Numerical Analysis of the Impact of Geometric Shape Patterns on the Performance of Miniaturized Chromatography Systems

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Abstract: Various chromatography systems are today widely applied for both analysis and preparation of chemical compounds from complex mixtures. Current trends aim at the miniaturization of such systems, for instance on microchips. One approach is to arrange arrays of small pillars in a micro channel. The pillar surfaces are functionalized such as to adsorb specific substances from a bulk fluid which flows through the channel. The performance of such miniaturized chromatography systems is particularly sensitive to the geometric shape pattern of the pillar array. Dead volumes that are often formed at the channel inlet, outlet and boundaries significantly contribute to the unwanted effect of bulk flow dispersion. The same is true for miniaturized chromatography systems using porous particles in a packed bed.

We hence have implemented a two dimensional chromatography model for the analysis and optimization of structured micro pillar arrays. Dynamic surface interaction of solved molecules is taken into account by the kinetic Langmuir model. Variations of the pillar array geometry lead to deviations in the outlet concentration profiles. These deviations can not be described by the one dimensional models that are typically used for the simulation of chromatography on larger scales where the sizes of the channel and of the functionalized media differ by several orders of magnitude.

We also have implemented a two dimensional model for studying the interplay of transport and sorption processes in packed bed chromatography with porous particles.

Keywords: Microfluidics, Chromatography, Flow in Porous Media, Adsorption and Desorption

1. Introduction

Miniaturized chromatography systems are potentially important as unit operations for the separation and analysis of complex mixtures in lab-on-microchip technology. The performance of such systems mainly depends on a large spread between residence times of the studied molecule species and at the same time on low axial dispersion [1]. Miniaturization helps to achieve the latter goal due to laminar flow and the absence of turbular mixing at low Reynolds numbers in the micro-channels. Another key advantage of miniaturized systems lies in the requirement of very small sample volumes. However, the technical separation must be achieved on a short axial distance, and numerical simulations must be able to preserve rather sharp-edged concentration profiles.

Chromatography systems are usually modeled in only one spatial dimension [2]. One dimensional models are computationally less complex and allow quite accurate simulations of large-scale chromatography systems. On the other hand, one dimensional simulations can not account for the specific 2D geometry of pillar arrays. We hence apply a two dimensional chromatography model for studying the impact of geometric shape patterns in microfluidic separation devices on the shape of breakthrough curves, and compare the results with one dimensional simulations.

Our analysis is based on hypothetical chromatography systems with micropillars that are arranged in several distinct shape patterns. The surfaces of these pillars are assumed to be functionalized with receptors that reversibly bind specific molecules from the fluid phase. The migration of molecules through the chromatography column is slowed down by these reversible binding processes as compared to the convective flow of the bulk fluid. Molecule species with high surface affinity are more strongly retained and hence separated from molecules with lower surface affinities.

2. Multiphysics Modeling

The two dimensional model is organized in submodels for transport, dispersion and adsorption. We first set up a model with adsorption on the pillar surfaces, and later

generalize this model by adding diffusion and sorption processes inside porous chromatography media.

2.1 Geometry

We compare chromatography devices with identical number and size of micropillars. Figure 1 shows two basic shape patterns.

2.2 Transport

We neglect changes of viscosity and density due to adsorption of molecules from the bulk liquid to the pillar surfaces and consider the velocity profile invariant and in particular independent of the local molecule concentration. The Navier-Stokes equation for incompressible media can consequently be calculated separately from the dispersion and adsorption processes of the transported molecules:

$$\rho \frac{\partial \vec{V}}{\partial t} = -\nabla P + \mu \Delta \vec{V} \qquad (1)$$

Here, P denotes pressure, μ viscosity and ρ density of the bulk fluid. The velocity profile $\vec{V}$ is precalculated and stored for later use in solving the convection-dispersion equation:

$$\frac{\partial c}{\partial t} = -\vec{V} \cdot \nabla c + D \cdot \Delta c \qquad (2)$$

Here, D denotes the dispersion coefficient and c the molecule concentration in the bulk fluid. The flow is laminar due to the microscale of the whole system.

2.3 Sorption

The molecules are transported through the chromatography column and temporarily immobilized at the pillar boundaries. For this immobilization process we assume a classical Langmuir kinetic:

$$\frac{\partial q}{\partial t} = k_a \cdot c \cdot (q_{\max} - q) - k_d \cdot q \qquad (3)$$

Here, q_{max} denotes the overall number of binding sites, q the receptors that are actually occupied, and k_{ads} and k_{des} quantify the adsorption and desorption rate, respectively. The molecule concentration c in the bulk fluid is also taken at the pillar boundaries.

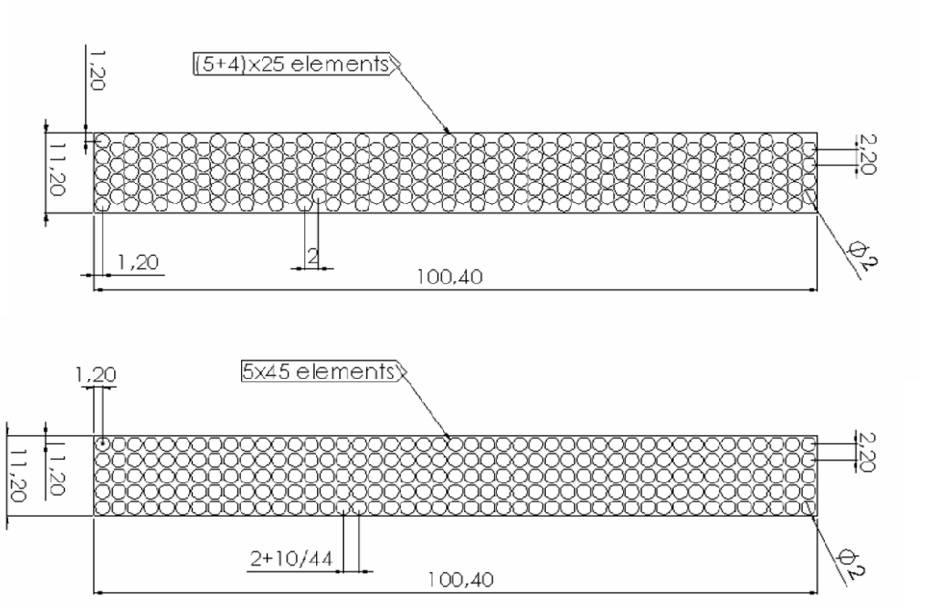

Figure 1: Two basic geometries. Top: (5+4)×25 shifted pillar geometry, bottom: 5×45 straight pillar geometry

3. Implementation

The model equations for transport, diffusion and sorption are numerically solved over the interstitial subdomain between the pillars and on the boundary of each pillar. The fluid velocity profile is first determined in Navier-Stokes application mode and then used as input for the coupled calculation of the convection-dispersion and sorption processes. Sorption is modeled as time dependent outward flux -J_n onto the pillar boundaries, resulting in a Neumann boundary condition:

$$J_n = \frac{\partial q}{\partial t} \tag{4}$$

The Langmuir model is implemented in a weak formulation on each pillar boundary (compare [3]). Table 1 shows the boundary conditions for all application modes (AM).

AM	Boundary	Condition	Variable & Value
ns	Inlet Outlet All other	Inlet velocity Pressure No slip	$v_{\sup}$ $p = 0$ –
cd	Inlet Outlet Pillars All other	Concentration Convect. flux Flux Insulation	c_0 – $-J_n$ –
wb	Pillars All other	Weak term inactive	*weak*/*dweak* –

Table 1: Boundary conditions

4. 1D/ 2D parameter conversion

In one dimensional chromatography models the geometry is only taken into account by means of the column porosity ε, that is the volume fraction of the interstitial column void. The fluid velocity acts in axial direction only, and the sorption process is usually considered as outflux. The convection-diffusion equation can hence be rewritten as follows:

$$\frac{\partial c}{\partial t} = -v_{\text{int}} \cdot \frac{\partial c}{\partial z} + D_a \cdot \frac{\partial^2 c}{\partial z^2} - \frac{1-\varepsilon}{\varepsilon} \cdot \frac{\partial q}{\partial t} \tag{5}$$

Here, z denotes the axial distance from the column inlet and D_a is the axial dispersion coefficient. In order to compare 1D and 2D simulations we need to determine consistent values of the interstitial velocity v_{int} and the receptor density $q_{\max}^{1D}$. If the superficial velocity in the 2D model is denoted by v_{sup} we get:

$$v_{\sup} = v_{\text{int}} \cdot \varepsilon \tag{6}$$

The receptor density $q_{\max}^{1D}$ that is used for q_{max} in the Langmuir sorption model (Equation 3) in the one dimensional model is defined with respect to the volume fraction that is occupied by the pillars. This value is hence a function of the receptor density per total column volume $\bar{q}_{\max}$ and column porosity ε:

$$q_{\max}^{1D} = \frac{\bar{q}_{\max}}{1-\varepsilon} \tag{7}$$

The total receptor density in the one dimensional model is proportional to the surface specific receptor density in the two dimensional model, which is only here denoted by $q_{\max}^{2D}$ in order to avoid ambiguity:

$$\bar{q}_{\max} = q_{\max}^{2D} \cdot \frac{n \cdot 2\pi r \cdot \cancel{h}}{l \cdot b \cdot \cancel{h}} \tag{8}$$

Here, n denotes the amount of pillars, and the channel height h cancels out.

5. Solution

The minimum element size of the finite element mesh was estimated by step-wise refinement, within the given limits of memory and computational time. We used the results on the finest mesh as reference in order to estimate the approximation error as illustrated in Figure 2. Based on these estimates we chose a maximum element size of $\Delta x = 1.5 \cdot 10^{-4} m$, resulting in 77348 finite elements.

The velocity profile of the liquid phase is first computed in COMSOL by solving the Navier-Stokes equations for incompressible flow with the direct PARDISO solver. This profile is then considered invariant. Convection, dispersion and sorption of the molecules are

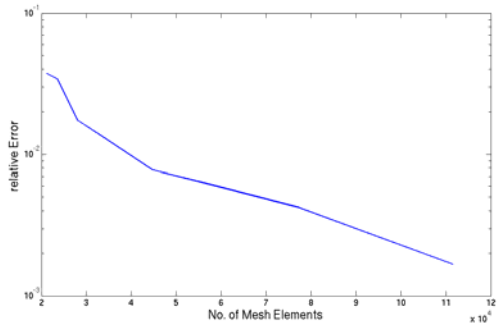

Figure 2: Relative approximation error over number of mesh elements

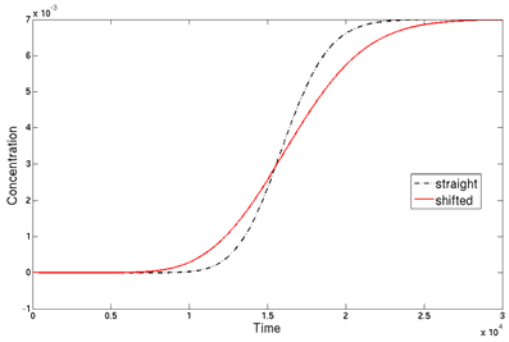

Figure 4: Cross section averaged outlet concentration profiles for different pillar arrays

subsequently calculated with the iterative GMRES solver and a geometric multigrid preconditioner.

6. Results

Figure 3 shows typical simulation results at an intermediate time during the column load phase for two different arrangements of the pillar array. The array pattern obviously influences the shape of the concentration front. The larger spaces at the channel walls in model *b)* cause smearing of the front. This is a major problem for miniaturized chromatography systems where the bed is less dense at the channel walls as compared to the channel center. A straight pillar arrangement as in model *a)* yields a much sharper and less smeared concentration front. Figure 4 shows the impact of the front smearing effects inside the chromatography column on the cross section averaged breakthrough curves at the column outlet.

The reduced steepness of the breakthrough curve of model *b)* usually indicates increased dispersion in the column. The difference between both breakthrough curves is exclusively caused by geometry and could not be explained by a one dimensional model. We will further analyze the analogy between 1D and 2D chromatography models in the next section.

7. Comparison with 1D Dispersion

In section 4 we show how to transfer several model parameters from the 1D to the 2D case. The system geometry impacts on both interstitial velocity v_{int} and receptor density q_{max} via column porosity ε. However, the impact of system geometry on axial dispersion in the one dimensional model is much more complex, since the dispersion in the two dimensional model can have a significant orthogonal component. We

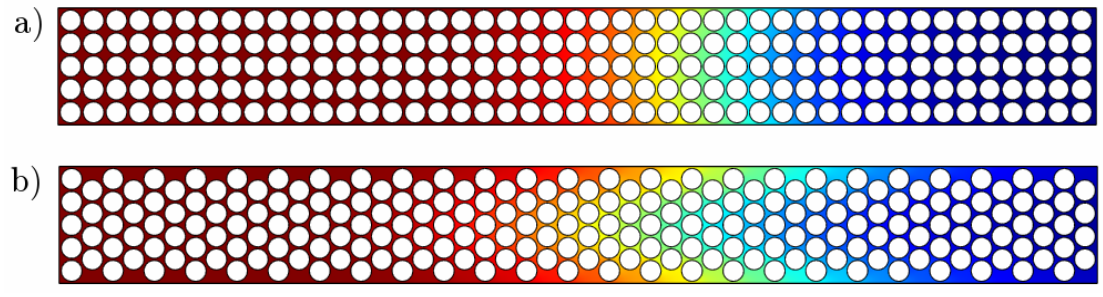

Figure 3: Simulation results at an intermediate time for varied geometries of the pillar array. a) straight b) shifted. Flow from left to right, blue: low concentration, red: high concentration

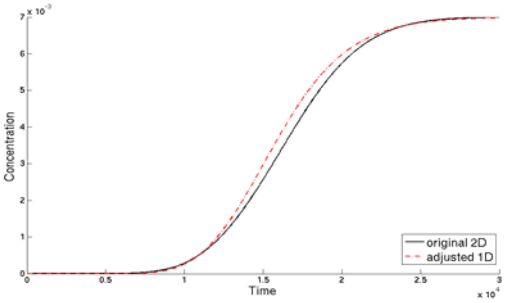

Figure 5: Best fit of breakthrough curves between 1D and 2D models with shifted pillar geometry

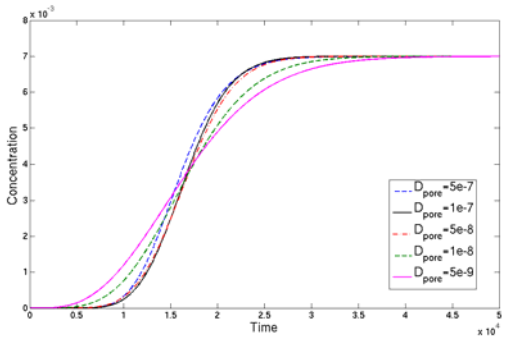

Figure 7: Outlet concentration profiles for different pore diffusion coefficients.

hence estimated effective dispersion coefficients by fitting the 1D model to 2D simulation results in order to quantify apparent axial dispersion.

The one dimensional chromatography model was implemented in MATLAB, solved with *ode15s*, and fitted with the Levenberg-Marquardt algorithm *lsqnonlin*. The 2D dispersion coefficient $D = 5 \cdot 10^{-7}$ results in apparent 1D dispersion coefficients of $3.42 \cdot 10^{-7}$ for the straight 5×45 pillar array and of $1.36 \cdot 10^{-6}$ for the shifted (5+4)×25 pillar array. The breakthrough curves of the 1D and 2D models match very well for the straight pillar geometry, but a significant residual remains in case of the shifted geometry, as illustrated in Figure 5. This result underlines the necessity to use 2D or even 3D models for the simulation of more complex geometric pillar geometries.

8. Porous Media

We also implemented a model for studying miniaturized separation devices with porous chromatography media. Here, the pillars are replaced by cylindrical porous particles. Figure 6 shows a typical result. The molecules are again subject to convection and dispersion in the column bulk fluid, but can penetrate the particle boundaries and diffuse into the porous media where they are also immobilized by specific receptors at the pore walls. Figure 7 shows simulated breakthrough curves for varied pore diffusion coefficients:

$$D_{pore} = [5 \cdot 10^{-7}, 1 \cdot 10^{-7}, 5 \cdot 10^{-8}, 1 \cdot 10^{-8}, 5 \cdot 10^{-9}]$$

A pore diffusion coefficient of $D_{pore} = 5 \cdot 10^{-7}$ yields a rather steep breakthrough curve at the column outlet. With decreasing diffusion coefficients the porous particles are filled and emptied more slowly, resulting in an earlier begin and a more pronounced tailing of the break through curve.

9. Conclusions

We implemented various models for miniaturized column chromatography in one and two dimensions. The impact of geometrical shape patterns was analyzed and compared. We found that local shape irregularities of the pillar array in particular at the channel boundaries can cause smearing of the internal concentration fronts and that the resulting impact on the external breakthrough curve at the column outlet can not be predicted with 1D models. However,

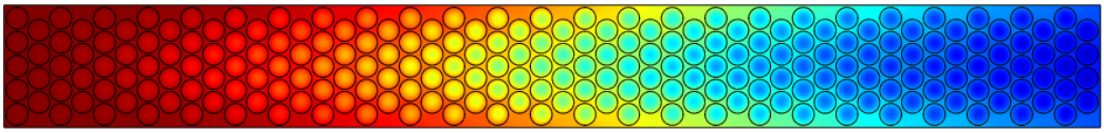

Figure 6: Simulation result for a chromatography system with porous media. Flow from left to right. Blue: low concentration, red: high concentration

adjusting the one axial dispersion coefficient in a one dimensional model to an apparent value can significantly decrease the inevitable discrepancy between 1D and 2D simulation results.

We also implemented a two dimensional model for the simulation of chromatography with porous particles. This model was applied for a parameter study with varied pore diffusion coefficients. However, a 3D model will be necessary for the analysis of packed bed chromatography where spherical particles are in direct contact, and the two dimensional projection leaves no channel for convective transport. This will be subject of further studies.

10. References

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11. Acknowledgements

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