Available online at www.sciencedirect.com
ScienceDirect
Journal of Chromatography A, 1165 (2007) 100–108
JOURNAL OF CHROMATOGRAPHY A
www.elsevier.com/locate/chroma

Experimental implementation of automatic 'cycle to cycle' control of a chiral simulated moving bed separation

Mohammad Amanullah [a], Cristian Grossmann [b], Marco Mazzotti [a,*], Manfred Morari [b], Massimo Morbidelli [c]

[a] Institute of Process Engineering, ETH Zurich, Sonneggstrasse 3, CH-8092 Zurich, Switzerland
[b] Automatic Control Laboratory, ETH Zurich, Physikstrasse 3, CH-8092 Zurich, Switzerland
[c] Institute of Chemical and Bio-Engineering, ETH Zurich, Wolfgang-Pauli-Strasse 10, CH-8093 Zurich, Switzerland

Received 16 May 2007; received in revised form 24 July 2007; accepted 26 July 2007
Available online 1 August 2007

Abstract

In the absence of a suitable controller, currently simulated moving beds (SMBs) are operated suboptimally to cope with system uncertainties and to guarantee robustness of operation. Recently, we have developed a 'cycle to cycle' optimizing controller that not only makes use of minimal system information, i.e. only the Henry constants and average bed voidage, but also optimizes the process performance and taps the full economic potential of the SMB technology. The experimental implementation of the 'cycle to cycle' optimizing controller had been carried out for achiral separation. For chiral separation however, application of any online controller has not been possible because an appropriate online monitoring system has not been avaiable. This work reports and discusses the first experimental implementation of the 'cycle to cycle' optimizing control for chiral separations. A mixture of guaifenesin enantiomers is separated on Chiralcel OD columns with ethanol as mobile phase in a eight-column four sections laboratory SMB unit. The results show that the controller, although using minimal information about the retention of the two enantiomers, is able to meet product and process specifications, can optimize the process performance, and is capable of rejecting disturbances that may occur during the operation of the SMB plant.

Keywords: Simulated moving bed; Optimizing control; Separation of enantiomers; Repetitive model predictive control

1. Introduction

Simulated moving bed (SMB) chromatography is a firmly established powerful technique for continuous chromatographic separation especially for fine chemicals and enantiomers [1]. SMB technology may be applied at all scales from laboratory to production, thus making it a suitable choice for new drug development where time to market is very crucial.

The scheme of an SMB is shown in Fig. 1. The SMB technique is based on a simulated countercurrent contact between the mobile phase and the stationary adsorbent phase approximating a true moving bed (TMB). This is achieved through the periodic movement of inlet and outlet ports in the same direction of the fluid flow as shown in Fig. 1.

In an SMB unit there are two inlet streams, namely the feed and the make-up solvent stream, and two outlet or product streams, namely extract and raffinate. The feed is injected between sections II and III, where the separation takes place. The less adsorbable component B is carried by the fluid flow and collected in the raffinate outlet. The more adsorbable component A is retained in the solid phase, until the switching of the ports takes it to section I, where it is eluted with fresh desorbent and collected from the extract outlet. Section IV is designed to adsorb the remaining species B in the fluid flow and prevent it from reaching section I through the recycle. On the other hand, desorbent flow in section I is set to desorb species A from the stationary phase and thus preventing it from reaching section IV after switching. A detailed description of the SMB plant and its working principle may be found elsewhere [2].

Although SMB chromatography significantly improves the productivity and reduces solvent consumption compared to single column chromatography, robust and optimum operation of

* Corresponding author. Tel.: +41 44 632 2456, fax: +41 44 632 1141.
E-mail address: marco.mazzotti@ipe.mavt.ethz.ch (M. Mazzotti).

0021-9673/$ – see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.chroma.2007.07.065

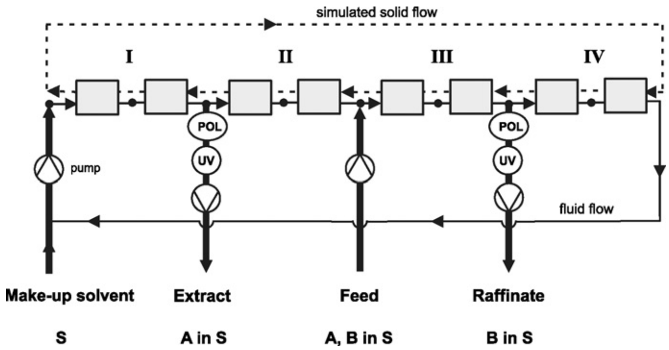

Fig. 1. Scheme of the laboratory scale SMB plant with online monitoring using a combination of polarimeter and UV detectors. The plant has a 2:2:2:2 configuration and the polarimeters and UV detectors are placed before the extract and raffinate pumps, respectively.

an SMB unit, especially long term operation, is a challenge due to reasons like aging of the stationary phase and change in ambient conditions. Currently, this is addressed by operating the plant suboptimally, i.e. by utilizing a safety factor, and by changing the operating parameters manually by experienced personnel when necessary. Consequently, SMB process control problem is receiving a lot of attention [3–16]. However, the underlying characteristics of the SMB process, such as its cyclic steady state, and nonlinear and hybrid nature, make the control problem challenging. Furthermore, many of these control strategies require accurate physical data of the plant, i.e. adsorption isotherm, column voidage, and dispersion parameters' determination, which are difficult, time consuming and may change over time due to aging of the stationary phase [3–9,16]. In previous papers an SMB control scheme has been proposed, which guarantees the fulfillment of product and process specifications, such as minimum purities and maximum allowable pressure drop, while optimizing the economics of the process [10–15]. The design of this controller requires only minimal information both on the adsorption isotherm of the components to separate, i.e. only the linear adsorption isotherm, and on the characteristics of the columns constituting the SMB plant, i.e. the average void fraction of the columns in the SMB unit. In this control scheme, the concentration profiles of the product streams measured at the two outlets of the SMB plant are used as the feedback information. In view of application in production units, this control scheme has been further modified and the concentrations of the product streams averaged over one cycle are used as the feedback information, the so-called 'cycle to cycle' controller [17]. It is common practice in industrial SMB applications to collect samples over one entire cycle, and to analyze them using an automated HPLC for quality control. A detailed description of the development of the 'cycle to cycle' controller and its implementation in an SMB unit for the separation of a mixture of nucleosides (uridine and guanosine) have been reported elsewhere [17].

For chiral separations, however, no experimental application of any online optimizing controller is reported in the literature. This work reports and discusses the first experimental implementation of the 'cycle to cycle' optimizing control for a chiral separation in a laboratory SMB unit. The paper is organized as follows: in Section 2, a brief overview of the control concepts and optimization problem are presented. In Section 3, materials, system characterization, and online monitoring scheme are discussed. In the last section, the performance of the controller for the separation of a mixture of guaifenesin enantiomers is assessed and conclusions are drawn.

2. On-line optimization based 'cycle to cycle' SMB control

The control concept, which is based on repetitive model predictive control (RMPC), is schematically shown in Fig. 2; a detailed description can be found elsewhere [18,19,17]. An important element of the controller is an explicit and simplified SMB model. The manipulated variables are the four internal flow rates in the four sections of the SMB unit. The measured variables are the products' (extract and raffinate) concentration profiles averaged over one cycle. The switching time, t^*, is predefined and chosen based on maximum allowable pressure drop considerations. The objectives are specified to the controller in terms of maximization of productivity and minimization of solvent consumption, whereas the product specifications are in terms of minimum purity requirement. The product concentrations are measured online by an appropriate sensor system, in this case a combination of polarimeter and UV detectors for chiral separation, and are used as feedback information. The measured concentrations of the product streams, averaged over one cycle, are used together with a Kalman filter and the SMB model to estimate the current state of the SMB plant.

With this information the controller is able, by using the simplified SMB model, to predict the future evolution of the SMB plant and to calculate a set of manipulated variables, i.e. flow rates, which is optimal for the specified economical objective, and fulfills the given product and process constraints. The controller acts on the SMB plant by changing, if necessary, the flow rates once every cycle. The dynamics of an SMB plant requires some time before a change in the flow rates is reflected on the products' concentration profiles. Therefore, the controller predicts and optimizes the performance of the plant over the prediction horizon, i.e. a time window comprising n_p cycles,

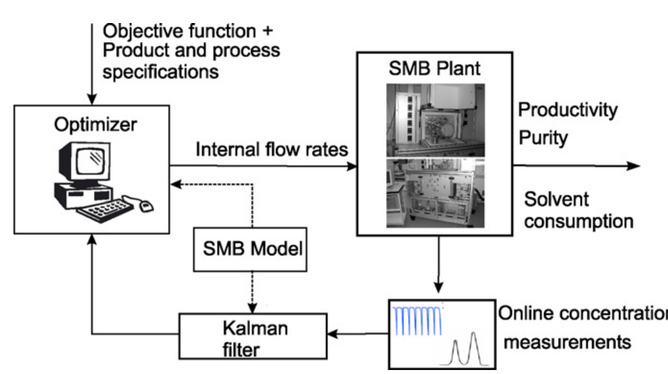

Fig. 2. Scheme of online 'cycle to cycle' optimization based SMB control concept. For chiral separation, the online monitoring of products' concentration profiles, averaged over one cycle, may be accomplished by either an HPLC or a combination of polarimeter and UV detectors. In the present work, the latter is used.