

# Optimal Operation and Control of Simulated Moving Bed Chromatography: A Model-Based Approach

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## Abstract

Chromatographic separations are an expanding technology for the separation of Life Science products, such as pharmaceuticals, food, and fine chemicals. The simulated moving bed (SMB) process as a continuous chromatographic separation is an interesting alternative to conventional batch chromatography, and gained more and more impact recently. The SMB process is realized by connecting several single chromatographic columns in series. A countercurrent movement of the bed is approximated by a cyclic switching of the inlet and outlet ports in the direction of the fluid stream. Because of its complex dynamics, the optimal operation and automatic control of SMB processes is a challenging task. This contribution presents an integrated approach to the optimal operation and automatic control of SMB chromatographic separation processes. It is based on computationally efficient simulation models and combines techniques from mathematical optimization, parameter estimation and control theory. The overall concept and the realization of the elements are explained, and the efficiency of the proposed approach is shown in a simulation study for the separation of fructose and glucose on an 8-column SMB plant.

## Keywords

Chromatographic separation, Simulated moving bed, Dynamic models, Optimization, Model-based control

## Introduction

The chemical process industry is currently undergoing a substantial restructuring: the classical bulk business is more and more substituted by Life Science products with higher profit margins. In this area, particularly in the development and production of pharmaceuticals, it is of the utmost importance to be ahead of the competitors in the race to the market. This requires a detailed and integrated process design already in the product development phase. In this context, product separation and purification is the critical element in many cases.

Chromatographic processes provide a versatile tool for the separation of substances which have different adsorption affinities. They are especially suitable for temperature-sensitive compounds and substances with similar molecular structure and physico-chemical properties. Chromatography is well established in the field of the chemical analysis, but in recent years it gained more and more importance on the preparative scale as a highly efficient, highly selective separation process. Due to their origin and the close relation to the instruments from chemical analysis (i.e. HPLC and gas chromatographic analyzers), chromatographic separation processes are mainly operated in the classical batch elution mode. To improve the economic viability, a continuous countercurrent operation is often desirable, but the real countercurrent of solids—such as the adsorbent in chromatographic processes—leads to serious operating problems. Therefore, the simulated moving bed (SMB) process is an interesting alternative since it provides the advantages of a continuous countercurrent

unit operation while avoiding the technical problems of a true moving bed.

The SMB process was first realized in the family of SORBEX processes by UOP (Broughton and Gerhold, 1961) and is increasingly used in a wide range of industries. Currently, the main applications of continuous chromatographic separations can be divided into two groups: the large-scale industrial production of relatively cheap specialty products, like xylene production or sugar separation, and the separation of high-value products in small amounts, which very often exhibit separation factors near unity (e.g. enantiomer separations in the pharmaceutical industry). The separation costs in both cases are very high in relation to the overall process costs and easily dominate those. An optimal design and operation might therefore be the only possibility to exploit the economic potential of the process and to make its application feasible.

In practice, the SMB process is nowadays mainly realized by connecting several single chromatographic columns in series. The countercurrent movement is then approximated by a cyclic switching of the feed stream and the inlet and outlet ports in the direction of the fluid flow. Thus, the process shows mixed continuous and discrete dynamics with complex interactions of the corresponding process parameters. If the SMB process is operated close to its economic optimum, high sensitivities to disturbances and changes in the operating parameters result. Furthermore, concentration measurements are expensive and can only be installed at the outlet of the separation columns. Therefore, the control of SMB chromatographic separation processes in order to ensure a safe and economical operation while guaranteeing the product specifications at any time is a challenging task.

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Currently, most processes are operated at some distance from the optimum to avoid off-spec production and to ensure sufficient robustness margins. In order to exploit the full economic potential of this increasingly applied technology, model-based optimization and automatic control of SMB processes are required.

Several publications on both process optimization and feedback control of SMB processes can be found in the literature but they predominantly do not treat optimization and control in an integrated manner. The purpose of this contribution is to propose such an integrated approach based on a rigorous dynamic process model. The overall concept and the realization of the elements are explained in the remainder of this paper. In each section, we review the state of the art and refer to related work of other authors. We start from a short description of chromatographic separations and SMB chromatography in particular, and then explain the generation and implementation of sufficiently accurate and computationally efficient process models, which are the essential prerequisite for model-based optimization and control. We proceed with the issue of determining the optimal operating regime of the process, followed by the description of the overall control concept and its components. The feasibility and the capabilities of the proposed approach are then demonstrated on an application example, the separation of fructose and glucose on an 8-column SMB laboratory plant. We finalize with some conclusions, highlighting unresolved issues and future research directions.

## Process Description

Chromatography is a separation technique which is based on the preferential adsorption of one component. In adsorption, the solutes are transferred from a liquid or gas mixture to the surface of a solid adsorbent, where they are held by intramolecular forces. Desorption is the reverse process whereby the solute, called adsorbate, is removed from the surface of an adsorbent. By the use of a suitable stationary phase, components that are difficult to separate by other methods can be obtained in very high purities. In comparison to other thermal separation methods, e.g. distillation, less energy is consumed. Chromatography is particularly useful for the separation of temperature-sensitive components because it can often be performed at room temperature (Hashimoto et al., 1993; Adachi, 1994).

The classical implementations of chromatographic separations are batch processes in elution mode (see Figure 1). A feed pulse, containing the components to be separated, is injected into a chromatographic column filled with a suitable adsorbent, alternating with the supply of pure solvent. On its way along the column, the mixture is gradually separated and the products can be fractionated at the column outlet. One of the major drawbacks of this method is the high amount of solvent

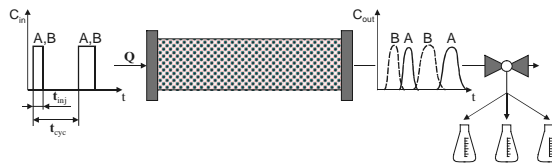


Figure 1: Batch elution chromatography.

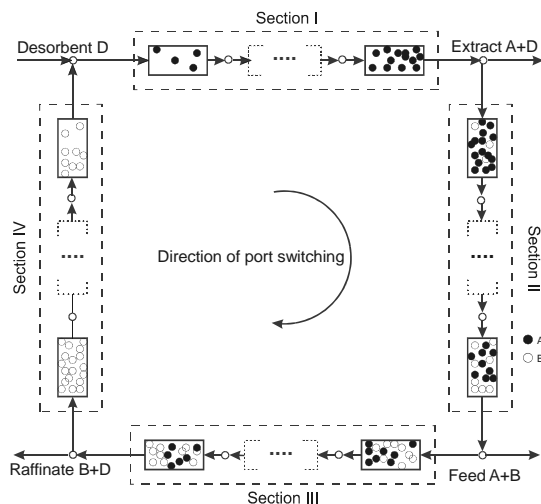
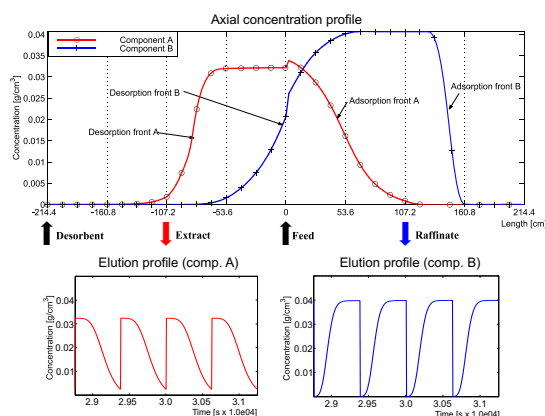


Figure 2: Simulated moving bed chromatography.

needed to perform the separation. This also leads to a high dilution of the products. During the migration of the components along the column, only a small part of the adsorbent is used for the separation. Another disadvantage is the batch operation mode of the process. In industrial applications, processes with continuous product streams are preferred.

These drawbacks led to the development of continuous countercurrent adsorption processes. The main advantage of such an arrangement is the countercurrent flow, as in heat exchangers or distillation columns, that maximizes the average driving force. Thus, the adsorbent is used more efficiently. However, the movement of the solid particles is very difficult to realize. One reason is the inevitable back-mixing of the solid that reduces the separation efficiency of the columns. Another problem is the abrasion of the particles which is caused by the movement.

The invention of the Simulated Moving Bed process overcame these difficulties, providing a profitable alternative mainly for the separation of binary mixtures. The countercurrent movement of the phases is approximated by sequentially switching the inlet and outlet valves of interconnected columns in the direction of the liquid flow. According to the position of the columns relative to the feed and the draw-off nodes, the process can be divided



**Figure 3:** Cyclic steady state of the simulated moving bed process. Top: axial concentration profile (end of period), Bottom: elution profiles.

into four different sections (see Figure 2). The flow rates are different in every section and each section has a specific function in the separation of the mixture. The separation is performed in the two central sections where component B is desorbed and component A is adsorbed. The desorbent is used to regenerate the adsorbent by desorption of component A in the first section, and component B is adsorbed in the fourth section to regenerate the desorbent. The net flow rates of the components have different signs in the central sections II and III, thus component B is transported from the feed inlet upstream to the raffinate outlet with the fluid stream and component A is transported downstream to the extract outlet with the “solid stream”.

The stationary operating regime of the SMB process is a cyclic steady state (CSS), in which in each section an identical transient takes place during each period between two valve switches. This periodic orbit is practically reached after a certain number of valve switches. The upper part of Figure 3 represents the axial concentration profile at the end of a switching period while operating in cyclic steady state. The resulting elution profiles below represent the time history of the product concentrations and highlight the periodic nature of the process dynamics.

## Modeling and Simulation

### Modeling of the SMB Process

The modeling and simulation of SMB processes has been a topic of intensive research in recent years. An overview can be found e.g. in Ruthven and Ching (1989), Ganetsos and Barker (1993), Zhong and Guiochon (1998) and Klatt (1999). The modeling approaches can be divided into two classes. In the first class, a rigorous SMB model

is assembled from dynamic process models of the single chromatographic columns under explicit consideration of the cyclic switching operation. Alternatively, an equivalent solid velocity is deduced from the switching time and the balance equations for the corresponding true moving bed (TMB) are used.

By neglecting the cyclic port switching, the model is distinctly simplified, and can be solved very efficiently. It can be shown that the steady state solution of a detailed TMB model reproduces the concentration profile of a SMB model reasonably well in case of three or more columns per zone and linear adsorption behavior, which justifies the use of this type of model for the design of such units (Storti et al., 1988; Lu and Ching, 1997; Pais et al., 1998). However, many of the recent applications of the SMB process, especially in the area of fine chemicals and pharmaceuticals, are operated with less columns per zone and at higher concentrations with nonlinear adsorption equilibrium for economic reasons. In these cases, the accuracy of the TMB approximation becomes poor. Furthermore, only the dynamic SMB model correctly represents the complete process dynamics, which is essential for an optimization of the operating policy and for model-based control.

The rigorous dynamic SMB model is closely related to the real process and directly describes the column interconnection and the switching operation. It mainly consists of two parts: the node balances to describe the connection of the columns combined with the cyclic switching, and the dynamic simulation models of the single chromatographic columns. The node balances are used to calculate the inlet flows and inlet concentrations of the four zones of the process based on the mass balances at the corresponding nodes (Ruthven and Ching, 1989):

$$\begin{aligned} Q_{IV} + Q_D &= Q_I \\ c_{i,IV}^{out} Q_{IV} + c_{i,D} Q_D &= c_{i,I}^{in} Q_I \end{aligned} \quad (1)$$

Extract node:

$$\begin{aligned} Q_I - Q_{Ex} &= Q_{II} \\ c_{i,I}^{out} &= c_{i,II}^{in} = c_{i,Ex} \end{aligned} \quad (2)$$

Feed node:

$$\begin{aligned} Q_{II} + Q_F &= Q_{III} \\ c_{i,II}^{out} Q_{II} + c_{i,F} Q_F &= c_{i,III}^{in} Q_{III} \end{aligned} \quad (3)$$

Raffinate node:

$$\begin{aligned} Q_{III} - Q_{Raf} &= Q_{IV} \\ c_{i,III}^{out} &= c_{i,IV}^{in} = c_{i,Raf} \end{aligned} \quad (4)$$

with  $Q_i$  being the respective flow rate in each of the four zones,  $Q_D$  the desorbent flow rate,  $Q_F$  the feed flow rate,  $Q_{Ex}$  the extract flow rate, and  $Q_{Raf}$  the raffinate flow rate. The switching operation can, from a mathematical point of view, be represented by shifting the

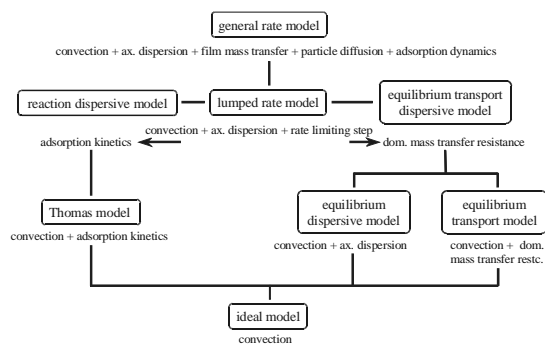


Figure 4: Classification of column models.

initial or boundary conditions for the single columns. Using the node model, the dynamic models of the single columns are interconnected. This modular approach allows the use of different column models which are appropriate for the problem at hand.

### Modeling of a Chromatographic Column

Modeling and simulation of chromatographic separation columns has been a topic of research since the 1950s. An overview can be found in Guiochon et al. (1994), an interesting presentation of the phenomenological background is given by Tondeur (1995). Mostly, apart from few outdated approaches using a stage model, the model is formulated by a differential mass balance on a cross section of the chromatographic column. Many different modeling approaches can be found in the literature, and those can be classified by the phenomena which they include and by their level of complexity (see Figure 4).

The simpler modeling approaches in the bottom of Figure 4 can partly be solved analytically, and therefore they can be evaluated very efficiently (see e.g. Rhee et al., 1989; Helfferich and Whitley, 1996; Zhong and Guiochon, 1996; Dünnebier and Klatt, 1998; Dünnebier et al., 1998). However, the idealistic assumptions on which they are based are very unrealistic for most real systems. For optimal operation and control, a model which is both accurate and computationally efficient is essential. The more complex process models mainly require an appropriate numerical solution strategy. The models consist of a set of partial differential equations of the convection-diffusion (or hyperbolic-parabolic) type. Some properties of this type of equations, like shock layers and almost discontinuous solutions, make the application of many standard discretization procedures difficult. A lot of research has been devoted to the development of suitable spatial discretization schemes for chromatography column models in order to transform the PDEs to a set of ODEs (see e.g. Kaczmarski et al., 1997; Kaczmarski and Antos, 1996; Strube and Schmidt-Traub, 1996; Poulain and Finlayson, 1993; Ma and Guiochon, 1991; Spieker et al., 1998). Common to most of the

known approaches is the need for large computational power which makes it difficult, even with modern computers, to perform simulations substantially faster than real time.

Therefore, the first objective of our research on model-based control of chromatography processes was the formulation and implementation of suitable process models. We followed a bottom up strategy, proceeding from the ideal model and increasing the complexity as far as necessary in order to achieve sufficient accuracy. From a mathematical point of view, it is useful to distinguish chromatographic processes by the type of adsorption isotherms, which describe the thermodynamic equilibrium of the separation system. Processes with a linear relation between the fluid phase concentration  $c_i$  and the solid phase concentration  $q_i$  (Henry's law)

$$q_i = K_{H,i} \cdot c_i \quad (5)$$

lead to systems of decoupled differential equations which are easier to solve than those with coupled nonlinear adsorption behavior, described for instance by competitive Langmuir isotherms

$$q_i = \frac{a_i}{1 + \sum_{j=1}^n b_j c_j} \cdot c_i \quad (6)$$

Van Deemter et al. (1956) have shown that in case of a linear isotherm the effects of axial dispersion and mass transfer resistance are additive and can be incorporated into a single parameter, the apparent dispersion coefficient  $D_{ap}$ . This results in the following quasi-linear parabolic partial differential equation for the fluid phase concentration of each component

$$\gamma_i \frac{\partial c_i}{\partial t} + u_L \frac{\partial c_i}{\partial x} - D_{ap,i} \frac{\partial^2 c_i}{\partial x^2} = 0 \quad (7)$$

The parameter  $\gamma$  is defined as

$$\gamma_i = 1 + \frac{1-\varepsilon}{\varepsilon} K_{H,i} \quad (i = A, B)$$

where  $\varepsilon$  represents the column void fraction, and the interstitial velocity  $u_L$  is assumed to be constant. Lapidus and Amundsen (1952) proposed a closed form solution of this type of equation for a set of general initial and boundary equations by double Laplace transform. From this, the dynamic SMB model can be generated by connecting the solutions for each single column by the respective node model (see Dünnebier et al., 1998, for details of the implementation). We denote this implementation as the DLI model (dispersive model for linear isotherms). It was shown that simulation times two orders of magnitude below real-time can be achieved while reproducing both the results obtained with more complex simulation models and experimental results very accurately.

In order to generate both an accurate and computationally efficient dynamic model also in the case of general nonlinear adsorption isotherms we first followed the same approach as in the linear case by analyzing a model where the non-idealities are lumped into a single parameter. However, a closed-form solution is no longer possible in the nonlinear case and the numerical solution using standard techniques for the spatial discretization did not improve the computational efficiency substantially. Fortunately, there exists a very effective numerical solution for the detailed general rate model

$$\begin{aligned} \frac{\partial c_i}{\partial t} - D_{ax} \frac{\partial^2 c_i}{\partial x^2} + u_L \frac{\partial c_i}{\partial x} + \frac{3(1-\varepsilon)k_{l,i}}{\varepsilon r_p} (c_i - c_{p,i}(r_p)) = 0 \\ (1 - \varepsilon_p) \frac{\partial q_i}{\partial t} + \varepsilon_p \frac{\partial c_{p,i}}{\partial t} - \varepsilon_p D_{p,i} \left[ \frac{1}{r^2} \frac{\partial}{\partial r} \left( r^2 \frac{\partial c_{p,i}}{\partial r} \right) \right] = 0 \end{aligned} \quad (8)$$

with complex nonlinear isotherms proposed by (Gu, 1995). Here,  $D_{ax}$  represents the axial dispersion coefficient,  $c_{p,i}$  the concentration within the particle pores, and  $q_i$  the solid phase concentration which is assumed to be in equilibrium with the pore-phase concentration.  $r_p$  denotes the particle radius,  $\varepsilon_p$  the particle porosity,  $k_{l,i}$  the respective mass transfer coefficient, and  $D_{p,i}$  the diffusion coefficient within the particle pores. A finite element formulation is used to discretize the fluid phase, and orthogonal collocation for the solid phase. We applied this formulation to SMB processes resulting in a superb accuracy and simulation times almost two orders of magnitude below real time (Dünnebier and Klatt, 2000). Due to the favorable numerical properties, this certain implementation of the complex general rate model in terms of computational efficiency even outperforms the state of the art simulation models for SMB processes (equilibrium transport dispersive model—second layer of complexity in Figure 4) which follow a linear driving force approach with a lumped mass transfer rate (e.g. Strube and Schmidt-Traub, 1996; Kaczmarski and Antos, 1996; Kaczmarski et al., 1997). Furthermore, in terms of physical consistency the general rate model is more exact, because the lumping of the different mass transfer phenomena is strictly valid only for systems with linear isotherms and incorrect for substances with large molecules (as they appear e.g. in bioseparations).

## Optimal Operating Regime

### State of the Art

Most of the known approaches for the determination of operating parameters for simulated moving bed separation processes are not based on mathematical optimization methods and rigorous dynamic process models. Two main approaches can be distinguished: The first is to derive short-cut design methodologies based on the equivalent TMB process. The second type of work uses heuristic strategies combined with experiments and dynamic

simulation of the SMB model.

By transforming the switching time  $\tau$  into an equivalent solid flow rate

$$Q_S = \frac{(1-\varepsilon)V_{col}}{\tau} \quad (9)$$

the operating parameters of a SMB process can be expressed in terms of the operating parameters of the corresponding TMB process. In case of the ideal model and linear adsorption isotherms according to Equation 5, the TMB model can be solved in closed form. On the basis of this solution Nicoud (1992) and Ruthven and Ching (1989) introduced new operating parameters  $\beta_i$  and stated bounds for which the desired separation can be achieved:

$$\begin{aligned} Q_F &= Q_S(K_{H,A}/\beta_{III} - K_{H,B}\beta_{II}) \\ Q_{Ex} &= Q_S(K_{H,A}\beta_I - K_{H,B}\beta_{II}) \\ Q_D &= Q_S(K_{H,A}\beta_I - K_{H,B}/\beta_{IV}) \\ Q_{IV} &= Q_S(K_{H,B}/\beta_{IV} + \frac{\varepsilon}{1-\varepsilon}) \end{aligned} \quad (10)$$

$$1 \leq \beta_i \leq \sqrt{\frac{K_{H,A}}{K_{H,B}}}, \quad K_{H,B} < K_{H,A}$$

The  $\beta$ -variables were originally intended as slack variables to formulate the conditions for proper operation of the separation unit as a set of inequalities. The bounds on those variables result from retaining the adsorption and desorption fronts in the appropriate zone of the unit, i.e. the  $\beta$ 's are safety factors for the ratio of the net mass flow rate of the solid and the liquid phase. A detailed exposition of this subject can be found in Zhong and Guiochon (1998).

As the objective function in this framework, the minimization of the specific desorbent consumption  $Q_D/Q_F$  or the maximization of the throughput  $Q_F$  can be used. Both objective functions lead to the same solution in the idealistic case, which is  $Q_D = Q_F$  at the boundary of the feasible region with  $\beta_i = 1$  and  $Q_D/Q_F = 1$ . The maximum feed inflow  $Q_F$  is bounded by the maximum allowed internal flow rates, which are limited by the pressure drop or the efficiency of the adsorbent. Storti et al. (1993), Mazzotti et al. (1997), and Migliorini et al. (1998) derived a graphical short-cut design methodology based on these ideas, the so-called *triangle theory* and extended the theory to systems with nonlinear adsorption isotherms. This methodology is currently state of the art and has been applied to a large number of separations. Due to the unrealistic assumptions of the ideal model, the triangle theory can only give initial guesses for a feasible operating point of the process because it does not permit a reliable prediction of the product purities which are the most important operating constraints.

To overcome the limitations of the ideal model, Ma and Wang (1997) and Wu et al. (1998) presented a stand-

ing wave design approach based on an equilibrium dispersive transport model of the TMB process. However, in case of systems with dominant mass transfer or diffusion effects the minimization of the desorbent consumption and the maximization of the throughput become conflicting. Additionally, as already mentioned, the quality of the prediction of the TMB model in general is only sufficient for a restricted range of applications. It is therefore necessary to develop design strategies based on rigorous dynamic SMB process models. The operating points determined with the triangle theory or the standing wave design can be used as initial guesses for the computation of an optimal operating point.

Strube et al. (1999) describe a heuristic design strategy based on the dynamic simulation of a SMB process model. The optimization objective is formulated in a set of competing and partly contradictory targets which are approached by parameter variation based on a heuristic strategy. The major advantage of this method is the use of a realistic process model, the disadvantage is the need for extensive manual simulation without any guarantee to determine the optimum, and the need for an experienced user.

From the shortcomings and the limitations of the previously described approaches, a list of desired properties for a model-based optimization strategy for simulated moving bed chromatographic processes can be stated as follows:

1. The algorithm has to be based on a realistic and efficient dynamic SMB process model.
2. The objectives for the optimization must be formulated in a single objective function avoiding competing and contradictory targets.
3. The product quality has to be included explicitly in the formulation since this is the most relevant constraint for the operation.
4. The strategy has to be based on a mathematical optimization procedure. This is the only way to ensure that, in combination with suitable initial guesses, a solution at least close to the optimum can be obtained in finite time and without requiring too much costly expertise.
5. The procedure should be as general as possible, so that it can be applied to a broad variety of SMB processes with linear or nonlinear adsorption equilibrium, any number of columns and any size of equipment.

### A New Model-Based Optimization Strategy

To the best of our knowledge, there are only two approaches documented in the literature which treat the calculation of the optimal operating regime in a rigorous mathematical formulation: the strategy suggested by Kloppenburg and Gilles (1998), and the approach

proposed in the sequel which is explained in detail in Dünnebier and Klatt (1999); Dünnebier et al. (2000).

We here consider the case where the plant design is fixed and the feed inflow is pre-specified, e.g. by the outflow of an upstream unit. In this case, the desorbent inflow  $Q_D$  constitutes the only variable contribution to the processing costs. By defining  $c_k$  as the axial concentration profile at the end of a switching period, and by expressing both the process dynamics between two switching operations and the switching operation itself by the operator  $\Phi$

$$c_{k+1} = \Phi(c_k) \quad (11)$$

we can write the following condition for the cyclic steady state:

$$\|\Phi(c_k) - c_k\| \leq \delta_{css} \quad (12)$$

The purity requirements for the products in the extract and raffinate stream are formulated as inequality constraints. Besides that, the efficiency and functionality of most adsorbents is only guaranteed up to a maximum interstitial velocity, which results in a constraint  $Q_{\max}$  for the flow rate in the first section of the process. The optimization problem can then be stated as follows:

$$\min_{Q_j, \tau} Q_D \quad (13)$$

subject to

$$\begin{aligned} \|\Phi(c_k) - c_k\| &\leq \delta_{css} \\ \int_0^\tau \frac{c_{A,Ex}(t)}{c_{A,Ex}(t) + c_{B,Ex}(t)} dt &\geq Pur_{Ex, \min} \\ \int_0^\tau \frac{c_{B,Raf}(t)}{c_{A,Raf}(t) + c_{B,Raf}(t)} dt &\geq Pur_{Raf, \min} \\ Q_I &\leq Q_{\max} \end{aligned}$$

Although the values for the optimization variables are constant during the switching periods, the optimization problem is inherently a dynamic one, because the operating regime of a SMB process is a periodic orbit and not a steady state. From a mathematical point of view, this is due to the dynamic nature of Equation 12 which is a system of partial differential equations with switching initial and boundary conditions, constituting the crucial constraint of the formulation given in Equation 13.

The natural choices of the degrees of freedom for the calculation of the optimal operating regime are the desorbent flow rate  $Q_D$ , the extract flow rate  $Q_{Ex}$ , the switching time  $\tau$  and the recycle flow rate  $Q_{IV}$ . Due to the complex interactions, this results in a strongly coupled system dynamics, since each of the independent variables affects every zone of the process. Furthermore, it is impossible to formulate explicit and independent bounds on those variables, and the optimization problem is not well-conditioned from a numerical point of view.

We therefore exploit the results of the analysis for the ideal process model in case of linear isotherms. Equation 10 sets up a transformation where the “natural degrees of freedom”  $Q_D$ ,  $Q_{Ex}$ ,  $Q_{IV}$ , and  $\tau$  are replaced by the variables  $\beta_i$ . Due to the physical meaning of the  $\beta_i$  (safety margins for stable process operation), the feasible region for the optimization problem is well-defined in terms of the bounds for the transformed variables given in Equation 10. Furthermore, due to the scaling effect and based on the feature, that any of the variables  $\beta_i$  mainly affects one zone of the process, the variable transformation results in a more favorably structured optimization problem. In case of nonlinear isotherms, the slope of the isotherm is concentration dependent and can no longer be represented by the constant Henry-coefficient  $K_H$ . In order to extend Equation 10 to the nonlinear case, we thus chose a reference concentration to formulate the transformation:

$$\begin{aligned}
 Q_S &= \frac{Q_F}{\frac{\partial g_A}{\partial c_A}(c_F)/\beta_{III} - \frac{\partial g_B}{\partial c_B}(c_F)\beta_{II}} = \frac{(1 - \varepsilon_b)AL}{\tau} \\
 Q_{Ex} &= Q_S \left( \frac{\partial g_A}{\partial c_A}(c_F)\beta_I - \frac{\partial g_B}{\partial c_B}(c_F)\beta_{II} \right) \\
 Q_D &= Q_S \left( \frac{\partial g_A}{\partial c_A}(c_F)\beta_I - \frac{\partial g_B}{\partial c_B}(c_F)/\beta_{IV} \right) \\
 Q_{IV} &= Q_S \left( \frac{\partial g_B}{\partial c_B}(c_F)/\beta_{IV} + \frac{\varepsilon}{1 - \varepsilon} \right)
 \end{aligned} \tag{14}$$

where

$$g_i = \varepsilon_p c_{p,i} + (1 - \varepsilon_p)q_i(c_A, c_B) \quad (i = A, B)$$

and describes the equilibrium isotherm. The feed concentration is a simple and suitable choice to calculate the slopes. The bounds on the variables  $\beta_i$  as given in Equation 10 are based on stability considerations for the ideal model and linear adsorption equilibrium and can therefore not simply be transferred to more complex systems. In case of nonlinear isotherms the bounds have to be relaxed suitably, and in terms of the triangle theory, the region limited by these bounds can be seen as a hull for the shaped triangle. However, the transformation Equation 14 helps to scale, structure and reduce the search space.

The crucial point in the solution of the optimization problem (13) is the efficient and reliable computation of the cyclic steady state. The solution of the associated fix-point problem given by Equation 12 corresponds to a mathematically similar formulation for pressure swing adsorption (PSA), the dynamics of which shows some similarities to SMB processes. Three main approaches have been identified and examined in the literature. Firstly, the solution can be achieved by direct dynamic simulation (Picard iteration). Alternatively, Equation 12 can be solved by a Quasi-Newton scheme (Unger et al.,

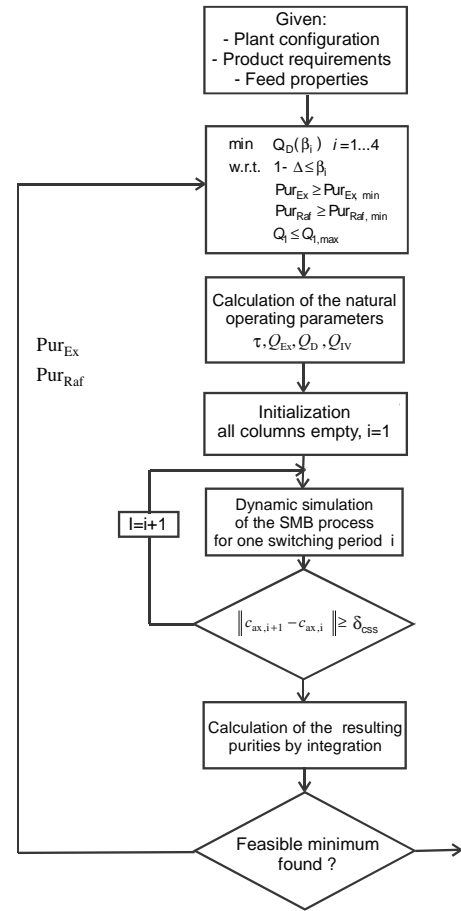


Figure 5: Optimization algorithm.

1997; Kvamsdal and Hertzberg, 1997; Croft and Le Van, 1994), or by discretizing the equations in space and time and solving the resulting system of algebraic equations (Nilchan and Pantelides, 1998; Kloppenburg and Gilles, 1998).

Even though there are many analogies between the SMB chromatography and PSA processes, the convergence of the direct dynamic simulation approach is much faster in the SMB case. For realistic SMB chromatography processes, the cyclic steady state is reached after a few hundred switching periods at the latest, whereas in the PSA case possibly several thousand cycles have to be evaluated. The inherent dynamics of the process are therefore much faster. On the other hand, especially for systems with nonlinear adsorption behavior and reaction kinetics, the system becomes very stiff and a very fine grid is needed, which makes the application of a global discretization approach difficult. We therefore choose the direct dynamic simulation as the most robust and efficient way for the calculation of the cyclic steady state within our optimization algorithm, which is schematically shown in Figure 5.

	Original	Run 1	Run 2
Pur <sub>Ex</sub> [%]	99.5	99.5	98.0
Pur <sub>Raf</sub> [%]	98.3	98.3	98.0
rel. Q <sub>D</sub> [%]	100	<b>60.9</b>	<b>41.7</b>
Q <sub>D</sub> [cm <sup>3</sup> /s]	0.8275	0.5043	0.3452
Q <sub>F</sub> [cm <sup>3</sup> /s]	0.2500	0.2500	0.2500
Q <sub>Ex</sub> [cm <sup>3</sup> /s]	0.77989	0.4683	0.3489
Q <sub>IV</sub> [cm <sup>3</sup> /s]	0.2695	0.1489	0.1423
$\tau$ [s]	1337.4	2096.7	2675.2

**Table 1:** Optimization results for the separation of phenylalanine and tryptophan.

We follow a staged sequential approach for the solution of the dynamic optimization problem. The degrees of freedom  $\beta_i$  are chosen by the optimizer in an outer loop and are then transformed back into flow rates and switching times according to Equation 14. In the inner loop, the cyclic steady state is then calculated by direct dynamic simulation of the rigorous SMB process model. The purity constraints are evaluated by integration of the elution profiles for the cyclic steady state. The nonlinear program in the outer loop is small and can be solved by a standard SQP algorithm, while the required gradients are evaluated by perturbation methods. The results of the optimization are the optimal cyclic operating trajectory (CSS), the minimum desorbent inflow for the specified product purities, and the corresponding operating parameters.

The optimization algorithm was tested for a number of different separation systems with both linear and nonlinear adsorption equilibrium. One impressive example is shown in Table 1, the separation of phenylalanine and tryptophan. Estimated model parameters and the reference operating conditions were taken from Wu et al. (1998), where the original operating point was optimized by a standing wave design. Because of the nonlinear adsorption equilibrium (Langmuir isotherms), the general rate model was used within our optimization algorithm. The convergence to the cyclic steady state was achieved after 75 switching periods in the average, and the SQP solver in the outer loop converged after 12-15 steps depending on the initial point. This resulted in approx. 6-8 hours CPU time for each run on a 400 MHz PentiumII PC. In the first run, the purities for the operating point obtained by Wu et al. (1998) were taken as constraints. It can be seen, that compared to the operating regime determined by the standing wave design technique, the desorbent requirement was cut down by almost 40% using the proposed optimization approach. Furthermore, the purity requirements can be directly specified. The results for run 2 show the economical impact of a reduction of the purity specifications to 98% each.

## Control Concept

In real applications, plant/model mismatch and disturbances will lead to more or less pronounced deviations from the optimal trajectory. However, the online optimization under real-time requirements is not possible with the computational power currently available. Therefore, a feedback control strategy based on suitable dynamic models and on-line measurement information is required in order to keep the process close to the optimal trajectory.

Only few publications can be found in the open literature which treat the automatic control of simulated moving bed chromatographic processes. Ando and Tanimura (1986), Cohen et al. (1997), Hotier and Nicoud (1996), and Hotier (1998) deal with the basic control of the internal flow rates, which itself is a difficult task and forms the basis for the more advanced control strategies. The concepts described in Holt (1995), Cansell et al. (1996), and Couenne et al. (1999) propose feedback control for certain operating variables (e.g. product purity, system yield) based on some concentration measurements. They are predominantly applied to the separation of aromatic hydrocarbons where on-line Raman spectroscopy (Marteau et al., 1994) can be utilized to measure the specific concentration of the compound at the outlet of the chromatographic columns. Those as well as the geometric nonlinear control concepts described in Kloppenburg and Gilles (1999) and Benthabet et al. (1997) are mainly based on a model for the corresponding true moving bed (TMB) process, where the cyclic port switching is neglected, and thus rely heavily on the applicability of the TMB model as a simplified model for the SMB process. This is particularly critical for SMB processes with a low number of columns—which are more and more utilized in industrial applications in order to reduce the investment costs—where the correspondence between the SMB dynamics and the TMB approximation may become poor. In a recent publication, Natarajan and Lee (2000) suggest to apply repetitive model predictive control on a reduced order linear state space model of the SMB process. They optimize the product yield for a given constraint on the purities using the reduced linear model for the control calculations. This approach definitely follows the right objective, i.e. the control of the process in the vicinity of an optimal operation point. However, in case of the SMB process, yield optimization even when considering the purity constraints does neither generically imply the economic optimum nor guarantee a stable process operation in the long run. Furthermore, the range of validity for the linear approximation and its impact on the control performance is not explicitly considered.

In order to overcome some of the shortcomings and limitations mentioned above, we proposed a two-layer control architecture which is shown schematically in Fig-



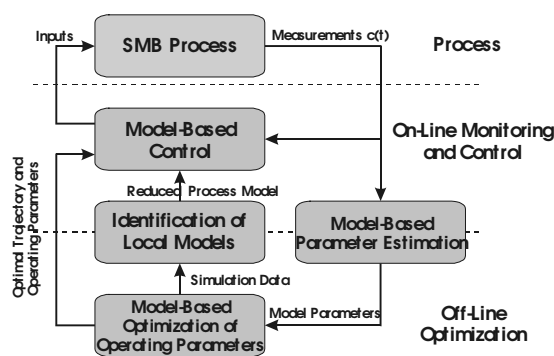


Figure 6: Control concept for SMB processes.

ure 6 (Klatt et al., 2000). The top layer features the off-line calculation of the optimal operating trajectory as described in the previous section, combined with an on-line estimation of the respective model parameters based on inline concentration measurements. The purpose of this estimation algorithm is twofold: It provides actual and reliable values for the model parameters, and together with the dynamic simulation model, it enables the monitoring of the complete axial concentration profile which is not directly measurable in the interior of the separation columns. If there is a too large discrepancy between the actual parameters and the parameter values used in the trajectory optimization (e.g. caused by aging of the adsorbent material), a new optimization run is initiated. The remaining control task then is to keep the process along the calculated nominal trajectory despite disturbances and plant/model mismatch, caused e.g. by small and non-persistent perturbations of the system parameters. This task is performed by the bottom layer where identification models based on simulation data of the rigorous process model along the optimal trajectory are combined with a suitable local controller. The realization of the remaining elements of the proposed control structure is explained below.

The model-based parameter estimation utilizes on-line measurement data from measurement devices located in the product outlets or in the connecting pipelines between the columns. Because of the high costs of on-line concentration measurements, measurements located after each single column will generally not be feasible. Typically, up to four measurement points can be found in real plants, if online measurement is employed at all. The devices are system specific and use either spectroscopic methods or combined measurement techniques to determine the concentration of each single species.

Starting from a complete set of model parameters determined in a priori experiments, the objective of the online estimation is to fit the model to the real process. The model parameters can be categorized in kinetic parameters (describing mass transfer, diffusion, dispersion)

and adsorption parameters (constituting the adsorption isotherms). Due to the limited measurement information available, we solve a reduced parameter estimation problem, where one crucial parameter per class and component is adapted by optimizing a quadratic cost functional

$$\min J = \int_{t_1}^{t_2} (c_{i,meas}(t) - c_{i,sim}(t))^2 dt, \quad i = A, B \quad (15)$$

where the measured outlet concentrations  $c_{i,meas}$  are compared to the outlet concentrations  $c_{i,sim}$  which are determined by the solution of the simulation model. The number and arrangement of the measurement devices depend on the mixture to be separated. In Zimmer et al. (1999) a measurement setup and estimation algorithm was proposed for systems with linear adsorption isotherms which is briefly sketched in the application example below.

The rigorous dynamic SMB model, consisting of PDEs (eqs. (7) and (8)) with switching initial and boundary conditions, is not well suited for a standard controller design. Thus, we base the trajectory control on a local model. In order to get rid of the hybrid system dynamics in the bottom layer of the control concept, we consider the reduced model as a discrete time model with the sampling interval equal to one switching period. The model predicts one characteristic parameter of the concentration profile per switching period, and therefore does not require the consideration of the discontinuities introduced by the switching operation.

Because of the favorable properties of the nonlinear transformation of the input space (14) which is utilized in the trajectory optimization, the variables  $\beta_i$ , resp. the deviations from their values on the nominal trajectory, are also chosen as inputs of the reduced model. This allows a variable switching time which is essential in case of inflow disturbances because feed flow-rate changes can be completely compensated only by a corresponding adaptation of the virtual solid stream. Furthermore, with an appropriate choice of outputs, the nonlinear transformation helps to create a nearly decoupled system dynamics, particularly for SMB separation processes with linear adsorption equilibrium.

One characteristic indicator of the separation performance of a SMB unit is the axial position of the adsorption and desorption fronts of the two components at a certain moment, e.g. at the end of a switching period (see Figure 3). They are referred to as front positions  $p_i$  in the sequel. Extensive simulation studies showed that the front positions do not only provide a suitable indicator for the long term stability of the system, but additionally exhibit an excellent correspondence with the product purities which are the relevant output variables. However, from a system dynamics point of view, the product concentrations are ill-suited as controlled variables due

to their strongly delayed response and their lack of sensitivity to changes in the manipulated variables. Thus, the deviations of the front positions from their nominal values on the optimized trajectory are chosen as outputs of the local model.

The axial concentration profile is not directly measurable, but assuming an on-line concentration measurement at the end of each column, an approximation of the complete axial concentration profile can be obtained by connecting all measurements of the elution profiles during one switching period. We call this representation the Assembled Elution Profile (AEP). If the system is at its cyclic steady state, the AEP can also be obtained by using the information of a single measurement over  $n_{col}$  switching periods. In case of a disturbed system, the AEP obtained from a system with less than  $n_{col}$  measurements becomes in some respect time variant, since the parts of the AEP are recorded at different instants during the transition, and the AEP constructed depends on the location of the measurements in the loop. Nevertheless, a reduction of the number of measurements below  $n_{col}$  is possible to a certain extent, and the effect on the AEP is comparable to a low pass filter. The required number and the exact location of the measurement devices depend on the specific system dynamics.

Three different methods for the calculation of the front positions from the AEP were evaluated:

- I. Functional approximation of the fronts, followed by the calculation of the inflection point of this function.
- II. Surface quadrature to calculate the center of gravity of the fronts.
- III. Wavelet analysis to determine the inflection points of the fronts.

For method I, a variation of the Gauss error function proved to supply a good approximation for the fronts of SMB separation processes with linear and moderately nonlinear adsorption isotherms. The desorption fronts are approximated by

$$f(t) = \frac{1}{2} \left[ 1 + \frac{2}{\sqrt{\pi}} \int_0^{k(t-z)} e^{-\theta^2} d\theta \right], \quad (16)$$

the adsorption fronts by

$$f(t) = \frac{1}{2} \left[ 1 - \frac{2}{\sqrt{\pi}} \int_0^{k(t-z)} e^{-\theta^2} d\theta \right]. \quad (17)$$

The two parameters of the function,  $k$  and  $z$  are calculated by a least-squares fit to the available measurements which is updated in each switching period, and the inflection point of the function which represents the front position is determined analytically afterwards.

In the second method, an upper and lower bound for the concentration front is assumed first. Then the front

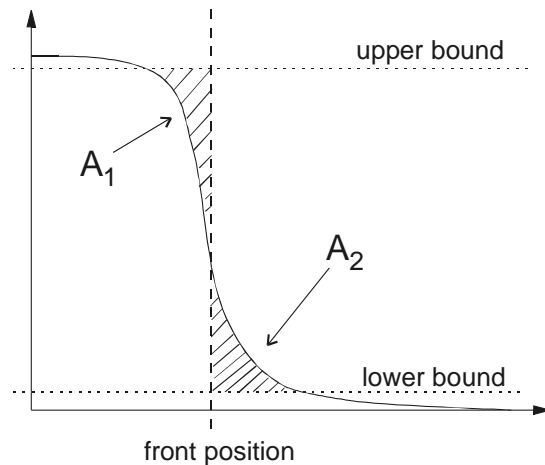


Figure 7: Evaluation by surface quadrature.

position is defined as the point where  $A_1 = A_2$  (see Figure 7). The integration is approximated by a summation over the available measurement points.

Wavelet analysis (III) is based on scale and position dependent coefficients of the form

$$C(a, k) = \int_{-\infty}^{\infty} f(t) \Psi(a, k, t) dt \quad (18)$$

and allows the multi-scale analysis and representation of arbitrary time series. It also enables the direct identification of inflection points from noisy data (see, e.g. Daubechies, 1992). The method of choice mainly depends on the characteristics of each different separation process, i.e. the shape and the position of the adsorption and desorption fronts. The different methods have to be evaluated trading off the computational requirements for the calculation, the robustness against noise, and the physical meaning of the calculated positions.

Having defined the inputs and outputs, the structure of the local model and the input signal for the identification need to be specified. In our work, we utilize the MATLAB System Identification Toolbox (Ljung, 1995) to perform the necessary computations. To obtain the necessary data for identification, the rigorous simulation model is excited around the nominal operation regime with a random binary signal. For MIMO identification, non-correlated signals in the different channels are to be preferred, which can be achieved with a slight modification of the Pseudo Random Binary Signal, the Pseudo Random Multistep Signal (Isermann, 1992). We tested prediction error models as well as subspace state space identification methods and found both approaches suitable for the SMB separation processes we have investigated so far.

After identification of the local linear model any standard linear control design approach or linear model predictive control can be used to realize the controller on

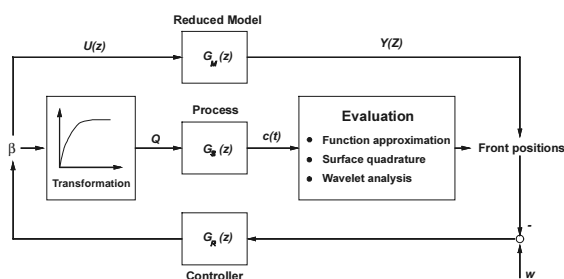


Figure 8: Structure of the trajectory control loop.

System Parameters			
$d_{col}$	2.6 cm	$L$	53.6 cm
$\varepsilon$	0.38	$d_p$	0.0325 cm
$\rho$	1 g/cm <sup>3</sup>	$\eta$	0.0058
$K_A$	0.54	$K_B$	0.28
Nominal Operating Parameters			
Concentration of feed $c_F$		0.5 g/cm <sup>3</sup>	
Feed flow rate $Q_F$		0.02 cm <sup>3</sup> /s	
Desorbent flow rate $Q_D$		0.0414 cm <sup>3</sup> /s	
Extract flow rate $Q_{Ex}$		0.0348 cm <sup>3</sup> /s	
Recycle flow rate $Q_{IV}$		0.0981 cm <sup>3</sup> /s	
Switching time $\tau$		1552 s	
Purity fructose		99.95%	
Purity glucose		99.95%	
$\beta$	[ 1.1371	1.0993	1.1164 1.1220 ]

Table 2: System and operating parameters for the separation of fructose and glucose on an 8-column SMB laboratory plant.

the bottom layer. At a glance, the structure of the trajectory control loop is depicted in Figure 8. The variables represent deviations from the nominal trajectory: four input variables  $u_i = \Delta\beta_i$ , and deviations of the four front positions (normalized to the scaled length of all interconnected columns between 0 and 1) as outputs  $y_i = \Delta p_i$ .

## Application Example

As an application example, we consider the separation of a fructose/glucose mixture on an 8-column laboratory scale SMB plant. Performing the proposed optimization algorithm, the plant was optimized for a product purity of 99.95% both in the extract and the raffinate stream. From a practitioner's point of view, this is an exceptionally high purity requirement for a sugar separation. Those are normally operated with a purity specification of at most 99%. However, the higher the purity specification the more challenging the control problem, because

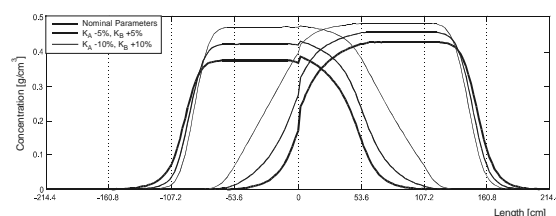


Figure 9: Axial profile (CSS, end of period) of the SMB fructose/glucose separation and its sensitivity to parameter perturbations.

the system is operated much closer to the stability margins. Furthermore, in pharmaceutical separations the purity requirements are generally very high. Thus we decided to operate the sugar separation under these high purity requirements to demonstrate the feasibility of the proposed approach.

The system and operating parameters are shown in Table 2. The plant is operated at 60 °C. The liquid density can be considered as constant for the given feed concentration, and the adsorption isotherms are well described by Henry's law (5). Thus, the DLI model (7) is utilized within the optimization and control framework. The optimal operating trajectory and parameters were determined using the optimization algorithm described above. Here, convergence to the cyclic steady state was achieved after 65 switching periods on the average, and the SQP solver in the outer loop converged after 10-15 steps depending on the initial point. This resulted in approx. 4 hours CPU time on a 400 MHz PentiumII PC. Because of the complex hybrid system dynamics, steady state multiplicities are possible in principle. We therefore tested different initial points within the feasible region, but for the separation task at hand they all converged to the optimal solution reported in Table 2. However, this is of course system dependent and has to be thoroughly inspected for each individual separation task.

Figure 9 shows the axial concentration profile for the optimal operation mode and its sensitivity against variations of the adsorption isotherm parameters, caused e.g. by a varying feed quality. We here perturbed the system into the direction where the separation becomes more difficult, i.e. decreasing  $K_A$  and increasing  $K_B$ . Table 3 depicts the corresponding product purities. It is obvious, that the optimal operating regime is quite sensitive against parameter variations and thus the results of the trajectory optimization illustrated above essentially depend on a reliable determination of the model parameters.

In Zimmer et al. (1999) an on-line parameter estimation algorithm for systems with linear adsorption isotherms based on concentration measurements only in the product outlets was proposed. A combination

	Nominal	$K_A$ -5% $K_B$ +5%	$K_A$ -10% $K_B$ +10%
Extract	99.95%	99.50%	97.04%
Raffinate	99.95%	99.61%	96.71%

**Table 3:** Product purities corresponding to the concentration profiles shown in Figure 9.

of a polarimeter and a densimeter is used to determine the specific concentrations of fructose and glucose (Altenhöner et al., 1997). Assuming the validity of the DLI model (7), the system has, in the case of a binary separation, four parameters describing the physical behavior, which are  $\gamma_i$  and  $D_{ap,i}$  ( $i = A, B$ ).  $\gamma$  incorporates the column void fraction  $\varepsilon$  and the respective adsorption parameter, the apparent dispersion coefficient  $D_{ap}$  lumps the kinetic effects. Thus, no further reduction of the parameter space is necessary in this case.

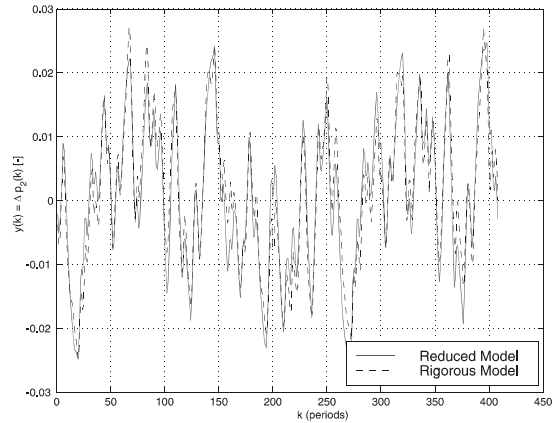
A linear adsorption isotherm implies that the components do not interact with regard to their adsorption behavior. Therefore, the two parameter sets  $(\gamma_A, D_{ap,A})$  and  $(\gamma_B, D_{ap,B})$  can be determined separately by solving the least-squares problem posed by Equation 15. The simulated axial concentration profile  $c_{i,sim}$  is determined by solving the PDE (7) for each column and each component. Unfortunately, the boundary and initial concentrations for each switching period are only partly available from the measurements. Therefore, a special approximation strategy was developed using the concentration of fructose and glucose in the extract and raffinate outflow in two consecutive switching periods. This parameter estimation additionally supplies an approximation of the non-measurable concentration profiles in the interior of the columns prior to the measurement. Because the measurement devices are located in the product outlets which are periodically switched downstream, the complete axial concentration profile can be reconstructed within a complete cycle (i.e. 8 switching periods).

The major task of the parameter estimation is to supply a set of actual model parameters which can be used for the trajectory optimization. Also they indicate if there is too large a deviation from the original set of parameters and thus a new optimization run has to be performed. However, as online optimization is not possible for the time being, smaller deviations and other disturbances have to be adjusted by the trajectory control loop.

For the fructose/glucose separation, a linear time invariant model of the ARX type was chosen as the local dynamic model:

$$\mathbf{A}(q)y(t) = \mathbf{B}(q)u(t) + e(t) \quad (19)$$

where  $\mathbf{A}$  and  $\mathbf{B}$  are  $4 \times 4$  matrices containing polynomial functions of the discrete time shift operator  $q$  in



**Figure 10:** Model validation.

each element. The amplitude of the input signal  $\Delta\beta_i$  for excitation of the rigorous DLI model was chosen to be 10% of the nominal  $\beta$ -value. This input range covers nearly the whole range of practically reasonable operating conditions. A first estimate of the necessary system order was obtained by the evaluation of step responses of the DLI model, which was then adapted based on the performance of the identified model. For the elements of the matrices  $\mathbf{A}$  and  $\mathbf{B}$ , polynomials of at most second order proved to be sufficient. The performance of the model was tested with a second validation data set. The prediction of the front positions (desorption front of glucose (component B) as one example) of the rigorous and of the reduced model are compared in Figure 10. The prediction horizon is infinite here, i.e. the simulation models are reconciled only for initialization and then run independently. The approximation is very good, only in regions far from the nominal trajectory, where the assumption of linearity is violated, slight deviations occur.

As postulated, the system dynamics are diagonally dominant in the vicinity of the optimal operating trajectory. As mentioned above, in principle, any standard linear controller design method could be applied. For this example, we transformed the ARX model (19) to a  $z$ -domain transfer function representation and applied internal model control following the guidelines proposed in Zafriou and Morari (1985) to design a discrete time SISO controller for each channel (i.e. the control of each single front position by manipulating the respective  $\beta$ -value). The design of the internal model controllers is very straightforward for the system at hand and allows the direct integration of the system dynamics into the controller.

In the conventional feedback representation, the internal model controller is of the form

$$C(z) = \frac{F(z)G^C(z)}{1 - F(z)G^C(z)G^M(z)} \quad (20)$$

where  $G^C$  is the internal model controller,  $G^M$  is the transfer function of the respective model, and  $F$  is a first order filter

$$F(z) = \frac{z(1-\alpha)}{z-\alpha} \quad (21)$$

where  $\alpha$  has to be suitably chosen in the range  $0 \leq \alpha < 1$ . After a cancellation of numerically induced pole/zero pairs, we obtained the following transfer functions for the respective input-output channels

$$\begin{aligned} G_1^M &= \frac{0.0349 \cdot z^2}{(z-0.145)(z-0.8011)} \\ G_2^M &= \frac{0.0256 \cdot z^2}{(z-0.7058+0.1106j)(z-0.7058-0.1106j)} \\ G_3^M &= \frac{-0.0365 \cdot z^2}{(z-0.6967+0.2277j)(z-0.697-0.2277j)} \\ G_4^M &= \frac{-0.0143 \cdot z^2}{(z-0.5743)(z-0.8270)} \end{aligned} \quad (22)$$

In this case, direct inversion of  $G_M$  is possible and the internal model controller is realized by

$$G_i^C = \frac{1}{z} \cdot \frac{1}{G_i^M(z)} \quad (23)$$

The filter parameters were selected from simulation studies as

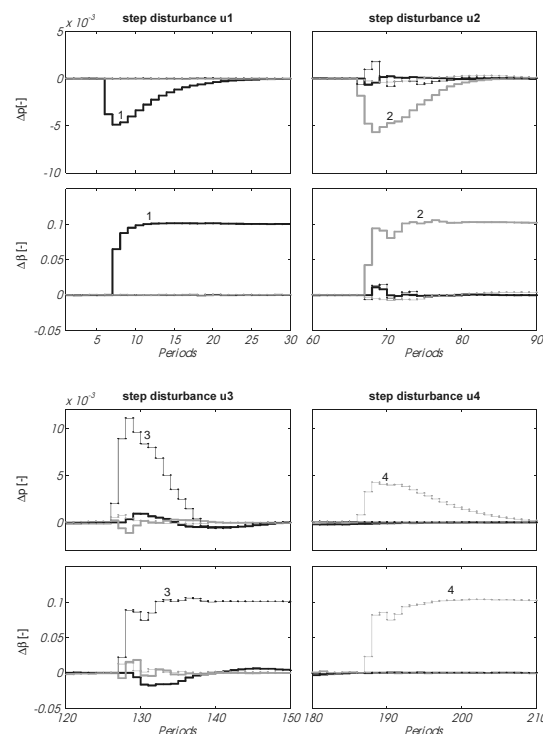
$$\alpha_1 = 0.4, \quad \alpha_2 = 0.4, \quad \alpha_3 = 0.6, \quad \alpha_4 = 0.6$$

and the range of the trajectory controller was chosen as a  $\pm 10\%$  deviation from its value at the optimal operating regime for each of the  $\beta_i$ .

In the following, some simulation studies are presented in order to demonstrate the capabilities of the proposed trajectory control. For the simulation scenarios, the general rate mode according to Equation 8 is used to represent the real plant. This introduces a structural deviation between the DLI model on which the control design is based and the simulation model for the validation experiments. The scenarios depicted below were performed both without and with noise added to the concentration measurements. White noise with a standard deviation of 1% of the maximum concentration value was assumed.

### Flow-Rate Disturbance

In this scenario it is assumed that a step disturbance in each of the internal flow rates occurs one at a time to analyze the effect on all front positions and possible coupling. Under practical considerations, these disturbances may be caused by an irregularity in the pumping and piping system or by an offset in the basic control layer. Each of the subplots in Figure 11 shows the manipulated variable and controlled variable moves resulting from the disturbance in the respective input channel,



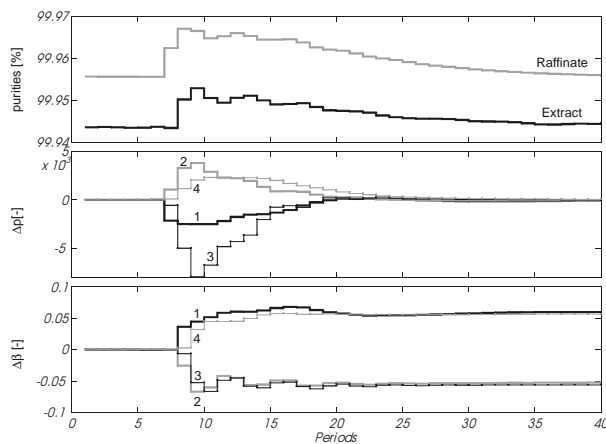
**Figure 11:** Closed loop reaction on input disturbance scenario.

where a 10% variation in terms of the  $\beta$ -variable corresponds to a 10-20% variation of the internal flow rates.

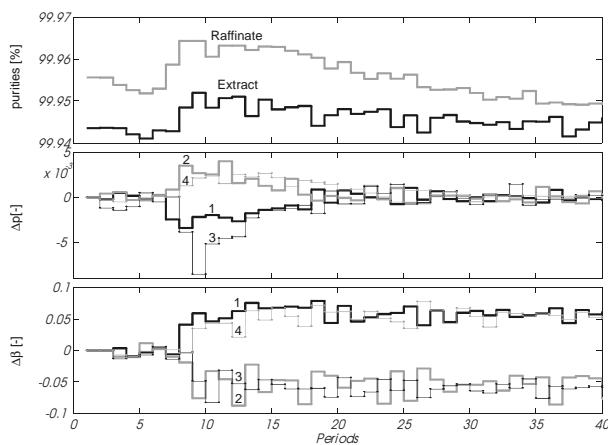
As can be clearly seen, the closed loop reacts in a mostly decoupled manner. The front position deviation is suppressed quickly by the controller, the maximum value of the deviation being about 0.01 in terms of scaled length. Though minor effects of coupling can be seen for disturbances in channels 2 and 3, the effects remain small. As expected, the results of the same sequence under noisy measurements show less smooth control actions and a slight wiggling of the front positions due to the noise's influence on the calculation of the inflection points. However, the results are principally the same with no major deterioration as compared to the noise-free setting. The corresponding plot is omitted here for the sake of brevity.

### Feed Batch Change

In real-world applications a separation process follows prior production steps which might be continuous or discontinuous, a typical example in the Life Science context being a fermenter or a batch reactor. Thus a continuous SMB chromatography has to face changes in the feed batch quality. In Table 3 and in Figure 9 we already considered this scenario, which corresponds to a change of the characteristic adsorption parameters, and its im-



**Figure 12:** Closed loop response to change of feed batch.



**Figure 13:** Closed loop response to change of feed batch in the presence of measurement noise.

pact on the axial concentration profile and the product purities within the cyclic steady state operating regime.

Starting from the optimal operating regime, after five periods we again perturbed the characteristic adsorption parameters by  $\pm 5\%$ , but now with the feedback control loop closed. The results are shown in Figure 12 for the case of noise-free concentration measurements. The trajectory controller quickly suppresses the disturbance and drives the corresponding front positions (controlled variables) back to their nominal values without any offset. The axial concentration profile therefore does not change its position as in the scenario without feedback control, but is kept in the immediate vicinity of the optimal profile. As a result, the product concentrations which are the essential quality parameters are thus indirectly con-

trolled and kept close to their optimal values. Figure 13 shows the same scenario under noisy measurements. The results are qualitatively the same and the effect on the product concentrations remains very small compared to the noise-free setting.

## Conclusions and Further Research

Simulated moving bed chromatographic separation processes pose a challenging control problem because of their complex hybrid dynamics. In this contribution, we proposed an integrated, model-based approach for the optimal operation and advanced control of a SMB chromatographic process. To our knowledge, it is the first approach which is based solely on a rigorous dynamic process model and does not utilize the simplified TMB model in any of its elements. Furthermore, the proposed strategy explicitly aims at controlling the process close to its economic optimum.

The control architecture features two cascaded layers where in the top layer the optimal operating trajectory is calculated off-line by dynamic optimization. Due to the associated computational complexity, online optimization based on a rigorous dynamic process model is currently not possible. The respective model parameters are determined by an online estimation algorithm which, in addition to providing actual and reliable model parameters for the trajectory optimization, enables the online monitoring of the non-measurable concentration profile within the separation columns. If the discrepancy between the actual parameters and the parameter values on which the trajectory optimization was based on becomes significant, a new optimization run should be initiated. The task of the second layer of the control architecture is to keep the process along the optimized trajectory. This trajectory control is based on a local linear model which is identified from simulation data of the rigorous dynamic process model along the optimized trajectory.

The capabilities of the proposed control concept could be demonstrated in a set of simulation studies for the separation of fructose and glucose on an eight column SMB plant which is currently operated manually in the Plant Design Laboratory at the University of Dortmund. Due to the particular choice of the inputs and outputs, the dynamics of the local ARX model are approximately decoupled in the vicinity of the optimal operating trajectory, and thus a simple decentralized internal model controller could be used for the trajectory control. It performs satisfactorily, rejecting different types of disturbances both in a noise-free setting and with noisy measurements.

The overall control architecture is currently being implemented in an industrial standard control system. It consists of a decentralized control system (DCS) of the SIEMENS S7-400 series (CPU S7-414-2DP) and the

Windows Control Center (WinCC) as human machine interface. The algorithms and programs of the components of the control structure are integrated via the C-script interface, Global Script. Due to the fact, that the trajectory optimization is performed off-line, this task can be swapped out to another machine.

The experimental verification of the proposed approach on the laboratory SMB plant is planned for the near future, followed by the extension of the concept to a real pharmaceutical separation. However, for this latter task, some open issues have to be addressed because pharmaceutical separations may show a very complex nonlinear adsorption behavior and not all of the components of the proposed concept are currently completely adapted to this challenge. The off-line trajectory optimization can be performed for arbitrary complex isotherms, the successful extension to reactive adsorption processes was recently reported in Dünnebier et al. (2000). The online parameter estimation concept is currently realized only for systems with negligible coupling of the adsorption isotherms. This has to be extended in order to get a reliable online estimate for the interaction parameters of the adsorption isotherm in case those have a significant impact on the system dynamics. Due to the limited measurement information, a reduced parameter estimation problem has to be posed in the case of complex nonlinear isotherms, restricting the online adaptation to the most significant model parameters only. The design strategy for the inner control loop is also subject to revision because the range of validity for the local linear model may be too small for very nonlinear and strongly coupled systems. Currently, the combination of NARX models based on neural networks and nonlinear model predictive control as an alternative to realize the trajectory control loop for this type of separations is investigated. Furthermore, the correspondence between the characteristic points used for control and the product purities—which is excellent in case of the sugar separation example—has to be validated for different types of substances and the need for alternative calculation methods or even different characteristics to represent the respective fronts has to be inspected.

The above mentioned issues are addressed in current research projects and we expect a medium term solution for most of the problems. However, in the long run also the cascaded control structure is under discussion. A real time optimization based on a dynamic process model redundantizing the inner loop would be desirable. To achieve this goal, the computational efficiency of the dynamic optimization has to be enhanced by at least one order of magnitude. For this, both the numerical solution of the model equation as well as the calculation of the cyclic steady state have to be improved. Adaptive gridding for the solution of the model equations in combination with the direct solution of the sensitivity equations seems to be a promising approach and provides an

interesting area for the cooperation between engineers and applied mathematicians.

## Acknowledgments

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