these species, we assume the continuity of the normal fluxes across \( \Gamma^f \), and a relation between the normal fluxes and the difference of concentrations across the interface:
\[
\begin{align*}
D_{f,i_k} \nabla c_{f,i_k} \cdot \mathbf{n}_f + D_{s,j_k} \nabla c_{s,j_k} \cdot \mathbf{n}_s &= 0 \quad \text{on} \quad \Gamma^f \\tag{10} \\
D_{f,i_k} \nabla c_{f,i_k} \cdot \mathbf{n}_f + \zeta_k (c_{f,i_k} - c_{s,j_k}) &= 0 \quad \text{on} \quad \Gamma^f.
\end{align*}
\]
Similar transmission conditions can be found e.g. in [26]. The coefficient \( \zeta_k \) describes the permeability of the interface \( \Gamma^t \) with respect to the chemical species. We assume that only \( \Gamma^t_1 \) is permeable for the chemical species, so \( \zeta_k = 0 \) on \( \Gamma^t_2 \). For chemical species present just in one of the domains \( \Omega^t_f \) or \( \Omega^t_s \), we prescribe zero flux condition on the interface \( \Gamma^t \).

We assume, that chemical reactions in the solid domain will induce the growth of material. Then the solid deformation is induced both by growth and elasticity. Therefore, we decompose the deformation gradient into two parts, one taking care of purely elastic response and the other one connected to the deformation due to growth. In doing so, we follow the approach of multiple natural configurations, see e.g. [1, 22, 32]. Hereby a new configuration, called natural configuration \( \Omega^t_{s,N} \) with the corresponding variables \( (\hat{x}_{N_s}, t) \) is introduced, see Figure 2, such that \( \Omega^0_s \) is deformed to \( \Omega^t_{s,N} \) at first with deformation gradient \( \hat{G}^s \), and then to \( \Omega^t_s \) with deformation gradient \( \hat{F}^e_s \). We suppose that \( \hat{G}^s \) and \( \hat{F}^e_s \) are invertible and thus the whole deformation gradient \( \hat{F}_s \) is decomposed as

\[
\hat{F}_s = \hat{F}^e_s \hat{G}^s \quad \text{in } \Omega^0_s.
\]

Here

\[
\hat{F}^e_s = \hat{F}^e_s(\hat{x}, t) = \hat{F}^e_s(T^N_s(\hat{x}, t), t) = \hat{F}^e_s(\hat{x}_N, t), \quad \hat{x} \in \Omega^0_s, \hat{x}_N \in \Omega^t_s, t \in I
\]

with the mapping \( T^N_s(\cdot, t) : \Omega^0_s \rightarrow \Omega^t_s \), and

\[
\hat{F}^e_s = \frac{\partial}{\partial \hat{x}_N} T_s(\hat{x}_N, t), \quad \hat{x}_N \in \Omega^t_s, t \in I,
\]

where the mapping \( T_s(\cdot, t) \) is defined as

\[
T_s(\cdot, t) : \Omega^t_s \rightarrow \Omega^t_s,
\]

\[
\hat{x}_N = T^N_s(\hat{x}, t) \Rightarrow T_s(\hat{x}_N, t) = x(\hat{x}, t), \quad t \in I.
\]

The tensor \( \hat{G}^s \) is associated with the deformation induced by growth and can therefore be called the growth tensor. The tensor \( \hat{F}^e_s \) describing the deformation from \( \Omega^t_s \) to \( \Omega^t_s \) is not related to growth, and is associated with the deformation induced by elasticity. The stress tensor \( \hat{\sigma}_s \) is dependent only on the component \( \hat{F}^e_s \) of the deformation gradient:

\[
\hat{\sigma}_s = \hat{\sigma}_s(\hat{F}^e_s) \quad \text{in } \Omega^0_s.
\]

To derive the expression of the growth tensor \( \hat{G}^s \), we follow the derivation in [1, 22, 32, 38], and its determinant \( J^g_s \) satisfies

\[
\frac{\partial J^g_s}{\partial t} = \frac{j^g_s(\hat{c}_{s,1}, \ldots, \hat{c}_{s,n_s})}{\rho_s^2} \quad \text{in } \Omega^0_s.
\]
where \( f_s^g(\cdot) \) is a function defining the growth depending on the chemical species. We assume that the growth is isotropic, i.e., growth is equal in all directions. Then the growth tensor is written as

\[
\hat{G}_s = \hat{g}_s I \quad \text{in} \quad \Omega_s^0.
\]  

(13)

The scaler function \( \hat{g}_s = \hat{g}_s(\hat{x}, t) \) is called the metric of growth, and we have \( \hat{J}_s^g = \det \hat{G}_s = \hat{g}_s^2 \), where 2 represents the dimension of the space \( \mathbb{R}^2 \). The formula \( d\hat{x}_N = \hat{J}_s^g d\hat{x} \) describes how the metric of the reference configuration is changed during the growth process. Now (12) is rewritten as

\[
2 \frac{\partial \hat{g}_s}{\partial t} = \frac{f_s^g}{\hat{\rho}_s} \hat{g}_s \quad \text{in} \quad \Omega_s^0.
\]  

(14)

This is the equation for the metric of growth in the Lagrangian framework, and in the Eulerian framework it is transformed to

\[
2 \left( \frac{\partial g_s}{\partial t} + \mathbf{v}_s \cdot \nabla g_s \right) = \frac{f_s^g}{\rho_s} g_s \quad \text{in} \quad \Omega_s^t.
\]  

(15)

Using the metric of growth and (13), we are able to calculate the tensor \( \hat{F}_s^e \) used in the constitutive equations of \( \hat{\sigma}_s \) as

\[
\hat{F}_s^e = \hat{g}_s^{-1} \hat{F}_s, \quad \hat{J}_s^e = \hat{g}_s^{-1} \hat{J}_s,
\]

such that the two material laws incorporating growth can be written as

\[
\hat{\sigma}_s = \begin{cases} 
-\hat{\rho}_s I + \hat{\rho}_s (\hat{g}_s^{-2} \hat{F}_s \hat{F}_s^T - I) & \text{(INH)} \\
-\hat{\rho}_s I + \hat{C}_1 \hat{g}_s^{-2} \hat{F}_s \hat{F}_s^T - \hat{C}_2 \hat{g}_s^2 \hat{F}_s^{-T} \hat{F}_s^{-1} & \text{(IMR)}
\end{cases}
\quad \text{in} \quad \Omega_s^0.
\]  

(16)

2.3 Final model

In this section we collect all equations and state the final mathematical model. It has two main parts which are strongly coupled. The fluid-structure interaction problem is obtained with the Navier-Stokes equations (1) and the elastic structure equations (5)

\[
\rho_f \frac{\partial \mathbf{v}_f}{\partial t} + \rho_f \mathbf{v}_f \cdot \nabla \mathbf{v}_f = \operatorname{div} \mathbf{\sigma}_f \quad \text{in} \quad \Omega_f
\]

\[
\operatorname{div} \mathbf{v}_f = 0 \quad \text{in} \quad \Omega_f
\]

\[
\hat{J}_s \hat{\rho}_s \frac{\partial \mathbf{v}_s}{\partial t} = \operatorname{div}(\hat{J}_s \hat{\sigma}_s \hat{F}_s^{-T}) \quad \text{in} \quad \Omega_s^0
\]

\[
\frac{\partial \mathbf{u}_s}{\partial t} = \hat{\mathbf{v}}_s \quad \text{in} \quad \Omega_s^0
\]  

(17)

and is used to describe the fluid dynamics and the structural mechanics. The reactive transport problem for the chemical species consists of equations (8) and (9):

\[
\frac{\partial c_{f,i}}{\partial t} + \operatorname{div}(c_{f,i} \mathbf{v}_f) - \operatorname{div}(D_{f,i} \nabla c_{f,i}) = R_{f,i}(c_{f,1}, \ldots, c_{f,n_f}) \quad \text{in} \quad \Omega_f^i, \quad \forall i = 1, \ldots, n_f
\]

(18)

\[
\frac{\partial}{\partial t}(\hat{J}_s \hat{c}_{s,j}) - \operatorname{div}((\hat{J}_s \hat{F}_s^{-1} \hat{D}_{s,j} \hat{F}_s^{-T} \nabla \hat{c}_{s,j})) = \hat{R}_{s,j}(\hat{c}_{s,1}, \ldots, \hat{c}_{s,n_s}) \quad \text{in} \quad \Omega_s^0, \quad \forall j = 1, \ldots, n_s.
\]

(18)

They are used to describe the motion and reaction of chemical species. The process by which the chemical reactions lead to growth of material is described by the equation for the metric of growth:

\[
2 \frac{\partial \hat{g}_s}{\partial t} = \frac{f_s^g(\hat{c}_{s,1}, \ldots, \hat{c}_{s,n_s})}{\hat{\rho}_s} \hat{g}_s \quad \text{in} \quad \Omega_s^0.
\]  

(19)
The stress tensors \( \sigma_f \) and \( \hat{\sigma}_s \) are given as
\[
\sigma_f = -p_f I + \rho_f \nu (\nabla v_f + \nabla v_f^T) \quad \text{in} \quad \Omega_f^0
\]
\[
\hat{\sigma}_s = \begin{cases} 
-\hat{p}_s I + \hat{\rho}_s (\hat{F}_s F_s^T - I) & \text{(INH)} \\
-\hat{p}_s I + \hat{\rho}_s (\hat{F}_s F_s^T - \hat{\chi}_2 F_s^{-1} \hat{F}_s^T) & \text{(IMR)}
\end{cases} \quad \text{in} \quad \Omega_s^0
\]
\[
\hat{F}_s c_s = \hat{F}_s G_s^{-1} = \frac{1}{\hat{g}_s} \hat{F}_s \quad \text{in} \quad \Omega_s^0.
\]

The model is closed by the initial and boundary conditions from equations (17) and (18):
\[
v_f|_{t=0} = v_f^0, \quad c_{f,i}|_{t=0} = c_{f,i}^0 \quad \text{in} \quad \Omega_f^0, \quad \forall i = 1, \ldots, n_f
\]
\[
v_f = v_f^D, \quad c_{f,i} = c_{f,i}^D \quad \text{on} \quad \Gamma_{f,\text{in}}, \quad \forall i = 1, \ldots, n_f
\]
\[
v_f = 0, \quad \nabla c_{f,i} \cdot n_f = 0 \quad \text{on} \quad \Gamma_{f,\text{wall}}, \quad \forall i = 1, \ldots, n_f
\]
\[
\rho_f \nu \nabla v_f \cdot n_f - p_f n_f = 0, \quad \nabla c_{f,i} \cdot n_f = 0 \quad \text{on} \quad \Gamma_{f,\text{out}}, \quad \forall i = 1, \ldots, n_f
\]
\[
\hat{g}_s|_{t=0} = 1 \quad \text{in} \quad \Omega_s^0
\]
\[
\hat{v}_s|_{t=0} = 0, \quad \hat{u}_s|_{t=0} = 0 \quad \text{in} \quad \Omega_s^0
\]
\[
\hat{c}_{s,j}|_{t=0} = 0 \quad \text{in} \quad \Omega_s^0, \quad \forall j = 1, \ldots, n_s
\]
\[
\hat{v}_s = 0, \quad \hat{u}_s = 0 \quad \text{on} \quad \Gamma_{s,\text{in}} \cup \Gamma_{s,\text{wall}} \cup \Gamma_{s,\text{out}}
\]
\[
\hat{F}_s^{-T} \nabla \hat{c}_{s,j} \hat{F}_s^{-T} \cdot \hat{n}_s = 0 \quad \text{on} \quad \Gamma_{s,\text{in}} \cup \Gamma_{s,\text{wall}} \cup \Gamma_{s,\text{out}}, \quad \forall j = 1, \ldots, n_s
\]

as well as the transmission conditions on the interface \( \Gamma^d \):
\[
\begin{align*}
\sigma_f \cdot n_f + \sigma_s \cdot n_s &= 0 \\
D_{f,ik} \nabla c_{f,ik} \cdot n_f + D_{s,ik} \nabla c_{s,ik} \cdot n_s &= 0 \\
D_{f,ik} \nabla c_{f,ik} \cdot n_f + \zeta_k (c_{f,ik} - c_{s,ik}) &= 0.
\end{align*}
\]

Here \( \hat{n}_s \) is the unit outer normal vector of \( \Gamma_{s,\text{in}} \cup \Gamma_{s,\text{wall}} \cup \Gamma_{s,\text{out}} \) with respect to \( \Omega_s^0 \), and the last boundary condition in (21) is obtained from the boundary condition \( \nabla c_{s,j} \cdot n_s = 0 \) by using the transformation formula. Based on these equations, in the next section the numerical methods will be introduced.

\section{3 Numerical Methods}

Here, we describe the discretization of the system of equations (17), (18) and (19), that govern the dynamics of reactive flow interacting with the solid structure. We choose a strictly monolithic approach for the complete set of coupled equations, to allow for a robust discretization with very large time steps. The main difficulty is given by the fluid-structure coupling, that leads to problems on moving (and a priori unknown) domains with large deformation.

### 3.1 Arbitrary Lagrangian Eulerian framework

To cope with the different coordinate frameworks, Eulerian for fluid and Lagrangian for solid and to realize the motion of domains, we base the coupled formulation on the \textit{Arbitrary Lagrangian Eulerian} framework (ALE) \cite{10, 11}. Instead of formulating the flow problem on the moving domain \( \Omega_f^0 \), we introduce the fixed reference domain \( \Omega_f^0 \), which is simply the well defined state at initial time \( t = 0 \). All computations are to be carried out on this reference state. Mapping of the complete set of equations...
to the reference state is via the ALE mapping \( \hat{T}_f(\cdot, t) : \Omega^0_f \to \Omega^T_f \), i.e. \( x = \hat{T}_f(\hat{x}, t) \). On the reference domain, we will denote velocity by \( \hat{\mathbf{v}}_f \) and pressure by \( \hat{p}_f \). This ALE mapping is defined via an artificial displacement \( \hat{\mathbf{u}}_f \) of the fluid domain, which is given as an extension of the solid’s displacement \( \hat{\mathbf{u}}_s \) from the interface \( \Gamma^0 \) to the fluid domain. Throughout this work, we use either a simple harmonic extension
\[-\hat{\Delta} \hat{\mathbf{u}}_f = 0 \quad \text{in} \quad \Omega^0_f, \quad \hat{\mathbf{u}}_f = \hat{\mathbf{u}}_s \quad \text{on} \quad \Gamma^0, \quad \hat{\mathbf{u}}_f = 0\] on \( \partial \Omega^0_f \setminus \Gamma^0 \),
or a biharmonic extension
\[-\hat{\Delta}^2 \hat{\mathbf{u}}_f = 0 \quad \text{in} \quad \Omega^0_f, \quad \hat{\mathbf{u}}_f = \hat{\mathbf{u}}_s, \quad \partial_n \hat{\mathbf{u}}_f = \partial_n \hat{\mathbf{u}}_s \quad \text{on} \quad \Gamma^0, \quad \hat{\mathbf{u}}_f = \hat{\Delta} \hat{\mathbf{u}}_f = 0 \quad \text{on} \quad \partial \Omega^0_f \setminus \Gamma^0, \]
and set
\[\hat{T}_f(\hat{x}, t) := \hat{x} + \hat{\mathbf{u}}_f(\hat{x}, t), \quad \hat{\mathbf{F}}_f := I + \hat{\nabla} \hat{\mathbf{u}}_f, \quad \hat{\mathbf{J}}_f := \text{det} \hat{\mathbf{F}}_f. \]

With help of these relations, we can map the complete system of equations (in variational form) to the reference system \( \Omega^0_f \) with transformation of integrals. Realization of the transmission conditions is achieved by variational principles, coupling test spaces for the momentum balance equations of fluid and solid and coupling trial spaces for velocity and displacement. In the case of harmonic extension, we search for the velocity and displacement defined by
\[\hat{\mathbf{v}} = \{\hat{\mathbf{v}}_f, \hat{\mathbf{v}}_s\} \in \hat{\mathbf{v}}^{\text{in}} + L^2[\Omega; \mathcal{V}], \quad \mathcal{V} := H^1_0(\Omega; \partial \Omega \setminus \Gamma_{f, \text{out}})^2, \]
\[\hat{\mathbf{u}} = \{\hat{\mathbf{u}}_f, \hat{\mathbf{u}}_s\} \in L^2[\Omega; \mathcal{W}], \quad \mathcal{W} := H^1_0(\Omega; \partial \Omega)^2. \]

Here \( L^2[\Omega; X] \) is the Lebesgue space involving time \( \Omega = [0; T] \), in which the functions map time into the Banach space \( X \). \( H^1_0(\Omega; \Gamma) \) is the Lebesgue space of square integrable functions \( L^2(\Omega) \) with first weak derivative in \( L^2(\Omega) \) and with trace zero on the boundary \( \Gamma \subset \partial \Omega \). Functions in the space \( \mathcal{V} \) are not restricted to zero on \( \Gamma_{f, \text{out}} \) to realize the do-nothing outflow condition, see (21). By \( \hat{\mathbf{v}}^{\text{in}} \) we denote an extension of the Dirichlet data on \( \Gamma_{f, \text{in}} \) into the domain \( \Omega \).

This global (on fluid and solid domain) space \( \mathcal{V} \) is also taken for the test function in the momentum equations. The pressure satisfies
\[\hat{p}_f \in L^2[\Omega; \mathcal{L}_f], \quad \mathcal{L}_f := L^2(\Omega^0_f).\]
The concentrations satisfy
\[\hat{c}_{f,i} \in \hat{c}^{\text{in}}_{f,i} + L^2[\Omega; \mathcal{V}_f], \quad \mathcal{V}_f := H^1_0(\Omega^0_f; \Gamma_{f, \text{in}}), \]
\[\hat{c}_{s,j} \in L^2[\Omega; \mathcal{V}_s], \quad \mathcal{V}_s := H^1(\Omega^0_s), \]
where by \( \hat{c}^{\text{in}}_{f,i} \) we denote an extension of the Dirichlet data on \( \Gamma_{f, \text{in}} \) into the domain \( \Omega^0_f \). For growth we consider the space
\[\hat{g}_s \in L^2[\Omega; \mathcal{L}_s], \quad \mathcal{L}_s := L^2(\Omega^0_s).\]
The variational formulation of the system (17), (18) and (19) are given as

\[
\left( \rho_f \dot{J}_f \frac{\partial \hat{v}_f}{\partial t}, \phi \right)_{\Omega_f^0} + \left( \rho_f \dot{J}_f \left( \tilde{F}_f^{-1} \left( \dot{\hat{v}}_f - \frac{\partial \hat{T}_f}{\partial t} \right) \right) \cdot \hat{\nabla} \hat{v}_f, \phi \right)_{\Omega_f^0}
\]

\[
+ \left( \dot{J}_f \hat{\sigma}_f \tilde{F}_f^{-T} \hat{\nabla} \phi \right)_{\Omega_f^0} + \left( \dot{J}_s \frac{\partial \hat{v}_s}{\partial t}, \phi \right)_{\Omega_s^0} + \left( \dot{J}_s \hat{\sigma}_s \tilde{F}_s^{-T} \hat{\nabla} \phi \right)_{\Omega_s^0} - \left( \hat{g}_f^{\text{out}}, \phi \right)_{\Gamma_f,\text{out}} = 0
\]

\[
\left( \text{div} \left( \dot{J}_f \tilde{F}_f^{-1} \hat{v}_f \right), \xi_f \right)_{\Omega_f^0} = 0
\]

\[
\left( \frac{\partial \hat{u}_s}{\partial t} - \hat{v}_s, \psi_s \right)_{\Omega_s^0} = 0
\]

\[
\left( \hat{\nabla} \hat{u}_f, \hat{\nabla} \phi \right)_{\Omega_f^0} = 0
\]

\[
\left( \tilde{F}_f^{-1} \tilde{D}_f \tilde{F}_s^{-T} \hat{\nabla} \hat{e}_{f,s,j}, \hat{\varphi}_s \right)_{\Omega_s^0} + \left( \dot{J}_s \tilde{D}_s \tilde{F}_s^{-T} \hat{\nabla} \hat{e}_{s,j}, \hat{\varphi}_s \right)_{\Omega_s^0} - \left( \ddot{R}_s, \hat{\varphi}_s \right)_{\Omega_s^0} + \left( \hat{g}_s^{\text{int}}, \hat{\varphi}_s \right)_{\Gamma_s} = 0
\]

\[
2 \frac{\partial \hat{g}_s}{\partial t}, \hat{\chi}_s \right)_{\Omega_s^0} - \left( \frac{\ddot{g}_s}{\rho_s}, \hat{\chi}_s \right)_{\Omega_s^0} = 0,
\]

for all
\[
\hat{\phi} \in \mathcal{V}, \quad \xi_f \in \mathcal{L}_f, \quad \hat{\psi}_s \in \mathcal{L}_s^2, \quad \hat{\varphi}_s \in \mathcal{V}_s^0, \quad \hat{\varphi}_f \in \mathcal{V}_f, \quad \hat{\psi}_s \in \mathcal{V}_s, \quad \hat{\chi}_s \in \mathcal{L}_s,
\]

where the space \( \mathcal{V}_s^0 := H^1_0(\Omega_f^0; \partial \Omega_0^0)^2 \), \( \mathcal{L}_s^2 := L^2(\Omega_0^0)^2 \), and the stress tensor \( \hat{\sigma}_f \) in the ALE framework is given as

\[
\hat{\sigma}_f = -\tilde{p}_f I + \rho_f \nu \left( \hat{\nabla} \hat{v}_f \tilde{F}_f^{-1} + \tilde{F}_f^{-T} \hat{\nabla} \hat{v}_f \right).
\]

The boundary terms in (26) contain the boundary and transmission conditions in (21) and (22), and are given as

\[
\hat{g}_f^{\text{out}} = \tilde{f}_f \rho_f \nu \left( \tilde{F}_f \hat{\nabla} \hat{v}_f \right) \tilde{F}_f^{-T} \hat{\nabla} \hat{n}_f
\]

\[
\hat{g}_f^{\text{int}} = \begin{cases} \zeta_k (\hat{e}_{f,i_k} - \hat{e}_{s,j_k}) |\tilde{F}_f^{-T} \hat{\nabla} \hat{u}_f| & \text{if } i = i_k \\ 0 & \text{if } i \neq i_k \end{cases}
\]

\[
\hat{g}_s^{\text{int}} = \begin{cases} \zeta_k (\hat{e}_{s,j_k} - \hat{e}_{f,i_k}) |\tilde{F}_s^{-T} \hat{\nabla} \hat{u}_s| & \text{if } j = j_k \\ 0 & \text{if } j \neq j_k \end{cases}
\]

For realization of a biharmonic extension of the deformation \( \hat{u}_s \) to the fluid domain, we introduce an artificial variable

\[
\hat{w}_f := -\Delta \hat{u}_f \in L^2[I; \mathcal{V}_f^1], \quad \mathcal{V}_f^1 := H^1_0(\Omega_f^0; \partial \Omega_f^0 \setminus \Gamma^0)^2,
\]
and replace the variational formulation
\[
\left( \hat{\nabla} \hat{u}_f, \hat{\nabla} \hat{\psi}_f \right)_{\Omega_f^0} = 0
\]
in (26) with
\[
\left( \hat{\nabla} \hat{u}_f, \hat{\nabla} \hat{\psi}_f \right)_{\Omega_f^0} - \left( \hat{w}_f, \hat{\psi}_f \right)_{\Omega_f^0} + \left( \hat{\nabla} \hat{w}_f, \hat{\nabla} \hat{\psi}_f' \right)_{\Omega_f^0} = 0
\]
for all test functions
\[
\hat{\psi}_f, \hat{\psi}_f' \in V_f^0.
\]
Details and a comparison of different mesh extension techniques are found in the literature, see [36, 37].

3.2 Temporal discretization

We are facing the situation of configurations involving several temporal scales. Whereas the dynamics of a pure fluid-structure interaction will be on the same time scale as the inflow, adding changes of the solid structure caused by transport and reactions leads to a corresponding second time scale, which is expected to be large compared to the first one. Growth and material changes will happen on a very large time scale. In particular, for plaque formation in blood vessel, the short scale is determined by blood inflow pulsating in the frequency of the heart beat, while the overall temporal range of structural changes extends to months or years.

However, numerical schemes so far cannot efficiently resolve both time scales together. Since we are interested to check if the model system is able to show plaque formation, we assume in our simulation that the inflow conditions in the fluid part are time independent, in order to simplify the situation numerically. This justifies the assumption in the numerical simulations that the velocity of the fluid \( \hat{v}_f \) and the concentrations of the transported species \( \hat{c}_{f,i} \) as well as the ALE mapping \( \hat{T}_f \) are quasi-stationary. That means their time derivatives can be set zero. Ongoing research is focussed to developing multi-scale methods in time solving the general problem (see section 5). A first step is found in [15]. Here, we may consider very large time step sizes for the resolution of the large scales only.

As numerical schemes cannot efficiently resolve both scales, we will assume, that the flow will always be in a pseudo-stationary limit. This is obtained by omitting the time derivatives of \( \hat{v}_f, \hat{T}_f \) and \( \hat{c}_{f,i} \) in Equation (26). This allows to consider very large time step sizes for the resolution of the long scales only.

We discretize System (26) by the backward Euler scheme. Second order schemes like the implicitly shifted (for robustness) versions of the trapezoidal rule [24] are easily implemented, it shows however, that the temporal resolution is not of substantial importance for the accuracy of the approximation of the remaining systems, see the numerical tests in Section 4.1.

For discretization in time, we choose a uniform step size \( k \) and introduce discrete time steps \( t_m = m \cdot k \). Hence, let \( \hat{\psi}_s^{\text{old}}, \hat{\psi}_s^{\text{old}}, \hat{c}_{s,i}^{\text{old}} \) and \( \hat{g}_s^{\text{old}} \) be the old solution at time \( t = t_{m-1} \). Then, we approximate
\[
\frac{\partial \hat{\psi}_s}{\partial t}(t_m) \approx \frac{1}{k}(\hat{\psi}_s(t_m) - \hat{\psi}_s^{\text{old}}), \quad \frac{\partial \hat{u}_s}{\partial t}(t_m) \approx \frac{1}{k}(\hat{u}_s(t_m) - \hat{u}_s^{\text{old}}),
\]
\[
\frac{\partial \hat{c}_{s,i}}{\partial t}(t_m) \approx \frac{1}{k}(\hat{c}_{s,i}(t_m) - \hat{c}_{s,i}^{\text{old}}), \quad \frac{\partial \hat{g}_s}{\partial t}(t_m) \approx \frac{1}{k}(\hat{g}_s(t_m) - \hat{g}_s^{\text{old}}).
\]
3.3 Finite elements

Let \( \Omega_h \) be a quadrilateral finite element mesh of the domain \( \Omega = \Omega_f^0 \cup \Gamma^0 \cup \Omega_s^0 \). We assume, that the triangulation \( \Omega_h \) satisfies the following principles:

1. \( \Omega_h = \{K_1, \ldots, K_N\} \) consists of open elements \( K_i \in \Omega_h \), that defined via bilinear mapping of the reference element \( T_K : \hat{K} := (0,1)^2 \rightarrow K \), with \( T_K \in Q_1^2 := \text{span}\{1,x,y,xy\}^2 \). By \( h_K := \text{diam}(K) \) we denote the diameter of an element \( K \in \Omega_h \) and by

\[
h := \max_{K \in \Omega_h} h_K
\]

the maximum diameter in the mesh \( \Omega_h \). For the reference map \( T_K : \hat{K} \rightarrow K \) it holds (shape regularity)

\[
\|\nabla T_K\|_{\infty} \cdot \|\nabla T_K^{-1}\|_{\infty} \leq c \quad \forall K \in \Omega_h \quad (h \rightarrow 0).
\]

2. \( \Omega_h \) is regular in a sense, that the elements cover the domain \( \bar{\Omega} = \bigcup_{K \in \Omega_h} K \), \( K_i \cap K_j = \emptyset \) \( \forall i \neq j \), and that the intersection of \( K_i \cap K_j \) for \( i \neq j \) is either empty, or a common corner point, a common edge or – to allow for local mesh refinement with hanging nodes – exactly one half of a common edge, see [8]. Degrees of freedom in such hanging nodes are replaced by the linear interpolation of the two adjacent regular nodes.

3. The triangulation \( \Omega_h \) is matching the partitioning, i.e., for every element \( K \in \Omega_h \) it holds \( K \cap \Gamma^0 = \emptyset \). We define sub-triangulations

\[
\Omega_{h,f} = \{K \in \Omega_h, K \subset \Omega_f^0\}, \quad \Omega_{h,s} = \{K \in \Omega_h, K \subset \Omega_s^0\}.
\]

On \( \Omega_h \), we define the space of continuous (isoparametric) finite elements of degree one:

\[
V_h := \{\phi \in C(\Omega), \phi\big|_K \circ T_K \in Q_1, K \in \Omega_h\},
\]

and the finite element spaces on the sub-domains

\[
V_{h,f/s} := \{\phi \in C(\Omega_{f/s}^0), \phi\big|_K \circ T_K \in Q_1, K \in \Omega_{h,f/s}\}.
\]

We choose an equal-order finite element discretization for all solution variables and search for

\[
\hat{\mathbf{v}}_h \in V_h^2, \quad \hat{\mathbf{v}}_{h,f} := \hat{\mathbf{v}}_h|_{\Omega_f^0}, \quad \hat{\mathbf{v}}_{h,s} := \hat{\mathbf{v}}_h|_{\Omega_s^0}
\]

\[
\hat{\mathbf{u}}_h \in V_h^2, \quad \hat{\mathbf{u}}_{h,f} := \hat{\mathbf{u}}_h|_{\Omega_f^0}, \quad \hat{\mathbf{u}}_{h,s} := \hat{\mathbf{u}}_h|_{\Omega_s^0}
\]

\[
\hat{p}_{h,f} \in V_{h,f}
\]

\[
\hat{c}_{h,(f,i)/(s,j)} \in V_{h,f/s}
\]

\[
\hat{g}_{h,s} \in V_{h,s}.
\]

Velocity and displacement are defined globally on the complete domain and share the same degrees of freedom on the interface \( \Gamma^0 \) each. The same holds for the test function \( \phi_h \in V_h^2 \) in the momentum balance equations. All other variables are split into fluid part coming from \( V_{h,f} \) and solid part in \( V_{h,s} \).
As the equal order pair of velocity and pressure elements does not satisfy the inf-sup condition, we add further stabilization terms to the variational formulation:

\[ s_{lp}(\hat{\mathbf{p}}_{h,f}, \hat{\xi}_{h,f}) := \sum_{K \in \Omega_{h,f}} \left( \alpha_K \nabla(\hat{\mathbf{p}}_{h,f} - \pi_2 h \hat{\mathbf{p}}_{h,f}), \nabla(\hat{\xi}_{h,f} - \pi_2 h \hat{\xi}_{h,f}) \right)_K. \]

Details on this local projection stabilization technique are given by Becker, Braack et al. [3, 5]. The operator \( \pi_2 h : V_{h,f} \to V_{2h,f} \) is a local interpolation operator into the finite element space of degree one on a coarser mesh. The stabilization parameter \( \alpha_K \) depends on the local mesh Peclet number

\[ \alpha_K := \alpha_0 \left( \frac{\nu_f}{h_K} + \frac{\|\mathbf{v}\|_{L^\infty(K)}}{h_K} \right)^{-1}. \] (27)

If transport gets dominant, we further need stabilization terms within the transport-diffusion reaction equations for the concentrations \( \hat{c}_{h,(f,i)} \). We are using the classical artificial diffusion method and add a further term to the variational formulation:

\[ s_{cad}(\hat{\mathbf{c}}_{h,(f,i)}, \hat{\phi}_{h,f}) := \sum_{K \in \Omega_{h,f}} \left( \delta_{K,i} \nabla(\hat{\mathbf{c}}_{h,(f,i)}), \nabla(\hat{\phi}_{h,f}) \right)_K. \]

For details, we refer to Johnson [21]. Similarly to \( \alpha_K \), the parameter \( \delta_{K,i} \) are given as

\[ \delta_{K,i} := \delta_0 \left( \frac{D_{f,i} h}{h_K} + \frac{\|\mathbf{v}\|_{L^\infty(K)}}{h_K} \right)^{-1}. \] (28)

For our problem, we could not find a benefit in using streamline diffusion terms.

### 3.4 Solution of the systems

Discretization of the system of partial differential equations (26) leads to a large nonlinear algebraic system of equations:

\[ A_h(U_h) = F_h, \]

where \( A_h \) describes the variational problem (26) and where

\[ U_h = \{ \mathbf{v}_h, \mathbf{u}_h, \hat{\mathbf{p}}_{h,f}, \hat{c}_{h,(f,i)}, \hat{c}_{h,(s,j)}, \hat{g}_{h,s} \} \]

is the combined solution vector. The right hand side \( F_h \) involves both the problem data and the last time step. We tackle the nonlinearity with a Newton scheme and find iterates \( U_h^{(n)} \):

\[ A_h'(U_h^{(n)}) W_h^{(n)} = F_h - A_h(U_h^{(n)}), \quad U_h^{(n+1)} := U_h^{(n)} + W_h^{(n)}, \quad n \geq 1, \] (29)

where \( U_h^{(0)} \) is a given initial guess. By \( A_h'(U_h) \) we denote the Jacobian of the coupled system. An analytical expression of this Jacobian must deal with implicit domain transformation, see [29] for a derivation. Here, we made good experience with a simple finite difference approximation.

Every step of the Newton iteration requires the solution of a very large, ill-conditioned, non-symmetric linear system of saddle point type (due to the velocity-pressure coupling). Efficient iterative standard solvers are not available. Usually, Krylov subspace methods, preconditioned by partitioned iterations are considered, see Heil et al. [18]. Another approach is to use monolithically coupled multigrid solvers, that apply a partitioning within the multigrid smoother, see [30]. Here, the problem structure also suffers from the coupling to different equations describing the chemical reactions and
the dynamics of the growth. Due to the lack of efficient alternatives, we solve the linear systems with
a direct solver using the library UMFPACK [9]. To increase efficiency, we choose an inexact Newton
approach and freeze the evaluation point of the Jacobian evaluation
\[ A_h(U_h^{(n)}) \approx A_h(\bar{U}_h) \]
for several iterations of the Newton-method and even keep this approximation over several time steps.
A new Jacobian is only assembled, if the convergence rate suffers, i.e. if
\[ \|F_h - A_h(U_h^{(n+1)})\| \geq \alpha \|F_h - A_h(U_h^{(n)})\| . \]
We usually choose \( \alpha \approx 0.05 \), which allows us to reuse a Jacobian for about 350 Newton steps, which
corresponds to about 180 time steps, as only an average of 2 Newton steps is required in every time
step for a reduction of the nonlinear residual by \( 10^{-8} \). The reuse of the Jacobian is important for an
efficient scheme, as assembling the system matrix and preparing the direct solver is most costly part
in the simulation.

4 Application to Plaque Formation and Numerical Results

In this section, we will focus on a prototypical application of this mechano-chemical fluid-structure
interaction problem: the formation of plaques in blood vessels, which is a main cause for diseases like
atherosclerosis.

Plaques are formed primarily in the innermost layer of the vessel wall, the intima. Their formation
is initiated by endothelial dysfunction, and involves several biochemical processes in the following.
Leucocytes, in particular monocytes, from the blood flow are attracted to the vessel wall. They
migrate into the inflamed intima. Here, a cytokine, known as macrophage colony-stimulating factor,
induces the differentiation of monocytes to macrophages. These immune cells take up low-density
lipoproteins, which carry cholesterol and triglycerides to the tissues, and are finally transformed into
foam cells, which are engorged with lipids [17].

The accumulation of foam cells in the vessel causes a swelling of the vessel walls. The subsequent
evolution of the plaques consists of formation of structures and components typical for a mature
plaque: a soft, lipid-rich atheromatous core and a hard, collagen-rich sclerotic tissue, called fibrous
cap [25]. A plaque with a large core and a thin cap becomes vulnerable and may rupture, if the
biomechanical forces reach a critical value. After plaque rupture, platelets in the blood flow adhere
to the ruptured region and lead to thrombus formation[12, 35]. This far spread disease of arteries is
related to coronary artery disease, stroke and other conditions.

We use our model derived in Section 2.3 to describe the atherosclerotic plaque formation. In this
section, the general problem reduces to the model derived in [37, 38]. It consists of both biochemical and
biomechanical processes, which are huge and complex. The main biomechanical process is the fluid-
structure interaction between blood flow and vessel wall, so we can use the fluid-structure interaction
problem (17) to describe it. The main biochemical processes we are interested in are the transport
and reaction of monocytes (with concentration \( c_f \)), macrophages (with concentration \( c_s \)) and foam
cells (with concentration \( c^*_s \)). The corresponding reactive transport problem for these cells is obtained as

\[
\frac{\partial c_f}{\partial t} + v_f \cdot \nabla c_f - D_f \Delta c_f = 0 \quad \text{in} \; \Omega_f \\
\frac{\partial}{\partial t}(\hat{J}_s \hat{c}_s) - \text{div}(\hat{J}_s \hat{F}_s^{-1} \hat{D}_s \hat{F}_s^{-T} \nabla \hat{c}_s) = -\beta \hat{J}_s \hat{c}_s \quad \text{in} \; \Omega_s^0 \\
\frac{\partial}{\partial t}(\hat{J}_s \hat{c}^*_s) = \beta \hat{J}_s \hat{c}_s \quad \text{in} \; \Omega_s^0.
\]
Since monocytes differentiate into macrophages as they move into the vessel wall, $c_f$ and $c_s$ have transmission conditions on the interface $\Gamma^t$:

\[
\begin{align*}
D_f \nabla c_f \cdot n_f + D_s \nabla c_s \cdot n_s &= 0 \\
D_f \nabla c_f \cdot n_f + \zeta (c_f - c_s) &= 0.
\end{align*}
\]

The equation for the metric of growth is still given as \eqref{eq:19}, and for the growth function $\hat{f}_s^g$, we assume a linear relation given by

\[
\hat{f}_s^g = \gamma \hat{\beta}_s \quad \text{in} \quad \Omega^0_s.
\]

The stress tensors $\sigma_f$ and $\hat{\sigma}_s$ are given as \eqref{eq:20}. Moreover, the model assumes that the increase of the concentration of foam cells not only lets the volume of solid phase grow, but also changes its mechanical properties. So the coefficients $\hat{D}_s$, $\hat{\mu}_s$, $\hat{C}_1$ and $\hat{C}_2$ are given by

\[
\begin{align*}
\hat{D}_s &= D_{s,d} + (D_{s,h} - D_{s,d}) e^{-a_1 c_s^*} \quad \text{in} \quad \Omega^0_s \\
\hat{\mu}_s &= \mu_{s,d} + (\mu_{s,h} - \mu_{s,d}) e^{-a_2 c_s^*} \quad \text{in} \quad \Omega^0_s \\
\hat{C}_1 &= C_{1,d} + (C_{1,h} - C_{1,d}) e^{-a_3 c_s^*} \quad \text{in} \quad \Omega^0_s \\
\hat{C}_2 &= C_{2,d} + (C_{2,h} - C_{2,d}) e^{-a_4 c_s^*} \quad \text{in} \quad \Omega^0_s,
\end{align*}
\]

see \cite{37, 38}. Based on this plaque formation model, we will carry out and discuss numerical simulations of an idealized plaque formation configuration. We consider a two-dimensional computational domain, shown in Figure 3. Table 1 collects all characteristics of the geometry. The domain $\Omega$ consists of two parts, the fluid domain $\Omega^f$ and the solid domain $\Omega^s$. The interface $\Gamma^0 := \partial \Omega^f_s \cap \partial \Omega^0_s$ is split into $\Gamma^0 = \Gamma^0_f \cup \Gamma^0_s$. Only the inner part $\Gamma^0_f$ shown as dashed line in Figure 3 is permeable for the monocytes. A second dashed line, indicated in Figure 3 marks an area of the solid domain $\Omega^s = (0mm, 35mm) \times (-0.0625mm, 0mm)$, where endothelial cells and smooth muscle cells are present, that are only slightly affected by plaque formation. In this transition layer, chemical reactions rarely take place, so the monocytes will not be converted to foam cells. This fact is confirmed by our medical partners. The upper boundary of $\Omega^f$ and the lower boundary of $\Omega^0_s$ are assumed to be fixed for simplicity, because we are mainly interested in the motion of the interface induced by the development of plaques, which has a different time scale from the oscillation of the upper and lower boundaries induced by heart beat. The multiple time scale problem by coupling the fast vessel oscillation with the slow plaque growth will be topic of further investigations. We refer to \cite{15} for a first study of plaque growth considering a temporal multi-scale approach.

The parameters of the model and the initial conditions are listed in Table 2. The parameters with the ”star mark”, e.g. the growth and reaction coefficients and the permeability of the interface, are chosen in a ”reasonable” range due to the lack of values obtained from real data. The other ones are taken from the medical literatures e.g. \cite{2, 16, 31, 33}. The diffusion coefficient $D_s$, the shear modulus $\mu_s$ and the other elastic coefficients $C_1$ and $C_2$ are defined by \eqref{eq:33}. From Table 2 we note, that the elastic coefficients decrease and that the diffusion coefficient increases in the diseased vessel wall, since, as the plaque is formed, the diseased tissue becomes softer and easier for molecules to diffuse. Concerning the reaction coefficient, it is given by

\[
\begin{align*}
\beta &= (\beta_0^* + (\beta_0 - \beta_0^*) e^{-a(y+0.0625)}) \quad \text{in} \quad \Omega^e_s \\
\beta &= \beta_0 \quad \text{in} \quad \Omega^0_s \setminus \Omega^e_s.
\end{align*}
\]

We take it equal to constant value $\beta_0$ under the lower dashed line and extend it by an exponentially decreasing function between the interface and the lower dashed line, in such a way that the value is
Figure 3: Configuration of the computational domain in the ALE framework

significantly smaller and the reaction can almost be neglected in this transition layer $\Omega_s^e$. Finally on the interface, we set a constant value $\zeta$ on $\Gamma_{1}^0$ and 0 on $\Gamma_{2}^0$. The corresponding initial and boundary conditions are given as (21). In particular, the initial velocity profile $\mathbf{v}^0$ of the blood flow is a parabola [10], and the initial value of the concentration of monocytes $c_f^0$ in $\Omega_f^0$ is a positive constant.

Table 1: Characteristics of the computational domain

<table>
<thead>
<tr>
<th>Domain</th>
<th>Fluid domain $\Omega_f^0$</th>
<th>Solid domain $\Omega_s^0$</th>
<th>Part of interface permeable for monocytes $\Gamma_1^0$</th>
<th>Transition layer $\Omega_s^e$</th>
</tr>
</thead>
<tbody>
<tr>
<td>length</td>
<td>35.0 mm</td>
<td>35.0 mm</td>
<td>2.5 mm</td>
<td>0.0625 mm</td>
</tr>
<tr>
<td>width</td>
<td>5.0 mm</td>
<td>0.5 mm</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

We visualize the numerical results in the whole domain $\Omega_f^t \cup \Omega_s^t$, with respect to the Eulerian framework, so that we can observe not only the evolution of the solution components (displacement, velocity, concentrations), but also the motion of the domain when the plaque is formed. In Figure 4, we show the position of the interface $\Gamma^t$ (indicated by the white line). At initial time, the interface is parallel to the upper and lower boundary of the domain $\Omega$. When time passes, the interface moves due to the formation and growth of the plaque in $\Omega_s^t$ and forms a hump around the permeable interface $\Gamma_1^t$ after $4.5 \times 10^7$ seconds. Figure 4 also presents the concentration of monocytes $c_f$ in the fluid domain $\Omega_f^t$ and the concentration of foam cells $c_s^*$ in the solid domain $\Omega_s^t$ at different points in time $t_1 = 0 sec$, $t_2 = 3 \cdot 10^7 sec$ and $t_3 = 4.5 \cdot 10^7 sec$. When the plaque formation starts, $c_f$ decreases mainly downstream of the permeable interface $\Gamma_1^t$. This decrease in $c_f$ is due to the penetration of monocytes into the vessel wall. $c_s^*$ increases as the plaque is growing, and reaches high value at the place with large deformation. This shows that plaque formation and growth are induced by the penetration of monocytes and the accumulation of foam cells.

To analyze the influence of the chemical reactions on the mechanical properties of the vessel walls, we indicate in Table 3 the maximum principal stress $\sigma_{s,p}$, which is given by the largest eigenvalue

Accepted for publication in IJNMF, 2016
Table 2: Parameter values and initial conditions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>density $\rho_f$</td>
<td>$0.00106 g/mm^3$</td>
</tr>
<tr>
<td>kinematic viscosity $\nu$</td>
<td>$3.0 mm^2/s$</td>
</tr>
<tr>
<td>diffusion coefficient $D_f$</td>
<td>$1.0 \times 10^{-6} mm^2/s$</td>
</tr>
<tr>
<td>density $\rho_s$</td>
<td>$0.00106 g/mm^3$</td>
</tr>
<tr>
<td>growth coefficient $\gamma^*$</td>
<td>$1.0 \times 10^{-6} g$</td>
</tr>
</tbody>
</table>
| shear modulus $\mu_s$      | $\mu_{s,h} = 1.0 \times 10^5 g/mm \cdot s^2$
|                            | $\mu_{s,d} = 0.05 \times \mu_{s,h}$|
| elastic coefficients $C_1$ and $C_2$| $C_{1,h} = C_{2,h} = 1.0 \times 10^5 g/mm \cdot s^2$
|                            | $C_{1,d} = C_{2,d} = 0.05 \times \mu_{s,h}$|
| diffusion coefficient $D_s$| $D_{s,h} = 1.0 \times 10^{-7} mm^2/s$
|                            | $D_{s,d} = 5.0 \times \mu_{s,h}$|
| reaction coefficient $\beta^*$| $\beta_0 = 1.0 \times 10^{-7} /s$
|                            | $\beta_0^* = 0.05 \times \beta_0$|
| permeability of the interface $\zeta^*$| $\zeta = 1.0 \times 10^{-4} mm/s$ on $\Gamma_1^0$
|                            | $\zeta = 0$ on $\Gamma_2^0$|
| initial velocity $v_{f,0}$  | $48x(5-x) mm/s$                    |
| initial concentration $c_{f,0}$ | $540.0/mm^3$                      |

* chosen in a "reasonable" range of the stress tensor $\sigma_s$, at different points in time $t_1 = 3 \cdot 10^7 sec$ and $t_2 = 4 \cdot 10^7 sec$ for different coefficients $\alpha_2$ used to define $\mu_s$ in (33). The results show, that the principal stress is decreasing, if the coefficient $\alpha_2$ is being increased.

### 4.1 Convergence of numerical solutions

In the first sequence of numerical test cases, we analyze the convergence properties of our numerical scheme with regard to spatial and temporal refinement of the discretizations. Figure 5 shows the evolution of the vertical displacement $u_{s,y}(x_0, t)$ at a point $x_0 = (17.5 mm, 0 mm)$ in the middle of the interface. In this figure, we collect simulations for three different levels of mesh refinement starting at a coarse mesh with $N_1 = 4221$ nodes, an intermediate mesh with $N_2 = 7865$ and a fine mesh with $N_3 = 15149$ nodes. The $x$–axis indicates time $t \in I := [0, 10^7 sec]$, and the $y$–axis denotes the displacement $u_{s,y}(x_0, t)$. For better assessment of these results, we enlarge the results for a small temporal subset $I_1 = [7.9 \cdot 10^6 sec, 8 \cdot 10^6 sec]$. The step size of the temporal discretization is taken as $k = 500 sec$. Comparing the results of the three different mesh levels reveals smaller differences between adjacent levels under mesh refinement, i.e., we observe spatial mesh convergence for $h \to 0$.

Similarly, in Figure 6, we show the results of the vertical displacement $u_{s,y}(x_0, t)$ under refinement of the temporal discretization. Here, we carry out all computations on a fixed mesh with $N = 7865$ nodes and vary the temporal step size from $k_1 = 1000 sec$ over $k_2 = 500 sec$ to $k_3 = 250 sec$. Again, we plot the displacement as function over time in the complete interval $I$ and enlarge a small subset $I_2 = [7.998 \cdot 10^6 sec, 8 \cdot 10^6 sec]$. As the difference between solutions with adjacent time steps sizes is
Figure 4: Motion of the interface, evolution of concentration of monocytes $c_f$ (in $/mm^3$) in the fluid domain $\Omega_f^t$ and evolution of concentration of foam cells $c_s^*$ (in $/mm^3$) in the solid domain $\Omega_s^t$. $k = 500 sec$ on a mesh with $N = 7865$ nodes. The white line indicates the interface location. Red color denotes high concentrations, while blue color denotes low value.

also decreasing, we again observe numerical convergence of the scheme for $k \to 0$. Comparing the convergence of the temporal discretization in Figure 6 with the spatial convergence in Figure 5, we conclude, that temporal accuracy effects play a lesser role, such that the backward Euler scheme is preferable over higher order schemes due to its robustness. The discrepancy between the different spatial refinement levels is about 0.25% while the temporal refinement yields values within 0.01% variation. We refer to the enlarged sections in Figures 5 and 6.

4.2 Mesh Maintenance

In the second test case, we analyze the quality of the mesh transformation, that enters the mapping of the set of equations to Arbitrary Lagrangian Eulerian coordinates, see Section 3.1. For comparison, we consider both the very simple (but standard) harmonic extension of the solid displacement $u_s$ to a fluid displacement $u_f$ and the more complex biharmonic extension.

In Figure 7, we show plots of the solution (and the deformed computational mesh) for both extensions at different points in time $t_1 = 0 sec$, $t_2 = 3 \cdot 10^7 sec$ and $t_3 = 4.5 \cdot 10^7 sec$. This last point in time is very close to the break down of the numerical scheme. Every plot contains a white line, that shows the interface $\Gamma^t$, evolving over time. The coloring indicates the distribution of the horizontal velocity $v_x$. We only show a subset of the computational domain that covers the significant part of the growth.
Figure 5: Evolution of the vertical displacement $u_{s,y}$ (in mm) at the point $(17.5\, mm, 0\, mm)$ with different levels of mesh refinement. Time interval $I = [0, 10^7\, sec]$ and subset $I_1 = [7.9 \cdot 10^6\, sec, 8 \cdot 10^6\, sec]$

Figure 6: Evolution of the vertical displacement $u_{s,y}$ (in mm) at the point $(17.5\, mm, 0\, mm)$ with different time step sizes. Time interval $I = [0, 10^7\, sec]$ and subset $I_2 = [7.998 \cdot 10^6\, sec, 8 \cdot 10^6\, sec]$
Figure 7: Motion of the interface and distribution of horizontal velocity \( v_x \) (in mm/sec) in the whole domain \( \Omega^f \cup \Omega^s \), \( k = 500 \) sec on a mesh with \( N = 7865 \) nodes. The white line indicates the interface location. Red color denotes high velocities, while blue color denotes low value. Left: computation using a harmonic mesh extension. Right: biharmonic extension.
Figure 8: Motion of the interface and distribution of horizontal velocity $v_x$ (in \textit{mm/sec}), concentration of monocytes $c_f$ (in \textit{/mm$^3$}) and concentration of foam cells $c^*_s$ (in \textit{/mm$^3$}) near the hump of the interface $\Gamma_1^t \cup \Gamma_2^t$ at $t = 4.5 \times 10^7 \text{sec}$. Both harmonic and biharmonic mesh models are used, and results are compared, showing better quality of fluid meshes in biharmonic extension. $k = 500\text{sec}$ on a mesh with $N = 7865$ nodes. The white line indicates the interface. Red color denotes high value, while blue color denotes low value.
Table 3: Principal stresses with different $a_2$

<table>
<thead>
<tr>
<th>maximal value of the principal stress $\sigma_{s,p}$</th>
<th>$t = 3.0 \cdot 10^7 \text{sec}$</th>
<th>$t = 4.0 \cdot 10^7 \text{sec}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$a_2 = 10^{-4}$</td>
<td>$\sigma_{s,p} = 1.572 \cdot 10^3 \text{Pa}$</td>
<td>$\sigma_{s,p} = 2.525 \cdot 10^3 \text{Pa}$</td>
</tr>
<tr>
<td>$a_2 = 10^{-3}$</td>
<td>$\sigma_{s,p} = 1.566 \cdot 10^3 \text{Pa}$</td>
<td>$\sigma_{s,p} = 2.509 \cdot 10^3 \text{Pa}$</td>
</tr>
<tr>
<td>$a_2 = 10^{-2}$</td>
<td>$\sigma_{s,p} = 1.547 \cdot 10^3 \text{Pa}$</td>
<td>$\sigma_{s,p} = 2.444 \cdot 10^3 \text{Pa}$</td>
</tr>
<tr>
<td>$a_2 = 10^{-1}$</td>
<td>$\sigma_{s,p} = 1.357 \cdot 10^3 \text{Pa}$</td>
<td>$\sigma_{s,p} = 2.0 \cdot 10^3 \text{Pa}$</td>
</tr>
</tbody>
</table>

The time step is chosen as $k = 500 \text{sec}$. For better resolution of the important interface line, we add two layers of mesh refinement along the interface. The resulting discretization with $N = 7865$ nodes corresponds to the intermediate mesh, that has been used in the previous section.

Here, we note, that all computations are performed in a strict interpretation of the ALE approach using a fixed reference mesh $\Omega_h$ of the initial domain $\Omega$ for all times. Mesh motion is hidden in the implicit ALE map. The distortions of the meshes in Figure 7 are added in a postprocessing step. The computation on the fixed ALE mesh however is equivalent to a Eulerian computation on the distorted meshes shown in the figures.

First, we observe, that no difference in interface location or velocity profile is visible between the results obtained using harmonic and biharmonic extension. Only a sharp look at the values reveals a slight difference in the maximum velocity at time $t = 4.5 \cdot 10^7 \text{sec}$. On the other hand, we observe, that the quality of the distorted meshes strongly deteriorates for large deformations at later times. Close to the interface, the harmonic mesh extension gives highly anisotropic and sheared elements, see Figure 8 for a close up look at a region with strong curvature at time $t = 4.5 \cdot 10^7 \text{sec}$. Here, the biharmonic extension yields very regular mesh elements in all areas of the mesh. It is very surprising, that this enormous difference in mesh quality does not relate to substantial variations in numerical results measured as output functionals like the displacement $u_s$ or concentration of monocytes. We will however expect larger differences, when observing the long time behaviour of the solution, that will also cause even larger deformations.

4.3 Incompressible Mooney-Rivlin (IMR) model

The two preceding numerical test cases both consider the incompressible neo-Hookean (INH) model as the material law for modeling the vessel walls. Here in the third test case, we investigate incompressible Mooney-Rivlin (IMR) model, which is more widely used in the field of hemodynamics. To get more stable solutions and regular mesh elements close to the interface, we use the biharmonic extension to generate the ALE map. In Figure 9, the evolutions of the vertical displacement $u_{s,y}(x_0,t)$ at the point $x_0 = (17.5 \text{mm}, 0 \text{mm})$ in the INH and IMR models are compared. We observe that they exhibit similar behavior in the time interval $I = [0, 3.0 \cdot 10^7]$. For larger times however, $u_{s,y}(x_0,t)$ keeps increasing in the INH model, whereas it suddenly decreases in the IMR model. From Figure 10 we can get more information. When time $t = 3.5 \cdot 10^7 \text{sec}$, there is a “dent” formed in the middle of the interface. Experiments using different levels of mesh refinement show that this behavior is stable under mesh convergence, implying that this “dent” is not a numerical artefact. Therefore, more numerical tests need to be taken in this case to understand the reason and signification of this behavior.
Figure 9: Evolution of the vertical displacement $u_{s,y}$ (in mm) at the point $(17.5\text{mm},0\text{mm})$ in the INH and IMR models. Time interval $I = [0, 3.5 \cdot 10^7 \text{sec}]$

5 Conclusions

In this paper, we formulated a mathematical model system for fluid-structure interactions including transport and reactions of chemical substances, changing the mechanical properties of the solid wall and causing volume growth, which may lead to rupture of the solid structure. Plaque formation in blood vessels, a prototype for this class of problems, is treated numerically, and the chosen numerical method delivers very reliable results. The main objectives of the investigation could be achieved, by demonstrating that the model system is able to develop permanent deformations of the solid structure, in case of blood vessels with plaques. Despite of the strong simplification in the specific model system, the numerical simulation remained challenging:

- structural changes in the solid are added to the common mechanical interactions of fluid and solid, increasing the complexity of the system;

- the changes to be described are long-time effects.

In this paper, we found surprising results when using the incompressible Mooney-Rivlin material. This IMR model is important and must be the subject of future work, as it is widely used in the field of hemodynamics. We only dealt with simulations in 2D and assumed that the inflow of fluid is not dependent on time, whereas in the blood system it is changing according to the frequency of the heartbeat. Next aims in on-going research are the numerical simulation in 3D, and the development of a mathematically based method to deal with the multi-scale problem in time. Analytic investigations of the systems of partial differential equations arising in the ALE approach are urgently required to design and support the numerical methods. Improving the calibration and validation of the plaque model system is strongly dependent on the acquisition and processing of biomedical and biomechanical data. Finally, we emphasize once again that the mathematical and computational concepts and methods are portable to other situations of multi-physics interactions between fluid and solid phases.
Figure 10: Motion of the interface and distribution of horizontal velocity $v_x$ (in mm/sec) in the whole domain $\Omega_{t_f} \cup \Omega_s$. $k = 500$ sec on meshes with different levels of refinement. The IMR model and biharmonic extension are used. The white line indicates the interface location. Red color denotes high velocities, while blue color denotes low value. Left: mesh with $N_1 = 4221$ nodes. Center: mesh with $N_2 = 7865$ nodes. Right: mesh with $N_3 = 15149$ nodes.
Acknowledgements

The work of the first author was supported in the framework the Twinning Project Plaque Formation in Blood Vessels - Mathematical Modeling, Simulation and Validation (PLAQUEFORM) of the Excellence Initiative at the University of Heidelberg.

References


Accepted for publication in IJNMF, 2016