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Continuous Chromatographic Processes with a Small Number of Columns: Comparison of Simulated Moving Bed with Varicol, PowerFeed, and ModiCon

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Abstract−The Simulated Moving Bed process and its recent extensions called Varicol, PowerFeed and ModiCon are studied, in the case where a small number of columns are used, i.e. from three to five. A multiobjective optimization approach, using genetic algorithms and a detailed model of the multicolumn chromatographic process, is applied to optimize each process separately, and allow for comparison of the different operating modes. The non-standard SMB processes achieve better performance than SMB, due to the availability of more degrees of freedom in the operating conditions of the process, namely the way to carry out asynchronous switches for Varicol, and the different flow rates and feed concentration during the switching interval for PowerFeed and for ModiCon, respectively. We also consider the possibility of combining two non-standard operating modes in a new hybrid process, and evaluate also in this case the possible performance. Finally, a critical assessment of the results obtained and of the potential for practical implementation of the different techniques is reported.

Key words: Simulated Moving Bed, Varicol, PowerFeed, ModiCon, Chiral Separations

INTRODUCTION

Preparative chromatography, in particular Simulated Moving Bed (SMB), is now one of the most important chiral separation techniques in the pharmaceutical industry. Compared to batch elution chromatography, SMB has the advantages of higher productivity, lower solvent consumption, lower product dilution and therefore lower operating costs, and the disadvantage of higher fixed costs. For preparative and production scale separations, where the low operating cost overcomes the high fixed cost, the overall separation cost of SMB is lower than that of batch chromatography.

Two approaches have been taken to further reduce the production cost or to further improve the separation efficiency of the SMB process. The first one is to design an SMB unit with a small number of highly efficient columns, so as to reduce the inventory of the expensive chiral stationary phase (CSP). In fact, there is a clear trend in applications to operate SMB with 5 or 6 columns, instead of 8, which was previously regarded as the minimum number of columns for SMB units. The second approach aims at improving the unit's separation efficiency either by optimizing the adsorptivity of the solutes in the different sections of the unit, such as in supercritical fluid SMB [Nicoud and Perrut, 1992; Mazzotti et al., 1997b; Di Giovanni et al., 2001; Denet et al., 2001], temperature gradient SMB [Migliorini et al., 2001] and solvent gradient SMB [Jensen et al., 2000; Antos and Seidel-Morgenstern, 2001; Abel et al., 2002; Houwing et al., 2003], or more recently by operating SMB under more complex dynamic conditions, as it is the case in the Varicol [Ludemann-Hombourger et al., 2000, 2002; Zhang et al., 2002, 2003a; Toumi et al., 2003; Pais and Rodrigues, 2003], PowerFeed [Kearney and Hieb, 1992; Kloppenburg and Gilles, 1999; Zang and Wankat, 2002a, b; Zhang et al., 2003b, 2004] and ModiCon [Schramn et al., 2002, 2003] processes. These new operation modes do not keep constant conditions during one switching period t^*, as in a standard SMB, but allow for variation of the column configuration, the fluid flowrates, or the feed concentration, respectively. This means that the SMB unit is no longer treated as a simulated implementation of the True Moving Bed (TMB) process, but it is a unit to be optimized independently by exploring and exploiting all its potential flexibilities in order to improve its separation performance.

These newly emerging operational options call for new criteria to identify which is the best solution in general, or at least for a specific separation problem. The definition of such criteria is a very important goal within our research program on SMB. In this context this work has two objectives. On the one hand, we investigate and compare the optimal separation behavior of SMB, Varicol, PowerFeed and ModiCon in a unit with a small number of columns, i.e. 3, 4, or 5 columns. On the other hand, we aim at further improving the unit's flexibility by combining two of the three above mentioned new operation modes in the same process, e.g., combining Varicol with PowerFeed, and at investigating the separation performance attainable using a multiobjective optimization technique based on a genetic algorithm [Zhang et al., 2002; Bhaskar et al., 2000]. As a model system we consider the chiral separation reported else-

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‡This paper is dedicated to Professor Hyun-Ku Rhee on the occasion of his retirement from Seoul National University. The importance of the seminal papers of Professor Rhee on first order partial differential equations and the theory of multicomponent chromatography (H.-K. Rhee, R. Aris, N. R. Amundson, *Philos. Trans. Roy. Soc. London,* **A267** (1970) 419-455; **A269** (1971) 187-215) for the SMB design and optimization tools (Triangle Theory) that the authors have developed over the years cannot be overestimated.

Table 1. Characteristics of the model chiral separation system [Biressi et al., 2000]

Column configuration	L_{com}=20 cm; Section Ω=1 cm^2
Stationary phase particle size	d_p=30 μm
External porosity	ε_b=0.565
Internal porosity	ε_p=0
Maximum unit pressure drop	$(\Delta P_{unit})_{max}$=70 bar
Isotherms	$\overline{C}_A=\dfrac{1.25\cdot C_A}{1+0.125\cdot C_A+0.1\cdot C_B}$
	$\overline{C}_B=\dfrac{1\cdot C_B}{1+0.125\cdot C_A+0.1\cdot C_B}$
Pressure drop correlation	$\Delta P(\text{bar})=960\ u/d_p^2\cdot L_{col}(\text{cm})$
Van Deemter equation	$\text{HETP(cm)}=0.0005d_p(\mu\text{m})$ $+0.00165d_p^2\cdot u(\text{cm/s})+0.001/u$

where [Biressi et al., 2000], whose relevant characteristics are summarized in Table 1.

COMPARISON OF THE SMB, VARICOL, POWERFEED AND MODICON PROCESSES

SMB is a practical implementation of the TMB process, where the counter-current movement of the solid and liquid phase is simulated by periodical and simultaneous shift by one column of the inlet and outlet ports in the direction of liquid flow. A schematic diagram of a typical four-section SMB is shown in Fig. 1a. Regardless of the location of the inlet and outlet ports, the distribution of the columns in the four sections (column configuration) or the section length is constant over the entire operation period. Moreover, in the standard SMB operation, the liquid flow-rates and the feed concentration are also constant in order to maintain equivalence with the TMB process.

However, in the Varicol process proposed recently [Ludemann-Hombourger, 2000, 2002], the inlet and outlet ports are shifted in an asynchronous manner. Therefore, the column configuration and the section length are no longer constant with time. If the column configuration, represented by the parameter χ (assuming discrete values associated to SMB configurations such as 2-2-2-2, or 3-1-3-1, etc.), is changed in three even subintervals during one switching period t^*, the difference between SMB and Varicol can be schematized in Fig. 1(b), where χ is constant for SMB but variable for Varicol. In such a way, more degrees of freedom are added to the classical SMB process, making it possible to achieve better performance [Zhang et al., 2002, 2003a; Toumi et al., 2003; Pais and Rodrigues, 2003].

The PowerFeed process [Zhang et al., 2003b, 2004], as we call it, since the feed flow-rate modulation is regarded as the most important one, is in turn based on the idea of variable liquid flow-rates, which was proposed originally in a patent [Kearney and Hieb, 1992]

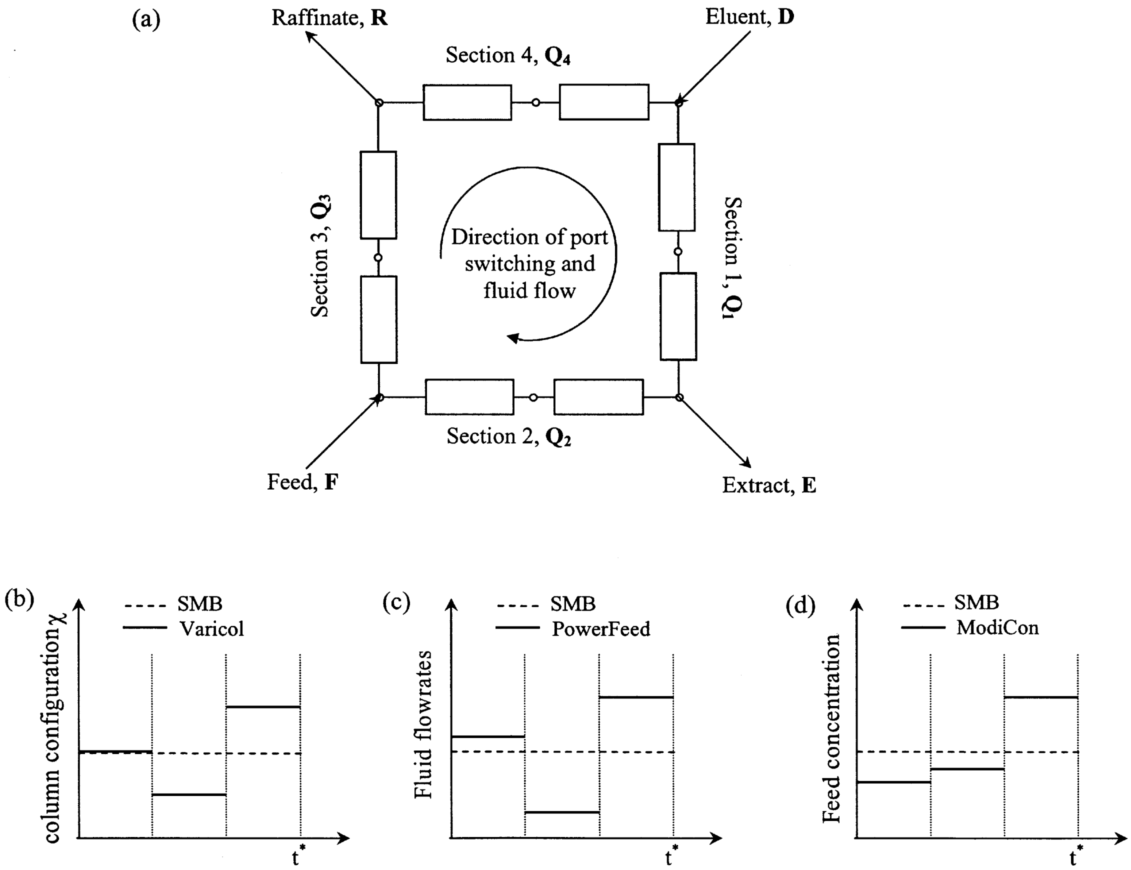

Fig. 1. (a) Schematic diagram of a 4-section SMB unit; (b) comparison of the column configuration policies of SMB and Varicol; (c) comparison of the fluid flowrates policies of SMB and PowerFeed; (d) comparison of the feed concentration policies of SMB and ModiCon.

and more recently in the scientific literature [Kloppenburg and Gilles, 1999]. The flow-rate policies for SMB and PowerFeed are compared in Fig. 1c, taking as example a PowerFeed process where t^* is divided in three subintervals. Different forms of PowerFeed processes have been investigated based on simulation studies on both linear and nonlinear separation systems [Zang and Wankat, 2002a, b; Zhang et al., 2003b, 2004]. Recently, we have been able to verify experimentally in the case of a chiral separation that the PowerFeed process can indeed outperform the SMB process [Zhang et al., 2004].

A third new SMB operation mode, ModiCon, has recently been proposed [Schramn et al., 2002, 2003], which is based on the concept of modulating the feed concentration of the SMB process during the switching period, as shown in Fig. 1d, while keeping the flow-rates and the column configuration unchanged. It was demonstrated that by cyclic modulation of the feed concentration the productivity can be increased and the eluent consumption can be reduced in a nonlinear separation system; the advantage of ModiCon over SMB was also validated experimentally [Schramn et al., 2003].

In the case of the SMB operations mentioned above, Varicol, PowerFeed and ModiCon, SMB is no longer regarded as a practical implementation of TMB, but as a unit with a larger number of degrees of freedom, which should be optimized to improve its separation performance. Figs. 1b, 1c and 1d show only one simplified column configuration, liquid flow-rates and feed concentration modulation example for Varicol, PowerFeed and ModiCon, respectively. In principle, one can conceive different cyclic modulation forms, e.g., uneven subintervals, larger subinterval number, or continuous variation of flow-rates and feed concentration. In order to keep the decision variables for the optimization relatively small, a simplified PowerFeed operation is considered in this work, where the feed flow-rate, F, only is varied in S equal subintervals, whereas Q_1, Q_2, and Q_4 are kept constant. Also Q_3 and the raffinate flow-rate, R, vary in time as a result of mass balance; in fact $Q_3=Q_2+F$, and $R=Q_3-Q_4$.

MATHEMATIC MODEL AND MULTIOBJECTIVE OPTIMIZATION PROCEDURES

The same stage model used in previous works [Zhang et al., 2003a] that has been extended to allow for column configuration, feed flow-rate and feed concentration to vary in time, has been adopted to simulate the SMB, Varicol, PowerFeed and ModiCon processes. We have selected the multiobjective optimization problem where one wants to simultaneously maximize the purity of the extract, where the desired product is collected, and the productivity, while keeping above a minimum value the raffinate purity, 90% in this case, to guarantee a good recovery of the desired product, and below the maximum the overall pressure drop. Moreover, we consider a plant with 3 to 5 columns of a given size. The optimization problem is described mathematically as follows [Zhang et al., 2003a]:

Max	$J_1=M_A^E/(M_A^E+M_B^E)=P_E\,[Q_1, \mathbf{F}, m_1, m_2, m_4, \mathbf{C}_T^F, \chi]$	(1a)
Max	$J_2=F\cdot C_T^F/V_{solid}=\text{Prod}\,[Q_1, \mathbf{F}, m_1, m_2, m_4, \mathbf{C}_T^F, \chi]$	(1b)
Subject to	$P_R=M_B^R/(M_A^R+M_B^R)\geq 90\%$	(1c)
	$\Delta P_{unit}\leq 70$ bar	(1d)
	$C_{T,ave}^F=8$ g/l and for ModiCon, $C_{T,j}^F\leq 12$ g/l	(1e)
	$L_{col}=20$ cm, $\Omega=1$ cm^2 and fixed values of N_{col}	(1f)

where extract purity, P_E and productivity, Prod are the two objective functions to be maximized; M_i^E and M_i^R are the masses of component i collected in the extract and in the raffinate, respectively, during one switching period at cyclic steady state. The optimization variables are the flow rate in section 1, Q_1, the feed flow rate, F, the flow rate ratios, m_1, m_2 and m_4, the total feed concentration C_T^F (with equimolar composition of the two enantiomers), and the unit configuration represented by the parameter, χ. By fixing Q_1, F, m_1, m_2 and m_4, the five operating variables Q_1, Q_2, Q_3, Q_4 and t^* are univocally determined through Eq. (2) defining the flow-rate ratio m_j [Mazzotti et al., 1997a]

$$m_j=\frac{Q_j t^*-V_{col}\varepsilon}{V_{col}(1-\varepsilon)} \quad (j=1, ..., 4) \tag{2}$$

and the mass balance relationship $F=Q_3-Q_2$.

For SMB, Varicol and PowerFeed, C_T^F is fixed as the average feed concentration, 8 g/l, while for ModiCon C_T^F represents an S-size vector of total feed concentration values in the S subintervals of the switching period t^*, i.e. $[C_{T,1}^F \ldots C_{T,S}^F]$, under the constraints that the average concentration is anyhow 8 g/l, and that the maximum concentration is not larger than 12 g/l, which in this work represents the solubility limit. Once the average feed concentration is fixed, only the concentrations in (S-1) subintervals are independent and therefore used as decision variables for ModiCon optimization. Feed flow-rate, F, for PowerFeed and unit configuration, parameter χ for Varicol in Eqs. (1a) and (1b) are also vectors, representing all the feed flowrate values and column configurations in the S subintervals for PowerFeed and Varicol, respectively. For example, if there are three subintervals (S=3) during a switching period, the decision variables are Q_1, F, m_1, m_2, m_4 and χ for SMB; Q_1, F, m_1, m_2, m_4, χ_1, χ_2 and χ_3 for Varicol; Q_1, F_1, F_2, F_3, m_1, m_2, m_4 and χ for PowerFeed; and Q_1, F, m_1, m_2, m_4, $C_{T,1}^F$, $C_{T,2}^F$ and χ for ModiCon.

In addition, a minimum 90% purity of the raffinate product and a maximum 70 bar pressure drop along the entire unit are required

Table 2. Possible column configurations (distribution) for N_{col}=5, 4 and 3

χ	Column configuration[#]	χ	Column configuration
	$N_{col}=5$		
A	2/1/1/1	C	1/1/2/1
B	1/2/1/1	D	1/1/1/2
	$N_{col}=4$		
χ	Column configuration	χ	Column configuration
A	1/1/1/1	E	2/1/1/0
B	0/2/1/1	F	1/2/1/0
C	0/1/2/1	G	1/1/2/0
D	0/1/1/2		
	$N_{col}=3$		
χ	Column configuration	χ	Column configuration
A	0/1/1/1	C	1/1/0/1
B	1/0/1/1	D	1/1/1/0

[#]Column distribution 2/1/1/1 means 2 columns in section 1 and one column in sections 2 to 4.

and given as constraints to the optimizer. The column length L_{col} and the column cross section Ω, with $V_{col}=L_{col}\Omega$, are fixed at 20 cm and 1 cm^2, respectively. Various values of the total number of columns N_{col} (5, 4 and 3) have been considered to study the separation performance of SMB, Varicol, PowerFeed and ModiCon, but in each optimization run the value of N_{col} has been kept fixed. The column configurations considered in this work are listed in Table 2. One should refer to the proper N_{col} category to look up the column configuration corresponding to a given χ parameter value, e.g. χ= B represents 1/2/1/1 for N_{col}=5, 0/2/1/1 for N_{col}=4 and 1/0/1/1 for N_{col}=3. Optimizations were carried out using the genetic algorithm, described in detail elsewhere [Zhang et al., 2002; Bhaskar et al., 2000].

RESULTS AND DISCUSSION

1. Optimization of SMB, Varicol, PowerFeed and ModiCon

The optimization results for the SMB, Varicol, PowerFeed and ModiCon processes are reported in Table 3 in the case of units with five columns: N_{col}=5. It is seen that as required the constraints on the raffinate purity P_R and on the overall pressure drop ΔP_{unit} are always satisfied. In particular, the value of P_R is always equal to its lower bound, 90%, as a consequence of maximizing P_E and productivity, while the value of ΔP_{unit} is always far below its upper bound, i.e., 70 bar. With the productivity increasing, the overall pressure drop (in the unit) increases, and the column efficiency in terms of number of theoretical plates, N_{NTP}, decreases. Since the particle size used in this work is rather large, d_p=30 μm, columns are not very efficient and low liquid flow-rates yield a better separation performance. The optimal separation performances of the 5-column SMB, Varicol, PowerFeed and ModiCon, in terms of the two objective functions, i.e. productivity and P_E, are compared in Fig. 2, where a different Pareto curve [Bhaskar et al., 2000] is obtained for each operation mode. It can readily be seen that increasing productivity yields a decrease of the maximum possible extract purity, as intuitively expected. All the three new, non-standard operating modes, i.e. Varicol, PowerFeed and ModiCon, perform better than SMB, in that for a given productivity they can achieve higher P_E or for a given P_E they can operate at higher productivity. For example, at Prod= 74.9 g/(l day), the P_E value increases from 89.6% for SMB, to 92.6% for Varicol, to 93.5% for PowerFeed, and to 93.7% for ModiCon. It is worth noting that there is a significant change from SMB to Varicol, i.e., 3% in P_E, whereas smaller differences are found among the three non-standard operating modes, being the maximum difference in P_E only 1%.

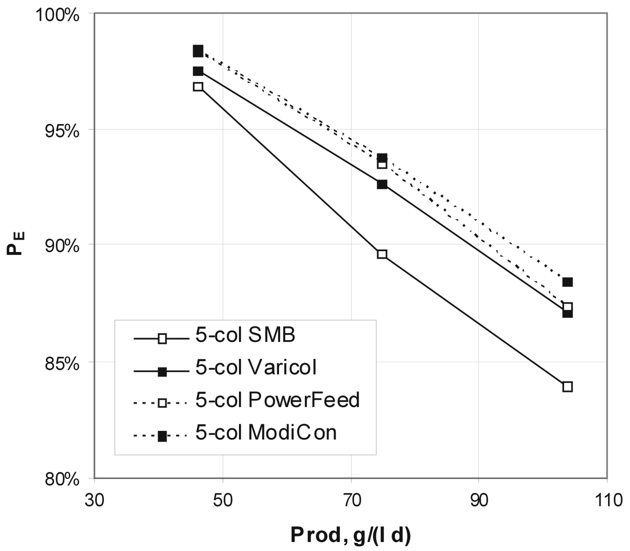

Fig. 2. Comparison of the optimal separation performances of the 5-column SMB, Varicol, PowerFeed and ModiCon processes.

The optimal column configuration for SMB and for Varicol changes from B (1/2/1/1) to C (1/1/2/1) and from C-B-B to C-C-B with increasing productivity or decreasing P_E, as shown in Table 3. The section of the unit with more than one column is mostly section 2 (configuration B for SMB and C-B-B for Varicol) when extract purity is large, and it is mostly section 3 (configuration C for SMB and C-C-B for Varicol) when extract purity decreases. The same trend was reported elsewhere [Zhang et al., 2003a]. In the case of PowerFeed, the optimal separation performance can be obtained

Table 3. Optimization results for SMB, Varicol, PowerFeed and ModiCon processes with N_{col}=5

Process	Prod. (g/*l* d)	Q_1 (ml/min)	m_1	m_2	m_4	$C_T^F(x_A=x_B=0.5)$ (g/*l*)	F (ml/min)	χ	N_{NTP}	ΔP_{unit} (bar)	P_R %	P_E %
SMB	46.1	22.775	1.434	0.911	0.762	8	0.40	B	41	33.99	90.04	96.86
	74.9	26.807	1.542	0.828	0.746	8	0.65	B	37	38.03	90.03	89.63
	103.7	30.415	1.362	0.836	0.664	8	0.90	C	31	45.46	90.15	83.92
Varicol	46.1	21.327	1.407	0.918	0.738	8	0.40	C-B-B	43	32.21	90.09	97.50
	74.9	27.998	1.441	0.864	0.704	8	0.65	C-B-B	34	41.26	90.11	92.63
	103.7	30.364	.437	0.817	0.622	8	0.90	C-C-B	32	44.06	90.05	87.13
PowerFeed	46.1	23.629	1.480	0.933	0.660	8	0.01-0.02-1.17	B	40	34.98	90.11	98.32
	74.9	27.382	1.466	0.859	0.683	8	0.00-0.02-1.93	B	35	40.19	90.05	93.52
	103.7	29.025	1.430	0.788	0.705	8	0.01-0.04-2.65	B	33	42.52	90.06	87.33
	103.7	31.128	1.418	0.828	0.555	8	1.31-1.39-0.00	C	31	45.59	90.06	87.22
ModiCon	46.1	22.129	1.419	0.923	0.719	0.05-11.99-11.96	0.40	B	42	33.15	90.02	98.41
	74.9	29.430	1.590	0.865	0.721	0.00-12.00-12.00	0.65	B	34	41.52	90.02	93.72
	103.7	30.966	1.487	0.802	0.700	0.01-11.99-12.00	0.90	B	32	44.14	90.01	88.43
	74.9	29.446	1.489	0.878	0.701	0.06-6.07-17.87	0.65	B	33	42.73	90.06	94.67

by introducing almost all the feed flow in the third subinterval so that there is almost no feed flow in the first two subintervals. This is different from the optimal feed flow-rate variation policies reported earlier [Zang and Wankat, 2002a, b; Zhang et al., 2003b, 2004], thus demonstrating that the optimal feed strategy for PowerFeed is indeed system dependent. Unlike SMB and Varicol, the optimal

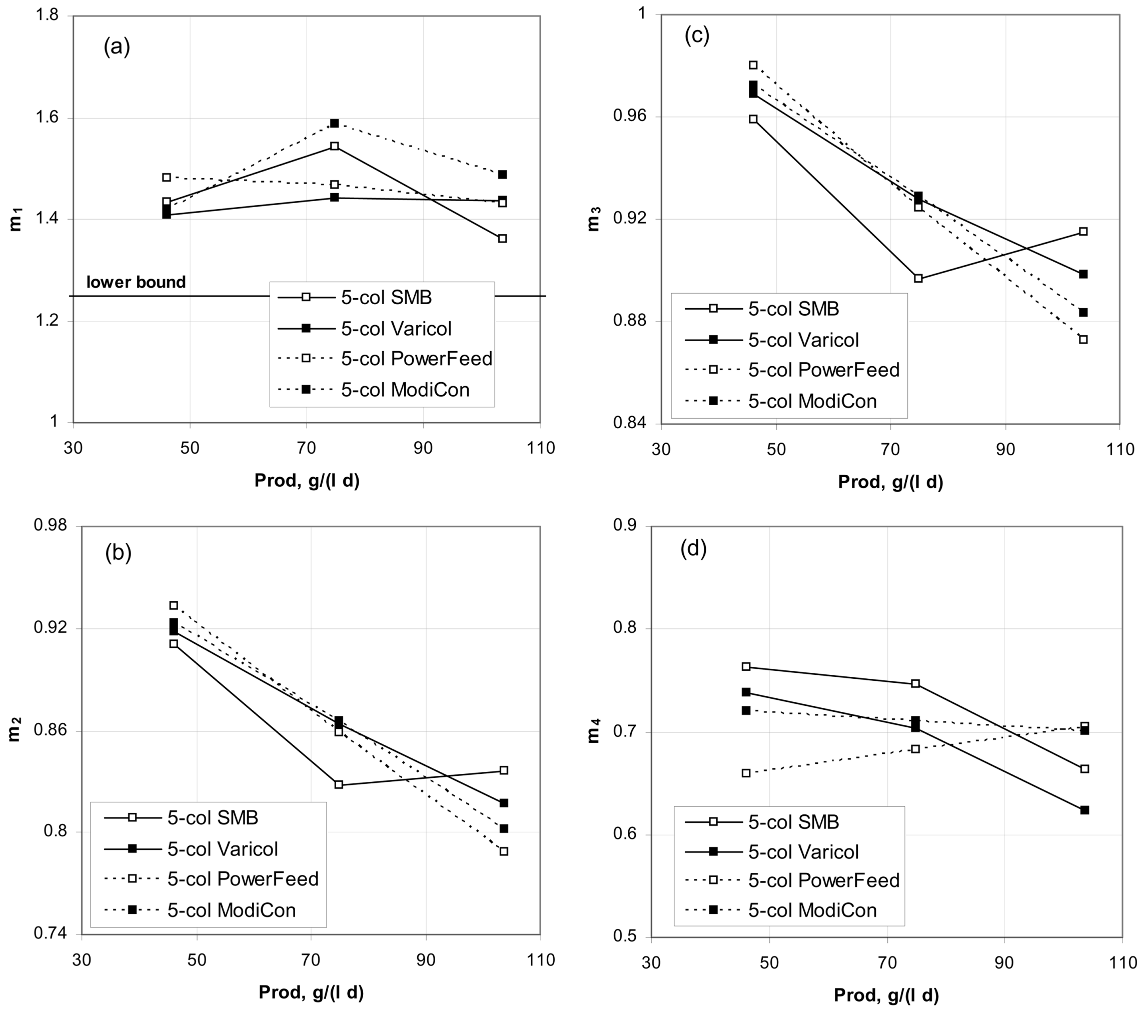

Fig. 3. Comparison of the optimal flowrate ratio parameter m values of the 5-column SMB, Varicol, PowerFeed and ModiCon processes.

Table 4. Optimization results for SMB, Varicol, PowerFeed and ModiCon processes with N_{col}=4

Process	Prod. (g/*l* d)	Q_1 (ml/min)	m_1	m_2	m_4	$C_T^F(x_A=x_B=0.5)$ (g/*l*)	F (ml/min)	χ	N_{NTP}	ΔP_{unit} (bar)	P_R %	P_E %
SMB	43.2	17.482	1.500	0.901	0.002	8	0.30	F	52	20.96	90.08	95.62
	72.0	21.726	1.365	0.889	0.001	8	0.50	G	41	27.11	90.06	88.61
	115.2	23.858	1.419	0.798	0.007	8	0.80	G	39	28.69	90.01	82.55
Varicol	43.2	20.088	1.579	0.947	0.288	8	0.30	B-G-F	48	24.08	90.10	98.63
	72.0	21.884	1.530	0.856	0.366	8	0.50	B-G-F	45	26.52	90.09	93.64
	115.2	26.252	1.535	0.792	0.147	8	0.80	A-G-F	38	30.56	90.07	85.18
PowerFeed	43.2	17.197	1.364	0.930	0.002	8	0.01-0.01-0.88	F	50	21.79	90.04	98.43
	72.0	22.097	1.418	0.867	0.019	8	0.01-0.09-1.40	F	41	27.14	90.10	94.03
	115.2	25.365	1.547	0.776	0.007	8	0.02-0.04-2.34	F	38	29.58	90.06	86.50
	115.2	26.278	1.408	0.809	0.004	8	1.24-1.16-0.00	G	35	32.05	90.01	85.71
ModiCon	43.2	16.158	1.420	0.919	0.000	0.11-11.93-11.96	0.30	F	55	19.91	90.03	98.22
	72.0	20.925	1.444	0.854	0.003	0.07-11.97-11.96	0.50	F	44	25.13	90.04	93.52
	72.0	21.823	1.381	0.870	0.002	11.97-11.97-0.06	0.50	G	41	26.96	90.23	92.00
	115.2	25.303	1.551	0.769	0.002	0.01-11.99-12.00	0.80	F	39	28.86	90.03	85.38

column configuration for PowerFeed is always B (1/2/1/1) even at low extract purity. In order to confirm this observation, another optimization run for the 5-column PowerFeed was carried out by fixing χ= C. It can be seen from the corresponding optimization results, reported also in Table 3, that a different F variation policy is obtained, which requires that the whole feed be introduced in the first two subintervals with an even distribution and that no feed flow be present in the last subinterval. However, this PowerFeed operation does not perform better than the PowerFeed with χ=B. The best separation performance is achieved by using the ModiCon mode, which allows the feed concentration to vary its value in three subintervals having the same average total feed concentration, 8 g/*l*, and not overcoming an upper constraint, 12 g/*l*. The optimal feed concentration variation policy, as reported in Table 3, implies that pure solvent be fed in the first subinterval, while a feed flows with the maximum feed concentration (12 g/*l*) be fed during the last two subintervals. A similar policy was also reported elsewhere [Schramn et al., 2002, 2003]. Like PowerFeed, the optimal column configuration for ModiCon is always B. Another optimization run at productivity=74.9 g/(*l* d) for ModiCon was carried out by relaxing the upper feed concentration constraint to 18 g/*l*. From the optimization results reported in Table 3, one can see that in this case the optimal feed concentration modulation policy is different from the case where $C^F_{T,j}$<12 g/*l*, and that a higher P_E is obtained. This leads to the conclusion that the best ModiCon operation is where the solute is fed as late as possible during a switching period.

The optimization results reported in Table 3 can be physically interpreted in the frame of triangle theory, in terms of the flowrate ratio parameters, m_j defined in Eq. (2). In Fig. 3, it is seen that for all operation modes, m_1 is larger than its lower bound and m_4 is smaller than its upper bound as defined by triangle theory [Mazzotti et al., 1997a]. This implies that enough solvent has been used to achieve sufficient regeneration of the solid and the liquid phases in sections 1 and 4, respectively. In this respect, it is worth noting that in this work solvent consumption is neither minimized nor constrained. The operating parameters m_2 and m_3 decrease as productivity increases, and this is fully consistent with the fact that this is accompanied by a decrease of extract purity [Mazzotti et al., 1997a]. This trend is not followed in the case of SMB, where the values of m_2 and m_3 go through a minimum value due to the column configuration change from B to C, as reported previously [Zhang et al., 2002, 2003a].

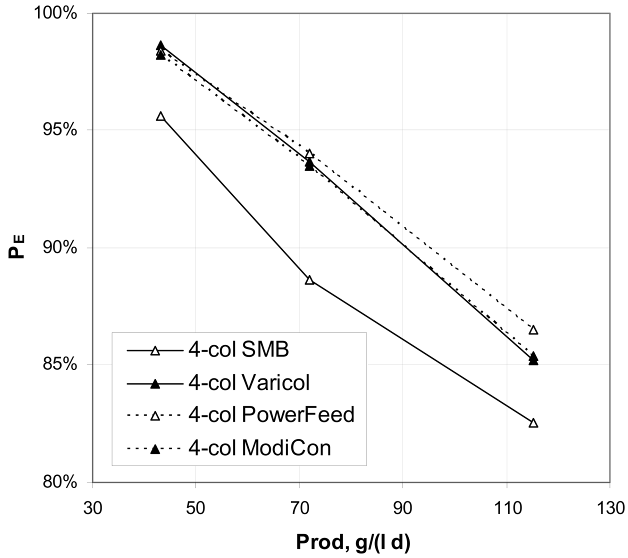

Fig. 4. Comparison of the optimal separation performances of the 4-column SMB, Varicol, PowerFeed and ModiCon processes.

The optimization of the SMB, Varicol, PowerFeed and ModiCon processes was also carried out in a unit with an even smaller number of columns: N_{col}=4 or 3. This is obtained by removing one or two columns while the column size is unchanged, so as to reduce the inventory of the stationary phase. For N_{col}=4, seven column configurations (reported in Table 2) were considered, which include not only the 4-section configuration 1/1/1/1 but also the 3-section configurations, i.e., no column in section 1 or 4. The optimization results with N_{col}=4 are reported in Table 4 for all processes, and their optimal separation performances are compared graphically in Fig. 4. Like in the case when N_{col}=5, Varicol, PowerFeed and ModiCon can achieve better separation performance than SMB, with PowerFeed performing slightly better than Varicol and ModiCon. The optimal column configuration for SMB changes from F (1/2/1/0) to G (1/1/2/0) with productivity increasing or P_E decreasing. No col-

Table 5. Optimization results for SMB, Varicol, PowerFeed and ModiCon processes with N_{col}=3

Process	Prod. (g/*l* d)	Q_1 (ml/min)	m_1	m_2	m_4	$C^F_T(x_A=x_B=0.5)$ (g/*l*)	F (ml/min)	χ	N_{NTP}	ΔP_{unit} (bar)	P_R %	P_E %
SMB	38.4	11.086	1.462	0.924	0.052	8	0.2	D	77	10.36	90.05	93.09
	57.6	13.422	1.421	0.873	0.002	8	0.3	D	65	12.50	90.00	88.50
	96.0	15.591	1.485	0.772	0.054	8	0.5	D	59	13.97	90.00	79.48
Varicol	38.4	11.623	1.496	0.930	0.411	8	0.2	A-D-D	78	10.79	90.18	94.06
	57.6	15.008	1.563	0.892	0.479	8	0.3	A-D-D	63	13.61	90.01	89.66
	96.0	16.347	1.696	0.780	0.528	8	0.5	A-D-D	62	14.06	90.06	81.49
PowerFeed	38.4	10.526	1.339	0.918	0.002	8	0.02-0.57-0.01	D	78	10.24	90.03	97.14
	57.6	14.011	1.395	0.886	0.004	8	0.00-0.90-0.00	D	61	13.38	90.09	93.50
	96.0	17.392	1.453	0.805	0.073	8	0.00-1.48-0.02	D	52	16.16	90.06	85.42
ModiCon	38.4	10.579	1.295	0.932	0.006	0.10-11.95-11.95	0.2	D	77	10.30	90.05	94.72
	57.6	13.517	1.349	0.900	0.008	0.10-11.99-11.91	0.3	D	63	12.89	90.03	91.28
	96.0	16.254	1.416	0.823	0.016	0.00-12.00-12.00	0.5	D	55	14.99	90.01	85.03

umn is utilized in section 4, meaning that the liquid stream from section 3, after partial withdrawal from the raffinate port, is recycled directly to section 1. Therefore, very low values of m_4 are necessary to minimize the pollution of the extract by the weakly adsorbed component. Depending on the productivity value, the optimal column configuration for Varicol is B-G-F or A-G-F, which, using the notation based on timed-average column lengths [Ludemann-Hombourger et al., 2000], corresponds to 0.67/1.67/1.33/0.33 or 1/1.33/1.33/0.33, which is very close to the result reported recently and obtained for a different separation [Toumi et al., 2003], i.e., 0.83/1.45/1.39/0.34. The same optimal feed flowrate and feed concentration modulation policies as in the case when N_{col}=5 are obtained for the 4-column PowerFeed and ModiCon processes, respectively, always with the optimal column configuration χ=F. Two comparison runs with column configuration G, one for PowerFeed and ModiCon each, result in different policies but lower P_E values, as reported in Table 4.

For a 3-column unit, there is at least one section without any column, so only the four different column configurations reported in Table 2 are possible. The optimization results are reported in Table 5 for all processes and their separation performances are compared

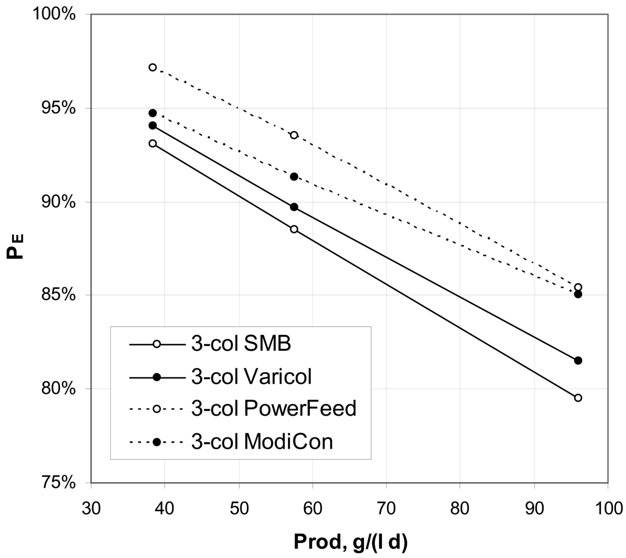

Fig. 5. Comparison of the optimal separation performances of the 3-column SMB, Varicol, PowerFeed and ModiCon processes.

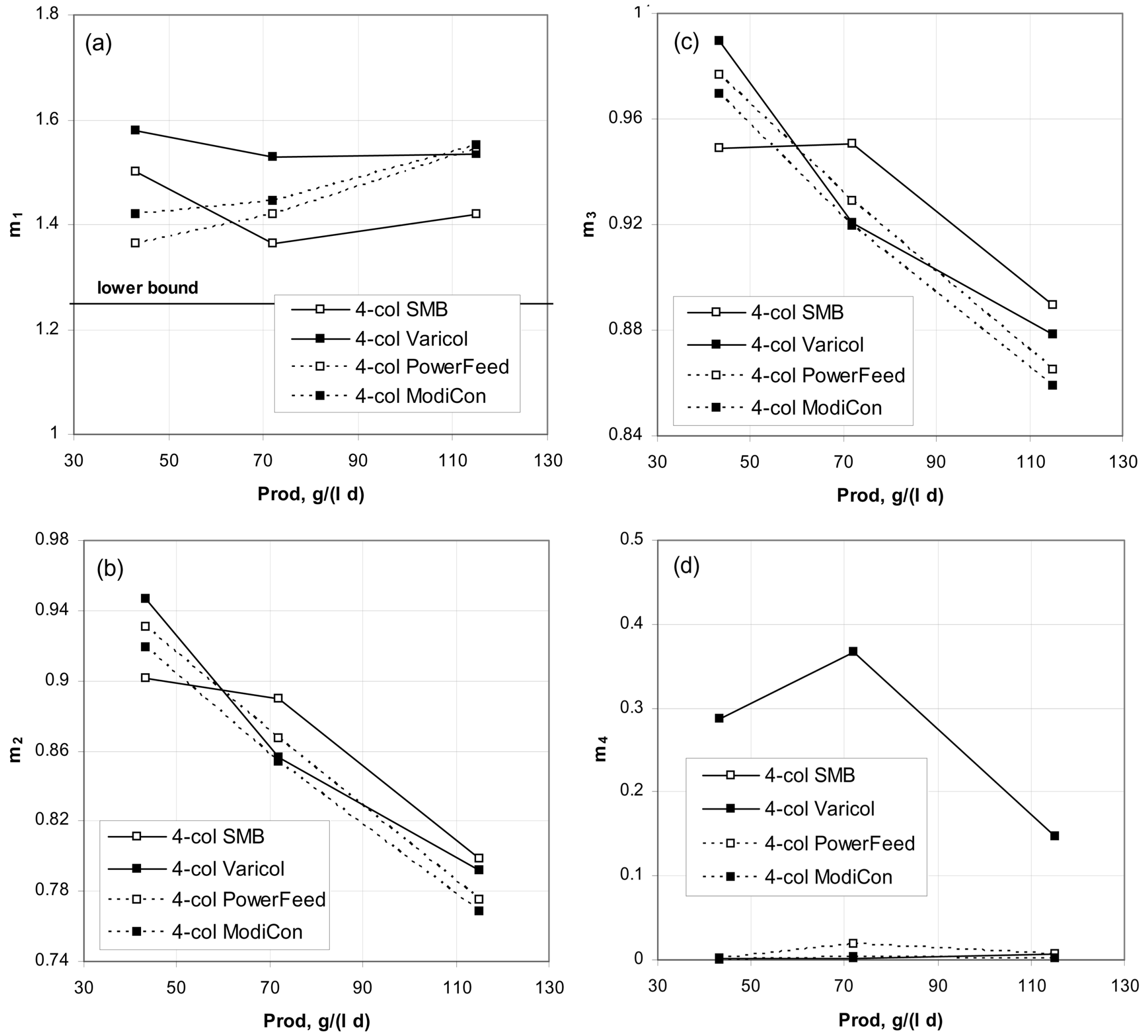

Fig. 6. Comparison of the optimal flowrate ratio parameter m values of the 4-column SMB, Varicol, PowerFeed and ModiCon processes.

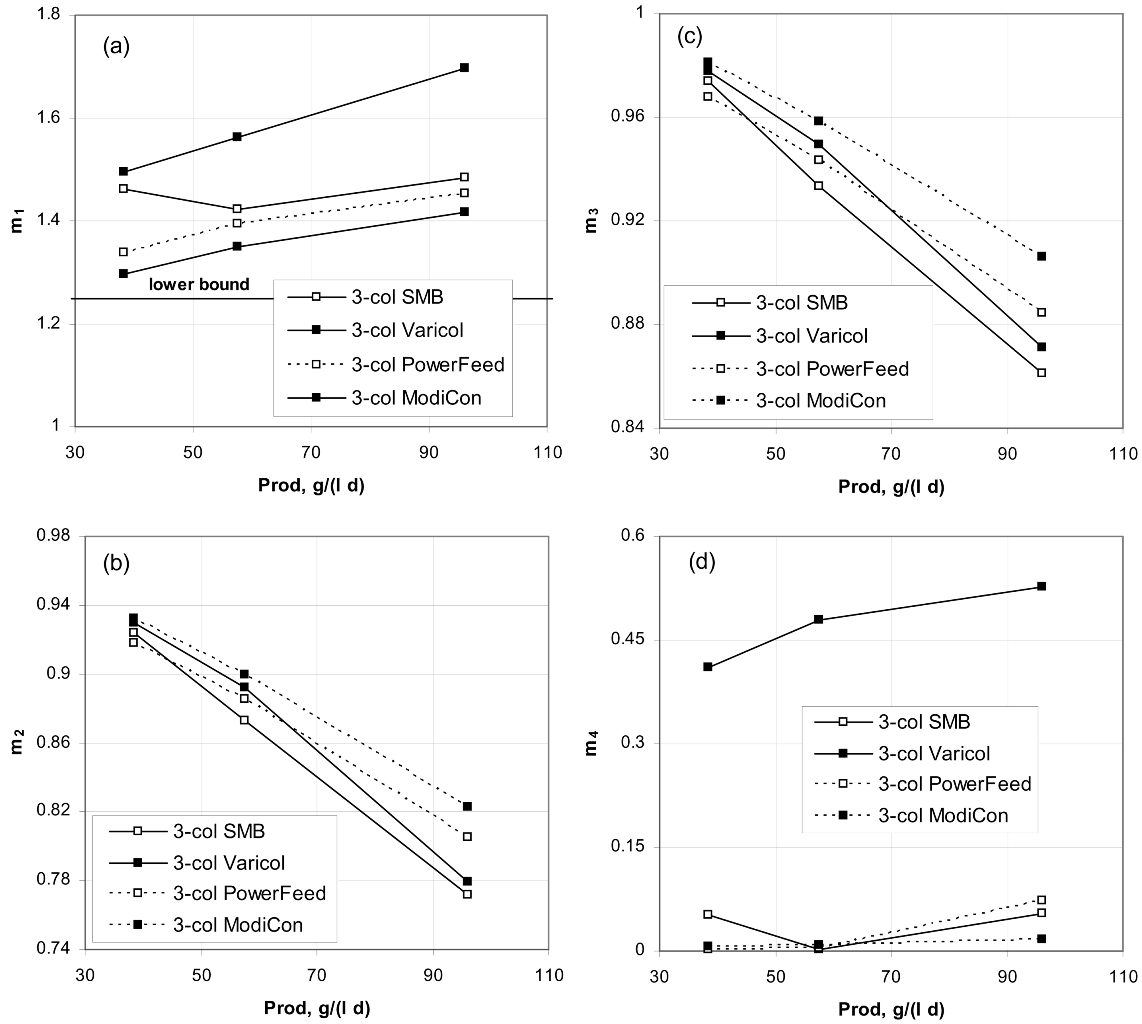

Fig. 7. Comparison of the optimal flowrate ratio parameter m values of the 3-column SMB, Varicol, PowerFeed and ModiCon processes.

in Fig. 5. The best performance can be obtained with PowerFeed, followed by ModiCon, Varicol and SMB. The optimal column configuration is always D (1/1/1/0) for SMB, PowerFeed and ModiCon, while for Varicol it is A-D-D, which corresponds to 0.67/1/1/0.33 based on the timed-average column lengths, also similar to the 0.29/1.21/1.15/0.35 reported elsewhere [Toumi et al., 2003]. The same optimal feed concentration policy as with N_{col}=4 and 5 is obtained for the 3-column ModiCon process, whereas for PowerFeed operation all the feed stream should be introduced during the second subinterval instead of during the last subinterval as in the case of the 4 and 5-column unit. This indicates that the optimal feed policy for the PowerFeed process is also dependent on the total number of columns. Nevertheless, it is also clear that PowerFeed has a remarkably good potential to improve performance with respect to the other modes when a small number of columns is used.

The optimal values of the flow-rate ratio parameters m_j are plotted in Fig. 6 and Fig. 7 for N_{col}=4 and N_{col}=3, respectively. The results are similar to those where N_{col}=5, with the only difference that the m_4 values are very close to zero for SMB, PowerFeed and ModiCon, since section 4 has no column in these cases. It should be noted that the optimal operating points calculated in this work are always outside the SMB complete separation region in the (m_2, m_3) plane as defined through triangle theory and shown in Fig. 8 [Mazzotti et al., 1997a]. This is due first to the high productivity and therefore relatively low product purities achieved; secondly, the actually complete separation region for a SMB unit with a small number of columns is smaller than that plotted by using equilibrium theory, which is based on the assumption of perfect equivalence between SMB and TMB. As a matter of fact, such equivalence is weaker and weaker with a decreasing number of columns [Storti et al., 1988]. This observation explains why the operating points in Fig. 8, which are very close to the complete separation region, achieve only relatively low purities. It is also worth noting again that only the 3-column SMB has only one possible configuration, D (1/1/1/0); hence the points in the operating plane in Fig. 8 for N_{col}=3 belong to a straight line. On the contrary, in the case of 4- and 5-column SMB the optimal configuration changes when increasing the productivity (see Tables 3 and 4), and the corresponding points in the (m_2, m_3) plane do not lie on straight lines.

In Fig. 9, for each overall number of columns, N_{col} value, the performance of the SMB operation is compared to that of the non-standard process that achieves the best performance: ModiCon for 5-column unit, and PowerFeed for 4-column and 3-column units (see Tables 3, 4 and 5). In general, the Pareto set for a unit with a larger

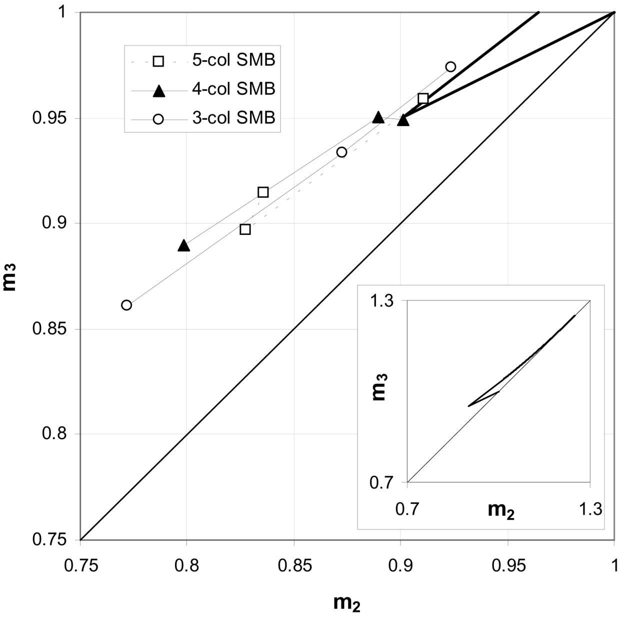

Fig. 8. Optimal operating points of 5-, 4- and 3-column SMBs in the (m_2, m_3) plane, together with the complete separation region calculated according to triangle theory with C_T^F= 8 g/*l* [Mazzotti et al., 1997a].

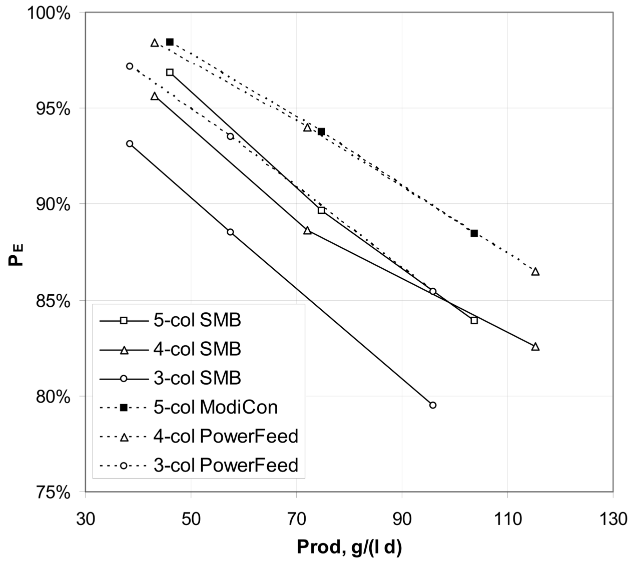

Fig. 9. Comparison of the optimal separation performances of the 5-column SMB and ModiCon in Fig. 2, the 5-column SMB and PowerFeed in Fig. 4, and the 3-column SMB and PowerFeed in Fig. 5.

number of columns is above that for a unit with a smaller number of columns--better performance is achieved with more columns. This is true for SMB even though the difference between four and five columns is rather small. It is also true for the non-standard operation modes, although also in this case the Pareto set of the 4-column PowerFeed and that of the 5-column ModiCon practically overlap (as a matter of fact, also the Pareto set for the 5-column PowerFeed is very similar to these, as shown in Fig. 2). These results indicate that for this particular case the PowerFeed operation mode is never worse that the others, i.e., standard SMB, as well as Varicol and ModiCon. It can also be observed that the 3-column PowerFeed process achieves a similar separation performance as that of the 5-column SMB, a unit that requires a much higher investment cost.

2. Combination of Varicol, PowerFeed and ModiCon in One Unit

It has been shown above that Varicol, PowerFeed and ModiCon perform better than the corresponding SMB, because in these cases more degrees of freedom are available to be adjusted to improve the separation behavior. Therefore, it is possible that the separation performance can be further improved by combining any two or all of Varicol, PowerFeed and ModiCon modes to obtain a new hybrid operation mode. For example, Varicol+PowerFeed, the combination of Varicol and PowerFeed, can be obtained by allowing the unit to change both its column configuration and its liquid flow-rates during the switching period, t^*. In the following, we will investigate the three possible binary combinations: Varicol+PowerFeed, Varicol+ModiCon, and PowerFeed+ModiCon. For the sake of simplicity, the optimization will be carried out at fixed value of productivity, by maximizing the extract purity. The optimization problem can be formulated as follows:

Max $\quad J_1=M_A^E/(M_A^E+M_B^E)=P_E\ [Q_1, \mathbf{F}, m_1, m_2, m_4, \mathbf{C}_T^F, \chi]$ (3a)

Subject to $\quad P_R=M_B^R/(M_A^R+M_B^R)\geq 90\%$ (3b)

$\Delta P_{unit}\leq 70$ bar (3c)

Table 6. Optimization results for different combinations of Varicol, PowerFeed and ModiCon with N_{col}=5, 4 and 3

N_{col}	Process[#]	Prod. (g/*l* d)	Q_1 (ml/min)	m_1	m_2	m_4	$C_T^F(x_A=x_B=0.5)$ (g/*l*)	F (ml/min)	χ	N_{NTP}	ΔP_{unit} (bar)	P_R %	P_E %
5	V+P	74.9	28.297	1.518	0.866	0.728	8	0.00-0.01-1.94	C-B-B	34	41.20	90.02	93.74
	V+M	74.9	27.766	1.513	0.870	0.696	11.84-0.89-11.27	0.65	C-B-B	35	40.18	90.12	93.79
	P+M	74.9	27.702	1.489	0.867	0.660	2.25-10.31-11.92	0.00-0.01-1.30	B	35	40.20	90.05	94.64
4	V+P	72.0	22.816	1.449	0.874	0.001	8	0.01-0.05-1.44	G-F-F	40	27.87	90.08	94.28
	V+M	72.0	20.607	1.489	0.854	0.391	12.00-11.90-0.10	0.50	B-G-F	47	24.66	90.12	94.54
	P+M	72.0	21.719	1.432	0.872	0.002	3.86-11.03-11.75	0.00-0.03-0.99	F	42	26.49	90.02	95.09
3	V+P	96.0	17.924	1.582	0.810	0.467	8	0.00-0.00-1.50	A-D-D	55	16.23	90.10	87.46
	V+M	96.0	16.565	1.560	0.818	0.448	11.97-0.15-11.88	0.50	A-D-D	59	14.79	90.08	85.25
	P+M	96.0	16.696	1.447	0.805	0.002	4.67-11.93-10.39	0.00-1.00-0.00	D	54	15.39	90.01	87.12

[#]V, P and M represent Varicol, PowerFeed and ModiCon, respectively.

$C^F_{T,j} \leq 12$ g/*l* (3d)

Fixed productivity value for each N_{col}, i.e.

$$\mathbf{Prod} = (F_1 C^F_{T,1} + F_2 C^F_{T,2} + F_3 C^F_{T,3})/(3V_{solid}) \quad (3e)$$

L_{col}=20 cm, Ω=1 cm^2 and fixed values of N_{col} (3f)

For each N_{col} value, one of the SMB runs reported previously is selected as the basis for comparison, e.g., the 5-column SMB run with Prod=74.9 g/(l d) and F=0.65 ml/min in Table 3. For the Varicol+PowerFeed operation, the decision variables are Q_1, F_1, F_2, m_1, m_2, m_4, χ_1, χ_2 and χ_3, while F_3 can be calculated from Eq. (3e) where $C^F_{T,1}=C^F_{T,2}=C^F_{T,3}=8$ g/*l*. Similarly for the Varicol+ModiCon process, the decision variables are Q_1, m_1, m_2, m_4, $C^F_{T,1}$, $C^F_{T,2}$, χ_1, χ_2 and χ_3, while $C^F_{T,3}$ can be calculated from Eq. (3e) where $F_1=F_2=F_3=0.65$ ml/min. The decision variables for the PowerFeed+ModiCon process are Q_1, F_1, F_2, F_3, m_1, m_2, m_4, $C^F_{T,1}$, $C^F_{T,2}$ and χ, with $C^F_{T,3}$ calculated from Eq. (3e). It should be noted that in all the cases, $C^F_{T,j}$ is upper bounded by the maximum concentration, i.e. 12 g/*l*.

The optimization results for these combined, hybrid processes are reported in Table 6. Comparing these to those in Table 3, one can see that at Prod=74.9 g/(*l* d) for N_{col}=5, any combination of two operation modes results in a higher P_E value than what is achievable with either single operation mode–either Varicol, PowerFeed, or ModiCon; however, the improvement is not significant. The highest P_E, 94.64% (about 5% and 0.9% higher than that of the SMB and ModiCon processes reported in Table 3, respectively), is obtained with the combination PowerFeed+ModiCon, which requires that almost all the feed be introduced in the last subinterval as in the optimal single PowerFeed, and that the feed fed during the last two subintervals contains the highest feed concentration as in the optimal single ModiCon. A similar situation occurs also where N_{col}=4, since the PowerFeed+ModiCon mode achieves the highest P_E value of 95.09%, i.e., 6.5% and 1.0% higher than the P_E value of SMB and PowerFeed reported in Table 4, respectively. With N_{col}=3, the best separation performance is obtained when Varicol is combined with PowerFeed, P_E=87.46%, which is 8.0% and 2.0% higher than the P_E value of SMB and PowerFeed reported in Table 5, respectively. It is remarkable that the improvement increases with decreasing N_{col} value.

CONCLUSIONS

In this work we have investigated numerically the separation performance of the three newly proposed extensions of an SMB process: Varicol, PowerFeed and ModiCon. These are based on asynchronous port shift, variable liquid flow-rates, and variable feed concentration during the switching period, respectively. Units with a small number of columns, between three and five, have been considered, since they look more promising for future applications of the SMB and related technologies. The analysis involves the comparison of the optimal separation performance that each operating mode can achieve; this is computed by carrying out a multiobjective optimization using a genetic algorithm and a detailed model of the multicolumn chromatographic process.

Even though one should be cautious in generalizing the results to other systems, these indicate that the new operating modes have a significant potential to improve over standard SMB performance. Industry has already recognized this, where the Varicol process is already applied in units with exactly the same hardware as a standard SMB unit. In the case considered here, and possibly also in other cases involving chiral separations, the PowerFeed and ModiCon modes allow one to achieve even better performance than Varicol. The implementation of the PowerFeed requires that the flow rates of the unit are changed during the switching time, thus possibly imposing more technical constraints on the pumps and valves of the unit as compared to a standard SMB unit. On a lab-scale, we have proven this feasible [Zhang et al., 2004].

As to the ModiCon operation, other considerations should be made. The overall feed concentration of an SMB-like process is upper bounded on the one hand by the solubility of the species to be separated, a constraint that cannot be overcome, and on the other hand by the requirement of operating the unit under robust conditions, where the complete separation triangle in the (m_2, m_3) plane is not too narrow (see Fig. 8). Whether either one or the other condition is controlling depends on the solubility of the solutes and on the non-linearity of their adsorption isotherm. In the case examined here, we have adopted a rather high feed concentration for the SMB, PowerFeed and Varicol processes, 8 g/*l*, where as shown in Fig. 8 the complete separation triangle is already rather small. On the other hand, maximum solubility has been taken as 12 g/*l*. These are conditions where the isotherm non-linearity is controlling the feed concentration, and ModiCon can indeed outperform SMB since it exploits the possibility of modulating the feed concentration during the switching interval, thus effectively weakening the non-linearity of the system. On the contrary, if the SMB feed concentration were dictated by the solubility limit, as can happen, whereas the adsorption behavior was still rather linear at the feed composition, then the ModiCon operation has no possibility to improve over SMB performance.

We believe that the results presented here, as well as those reported elsewhere by our group and by other groups, demonstrate that significant performance improvements can be achieved by choosing the proper non-standard SMB configuration, and by using units with a small number of columns. Our findings point also at the importance of using multiobjective optimization tools that allow for a fair and comprehensive comparison of the performance of the different techniques. This is an exciting field of research, where further improvements and more application possibilities for SMB and related technologies can be envisaged.

NOMENCLATURE

C_i : liquid phase concentration of component i [g/*l*]
$\overline{C}_i$: solid phase concentration of component i [g/*l*]
C^F_T : total feed concentration [g/*l*]
d_p : particle diameter [μm]
D : eluent flow rate [ml/min]
E : flow rate of extract stream [ml/min]
F : feed flow rate [ml/min]
HETP: height equivalent to a theoretical plate [cm]
J : objective function
L_{col} : length of each column [cm]
m : flow rate ratio parameter
M_i : mass of component i collected or introduced during one switching period [g]

N_{col} : total number of columns
N_{NTP} : number of theoretical plates
Prod : productivity [g/(l d)]
P_E : purity of extract stream [%]
P_R : purity of raffinate stream [%]
Q_j : fluid flow rate in section j [ml/min]
R : flow rate of raffinate stream [ml/min]
S : number of subintervals in Varicol, PowerFeed and ModiCon
t : time [min]
t^* : switching time [min]
u : velocity [cm/s]
V_{col} : column volume [ml]
x : mole fraction

Greek Letters

χ : column configuration
ΔP_{unit} : unit pressure drop [bar]
ε : total porosity
ε_b : bed porosity
ε_p : particle porosity
Ω : column cross section [cm^2]

Subscripts and Superscripts

A : strong component of the feed
B : weak component of the feed
i : component i
j : section j

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