Model-based conversion of a single-column batch process to 3- and 4-column periodic counter-current chromatography

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BACKGROUND

As fully integrated continuous processing is being adopted by the biopharmaceutical industry, the individual batch-wise processes have to be replaced by continuous equivalents.

Periodic counter-current chromatography (PCCC) systems are able to cope with ternary mixtures. PCCC has been successfully employed as first capture step and design charts have been developed for such cases by Carta and Perez-Almodovar. However, intermediate purification steps are much more sensitive to small changes in the process parameters.

MATERIALS AND METHODS

In the presented ion exchange case study using SP Sepharose FF, the target component was an intermediate binding IgG. The model was calibrated using three gradient elutions in linear mode and one in nonlinear mode.

All simulations, parameter estimation and process optimization were performed with GoSilico’s software ChromX. An NSGA-II evolutionary algorithm was used for multi-criteria optimization. MVDA was performed with the software Simca by Umetrics.

RESULTS: PROCESS CONVERSION

Because of the many degrees of freedoms of PCCC set-ups, such as flow rates, buffer concentrations, cycle duration, etc., model-based process development is the method of choice to identify the design space and optimal conditions.

As the protein-parameters can be taken directly from the batch-mode model, only the flow sheet is substituted.

RESULTS: PROCESS OPTIMIZATION

The optimal process conditions for single-column batch, 3-column (3C) and 4-column (4C) PCCC processing were determined with an evolutionary multi-objective optimization regarding yield, purity and production rate. All optimization variables are listed on the right together with the resulting Pareto surface for 3C-PCCC. Black dots indicate single simulation results.

SUMMARY: PERFORMANCE COMPARISON

The results show comparable values for yield and purity. However, the production rates of the simulated 3C-PCCC and 4C-PCCC were increased by 100% and 280% compared to the batch process. The MVDA results indicate that the 3C-PCCC process is sensitive to the chosen cycle time. The 4C process is more robust in this sense. Also, it achieves the highest production rate.

RESULTS: MVDA

Multi-variate data analysis was employed to identify the main factors of influence on the three sub-objectives. MVDA was unable to explain the variation in the whole design space. However, applying MVDA to the Pareto fronts allowed to identify different clusters of critical parameters.

GoSilico is a spin-off project of the Karlsruhe Institute of Technology (KIT) that develops software and methods for computer-aided – in silico – bioprocess development.

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