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# Supercritical fluid simulated moving bed chromatography<sup>1</sup>

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## Abstract

Continuous chromatographic separation processes have gained increasing industrial importance for fine chemical and pharmaceutical applications. These are based on the simulated moving bed (SMB) technology, of which the implementation using a supercritical eluent (SF-SMB) is dealt with in this work. Criteria for the choice of the operating conditions of SF-SMBs to achieve optimal separation performance are derived. Through these a thorough analysis of the two operating modes of these units, isocratic and pressure gradient mode, is made. The theoretical findings are supported by comparison with experimental data previously published in the literature. © 1997 Elsevier Science B.V.

**Keywords:** Simulated moving bed chromatography; Supercritical fluid chromatography; Pressure gradient; Fatty acid ethyl esters

## 1. Introduction

Preparative scale chromatography is spreading more and more in fine chemical and pharmaceutical industries, for the separation of natural products, aroma and in particular for the resolution of racemates. This is mainly due to the understanding that chromatographic analytical methods can be scaled up to preparative applications or even to continuous processes using the simulated moving bed (SMB) technology [1]. The latter has been applied for more than thirty years in the petrochemical and sugar industries [2], but only recently has it been successfully proposed for small scale fine chemical applications [3,4]. The efficient use of the stationary and

mobile phases in SMB units leads to significant performance improvements in terms of solvent consumption and specific productivity with respect to classical batchwise preparative chromatography [5].

SMB applications may be based on either displacement or elution chromatography. The former, which implies the use of a desorbent having a non-negligible affinity for the stationary phase, is normally applied in large scale hydrocarbon separations, where the feed mixture is constituted of the components to be separated only. The latter, where the mobile phase exhibits a weaker interaction with the stationary phase than the species to be separated, is the most common case in fine chemical applications, where usually the species to be separated are dissolved in the eluent before entering the SMB unit. In both cases the displacement or elution strength of the mobile phase plays a key role in determining the separation performances. As discussed in the next

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<sup>1</sup>Dedicated to Professor Dieter Seebach on the occasion of his 60th birthday.

sections, the choice of the mobile phase is the result of a compromise between different and often opposite needs.

In this work a new chromatographic separation process which has been recently proposed [6,7] is analyzed. This is based on the SMB technology and the use of a supercritical eluent, and it is referred to as supercritical fluid simulated moving bed (SF-SMB). This process is the rather natural scale up of the well established analytical supercritical fluid chromatography. Its main feature is the rather unique opportunity to tune the elution strength of the mobile phase in the different zones of the SF-SMB unit, in order to optimize its separation performances. Therefore, the SF-SMB technology couples the well known advantages of supercritical fluid chromatography (SFC), namely easy separation of products and solvent and full compatibility of the most common solvent (i.e. carbon dioxide) with any product bound to be used on humans, with the SMB performance improvements due to the possibility of tuning the elution strength. These features have been recently demonstrated through experiments [6]. The aim of this work is to provide the theoretical basis for the interpretation of these results and the development of optimal design and operation procedures of SF-SMB units.

After reviewing the relevant aspects of SFC thermodynamics, the SF-SMB technology and its two possible implementations, i.e. isocratic and pressure-gradient mode, will be discussed. Next, criteria for the choice of the operating conditions of SF-SMB units to achieve the desired separation performance will be derived. Differences between the two operating modes will be shown and discussed with emphasis on the effect of selectivity on separation performance. Finally, these theoretical results will be discussed in the light of their comparison with the experimental results reported in the literature.

## 2. Solute retention in supercritical fluid chromatography

Supercritical fluid chromatography is a consolidated analytical technique used for several applications [8], which is gaining more and more interest in

preparative applications [9,10]. One of its main features is the possibility of controlling solute retention, since in the near-critical region retention is very sensitive to thermodynamic conditions.

In the case of carbon dioxide, which is the most common supercritical solvent, critical parameters are:  $T_c = 31^\circ\text{C}$ ,  $P_c = 73$  bar and  $d_c = 470$  kg/m<sup>3</sup>. In the supercritical region the solvating power of the fluid is highly dependent on temperature and pressure, and so is the affinity of a given solute for the supercritical fluid phase itself. The affinity of the same solute for a given stationary phase is also a function of temperature. The coupling of these two effects yields a temperature and pressure dependence of the partition constant of a given solute between the stationary phase and the supercritical solvent at equilibrium [9].

In linear chromatography the partition constant, i.e. the ratio  $q_i/c_i$ , where  $q_i$  and  $c_i$  are the adsorbed and the fluid phase concentrations of the  $i$ th species, respectively, is given by the Henry constant,  $H_i$ . This is related to the retention time in a chromatographic column,  $t_{R,i}$ , by the following well known equation:

$$t_{R,i} = t_0 \left( 1 + \frac{1 - \epsilon^*}{\epsilon^*} \cdot H_i \right), \quad (1)$$

where  $t_0$  is the residence time of a non-retained species and  $\epsilon^*$  is the overall void fraction of the bed. Thus, the retention time depends on temperature and pressure, through  $H_i$ .

For the purpose of the following analysis it is not necessary to address the complex issues of determining the partition constant under supercritical conditions [11]. We will use in fact a simple equation, which can be derived directly from experimental measurements, relating the Henry constant to the density of the supercritical solvent,  $d$ , which in turn depends upon temperature and pressure [9,12,13]:

$$H_i = H_{i,0} \left( \frac{d_0}{d} \right)^{b_i}. \quad (2)$$

Here  $H_{i,0}$  is the Henry constant at the reference density  $d_0$ , whereas  $b_i$  is an empirical parameter. Both these solute specific parameters depend not only on temperature but also on the chromatographic system, i.e. the supercritical solvent and the stationary phase. Typical values of  $b_i$  are in the range 1 to 10. For example  $b$  equals 2.77 in the case of naphthalene on a SB-Methyl-100% capillary SFC

column using carbon dioxide as mobile phase at 125°C [13]. Using Eq. (1) this implies that the retention time of naphthalene on this stationary phase exhibits a ten fold reduction when pressure is increased from 116 bar (corresponding to  $d=200 \text{ kg/m}^3$ ) to 221 bar ( $d=450 \text{ kg/m}^3$ ).

### 3. SF-SMB technology

In its simplest implementation the SF-SMB technology is nothing but the SMB technology where the mobile phase consists of a supercritical fluid. SMB separation is a continuous process, which can be simply described with reference to the equivalent true counter-current (TCC) unit schematically illustrated in Fig. 1. This is divided into four sections,

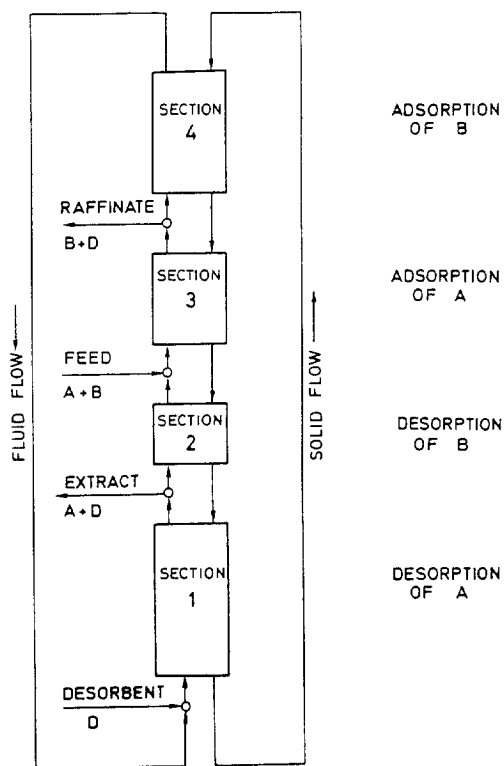


Fig. 1. Scheme of a four section true counter-current unit for continuous chromatographic separations: the binary separation of a more retained species A and a less retained species B is considered.

each consisting of a counter-current adsorption column and playing a specific role in the separation.

Let us refer to a two component feed mixture consisting of the more retained species, A, and the less retained one, B, which are to be collected in the extract and the raffinate stream, respectively. Components A and B in the feed stream may or may not be dissolved in a proper solvent; if this is the case the mobile phase consists of the solvent itself. The separation must be obtained in the two central sections, in such a way that A is carried by the solid phase to the extract outlet and B is carried by the mobile phase to the raffinate outlet. The mobile phase (i.e. a solvent which as discussed in the introduction can be either a desorbent or an eluent) is fed to the bottom of section 1, so as to desorb A and regenerate the adsorbent before it is recycled to section 4. Finally, component B is retained by the solid phase in section 4, so as to regenerate the mobile phase, which is mixed with its make-up stream and recycled to column 1.

Due to the unavoidable inefficiencies connected to the movement of the solid phase, in practice the TCC configuration is replaced by the SMB configuration, illustrated in Fig. 2. Here the solid beds are fixed and

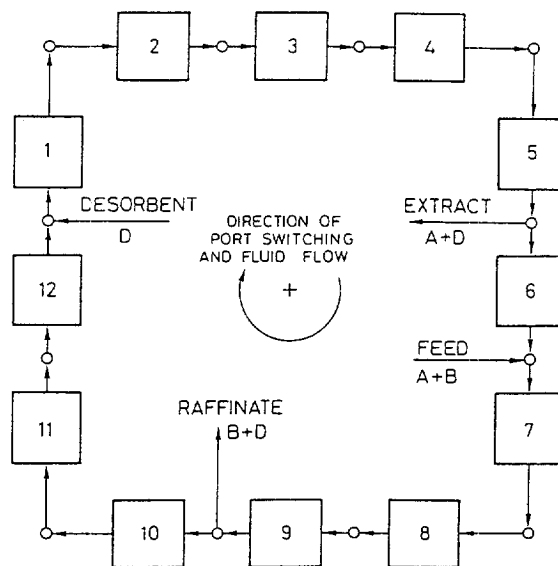


Fig. 2. Scheme of a four-section simulated moving bed unit for continuous chromatographic separations with port distribution 5-1-3-3 (same separation as in Fig. 1).

the continuous movement of the solid is simulated by periodically switching the inlet and outlet ports of the unit in the same direction of the mobile phase flow. Each section of the SMB unit is divided into a number of subsections so as to closely mimic the counter-current movement of the solid phase. Each subsection consists of a chromatographic column, equipped with sufficient valves to connect it to all the outlets (extract and raffinate) and to all the inlets (feed and solvent make-up) of the process. After mixing with or withdrawal of an external stream the resulting stream is fed to the following chromatographic column. Notice that SMB units are usually operated under isothermal conditions.

In order to best exploit the potential of these units, their operating conditions should be carefully selected in order to optimize the separation performance, for example by minimizing the mobile phase consumption, i.e. the mobile phase make-up flow-rate [5,14,15]. With reference to Fig. 1 and assuming a given solid flow-rate, this objective, i.e. the objective of reducing the mobile phase make-up flow-rate, can be achieved either by reducing, in theory by minimizing, the fluid flow-rate in section 1, or by increasing, in theory by maximizing, the fluid flow-rate in section 4.

In the case of displacement chromatography (e.g., hydrocarbon separations) this implies the use of a strong desorbent in section 1, where the objective is that of displacing all adsorbed species, and of a weak desorbent in section 4, that would favor the retention of the weak component which is the objective of section 4. This situation calls for a compromise. A desorbent with an intermediate adsorptivity with respect to the two species to be separated is in fact used wherever possible [1]. This conclusion is also suggested by considerations about the operation of sections 2 and 3, which are not discussed here [16].

In the case of SMB separations based on elution chromatography, the major problem is typically the regeneration of the solid phase in section 1 which will imply the use of exceedingly large amounts of mobile phase whenever the more retained component exhibits a too strong affinity for the stationary phase. In practice, the mobile phase composition is selected so as to obtain a reasonable retention of the strong component [17].

The SF-SMB technology allows for a novel

approach to this optimization problem, based on the enforcement of an elution strength gradient in the SMB unit. A SF-SMB unit can be operated in two ways: the isocratic mode, where the pressure in the unit is uniform (apart from negligible pressure drops due to the fluid flow through the chromatographic columns), and the pressure gradient mode, where different pressure levels are imposed in the four sections of the unit (cf. Fig. 3). In the former case the situation is not at all different from the case of the eluting mobile phase discussed above. In the latter case different pressure values are imposed in two adjacent sections by locating a pressure control valve after each column, between outlet and inlet valves [6]. Thus, since the density of the supercritical mobile phase decreases with decreasing pressure, according to Eq. (1) and Eq. (2) the Henry constants of the components to be separated and their retention times increase. Accordingly, by imposing a decreasing pressure gradient from section 1 to section 4, we realize also a decreasing gradient of the elution strength of the mobile phase, thus achieving the optimal condition envisaged above. In fact the elution strength is maximum in the first section, where the more retained component must be eluted, and it is minimum in the fourth section, where the less retained component must be retained by the stationary phase. Together with a similar positive effect on the performances of sections 2 and 3 that will be discussed in the following, this allows one to optimize the separation performance with particular

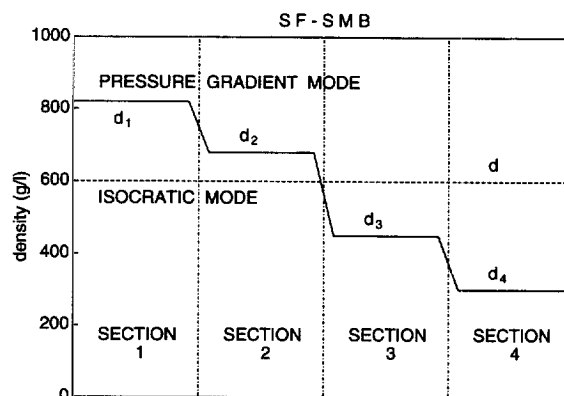


Fig. 3. Density profile in the four sections of a SF-SMB separation unit: (---) isocratic mode; (—) pressure gradient mode.

reference to productivity and mobile phase consumption.

#### 4. Design of operating conditions

In this section the qualitative considerations developed above are quantitatively demonstrated. Although these are valid for systems described by both linear and nonlinear adsorption isotherms, for the sake of simplicity in the following we limit our analysis to linear systems described by Henry isotherms. Following the approach described elsewhere [5,14,18] and in the frame of equilibrium theory (i.e. neglecting axial dispersion and mass transfer resistances) it is possible to demonstrate that the performance of simulated counter-current chromatographic separation units depends on the choice of four operating parameters, one for each section, defined as ( $j=1, \dots, 4$ ):

$$m_j = \frac{Q_j t^* - V\epsilon^*}{V(1 - \epsilon^*)}, \quad (3)$$

where  $Q_j$  is the volumetric fluid flow-rate in section  $j$ ,  $V$  is the overall volume of the chromatographic column and  $t^*$  is the switch time of the SMB unit, i.e. the time period between two successive switches of the inlet and outlet ports.

Let us assume that complete separation is sought, i.e. the situation illustrated in Fig. 1 and Fig. 2, where species A and B are collected only in the extract and raffinate stream, respectively. Necessary and sufficient conditions for complete separation are given by the following constraints on the operating parameters of the unit [5,18]:

$$H_{A,1} < m_1 \quad (4)$$

$$H_{B,2} < m_2 < H_{A,2} \quad (5)$$

$$H_{B,3} < m_3 < H_{A,3} \quad (6)$$

$$m_4 < H_{B,4} \quad (7)$$

The Henry constant  $H_{i,j}$  is characterized by two labels:  $i$  refers to the solute, either A or B, whereas  $j$  indicates the section of the SMB unit. These inequalities define a region in the four-dimensional

space spanned by the operating parameters  $m_j$ ,  $j=1, \dots, 4$ , whose points correspond to operating conditions which in the frame of equilibrium theory guarantee the achievement of complete separation. From the physical point of view, the meaning of constraints 5 and 6 is that the operating parameters  $m_2$  and  $m_3$  must be large enough so that component B is carried towards the raffinate outlet, but on the other hand they must not be too large so as to guarantee that component A is carried towards the extract outlet and to avoid that it is also carried towards the raffinate port [5]. As far as constraints 4 on  $m_1$  and 7 on  $m_4$  are concerned, these impose that both components are eluted in section 1 and retained in section 4, so as to regenerate the mobile and the stationary phase, respectively.

##### 4.1. Isocratic operating mode

When SF-SMBs are operated in the isocratic mode, i.e. at constant pressure and mobile phase density, the elution strength of the mobile phase as well as the Henry constants of the species to be separated are uniform through the unit. By indicating the latter as  $H_i$ , with  $i=A,B$ , the adsorption selectivity is defined as:

$$S_{AB} = \frac{q_A/q_B}{c_A/c_B} = \frac{H_A}{H_B}, \quad (8)$$

and it is also uniform in the SMB unit.

From the above considerations it follows that the degrees of freedom of a SF-SMB separation unit in the isocratic mode are the four operating parameters,  $m_j$ , and the pressure in the unit (hence the density  $d$ , since we assume that temperature is given), which according to Eq. (2) determines the exact values of  $H_i$ . According to Eq. (3) a positive feed flow-rate requires  $m_3 > m_2$ , hence the constraints 5 and 6 can be recast in the following form:

$$H_B < m_2 < m_3 < H_A \quad (9)$$

These constraints refer to the two key sections of the SMB unit, i.e. the sections where separation takes place, and define the projection of the four-dimensional region of complete separation onto the ( $m_2, m_3$ ) plane. This is illustrated in Fig. 4, where the complete separation region corresponds to the square triangle indicated as region I. Note that constraints

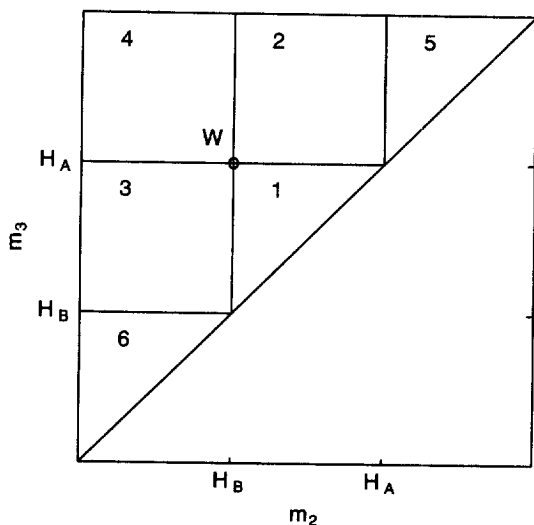


Fig. 4. SF-SMB: isocratic mode. Regions of the  $(m_2, m_3)$  plane with different separation regimes in terms of purity of the outlet streams. Region 1: both extract and raffinate pure; 2: extract pure,  $P_R < 100\%$ ; 3: raffinate pure,  $P_E < 100\%$ ; 4:  $P_E$  and  $P_R < 100\%$ ; 5: extract flooded with pure solvent, A and B are collected in the raffinate; 6: raffinate flooded with pure solvent, A and B are collected in the extract. W: optimal operating point.

in sections 2 and 3 are decoupled: this is a typical feature of linear systems, which is not shared by nonlinear systems where on the contrary they are tightly coupled [5,18].

It is worth emphasizing that the correct constraints on  $m_2$  and  $m_3$  are given by Eq. (5) and Eq. (6) and not by those sometimes reported in the literature, i.e.  $H_B < m_2$  and  $m_3 < H_A$  [19,20]. It is clear that these can also be cast in the same form as Eq. (9), however, they are not complete since they omit to specify the upper constraint on  $m_2$  and the lower constraint on  $m_3$ . This does not allow one to analyze the zones of the operating parameter plane different from the complete separation region as we see in the next paragraph with reference to Fig. 4. Moreover, this error leads to wrong conclusions about the complete separation region itself in the case of SF-SMBs operated in the pressure gradient mode (cf. Section 4.2).

With reference to Fig. 4, it is rather useful to analyze the whole  $(m_2, m_3)$  plane in terms of purities of the product streams ( $P_E = 100 \times c_A^E / (c_A^E + c_B^E)$  for the extract and  $P_R = 100 \times c_B^R / (c_A^R + c_B^R)$  for the raffi-

nate) [5]. In regions 2, 4 and 5, where  $m_3 > H_A$ , the upper constraint in Eq. (9) is not fulfilled. Hence these are constituted of operating points corresponding to conditions for which the more retained component A pollutes the raffinate stream, whose purity drops below 100%. Similarly, in regions 3, 4 and 6, where  $m_2 < H_B$ , the lower constraint in Eq. (9) is not fulfilled. Hence these are constituted of operating points corresponding to conditions for which the less retained component B pollutes the extract stream, whose purity drops below 100%. It follows that in region 2 only the extract stream is pure, whereas in region 3 only the raffinate stream is pure. In region 4 neither product stream is pure, since both species distribute in both the extract and the raffinate. Region 5 is constituted of points where both  $m_2$  and  $m_3$  are larger than the upper bounds given by Eqs. (5) and (6). This implies that both A and B are removed by the mobile phase from section 2. Therefore the extract stream is constituted of pure mobile phase and the whole amount of A and B fed to the unit is collected in the raffinate. This is a no-separation region where the extract port is flooded with pure solvent. Similarly, it can be shown that region 6 is a no-separation region where the raffinate outlet is flooded with pure solvent and A and B are entirely collected in the extract.

Thus summarizing, in the frame of Equilibrium Theory, if the operating parameters  $m_1$  and  $m_4$  fulfill their relevant constraints 4 and 7, the relative position of the operating point in the  $(m_2, m_3)$  plane with respect to the six regions of separation shown in Fig. 4 provides thorough and precise indications about the separation performance of the SMB unit. It is worth recalling that within the complete separation region the furthest point from the diagonal, i.e. vertex W with coordinates  $(H_B, H_A)$ , represents operating conditions corresponding to optimal separation performances (in terms of productivity, mobile phase consumption, recovery, enrichment). It is worth pointing out that identical conclusions hold for nonlinear equilibrium isotherms, the only difference being the shape of the separation regions in Fig. 4 [5,14].

#### 4.2. Pressure gradient operating mode

As illustrated in Fig. 3, when SF-SMBs are

operated in the pressure gradient mode, pressure and density of the supercritical mobile phase are different in each section of the unit. Therefore, the Henry constant of the same solute changes in going from one section to the following one as implicitly accounted for in Eqs. (4)–(7). Let us express these Henry constants through Eq. (2) ( $i = A, B$  and  $j = 1, \dots, 4$ ):

$$H_{i,j} = H_{i,0} \left( \frac{d_0}{d_j} \right)^{b_i} \quad (10)$$

Assuming a given temperature, the degrees of freedom of a SF-SMB separation in the pressure gradient mode are the four operating parameters,  $m_1, m_2, m_3, m_4$ , and the four pressures in the unit, i.e. the corresponding density values,  $d_1, d_2, d_3$  and  $d_4$ . With reference to Fig. 3, note that for the sake of comparison it has been assumed that the pressure level in the isocratic mode is intermediate between those of the second and third section in the pressure gradient mode, hence  $d_1 > d_2 > d > d_3 > d_4$ . One could repeat the analysis assuming a different value of the isocratic mode pressure with respect to those in the pressure gradient mode, thus reaching similar results and same conclusions. As a consequence of the above assumption and of Eq. (10), it is readily observed that:

$$H_{i,1} < H_{i,2} < H_i < H_{i,3} < H_{i,4} \quad (i = A, B) \quad (11)$$

Since the retention of both solutes decreases, the elution strength of the mobile phase increases along the SF-SMB unit operated in the pressure gradient mode, as required.

By applying the inequalities Eqs. (4)–(7), the region of complete separation in the operating parameter space can be easily determined. As in the isocratic case it is useful to consider its projection onto the  $(m_2, m_3)$  plane. Accounting for Eq. (11) and recalling that  $H_{A,j} > H_{B,j}$ , two qualitatively different situations may occur, depending on whether  $H_{A,2} > H_{B,3}$  (Fig. 5) or  $H_{A,2} < H_{B,3}$  (Fig. 6). It is noteworthy that the complete separation region, i.e. region 1 in both figures, is not a square triangle any more but either a truncated rectangle or a full rectangle. The coordinates of the optimal point Y are  $(H_{B,2}, H_{A,3})$ , which according to Eq. (11) correspond to a point that is further away from the diagonal than the

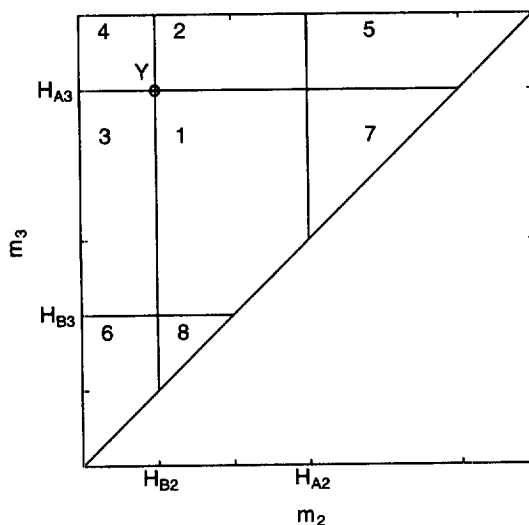


Fig. 5. SF-SMB: pressure gradient mode ( $H_{A,2} > H_{B,3}$ ). Regions of the  $(m_2, m_3)$  plane with different separation regimes in terms of purity of the outlet streams. Regions 1 to 6 as in Fig. 4; region 7: extract flooded with pure solvent, B is collected in the raffinate, A accumulates in the unit; 8: raffinate flooded with pure solvent, A is collected in the extract, B accumulates in the unit. Y: optimal operating point.

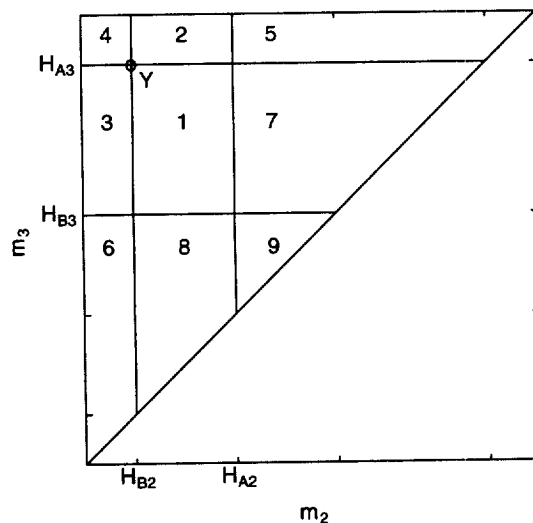


Fig. 6. SF-SMB: pressure gradient mode ( $H_{A,2} < H_{B,3}$ ). Regions of the  $(m_2, m_3)$  plane with different separation regimes in terms of purity of the outlet streams. Regions 1 to 8 as in Fig. 5; region 9: both extract and raffinate flooded with pure solvent, both A and B accumulate in the unit. Y: optimal operating point.

isocratic optimal point W ( $H_B$ ,  $H_A$ ). This is well illustrated by the comparison between the complete separation regions in the isocratic mode (dashed boundaries) and in the pressure gradient mode (solid boundaries, referring to the case where  $H_{A,2} > H_{B,3}$ ) shown in Fig. 7. This result has important consequences on the separation performance, as discussed in the next section. A similar situation occurs in the case where  $H_{A,2} < H_{B,3}$ .

Let us analyze the other separation regions shown in Figs. 5 and 6, assuming that the relevant constraints on  $m_1$  and  $m_4$ , i.e. Eqs. (4) and (7), are fulfilled. Regions 2 to 6 represent the same separation regimes as in Fig. 4, as it can easily be demonstrated by applying the inequalities, Eqs. (5) and (6). Region 7 is the result of the ideality assumptions involved in the adopted linear equilibrium model and in fact it does not appear in reality. To understand this we note that in region 7, similarly to region 5, the extract outlet is flooded with pure solvent; however, in this case the operating parameter  $m_3$  is such that only component B is carried towards the raffinate outlet, whereas component A is retained by the stationary phase. In other words, the

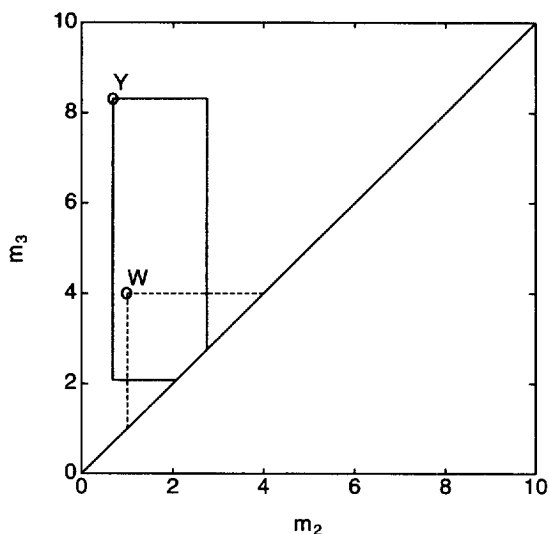


Fig. 7. Comparison of the regions of complete separation in the ( $m_2, m_3$ ) plane for a SF-SMB separation unit operated in the isocratic (---) or in the pressure gradient mode (—). Operating parameters (densities in  $\text{kg}/\text{m}^3$ ):  $d=600$ ,  $d_1=720$ ,  $d_2=680$ ,  $d_3=470$ ,  $d_4=400$ . Retention parameters (dimensionless):  $H_A=4$ ,  $H_B=1$ ;  $b_A=b_B=3$ .

operating regime of section 3 is such that the separation of A and B is realized, while on the other hand that in section 2 prevents both components from reaching the extract. This means that component A is fed to the unit but it comes out from neither the extract nor the raffinate and it actually accumulates indefinitely within the unit, thus implying a correspondent indefinite increase of its concentration. This result, which is obviously physically unrealistic, is actually consistent with a linear equilibrium model, which implies that the concentration in the fluid and adsorbed phases can increase indefinitely without reaching any saturation limit. In reality, the fluid phase concentration is typically upper bounded by the solute solubility, whereas the concentration in the adsorbed phase reaches a saturation value for large enough values of the fluid phase concentrations, depending upon the solutes and the chromatographic system. When these effects are accounted for through an appropriate nonlinear equilibrium model, the shape of all separation regions changes [5,18] and region 7 disappears. On the basis of similar arguments it can be seen that in region 8 the raffinate is flooded with pure solvent and component B accumulates within the unit, whereas in region 9 (which appears only in the case illustrated in Fig. 6) both the extract and the raffinate are flooded with pure solvent and both species accumulate indefinitely within the unit. Accordingly, these regions are also artifacts of the linear equilibrium model and do not exist in reality.

Thus summarizing, regions 7 to 9 represent anomalous operating conditions which during the transient regime of the unit may cause solubility problems or a shift from linear to nonlinear equilibria. Moreover, these regions of operations, as well as regions 4 and 6, do not provide even a single pure stream (neither the extract nor the raffinate) and should therefore be avoided.

## 5. Discussion and conclusions

The effect of the degrees of freedom characteristic of the pressure gradient operating mode on the separation regions in the operating parameter space has been elucidated in the previous section. In particular, we have seen that the optimal operating



point is driven further away from the diagonal of the operating plane ( $m_2, m_3$ ) when going from the isocratic to the pressure gradient operating mode (cf. Fig. 7). According to previous analyses [5,14] this implies an improvement in process performances as demonstrated both theoretically and experimentally in the following.

5.1. Separation performances

Besides purity of product streams, several parameters may be used to evaluate the separation performance of SMB units. These include productivity with respect to the overall inventory of stationary phase, mobile phase consumption with respect to separated amount of feed mixture and enrichment of the outlet streams [5,14,15]. In the case of SF-SMB units, the solvent (typically carbon dioxide) per se does not represent a significant contribution to the production cost, which is instead strongly affected by the energy required to pressurize the inlet streams. Accordingly, the process performance can be best evaluated by expressing productivity as the ratio between the solute flow-rate treated by the unit and the overall flow-rate of the two pressurized inlet streams [6]:

$$PR = \frac{G_F w_T^F}{G_1 + G_F} = \frac{d_F Q_F w_T^F}{d_1 Q_1 + d_F Q_F} \tag{12}$$

where  $G$  represents mass flow-rate and  $w_T^F$  is the overall mass fraction of solutes in the feed stream. Using Eq. (3) and noting that  $d_F = d_3$ , since the feed port is located after the pressure control valve between sections 2 and 3, the previous equation can be recast in the following form:

$$PR = w_T^F \left[ 1 + \frac{d_1 m_1}{d_3 (m_3 - m_2)} \right]^{-1} \tag{13}$$

From this equation it is clear that the optimal productivity within the complete separation region is achieved by operating points located as far as possible from the diagonal, i.e. in its upper left vertex (point W in Fig. 4 for the isocratic mode and point Y in Figs. 5 and 6 for the pressure gradient mode). In terms of the reference selectivity  $S_{AB}$ , defined by Eq. (8), and of the proportionality factors

$r_{i,j} = (d/d_j)^{b_i}$ , the optimal productivity PR is given by:

$$\begin{aligned} PR_{opt} &= w_T^F \left[ 1 + \frac{d_1 H_{A,1}}{d_3 (H_{A,3} - H_{B,2})} \right]^{-1} \\ &= w_T^F \left[ 1 + \frac{d_1 r_{A,1} S_{AB}}{d_3 (r_{A,3} S_{AB} - r_{B,2})} \right]^{-1} \end{aligned} \tag{14}$$

Using this equation the optimal productivities achieved in the two SF-SMB operating modes can be compared:

$$\frac{PR_{opt}^{PG}}{PR_{opt}^{ISO}} = \frac{2S_{AB} - 1}{S_{AB} - 1} \left[ 1 + \frac{d_1 r_{A,1} S_{AB}}{d_3 (r_{A,3} S_{AB} - r_{B,2})} \right]^{-1} \tag{15}$$

This relationship involves the densities in the sections of the unit and the reference selectivity. The productivity ratio, which is always larger than 1, is shown in Fig. 8 (solid line) as a function of the reference selectivity, for reasonable values of the other involved parameters. It is remarkable that in switching from the isocratic to the pressure gradient operating mode the productivity may increase by

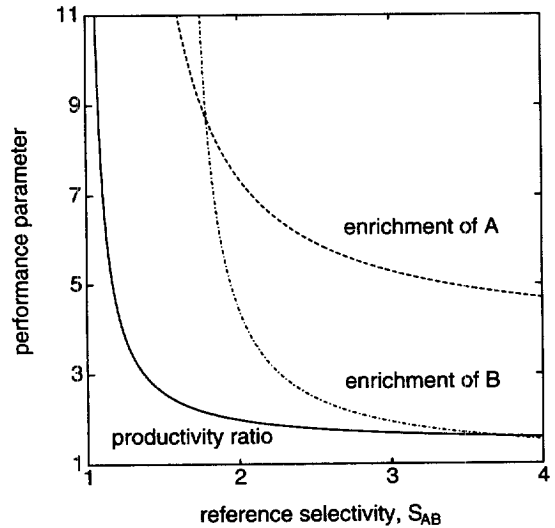


Fig. 8. Comparison of the optimal separation performances of SF-SMBs in the two operating modes as a function of the reference selectivity,  $S_{AB}$ : (—) productivity ratio,  $PR_{opt}^{PG}/PR_{opt}^{ISO}$ ; (---) enrichment of A (pressure gradient mode),  $E_{A,opt}^{PG}$ ; (- · -) enrichment of B (pressure gradient mode),  $E_{B,opt}^{PG}$ . Operating and retention parameters as in Fig. 7.

Table 1

Separation of two fatty ethyl esters in a SF-SMB pilot unit: operating conditions of the experimental runs [6]

Run	$w_T^F$ (%)	$t^*$ (s)	Pressure (bar)				Flow-rate (kg/h)			
			$P_1$	$P_2$	$P_3$	$P_4$	$G_F$	$G_E$	$G_R$	$G_4$
Isocratic mode	0.20	694	158	154	150	146	0.69	1.49	0.67	3.18
Pressure gradient mode	0.23	276	195	175	125	115	2.2	1.3	0.79	7.15

several times and that the smaller the reference selectivity the larger this improvement. Thus, the pressure gradient mode provides the largest improvements for difficult separations, which is where they are obviously more welcome.

Let us now consider the enrichment parameters [5]. The enrichment of species A (B),  $E_A$  ( $E_B$ ), is defined as the ratio between the concentration of A in the extract (of B in the raffinate) and its concentration in the feed stream. Under the assumption of complete separation, i.e. for operating points within the complete separation region, a simple material balance indicates that  $E_A$  ( $E_B$ ) is given by the ratio between the feed flow-rate and the extract (raffinate) flow-rate. Whereas the optimal enrichment in the isocratic mode is constant and equal to 1, that in the pressure gradient mode is a function of the operating conditions in the unit as given by:

$$E_{A,opt}^{PG} = \frac{r_{A,3}S_{AB} - r_{B,2}}{r_{A,1}S_{AB} - r_{B,2}}; \quad (16)$$

$$E_{B,opt}^{PG} = \frac{r_{A,3}S_{AB} - r_{B,2}}{r_{A,3}S_{AB} - r_{B,4}}. \quad (17)$$

They are both always larger than one, and, as shown in Fig. 8, as a function of the reference selectivity exhibit the same qualitative behavior as the productivity ratio.

## 5.2. Comparison with experimental results

The above theoretical findings are supported by a

comparison with available experimental data. These refer to the separation of two fatty ethyl esters (A: docosahexaenoic ethyl ester; B:  $\gamma$ -linolenic ethyl ester) on  $C_{18}$  bounded silica using supercritical carbon dioxide as mobile phase [6]. Two experiments, in the isocratic and in the pressure gradient operating mode, respectively, have been performed in a SF-SMB pilot unit constituted of 8 columns. The operating conditions of the experiments are summarized in Table 1. It is worth noting that in the isocratic operating mode the pressure in the unit is substantially uniform and equal to  $152 \pm 6$  bar, whereas in the pressure gradient mode an overall pressure drop of about 80 bar is obtained. Since information about the geometry of the columns and the retention times of the two solutes (i.e. equilibrium isotherms) are not available, we cannot determine the operating points and the complete separation regions in the operating parameter space. However, on the basis of the experimental purity values reported in Table 2 (above 98%), we can expect that the operating point of the isocratic mode experiment is outside the complete separation region but rather close to the optimal point (point W in Fig. 4) whereas that of the pressure gradient mode experiment is within the complete separation region, but also close to the optimal point, since the other performance parameters are rather good (point Y in Figs. 5 and 6).

Based on the arguments above, we assume that the two experimental runs are well representative of the optimal operating conditions in the two operating modes of the SF-SMB unit. Under this assumption

Table 2

Separation of two fatty ethyl esters in a SF-SMB pilot unit: experimental separation performances [6]

Run	$P_E$ (%)	$P_R$ (%)	$E_A$	$E_B$	PR (g/kg)
Isocratic mode	97.8	97.7	0.24	1.0	0.26
Pressure gradient mode	99.9	100.0	1.9	5.0	0.55

the experimental results can be compared with the theoretical findings presented in this work about optimally operated units. In particular, it was found experimentally that in the pressure gradient mode productivity is more than two times larger than in the isocratic mode, whereas the enrichments of A and B are 8 and 5 times larger, respectively. As discussed above with reference to Fig. 8, these values are indeed realistic and are satisfactorily explained by the analysis presented in this paper. From a quantitative point of view the above experimental values are very close to those calculated in Fig. 8 for a reference selectivity  $S_{AB}=2$ , and using the density values corresponding to the experimental pressure values reported in Table 1 and an operating temperature of 60°C.

Thus summarizing, in this work we have analyzed the operating conditions and the separation performances of a new adsorptive separation process, the supercritical eluent simulated moving bed process, under linear chromatographic conditions. The two operating implementations of this technology proposed by Clavier et al. [6], isocratic and pressure gradient mode, have been examined through the developed theory. It is shown that this theory explains the interesting and rather surprising experimental results obtained earlier. Moreover, the theoretical predictions indicate that SF-SMB has a very strong potential for achieving rather unique separation performances. This technology is further supported by the large number of highly efficient supercritical chromatographic systems that have been developed in the last few years for analytical and preparative purposes. These make SF-SMB a very promising continuous chromatographic process for small and medium scale applications, where the required high pressure values do not impose exceedingly expensive apparatus.

## 6. Notation

$b$	exponent in Eq. (2) and Eq. (10)
$c$	fluid phase concentration
$d$	fluid phase density
$E$	enrichment
$G$	mass flow-rate

$H_{i,j}$	Henry constant of species $i$ in section $j$ , defined by Eq. (2) and Eq. (10)
$m_j$	mass flow-rate ratio in section $j$ , defined by Eq. (3)
$P$	pressure
$P_E$	desorbent free extract purity
$P_R$	desorbent free Raffinate purity
PR	productivity, defined by Eq. (12)
$q$	adsorbed phase concentration
$Q$	volumetric flow-rate
$r_{i,j}$	proportionality factor of species $i$ in section $j$ , $r_{i,j} = (d/d_j)^{b_i}$
$S_{AB}$	reference selectivity defined by Eq. (8)
$t^*$	switch time in a SMB unit
$t_R$	retention time in a chromatographic column
$t_0$	residence time of a non-retained species in a chromatographic column
$T$	temperature
$V$	volume of the column
$w_T^F$	overall mass fraction of solutes in the feed stream
<i>Greek</i>	
$\epsilon^*$	overall void fraction of the bed

## Subscripts and superscripts

A	more retained species in the feed
B	less retained species in the feed
$c$	critical parameter
D	desorbent
E	extract
F	feed
$i$	component index, $i=A,B$
ISO	isocratic operating mode
$j$	section index, $j=1, \dots, 4$
PG	pressure gradient operating mode
R	raffinate
0	reference value

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