Optimization and Control of Chromatography

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Abstract

Chromatography has developed from an analytical technology to a well-established separation process in industry. It is the method of choice for difficult separation tasks especially when temperature-sensitive components or species exhibiting very similar thermodynamic properties are involved. Large-scale industrial applications have been reported from different industrial fields, e. g. in the petrochemical, pharmaceutical, bio-chemical, and also in the food industry. Chromatographic separations often cause a large fraction of the overall production cost, so efficient design and operation become mandatory when production cost matters for competitiveness. In this paper we present an overview of model-based techniques for optimisation and control of batch as well as continuous chromatographic separation processes. These methods also help to speed up process development which may even be more critical than the reduction of production cost.

Keywords: chromatography, online optimisation, nonlinear control.

1. Chromatographic separations

The chromatographic separation is based on the different adsorptivities of the components to a specific adsorbent which is fixed in a chromatographic column. The most widespread process, batch chromatography, involves a single column which is charged with pulses of the feed solution. These feed injections are carried through the column by pure desorbent. While travelling through the column, the more adsorptive species is retained longer by the adsorbent thus leaving the column after the less adsorptive specie. As indicated in Fig. 1(a), the separated peaks can be withdrawn as different fractions at the end of the column with the desired purities.

Batch chromatography has the usual drawbacks of a batch operation, and leads to highly diluted products. On the other hand, it is extremely flexible, several components may be recovered from a mixture during one operation and varying compositions of the desorbent can be used to enhance separation efficiency. The idea of a continuous operation with counter-current movement of the solid led to the development of the Simulated Moving Bed (SMB) process (Broughton 1966). It is gaining increasing attention due to its advantages in terms of productivity and eluent consumption (Guest 1997, Juza et al. 2000). A simplified description of the process is given in Fig. 1(b). It consists of several chromatographic columns connected in series which constitute a closed loop. A counter-current motion of the solid phase relative to the liquid phase is simulated by periodically and simultaneously moving the inlet and outlet lines by one column in the direction of the liquid flow.

After a start-up phase, SMB processes reach a cyclic steady state (CSS). Fig. 1(b) shows the CSS-evolution of a binary separation along the columns plotted for different

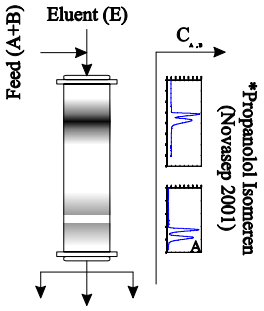

Figure 1(a). Batch operation

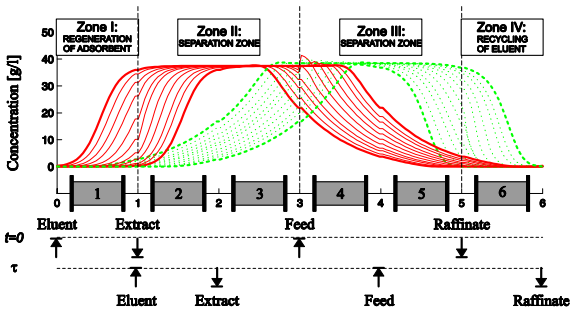

Figure 1(b). Simulated Moving Bed Process

time instants within a switching period. At every axial position, the concentrations vary as a function of time, and the values reached at the end of each switching period are equal to those before the switching, relative to the port positions.

Several new operating regimes have been introduced recently for the SMB process. Ludemann-Hombourger & Nicoud (2000) proposed the VARICOL process which uses an asynchronous shift of the inlet/outlet lines leading to a better allocation of the adsorbent (Ludemann-Hombourger et al. 2002, Toumi et al. 2003) and hence reduced desorbent consumption. (Zhang et al. 2003) showed the potential of the variation of flow rates (PowerFeed). In the ModiCon process (Schramm et al. 2002), a feed solution with variable concentrations is injected using a gradient pump and a significantly higher productivity for mixtures with highly nonlinear adsorption is obtained.

The design and the operation of chromatographic separations, especially of the newly introduced processes, require the choice and the adaptation of a large number of parameters which affect the separation in a highly nonlinear and interacting fashion. Even for the simple batch process, a trial-and-error procedure is time-consuming and will usually not lead to optimal performance. For SMB and its variants, only a systematic, model-based approach can make full use of the available degrees of freedom.

The remainder of this paper is structured as follows: in the next section, we give an overview over the issues in model-based design and operation and introduce a general process model. In section 3, model-based optimisation and control strategies are discussed for batch processes, while section 4 is devoted to optimisation and feedback control of SMB and similar processes which is currently a subject of intensive academic research. Finally, a summary and some perspectives for future research are given.

2. Model-based design

Fig. 2 shows the steps generally required for model-based design and operation of a unit operation, in our case a chromatographic process. Of course, the formulation of a mathematical model is the first crucial step of the process. For chromatographic separations this is relatively easy in principle, as several standard models are well-known. Guiochon (2002) in a recent article reviewed different modelling approaches and pointed out that all of them can be derived from the General Rate Model (GRM) of chromatography.

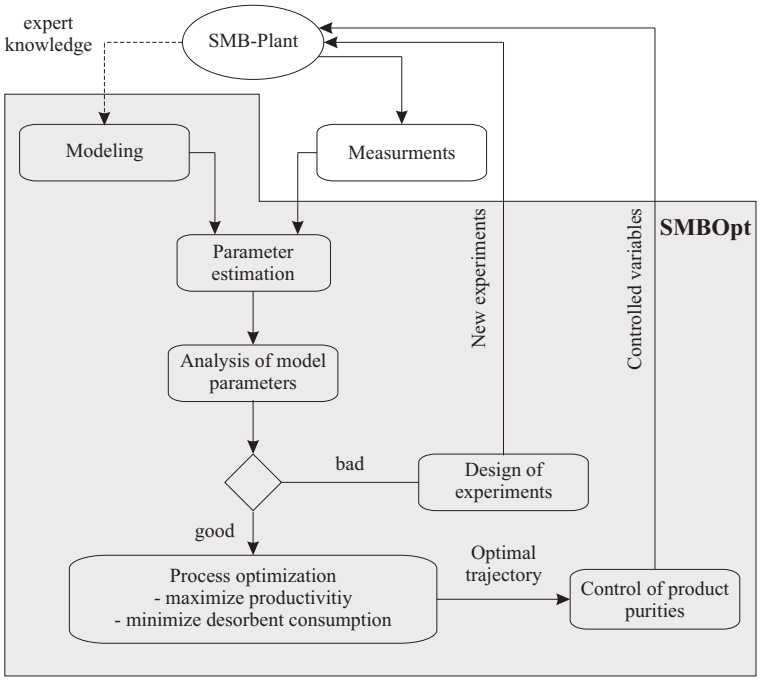

Figure 2. Integrated approach to process design and operation

The difficult step in modelling chromatographic separations is the determination of the model parameters. In particular, the adsorption isotherm is of crucial importance for the behaviour of the process. The precise determination of the model parameters can either be performed in specific experiments which causes a considerable effort in terms of experimental time and test material, or by numerical parameter estimation from test runs. Frontal analysis (FA), frontal analysis by characteristic points (FACP) or elution by characteristic point (ECP) are some practical methods for the determination of the adsorption isotherm (Guiochon 2002). Usually such standard test methods are combined with model-based estimation methods where the model parameters are adapted at the real process using numerical techniques (Felinger et al. 2003, Altenhöhner et al. 1997). However, often not all parameters of the model can be identified well from production runs due to the lack of sensitivity of the concentration profiles to these parameters, especially in batch chromatography. In this case, it is necessary to design new experiments to estimate the model parameters reliably. During plant operation, some physical parameters may change due to degradation. This can be detected and compensated by periodic on-line re-estimation.

The goal of process optimization is to calculate those operating conditions which lead to minimal separation costs while satisfying the product purity requirements and the plant constraints. In this context, the validated process model is used to evaluate the process behaviour. If the process is operated at the optimal point, where usually at least some of the purity constrains are active, the inevitable model/plant mismatch and disturbances may lead to off-spec products. Therefore, feedback control must be used to stabilize the plant at the desired conditions. This is a challenging task since chromatographic processes exhibit a strongly non-linear behaviour and only the profiles at (some)

column outputs can be measured. Besides, on-line concentration measurements in most cases are not highly accurate, so additional feedback of information gained from process analytics (e. g. HPLC) must be introduced.

2.1. Mathematical Modelling

The mathematical modelling of single chromatographic columns has been extensively described in the literature by several authors, and is in most cases based on differential mass balances (see e. g. Guiochon, 2002). From a mathematical point of view, it is useful to distinguish chromatographic processes by the type of adsorption isotherms. Processes with linear or simple Langmuir isotherms lead to systems of uncoupled differential equations which are easier to solve than those with coupled non-linear adsorption behaviour, e. g. the competitive Langmuir isotherm

$$q_i = \frac{H_i c_i}{1 + \sum_{j=1}^{n_{sp}} k_j c_j}, \tag{1}$$

or Bi-Langmuir isotherms. Moreover, the modelling approaches can be classified by the physical phenomena which they include and thus by their level of complexity. Fig. 3 shows this classification schematically. More details on models and solution approaches, especially for the SMB process, can be found in (Dünnebier & Klatt 2000). In the case of linear adsorption isotherms, a model of the class Equilibrium Dispersive Model where all kinetic and non-ideal effects are lumped into a single parameter can be formulated. This model can be solved analytically while still having a sufficient accuracy of prediction (Dünnebier et al. 1998).

As mentioned above, the most general one-dimensional model (ignoring radial inhomogenities) is the General Rate Model (GRM):

$$\frac{\partial c_{\mathrm{b},i}}{\partial t} + \frac{(1-\varepsilon_\mathrm{b})3k_{\mathrm{l},i}}{\varepsilon_\mathrm{b} R_\mathrm{p}}(c_{\mathrm{b},i} - c_{\mathrm{p},i|r=R_p}) + r^{\mathrm{liq}}_{\mathrm{kin},i} = D_\mathrm{ax}\frac{\partial^2 c_{\mathrm{b},i}}{\partial x} + u\frac{\partial c_{\mathrm{b},i}}{\partial x}, \tag{2}$$

$$(1-\varepsilon_\mathrm{p})\frac{\partial q_i}{\partial t} + \varepsilon_\mathrm{p}\frac{\partial c_{\mathrm{p},i}}{\partial t} - \varepsilon_\mathrm{p} D_{\mathrm{p},i}\left[\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial c_{\mathrm{p},i}}{\partial r}\right)\right] - r^{\mathrm{sol}}_{\mathrm{kin},i} = 0, \tag{3}$$

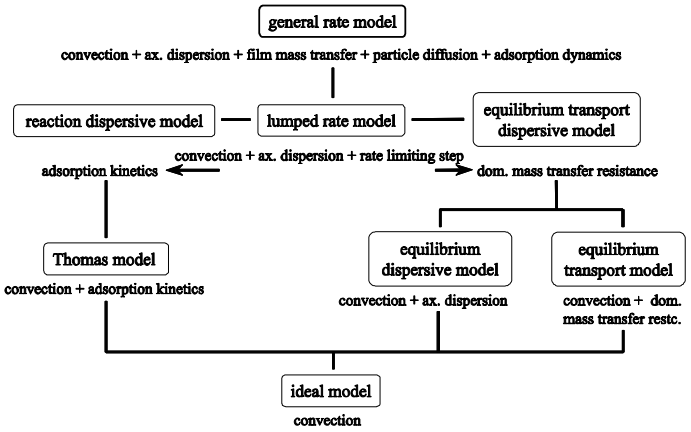

Figure 3. Classification of Column Models

with appropriate initial and boundary conditions. More details can be found in (Dünnebier & Klatt 2000b). The adsorption equilibrium q_i and eventual reaction terms r_{kin} are expressed by additional algebraic relationships. GRM is a rigorous first-principles model which takes into account all main effects in the chromatographic column: multi-component adsorption, mass transfer, diffusion, axial dispersion and reaction kinetics. From this general model, simplified ones which ignore one or more of the effects in a real column can be derived. Although being the most complex model, the General Rate Model is advantageous in terms of simulation efficiency. An efficient discretisation scheme has been proposed by Gu (1995), using orthogonal collocation for the solid phase and a Galerkin approximation on finite elements for the bulk phase.

2.2 Parameter estimation

Accurate values of the model parameters are needed to use the process model for optimisation and control, as the process is very sensitive to some of the parameters. These can be obtained by mathematical fitting of simulation runs to experimental data using the model parameters as optimisation variables. But one must pay attention to the fact that certain model parameters cannot be estimated well from given experiments. One mathematical approach to investigate this issue is based on the Fisher Information Matrix:

$$\mathbf{F} = \sum_{k=1}^{N} \mathbf{S}(t_k)\mathbf{C}^{-1}(t_k)\mathbf{S}(t_k). \tag{4}$$

$\boldsymbol{S}(t_k)$ contains the partial derivatives of the model outputs $\boldsymbol{y}$ (e.g. measured concentrations at the outlet of a chromatographic column) with respect to the model parameters $\boldsymbol{p}$ at the time instants t_k. $\boldsymbol{C}$ describes the covariance matrix of the measurement errors. The eigenvalues of the Fisher Information Matrix provide lower bounds for the parameter variances (Majer 1998). Toumi & Engell (2004) applied this method successfully to an integrated chromatographic process for glucose isomerisation. In this case, only a subset of the isotherm parameters can be estimated reliably based on batch experiments. Although the column is overloaded, the separation takes place mainly in the region of linear adsorption. A reduction of the set of estimated parameters also leads to better conditioning of the parameter estimation problem and thus reduces the numerical effort and improves convergence and robustness.

3. Optimisation and control of batch processes

For a chromatographic batch process with given design parameters (combination of packing and desorbent, column dimensions, maximum pump pressure), the determination of the optimal operating regime can be posed as follows: a given amount (or flow) of raw material has to be separated into the desired components at minimal cost while respecting constraints on the purities of the products. The operation cost may involve the investment into the plant and the packing, labour and solvent cost, the value of lost material (valuable product in the non-product fractions), and the cost of the further processing, e. g. removal of the solvent.

If the column is operated as a batch-column in elution mode, in certain time intervals a specified amount of raw material is injected into the column, transported through the

column by a flow of solvent, and separated into fractions at the outlet. The free operating parameters are:

- the throughput of solvent and feed material, represented by the flow rate Q or the interstitial velocity u, constrained to the maximum allowed throughput which in turn is limited by the efficiency of the adsorbent or the pressure drop,
- the injection period t_{inj}, representing the duration of the feed injection as a measure of the size of the feed charge,
- the cycle period t_{cyc}, representing the duration from the beginning of one feed injection to the beginning of the next one,
- the fractionating times.

The requirements on the products can usually be formulated in terms of minimum purities, minimum recoveries or maximum losses. In the case of a binary separation without intermediate cuts, these constraints can be transformed into each other, so either the recovery or the product purity may be constrained. A simple objective function is the productivity, i. e. the amount of product produced per amount of adsorbent. This formulation results in the following nonlinear dynamic optimization problem:

$$\begin{aligned} \max \quad & \Pr(u, t_{\text{cyc}}, t_{\text{inj}}) = \frac{\dot{m}_{\text{Product}}}{m_{\text{Adsorbent}}} \\ \text{s.t.} \quad & \text{Rec}_i \geq \text{Rec}_{\min,i}, \quad i = 1, \cdots, n_{\text{sp}} \\ & 0 \leq u \leq u_{\max}, \\ & 0 \leq t_{\text{inj}}, t_{\text{cyc}}. \end{aligned} \tag{5}$$

This type of problem can be solved by standard optimisation algorithms. In order to reduce the computation times to enable online optimisation, Dünnebier et al. (2001) simplified the optimisation problem and decomposed it in order to enable a more efficient solution. They exploited the fact that the recovery constraints are always active at the optimal solution and consider them as equalities. The resulting solution algorithm consists of two stages, the iterative solution of the recovery equality constraints, and the solution of the remaining unconstrained static non-linear problem.

In industrial practice, chromatographic separations are usually controlled manually. However, automatic feedback control leads to a uniform process operation closer to the economic optimum, and it can include online re-optimisation. Dünnebier et al. (2001) proposed the model-based online optimisation strategy shown in Fig. 4. To improve the model accuracy and to track changes in the plant, online parameter estimation is performed. Note that this scheme contains feedback only in the parameter estimation path. Therefore it will lead to good results if the model is structurally correct so that the parameter estimation leads to a highly accurate model. The scheme has been tested successfully at pilot scale for a sugar separation with linear adsorption isotherm (Dünnebier et al. 2001). A similar run-to-run technique has been proposed by (Nagrath et al. 2003).

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 Altenhöhner et al. (1997) was implemented and adapted for the use in the model-based control concept. In case of sugar separation, Dünnebier et al. (2001) used a densimeter for the measurement of the total concentration of fructose and

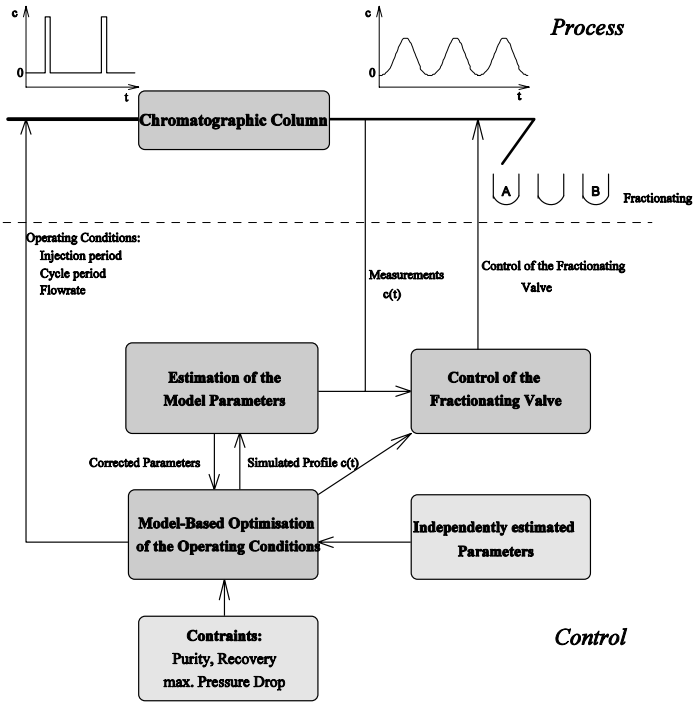

Figure 4. Control Scheme for Chromatographic Batch Separations

glucose and a polarimetric detector for the determination of the total rotation angle which are connected in series at the plant outlet.

Fig. 5 shows an experimental validation of the control scheme presented above for a linear sugar system (Dünnebier et al. 2001). First the operating parameters are modified in order to meet the product purity and recovery of 80 % each. After about 28 hours, the controlled operating parameters reach a stable steady state. At this point a set point change takes place in the product specifications: purity and recovery are now required to be 86 %. The control scheme reacts 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. Fig. 5 shows an overshoot of the controlled variables; this leads to a less than optimal throughput. However the controlled system quickly converges to a new steady state.

However, most chromatographic separation processes are characterised by nonlinear adsorption isotherms which often cannot be matched exactly by the standard isotherm models (e.g. Langmuir, Bi-Langmuir). Another cause of structural model-plant mismatch is the presence of additional components in the mixture. In this case, the purity constraints must be established by an additional control layer (Hanisch 2003), causing a loss of performance. Recently, Gao & Engell (2004) re-designed the formulation of the optimisation problem to take the plant-model mismatch into account, using the iterative scheme proposed by Tatjewski (2002). Here actual measurements are used in each step to correct the cost function rather than to re-estimate model parameters.

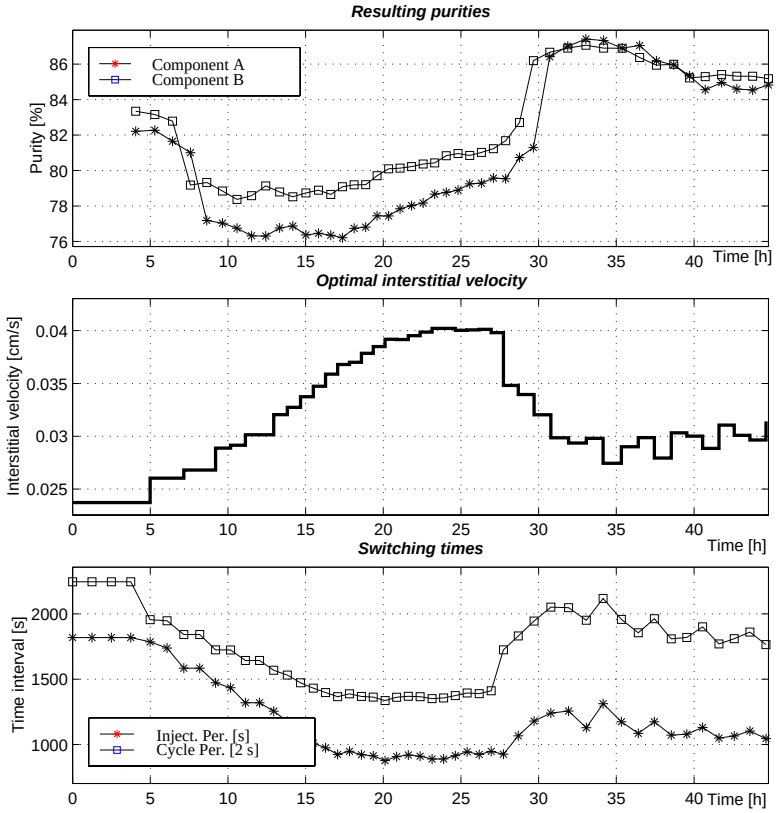

Figure 5. Product purities and operating parameters during experimental run (set-point change for required purity at approx. 28 hours from 80% to 85%) Dünnebier et al. (2001)

4. Optimisation and control of simulated moving bed processes

The group of Mazzotti, Storti and Morbidelli derived a graphical short-cut design methodology based on a simple ideal True Moving Bed model, the so-called **triangle theory,** and extended this theory to systems with nonlinear adsorption isotherms (Migliorini et al. 1998). This methodology is currently state-of-the-art and has been applied to a large number of separations (Miller et al. 2003). However, in the pharmaceutical field and due to highly expansive chiral stationary phases (CSP), small SMB processes with a small number of columns are preferred. Such systems cannot be accurately approximated by TMB models and the applicability of the triangle theory is questionable.

In order to exploit the full potential of SMB processes, recent research has focused on the design of the process, in particular the choice of the operation parameters for a given selection of adsorbent, solvent and column dimensions, using mathematical optimisation. As the optimum should be determined precisely while meeting all constraints, rigorous models which include the discrete dynamics are used (Klatt et al. 2000, Zhang et al. 2003). In addition to a higher reliability compared to short-cut methods, this approach is applicable to a broad variety of SMB-like operating regimes. The optimisation problem can be stated as (Toumi et al. 2003):

$$\begin{aligned} \min_{Q_i, N_i, \tau} \quad & \text{Cost}_{\text{spec}} \\ \text{s.t.} \quad & \Gamma(\mathbf{c}_{ax}(\tau)) - \mathbf{c}_{ax}(0) \le \varepsilon, \\ & \text{Pur}_{\text{Ex}} \ge \text{Pur}_{\text{Ex,min}}, \\ & \text{Pur}_{\text{Ex}} \ge \text{Pur}_{\text{Ex,min}}, \\ & 0 \le Q_i \le Q_{\max}. \end{aligned} \tag{6}$$

The goal is to determine the optimal cyclic steady state with minimal separation costs $\text{Cost}_{\text{spec}}$ while the purity requirements at both product outlets are fulfilled. (6) constitutes a complex dynamic optimization problem the solution of which essentially depends on an efficient and reliable computation of the cyclic steady state:

$$\Gamma(\mathbf{c}_{\text{ax}}(\tau)) - \mathbf{c}_{\text{ax}}(0) \le \varepsilon, \tag{7}$$

where Γ summarizes the dynamics of a SMB process during one switching period τ, including the discrete shifting of the ports. $\boldsymbol{c}_{\mathbf{ax}}$ denotes the axial concentration profile along the chromatographic columns. The free optimization variables are the flow rates in the different columns Q_i and the switching period τ. They are transformed to the so-called β-factors which represent the ratio between the flow rates Q_i and the hypothetical solid flow rate. This non-linear transformation leads to a better-conditioned optimization problem (Dünnebier et al. 2001). In the VARICOL operating mode, the average lengths of the zones N_i are additional degrees of freedom. Other variables as the column lengths or the feed concentrations can be also considered (Ludemann-Hombourger & Nicoud 2000). An additional constraint takes the maximum pressure drop into account. The main difficulty of the optimisation problem results from the large dimension of the cyclic steady state equations when a first-principles plant model is used. A simple and robust optimisation approach consists of integration of the model equations starting from initial values until the cyclic steady state is reached (sequential approach). At the cyclic steady state the objective function as well as the constraints are evaluated and returned to an optimizer. In this approach, the number of free parameters is small and hence the optimisation problem is not very demanding. The number of cycles required to reach a cyclic steady state usually is moderate (about 100) compared to other periodic processes like PSA/RSPA where 1000 or more periods have to be simulated. The computational effort therefore is reasonable.

Table 1 compares the optimal operating points obtained for a reactive SMB process for glucose isomerisation. Within this process, a pure glucose feed is fed to the plant, glucose reacts to fructose while a parallel chromatographic separation takes place. Such an integrated process is suitable for equilibrium limited reactions where conversion beyond thermodynamic equilibrium can be reached (Toumi & Engell 2004a).

In this case study, the objective was to minimise the desorbent consumption while producing a high fructose corn syrup with a purity of 70% (Toumi *et al.* 2004b). In Table 1, the classical SMB operating regime is compared to the VARICOL process. 40 % less desorbent consumption can be reached by asynchronously rather than synchronously switching the inlet/outlet lines. The optimal average distribution of the zones in the VARICOL case was [0.99, 1.6, 3. 4], i.e. zone III should be chosen larger than zones I and II. If the VARICOL distribution is rounded to the next integer distribution, an SMB process with section lengths [1, 2, 3] results. By this distribution

Table 1. Reactive Simulated Moving Bed process for glucose isomerisation, comparison of different column distributions (Pur_{Ex}*=70 %,* Q_{Fe}*=1.3* ml/min*)*

	SMB I	VARICOL	SMB II
rel. Q_{De} [%]	100.00	60.00	62.00
Q_{De} [ml/min]	3.70	2.26	2.31
Q_{Re} [ml/min]	17.60	15.51	15.25
τ [min]	10.40	12.12	12.26
Q_{Ex}	5.0	3.56	3.61
N_i	[2,2,2]	[0.99,1.61,3.4]	[1,2,3]

the desorbent consumption can be reduced by 38 %. Based on the result obtained for the VARICOL process a considerably better SMB configuration was obtained after only two optimization runs. Thus the VARICOL idea can be used to optimise the column distribution of a classical SMB process avoiding the solution of a complex Mixed Integer Nonlinear Optimization Problem (MINLP).

4.2 Control of SMB processes

In current industrial applications, chromatographic processes usually are not governed by advanced feedback control. Conventional control strategies are unsuitable for these processes due to their unconventional structure with extremely long time delays, distributed parameters and mixed discrete and continuous dynamics.

Automatic control has been reported for the separation of aromatic hydrocarbons where on-line Raman spectroscopy can be utilised to measure the concentrations of the compounds at the outlet of the chromatographic columns (Marteau et al. 1994). This approach, as well as the geometric nonlinear control concept described in (Kloppenburg & Gilles 1999), is based on a model of the corresponding true moving bed (TMB) process, where the cyclic port switching is neglected. In case of SMB processes with a few number of columns (8 or less), the TMB process does not approximate the SMB process accurately, so that the applicability of this control scheme to plants with few columns seems to be problematic.

Natarajan & Lee (2000) investigated the application of a repetitive model predictive control (RMPC) technique to SMB processes. RMPC is a model-based control technique that results from incorporating the basic concept of repetitive control into the model predictive control framework. The switching period of the process is assumed to be constant. This is limiting, since the switching time can be manipulated to control the process. The rigorous model is linearised along the optimal trajectory and reduced to a low dimensional linear model, based on which a linear MPC controller scheme was developed. In the presence of strong non-linearities as they occur in enantiomer separation and in the reactive case, this approach will work only close to a fixed operating regime.

Schramm et al. (2001) presented a model-based control approach for the direct control of the product purities of SMB processes. Based on wave theory, they derived relationships between the front movements and the flow rates of the equivalent TMB process. Based on these relationships, they proposed a simple control concept with two standard PI controllers. This concept is easy to implement. Similar relationships are

however difficult to determine analytically in the case of nonlinear reactive chromatography.

Klatt et al. (2002) proposed a two-layer control architecture similar to the one used for batch chromatography where the optimal operating trajectory is calculated at a low sampling rate by dynamic optimisation based on a rigorous process model. The model parameters are adapted based on online measurements. The low-level control task is to keep the process on the optimal trajectory despite disturbances and plant/model mismatch. The controller is based on identified models gained from simulation data of the rigorous process model along the optimal trajectory. For the linear adsorption isotherm case, linear ARX models are sufficient (Klatt et al. 2002), whereas in the nonlinear case neural networks (NN) were applied successfully (Wang et al. 2003). A disadvantage of this two-layer concept is that the stabilised front positions do not guarantee the product purities if plant/model mismatch occurs. Thus an additional purity controller is required.

Toumi & Engell (2004a) recently presented a nonlinear model predictive scheme based on a full nonlinear process model and applied it successfully to a 3-zones reactive SMB process for glucose isomerisation (Toumi & Engell 2004b). The key feature of this approach is that the production cost is minimised on-line while the product purities are considered as constraints, thus real online optimisation is performed, not trajectory tracking. In the experimental control result shown in Fig. 6, the desired purity of fructose was set to 55.0 % and the controller was started at the 60th period (after 10 cycles). The control horizon was set to H_r=1 cycle and the prediction horizon is H_r=10 cycles. Fig. 5 shows the evolution of the product purity as well as of the control variables. In the open-loop mode where the operating point was calculated based on the

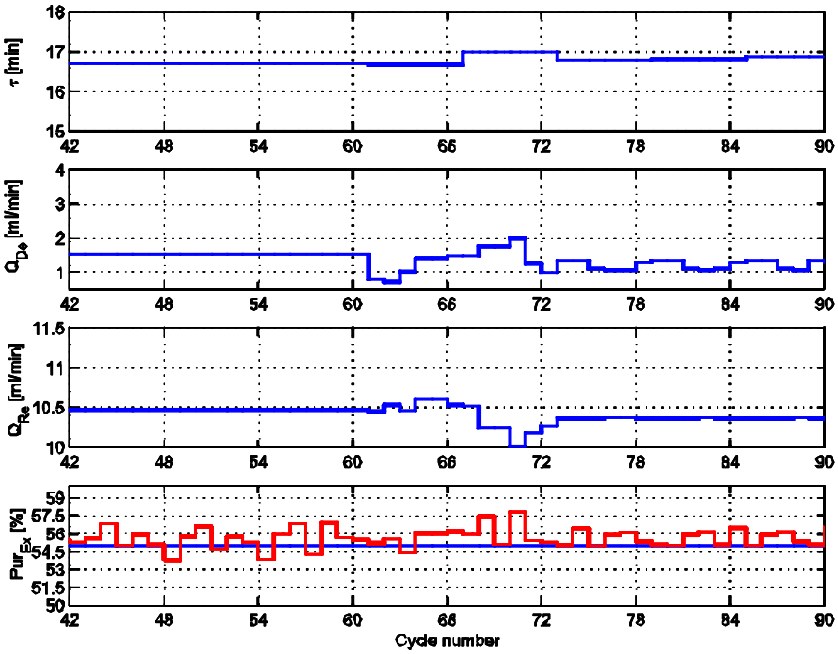

Figure 6. Control Experiment for a target purity of 55.0 %

initial model, the product purity was violated at periods 48 and 54. After one cycle, the controller drove the purity above 55.0 % and kept it there. The controller initially reduced the desorbent consumption. This action seems to be in contradiction to the intuitive idea that injection of more desorbent should enhance the separation. In the presence of a chemical reaction this is not true anymore, as shown by this experiment.

5. Summary and future work

This paper presented a fully optimisation-based integrated approach to the parameter estimation, the computation of optimal operating parameters and the on-line control of chromatographic processes in batch and continuous mode. User friendly software has been developed to support all these steps (Toumi & Engell 2003b). As new operating regimes such as VARICOL and PowerFeed (Ludemann-Hombourger & Nicoud 2000, Zhang et al. 2003) offer an even larger potential for off-line and online optimisation but constitute more difficult optimisation problems, our future work will concern the development of new efficient optimisation techniques. The optimisation of SMB processes essentially depends on an efficient calculation of the cyclic steady state. The sequential approach presented in this article is robust and simple. The disadvantages are that only stable cycles can be found, that there are no a priori estimates for the convergence behaviour (at most linear convergence can be achieved), and that the convergence is determined by the properties of the respective system and can not be controlled.

The disadvantages of the sequential approach can be overcome by a simultaneous approach where both the operating point and the cyclic steady state are evaluated within one step. However a straightforward simultaneous approach is prohibitively expensive in the Simulated Moving Bed context given the size of the problem and the related computational effort. A promising alternative is the simultaneous multiple shooting approach (Bock et al 2000). First numerical experiments demonstrated good numerical performance for a more general problem formulation than in the standard SMB case.

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