



MODELLING AND SIMULATION OF CHROMATOGRAPHY WITH SPHERICAL BEADS

In the BMBF joint research project AMSCHA, we develop models for the simulation of separation processes of protein and cell suspensions. The abbreviation stands for “Analysis, modelling and simulation of chromatographic purification processes”. In collaboration with researchers from the Technical University Kaiserslautern and the University of Applied Sciences Darmstadt, the processes are investigated on different length scales. The chemical and pharmaceutical company Merck KGaA and the manufacturer of optical microscopes Leica Microsystems support the research project as industrial partners.

The separation of target substances from a suspension is an important and often undervalued step in the manufacturing of agents in the pharmaceutical industry, although one cannot imagine laboratory and industrial work without chromatography as a separation process. One well-established form is column chromatography. The efficiency and the throughput of these columns strongly depend on the process conditions and the used chromatographic media.

Model, simulate and optimize protein purification

In one part of the project, we consider the separation of protein suspensions using chromatographic purification. The goal is to extract one target protein from a mixture. This is done with the help of spherical, microporous beads (pearls). In column chromatography, a cylindrical tube – the separating column – is packed with the stationary phase – the beads – and is flowed through by a protein suspension. In this connection, part of the proteins is deposited within the beads.

The industry partner Merck conducts for this application several experiments in the laboratory. To reproduce the processes in the simulation, we determine suitable model parameters based on static and dynamic measurements of the binding capacities (protein concentration). Additionally, Merck visualizes the concentration profiles in the static experiments using confocal laser scanning microscopy.

1 Microscopy image of a chromatography bead. Confocal laser scanning microscopy image of a labeled bead. The dye intensity is indicating the loading (lightest red strongest loading).

2 Overview on the simulation of a chromatography column (dynamic process conditions; left: concentration profile in the column, right: the loading of single beads at different positions in the column)

3 Comparison of the simulated protein breakthrough curve with experimental data

