FINITE HORIZON OPTIMIZING CONTROL OF ADVANCED SMB CHROMATOGRAPHIC PROCESSES

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Abstract: Simulated Moving Bed (SMB) chromatography is attracting increasing attention for complex separation tasks. Chromatography is the method of choice in different fields (e.g. in the production of fine chemicals and pharmaceuticals) if the components have physicochemical properties which differ little or are thermally unstable. In these cases, standard separation techniques as, e.g. distillation or extraction, are not applicable.
Control of SMB processes is a challenging task, as these processes exhibit a strongly nonlinear behavior and are of hybrid and periodic nature. In this contribution, we investigate the optimizing control of the new advanced SMB-like processes VARI*COL* and PowerFeed. The online optimization is based on a full rigorous process model. An efficient numerical approach for the solution of the control problem is described and the control performance is demonstrated in simulations of a benchmark enantiomer separation.

Keywords: Optimizing control, NMPC, Chromatography, Simulated Moving Bed, VARI*COL* , PowerFeed, Direct multiple shooting, Nonlinear optimization

1. INTRODUCTION

Chromatographic separations are based on the different adsorptivities of the components of a fluid mixture to a solid 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 species. The separated peaks can be withdrawn as different fractions at the end of the column with the desired purities.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. 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).

The SMB process 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

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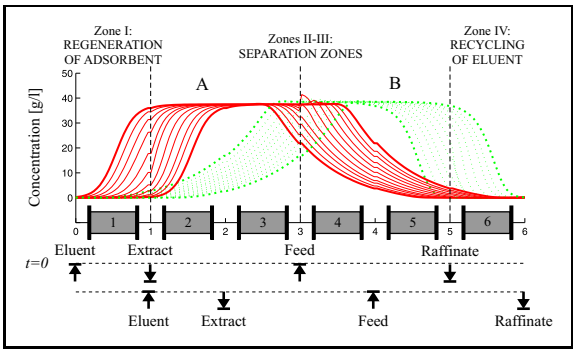

Fig. 1. Principle of the SMB process

moving the inlet and outlet lines by one column in the direction of the liquid flow (Fig. 1).

After a start-up phase, SMB processes reach a Cyclic Steady State (CSS). Fig. 1 shows the CSS of a binary separation along the columns plotted for different 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 reported recently for the SMB process. Ludemann-Hombourger and Nicoud (2000) proposed the VARI*COL* process which uses an asynchronous shift of the inlet/outlet lines leading to a better allocation of the adsorbent (Toumi *et al.*, 2003) and hence reduced desorbent consumption. Zhang *et al.* (2003) showed the potential of the variation of the 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 isotherms is obtained.

The operation of chromatographic separations, especially of the newly introduced advanced SMB processes, requires 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.

Toumi and Engell (2004) have presented an NMPC control concept for SMB processes where the operating degrees of freedom (the flow rates and the switching period) are adjusted such that an economic criterion for optimal operation is optimized over the prediction horizon, and the concept was experimentally validated at a real pilot plant scale reactive SMB process. For the online optimization, a sequential (or direct single shooting) approach was used, where a rigorous process model is simulated and the resulting performance is given back to the optimizer. The requirements on the product purities are integrated as constraints in the optimization which is performed by a feasible path SQP-solver. The numerical effort thus mainly occurs in the repeated simulation of the process with typically several hundred state variables while the nonlinear optimization problem is of relatively small scale. However, the chosen sequential approach becomes considerably more expensive when many control degrees of freedom are present.

In this paper we present an alternative approach to the formulation and the solution of the optimization problem that is based on the direct multiple shooting method (Bock and Plitt, 1984), using the package MUSCOD-II (Leineweber *et al.*, 2003). This dynamic optimization method is particularly advantageous for strongly nonlinear systems with state constraints, and in the case where many control variables are present.

2. PROCESS MODEL

Modeling of chromatographic processes has been the focus of many publications in recent years. Rigorous models of SMB plants consist of dynamic models of each column and periodic shifting of the ports. From mass balances around the inlet and outlet nodes, the following expressions for the internal flow rates $Q_{\mathrm{I}}, Q_{\mathrm{II}}, Q_{\mathrm{III}}, Q_{\mathrm{IV}}$ and the inlet concentrations $c^{\mathrm{in}}_{i,\mathrm{I}}, c^{\mathrm{in}}_{i,\mathrm{III}}$ after the mixing nodes can be derived:

$$\begin{aligned} Q_{\mathrm{IV}} + Q_{\mathrm{De}} &= Q_{\mathrm{I}} && \text{Desorbent node} \\ c^{\mathrm{in}}_{i,\mathrm{I}} Q_{\mathrm{I}} &= c^{\mathrm{out}}_{i,\mathrm{IV}} Q_{\mathrm{IV}}, \\ Q_{\mathrm{I}} - Q_{\mathrm{Ex}} &= Q_{\mathrm{II}} && \text{Extract node} \\ c^{\mathrm{in}}_{i,\mathrm{II}} &= c^{\mathrm{out}}_{i,\mathrm{I}} \\ Q_{\mathrm{II}} + Q_{\mathrm{Fe}} &= Q_{\mathrm{III}} && \text{Feed node} \\ c^{\mathrm{out}}_{i,\mathrm{II}} Q_{\mathrm{II}} + c_{i,\mathrm{Fe}} Q_{\mathrm{Fe}} &= c^{\mathrm{in}}_{i,\mathrm{III}} Q_{\mathrm{III}}, \\ Q_{\mathrm{III}} - Q_{\mathrm{Ra}} &= Q_{\mathrm{IV}} && \text{Raffinate node} \\ c^{\mathrm{in}}_{i,\mathrm{IV}} &= c^{\mathrm{out}}_{i,\mathrm{III}}. \end{aligned}$$

$Q_{\mathrm{De}}, Q_{\mathrm{Ex}}, Q_{\mathrm{Fe}}, Q_{\mathrm{Ra}}$ denote the external flow rates while $c^{\mathrm{out}}_{i,z}$ denotes the concentration of component i leaving the respective zone z. The chromatographic columns are described accurately by the general rate model which accounts for all important effects of the column, i.e. mass transfer between the liquid and solid phase, pore diffusion, and axial dispersion (Guiochon *et al.*, 1994). It is assumed that the particles of the solid phase are uniform, spherical, porous (with a constant void fraction ϵ_{b}), and that the mass transfer between the particle and the surrounding layer of the bulk is in a local equilibrium. The concentration of

component i is given by $c_{\mathrm{b},i}$ in the liquid phase and q_i in the solid phase. $D_{\mathrm{ax},i}$ is the axial dispersion coefficient, u the interstitial velocity, ϵ_{b} the void fraction of the bulk phase, c_i^{eq} the equilibrium concentration, $k_{\mathrm{l},i}$ the film mass transfer resistance, and $D_{\mathrm{p},i}$ the diffusion coefficient within the particle pores. The concentration within the pores is denoted by $c_{\mathrm{p},i}$. With the assumption that u and c_i are uniformly distributed over the radius of the column the following set of partial differential equations can be obtained from a mass balance around an infinitely small cross-section of the column:

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

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

The initial and boundary conditions are

$$c_{\mathrm{b},i,0} = c_{\mathrm{b},i}(t=0,x), \quad c_{\mathrm{p},i,0} = c_{\mathrm{p},i}(t=0,x,r),$$
$$\frac{\partial c_{\mathrm{b},i}}{\partial x}(0) = \frac{u}{D_{\mathrm{ax},i}}(c_{\mathrm{b},i} - c_i^{\mathrm{in}}), \quad \frac{\partial c_{\mathrm{b},i}}{\partial x}(L) = 0,$$
$$\frac{\partial c_{\mathrm{p},i}}{\partial r}(0) = 0, \quad \frac{\partial c_{\mathrm{p},i}}{\partial r}(R_{\mathrm{p}}) = \frac{k_{\mathrm{l},i}}{\epsilon_{\mathrm{p}} D_{\mathrm{p},i}}(c_{\mathrm{b},i} - c_{\mathrm{p},i,R_{\mathrm{p}}}).$$

The above partial differential equations for the coupled columns are spatially discretized with finite elements in the axial direction (1) and collocation within the particles (2). In the chosen discretization, this yields a nonlinear system of semi-explicit ordinary differential equations (ODE) with about 600 states.

3. OPTIMIZATION OF ADVANCED SMB PROCESSES BY A MULTIPLE SHOOTING APPROACH

Many dynamic process optimization problems can be expressed as multi-stage optimal control problems with ODE or, more generally, differential algebraic equation (DAE) models. The time horizon of interest $[t_0, t_M]$ is divided into M subintervals, i.e. M corresponds to the number of stages of the SMB process times the number of predicted cycles. Note that the stages may have different DAE models, as e.g. in the VARI*COL* process where the relative positions of inlet and outlet ports are varied. Such kind of problems can be efficiently solved with the software package MUSCOD-II (Leineweber *et al.*, 2003) based on the direct multiple shooting method (Bock and Plitt, 1984). The manipulated variables u_i are approximated by a piecewise representation. This is done by first dividing each model stage into a number of subintervals called multiple shooting intervals as indicated in Fig. 2. Additional variables s_{ij}^x, s_{ij}^z are added as initial values for the differential and algebraic variables. The basic concept of the direct multiple shooting method is to solve the DAE initial value problems independently on each of the multiple shooting intervals, using an adaptive error controlled DAE solver that is also able to compute accurate derivatives. The infinite dimensional optimal control problem is thus transformed into a Nonlinear Program (NLP) which is then solved by a specially designed sequential quadratic programming (SQP) algorithm (Leineweber *et al.*, 2003). Consistency of the algebraic equations and, particulary, continuity of the state trajectory at the multiple shooting grid points are incorporated as constraints into the NLP. They are satisfied only at the solution of the problem, but not necessarily during the SQP iterations.

The efficiency of the approach, which has been observed in many practical applications, has several reasons. Among the most important ones is the inclusion of information about the behavior of the state trajectory (which is often well-known) into the initial guess in the iterative solution procedure; this can damp the influence of poor initial guesses of the optimization variables (which are usually much less known). This in particular enables an efficient initialization of subsequent online problems (Diehl *et al.*, 2002).

We want to mention that an offline optimization of the cyclic steady state can also be performed by a novel direct multiple shooting technique that directly exploits the periodicity (Toumi, 2004).

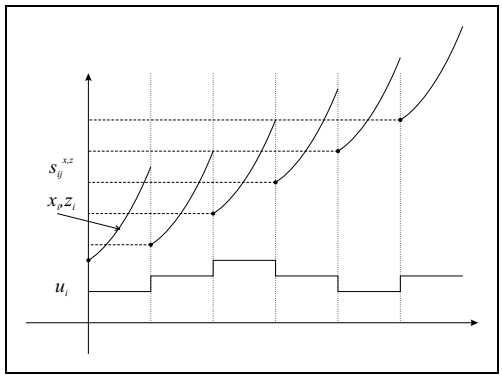

Fig. 2. Direct Multiple Shooting Method

4. FORMULATION OF THE ONLINE OPTIMAL CONTROL PROBLEM

In contrast to other approaches where in a first step an optimal operating regime is computed offline and this regime is corrected online using feedback control of the product purities or the concentration fronts (Klatt *et al.*, 2002), we propose to perform a direct online optimization of the process operation over a finite horizon and to formulate the demands on the product purities

as constraints within this optimization problem. The control vector consists of the flow rates of the eluent, extract, feed and recycle streams in each subperiod of a switching period as well as of the lengths of the subperiods:

$$\mathbf{u}_k = (Q^l_{\mathrm{De}}, Q^l_{\mathrm{Ex}}, Q^l_{\mathrm{Fe}}, Q^l_{\mathrm{Re}}, \delta t^l)^T. \qquad (3)$$

The overall switching period (or cycle time) results as

$$\tau^l = \sum_{j=1}^{n_{\mathrm{stages}}} \delta t^j. \qquad (4)$$

The sampling time of the controller is equal to the cycle time. In each cycle of the process, the optimization problem:

$$\begin{aligned}
\min_{[\mathbf{u}_k, \cdots \mathbf{s}_k, \cdots]} \quad & \sum_{j=k}^{k+H_{\mathrm{p}}} \left(\mathrm{Cost}(j) + \Delta\mathbf{u}_j^T \mathbf{R}_{u,j} \Delta\mathbf{u}_j + \mathbf{r}_{s,j}^T \mathbf{s}_j\right) \\
\text{s.t.} \quad & \text{Model Equations are fulfilled} \\
\text{and} \quad & \mathrm{Pur}^j_{\mathrm{Ex},k} + s^j_{\mathrm{Ex}} \geq \mathrm{Pur}_{\mathrm{Ex,min},k}, \\
& \mathrm{Pur}^j_{\mathrm{Ra},k} + s^j_{\mathrm{Ra}} \geq \mathrm{Pur}_{\mathrm{Ra,min},k}, \\
& s^j_{\mathrm{Ex}} \geq 0, s^j_{\mathrm{Ra}} \geq 0, \\
& Q_{\min} \leq Q^j_{\mathrm{I}} \leq Q_{\max}, \\
& \mathbf{h}(\mathbf{u}_j) \geq \mathbf{0}, \quad j = k, \ldots, k + H_{\mathrm{p}},
\end{aligned}$$

is solved and the resulting controls are applied for the next cycle.

The purity requirement on the simulated purities $\mathrm{Pur}^j_{\mathrm{Ra},k}$ and $\mathrm{Pur}^j_{\mathrm{Ex},k}$ is softened by introducing positive slacks

$$\mathbf{s}_j = (s^j_{\mathrm{Ex}}, s^j_{\mathrm{Ra}})^T, \quad j = k, (k+1), \cdots, (k+H_{\mathrm{p}}),$$

and by penalizing the violations of the purity constraints in the objective. If the weighting factors $\mathbf{r}_{s,j}$ of the slack variables are chosen sufficiently high, this soft constraint formulation is equivalent to hard constraints for feasible problems; if the purity requirements cannot be met, the optimizer tries to find a relaxed solution which is in line with the goal of the best possible process operation.

Additional inequality constraints $\mathbf{h} \geq 0$ are formulated to force the controls and switching times to be positive.

The optimization is based on a rigorous process model which however will always differ from the behaviour of the true plant. Feedback is introduced to compensate for this by an adaptation of the required purities $\mathrm{Pur}_{\mathrm{Ra,min},k}$ and $\mathrm{Pur}_{\mathrm{Ex,min},k}$ within the optimization that is based on the mismatch of simulated and measured concentrations.

5. SIMULATION STUDIES

In the sequel we apply the proposed online optimizing control scheme to the separation of the enantiomer mixture EMD-53986. The substance involved is a precursor of a potential active ingredient in a pharmaceutical product. The separation is characterized by a strongly nonlinear adsorption isotherm. Details on the model parameters can be found in (Toumi, 2004). We consider an SMB process with only 4 columns. The chosen parameters of the optimizing controller are given in Table 1. We chose a control horizon of two cycles and a prediction horizon of 8 cycles (two periods of the process). We restricted the number of SQP iterations of the underlying direct multiple shooting optimizer to 10, to guarantee real-time feasibility. The optimization problems are initialized using a shift strategy to exploit the knowledge from the previous iteration.

Table 1. Controller parameters

Quantity	Value
control horizon H_{r}	2 cycles
prediction horizon H_{p}	8 cycles
regularization $\mathbf{R}_{u,j}$	$\mathbf{0}_{(n_u,n_u)}$
penalty $\mathbf{r}_{s,j}$	$(1.0 \cdot 10^3, 1.0 \cdot 10^3)^T$
flow constraints $(Q_{\min}, Q_{\max})^T$	$(20, 500)^T$ [ml/min]
desired purity $\mathrm{Pur}^{\mathrm{ref}}_{*,\mathrm{min},k}$	$(98.0, 98.0)^T$ [%]

We assume that the column is started up with controls that would yield product purities of 90 % in an open loop regime. The optimizing controller is started after the eighth cycle.

5.1 Conventional SMB process

Fig. 3 shows the transient from this initial condition to the steady state under closed-loop control for a conventional SMB process. The control objective is the maximization of the productivity (i.e. of the feed flow) for the specified product purities. The NMPC corrects the flow rates in such a way that the plant is in the desired cyclic steady state after 100-120 minutes. The recycle flow is steered to its lower bound. The optimal operating parameters at the steady state are listed in Table 2. The switching period is 5.14 minutes, yielding a productivity of 51.7 mg feed per minute.

5.2 Four Stage PowerFeed process

In the PowerFeed process, the flow rates are varied during each cycle. We assume that four different constant values of the flow rates can be set by the controller. The number of degrees of freedom consequently is four times larger than for the conventional SMB process. The resulting closed-loop responses with the online optimizing controller are shown in Fig. 4. The PowerFeed process reaches the desired purities significantly faster than the conventional SMB process. The steady state is reached after about 80 minutes. It is very interesting to analyze the resulting steady state. The flows vary strongly over a switching period. When the

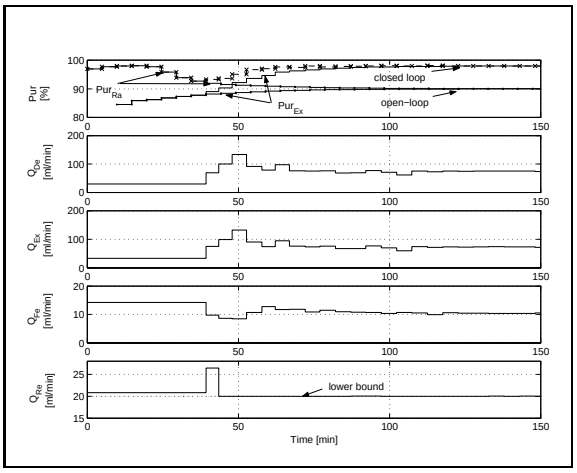

Fig. 3. Conventional SMB process under the control of the optimizing controller: purities and manipulated variables

unwanted fractions reach the extract and raffinate ports, the flow rates are reduced. The optimal cyclic steady state operation that is characterized in Table 2 is a mixture of batch and continuous operation. The lower bound $Q_{\min} = 20$ [ml/min] is active for the recycle stream Q_{Re} for three of the four intervals. The switching period is now 4.93 minutes and the productivity has been increased to 56.10 mg feed per minute, a gain of 8% without any additional cost for hardware.

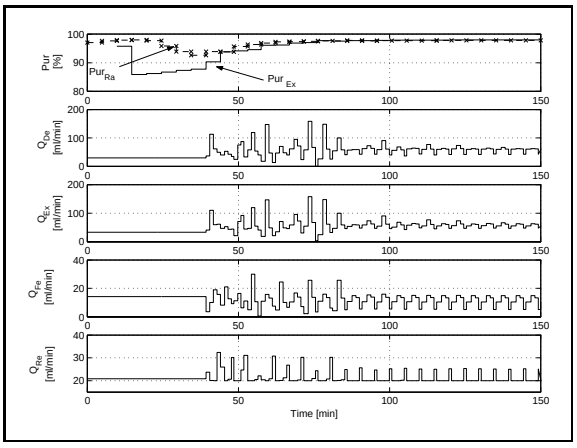

Fig. 4. Four stage PowerFeed process under the control of the optimizing controller: purities and manipulated variables

5.3 Combination of PowerFeed and VARICOL

Finally we consider the combination of PowerFeed and the VARI*COL* concept. We choose a configuration as shown in Fig. 5 for the VARI*COL* process. The extract port is initially placed after the fourth (before the first) column. The extract port is switched first to the output of the first column after the tail of the peak of the unwanted component has passed this column. Then the raffinate port is switched from the output of the third column to the output of the fourth column after the component peak that spoils the purity of the raffinate flow has passed. Then the feed is switched from the input of the third column to the input of the fourth column.

Thus extract and feed port change their positions within one period. The corresponding flow rates are composed of two different sections, one before and one after the change of the order of the ports. This can be seen in Fig. 6. In the process under optimizing control, the desired purities are reached after about 60 minutes, only about half the time needed in the classical SMB process. The switching period is reduced to 3.37 minutes and the productivity is increased by more than 18% compared to the usual process. This is however achieved at the expense of an increased dilution of the products.

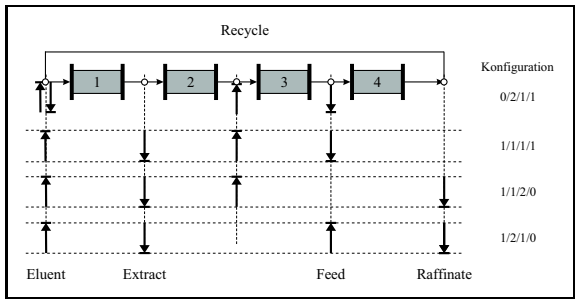

Fig. 5. The chosen VARI*COL*-configuration

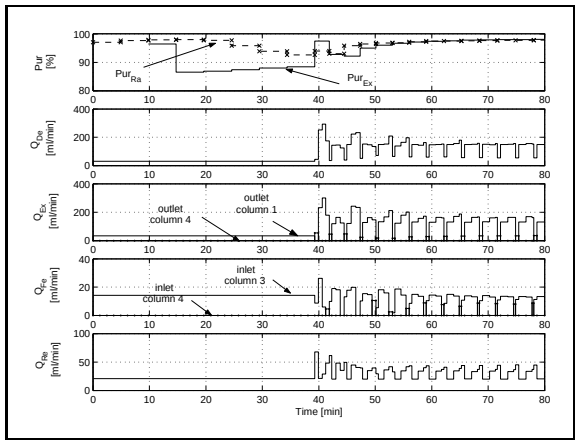

Fig. 6. Combined four stage PowerFeed & VARI*COL* process under control of the optimizing controller: purities and manipulated variables

6. CONCLUSIONS

In this contribution, we discussed the application of a direct multiple shooting approach to the online optimizing control of advanced SMB processes. As demonstrated by the simulations, the controller guarantees the purity specifications while driving the process to an economically optimal periodic steady state. The direct multiple shooting approach is able to perform the

Table 2. Comparison of cyclic steady states

Process	Intervals	δt [min]	Q_{De} $[\frac{ml}{min}]$	Q_{Ex} $[\frac{ml}{min}]$	Q_{Fe} $[\frac{ml}{min}]$	Q_{Re} $[\frac{ml}{min}]$
SMB	1	5.19	75.19	73.58	10.34	20.0
PowerFeed	1	1.67	60.33	55.16	10.32	20.0
	2	1.33	62.21	62.20	14.81	20.0
	3	1.06	61.12	61.13	13.33	20.0
	4	0.86	42.63	47.61	4.99	25.15
PowerFeed & VARI*COL*	1	0.63	51.89	35.59[1]	11.69	45.38
	2	1.35	148.4	131.5	12.89	20.0
	3	1.07	151.7	164.3	12.59	32.59
	4	0.24	154.9	163.8	9.27[2]	36.50

Process	τ [min]	Pr $[\frac{mgFe.}{min}]$	rel. Pr [%]
SMB	5.148	51.70	100.0
PowerFeed	4.932	56.10	108.51
PowerFeed & VARI*COL*	3.375	61.481	118.91

[1] outlet column 4, [2] inlet column 4

online optimization of the PowerFeed and the VARI*COL* processes that have considerably more degrees of freedom than the standard SMB process. As the flow rates and the port positions are varied within a cycle, each cycle is naturally decomposed into multiple shooting subintervals. It was demonstrated that the novel concepts for the operation of SMB-like processes have a large potential for improvements of the productivity. The ModiCon process can be controlled by an optimizing controller in the same fashion.

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REFERENCES

Bock, H.G., and K. Plitt (1984). A multiple shooting algorithm for direct solution of optimal control problems. In: Proc. 9th IFAC World Congress, Budapest, Pergamon Press, 243-247.

Broughton, D. (1966). Continuous simulated counter-current sorption process employing desorbent made in said process. US Patent 3.291.726.

Diehl, M., H.G. Bock, J.P. Schlöder, R. Findeisen, Z. Nagy, and F. Allgöwer (2002). Real-time optimization and nonlinear model predictive control of processes governed by differential-algebraic equations. J. Proc. Contr. **12** (4), 577–585.

Guiochon, G., S. Golshan-Shirazi and A. Katti (1994). Fundamentals of Preparative and Nonlinear Chromatography, Academic Press, Boston.

Leineweber, D.B., A. Schäfer, H.G. Bock and J.P. Schlöder (2003). An efficient multiple shooting based reduced SQP strategy for large-scale dynamic process optimization. Part II: Software aspects and applications. *Comp. & Chem. Eng.* **27**, 167–174.

Ludemann-Hombourger, O. and R. M. Nicoud (2000). The VARICOL process: A new multicolumn continuous chromatographic process, *Separation Science and Technology* **35**, 1829-1862.

Klatt, K.-U., F. Hanisch, and G. Dünnebier (2002). Model-based control of a simulated moving bed chromatographic process for the separation of fructose and glucose, *Journal of Process Control* **12**, 203-219.

Schramm, H., M. Kaspereit, A. Kienle and A. Seidel-Morgenstern (2002). Improving simulated moving bed processes by cyclic modulation of the feed concentrations, *Chem. Eng. Technol.* **25**, 1151-1155.

Toumi, A. and S. Engell (2004). Optimization-based control of a reactive simulated moving bed process for glucose isomerization, *Chemical Engineering Science* **59**, 3777-3792.

Toumi, A., S. Engell, O. Ludemann-Hombourger, R. M. Nicoud and M. Bailly (2003). Optimization of simulated moving bed and VARICOL processes, *Journal of Chromatography A* **1006**, 15-31.

Toumi, A. (2004). Optimaler Betrieb und Regelung von Simulated Moving Bed Prozessen. Dr.-Ing. Dissertation, Fachbereich Bio- und Chemieingenieurwesen, Universität Dortmund, and Shaker Verlag, Aachen.

Zhang, Z., M. Mazzotti and M. Morbidelli (2003). PowerFeed operation of simulated moving bed units: Changing flow-rates during the switching interval, *Journal of Chromatography A* **1006**, 87-99.