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Nina Brestrich
Karlsruhe Institute of Technology, nina.brestrich@kit.edu

Tobias Hahn
Karlsruhe Institute of Technology

Adrian Sanden
Karlsruhe Institute of Technology

Till Briskot
Karlsruhe Institute of Technology

Jurgen Hubbuch
Karlsruhe Institute of Technology

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PAT CONCEPTS FOR CHROMATOGRAPHY: REAL-TIME MONITORING, REAL-TIME CONTROL, AND CAUSE OF ERROR DIAGNOSTICS

Nina Brestrich, Karlsruhe Institute of Technology
nina.brestrich@kit.edu
Tobias Hahn, Karlsruhe Institute of Technology
Adrian Sanden, Karlsruhe Institute of Technology
Till Briskot, Karlsruhe Institute of Technology
Jürgen Hubbuch, Karlsruhe Institute of Technology

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In the recent years, the growing competition in the biopharmaceutical industry due to biosimilars combined with market fluctuations and increasing product pipelines have given rise to the evaluation of continuous processing. Advantages include smaller equipment that may be disposable, an overall process intensification as well as steady-state operation. As variability should be managed by the continuous process itself to insure a consistent product quality, the development of advanced Process Analytical Technology (PAT) concepts is one crucial aspect for the implementation of continuous processing.

In chromatographic protein purification, process variability can lead to variations in retention volumes or peak shapes of the eluting species. If the contaminants are co-eluting with the product, a peak deconvolution is required to enable real-time process monitoring and control. In order to overcome this analytical bottleneck, a tool will be presented, which allows for real-time peak deconvolution and pooling decisions in chromatography [1]. The peak deconvolution is obtained by Partial Least Squares Regression (PLS) modelling with spectroscopic data. The applicability of the peak deconvolution tool for real-life applications was successfully demonstrated in a case study with co-eluting monoclonal antibody, its aggregates, and fragments as well as in case study with co-eluting serum proteins [2].

Aside from the detection of variations in elution profiles, a fast diagnostics of their causes is crucial for a comprehensive process understanding and control. The identification of causes for variations in chromatography processes requires however a mechanistic understanding. In this presentation, a case study will be shown, where the deconvoluted peaks of three co-eluting model-proteins of several linear gradient elutions were used for the calibration of a mechanistic chromatography model. Variations in the elution profiles of all proteins were subsequently induced by deliberately generated errors in the process parameters flow rate, salt concentration in loading buffer, and salt concentration in elution buffer. The individual elution profiles of all proteins were determined by the peak deconvolution tool. The peak deconvolution in combination with the mechanistic model allowed for a fast estimation of the actual values of the three process parameters by curve fitting.

In summary, peak deconvolution by PLS modelling with spectroscopic data might enable real-time monitoring and control in future chromatographic processes. A combination of peak deconvolution with mechanistic modelling allows furthermore for a fast cause of error-diagnostics, which might contribute to better process understanding and control and might minimize lot rejections.

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