

# A hierarchical approach to optimal control of a hybrid chromatographic batch process<sup>\*</sup>

Dmitry Gromov<sup>\*</sup> Suzhou Li<sup>\*\*</sup> Jörg Raisch<sup>\*,\*\*</sup>

<sup>\*</sup> *Fachgebiet Regelungssysteme, Technische Universität Berlin  
e-mail: {gromov,raisch}@control.tu-berlin.de*

<sup>\*\*</sup> *Max-Planck-Institut für Dynamik komplexer technischer Systeme,  
Magdeburg, Germany  
e-mail: suzhou@mpi-magdeburg.mpg.de*

---

**Abstract:** In this paper we consider a hierarchical approach to solve an optimal control problem for a hybrid chromatographic batch process. The plant consists of several chromatographic columns which can be connected in an arbitrary way. The plant configuration can therefore be considered as a discrete-valued control input. The dynamics of each chromatographic column is described by two coupled nonlinear partial differential equations. Hence, we have a hybrid optimisation problem with highly nonlinear dynamics.

To handle complexity, we propose a hierarchical two-level optimisation scheme: first, we solve a number of continuous optimisation problems that correspond to fixed configurations. In a subsequent step, on the basis of these solutions, we solve a discrete optimisation problem to generate the optimal configuration or configuration signal.

Because of the imposed structure, we can of course not expect the overall solution to be optimal. However, we demonstrate that, by using the plant configuration as an additional control input, performance may be considerably improved when compared to the constant configuration scenario.

*Keywords:* Hierarchical optimisation, optimal control, hybrid systems, batch chromatography

---

## 1. INTRODUCTION

Column chromatography using solid and liquid phases is a key technique for the isolation and purification of valuable products, which has found a large number of successful applications in petrochemical, food and pharmaceutical industries during the last decades. Chromatographic separation processes can be operated in continuous or batch mode. Continuous separation is usually realised by the well-known simulated moving bed (SMB) process and its various modifications. This scheme has been proven to be very efficient for large-scale separation tasks. A drawback is, however, that the start-up procedure may take considerable time. Hence, this technology may not be suitable for the separation of relatively small amounts of mixtures. In this case, batch chromatography is an attractive alternative. Currently, a considerable number of chromatographic separations are operated in batch mode. Therefore the efficient operation and control of these processes is an important topic in order to exploit the economic potential and reduce the production cost.

There are a number of papers devoted to the optimisation and parameter identification of batch separation processes, see, e.g., (Dünnebier et al., 2001; Gao and Engell, 2005; Nagrath et al., 2003; Piątkowski, 2006) for details and references. These papers study the problem of optimisation of the process w.r.t. different performance criteria (e.g.,

productivity, or more specific criteria, like in (Felsing and Guiochon, 1996, 1998)). These criteria describe the overall (integral) performance of the system, but they are not very suitable if there are additional operational restrictions such as fixed batch volume, separation time and so on. Such restrictions naturally appear if the chromatographic system is a part of a complex chemical plant whose operation must follow a certain schedule. Moreover, in some applications the configuration of the plant is an additional degree of freedom, as the plant consists of a number of chromatographic columns that can be arranged in different ways. This degree of freedom has not been widely investigated up to now. An exception is (Ziomek et al., 2006), where the plant configuration is a design parameter, but constant over time. Also, additional operational restrictions (e.g., fixed batch size etc.) are not considered there.

In this contribution, we aim to develop a general framework to optimal (open loop) control of a chromatographic batch process. It includes several practically important problem statements and covers the scenario where the plant configuration may change during the operation of the plant. The latter introduces an additional, discrete-valued, degree of freedom, which makes the overall control problem an intrinsically hybrid one. To deal with the inherent complexity of this hybrid problem, we suggest a hierarchical approach, where a lower control level determines the continuous inputs and a higher control level solves the remaining discrete optimisation problem.

---

<sup>\*</sup> Work has been done in the framework of the project “Methods from Discrete Mathematics for the Synthesis and Control of Chemical Processes”, DFG-FG 468

This paper is organised as follows: In Section 2, we define the plant and a suitable PDE model. In Section 3, we motivate different optimisation problems for this plant. Section 4 suggests a hierarchical approach to solve these problems, and Section 5 presents a numerical example.

## 2. PLANT DESCRIPTION

### 2.1 Mathematical model

The system consists of  $N$  identical chromatographic columns, which can be arranged in  $N_\ell \leq N$  parallel lines. Via valves connected to the columns, their configuration can be changed within a very short time. The column configuration can therefore be interpreted as a control input. The number of columns in the  $i$ -th line is denoted by  $N_{col}^i(t)$ , with the obvious restriction  $\sum_{i=1}^{N_\ell(t)} N_{col}^i(t) = N$ ,  $\forall t$ .

Figure 1 shows a configuration with (at time  $t$ )  $N = 5$ ,  $N_\ell(t) = 2$ ,  $N_{col}^1(t) = 3$ , and  $N_{col}^2(t) = 2$ .

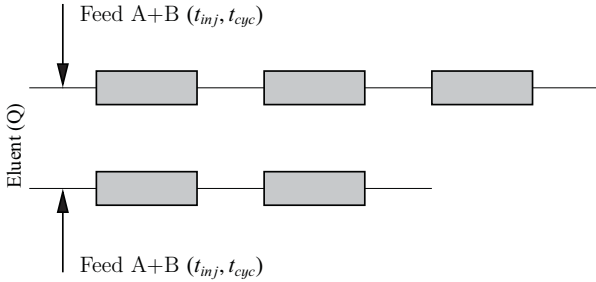


Fig. 1. Example configuration.

The dynamics of a single column is described by two nonlinearly coupled second order PDEs (so called equilibrium-dispersive model, (Guiochon et al., 2006)):

$$\frac{\partial c_k(t, x)}{\partial t} + F \frac{\partial q_k(t, x)}{\partial t} + u \frac{\partial c_k(t, x)}{\partial x} = D_{ap} \frac{\partial^2 c_k(t, x)}{\partial x^2}, \quad k \in \{A, B\},$$

where  $c_k$  and  $q_k$  are the liquid phase and solid phase concentrations,  $t, x$  are the temporal and spatial coordinates,  $u$  is the velocity of the liquid phase in the column,  $F = (1 - \epsilon_t)/\epsilon_t$  is the phase ratio, and  $\epsilon_t$  is the column total void fraction.  $D_{ap}$  is the apparent axial dispersion coefficient defined as a function of  $u$ :  $D_{ap} = uf(u)/2$ , where  $f(u) = (\alpha_D + \beta_D u)$  represents the linearised van Deemter equation,  $\alpha_D$  and  $\beta_D$  are constant coefficients. In the following, we shall often use the volumetric flowrate  $Q = u\pi D^2 \epsilon_t/4$  instead of  $u$ , where  $D$  is the diameter of the column.

The concentrations of the components in the solid and liquid phases are related via the isotherm equation. To describe adsorption, the competitive Langmuir model is employed:

$$q_k(c_A, c_B) = \frac{H_k c_k}{1 + K_A c_A + K_B c_B}, \quad k \in \{A, B\},$$

where  $H_k$  and  $K_k$  are the Henry and the equilibrium constants. Component A is assumed to be less retained than component B, therefore,  $H_A < H_B$ .

The initial and boundary conditions are defined in a standard way: the initial concentration of the components in the columns is equal to zero. We employ the Danckwerts boundary conditions for the inlet of the first and the outlet of the last column in each line:

$$\begin{cases} uc_k(t, x) - D_{ap} \frac{\partial c_k(t, x)}{\partial x} \Big|_{x=0} = uc_{k,in}(t) \\ \frac{\partial c_k(t, x)}{\partial x} \Big|_{x=L} = 0, \end{cases}$$

where  $k \in \{A, B\}$ ,  $L$  is the column length. The ‘‘inter-column’’ boundary conditions reflect the continuity of the concentrations profiles.

The functioning of a single chromatographic column is shown schematically in Fig.2. The solution containing a binary mixture is injected at the inlet of the column during the time interval  $t_{inj}$ . Injections are repeated cyclically, with the interval between two subsequent injections  $t_{cyc}$  (Fig.2a). The mixture is transported through the column with velocity  $u$ . During transportation, separation occurs because one of the components (in our example component A) is less retained than the other one. Fig.2b shows a snapshot of the concentration profiles within the column at two time instants: at an ‘‘early’’ time instant, the separation effect is weak, and the concentration profiles for the two components are very close (dashed lines). At a later time instant, the profiles have moved further apart. Finally, component A is collected from the outlet during the fractionation interval  $t_{fr}$ . Fig.2c shows the concentration signals  $c_{A,out}(t)$  and  $c_{B,out}(t)$  at the outlet of the column.  $t_1$  denotes the time instant when the concentration of the less retained component A exceeds a given threshold  $c_{A,thr}$  and  $t_4$  denotes the time when the concentration  $c_B$  becomes less than another threshold.

The following entities are used to characterise the separation process within each line and during each injection cycle. For component A, they are:

- The mass output

$$m_{A,out} = \int_{t_1}^{t_2} c_{A,out}(t) Q dt.$$

- The purity

$$Pur_A = \frac{\int_{t_1}^{t_2} c_{A,out}(t) dt}{\int_{t_1}^{t_2} c_{A,out}(t) dt + \int_{t_1}^{t_2} c_{B,out}(t) dt}.$$

- The yield

$$Y_A = \frac{m_{A,out}}{V_{inj} c_{A,in}},$$

where  $V_{inj} = Q t_{inj}$  is the injection volume.

- The productivity

$$Pr_A = \frac{m_{A,out}}{t_{cyc}} = \frac{V_{inj} c_{A,in} Y_A}{t_{cyc}}. \quad (1)$$

For component B, they are defined in an analogous way.

There are also a number of technological constraints imposed on the system. Some of them are listed below (for details see Ziomek et al. (2006)). For example, for each line of columns, we have:

- Two restrictions on the volumetric flowrate. The first one is caused by the the maximal pressure drop  $\Delta P_{max}$ , namely  $Q \leq Q_{max}(\Delta P_{max})$ . The maximal

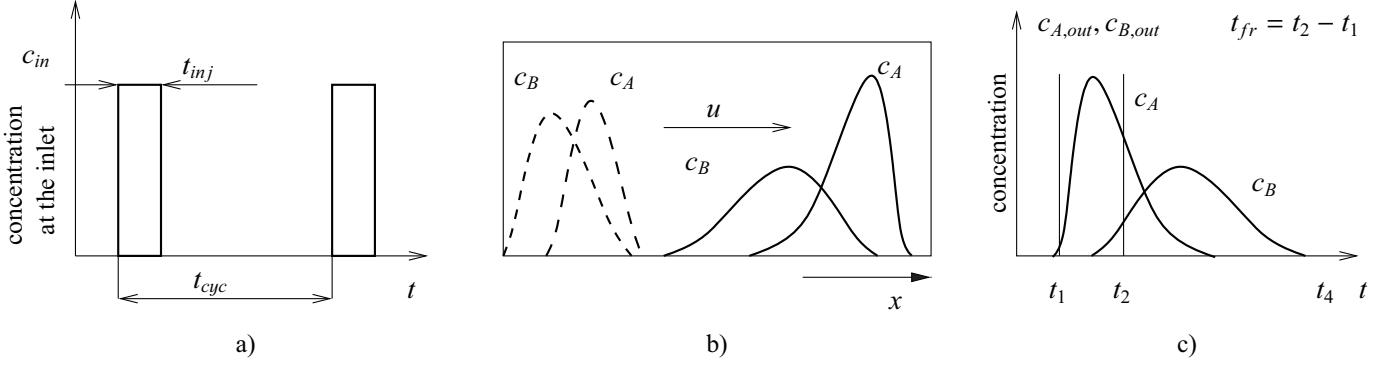


Fig. 2. a) input signal; b) concentration profiles within the column; c) concentration signals at the outlet.

pressure drop is calculated from the Darcy equation. Furthermore, there is a restriction on the maximal capacity of the pump  $Q_{max}^p$ . Hence, the resulting constraint is written as follows (Guiochon et al., 2006):

$$Q \leq \min(Q_{max}(\Delta P_{max}), Q_{max}^p).$$

- Minimal fractionation time caused by technical limitations:  $t_{fr} \geq t_{fr,min}$ .

## 2.2 Decision parameters

There are a number of parameters that can be chosen to optimise the process. We can divide them into two groups: discrete parameters, which can take values in a finite set, and continuous parameters, which can take values in a dense subset of  $\mathbb{R}$ . The continuous parameters are defined for each line  $i \in \{1, N_\ell\}$ :

- (1) The velocity of the liquid phase,  $u^i$ ,
- (2) The injection time,  $t_{inj}^i$ ,
- (3) The cycle period,  $t_{cyc}^i$ ,
- (4) The fractionation time,  $t_{fr}^i$ .

The first parameter enters the PDEs directly whereas the second and the third one enter the boundary conditions of the first column within a line. The last parameter is usually determined to satisfy purity requirements.

The discrete parameters are the number of lines,  $N_\ell$ , and the number of columns in the  $i$ -th line,  $N_{col}^i$ . These parameters describe the configuration of the plant. Furthermore, for a given configuration, the number of injections  $N_{inj}^i$  in line  $i$  is also a degree of freedom. In the following, we shall consider two cases:

- (1) The configuration is constant during the entire operation of the process.
- (2) The configuration changes over time.

In the second case, the sequence

$$\{(N_\ell(j), N_{col}^1(j), \dots, N_{col}^{N_\ell(j)}(j), N_{inj}^1(j), \dots, N_{inj}^{N_\ell(j)}(j), \tau(j))\},$$

$$j = 0, N_s$$

can be interpreted as a control signal, with  $N_s$  the (a priori fixed) number of configuration changes,  $\tau(j)$  the time interval during which the plant is operated in the  $j$ -th configuration,  $N_\ell(j)$  the number of lines for this configuration,  $N_{col}^i(j)$  the number of columns in the  $i$ -th

line in the  $j$ -th configuration, and  $N_{inj}^i(j)$  the number of injections for the  $i$ -th line in the  $j$ -th configuration.

In the remainder of this paper, we will use the following assumptions:

- A1** The continuous control parameters for all parallel lines can be adjusted separately.
- A2** The only component we are interested in is component A (less retained). In the following, we shall omit the subscript identifying the component if this is clear from the context.
- A3** The continuous control parameters do not change within the interval of constant configuration  $\tau(j)$ .
- A4** The cycle time is chosen to be equal to the duration of the chromatogram:  $t_{cyc}^i = t_4^i - t_1^i$ ,  $i \in \{1, N_\ell\}$ .
- A5** The inlet concentrations  $c_{k,in}$ ,  $k \in \{A, B\}$  are assumed to be known and fixed  $\forall t$ .

## 3. OPTIMISATION PROBLEMS

We shall investigate the following overall optimisation problems:

- (1) Yield maximisation for fixed overall time span  $T_{max}$ :

$$\text{maximise } Y_\Sigma$$

$$s.t. T_\Sigma \leq T_{max},$$

where overall yield  $Y_\Sigma$  is defined as

$$Y_\Sigma = \frac{\sum_{j=0}^{N_s} V_\Sigma(j) Y_\Sigma(j)}{\sum_{j=0}^{N_s} V_\Sigma(j)}.$$

In (3),  $V_\Sigma(j)$  and  $Y_\Sigma(j)$  are the processed volume and the yield for the  $j$ -th configuration:

$$V_\Sigma(j) = \sum_{i=1}^{N_\ell(j)} N_{inj}^i(j) V_{inj}^i(j),$$

$$Y_\Sigma(j) = \frac{\sum_{i=1}^{N_\ell(j)} N_{inj}^i(j) m_{out}^i(j)}{c_{in} V_\Sigma(j)}.$$

Overall time  $T_\Sigma$  is given by  $T_\Sigma = \sum_{j=0}^{N_s} \tau(j)$ , where

$$\tau(j) \geq \max_{i=1, N_\ell(j)} (N_{inj}^i(j) t_{cyc}^i(j)).$$

- (2) Produce required yield  $Y_{min}$  in minimal time:  
 minimise  $T_\Sigma$   
 s.t.  $Y_\Sigma \geq Y_{min}$ . (4)

In both cases, we have additional constraints for overall batch size (volume):  $V_\Sigma = V_{batch}$ , and for overall purity:

$$Pur_\Sigma = \frac{\sum_{j=0}^{N_s} V_\Sigma(j) Y_\Sigma(j)}{\sum_{j=0}^{N_s} \frac{V_\Sigma(j) Y_\Sigma(j)}{Pur_\Sigma(j)}} \geq Pur_{min},$$

where

$$Pur_\Sigma(j) = \frac{\sum_{i=1}^{N_\ell(j)} N_{inj}^i(j) m_{out}^i(j)}{\sum_{i=1}^{N_\ell(j)} N_{inj}^i(j) \frac{m_{out}^i(j)}{Pur^i(j)}}.$$

Note that  $m_{out}^i$  and  $Pur^i$  are the mass output and the purity in the  $i$ -th line for one cycle and depend on the continuous decision parameters as well as on the number of columns in line  $i$ ,  $N_{col}^i$ .

#### 4. HIERARCHICAL APPROACH

The optimisation problems posed in Sec.3 are highly complex tasks. In the variable configuration case, there is a large number of discrete and continuous decision parameters. In each iteration step during the optimisation procedure,  $2N_\ell$  partial differential equations have to be solved. Moreover, the values of the cost functions cannot be found analytically and have to be calculated from the results of numerical simulation. Since information about the derivatives of the cost functions is not available, derivative-free methods must be used, which substantially reduces the efficiency of numerical optimisation. Therefore, standard solvers normally fail to deliver a solution to these optimisation problems in reasonable time (if they provide a solution at all).

Therefore, we propose to use a hierarchical optimisation scheme to cope with complexity. In this scheme, optimisation of discrete and continuous decision variables is decoupled.

##### 4.1 Low-level (local) optimisation

On the low level, we define a set of continuous optimisation problems for one line of columns over one cycle period. The cost function for the low-level problem is productivity (Eq.1). The set of low-level problems is parametrised by the number of columns  $n$  ( $n=1, N$ ) in a line and a (finite) number of purity constraints  $Pur \geq p_m$ ,  $m = 1, M$ :

$$\begin{aligned} & \text{maximise } Pr \\ & (Q, t_{inj}, t_{fr}) \\ & \text{s.t. } N_{col} = n, \\ & Pur \geq p_m. \end{aligned} \quad (5)$$

For each low-level problem, the optimal solution ( $Q^*, V_{inj}^* = t_{inj}^* Q^*, t_{fr}^*$ ) and the corresponding values ( $t_{cyc}^*, m_{out}^*$ ) need to be stored and will be used for the solution of a high-level

problem. This information can be conveniently collected in the following table.

		Pur		
		$p_1$	$\dots$	$p_M$
$N_{col}$	1	.	.	.
	$\vdots$	.	.	.
	$n$	.	.	$Q^*, V_{inj}^*, t_{fr}^*,$ $t_{cyc}^*, m_{out}^*$
	$\vdots$	.	.	.
	$N$	.	.	.

Table 1. Results of the local optimisation

##### 4.2 High-level optimisation

###### a) Constant configuration case:

On the high level we maximise overall productivity

$$Pr_\Sigma = \frac{\sum_{i=1}^{N_\ell} N_{inj}^i m_{out}^i}{T_\Sigma} \quad (6)$$

$$\text{s.t. } Pur_\Sigma = \frac{\sum_{i=1}^{N_\ell} N_{inj}^i m_{out}^i}{\sum_{i=1}^{N_\ell} N_{inj}^i \frac{m_{out}^i}{Pur^i}} \geq Pur_{min} \quad (7)$$

$$V_\Sigma = \sum_{i=1}^{N_\ell} N_{inj}^i V_{inj}^i = V_{batch} \quad (8)$$

and such that

$$T_\Sigma = \max_{i=1, N_\ell} (N_{inj}^i t_{cyc}^i), \quad (9)$$

or such that

$$Y_\Sigma = \frac{\sum_{i=1}^{N_\ell} N_{inj}^i m_{out}^i}{c_{in} V_\Sigma}. \quad (10)$$

Note that for fixed time  $T_\Sigma$  and fixed batch volume  $V_\Sigma$ , the maximisation of overall productivity is equivalent to the maximisation of overall yield. Conversely, for fixed batch volume and fixed overall yield, the maximisation of productivity is equivalent to the minimisation of the overall processing time. Therefore, the optimisation problem (6-8) and (9) or (10) can be seen as a general formulation encompassing both our original optimisation problems described in Sec. 3.

The decision variables for the high-level optimal problem are  $N_\ell$ ,  $N_{inj}^i$ ,  $i = 1, N_\ell$ , and pairs  $(n^i, m^i)$  representing the entry in the  $n^i$ -th row and  $m^i$ -th column of Table

1. Naturally, the restriction  $\sum_{i=1}^{N_\ell} n^i = N$  has to hold. As  $N_{inj}^i$ , the number of injections in the  $i$ -th line, is always bounded by the problem setup, the high-level problem has

a finite search space. Note that to evaluate the overall cost function, only the values of the decision variables and the corresponding entries in Tab. 1 are needed. In particular, no numerical simulations are required. In effect, this means that we assemble an overall solution from the solutions of the low-level optimisation problem.

While we cannot expect the resulting solution to be globally optimal, it seems reasonable that we shall obtain a decent approximation.

*b) Variable configuration case:*

In the variable configuration case, the overall cost function (6) changes to

$$Pr_{\Sigma} = c_{in} \frac{\sum_{i=0}^{N_s} V_{\Sigma}(j) Y_{\Sigma}(j)}{\sum_{i=0}^{N_s} \tau(j)} \quad (11)$$

with the obvious corresponding changes in (7)-(10). The only difference in terms of the optimisation procedure is an increase of the cardinality of the search space.

From a practical point of view, the question whether a significant improvement is possible when allowing a variable configuration is of prior interest. Our example in the next section indicates that switching configuration may indeed improve performance.

## 5. NUMERICAL EXAMPLE

As an example of the proposed approach we consider a case with 5 chromatographic columns,  $N = 5$ . The numerical values of parameters and restrictions for a single column are listed in Appendix A. We investigate the maximisation of yield within a given time. The required minimal purity is 95%. Time  $T_{max}$  is equal to 20000s. Different overall batch volumes are considered.

### 5.1 Low-level optimisation

First, we solved a set of low-level optimisation problems of the form (5). Optimisation was performed for the following values of required purity:  $p_m \in \{0.9, 0.91, \dots, 0.99\}$  and for different numbers of columns in the line:  $N_{col} \in \{1, 2, 3, 4, 5\}$ . The optimal values of the continuous decision variables ( $Q^*$ ,  $V_{inj}^*$ ,  $t_{fr}^*$ ), as well as the corresponding values ( $t_{cyc}^*$ ,  $m_{out}^*$ ) were stored as a table as indicated in the previous section.

An improved derivative-free Nelder-Mead method (Nelder and Mead, 1965; Kelley, 1999) was used to solve these nonlinear constrained optimisation problems. In the proposed variant, the initial simplex was generated randomly and a multi-restart strategy was taken to increase the probability of locating the global optimum. For each subsequent restart, only the vertex with the best solution found previously was retained and the other vertices were replaced with new random points. Moreover, the algorithm was capable of handling the nonlinear constraints by using the penalty function technique. During the optimisation, a numerical simulation procedure was used to generate the outlet concentration signals for given values of decision variables. From this, we evaluate the objective function

and check the constraints. This information was then used by the optimiser to find a new direction in the continuous search space to improve the cost.

The coupled PDE model of the considered process with  $N_{col}$  columns connected in series was discretised using the method of orthogonal collocations on finite elements (Ma and Guiochon, 1991; Kaczmarski et al., 1997). The resulting system of differential algebraic equations was solved by ode15s, a variable step-size and variable order integrator implemented in Matlab (Shampine and Reichelt, 1997). Information about the Jacobian contained in the discretised model equations was fully exploited by the solver, thereby significantly accelerating the integration.

### 5.2 High-level optimisation

*a) Constant configuration case:*

Next, we solved the discrete optimisation problem (2) for the constant configuration case, as described in Sec.4.2a. The results of the optimisation procedure are presented in Tab. 2.

Volume of the batch, $V_{batch}$ , ml	Optimal configuration	Optimal purities, $Pur^i$ , %	Resulting productivity $Pr$ , g/s	Resulting yield $Y$
23000	{3 2}	0.94 0.97	5.942 e-4	0.517
25000	{3 2}	0.95 0.95	6.2404 e-4	0.4992
27000	{3 2}	0.96 0.94	6.4118 e-4	0.475
28000	{2 2 1}	0.95 0.96 0.97	6.0756 e-4	0.424
29000	{2 2 1}	0.95 0.95 0.98	6.2808 e-4	0.421
31000	{2 2 1}	0.95 0.96 0.94	6.6047 e-4	0.3901

Table 2. Results of high-level optimisation for constant configuration scenario

*b) Variable configuration case:*

It can be seen from Table 2 that the configuration {3 2} ensures high productivity for smaller batch volumes. For higher volumes, this configuration cannot process the required volume within the required time. Hence, from the certain batch volume  $V_{batch}$ , one has to use another configuration, for example {2 2 1}. This configuration ensures higher throughput at the cost of productivity. Therefore, it is intuitive to consider configuration as a time-variant degree of freedom, i.e., a control variable. In this way one expects to combine the advantages of both configurations.

We considered the case with one possible configuration change, i.e.,  $N_s = 1$ . Indeed, our optimisation results show an increase of performance for the variable configuration case. The results are shown in Table 3. It is worth noting that the improvement could be much bigger if there were bigger differences in the productivity and in the throughput between the different configurations.

## ACKNOWLEDGEMENTS

We acknowledge many helpful discussions with A. Seidel-Morgenstern, L.C. Keßler and G. Ziomek.



Volume of the batch, $V_{batch}$	Optimal configuration	Time, $\tau(j)$ , $j = 0, 1$	Volume, $V_{\Sigma}(j)$	Optimal purities, $Pur^i(j)$	Resulting productivity, $Pr_{\Sigma}$	Resulting yield, $Y_{\Sigma}$	Improvement compared to constant configuration case
28000	{2 2 1}	10600	16100	0.95 0.95 0.96	6.4305 e-4	0.4603	+5.84%
	{3 2}	9400	11900	0.95 0.95			
29000	{2 2 1}	10800	16675	0.95 0.95 0.96	6.5115 e-4	0.4509	+3.7%
	{3 2}	9200	12325	0.96 0.94			

Table 3. Results of the high-level optimisation with the change of structure

## REFERENCES

- Dünnebier, G., Engell, S., Epping, A., Hanisch, F., Jupke, A., Klatt, K.U., and Schmidt-Traub, H. (2001). Model-based control of batch chromatography. *AIChE Journal*, 47(11), 2493–2502.
- Felinger, A. and Guiochon, G. (1996). Optimizing preparative separations at high recovery yield. *Journal of Chromatography A*, 752, 31–40.
- Felinger, A. and Guiochon, G. (1998). Comparing the optimum performance of the different modes of preparative liquid chromatography. *Journal of Chromatography A*, 796(1), 59–74.
- Gao, W. and Engell, S. (2005). Iterative set-point optimization of batch chromatography. *Computers & Chemical Engineering*, 29(6), 1401–1409.
- Guiochon, G., Felinger, A., and Shirazi, S. (2006). *Fundamentals of Preparative and Nonlinear Chromatography*. Elsevier.
- Kaczmarek, K., Mazzotti, M., Storti, G., and Morbidelli, M. (1997). Modelling fixed-bed adsorption columns through orthogonal collocations on moving finite elements. *Comput. Chem. Eng.*, 21(6), 641–660.
- Kelley, C. (1999). *Iterative Methods for Optimization*. SIAM.
- Ma, Z. and Guiochon, G. (1991). Application of orthogonal collocation on finite elements in the simulation of nonlinear chromatography. *Comput. Chem. Eng.*, 15(6), 415–426.
- Nagrath, D., Bequette, B.W., and Cramer, S.M. (2003). Evolutionary operation and control of chromatographic processes. *AIChE Journal*, 49(1), 82–95.
- Nelder, J. and Mead, R. (1965). A simplex method for function minimization. *Comput. J.*, 7(4), 308–313.
- Piątkowski, W. (2006). Analysis of the design and optimization of preparative chromatography on the basis of the separation of a real post-reaction mixture. *Acta Chromatographica*, 16, 92–118.
- Shampine, L. and Reichelt, M. (1997). The MATLAB ODE suite. *SIAM J.Sci.Comput.*, 18.
- Ziomek, G., Antos, D., Tobiska, L., and Seidel-Morgenstern, A. (2006). Comparison of possible arrangements of five identical columns in preparative chromatography. *Journal of Chromatography A*, 1116, 179–188.

## Appendix A. LIST OF PARAMETERS

Name	Unit	Description	Value
<b>Physical (geometric) parameters</b>			
L	cm	Column length	25
D	cm	Column diameter	2
$\epsilon_t$	-	Column total void fraction	0.78
$\alpha_D$	-	Coefficient of the linearised van Deemter equation	0.012
$\beta_D$	-	Coefficient of the linearised van Deemter equation	0.156
$H_1$	-	Henry constant	5.7
$H_2$	-	Henry constant	7.4
$K_1$	ml/g	Equilibrium constant	170
$K_2$	ml/g	Equilibrium constant	370
<b>Operating parameters</b>			
$C_{i,in}$ , $i=A, B$	g/ml	Feed concentrations	0.001
$C_{i,thr}$	g/ml	Threshold concentrations	$0.001C_{i,in}$
$N$	-	Number of columns	5
$t_{fr}^{min}$	s	Minimal collecting (fractionating) time	5
$\Delta P_{max}$	bar	Maximal pressure drop	100
$Q_{max}$	ml/s	Volumetric flowrate corresponding to the maximal pump capacity	8.33