Abstract

We present optimization problem for Asymmetric Flow Field Flow Fractionation, which is a widely used technique for segregation of two or more particles of submicron scale, according to their hydrodynamic radius. We give a short description of AF4 and present one way coupled model. For an optimization problem we use the sensitivities due to the special structure of the objective functional for this specific application and memory constraints.

1 Introduction

We consider an optimal control problem for the focusing-injection stage of an Asymmetric Flow Field Flow Fractionation (AF4) process, in which the distribution of particles suspended in a liquid needs to be controlled. The dynamics of concentrations of small particles suspended in liquids is also of great importance in a number of different processes in medicine, biology, chemistry, etc. [17]-[19].

In many of these applications the evolution of the particle concentration can be influenced only by the inflow/outflow of the liquid. From the mathematical point of view this leads to a constrained optimal boundary control problem for a convection-diffusion equation coupled with Stokes equation. The theory to handle PDE constrained optimal problems is meanwhile well developed [4]. In particular, optimal control problems for convection-diffusion problems were considered in [10], for the Stokes and Navier-Stokes equations in [11, 12, 13, 14] and for the coupled problems in [7, 8, 9]. In these works the necessary derivative information was mainly provided by the solution of the adjoint equations.

Here, in contrast, we use the sensitivities due to the special structure of the objective functional for this specific application. This allows for the construction of a fast optimization algorithm, which is easy to parallelize. Parallelization is here essential, since the computing times for the forward problem are large already for the two-dimensional problem.

Computational challenges. Numerical simulation of the AFFFF process is a challenging task due to the dominance of the convection in the transport of the particles, the highly stretched grids needed in order to resolve the appearing boundary layers, etc. The computational challenges are even bigger when optimization problems are solved, and solving optimization problems, in general, is possible only if advanced numerical algorithms are used.

Also, it this industrial application it is common to use piecewise constant control of the flow on the boundary and it desired to use as few switches in the control as possible.

Goals. Our long term goal is shape optimization of AFFFF device and optimal control of the fractionation process in the full geometry. The goal of this paper is to present important ingredients for optimization algorithms. More precisely,

- present a mathematical model for the optimization problem and define objective functional, which will satisfy needs of the engineers
- present efficient and easy parallelizable optimization algorithms
- discuss our first numerical examples

Section 2 of our work is devoted to description of Asymmetric Flow Field Flow Fractionation process, where we also describe the problems, which engineers from Wyatt Technology have posed for us. We will also discuss the main difficulties which arise during the numerical modeling of AF4 and some additional features of the problem. In section 3 we introduce a mathematical description of AF4 process. Optimal control problem setting and optimization algorithm are described in Section 4. Numerical solution of state equation and its nuances are discussed in Section 5. Section 6 is devoted to numerical results and their discussion.

2 Modeling of AF4 processes: state-of-the-art

Asymmetric Flow Field Flow Fractionation, denoted further as AF4, is a special case of the Field Flow Fractionation technique. During the AF4, the particles get separated according to their size, more exactly to their hydrodynamic radius. The fractionation relies on the interplay between laminar flow and Brownian
diffusion. The fractionation occur in a thin channel equipped with inlet and outlet, and a special membrane as a bottom wall (see, e.g., 3D of Eclipse device on Fig. 1; for more details see, e.g., www.wyatt.eu). A horizontal flow of a solvent along a membrane is combined with a strong cross flow across the membrane. The membrane is impermeable for the particles, while the solvent can flow throughout it.

AF4 consists of two main stages: a focusing—
injection stage and an elution stage.

**Focusing—Injection stage.** A sketch of flow directions during the focusing—
Injection stage can be seen in Figure 2. During the focusing—
injection stage, the solvent is entering the channel from both sides, and leaves through the membrane (see Figure 2).

The ratio between the left and the right volumetric fluxes determines the position of the focusing line. In the real devices, this ratio is usually considered as piecewise-constant function of time. The particles are injected from the left side during a certain time interval (shorter than the total duration of the focusing—
injection stage), and they are transported towards the membrane due to the strong cross flow. The injection can be done either through a special injection port, or through the inlet. The Brownian diffusion, which acts isotropically, prevents particles from resting at the membrane surface. The interplay between the force induced by the cross flow and the Brownian diffusion results in forming a boundary layer with average distance from the membrane depending on the particle size (i.e., on the diffusion coefficient) and on the intensity of the cross flow (see, e.g., [5], [16]). Smaller particles with their larger diffusion coefficient form a layer which has a larger average distance to the membrane.

At the end of the focusing—
injection stage the injected particles are located in a thin layer on the membrane, within a focusing zone around the focusing line, and this is the starting point of the consecutive horizontal transport of the particles.

The main goals of the focusing-injection stage are

1. to concentrate almost all particles in some region $\Omega_1$ by the end of the focusing stage
2. to avoid very high concentration of particles in some regions of $\Omega_1$, otherwise the particles will start to interact with each other, which can lead to a poor separation or non-durable use of the membrane

**Elution stage.** A sketch of flow directions during the elution stage can be seen in Figure 3. Due to the parabolic profile of the horizontal velocity, a horizontal separation of the particles is achieved at a certain distance from the focusing line. During the elution stage, smaller particles are transported faster than the bigger particles towards the channel outlet, because they experience a higher tangential flow velocity. For a more detailed description of AF4 process see, e.g., [1], [16].

The main goal of the elution is to achieve the best possible separation of the particles, having in mind, that the whole elution stage should be as fast as possible.

### 3 Mathematical Model of the AF4 Process

In this section we specify the state system for the upcoming optimization of the AF4 process.

#### 3.1 Motivation and Simplifications

The solvent is usually a slow incompressible liquid and therefore Stokes equation can be used to describe the flow in the channel (see the sketch of the fractionation device geometry in Figure 1), as well as the flow in the free space under the membrane/frit (crossflow) region. The flow through the porous membrane and the underlying frit can either be described by the Darcy or the Brinkman model. Based on our previous experience, we consider only the Stokes-Brinkman model (for de-
tails see [6]). Further, our flow simulations with the 3D Stokes-Brinkman problem, demonstrate that for the regimes which are relevant for the fractionation process, the velocity on the surface of the membrane is almost constant, with zero tangential component and non-zero vertical component. Based on this, even the Stokes-Brinkmann equations can be replaced by just the Stokes problem in the channel. Numerical studies have also shown, that even when we consider time-dependent Stokes equation with fixed boundary conditions, then its solution stabilizes in few seconds ([6]).

**Remark 3.1.** Note, that this simplification is used also by pioneers of AF4 [16]. Furthermore, because our main goal is flow control for optimization of the fractionation procedure, we consider one more simplification used by [16]: We reduce the 3D problem to an effective 2D one.

By definition we have

\[ \langle \partial_t c, \varphi \rangle_{L^2(Q)} = \langle \partial_t c, \varphi \rangle_{W^*,W}. \]

Divergence-free property \( \nabla \cdot \vec{V} = 0 \) enables us to rewrite \( \vec{V} \cdot \nabla = \nabla \cdot (\vec{V} c) \), therefore

\[ \langle \partial_t c, \varphi \rangle_{W^*,W} + \langle \nabla \cdot (\vec{V} c - D \nabla c), \varphi \rangle_{L^2(Q)} = 0. \]

Using divergence theorem we obtain

\[ \langle \nabla \cdot (\vec{V} c - D \nabla c), \varphi \rangle_{L^2(Q)} = -\langle \vec{V} c - D \nabla c, \nabla \varphi \rangle_{L^2(Q)} + \langle (\vec{V} c - D \nabla c) \cdot \vec{n}, \varphi \rangle_{L^2(\partial \Omega \times (0,T))}. \]

Applying boundary conditions from (3.2), the boundary term from the last equality vanishes.

Then the weak formulation of (3.2) reads: Find \( c \in X \) s.t. \( c(0) = c_0 \) in \( L^2(\Omega) \) and \( \forall \varphi \in W \)

\[ \langle \partial_t c, \varphi \rangle_{W^*,W} - \langle \vec{V} c - D \nabla c, \nabla \varphi \rangle_{L^2(Q)} = 0. \]

### 3.3 Properties of Stokes equation

For the existence and uniqueness of the Stokes system (3.1) we refer to [15].

The linearity of the Stokes system directly yields the following result, which will be essential for the setup of our fast optimization algorithm.

**Lemma 3.1.** Consider the Stokes system (3.1) with boundary function \( \vec{g} = u_1 \vec{g}^{(1,0)} + u_2 \vec{g}^{(0,1)} \), where \( \vec{g}^{(1,0)}, \vec{g}^{(0,1)} \in H^{1/2}(\partial \Omega) \) and \( u_1, u_2 \in \mathbb{R} \). Then, the solution \( (\vec{V}, p) \) depends linearly on \( (u_1, u_2)^T \), i.e.

\[ \vec{V} = u_1 \vec{V}^{(1,0)} + u_2 \vec{V}^{(0,1)}, \quad p = u_1 p^{(1,0)} + u_2 p^{(0,1)} \]
where \((\tilde{V}^{(1,0)}, p^{(1,0)})\) corresponds to the boundary function \(\tilde{g}^{(1,0)}\) and \((\tilde{V}^{(0,1)}, p^{(0,1)})\) corresponds to \(\tilde{g}^{(0,1)}\), respectively.

### 4 The Optimal Control Problem

Now we state a specific optimal control problem on the domain \(\Omega = (0, L) \times (0, w)\) shown in Figure 4.

We define the subdomain \(\Omega_1 = (x_1^{(1)}, x_1^{(2)}) \times (0, \alpha w)\), where \(0 < x_1^{(1)} < x_1^{(2)} < L\) and \(0 < \alpha < 0.5\). The functional we are going to minimize is defined as

\[
J(c, u) = \frac{1}{2} \int_{x_1^{(1)}}^{x_1^{(2)}} \left( \left[ \int_0^w c(x_1, x_2, T) \, dx_2 - K \right]_+ \right)^2 \, dx_1
\]

\[
+ \frac{\mu}{2} \left( \int_{\Omega \setminus \Omega_1} c(x, T) \, dx \right)^2,
\]

where \(c = c(u)\) is the concentration computed from (3.2) and \(\tilde{V} = \tilde{V}(u)\).

It holds \((f)_+ = \max(f, 0)\) and \(K > 0\) is a constant which gives the desired average concentration on the sets \(\{x_1\} \times [0, w]\). The second term in \(J\) penalizes particles outside of \(\Omega_1\), in which we aim to accumulate the particles. Both aims can be adjusted by the positive constant \(\mu\).

**Remark 4.1.** We choose functional (4.4), because it meets the requirements presented by our industrial partner. The second term measures concentration outside the region \(\Omega_1\), while the first term is a measure for concentration exceeding certain level \(K\).

Consider the following linear operator

\[
Bc = \int_{0}^{w} c(x_1, x_2) \, dx_2, \quad B : L^2(\Omega) \rightarrow L^2(0, L)
\]

Then, the functional \(J\) can be rewritten in a more convenient operator form

\[
J(c, u) = \frac{1}{2} \langle (Bc - K)_+, (Bc - K)_+ \rangle_{L^2([x_1^{(1)}, x_1^{(2)}])}
\]

\[+ \frac{\mu}{2} \|c(T)\|_{L^1(\Omega \setminus \Omega_1)}^2.
\]

#### 4.1 Selection of control space

By problem definition, functions \((u_1, u_2)\) that rule Stokes equation (3.1) are control parameters at any time \(t\). We impose natural box constraints on the control:

\[
u_1^{a_i} \leq u_1(t) \leq u_1^{b_i}, \quad u_2^{a_i} \leq u_2(t) \leq u_2^{b_i}.
\]

We obtain a parametric set \(U\):

\[
U = \{(v_1, v_2) : v_1 \in [u_1^{a_i}, u_1^{b_i}], v_2 \in [u_2^{a_i}, u_2^{b_i}]\},
\]

which is a convex polygon.

Based on the requirements of our industrial partner, we will choose control functions \((u_1, u_2)\) to be piecewise continuous, i.e. they have a finite number of discontinuities of first kind on the interval \([0, T]\).

For the piecewise constant function we will need to evaluate derivatives with respect to an increment of arguments \(u_1^1 = u_1(t_{i-1}), \text{ as well as of } u_2^2 = u_2(t_{i-1})\) \((i = 1, \ldots, N)\).

For example, designating \(\frac{\partial}{\partial u_1^1} c(x, t) = f_1^1(x, t)\) and noting that

\[
\frac{\partial}{\partial u_1} \tilde{V} = \sum_{i=1}^N \chi_i(t) \tilde{V}(1,0),
\]

where \(\chi_i(t) = \mathcal{I}_{[t \in [t_{i-1}, t_i]]}\), we have

\[
\begin{aligned}
& \langle \frac{\partial}{\partial u_1^1} f_1^1, \varphi \rangle_{W^{1,\infty}} - \langle \tilde{V} f_1^1 - D \nabla f_1^1, \nabla \varphi \rangle_{L^2(Q)} \\
= & \langle \tilde{V}(1,0) c, \nabla \varphi \rangle_{L^2(\Omega \times [t_{i-1}, t_i])},
\end{aligned}
\]

\[f_1^1(0) = 0.
\]

It is clear, that equations for (3.3) and (4.7) are solved in parallel, so we do not need to store concentration \(c(x, t)\), except for its value at the terminal moment. This allows us to solve optimization problem in the cases when we have memory constraints.

#### 4.2 Projection gradient method

As a result, after solving the systems for

\[
c(x, t), \quad f_1^1(x, t), f_2^2(x, t) \quad (i = 1, \ldots, N)
\]

we obtain a \(2N\)-dimensional gradient vector of \(c(x, t)\):

\[
(f_1^1(x, t), \ldots, f_1^N(x, t), f_2^1(x, t), \ldots, f_2^N(x, t))
\]

\[=: \tilde{u}(x, t) \in [L^2(\Omega \times (0, T))]^{2N}.
\]

Then we derive an expression for the gradient of the reduced cost functional \(\tilde{J}(u)\): the \(i\)-th component of \(2N\)-dimensional vector \(\tilde{J}'(u)\) can be written as

\[
\langle \tilde{J}'(u) \rangle^i = \langle (Bc - K)_+, B d_i^u \rangle_{L^2([x_1^{(1)}, x_1^{(2)}])}
\]

\[+ \mu \|c(T)\|_{L^1(\Omega \setminus \Omega_1)} \int_{\Omega \setminus \Omega_1} d_i^u(x, T) \, dx,
\]

where \(d_i^u\) is \(i\)-th component of the gradient vector \(\tilde{u}(x, t)\).

**Remark 4.2.** Similarly to the case with derivative of the solution \(c'(u)\), gradient \(\tilde{J}'(u)\) is an approximation of Frechet derivative of functional \(\tilde{J}(u)\) with respect to control parameter \(u = u(t)\).

Using these results, we can formulate projection gradient (see [4]) method for minimization problem (4.6) with control set

\[
U = \{u_1^{1}, \ldots, u_1^{N}, u_2^{1}, \ldots, u_2^{N} : (u_1^{1}, u_2^{1}) \in U\}.
\]
This control set is convex and closed (which follows from the convexity of \( U \)), therefore, projection \( \mathcal{P}_U \) is well-defined and unique.

Denote initial guess \( u_0 \) be in the interior of \( \mathcal{U} \). Calculate the corresponding gradient \( d_0 \). The algorithm has the following form.

1: Set \( k := 0, \sigma \in (0, 1), \gamma, \gamma \)
2: do
3: Evaluate \( d_k := -\tilde{J}'(u_k) \)
4: Set \( u_{k+1} := \mathcal{P}_U(u_k + \gamma d_k) \)
5: Compute \( J(u_{k+1}) \)
6: If \( u_{k+1} \) satisfies Armijo’s rule, increase \( k \) and Go to 3.
7: Else \( \gamma := \gamma \cdot \sigma \) and Go to 4.
8: while \( ||u_k - \mathcal{P}_U(u_k + d_k)||/||u_0 - \mathcal{P}_U(u_0 + d_0)|| \geq \gamma \)

5 Numerical experiments

We present here some numerical results of minimization problem with simplified (compared with practical tasks) parameters of PDE and control.

For evaluating \( c(x, t), f_1(x, t), f_2(x, t) \) \( (i = 1, \ldots, N) \) we applied edge-averaged finite element (EAFZ) scheme, following the articles [2], [3].

At first we consider a certain case of boundary conditions for velocity flow \( \dot{V} \) shown on Figure 4. The solution for the Stokes equation (3.1) will read as

\[
V_1 = -6(u_1 + u_2) \frac{x_1}{L} \cdot \frac{x_2}{w} \left( 1 - \frac{x_2}{w} \right) + 6u_1 \frac{x_2}{w} \left( 1 - \frac{x_2}{w} \right),
\]

\[
V_2 = -(u_1 + u_2) \left( 1 - 3 \left( \frac{x_2}{w} \right)^2 + 2 \left( \frac{x_2}{w} \right)^3 \right) \cdot \frac{1}{L}.
\]

Rectangular domain \( \Omega \) has length \( L = 0.1 \) m and width \( w = 290 \cdot 10^{-6} \) m. Subdomain \( \Omega_1 \) is described as \( \Omega_1 = \{(x_1, x_2): x_1 \in [0.1 \cdot L, 0.2 \cdot L], x_2 \in [0, 0.1 \cdot w]\} \).

We consider a diffusion coefficient \( D = 8 \cdot 10^{-11} \) m\(^2\)/sec, while the focusing time is \( T = 100 \) seconds.

Number of switching moments was selected \( N = T/\Delta t \) with fixed switching time steps \( \Delta t_1 = 5 \) sec and \( \Delta t_2 = 10 \) sec. Moreover, as an initial guess for optimization problem with \( \Delta t_2 = 5 \) we use the answer of the optimization problem with \( \Delta t_1 = 10 \) sec.

Two cases of box constraints on \( u_1 \) and \( u_2 \) are considered. Corresponding constraining sets we denote by \( U_1 \) and \( U_2 \). Then

\[
U_1 = \{(v_1, v_2): v_2 \geq 0, 0.1 \leq v_1 \leq 1/3\},
\]

\[
U_2 = \{(v_1, v_2): v_2 \geq 0, 0.1 \leq v_1 \leq 1/3\}.
\]

Figure 5: Concentration in \( \Omega_1 \), integrated in \( y \)-direction. Flat distribution case.

5.1 Discussion of the results. Our first numerical results are very promising. For the realistic setting with \( K = \frac{1}{\Omega} \int \Omega c_0(x) dx \) the functional value is sufficiently small for already 10 switches. Moreover, we have seen, that for some cases, we do not benefit from increasing number of switching points.
Our next work will be devoted to more extensive research for this type of optimization problem. We will present soon extended numerical simulations and do tests for full geometries. Moreover, in order to speed up calculations, we will consider using Reduced Basis technique ([20], [21]) for the optimization problem ([22]). Our long term goal will be shape optimization of the 3D devices.

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