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OPTIMIZING CONTROL OF VARIABLE CYCLE TIME SIMULATED MOVING BEDS

Cristian Grossmann * **Mohammad Amanullah** ** **Marco Mazzotti** ** **Massimo Morbidelli** *** **Manfred Morari** *

* *ETH Zurich, Automatic Control Laboratory, Physikstrasse 3, 8092 Zürich, Switzerland.*
** *ETH Zurich, Institute of Process Engineering, Sonneggstrasse 3, 8092 Zürich, Switzerland.*
*** *ETH Zurich, Institute for Chemical and Bio-Engineering, 8093 Zürich, Switzerland.*

Abstract:
Simulated moving bed (SMB) is a cost-efficient chromatographic technique employed for difficult separation tasks. SMB processes exhibit complex dynamics, e.g., its hybrid nature due to the inlet/outlet port switches with nonlinearities and delays. The novel feature presented in this work is the extension of the ′cycle to cycle′ control concept to make use as manipulated variables, of the four sectional flow rates and the switch time. Its effectiveness is demonstrated through two case studies; the startup of a SMB unit under plant-model mismatch and the rejection of a pump disturbance.

Keywords: Optimization, Repetitive Model Predictive Control, Automatic Process Control, Simulated Moving Bed

1. INTRODUCTION

Simulated Moving Bed (SMB) is a continuous chromatographic process to separate mixtures into two fractions. The separation principle is the different affinity of the components in the mixture to the solid phase which moves countercurrently to the direction of the fluid. The generation of a real countercurrent flow between a solid and a fluid phase is infeasible in practice, but it can be overcome by a technical approximation of the process, the SMB. The SMB consists of a loop of fixed-bed columns where the fluid circulates in one direction (Fig. 1). The desired countercurrent flow is achieved by periodically switching the inlet and outlet streams in the direction of the fluid flow, which results in a "simulated" countercurrent movement of the solid with respect to the fluid. A detailed description and analysis of the process can be found elsewhere (Mazzotti and Morbidelli, 1997).

In recent years, SMB has been firmly established in the areas of pharmaceuticals, fine chemicals and biotechnology, because of its significant economical advantages. SMB is currently gaining attention for purification of species characterized by low selectivities such as chiral molecules for single enantiomer drug development (Juza and Morbidelli, 2000).

Nevertheless, the full exploitation of the economical advantages of SMB has been hindered by mainly two factors. On the one hand, regulatory agencies (FDA, EMEA) dictate increasingly

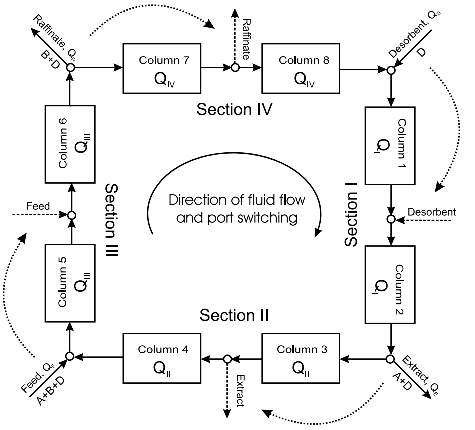

Fig. 1. Scheme of a Simulated Moving Bed (SMB) unit. The dashed lines indicate the inlet/outlet positions after the first switch.

stricter regulations and hard constraints on the purity and quality of chiral drugs. These requirements enforce the selection of operating conditions that will guarantee their fulfillment under any circumstances. In SMB practice and due to the nature of the process, these regulations translate into a conservative operation of the unit that guarantees the necessary robustness, at the price, of course, of sacrificing some productivity. On the other hand, any optimization of the operation that takes into account these facts will be limited by the precision and accuracy of the parameters of the mixture to be separated, i.e. the complete nonlinear isotherm information, which is by itself a very difficult and time-consuming task. So, the regulatory issues together with the lack of accurate data about the system lead to suboptimal performances in industrial SMB applications.

Hence, the robust and optimal operation of the SMB process is still an open problem. The full economical potential of the SMB can be exploited by using a proper feedback control scheme. Several approaches have been proposed. For a detailed literature review please refer to (Erdem *et al.*, 2004). In general, the drawback of these approaches is again, the need for accurate data about the system.

Here, a modified version of the recently introduced repetitive model predictive control (RMPC) method is applied (Natarajan and Lee, 2000). The control scheme presented in this paper integrates the optimization and control of the SMB, guaranteeing the fulfillment of product and process specifications, while optimizing the economics of the process. A significant feature of the controller is that only minimal information of the system has to be provided, i.e. the linear adsorption behavior of the mixture to be separated and the average void fraction of the columns. Therefore a full characterization of the system is no longer needed.

This work presents an extension of the 'cycle to cycle' control concept (Grossmann *et al.*, 2007) in order to make use of all five operating parameters of the SMB unit, i.e. the four sectional flow rates and newly, the switch time, as manipulated variables to optimize and control the process.

2. PROCESS DESCRIPTION

The description and modelling of the SMB process considered in this work has been reported in previous works (Erdem *et al.*, 2004). For the sake of completeness, a short summary is given here. A detailed description of the SMB process and its working principle may be found elsewhere (Mazzotti and Morbidelli, 1997).

The mixture of guanosine (A) and uridine (B) is to be separated in a closed-loop four-section eight-column SMB unit arranged in a 2-2-2-2 configuration (Fig. 1). The dynamical model for simulation of the SMB unit is obtained by interconnecting the dynamical models of each chromatographic column. The single-column dynamics are modelled with the equilibrium dispersive model (EDM) and the adsorption behavior of both components inside the columns is described by a linear adsorption isotherm, with Henry's constants H_A and H_B. The mathematical model is completed by considering the corresponding node balances between the columns and the proper boundary and initial conditions. The physical parameters of the system under consideration are summarized in Table 1.

Table 1. Physical parameters of the system to be separated and the SMB unit used for simulation.

Parameter	*Value*
Mixture to be separated	Guanosine and Uridine
Mobile phase	5% ethanol in water
Stationary phase	Source 30 RPC
Temperature,	$23\,°C$
Henry's constants	$H_A^{plant} = 2.140$
	$H_B^{plant} = 1.316$
Number of columns	8
Column distribution	2/2/2/2 Closed loop
Column diameter,	$1\,cm$
Column length,	$10\,cm$
Total packing porosity	$\varepsilon = 0.375$
Theoretical plates per column	100

3. 'CYCLE TO CYCLE' OPTIMIZING CONTROL SCHEME

The core of the control concept is the integration of the optimization and control of the SMB unit (Erdem *et al.*, 2004). The novel feature presented in this work is the extension of the 'cycle to cycle' control concept (Grossmann *et al.*, 2007) to also make use of the switch time as a manipulated variable. In this way, all five operating parameters of the SMB unit, i.e. the four sectional flow rates and the switch time, can be used to optimize and control the process. A scheme of the control concept is shown in Fig. 2.

The control problem is formulated as a con-

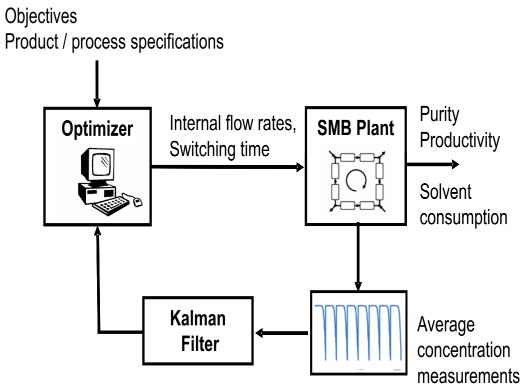

Fig. 2. Scheme of the $'$cycle to cycle$'$ control concept.

strained dynamic optimization problem within the RMPC framework. The productivity and solvent consumption represent the cost function to be optimized, while the hardware restrictions and product quality specifications are imposed as constraints. The controller makes use of a simplified $'$cycle to cycle$'$ SMB model to predict and optimize the performance of the unit over a predefined number of cycles, the so-called prediction horizon, n_p. The simplified $'$cycle to cycle$'$ SMB model requires only the linear isotherm information, H_A and H_B, and the average bed porosity of the unit, ε_{ave}. The solution of the optimization problem yields a sequence of optimal control actions for a chosen number of cycles, namely the control horizon n_c. This scheme is implemented according to a receding horizon strategy, i.e. the first element of the calculated optimal control actions sequence corresponding to the current cycle is implemented, and the remaining calculated optimal inputs are discarded. The prediction horizon is shifted by one cycle and as new measurements of the average concentrations of both species in extract and raffinate are available and an optimization problem based on the new estimate of the plant state is solved. The new state estimate is calculated using a Kalman filter. The measurements, optimization and control actions are performed only once every cycle, i.e. on a $'$cycle to cycle $'$ basis.

3.1 Simplified $'$cycle to cycle$'$ SMB model

The model used by the controller is of paramount importance for its performance. A detailed dynamic model of SMB would demand excessive computation for on-line optimization. Therefore a simplified linear time-invariant model of the process is considered. A detailed derivation of the model for control purposes has been reported (Erdem *et al.*, 2004; Grossmann *et al.*, 2007).

For this work, the modelling procedure presented in (Grossmann *et al.*, 2007) is followed. The space discretization of the system of partial differential equations (PDEs) describing the SMB unit yields a system of ordinary differential equations (ODEs). The ODE system is linearized with respect to the four internal flow rates and the new manipulated variable, the switch time t^* around a cyclic steady state concentration profile. This allows the controller to predict the effect of the switch time on the future performance of the plant. The model takes the form

$$\begin{aligned} x_{k+1} &= \mathbf{A}x_k + \mathbf{B}u_k \qquad x \in \mathbf{R}^{n_x},\ u \in \mathbf{R}^{n_u} \\ y_k &= \mathbf{C}x_k + \mathbf{D}u_k \qquad y \in \mathbf{R}^{n_y} \end{aligned} \tag{1}$$

where k is the cycle index. x is the state vector comprising the internal concentration profiles. u is the input vector containing the internal flow rates and the switch time. The average concentration levels of both species at both outlet streams, constitute the output vector y. n_x, n_y and n_u indicate the dimension of the state x and the number of process inputs u and outputs y, respectively. x, u and y are defined in terms of deviation variables. $\mathbf{A}$, $\mathbf{B}$, $\mathbf{C}$ and $\mathbf{D}$ are the state space matrices of the system.

The equations in (1) are used to derive along the lines of RMPC, the simplified $'$cycle to cycle$'$ model that constitutes the basis for the formulation of the control problem. The RMPC formulation is based on the assumption that possible model prediction errors and the effect of disturbances on the plant output are likely to repeat due to the periodic nature of the process, and therefore the information of the past cycles can be used to correct for model errors in the future cycles. We refer to the available literature for the description and implementation details of RMPC (Natarajan and Lee, 2000; Grossmann *et al.*, 2007).

It is relevant to note that RMPC was formulated under the assumption of a fixed period duration. Including the switch time as a manipulated variable leads inevitably to the violation of this assumption. Nevertheless, the $'$cycle to cycle$'$ formulation of the control problem allows to profit from the advantages of RMPC for periodic process even with a varying period duration.

3.2 Optimization problem

The economic objective considered in this work is defined to maximize the feed throughput and to minimize the solvent consumption. The decision variables in the optimization problem are the manipulated variables, i.e. the four internal flow rates $Q_I...Q_{IV}$ and the switch time t^*. These are constrained during the whole operation with lower and upper bounds.

$$Q_j^{max} \geq Q_j \geq Q_j^{min} \quad \text{for} \quad j = I, ..., IV \tag{2}$$

$$t^{*max} \geq t^* \geq t^{*min} \tag{3}$$

Furthermore, due to technical requirements, the switch time t^* is restricted to take only integer values which results in a MILP formulation. The required product specifications are enforced by constraining the average purities P^{ave} for each cycle of the prediction horizon with a lower bound P^{min}.

$$P_E^{ave} \geq P_E^{min} \tag{4}$$

$$P_R^{ave} \geq P_R^{min} \tag{5}$$

where P_E and P_R represent the purities in extract and raffinate, respectively.

The cost function of the MILP is defined to maximize the feed flow rate Q_F and minimize the desorbent consumption Q_D over a given prediction horizon n_p.

$$\min_{\mathbf{Q}^{(n_c)},\ \mathbf{t}^{*(n_c)}} \left[\lambda_D \underbrace{Q_D^{(n_p)}}_{Q_I - Q_{IV}} - \lambda_F \underbrace{Q_F^{(n_p)}}_{Q_{III} - Q_{II}} \right] \tag{6}$$

where $Q_D^{(n_p)}$ and $Q_F^{(n_p)}$ are the cumulative solvent consumption and feed throughput, respectively, over the prediction horizon n_p. λ_D and λ_F are the weights assigned to each term in the cost function and reflect the relative preference given to the desorbent consumption minimization and the feed throughput maximization, respectively. $\mathbf{Q}^{(n_c)}$ and $\mathbf{t}^{*(n_c)}$ are vectors consisting of the four internal flow rates $Q_I...Q_{IV}$ and the the switch times t^*, respectively, for the control horizon n_c.

The problem comprised 369 variables, and 462 constraints. A commercial solver, ILOG CPLEX 9.0 was used to solve the optimization problem. The maximum computation time was found to be less than 0.1 s in a PC with a 3 GHz processor.

4. CONTROLLER PERFORMANCE

The results are presented in terms of the triangle theory. For the sake of completeness, the main concepts are summarized here. The separating conditions are derived on the basis of the equilibrium theory model. The key operating parameters are the ratio of the net fluid and solid phase flow rates in each section of the SMB unit.

$$m_j = \frac{Q_j t^* - V\varepsilon}{V(1-\varepsilon)} \qquad (j = I, ..., IV) \tag{7}$$

where V is the volume of one column and ε is the total packing porosity. The necessary and sufficient conditions for the complete separation of a system characterized by a linear adsorption isotherm are given by the following inequalities

$$H_A < m_I < \infty \tag{8}$$

$$H_B < m_{II} < m_{III} < H_A \tag{9}$$

$$0 < m_{IV} < H_B \tag{10}$$

under the assumption that nonporous particles constitute the solid phase. Given that the inequalities (8) and (10) are fulfilled, i.e. the liquid and solid phases, respectively, are fully regenerated, then the position of the operating point in the (m_{II}, m_{III}) plane allows to make a prediction of the separation performance. Consider the different regions that Eq. (9) defines in the bottom Fig. 3. Note that the point on the (m_{II}, m_{III}) plane that maximizes the feed throughput, that is proportional to the difference between m_{II} and m_{III}, is located at the vertex of the complete separation region. More details on the triangle theory can be found elsewhere (Mazzotti and Morbidelli, 1997; Mazzotti, 2006).

In the following case studies, two different scenarios are presented to illustrate the performance of the controller. Section 4.1 shows how the controller can find the correct operating conditions to fulfill the specified minimum purities by manipulating the four sectional flow rates and the switch time regardless of the plant-model mismatch. Section 4.2 shows how the controller responds to a disturbance to recover the required purities and to drive the operation of the plant to the new optimal operating conditions, which were altered significantly by the disturbance.

Table 1 and 2 report the parameters used for the simulations and the development of the controller.

Table 2. Parameters used for the development of the controller.

Parameter	*Value*
λ_F	20
λ_D	1
$t^{*,ref}$	120 s
$m_{j=I...IV}^{ref}$	2.28, 1.25, 2.29, 1.29
n_p	8 cycles
n_c	1 cycle
$P_{min}^R = P_{min}^E$	99.0%
Henry's constants	$H_A^{model} = 2.248$
	$H_B^{model} = 1.303$
Average packing porosity	$\varepsilon_{ave} = 0.375$
n_x	26
n_u	5
n_y	4

4.1 Case study 1: Plant-model mismatch

The controller is developed using information from pulse injection under dilute condition, i.e. only the Henry's constants and the average porosity. However, it is common to have uncertainties and errors in these measurements. Besides, temperature deviations, plant dead volumes and aging of the solid phase affect the retention behavior of the species. This may lead to a difference between the actual Henry's constants characterizing the plant and the ones provided to the model. In order to demonstrate the controllers performance under such circumstances, the model is developed based on $H_A^{model} = 2.248$ and $H_B^{model} = 1.303$ (triangle with solid lines in Fig. 3), which are different from the Henry's constants characterizing the plant, namely $H_A^{plant} = 2.140$ and $H_B^{plant} = 1.316$ (triangle with dashed lines in Fig. 3), i.e., 5% smaller and 1% larger, respectively. The plant was started

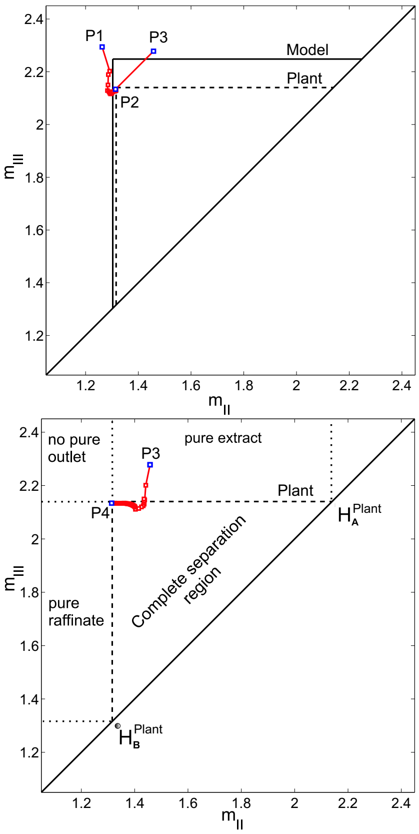

Fig. 3. Controller action represented in the (m_{II}, m_{III}) operating parameter space. *Top:* Trajectory before the disturbance at cycle 150. *Bottom:* Trajectory after the disturbance

up at the reference flow rates and switch time reported in Table 2, with initially clean columns and the controller was switched on at cycle 1. The startup point (P1 in Fig. 3) falls within the region, where none of the outlets is pure. The controller fulfills the outlet purities within 20 cycles (Fig. 4) and then takes the operating point to the vertex of the triangle of complete separation regime (P2 in Fig. 3) which is the theoretical optimum. This demonstrates the capability of the controller to fulfill the required purities and optimize the operation under a plant-model mismatch scenario using the flow rates and the switch time (Fig. 5). The optimal operating conditions are held constant until it is disturbed at cycle 151 (P3 in Fig. 3).

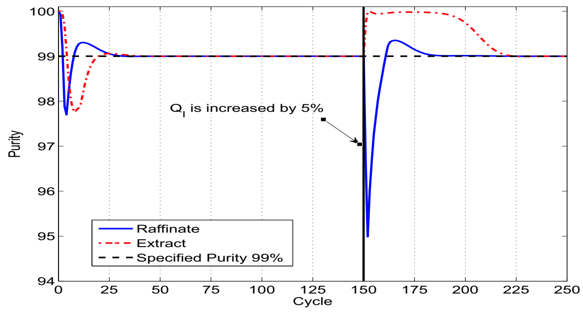

Fig. 4. Average output purities for the controlled plant over cycles.

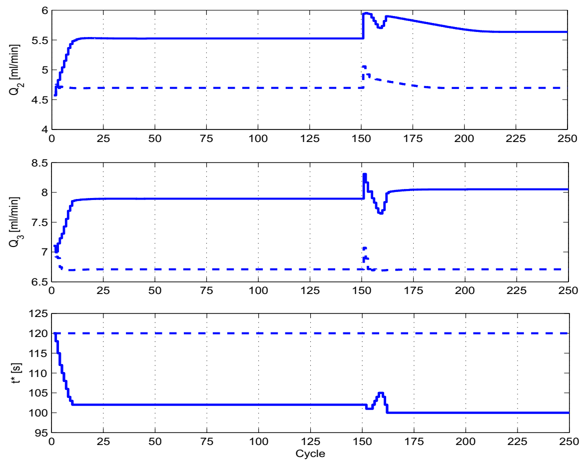

Fig. 5. Internal flow rates in section II and III and switch time t^* implemented in the plant for two different cases: *Continuous lines*, t^* was used as manipulated variable. *Dashed lines*, t^* was fixed throughout the operation.

4.2 Case study 2: Disturbance rejection

This case study addresses one of the common disturbances in a SMB unit, namely the malfunctioning of a pump during the steady state operation of the unit. The results are shown in the second part of Fig. 4, between cycle 151 and 250. The steady state operation at cycle 151 was disturbed by increasing the flow rate delivered by the pump before section I by 5%, thus affecting the rest of the sections as well. Note that this change is unknown to the controller, and it only realizes the disturbance from the measurements. The disturbance increases the flow rate in all four sections, which can be represented in the $m_{II} - m_{III}$ plane as a shift of the operating point up to the right (P3 in Fig. 3). This point lies in the pure extract region making the purity of extract and raffinate increase and decrease, respectively. The bottom part of Fig. 3 shows the operating trajectory after the disturbance and how the controller brings back the operating point to the vertex of the complete separation region (P4 in Fig. 3) in order to fulfill again the minimum specified purities and optimize the performance. It is interesting to observe how the controller, in order to recover as fast as possible the low raffinate purity, first approaches the complete separation region until it reaches the border. Once the minimum purity of the raffinate has been fulfilled, the operation is optimized by moving the operating point towards vertex of the triangle. In this way, the controller manages to reject the disturbance and the operation reaches a steady state that fulfills the requested product specifications.

For comparison, a further run under was made, keeping the switch time fixed throughout the operation of the plant. The same conditions and optimization problem were considered in this case. For the interpretation of these results note that the productivity is proportional to the feed flow rate $Q_F = Q_{III} - Q_{II}$ and inverse proportional to the switch time for constant purities, i.e. when $m_j \propto Q_j t^*$ is constant. Fig. 5 shows that the flow rates in sections II and III are lower when the switch time is fixed. This translates into a lower productivity than with variable switch time, when keeping the purities constant.

5. DISCUSSION AND CONCLUSIONS

In this study, an extension of the ′cycle to cycle′ control concept developed earlier (Erdem *et al.*, 2004; Grossmann *et al.*, 2007) has been presented. This extension allows the controller to make use of the full set of operating parameters, i.e. the four internal flow rates and the switch time, to control and optimize the unit. Our control scheme is formulated within the framework of MPC, thus providing the possibility to contemplate any economical objective function or include any type of process or product requirement in a clean and straightforward manner.

Incorporating the switch time as manipulated variable implies the violation of the basic assumption of constant period length in RMPC (Natarajan and Lee, 2000). Nevertheless, the ′cycle to cycle′ formulation constitutes a way to overcome this limitation that is restrictive for cyclic processes, where the period length is an important manipulated and optimization variable.

Motivated by the future experimental implementation of this approach and considering the software restrictions in our laboratory plant, the switch time was restricted to be an integer value. This led to solving MILP when optimizing the SMB unit at every cycle, contrary to the LP formulation presented in (Grossmann *et al.*, 2007). This approach had been mentioned in the literature, though derived from the idea of modelling SMB as a hybrid system (Natarajan and Lee, 2000). In our formulation and from a conceptual point of view, this constraint is not necessary and can be relaxed to allow the switch time to be continuous.

The performance of the controller to find the optimum predicted by the triangle theory has been illustrated through two case studies. The results have shown that the controller can assure the product quality and optimize the performance of the plant in terms of maximum feed throughput and minimum desorbent consumption despite uncertainties in the system parameters and major disturbances in the SMB operation.

The flexibility and potential of this controller resides in its ability to rely only on the concentration of each solute at the outlet streams, *averaged over one cycle*, as feedback information. The ′cycle to cycle′ formulation does not only allow an enhancement in the set of manipulated variables, but provides the flexibility to apply the controller to a wider range of separation tasks which will be studied in the future.

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