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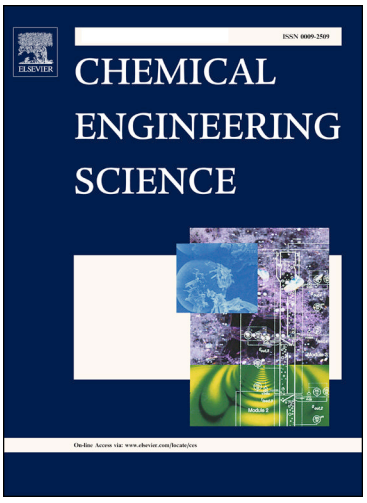

Selective Protein Quantification for Preparative Chromatography using Variable Pathlength UV/Vis Spectroscopy and Partial Least Squares Regression

Nina Brestich, Matthias Rüdt, Daniel Büchler, Jürgen Hubbuch

PII: S0009-2509(17)30646-2
DOI: https://doi.org/10.1016/j.ces.2017.10.030
Reference: CES 13862

To appear in: *Chemical Engineering Science*

Received Date: 31 March 2017
Accepted Date: 22 October 2017

Please cite this article as: N. Brestich, M. Rüdt, D. Büchler, J. Hubbuch, Selective Protein Quantification for Preparative Chromatography using Variable Pathlength UV/Vis Spectroscopy and Partial Least Squares Regression, *Chemical Engineering Science* (2017), doi: https://doi.org/10.1016/j.ces.2017.10.030

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Selective Protein Quantification for Preparative Chromatography using Variable Pathlength UV/Vis Spectroscopy and Partial Least Squares Regression

Nina Brestich[a,1], Matthias Rdt[a,1], Daniel Bchler[a], Jrgen Hubbuch[a,*]

[a] *Institute of Engineering in Life Sciences, Section IV: Biomolecular Separation Engineering, Karlsruhe Institute of Technology, Engler-Bunte Ring 3, 76131 Karlsruhe, Germany*

Abstract

In preparative protein chromatography, broad dynamic ranges of protein concentrations as well as co-elution of product and impurities are common. Despite being the standard in biopharmaceutical production, monitoring of preparative chromatography is generally limited to surrogate signals, e.g. UV absorbance at 280 nm. To address this problem, variable pathlength (VP) spectroscopy in conjunction with Partial Least Squares regression (PLS) was used to monitor preparative chromatography. While VP spectroscopy enabled the acquisition of absorbance data for a broad concentration range, PLS modelling allowed for the differentiation between the protein species. The approach was first implemented for monitoring the separation of lysozyme from cytochrome c at an overall loading density of 92 g/l. The same method was then applied to the polishing step of a monoclonal antibody (mAb) at 40 g/l loading density. For PLS model prediction of the mAb monomer and the high molecular weight variants (HMWs), the root mean square error (RMSE) was 1.07 g/l and 0.42 g/l respectively. To demonstrate the usability of the approach for in-line control, pooling decisions for both separation problems were subsequently taken based on the computed concentrations or thereof derived purities. In summary, VP spectroscopy in conjunction with PLS modelling is a promising option for in-line monitoring and control of future chromatography steps at large scale.

Keywords: Preparative Chromatography, Process Analytical Technology, Partial Least Squares Regression, In-Line Monitoring, Variable Pathlength Spectroscopy, Selective Protein Quantification

*Corresponding author. Tel.: +49 721 608 42557; fax: +49 721 608 46240
Email address: juergen.hubbuch@kit.edu (Jrgen Hubbuch)
[1] Contributed equally

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