Model-Based Control of Batch Chromatography

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In the chemical industry, life science products are considered the most promising markets for the near future. Since pharmaceutical products, food, and fine chemicals are subject to increasingly more complex standards and stricter legal restrictions, efficient methods for the separation of thermally unstable products are needed. Chromatographic separations, for example, usually create the main costs of the overall production process. To realize the full potential of the chromatographic separation, the desired product quality has to be maintained, while operating the process at the economic optimum by reliable and efficient process monitoring and control. For control of batch chromatography, model parameters were estimated and operating parameters were optimized online. The concept has been tested on a laboratory-scale column with an industrial process control system. Experimental results for a sugar separation are given.

Introduction

In the context of life sciences chromatographic separations are applied to high-value products with separation factors near unity, or if thermally unstable substances are involved. Despite the fact that the process size differs from the separation of several grams to many tons of mixture and the concentrations differ by several orders of magnitude, the goal of the separation is the same in any case: an efficient production within the specified range of purity and recovery, while minimizing separation costs. The separation costs are very high and often dominate the overall production costs. The optimal design and operation is therefore often required to exploit the economic potential of the process, and to make its application feasible. Since the economically optimal operation is close to an operation with impure products, safety margins are usually respected in the conventional operating strategy, leading to a suboptimal operation. A complete automation of the process using all available measurements exhibits a large economic potential, and enables the operation of the process close to the cost optimal operating point, while keeping the product specifications at any time.

Chromatographic separations are frequently operated in batch mode. The elution mode considered in this work is, besides displacement, frontal or recycle chromatography, the most commonly used operation. In elution mode, one charge of the mixture to be separated is injected into the column together with a suitable solvent (desorbent). This is usually realized by an injection valve, and the charge is carried through the column by continuously injecting additional desorbent. Due to the different adsorption affinities, the different components have different migration velocities and the mixture is gradually separated, while moving through the column. The eluting solvent is analyzed with a suitable detector at the outlet of the column, and a fractionating valve is controlled based on the measurement information to separate the mixture into its components. A detailed description of the process can be found (Guiochon et al., 1994).

This contribution describes the realization of a new control framework for batch chromatographic processes, based on parameter estimation and model-based online optimization. A brief overview of different modeling approaches for chromatographic separation processes is given afterwards. A procedure for the determination of some additional model parameters in a set of independent experiments is briefly described followed by the presentation of the new control strategy. This strategy is based on two main blocks: the adaptation of the process model to the actual behavior of the plant by online parameter estimation and an online model-based optimization of the operating parameters. The implementation of the concept and the necessary online concentration measurements and an experimental study conclude this contribution.

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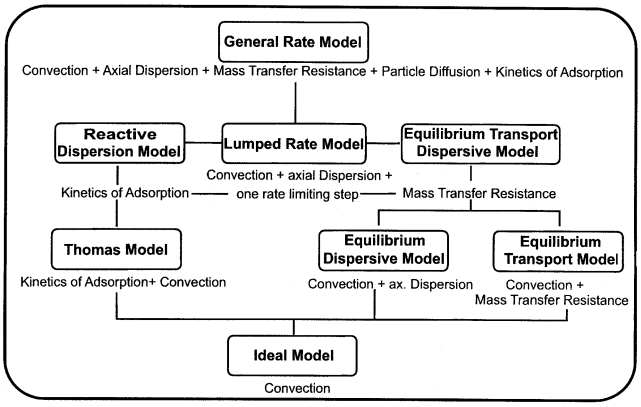

Figure 1. Different modeling approaches.

Modeling of Chromatographic Processes

The mathematical modeling of single chromatographic columns has been extensively described in the literature by several authors (see Guiochon et al., (1994) for a recent review). From a mathematical point of view, it is useful to distinguish chromatographic processes by the type of adsorption isotherms. The type of isotherm which describes the thermodynamic behavior of the modeled system influences the structure of the resulting mathematical problem substantially. Processes with linear or simple Langmuir isotherms lead to systems of decoupled differential equations, which are easier to solve than those with coupled nonlinear adsorption behavior, such as competitive Langmuir and Bi-Langmuir isotherms. Moreover, the modeling approaches can be classified by the physical phenomena which they include and thus by their level of complexity. Figure 1 shows this classification.

Many process models reported in the literature so far use an *equilibrium transport dispersive* column model. It is based on the adsorption equilibrium isotherm and a linear driving force approach for the mass transfer from bulk to solid phase. This results in a set of partial differential equations (PDEs) for the bulk phase and ordinary differential equations (ODEs) for the solid phase

$$\frac{\partial c_i}{\partial t} = D_{ax}\frac{\partial^2 c_i}{\partial x^2} - u\frac{\partial c_i}{\partial x} - \frac{1-\epsilon_b}{\epsilon_b}\frac{\partial q_i}{\partial t} \tag{1}$$

$$\frac{\partial q_i}{\partial t} = k_{eff,i}\left(c_i - c_i^{eq}\right) \tag{2}$$

Finite difference, finite element, or collocation methods are used to solve the system of model equations (Strube and Schmidt-Traub, 1996, Kaczmarski et al., 1997). A model of this type is used in the parameter estimation scheme described later. The computation times of these approaches are often within the range of the real process time. Therefore, they are not well suited for online optimization and control applications. For the application within an online optimization and control framework, computationally more efficient simulation models are required, which, on the one hand, still have a sufficiently good accuracy of prediction and, on the other hand, can be solved substantially faster. More details on the models and solution approaches developed in this framework can be found in Dünnebier et al., (1998) and Dünnebier and Klatt (1999a).

In case of systems with linear adsorption isotherms, the effects of mass-transfer resistance and axial dispersion are additive and can be incorporated into a single parameter, the apparent dispersion coefficient $D_{ap,i}$ (Van Deemter et al., 1956). This results in an *equilibrium dispersive model*, consisting of one quasi-linear parabolic partial differential equation for each species

$$\left(1+\frac{1-\epsilon}{\epsilon}K_{H,i}\right)\frac{\partial c_i}{\partial t} = D_{ap,i}\frac{\partial^2 c_i}{\partial x^2} - u\frac{\partial c_i}{\partial x}. \tag{3}$$

A closed form solution of this type of equation for a set of general initial and boundary equations by double Laplace transform was derived in Lapidus and Amundson (1952). In case of a step injection into a column, the solution of the equation can be given in closed form as follows

$$F_i(x,t) = \frac{c_i(x,t)}{c_i^e} = \frac{1}{2}\left[\begin{array}{l} 1+erf\left(\sqrt{\dfrac{\upsilon u}{4\gamma\epsilon D_{ap,i}}} - x\sqrt{\dfrac{\gamma\epsilon u}{4\upsilon D_{ap,i}}}\right) \\ + e^{\frac{ux}{D_{ap,i}}}erfc\left(\sqrt{\dfrac{\upsilon u}{4\gamma\epsilon D_{ap,i}}} + x\sqrt{\dfrac{\gamma\epsilon u}{4\upsilon D_{ap,i}}}\right) \end{array}\right] \tag{4}$$

with

$$\gamma_i = 1+\frac{1-\epsilon}{\epsilon}K_{H,i} \quad \upsilon = ut\epsilon \tag{5}$$

The pulse injections relevant in the elution mode can be generated by adding positive and negative steps. The solution then is not similar to a Gaussian distribution as sometimes assumed in literature; this assumption is only correct in case of the injection of a Dirac pulse. Even the assumption of a symmetric pulse is only correct as a first approximation. Several approximations of the Gaussian error function *erf* are known; due to the high accuracy, an approximation by Chebycheff-polynomials was chosen here.

In case of a nonlinear adsorption equilibrium, the modeling and solution approach by Gu (1995) (a model of the *general rate model* class) can be applied in an online control framework, as shown in Dünnebier et al., (1999).

Parameter Estimation

The parameter estimation strategy presented was developed for the design and scale-up of chromatographic separations using dynamic simulations of complex process models (Altenhöner et al., 1997). In the model-based control concept, the full set of independently determined model parameters are used to provide a good initial model for the reduced online parameter estimation procedure. This is of particular importance in case of more complex separations with nonlin-

ear adsorption equilibrium, where only a subset of the model parameters can be estimated in the online parameter estimation procedure to locally adapt the process model. In case of a sugar separation with linear adsorption equilibrium, most of the relevant system parameters can be determined online. Therefore, we only intend to give an overview of the possible extension of the approach to more complex systems.

The main idea of the parameter estimation concept is to determine the parameters in a sequence of several independent experiments. This procedure ensures the consistency between the parameters and the physical or chemical effects which should be described. It has been shown that extra column effects can lead to significant peak deformation (Hejtmanek and Schneider, 1993). To avoid these peak deformations being lumped into column fluid dynamics, they have to be taken into account separately. The experimental procedure starts with the determination of the extra column effects by injecting a pulse of a tracer substance into the plant without the column. From the mean residence time τ_{Dead} of the peak, the total dead volume (Eq. 6) of the system can be calculated

$$V_{\text{Dead}} = \tau_{\text{Dead}} \dot{V}. \tag{6}$$

The total dead volume V_{Dead} of the plant results from the piping and the dead volume of the detector cells that leads to time delay and back mixing, respectively. An ideal plug-flow tube and an ideal stirred tank are connected in series with the column to model the fluid dynamics of the plant. The volumes of the tube and of the tank are fitted to the experimental data by using the commercial process simulation tool *gPROMS* (gPROMS is a trademark of Process Systems Enterprise, London). The two volumes are added to determine the total dead volume of the plant. The values for V_{Dead} determined from the mean residence time (Eq. 6) of the peak and the fitting procedure only differ in the range of the measurement accuracy.

The second step is to determine the void fraction ϵ of the chromatographic column. For this pulse injection, experiments with a nonadsorbable tracer substance are carried out. To determine the void fraction of the packing, a tracer which cannot diffuse into the pores of the adsorbent was used. From the mean residence time $t_{\text{res,ext}}$ of such a peak, the void fraction can be calculated

$$\epsilon = \frac{t_{\text{res,ext}} \dot{V} - V_{\text{Dead}}}{V_{\text{col}}}. \tag{7}$$

The same experiment can be used to estimate the axial-dispersion coefficient D_{ax}. In two following steps, the isotherm parameter and the mass-transfer resistance can be determined. This is particularly required in the case of nonlinear and interacting adsorption isotherms.

Control Strategy for Batch Chromatography

In industrial applications, chromatographic processes are usually not equipped with a feedback control system. Only very recently, control concepts for continuous chromatographic processes have been presented in the literature, such as the work based on dynamic optimization of the simulated moving bed process by Kloppenburg and Gilles (1998) or Dünnebier and Klatt (1999b).

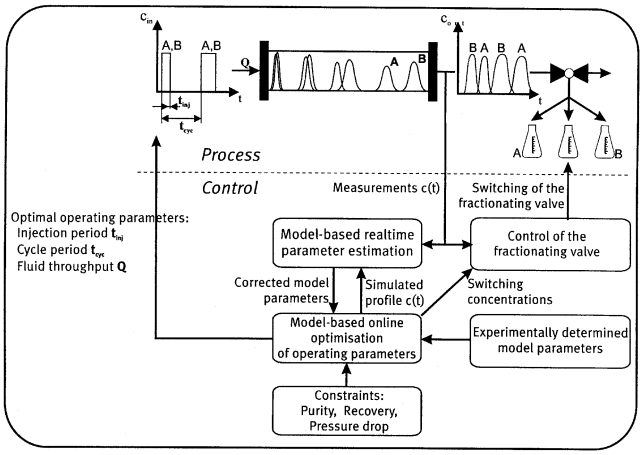

Figure 2. Process control concept.

Chromatographic separations cannot easily be controlled by conventional control strategies due to their complex dynamics with extremely long time delays, distributed parameters, and switchings.

This contribution proposes a new control structure for batch chromatographic processes, consisting of an online estimation of a reduced set of model parameters from the measurements at the column outlets only and a model-based online optimization of the operating parameters. The control scheme is shown in Figure 2. The concentration of the single components is measured online at the column outlet (elution profile) and is used to control the fractionating valve and to adjust the model parameters. In the estimation procedure, the model parameters are adapted to obtain an optimal fit of the model prediction to the measurements. The parameter estimation returns an updated set of model parameters for the chosen process model, which is then used by the optimization algorithm. The online optimization routine calculates the optimal injection period and cycle period, and the optimal flow rate based on the adapted process model.

Online parameter estimation

The starting point of the online parameter estimation strategy is a complete set of model parameters which was previously determined in a set of independent experiments, as described above. The complete set of model parameters should, especially for systems with nonlinear adsorption isotherms, be known with a reasonable initial accuracy in the range of 10–15%.

The large number of parameters and their strong interaction does not allow especially in the case of nonlinear adsorption behavior, for the estimation of all parameters based on the information available from the measured elution profile. Therefore, the intention of the online parameter estimation strategy is not the determination of a set of consistent parameters which completely describe the system and can be used for an extrapolation over a wide range of operating regions.

For the application within the control framework proposed here, a set of model parameters which allows for the extrapolation in a region close to the operating trajectory is sufficient.

The model parameters can in principle be divided in two classes:

Kinetic parameters describe the effects of mass transfer, diffusion, and axial dispersion.

Adsorption parameters describe the thermodynamic equilibrium of adsorption.

For the reduced online parameter estimation procedure, one dominant parameter from each class is chosen for each of the *nc* characteristic components of the mixture.

In the case of a linear adsorption isotherm, the effects of the two parameter classes are decoupled. The first class mainly influences the deformation of the peaks, the second the velocity of migration. For the separation of a mixture of *nc* components with linear adsorption behavior, the *DLI model* contains exactly *nc* parameters from each class, ($D_{ap,i}$ and γ_i), so there is no choice to be made. The only model parameters to be estimated *a priori* are the column void fraction ϵ and the extra column dead volumes.

Although the classification of the parameters and the decoupling of their effects is only a rough approximation in the case of nonlinear adsorption behavior, this classification is a useful means for the choice of the dominant parameters. The effects of the kinetic parameters are additive in a first approximation; therefore, an experimentally determined elution profile can be approximated by only fitting one kinetic parameter and the adsorption parameters (Golshan-Shirazi and Guiochon, 1992). Simulation studies for several tested physical systems led to the conclusion that for those systems the parameters $k_{l,i}$ and $K_{H,i}$ are the dominant parameters and, hence, chosen for parameter estimation (Dünnebier et al., 1999).

Therefore, the reduced online parameter estimation problem in both cases contains 2 *nc* parameters. As soon as the set of peaks resulting from one injected charge is eluted, this data is used for a batchwise parameter adaptation which adjusts the prediction of the model to the signals of the detector by a least-squares type algorithm.

Online optimization

The term optimization in the context of batch chromatography is only rarely used in connection with model-based mathematical optimization to determine the optimal design or the optimal operating conditions. Most of the work is concerned with the semi-empirical improvement of the system of desorbent/adsorbent. The design of a separation using mathematical models is reported in Felinger and Guiochon (1998). The models used there are rather simple and the problem formulation does not carry over to an application in an online optimization framework.

For a chromatographic column with given design parameters, the determination of the optimal operating regime is equivalent to the solution of the following problem: a possibly large amount of raw material has to be separated into the desired components, while strictly respecting the constraints on purity and recovery. The column here is operated as a batch-column in elution mode, where in specific time intervals a certain amount of raw material is injected into the column. By the solution of the optimization problem, the following set of operating parameters are determined:

(a) The throughput of solvent and educt, represented by the flow rate Q or the interstitial velocity u, while respecting the maximum throughput allowed, limited by the efficiency of the adsorbent or the pressure drop.

(b) The injection period t_{inj}, representing the duration of the feed injection as a measure of the size of the feed charge.

(c) The cycle period t_{cyc}, representing the duration from the beginning of one feed injection to the beginning of the next one.

Furthermore, the switching points of the fractionating valve $\tau_{\text{switch},i}$ can be considered as degrees of freedom of the optimization problem. In the case of total separation, the valve is switched when pure desorbent is eluting between two product peaks. In order to avoid intermediate fractions, in case of a nontotal separation, two switching times $\tau_{\text{switch},i}$ must be determined per batch to maximize the product quality.

The requirements on the products can usually be formulated in terms of minimum purities, minimum recoveries or maximum losses. In case of a binary separation, these constraints can be transformed into each other. In the sequel, we choose the product recovery Rec_i as a measure for the product quality. The objective function for the optimization is the productivity $Pr_i = \dot{m}_{\text{Product},i}/m_{\text{Adsorbent}}$ representing the amount of product produced per amount of adsorbent. If a detailed cost function is available, it can replace the simpler objective function used here.

This formulation results in the following nonlinear dynamic optimization problem

$$\begin{aligned} \max \quad & Pr\left(u, t_{\text{cyc}}, t_{\text{inj}}, \tau_{\text{switch},i}\right) \\ \text{s.t.} \quad & Rec_i \geq Rec_{\min,i}\, i = A, B \\ & 0 \leq u \leq u_{\max} \\ & t_{\text{inj}}, t_{\text{cyc}} \geq 0. \end{aligned} \tag{8}$$

This type of problem can in principle be solved by standard optimization algorithms, but the resulting computation times are unsuitable for online applications. The optimization problem is therefore simplified and decomposed in order to enable a more efficient solution.

Here, we exploit the fact that the recovery constraints are always active at the optimal solution, since a solution cannot be cost optimal if higher product qualities than required are obtained. Therefore, we consider those inequality constraints as equality constraints

$$Rec = \Phi\left(u, t_{\text{inj}}, t_{\text{cyc}}, \tau_{\text{switch},i}\right). \tag{9}$$

If, for a specified recovery, the solution of Eq. 9 could be given in the following form

$$\begin{pmatrix} t_{\text{inj}} \\ t_{\text{cyc}} \\ \tau_{\text{switch},i} \end{pmatrix} = f\left(Rec_{Spec}, u\right) \tag{10}$$

where f is a static mapping of the range which is restricted to the positive Euclidian space; then, by inserting Eq. 10 into Eq. 8, one could reformulate the problem as a static optimization problem with one degree of freedom

$$\begin{aligned} \max \quad & Pr(u) \\ \text{s.t.} \quad & 0 \le u \le u_{\max}. \end{aligned} \tag{11}$$

Because the objective function is unimodal, Eq. 11 can be treated as an unconstrained optimization problem without considering the pressure drop constraint. If the solution found lies above the maximum throughput, the optimal solution is obtained at the maximum throughput.

Unfortunately, a closed form solution of the system dynamics, as depicted in Eq. 10, cannot be given, but its structure allows for a very efficient iterative solution. The resulting solution algorithm then consists of two stages, the iterative solution of the dynamic equality constraints (Eq. 10) in an inner loop, and the solution of an unconstrained static nonlinear optimization problem (Eq. 11) in an outer loop. By introducing the additional inner loop, the optimization problem could therefore be substantially simplified. The resulting structure of the optimization algorithm is shown in Figure 3.

To solve the equality constraints in the inner loop, the cycle time t_{cyc}, the injection period t_{inj}, and the switching times $\tau_{\text{switch},i}$ for a given interstitial velocity u have to be determined such that the recovery constraints are fulfilled exactly.

The iterative solution commences with a dynamic simulation of the process model for the respective u with initial guesses for t_{inj} and t_{cyc}. By integration of the resulting elution profiles, a set of switching times $\tau_{\text{switch},i}$ is determined which gives exactly the desired product recovery. In general, these switching times are either not feasible, since the collecting intervals for the two fractions overlap, or not optimal, since a fraction of pure solvent lies between the two collecting intervals. A simple gradient-based search converges to the optimal and feasible solution in a few steps by adjusting the injection and cycle periods t_{inj} and t_{cyc} to force the collecting intervals to touch each other, and, therefore, gives the solution of the equality constraints for a given interstitial velocity u.

In the outer loop, a NEWTON type method is used to determine the optimal interstitial velocity. As mentioned earlier, the cost function of the reduced optimization problem (Eq. 11) is unimodal. Two competing physical effects are the main reasons for the shape of the objective function. By increasing the flow rate, the amount of product separated increases linearly. At the same time, the effectivity of the columns decreases due to the growing dominance of the kinetic effects which drive the column further and further away from the conditions of thermodynamic equilibrium. Because of this property, the one-dimensional static optimization problem has a unique global optimum within the interval $0 \le u \le u_{\max}$, which can be determined by a simple Newton type method in the outer loop of the overall optimization algorithm.

The objective function of the reduced optimization problem normally has an optimum within the feasible velocity range. As an example, the productivity is plotted over the interstitial velocity for a sugar separation in the upper part of Figure 4, and, in the lower part, the corresponding switching times are shown, which result from the solution of the inner loop.

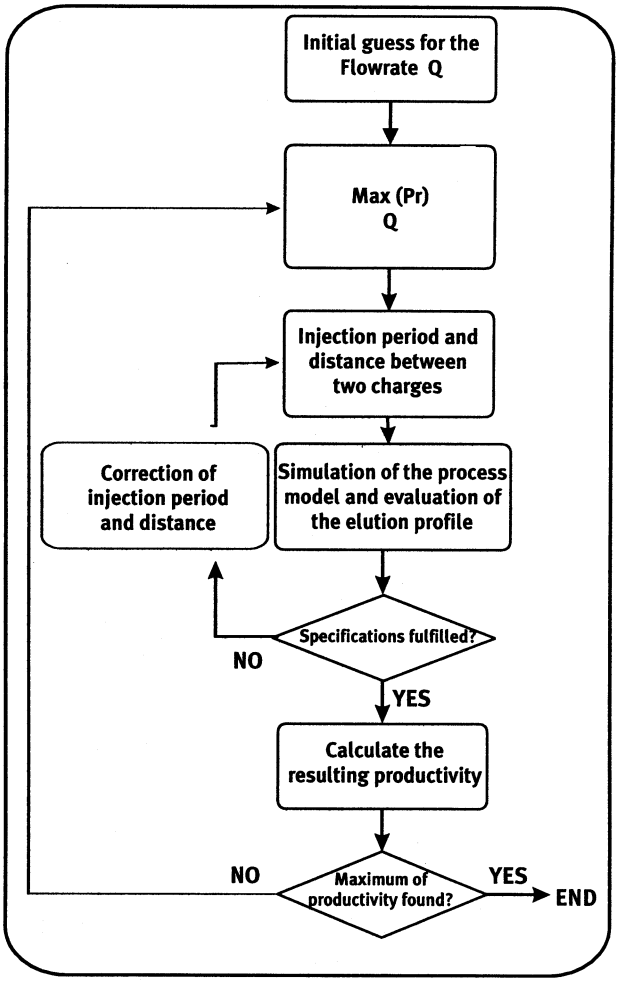

Figure 3. Optimization algorithm.

Implementation and Experimental Validation

Experimental setup and materials

The pilot plant is shown in Figure 5. It can be divided into three main parts. The first part is the conventional chromatographic separation system containing the pump, piping, injection valve, hand valves, storage vessels, and the chromatographic column. The second part is the online monitoring system, which is described in the following section and contains a densimeter, a polarimetric detector, and a PC for data acquisition and concentration calculation. The third part is the process control system.

For the conventional part of the pilot plant, the preparative HPLC solvent delivery system *NovaPrep* model NP200 from Merck, Darmstadt, Germany, was used. It is controlled by the process control system. Two types of chromatographic columns were used. For the determination of the parameters and the validation of the process models, a *Superformance* 600-26 column from Merck was used. Sugar separations are

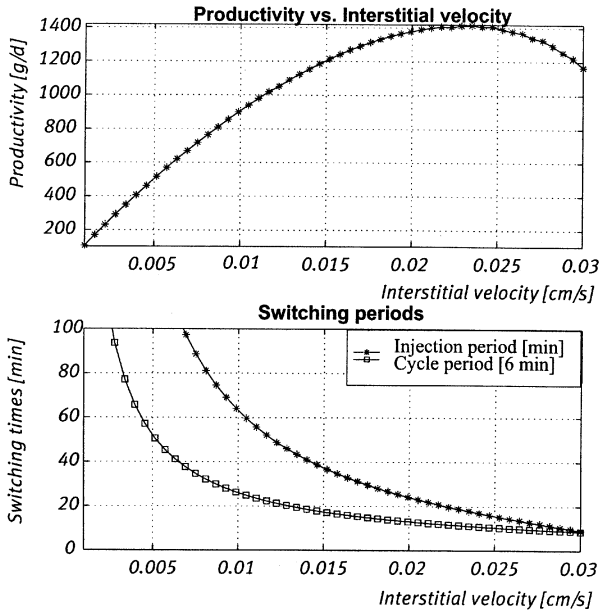

Figure 4. Sugar separation with a recovery of 90%.

usually carried out on ion-exchange resins with a large mean diameter and a high HETP value. To achieve a purity of 80% —90% at sufficiently high flow rates in the control experiments, a second column with column tops from AMICON, 43, 8 mm ID and a length of 1,500 mm was built. The bed length in the packed column was 1,300 mm. The voidage was determined as $\epsilon = 0.373$. The total dead volume of the plant was determined as $V_{\text{dead}} = 17$ mL.

Both columns and most of the piping consist of double-walled jackets for tempering the system. The adsorbent, a calcium type cation-exchange resin *ImacHP*1320*Ca* with a mean particle diameter of 350 μm, was donated by Rohm and Haas, Germany. Both columns were packed with a slurry technique. The D(-)-Fructose pure and D(+)-Glucose water free were purchased from Merck KGaA, Germany. The water was cleaned with a *MilliQ* + from Millipore Corporation, USA. The tracer Dextran T70 was purchased from Pharmacia, Sweden.

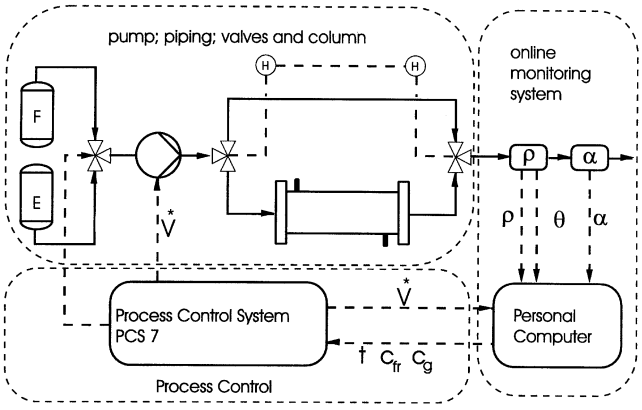

Figure 5. Pilot plant.

Online measurement concept

For model-based process control, online concentration measurements are an essential prerequisite. Therefore, an online monitoring system based on a two detector concept as first proposed by Altenhöner et al. (1997) was implemented and adapted for the use in the model-based control concept. A densimeter (symbol ρ in Figure 5) for the measurement of the total concentration of fructose and glucose and a polarimetric detector (symbol α in Figure 5) for the determination of the total rotation angle as substance specific information were connected in a series at the plant outlet.

The polarimetric detector was of the type $POLAR_{\text{Monitor}}$ from IBZ Messtechnik, Hannover, Germany. The exchangeable cell used has an optical path length of 100 mm and a holdup of 450 μL. The densimeter used was of the type *L-DENS* from Physica Meβtechnik, Austria. The variation of density with concentration is in the same order of magnitude as the variation of density with temperature. As the flow rate has to be changed during the online optimization process, the temperature in the densimeter cannot be kept constant during the whole experiment. Therefore, a temperature compensation algorithm based on the temperature measurement (symbol θ in Figure 5) in the densimeter was implemented. It turned out that a linear compensation of the temperature is sufficient. Thus, the concentration of the single components in the mixture results from

$$\begin{pmatrix} \alpha \\ \rho \end{pmatrix} = \begin{pmatrix} \alpha_0 + \dfrac{\partial \alpha}{\partial \theta}\theta \\ \rho_0 + \dfrac{\partial \rho}{\partial \theta}\theta \end{pmatrix} + \begin{pmatrix} \dfrac{\partial^2 \alpha}{\partial c_g \partial \theta}\theta + \dfrac{\partial \alpha}{\partial c_g} \\ \dfrac{\partial^2 \rho}{\partial c_g \partial \theta}\theta + \dfrac{\partial \rho}{\partial c_g} \end{pmatrix} c_g + \begin{pmatrix} \dfrac{\partial^2 \alpha}{\partial c_g \partial \theta}\theta + \dfrac{\partial \alpha}{\partial c_{fr}} \\ \dfrac{\partial^2 \rho}{\partial c_{fr} \partial \theta}\theta + \dfrac{\partial \rho}{\partial c_{fr}} \end{pmatrix} c_{fr} \quad (12)$$

In Eq. 12, α_0, ρ_0 and all partial derivatives are constants which were determined in preliminary calibration experiments.

The dead volume between the two detectors causes a time delay between the signal in the densimeter and the polarimetric detector. This time delay depends on the actual flow rate in the system and can lead to wrong concentration measurements in the case of low flow rates. It has to be compensated by correlating the actual signal of the polarimetric detector with the densimeter signal of the preliminary time $t - \tau_{\text{Delay}}$.

Model validation

To validate the process model, the parameter estimation procedure described above was applied. A void fraction of 0.37 was determined from the retention time of a dextran pulse (see Eq. 7). In order to determine the equilibrium isotherms for the chosen operating temperature of 40°C, a

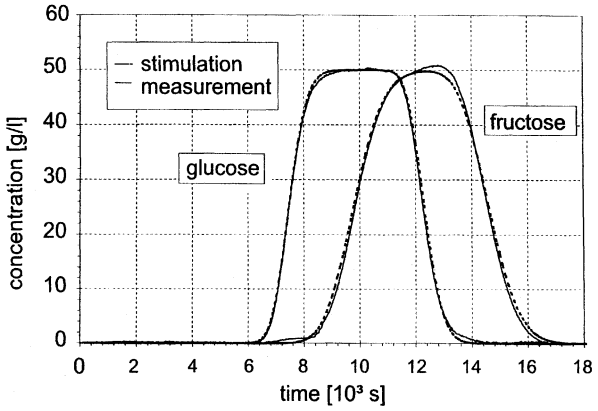

Figure 6. Experimental and simulated elution profiles.

series of breakthrough curve experiments were carried out on the small chromatographic column (2.6 cm ID). The solid-phase concentration was calculated by a mass balance. It is worth noticing that the slope of both isotherms appears to be very close to linear up to a solute concentration of approximately 50 g/L. At higher solute concentrations, there is a significant deviation from linearity. Based on these results, the maximum feed concentration for the following validation experiments was chosen to be 50 g/L in order to obtain linear adsorption conditions. The resulting distribution coefficient (Henry coefficient) is 0.28 for glucose and 0.55 for fructose in the linear case.

The measured and calculated elution profiles of an experiment to separate fructose and glucose under process conditions are plotted in Figure 6. This experiment was carried out on eight chromatographic columns (2.6 cm ID) connected in series with a total column length of 424 cm, a flow rate of 10 mL/min, and an injection time of 4,850 s. The individual concentrations of fructose and glucose were measured using the online monitoring system. The good agreement proves the precision of the process model.

Process control system

The control strategy introduced here was implemented in an industrial control environment, the process control system PCS 7 by Siemens. It consists of a decentralized controller (DCS) of the S7-400 series (CPU S7-414-2DP) on the process level and of the Windows Control Center (WinCC) running on the operator station for monitoring, data storage, and operation of the plant (see Figure 7).

The basic control algorithms which run on the DCS implement the computed optimal operating parameters and control the column pressure. In the development stage, the concentration measurements are managed by a separate computer. In an industrial environment, the concentration measurements could easily be integrated into the DCS, thus saving the extra PC; this would require two additional serial ports for the DCS. The calculations are simple enough not to put any significant load on the CPU.

The advanced control routines are implemented on the WinCC level. User defined functions and also external process calls can be implemented using its integrated C-script,

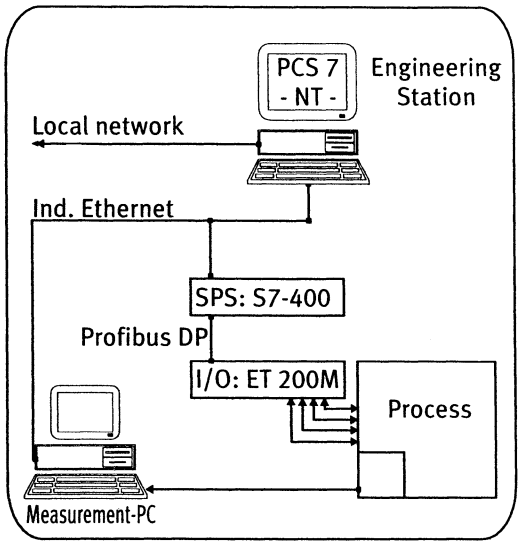

Figure 7. Process control system for batch chromatography.

called Global Script. Here, it consists of a monitoring procedure that continuously calculates the concentration gradients for both components and detects the elution of peaks at the column outlet. Once a complete pair of peaks has been detected, the history of injection data is analyzed to guarantee that the operating parameters varied only within certain bounds, while the peaks passed through the column. Then, the external algorithm for model adaptation and optimization of operating parameters is called with the concentration measurements and injection data. It returns adapted model parameters and optimal values for the operating parameters based on the updated model. These new set points are implemented on the process by the DCS when the next injection occurs.

Experimental results

With the system described above, a thorough experimental validation of the measurement, control, and optimization concept was carried out. The control scheme should:

- bring the process to the optimum from an initial disturbance at startup; and
- follow set point changes during operation.

Here, a feed mixture containing each 30 mg/mL fructose (component A) and glucose (component B) was to be separated. Prior to the experiment, the plant specific parameters such as void fraction, time delays between measurements, calibrating parameters, and adsorption coefficients were determined at a temperature of 40°C. With this data, initial operating parameters were calculated in an off-line optimization for required purities and recoveries of 80% for each of the components. Table 1 summarizes the initial values for the experiment.

When the automatic injection procedure is started, the monitoring algorithm (implemented in WinCC) begins to detect the peaks in the concentration profiles at the column outlet. Due to the time delay of the column, several batches

Table 1. Initial Parameters for Batch Chromatography Experiment

Parameter	Value
Feed conc. c_A/c_B	30/30 mg/mL
Required purity, A/B	80/80%
Required recovery, A/B	80/80%
Flow rate	8.00 mL/min
⇔ Interstitial velocity	0.0237 cm/s
Injection time	1,818 s
Cycle time	4,491 s
Column temp.	40°C

are injected into the column before the first peak elutes. This is reflected in constant values for interstitial velocity and injection and cycle time during the first 4 h of the experiment in Figure 8. After the first pair of peaks has been eluted, the process monitor collects the concentration measurements and the injection data corresponding to these peaks and calls the external optimization routine. The model parameters are updated (see Figure 9) and new optimal values for t_{inj}, t_{cyc}, and u are calculated, which are transferred back to WinCC and applied to the next batch by the DCS.

Figures 8 and 9 show how the initial disturbance from startup is compensated and how the operating parameters are modified in order to meet the desired purity and recovery rates. From Figure 9, it is apparent that the effective mass-transfer coefficients are adapted significantly to reduce the model error while the adsorption parameters were determined quite well in the preceding experiments and do not change much. The parameters $k_{eff,i}$ are calculated from the

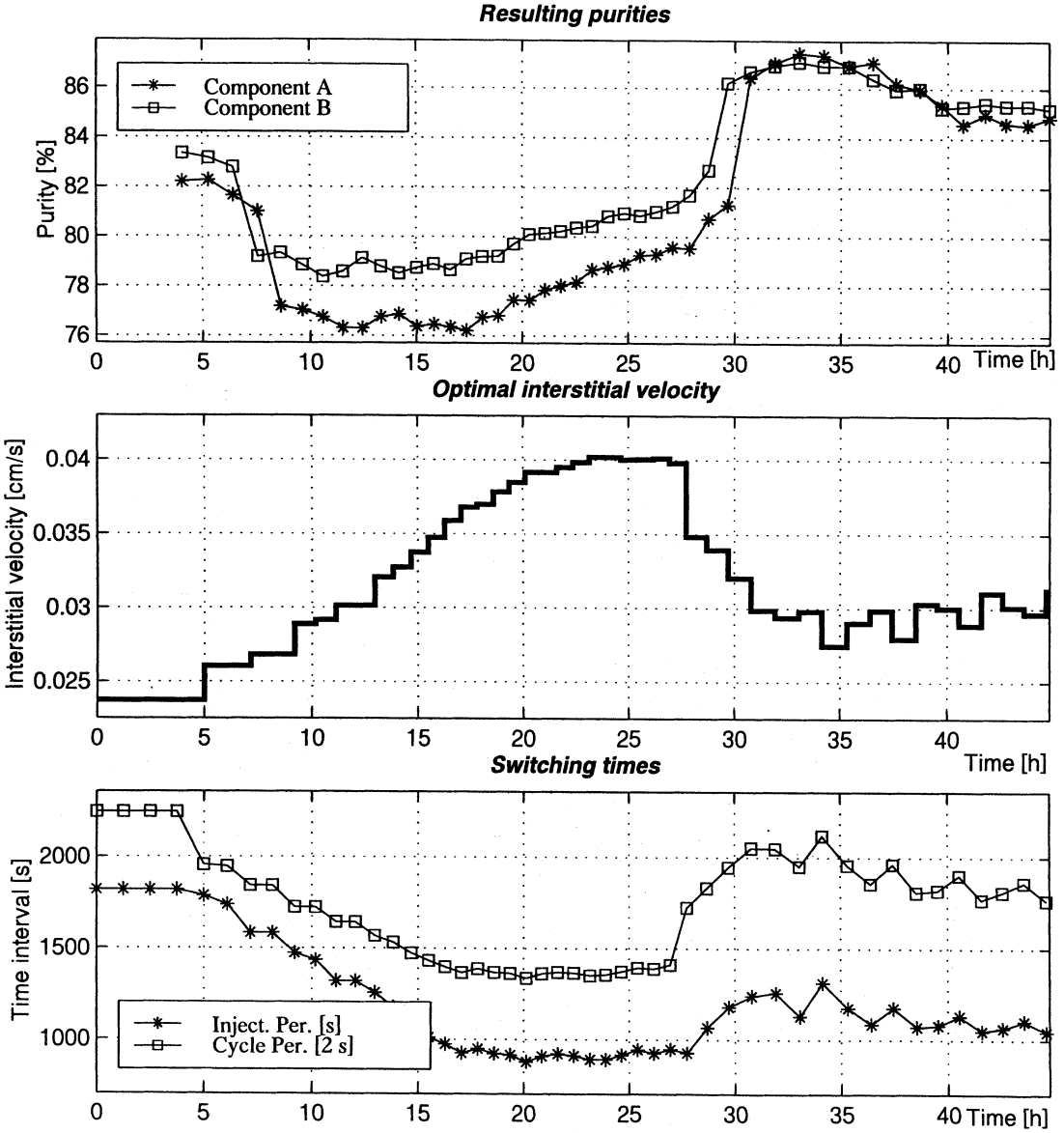

Figure 8. Product purities and operating parameters during experimental run.

Setpoint change for required purity at approx. 28 h from 80% to 85%.

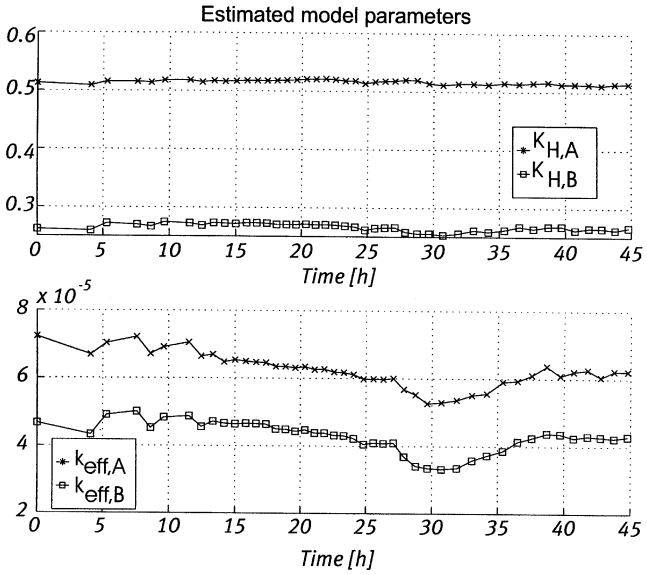

Figure 9. Adapted model parameters Henry coefficients $K_{H,i}$ and effective mass transfer resistance $k_{\text{eff},i}$.

estimated $D_{ap,i}$ using the correlation given in Dünnebier et al. (1998).

After about 28 h, the controlled operating parameters reach a stable steady stage. The average product purities meet the specifications. At this point, a set point change takes place in the product specifications: purities and recoveries are now required to be 85%. The control scheme reacts by immediately reducing the interstitial velocity and increasing the injection and cycle intervals. This leads to a better separation of the two peaks and to an increase in purity as desired. Figure 8 shows a slight overshoot of the controlled variable product purity for glucose and fructose; this results in a less than optimal throughput. However, the controlled system quickly converges to a new steady state. The effective mass-transfer coefficients $k_{\text{eff},A,B}$ vary in the transition phase due to the rapid change of operating conditions, especially of the interstitial velocity that affects the mass transport (Figure 9). At the new steady state, however, the coefficients settle to almost the same values, as can be expected from a theoretical analysis.

Conclusions

Since the economic potential of chromatographic separations cannot be exploited by the conventional manual operation, there is a growing need for reliable and stable process control and automation. This contribution presented a process control concept for batch-chromatography, consisting of an online parameter estimation and a model-based online optimization routine, based on an computationally efficient process model. An implementation of this algorithm in an industrial standard control system combined with an online measurement concept was used to validate the concept for a laboratory-scale sugar separation.

The applicability to more complex systems has already been shown in simulation studies elsewhere (Dünnebier et al., 1999), and the experimental validation for this case is currently under way.

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Notation

α = rotation angle, rad
c_i = concentration in the bulk phase, g/cm^3
$c_{\text{in},i}$ = inlet concentration, g/cm^3
c_i^{eq} = equilibrium concentration bulk phase, g/cm^3
D = column diameter, cm
D_{ax} = axial dispersion coefficient, cm^2/s
$D_{\text{ap},i}$ = apparent dispersion coefficient, cm^2/s
ϵ = void fraction bulk
γ_i = parameter defined in Eq. 5
k_{eff} = effective mass transport resistance (Equilibrium Dispersive Model), 1/s
$K_{H,i}$ = Henry coefficient
L = column length, cm
Pur_i = Product purity, %
q_i = concentration in the solid phase, g/cm^3
Q = flow rate, cm^3/s
ρ = density; g/cm^3
r_p = particle radius, cm
Rec_i = product recovery, %
Θ = temperature, C
t = time, s
t_{Delay} = time delay between sensors, s
t_{inj} = injection period, s
t_{cyc} = cycle period, s
$t_{\text{res,ext}}$ = residence time of tracer, s
$\tau_{\text{switch},i}$ = switching times fractionating valve, s
u = interstitial velocity, cm/s
υ = parameter defined in Eq. 5
V_{Dead} = total dead volume, cm^3
v_{Col} = column volume, cm^3
V = volumetric flow rate, cm^3/s
x = axial coordinate, cm

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