Fall 11-2-2015

Continuous production of proteins: Integration of polishing using MCSGP

Fabian Steinebach
Institute for Chemical and Bioengineering, ETH Zürich, fabian.steinebach@chem.ethz.ch

Daniel Karst
Institute for Chemical and Bioengineering, ETH Zürich

Massimo Morbidelli
Institute for Chemical and Bioengineering, ETH Zürich

Continuous production of proteins: Integration of polishing using MCSGP

Fabian Steinebach, Institute for Chemical and Bioengineering, ETH Zürich
fabian.steinebach@chem.ethz.ch
Daniel Karst, Institute for Chemical and Bioengineering, ETH Zürich
Thomas Müller-Späth, ChromaCon AG, Zürich
Massimo Morbidelli, Institute for Chemical and Bioengineering, ETH Zürich

Continuous counter-current processes for polishing steps overcome the purity-yield tradeoff of classical batch chromatography by internal recycling of overlapping regions of the chromatogram. Particularly in the case of challenging separation tasks this leads for the same product quality to significantly higher yields and productivity. Processes using these fundamental principals have been successfully implemented in the chemical industry up to multi-ton production.

In an integrated continuous process, with a perfusion bioreactor and a continuous capture process, the product quality of the capture product is different compared to classical batch processing. The lower residence time in the bioreactor and the higher loading in multi-column capture steps lead to polishing feed streams with higher concentration and less impurities. A cascade of beneficial correlations results in higher titer. Hence the polishing process parameters need to be adjusted accordingly.

In this work the process design as well as the results for monoclonal antibody polishing with a twin-column MCSGP setup is presented, where the feed stream was obtained from an integrated continuous cultivation and capture process. The process was designed accordingly and the resulting product quality in terms of aggregate and fragment content, as well as charge isoforms is compared to classical batch chromatography. The internal recycling of the product resulted in a higher productivity and yield for the multicolumn setup.