DYNAMIC PROCESS CONTROL OF TWIN-COLUMN PERIODIC COUNTERCURRENT CHROMATOGRAPHY PROCESSES

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Twin-column periodic countercurrent chromatography has become a promising solution for continuous downstream processes as chromatography equipment for both process development and GMP manufacturing has become available.

Twin-column periodic countercurrent processes have been utilized successfully in many applications including purification of biologics, such as monoclonal antibodies (mAbs), bispecific antibodies and fusion proteins, the purification of peptides and also small molecules such as antibiotics and fatty acid ethyl esters.

This presentation deals with the online UV-based control of two twin-column periodic countercurrent processes, 2C-PCC and MCSGP, covering applications in chromatographic capture and polishing.

2C-PCC is a capture process significantly improving the process performance (productivity, resin utilization, buffer consumption, product concentration) of affinity capture, e.g. the capture of mAbs, in comparison to traditional single column chromatography.

MCSGP is a polishing process to solve difficult ternary separation challenges, allowing purification with high product yield and purity in situations where traditional single column chromatography faces a yield-purity trade-off.

For robust operation in view of commercial manufacturing using these two cyclic processes, UV-based dynamic control strategies have been developed and tested.
In this presentation a UV-based control strategy for 2C-PCC based on online-determination of breakthrough curve signals is introduced and case studies for its application in protein A chromatography are shown. The control strategy accounts for changes in resin capacity and, in case of continuous upstream, for changes in titer occurring over time, and adjusts the operating parameters such that capacity utilization and yield are kept constant.

A second control strategy for MCSGP based on the online evaluation of the elution peak signal is presented based on a case study. The method accounts for shifts of the product peak e.g. due to changes in temperature and buffer preparation (e.g. during buffer refill). An application of the control strategy in protein purification is presented. The presented methods represent important tools for robust manufacturing using twin column processes