



Automatic Control of Simulated Moving Beds—Experimental Verification

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Abstract. Simulated moving bed (SMB) chromatography has become the state of the art technology applied for the complex separation tasks in the pharmaceutical and fine chemical industry. Nevertheless, operation of SMB units at their optimal operating conditions is still an issue challenging SMB practitioners due to absence of proper process control schemes. We have developed a feedback control scheme that integrates the on-line optimization and control of SMB units. A significant feature of the developed SMB control concept is that only a minimum of system information has to be provided, i.e., the average packing characteristics of the SMB columns and the linear adsorption isotherm, regardless of the type of isotherm characterizing the mixture to be separated. Therefore a detailed characterization of the columns and the separation system is no longer required. This paper demonstrates the experimental implementation of this control concept and presents results referring to two different experimental runs.

Keywords: simulated moving bed chromatography, RMPC, optimization, control

1. Introduction

The Simulated Moving Bed (SMB) is a continuous countercurrent chromatographic process to separate a chemical mixture into two fractions. The separation principle is the different affinity of the components in the mixture to the solid phase in the solid/liquid countercurrent contact. To generate a real countercurrent flow is technically infeasible, which can be overcome by a technical approximation of this process, the SMB. The SMB consists of a fixed-bed column loop where the solvent circulates in one direction. To obtain the desired countercurrent flow, the inlet and outlet streams are periodically switched by one column position in the direction of the liquid flow, which results in a “simulated” solid movement in the opposite direction with respect to the inlet and outlet flow positions. A more detailed description of the SMB process can be found elsewhere (Mazzotti et al., 1997).

There are two striking advantages of SMB technology. Firstly, compared to the batch process it has a high

productivity and low solvent consumption. Secondly, SMB technology allows a fast and reliable scale-up of separations from analytical chromatography and therefore a shorter time to market can be achieved. These two advantages make SMB chromatography an effective tool, particularly for the pharmaceutical and fine chemical industry demanding short development times and high productivity at low cost.

Improvement of the process performance has attracted a significant amount of attention, and new SMB schemes allowing for further improvements in the separation efficiency have been introduced (Ludemann-Homburger et al., 2000; Zhang et al., 2003; Schramm et al., 2003b). Nevertheless, the operation of SMB units at their economic optimum is still an open issue. Close to the optimal point, the operation becomes less robust. In addition to this, system uncertainties and aging make the operation at the optimum even more difficult. Therefore, it is common practice to choose a sub-optimal operating point in order to avoid off-spec production.

Implementation of a proper feedback control scheme has the potential to allow for the operation of SMB units

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at their economic optimal conditions. However, control of SMB units has its own challenges related to the underlying characteristics of the process, such as its non-steady-state, nonlinear and hybrid nature. Several SMB control approaches have been proposed (Kloppenborg and Gilles, 1999; Klatt et al., 2000; Schramm et al., 2001; Klatt et al., 2002; Schramm et al., 2003a; Song et al., 2003). The common drawback of these approaches is the need for accurate physical data about the system. Here, we propose a control strategy that integrates the on-line optimization and control of the SMB process addressing the difficulties mentioned above. A significant feature of the developed SMB control concept is that it is based on the knowledge of the linear adsorption isotherm and the overall average packing characteristic of the SMB unit only, which removes the necessity of detailed characterization of the columns and the behavior of the mixture to be separated.

2. On-Line Optimization Based Feedback Control Scheme

The proposed control scheme makes use of an explicit SMB model in order to predict the future evolution of the plant based on its current state (see Fig. 1). The internal flow rates in the four sections and the concentration levels in the two outlet streams are used as the manipulated and the measured variables, respectively. The switching period is defined at the beginning of the operation and kept constant. The control problem is defined as a dynamic optimization problem, and the performance of the plant is optimized over a

defined future time window, i.e., prediction horizon. The on-line solution of the constructed optimization problem provides the optimal flow rate sequence, i.e., resulting in optimal performance, for a chosen future time window, i.e., control horizon. The optimal flow rate sequence is implemented according to a receding horizon strategy, i.e., the element corresponding to the current time is implemented on the plant and the remaining elements are discarded. As new information becomes available with the new measurements collected from the plant, a new optimization problem is solved on the basis of updated state of the plant. Here, we make use of a periodic time-varying Kalman filter that provides a recursive correction for the model errors by combining the model estimation and the available measurements in an optimal sense (Erdem et al., 2004b). Note that because it is hard to access the internal flow rates directly, the calculated sectional flow rates are implemented by acting on three external and one internal flow rates, e.g., Q_E , Q_R , Q_F and Q_I .

2.1. SMB Model

The SMB model is a critical component of the control scheme. Because the dynamic models of SMB would demand excessive computation for on-line optimization, a time-varying linear model of the process has been obtained that is based on the linearization of the equilibrium dispersive SMB model, which is described in detail in (Erdem et al., 2004b; Abel et al., 2004). The obtained time-varying linear model of the SMB process constitutes the basis for the formulation of the control problem, which is constructed along the

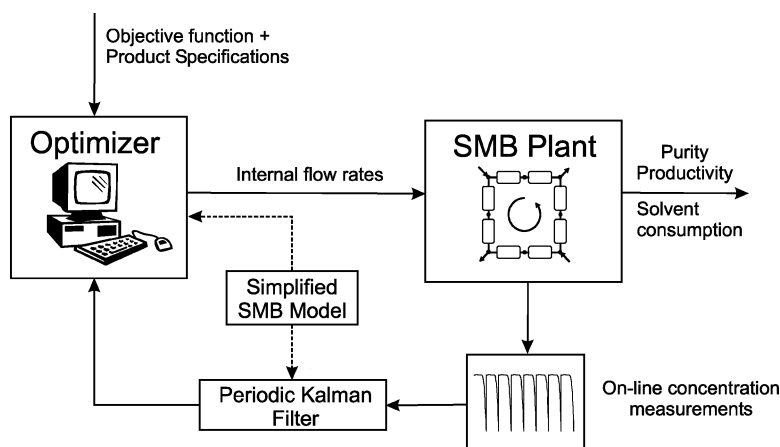


Figure 1. Scheme of the on-line optimization based feedback control concept.

lines of repetitive model predictive control (RMPC) (Natarajan and Lee, 2000; Lee et al., 2001). The RMPC formulation is based on the assumption that possible model prediction errors and/or the effect of disturbances on the plant output are likely to repeat due to the periodic nature of the process, and therefore the information from the past cycles can be used to correct for the model errors in the future cycles. We refer to the available literature for the description and implementation details of RMPC (Erdem et al., 2004b; Lee et al., 2001; Erdem et al., 2004a).

2.2. Optimization Problem

For a given plant layout and a switch time, the economic objective of the operation can be defined as maximizing the throughput, i.e., feed input, and minimizing the solvent consumption. The switch time is not used as a decision variable in the optimization problem because the SMB model is developed on the basis of a defined process period. The defined objective should include constraints on the product specifications, i.e., outlet purities, as well as on the operating conditions related to the hardware limitations, which can be considered explicitly as a part of the optimization problem. Here, the required product specifications are enforced by constraining the average purities over the prediction horizon, e.g., 2 cycles in our case, with a lower bound.

$$P_E^{\text{ave}} \geq P_E^{\text{min}} - s_1 \quad \text{where } s_1 \geq 0 \quad (1)$$

$$P_R^{\text{ave}} \geq P_R^{\text{min}} - s_2 \quad \text{where } s_2 \geq 0 \quad (2)$$

Introducing slack variables, i.e., s_1 and s_2 , is a standard method in order to eliminate the infeasibility problems that may occur during the on-line optimization. Note that the feasibility of the purity constraints (Eqs.(1)–(2)) is guaranteed for sufficiently large values of s_1 and s_2 . Excessive usage of slack variables is penalized by including them in the cost function.

The operating constraints due to hardware limitations such as maximum allowable flow rate related to pressure drop limitations for the columns are also incorporated into the optimization problem as linear inequality constraints.

$$0 \leq Q_j \leq Q_j^{\text{max}} \quad \text{for } j = I, \dots, IV \quad (3)$$

The cost function of the optimization problem is defined as minimizing the cumulative solvent

consumption and maximizing the cumulative throughput over the control horizon, e.g., $n_c = 1$ cycle in our case.

$$\min_{Q^{n_c}, s} [\lambda_D Q_D^{n_c} - \lambda_F Q_F^{n_c} + \lambda_1 s_1 + \lambda_2 s_2] \quad (4)$$

In the equation above, $Q_D^{n_c}$ and $Q_F^{n_c}$ are the cumulative solvent consumption and throughput over the control horizon, respectively; λ_D and λ_F are the weights of the corresponding terms, e.g., $\lambda_D = 4$ and $\lambda_F = 20$ in our case. Q^{n_c} consists of the manipulated variables, i.e., internal flow rates, for the complete control horizon. λ_1 , λ_2 are the weights of the corresponding slack variables in the cost function, which are kept large in order to punish their excessive use, e.g., $\lambda_1 = \lambda_2 = 100$ in our case. The linear cost function (Eq.(4)) together with the linear constraints (Eqs.(1)–(3)) constitutes a linear program (LP) to be solved on-line. ILOG CPLEX 7.0 is used as the commercial LP solver, and the maximum calculation time to solve the LPs was 1.2 seconds on a PC with a 3 GHz processor. The effectiveness of this control approach has been demonstrated through extensive simulations in different cases (model/plant mismatch; disturbances), and for different linear and non-linear adsorption isotherms (Erdem et al., 2004b; Abel et al., 2004; Erdem et al., 2004a).

3. Experimental Implementation of SMB Control

3.1. Model System

As a model system the separation of the nucleosides uridine and guanosine, purchased from Sigma-Aldrich Chemie GmbH, on the reversed phase SOURCE™ 30RPC (Amersham Biosciences), was considered. As a mobile phase a mixture of 5% ethanol in water was used. For a feed concentration of 0.05 g/l of each nucleoside both adsorption isotherms were found to be linear. The 8-column (each has a length of 10 cm and a diameter of 1 cm) SMB was operated in a 2-2-2-2 configuration at 23°C.

3.2. On-Line Monitoring

To implement a monitoring system suitable for on-line control, two sensors, one at each of the extract and raffinate outlets, are needed. Each sensor should be able to monitor on-line the concentrations of a binary mixture, hence two different signals are needed from each

sensor. This results into a system of two equations (one for each signal) with two unknowns (concentrations of the two components), which can then be solved for the concentrations of the individual compounds. For our system of nucleosides two multi-wavelength UV 2077 detectors (Jasco) have been chosen as sensors. The two different signals could be obtained by a simultaneous measurement at two different wavelengths, which exploit the difference in the UV spectra of uridine and guanosine. For a better measurement accuracy additional signals at two other wavelengths have been used and the system of equations thus obtained was solved by regression. The feed concentrations of the SMB experiments were chosen low enough to allow for a linear calibration of the detectors.

4. Results

The developed controller has been implemented experimentally on the separation of nucleosides, and the results obtained from the two test runs are reported here. For both runs, the plant was started up at an operating point that would lead to unsatisfactory purities for both outlets, i.e., below 94% and 90% for extract and raffinate respectively, if the unit were run without the controller. This is not only because the operating point in the (m_2, m_3) operating plane is located above the region of complete separation (see the operating point indicated as “cycle 1” in Fig. 2(e) but also because

the flow rates of section one and four lead to poor regeneration of the adsorbent and of the mobile phase, respectively.

In the first run, the minimum purity requirement was chosen as 98% for both product streams. The controller was activated after the first cycle, and it successfully adapted the operating conditions in order to fulfill the product specifications for both outlets. Figure 2(a) to (d) show the controller action in terms of flow rate ratios, i.e., m_j , in the four SMB sections. Figure 2(e) illustrates the controller action in the (m_2, m_3) operating plane. The complete separation region depicted by dash lines is based on the adsorption isotherm information that is used to develop the controller, whereas the one given by solid lines corresponds to the real plant, hence there exists a plant/model mismatch. It is worth mentioning that the temperature in the SMB can be controlled with an accuracy of $\pm 1^\circ\text{C}$, and since the adsorption behavior is temperature dependent, this constitutes an additional disturbance on the system, i.e., the complete separation region applied to the plant is subject to changes. One can see that the controller changes the flow rates of section two and three so as the operating point moves towards the complete separation region. Moreover, it increases and decreases the flow rates in section one and four, respectively, in order to have a better regeneration of the adsorbent and of the mobile phases (see Figs. 2(a) and (d)). It is worth noting that the steady state operating point (see the operating point indicated as “cycle 55” in Fig. 2(e)) is close to the

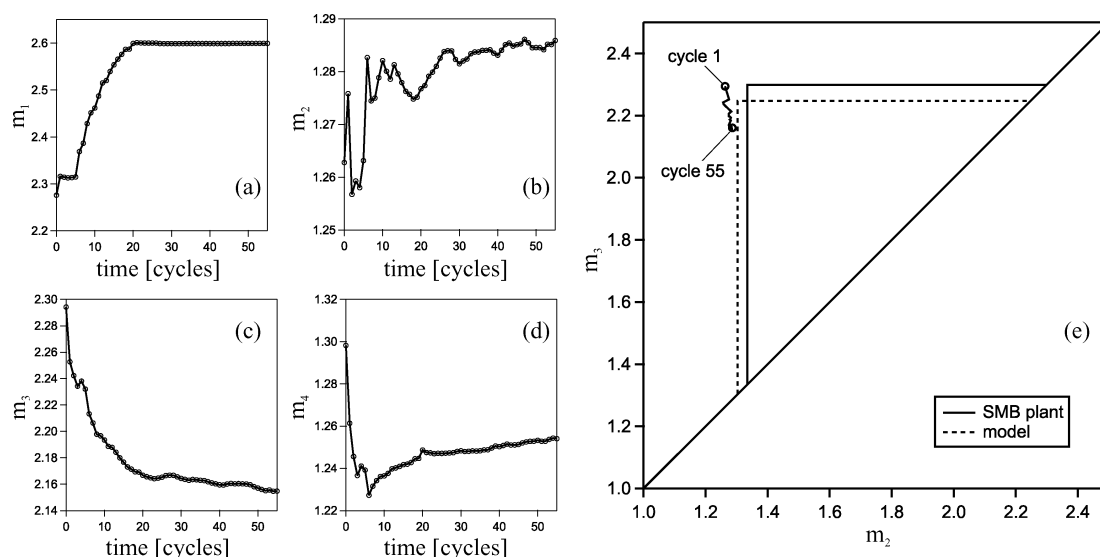


Figure 2. (a) to (d): Controller action in terms of the flow rate ratios m_1 to m_4 in the four sections of the SMB. (e): Controller action represented in (m_2, m_3) operating parameter space. The flow rate ratio is defined as $m_j = (Q_j t^* - V\varepsilon)/(V(1 - \varepsilon))$.

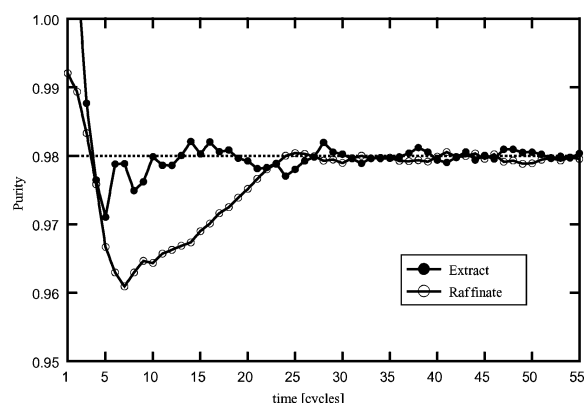


Figure 3. Measured outlet purities for the controlled SMB. The controller is switched on one cycle after the plant startup in order to bring the raffinate and extract outlet purities above minimum 98%.

vertex of the complete separation region, i.e., the optimal operating point according to “Triangle Theory” (Mazzotti et al., 1997). One can see from Fig. 3 that both raffinate and extract purity meet the specification after 28 cycles thanks to the controller action.

The second run refers to a separation with higher purity specifications, i.e., minimum purity of 99% for both extract and raffinate. The SMB unit is operated without the controller for a longer time than in the previous run, i.e., for 9 cycles, in order to show how the controller is able to recover the specified purities even when starting far away from the set point. One can see from Fig. 4 that the product specifications are fulfilled for both outlets after 28 cycles following the activation of the controller. It is worth mentioning that the accuracy of the on-line monitoring system was verified by off-line HPLC measurements of the product purities, and it was verified that the on-line monitoring system can be used effectively, i.e., the difference between off-line and on-line values was 0.1 to 0.5%.

These experimental runs demonstrate that the developed control concept is effective and promising also for applications. We expect that the performance of the controller can be improved, e.g., by proper tuning. It is worth noting that this is the first time a standard experimental SMB plant, i.e., an 8-column 4-section unit, is successfully optimized and controlled on-line.

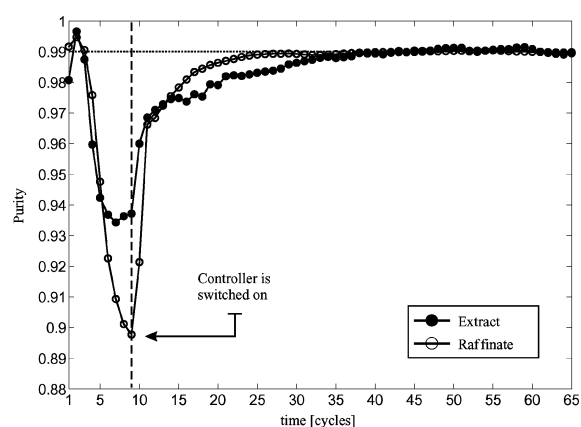


Figure 4. Measured outlet purities for the controlled SMB. The controller is switched on after cycle 9 in order to bring the raffinate and extract outlet purities above minimum 99%.

References

- Abel, S., G. Erdem, M. Mazzotti, M. Morari, and M. Morbidelli, *J. Chromatogr. A*, **1033**, 229–239 (2004).
- Erdem, G., S. Abel, M. Morari, M. Mazzotti, and M. Morbidelli, *Ind. Eng. Chem. Res.*, **43**, 3895–3907 (2004a).
- Erdem, G., S. Abel, M. Morari, M. Mazzotti, M. Morbidelli, and J.H. Lee, *Ind. Eng. Chem. Res.*, **43**, 405–421 (2004b).
- Klatt, K.U., F. Hanisch, and G. Däünnebieber, *J. Process Control*, **12**, 203–219 (2002).
- Klatt, K.U., F. Hanisch, G. Däünnebieber, and S. Engell, *Computers and Chem. Eng.*, **24**, 1119–1126 (2000).
- Kloppenborg, E. and E.D. Gilles, *J. Process Control*, **9**, 41–50 (1999).
- Lee, J.H., S. Natarajan, and K.S. Lee, *J. Process Control*, **11**, 195–207 (2001).
- Ludemann-Hombourger, O., R.M. Nicoud, and M. Bailly, *Separation Science and Technology*, **35**, 1829–1862 (2000).
- Mazzotti, M., G. Storti, and M. Morbidelli, *J. Chromatogr. A*, **769**, 3–24 (1997).
- Natarajan S. and J.H. Lee, *Computers and Chem. Eng.*, **24**, 1127–1133 (2000).
- Schramm, H., S. Gräner, and A. Kienle, *J. Chromatogr. A*, **1006**, 3–13 (2003a).
- Schramm, H., S. Gräner, A. Kienle, and E.D. Gilles, in *Proceedings of European Control Conference 2001, Porto, Portugal*, pp. 2528–2533, 2001.
- Schramm, H., M. Kaspereit, A. Kienle, and A. Seidel-Morgenstern, *J. Chromatogr. A*, **1006**, 77–86 (2003b).
- Song, I.-H., H.-K. Rhee, and M. Mazzotti, in *Proceedings of the 3rd Pacific Basin Conference on Adsorption*, Science and Technology, Kyongju, Korea, 2003.
- Zhang, Z., M. Mazzotti, and M. Morbidelli, *J. Chromatogr. A*, **1006**, 87–99 (2003).