High-Definition Simulation of Packed-bed Chromatography in Laterally Unconfined Compartments

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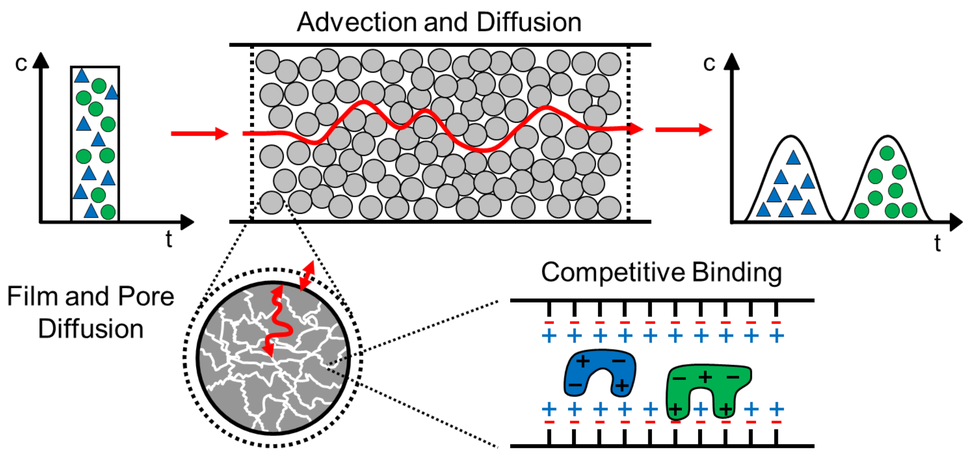
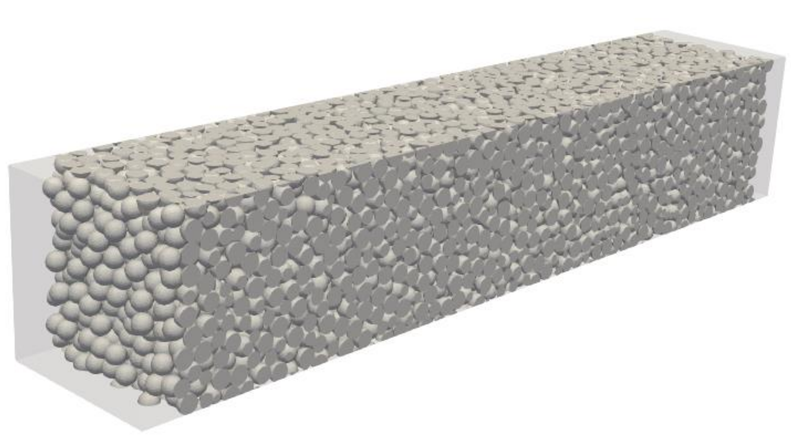
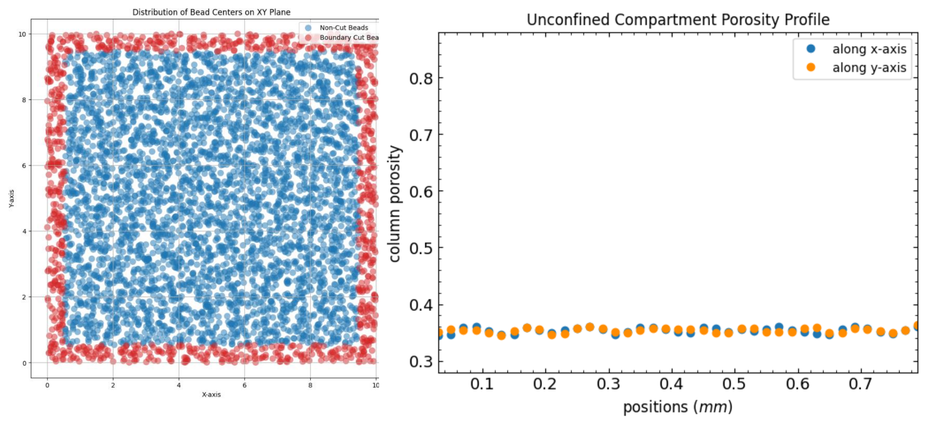
Introduction

Packed-bed liquid chromatography is widely used in biotechnology and other industries for the purification of molecules. While reduced-order models enable efficient simulations, they require extensive calibration based on experimental data and do not provide mechanistic insights into how specific morphological features influence local hydrodynamic profiles and separation performance within the column. These characteristics include particle size distribution, particle geometry, local packing irregularities, and wall effects. High-definition chromatography modeling addresses these limitations by fully resolving spatial details; yet previous studies have been restricted to confined cylindrical packings within unrealistically narrow columns. These constraints introduce substantial wall effects, altering the local hydrodynamic behavior, and limiting the applicability of the results to larger-scale applications.

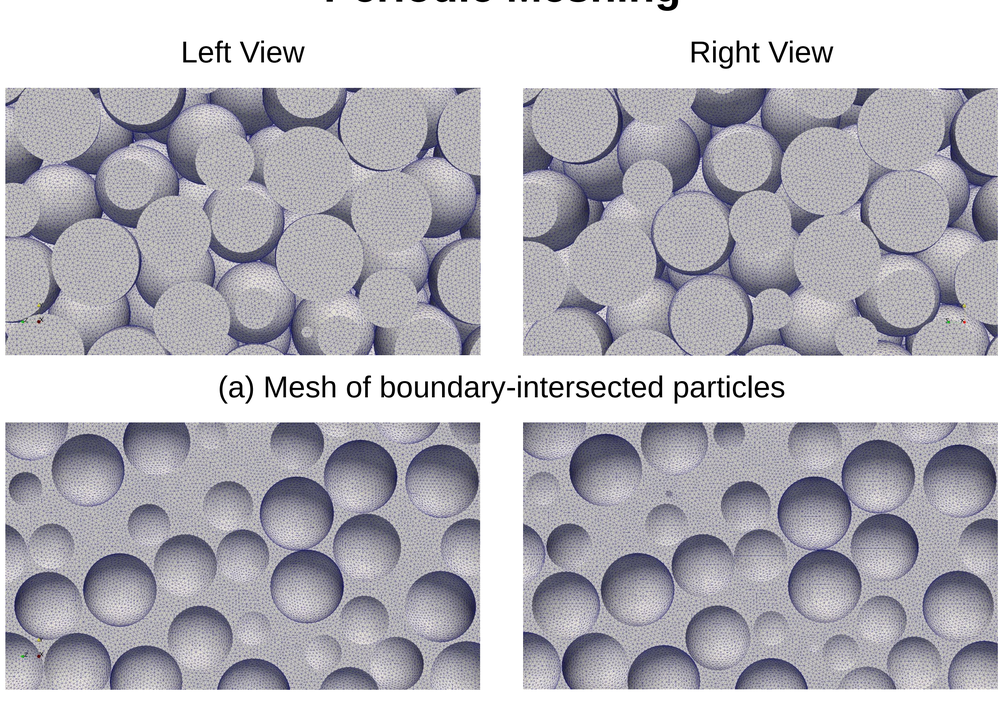


Laterally Periodic Packings





Periodic Meshing

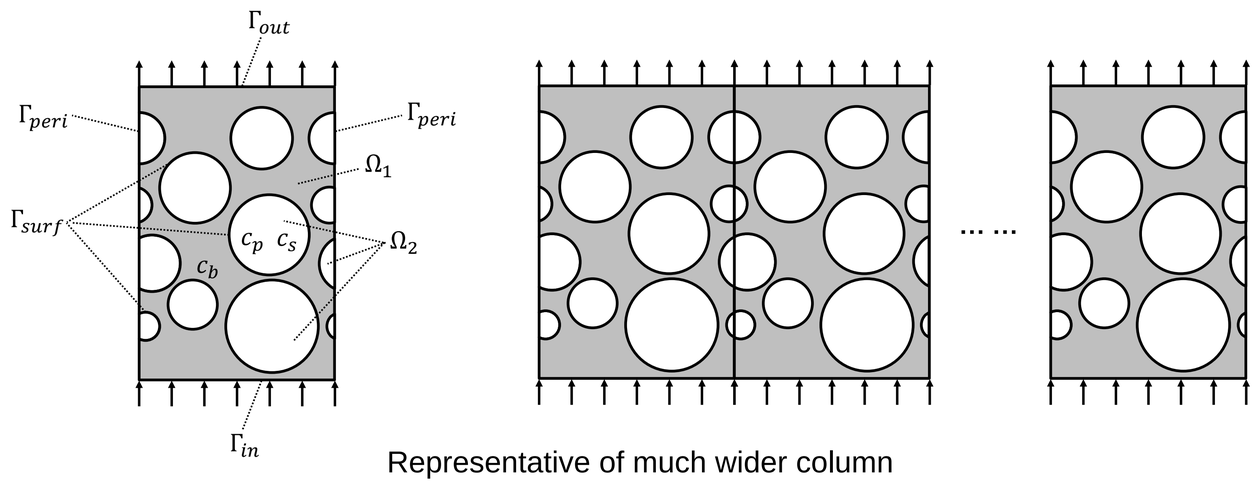


(a) Mesh of boundary-intersected particles

(b) Mesh of bulk regions excluding particles

Unconfined HD Chromatography Model

Schematic Representation



Representative of much wider column

Mathematical Representation

Stationary Stokes Flow

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

Mass Transport

$$\frac{\partial c_b}{\partial t} + (\boldsymbol{u} \cdot \nabla)c_b = D_b\nabla^2 c_b, \quad in \ \Omega_1$$
$$\varepsilon_p \frac{\partial c_p}{\partial t} + (1 - \varepsilon_p)\frac{\partial c_s}{\partial t} = D_p\varepsilon_p\nabla^2 c_p, \quad in \ \Omega_2$$

Langmuir Adsorption

$$\frac{\partial c_s}{\partial t} - k_a c_p(c_{s,max} - c_s) + k_d c_s = 0, \quad in \ \Omega_2$$

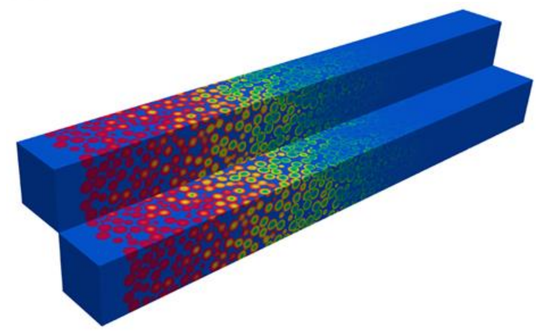
Multi-domain Coupling

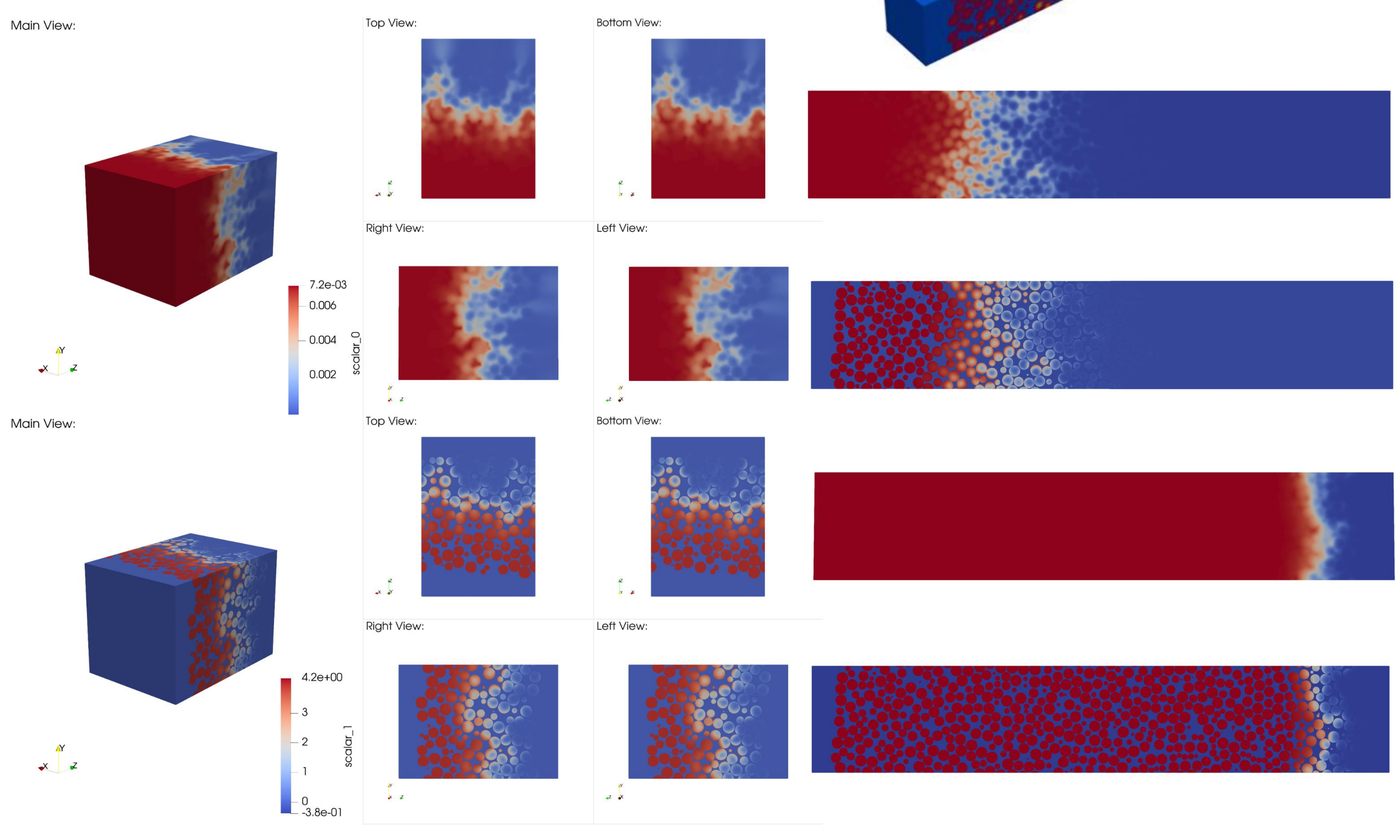
$$\boldsymbol{n}_1 \cdot (D_b\nabla c_b) = \boldsymbol{n}_2 \cdot (D_p\varepsilon_p\nabla c_p), \quad on \ \Gamma_{surf}$$

This work extends high-definition chromatography simulation from confined to unconfined compartments by establishing a validated workflow encompassing periodic packing generation, meshing, partitioning, XNS (CATS inhouse multi-physics solver) configurations and post-processing tools. Through systematic validation at each stage, we verify the correct implementation of periodic boundary conditions (PBCs). The successful resolution of mesh generation challenges enables scaling of mono-disperse packings from 1,000 to 10,000 particles in unconfined compartments, facilitating the investigation of local hydrodynamics without wall effects in industrial-scale applications. While double periodicity in XNS remains an open issue and requires further development, the validated performance of all other workflow components establishes a systematic framework for high-definition, large-scale simulations of packed-bed chromatography in laterally unconfined domains.

Test Framework

- Geometric periodicity in the packing
- Consistent distribution of grid nodes on PBCs
- Consistent connectivity between grid nodes on PBCs
- Block-swap approach for double periodicity validation





(a) Liquid and solid phase concentrations in small mono-disperse column at $t \approx 8000\ s$

(b) Liquid and solid phase concentrations in medium mono-disperse column at $t \approx 5000\ s$ and $t \approx 52900\ s$

Acknowledgements

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References

[1] Jayghosh Rao et al.: *High-definition simulation of packed-bed liquid chromatography*, Computers & Chemical Engineering 178 (2023): 108355.

[2] Xiang Xu. *Massively parallel high-definition simulation of packed-bed chromatography in laterally unconfined compartments*, Master Thesis, RWTH Aachen, 2025.

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