MODEL-BASED EVALUATION AND PROCESS DEVELOPMENT OF CONTINUOUS CHROMATOGRAPHY

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Multi-column periodic counter-current (PCC) chromatography has been proposed as continuous capturing technology to improve the process productivity and resin capacity utilization, as well as reduce buffer consumption and equipment footprint, which is applying for monoclonal antibody (mAb) capture with Protein A affinity resin. Due to the complexity of continues chromatography, some mathematical framework should be developed to aid the process development.

For continuous process, more factors should be considered and non-linear and phase-based relationships have to be faced as shown in Figure 1, which would certainly trouble the process development. To better understand and describe continuous capturing process, an integrated approach was developed to combine the Equilibrium Dispersive Model of column, General Rate Model of resin, as well as the Equilibrium Adsorption Model for fitting and predicting breakthrough curves, as well as the continuous process models for evaluating the operation conditions. Considering process productivity and capacity utilization together, a working window could be proposed for continuous chromatography. The model-based approach developed were tested with different PCC modes, including twin-column CaptureSMB from ChromaCon, 3/4-column PCC from GE Healthcare and multi-column BioSMB from Pall. A software platform with the interactive interface was also developed to easily input the data and visually output the results. In addition, artificial intelligence method was introduced to improve the data treatment, and different PPC modes could be evaluated in a fast way. The results indicated that model-based approach could aid the process development and promote the target-orientated process design for continuous process.

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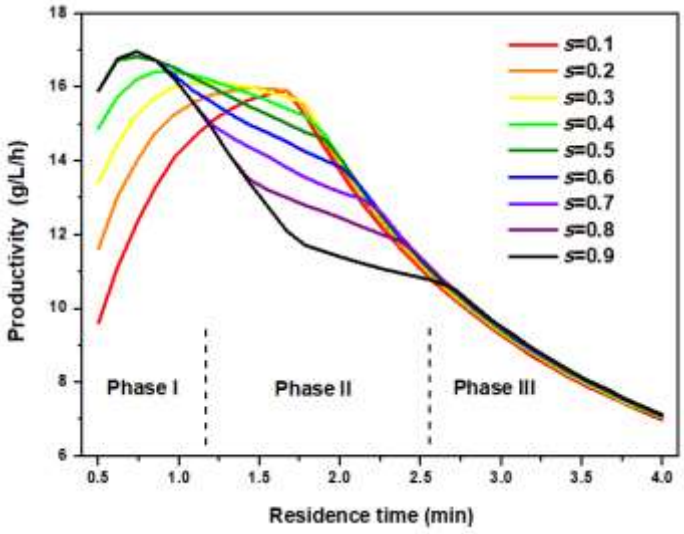

Figure 1. Productivity of continuous process with twin-column CaptureSMB at different residence times and breakthrough point control.