Multi-Column Chromatography Process Modelling for Process Performance Prediction

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Introduction

Multi-column capture chromatography methods performed on the BioSMB platform have the potential to unlock increases in process performance. However, experimental methods to determine optimal process conditions are time and resource intensive. Modelling strategies can help to reduce time and resources necessary to optimize the process. In this study, we evaluate three modelling approaches, and the most accurate of the three was chosen to explore how the number of columns and the column configuration strategy can impact productivity and binding capacity.

Model Evaluation

Figure 2: A Simple Computational Model to Predict Product Breakthrough Curves

Three experimental points were compared to the computational and empirical models. Residual sum of squares analysis was conducted on 12 experimental points per model to determine goodness of fit.

Process Performance

For the BioSMB processes at each load residence time, varying load amounts were simulated in ChromWorks, and the amount that corresponded to 99% capture efficiency is reported as the operating load capacity in figures 6 & 8. The 2 column processes were simulated in ChromWorks to validate the absence of significant process loss.

A duration of 1500 seconds, corresponding to 25 total column volumes at a 1 minute residence time, was allocated in each cycle for wash, elution, and regeneration steps. Residence times between 0.6 minutes and 3 minutes were simulated.

Conclusions

A hybrid experimental and modelling approach for process optimization and productivity gains were observed. The number of columns necessary to run the most productive scenario at a fixed feed concentration of 0.9 g/L, BioSMB Scenario 2 with 2 columns in the load zone, was reduced from 30 to 12 experimental points per model to determine goodness of fit.

The design space for each loading scenario is bound by low and high feed concentrations at 0.6 min. load residence time.

Residence times between 0.6 minutes and 3 minutes were simulated.

Product breakthrough curves were generated by loading a single Protein A column with 100 g mAb/L resin.

Three different loading scenarios were examined:

- BioSMB Scenario 1 with 2 columns in the load zone
- BioSMB Scenario 2 with 3 columns in the load zone
- 2 column multi-phase flow load

The design space for each loading scenario is bound by low and high feed concentrations at 0.6 min. load residence time. For each point, three HEC experiments were conducted to confirm the maximum capacity usage of the column. Capture efficiencies of 99%, 95% and 90% were targeted.

A simplified computational model which assumes a linear isotherm was used to model the breakthrough data.

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