High Definition Simulation of Packed Bed Chromatography

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Introduction

Chromatography is widely used in biotechnology and pharmaceutical industry as a downstream process for separating target molecules from fermentation broth or natural sources. In packed bed chromatography, a mixture of components in liquid solution flows through a cylindrical column filled with stationary porous particles (packed bed). Selective adsorption of the target components to functionalized inner surfaces of the particles enables their separation from unwanted components. Microscale columns contain about 100,000 particles while production scale columns contain billions of particles.

Motivation

Chromatography is conventionally simulated with reduced order models, such as the so-called general rate model, which describe the transport and adsorption in the column with varying degrees of complexity. However, these models are spatially homogenized and thus cannot capture packing morphology and are further simplified by neglecting radial concentration gradients in the column. Some of these issues can be addressed by a 2D general rate model with particle size distribution. However, high definition 3D CFD simulations provide a spatially resolved view of the impact of packing morphology on the flow and particle loading within the column.

Stationary Stokes Flow

$$-\eta\nabla^2\mathbf{u} + \nabla p = 0, \quad in\ \Omega_1$$
$$\nabla\cdot\mathbf{u} = 0, \quad in\ \Omega_1$$

Mass Transfer

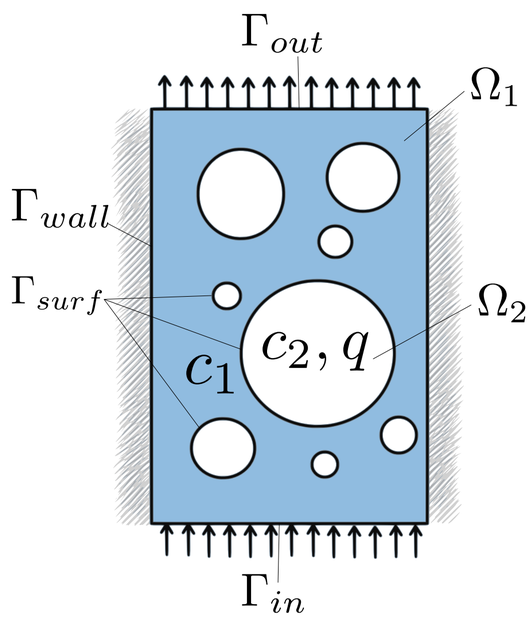
$$\frac{\partial c}{\partial t} = D_1\Delta c - \mathbf{u}\cdot\nabla c, \quad in\ \Omega_1$$
$$\frac{\partial c}{\partial t} + \frac{1-\varepsilon}{\varepsilon}\frac{\partial q}{\partial t} = D_2\Delta c, \quad in\ \Omega_2$$

Adsorption

$$\frac{\partial q}{\partial t} = k_a c\,(q_m - q) - k_d q, \quad in\ \Omega_2$$

Multi-domain coupling

$$\mathbf{n_1}\cdot(-D_1\nabla c_1) = \mathbf{n_2}\cdot(-D_2\nabla c_2), \quad in\ \Gamma_{surf}$$



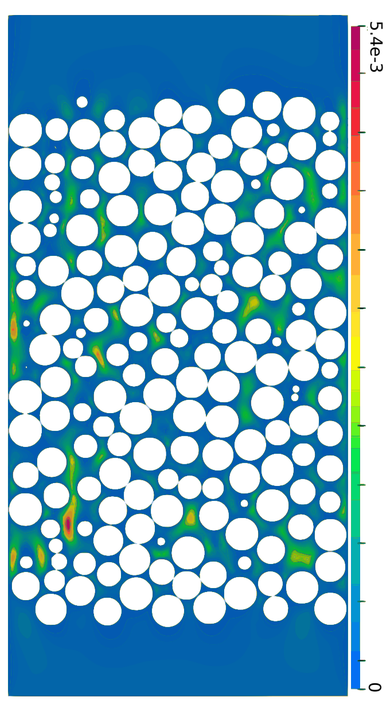
Parameter	Symbol	Value	Unit
Interstitial diffusivity	D_1	$1.15\cdot10^{-10}$	m^2/s
Effective pore diffusivity	D_2	$7.07\cdot10^{-11}$	m^2/s
Bead porosity	ε	0.75	–
Adsorption coefficient	k_a	1.144	$m^3/(mol\cdot s)$
Desorption coefficient	k_d	$2\cdot10^{-3}$	$1/s$
Maximum capacity	q_m	4.88	mol/m^3
Inlet concentration	c_{in}	$7.14\cdot10^{-3}$	mol/m^3
Inlet velocity	u_{in}	$2.09\cdot10^{-4}$	m/s
Column length	L	$2.01\cdot10^{-3}$	m
Column radius	R	$5\cdot10^{-4}$	m
Particle radius	r	$5\cdot10^{-5}$	m

Preliminary Results

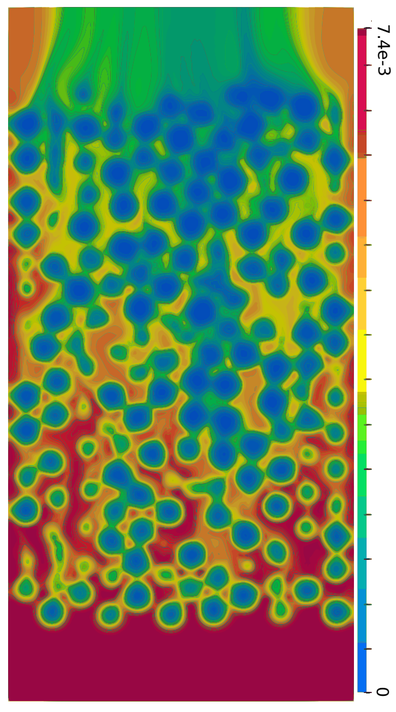
The system is simulated using the parallel multi-physics solver XNS, developed at CATS, RWTH Aachen. XNS utilizes a stabilized space-time Galerkin finite element method. The time and space domains are both discretized using finite elements (linear 4D tetrahedrons), yielding unconditionally stable linear systems. Mesh convergence was studied with a test column with 1360 monodisperse particles. Results for a mesh with 16.74M elements are shown below.

Geometry

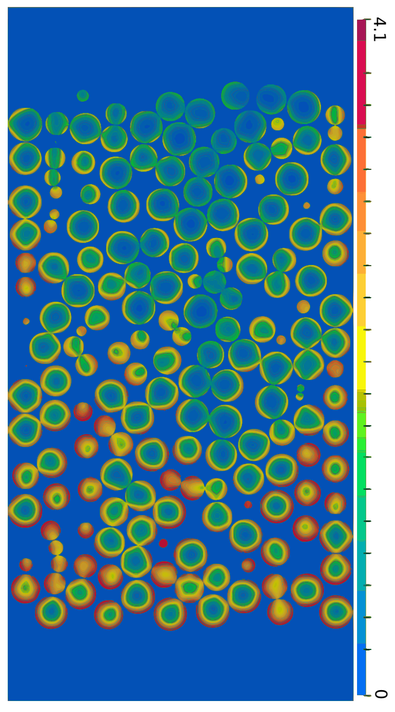
Velocity



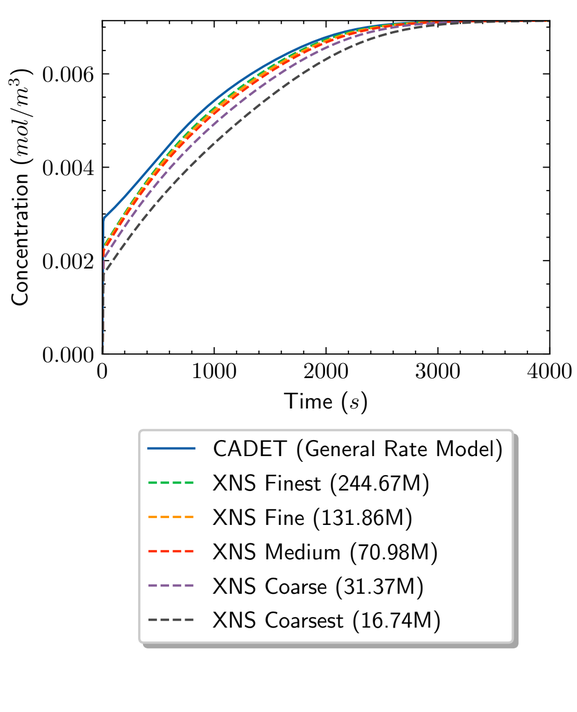
Mobile Phase



Bound Phase



Mesh Convergence



Conclusions

Preliminary results show that the simplifying assumptions of the so-called general rate model do not always hold:

- The velocity profile is not constant, but highly nonlinear.
- The radial concentration profile is not constant.
- The bead loading is not radially symmetric.

Planned Work

We are currently simulating columns with up to 10,000 particles. In the future, we will

- Implement hybrid parallelization to improve performance.
- Use second order elements to better capture flowfield.
- Use periodic boundaries to simulate production scale columns.

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