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## Supercritical fluid simulated moving bed chromatography II. Langmuir isotherm

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### Abstract

The simulated moving bed (SMB) technology offers the possibility of scaling up single column, batch chromatographic separations to continuous operation. This has proved particularly effective for the separation of enantiomers, and has been applied in the liquid and gas phase, as well as using a supercritical fluid as eluent (SF-SMB). In the last case, the main performance improvements are due to the possibility of tuning the elution strength of the mobile phase, by changing the pressure in the four sections of the SMB unit. Thus a SF-SMB can be operated in two modes, i.e. the isocratic and the pressure gradient mode. In this research, design criteria for these two operating modes have been developed, which can be applied to systems described by linear as well as nonlinear Langmuir adsorption isotherms. The role and effect of an appropriate modifier in increasing solubility and reducing retention times have been investigated. The results reported allow to identify the operating conditions, including the pressure levels and the modifier concentration, which lead to optimal separation performance in terms of productivity and desorbent requirement.   2001 Elsevier Science B.V. All rights reserved.

**Keywords:** Simulated moving bed chromatography; Supercritical fluid chromatography; Langmuir isotherm; Adsorption isotherms

### 1. Introduction

The simulated moving bed (SMB) technology has attracted more and more attention in the last few years for the separation of fine chemicals and pharmaceuticals, particularly for the case of chiral compounds. This is a continuous unit operated in a

cyclic mode which reproduces the performance of the equivalent true moving bed (TMB) unit illustrated in Fig. 1. This is divided into four sections, each constituted of a counter current adsorption column which plays a specific role in the separation. Let us consider a feed mixture consisting of a more retained species (A) and a less retained one (B) dissolved in the eluent. The separation is obtained in the two central sections, where A is carried by the solid-phase to the extract outlet and B is carried by the mobile phase to the raffinate outlet. The eluent is

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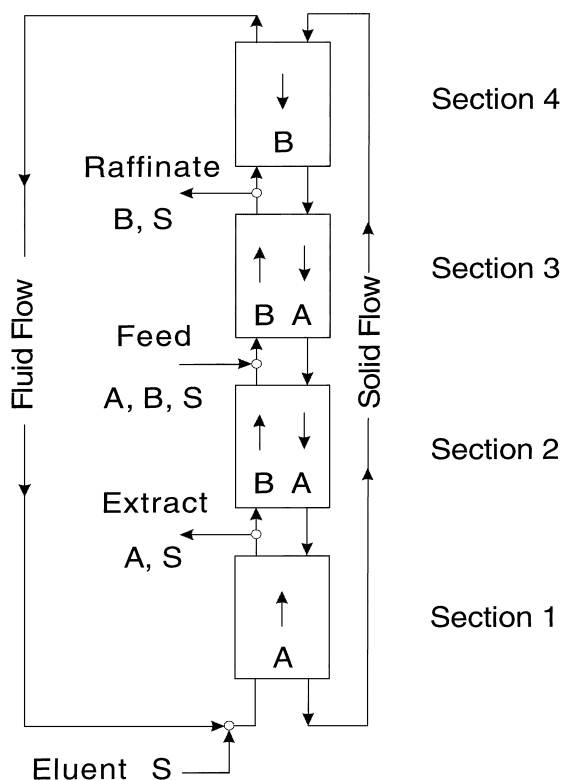


Fig. 1. Scheme of a four-section true moving bed (TMB) unit for the binary separation of a more retained species A and a less retained species B.

fed to the bottom of section 1, so as to desorb A and regenerate the adsorbent solid, before it is recycled to section 4. On the other hand B is retained in section 4 and the pure eluent is recycled to section 1. In practice the movement of the solid is not feasible (especially in terms of retaining the separation efficiency) and the TMB is replaced by the SMB configuration (Fig. 2) where the adsorption beds are fixed and the counter-current solid movement is simulated by periodically switching the inlet and outlet ports of the unit in the same direction of the fluid flow. An open loop 3-3-3-3 configuration (three chromatographic columns per section) is shown in Fig. 2, where the outlet from section 4 is not recycled directly, but collected and recycled off line.

Most SMB applications use liquid eluents (HPLC-SMB) [1–3], although a few examples exist of units operated in the gas phase (GC-SMB) [4]. On the other hand, chromatographic separations using super-

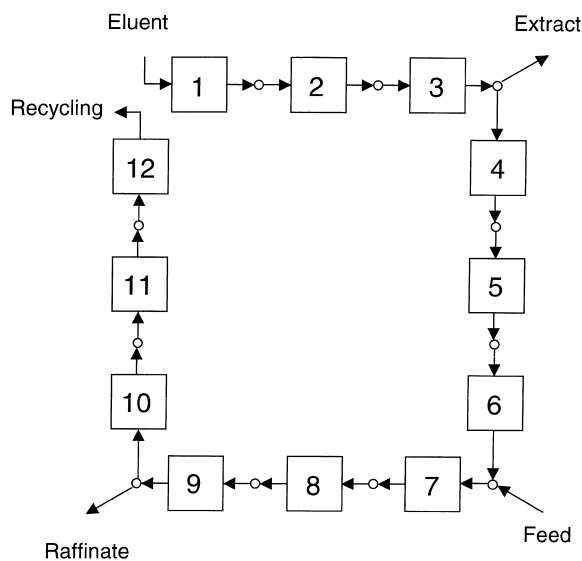


Fig. 2. Scheme of a four-section simulated moving bed (SMB).

critical eluents (SFC) for both analytical and preparative purposes are becoming more frequent [5] and in several instances the question arises about scaling up these techniques to a continuous SF-SMB unit (SMB using a supercritical fluid as eluent). The well known advantages of SFC, namely easy separation of products and solvent and full compatibility of the most common solvent (i.e.  $\text{CO}_2$ ) with products used by humans, are in fact maintained also in the SMB process.

However, in order to make this technology competitive in the market and to exploit its potential, it is necessary to fully understand its operational characteristics. An important characteristic of SF-SMB is that its performance can be improved by taking advantage of the tunability of the physical properties of near critical solvents [6]. For example, since the partition coefficient of a solute between stationary phase and supercritical solvent depends on the solvent density, this can be significantly altered by changing the operating temperature and pressure. For a chromatographic process, operating at higher supercritical fluid density results in the solute eluting faster. In terms of the different function of each section in the TMB unit described above, it is clear that a decreasing density gradient in the four sections of the unit, produces a correspondingly decreasing gradient of elution strength, thus leading to a better

performance when compared to a constant density profile, where a constant elution strength is kept in the unit. This is clearly obtained by setting the elution strength at a maximum in section 1, where the more retained component must be eluted, and at a minimum in section 4, where the less retained component must be adsorbed by the stationary phase.

This concept has been applied experimentally by inducing the density gradient through a suitable pressure gradient. In particular different pressure values in each section of the unit have been realized using a system of back pressure valves placed between each pair of columns, while pressure drop in each column in this context represents only a minor variation. A quantitative comparison of the SF-SMB performance when a pressure gradient is applied (pressure gradient mode) or when pressure is maintained uniform (isocratic mode) has been shown for the separation of two fatty ethyl esters (GLA, i.e.  $\gamma$ -linoleic ethyl ester; and DHA, i.e. docosahexaenoic ethyl ester) on  $C_{18}$  bounded silica [6].

Another important aspect of SF-SMB relates to the possibility of using a solvent modifier. Most of the separation processes of industrial interest involve high molecular mass, polar organic molecules that show a low solubility in pure carbon dioxide and cannot be eluted on standard stationary phases, e.g. those based on silica. To overcome this problem, small amounts of an organic solvent (modifier) are usually added to  $CO_2$ . The modifier is believed to act both in the fluid phase (by increasing the solubility of the solute) and in the stationary phase (by deactivating strongly polar groups, e.g. silanols). The net effect is a decrease of the retention time when increasing the modifier concentration. Therefore the choice of the modifier concentration increases the degrees of freedom of the process and must be considered while designing the operating conditions of SF-SMBs.

Finally, in order to best take advantage of these operational parameters, a simple and synthetic design procedure for the SF-SMB unit is needed where all these different aspects can be accounted for. In the case of liquid phase SMBs, such procedures are based on the so-called triangle theory [7]. Recently, this theory has been extended to derive criteria for the design of optimal and robust operating conditions for an SF-SMB unit, where the system is described

by linear adsorption equilibria [8]. The shape and position of the complete separation region in the operating parameter space for pressure gradient and isocratic operating mode have been determined and compared. The obtained results confirm the experimental observations mentioned above.

However, SMBs are most conveniently operated under overload conditions, since in general when increasing the overall feed concentration of the species to be separated, both productivity and solvent consumption improve. However, this usually implies operating the unit in the region where nonlinear competitive adsorption equilibria apply. Accordingly, we need criteria for the design of binary separations under such nonlinear overload conditions.

In this work we extend the triangle theory to the design of an SF-SMB separation carried out in the pressure gradient mode. To do this, two main features must be taken into account. First, since the adsorption thermodynamics depends on the solvent density value in each section of the unit, different adsorption isotherms must be used in the different sections of the unit. Secondly, rather complex hydrodynamic phenomena must be accounted for; these occur at the beginning of each time period when the valves and the columns switch and the set-point pressure values in each SMB section are stabilised.

The models used to describe the adsorption equilibria corresponding to different solvent density values are presented and discussed in Section 2. In Section 3 the equivalence between a SMB and a TMB unit is revised in general first, and then specialized to the case of SF-SMBs. The design criteria for SF-SMB units are derived in Section 4 using the same approach adopted for a SMB unit, where the elution strength gradient is realized through a temperature gradient imposed along the sections of the unit [9]. Finally, in Section 5, a procedure is developed to analyse the SF-SMB performance in order to determine the optimal operating conditions.

## 2. Adsorption isotherm models

In the case of low fluid phase concentration of the components to be separated, the adsorption equilibria under supercritical conditions can be described by a

linear relationship between adsorbed and fluid phase mass concentrations:

$$n_i = H_i c_i \quad (i = A, B) \quad (1)$$

where the coefficient  $H_i$  is the dimensionless Henry constant of component  $i$  and its dependence on density can be empirically accounted for through the following relationship [10]:

$$H_i = H_i^0 \left( \frac{\rho^0}{\rho} \right)^{b_i} \quad (i = A, B) \quad (2)$$

where  $H_i$  and  $H_i^0$  are the Henry constants of component  $i$  at the operating and reference densities  $\rho$  and  $\rho^0$ , respectively, and  $b_i$  is an empirical coefficient specific for the fluid and solid-phase at equilibrium, which depends upon temperature.

The addition to the eluent of a modifier, e.g. a polar alcohol to supercritical carbon dioxide, results in a reduction of the Henry constant. Although in general the dependence of  $H_i$  on the modifier concentration,  $c_m$ , can assume different functional forms, for the sake of simplicity but without loss of generality in our analysis the following relationship derived from chromatographic measurements is adopted [11]:

$$\frac{1}{H_i} = a_i c_m + d_i \quad (i = A, B) \quad (3)$$

Here  $c_m$  is the modifier concentration and  $a_i$  and  $d_i$  are two empirical constants, which depend on the chromatographic system considered. Thus, in order to account for the effect of both density and modifier concentration on the Henry constant, we use Eq. (3) to express the Henry constant at the reference density,  $H_i^0$ , and substitute it into Eq. (2). The resulting expression for  $H_i$  as a function of both  $\rho$  and  $c_m$  is:

$$H_i = \frac{1}{a_i c_m + d_i} \left( \frac{\rho^0}{\rho} \right)^{b_i} \quad (i = A, B) \quad (4)$$

In the following we also use Eq. (1) in the form:

$$n_{i,j} = H_{i,j}^* w_{i,j} \quad (i = A, B \quad j = 1, \dots, 4) \quad (5)$$

where  $w_{i,j}$  is the weight fraction of component  $i$  in the  $j$ th section of the SMB and:

$$H_{i,j}^* = H_i \rho_j \quad (6)$$

where  $\rho_j$  is the fluid density in section  $j$ .

As mentioned above, increasing the fluid phase concentration value leads to nonlinear competitive adsorption equilibria. The simplest effective model to describe this behavior is the classical Langmuir isotherm:

$$\begin{aligned} n_{i,j} &= \frac{N_i K_i c_{i,j}}{1 + \sum_l K_l c_{l,j}} \\ &= \frac{N_i K_{i,j}^* w_{i,j}}{1 + \sum_l K_{l,j}^* w_{l,j}} \quad (i = A, B \quad j = 1, \dots, 4) \end{aligned} \quad (7)$$

where  $K_{i,j}^* = K_i \rho_j$ , while  $N_i$  and  $K_i$  indicate the loading capacity and the equilibrium constant of the solute  $i$ , respectively. Note that, in the limit of small fluid phase concentrations, the Langmuir isotherm approaches the linear isotherm, where  $H_i = N_i K_i$ , hence Eq. (4) applies.

### 3. Analysis and modeling of an SF-SMB unit

The pressurization and depressurization dynamics after valve and column switch is of key importance for an SF-SMB unit operated in the pressure gradient mode, since it affects both the adsorption fronts position and the mass balances. Furthermore, only when this phenomenon is properly taken into account, consistent equivalence relationships between the SF-SMB and the SF-TMB units can be established, and the design criteria derived for the SF-TMB unit can be applied to the SF-SMB.

#### 3.1. Pressure changes during SF-SMB operation

The goal of this section is to describe the behavior of the SF-SMB unit during the pressurization/depressurization period that occurs at the beginning of each time period after valve switch.

Let us consider the SF-SMB unit in Fig. 2, when operating in the pressure gradient mode. Each section  $j$  is in general constituted of  $n_j$  chromatographic columns and it is kept at a pressure  $P_j$ , with  $P_1 \geq P_2 \geq P_3 \geq P_4$  and accordingly  $\rho_1 \geq \rho_2 \geq \rho_3 \geq \rho_4$ . Obviously the isocratic mode can be regarded as a

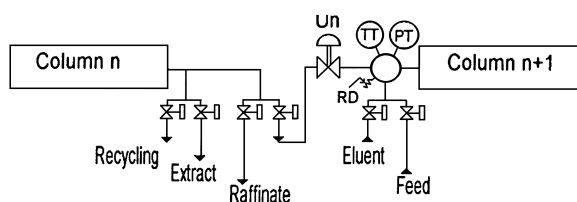


Fig. 3. Detailed scheme of the unit between each pair of columns.

special case of the pressure gradient mode defined above, where all pressure levels are the same. As shown in Fig. 3, each node between two columns is connected to the five inlets and outlets through on-off valves, while a back-pressure regulator keeps the pressure in the upstream column at the set-point level. After a valve and column switch occurs, one column leaves and a new column enters each section. The column that enters section  $j$  must be pressurized from pressure  $P_{j+1}$  to pressure  $P_j$  with  $j = 1, 2, 3$ , while in section 4 it must be depressurized from  $P_1$  to  $P_4$ . Since beside the back-pressure regulators four mass flow-meters and controllers are installed on the feed, extract, raffinate and recycle flows, pressurization of sections 1, 2 and 3 and depressurization of section 4 are made possible by feeding more eluent in section 1 and by removing more fluid from section 4, respectively. It is worth noting that the four flow-rate set points defined above, i.e.  $E$ ,  $F$ ,  $R$  and  $G_4$ , determine a set of nominal internal flow-rates  $G_j$ , given by:  $G_3 = G_4 + R$ ,  $G_2 = G_3 - F$ ,  $G_1 = G_2 + E$ .

The pressurization of the first three sections proceeds in series starting from section 1. In fact the back pressure valves that are placed between two sections open only when the pressure set point has been reached. Therefore a mass  $V\varepsilon(\rho_1 - \rho_2)$  of eluent is needed to reach the pressure set point in section 1, being  $V$  and  $\varepsilon$  the volume and the void fraction of the column, respectively; then the back pressure valve between section 1 and 2 opens and the last column of section 2 is pressurized using a mass of fluid phase equal to  $V\varepsilon(\rho_2 - \rho_3)$ ; finally the pressure set point in section 3 is reached by feeding to that section a mass of fluid phase equal to  $V\varepsilon(\rho_3 - \rho_4)$ . From the above description it can be concluded that the overall mass of eluent needed to pressurize the first three sections and that to be removed from section 4 are exactly the same and equal to  $V\varepsilon(\rho_1 - \rho_4)$ . This demonstrates that also during the initial pressurization/depressurization stage of the time period between two valve

switches the overall material balance is maintained although the flow-rates differ initially from the nominal ones. In particular, the additional mass to be fed to each section of the unit during the pressurization–depressurization stage is simply  $V\varepsilon(\rho_j - \rho_4)$  ( $j = 1, \dots, 4$ ) and this contribution reduces to zero for section 4, from which mass is only discharged to achieve pressure equilibration after valve switch.

Considering that a typical recycle flow-rate is equal to about 5 kg/h [6] and the mass to be discharged, for a column of  $\varepsilon V = 0.1$  l and  $\Delta\rho = 100$  g/l, is usually less than 10 g, the equilibration time of the fourth section is a few seconds. Similar considerations apply to the pressurization of the first three sections. Therefore in the following we will assume that the equilibration time is negligible in comparison to the switch time  $t^*$ , which is normally in the order of at least 1 min. With reference to a point located at the beginning of the first column of each section (cf. Section 3.3), in addition to the nominal flow-rate, only the mass entering the section must be considered and averaged over the time  $t^*$ , thus yielding:

$$\bar{G}_j = G_j + \frac{V\varepsilon(\rho_j - \rho_4)}{t^*} \quad (j = 1 \dots 4) \quad (8)$$

### 3.2. Dynamics of the adsorption fronts

In this section the pressurization effect on the dynamics of the adsorption front is analysed, thus showing that it is always very small. Therefore the retention times of the two solutes in the unit can be evaluated with reference to the nominal flow-rates, thus neglecting the pressurization contribution. However, the pressurization stream must be taken into account when defining the equivalence conditions between SF-TMB and SF-SMB in order to fulfill the mass balances, as it is discussed in Section 3.3.

Let us consider for the sake of simplicity a single chromatographic column at a density  $\rho_2$ , where no solute is present. At time  $t = 0$  a stream at a higher density level  $\rho_1$  enters the column, where the solute is at a concentration such that linear adsorption isotherm with Henry constant,  $H$ , applies. Before the column is equilibrated at the higher density value  $\rho_1$ , i.e. during the time period  $0 < t < t_{eq}$ , a flow-rate

$V\varepsilon(\rho_1 - \rho_2)/t_{\text{eq}}$  goes through it in addition to the nominal flow-rate  $G$ . For the sake of simplicity, instead of considering the rigorous hydrodynamic analysis, where the evolution of the density in the column from  $\rho_2$  to  $\rho_1$  is taken into account, two limiting cases are analysed, i.e. one where the entire column is assumed to be already at the final density  $\rho_1$  during the whole equilibration time (case A) and one where the column is assumed to remain at the initial density  $\rho_2$  during the whole equilibration time (case B). It is clear that the real behavior will be somehow intermediate between these two extremes. In the following, the variation of the retention time of the solute, due to the additional pressurization contribution, with respect to the case where the initial density in the column is the same as that of the feed, i.e.  $\rho_2 = \rho_1$ , is shown to be negligible in both cases.

The end of the column of length  $L$  and cross sectional area  $S$  is reached at time  $t_{\text{R}}^{\text{A}}$ , which is implicitly given in the first case A by the relation:

$$L = \left( \frac{G + \frac{V\varepsilon(\rho_1 - \rho_2)}{t_{\text{eq}}}}{\varepsilon S \rho_1} t_{\text{eq}} + \frac{G}{\varepsilon S \rho_1} (t_{\text{R}}^{\text{A}} - t_{\text{eq}}) \right) \cdot \frac{\varepsilon}{\varepsilon + (1 - \varepsilon)H} \quad (9)$$

while in the second case B the corresponding retention time  $t_{\text{R}}^{\text{B}}$  is given by:

$$L = \left( \frac{G + \frac{V\varepsilon(\rho_1 - \rho_2)}{t_{\text{eq}}}}{\varepsilon S \rho_2} t_{\text{eq}} + \frac{G}{\varepsilon S \rho_1} (t_{\text{R}}^{\text{B}} - t_{\text{eq}}) \right) \cdot \frac{\varepsilon}{\varepsilon + (1 - \varepsilon)H} \quad (10)$$

It is worth noting that the Henry constant  $H$  does not change in Eqs. (9) and (10). Eq. (9) yields:

$$t_{\text{R}}^{\text{A}} = t_{\text{R}}^{\text{ISO}} - \frac{V\varepsilon}{G}(\rho_1 - \rho_2) \quad (11)$$

while on the other hand Eq. (10) leads to:

$$t_{\text{R}}^{\text{B}} = t_{\text{R}}^{\text{ISO}} - \left( \frac{\rho_1}{\rho_2} - 1 \right) \left( \frac{V\varepsilon}{G} \rho_1 + t_{\text{eq}} \right) \quad (12)$$

where  $t_{\text{R}}^{\text{ISO}}$  represents the retention time observed

when the column is initially at the same density of the feed, i.e.  $\rho_2 = \rho_1$ , which is given by:

$$t_{\text{R}}^{\text{ISO}} = \frac{V\varepsilon\rho_1}{G} \left( 1 + \frac{1 - \varepsilon}{\varepsilon} H \right) \quad (13)$$

In order to evaluate the relative importance of the variation between  $t_{\text{R}}^{\text{ISO}}$  and either  $t_{\text{R}}^{\text{A}}$  or  $t_{\text{R}}^{\text{B}}$ , we consider some typical values of the operating parameters, namely a column volume  $V = 0.2$  l and a bed void fraction  $\varepsilon = 0.4$ , where  $G = 70$  g/min,  $\rho_1 = 850$  g/l and  $\rho_2 = 750$  g/l, which correspond to  $P_1 = 210$  bar and  $P_2 = 132$  bar in the case of carbon dioxide at  $T = 40^\circ\text{C}$ , respectively. As shown in Section 3.1, we assume that the equilibration time,  $t_{\text{eq}}$  is negligible when compared to the retention time in Eq. (12). Thus from Eqs. (11)–(13), it can be shown that  $t_{\text{R}}^{\text{A}}$  and  $t_{\text{R}}^{\text{B}}$  differ from  $t_{\text{R}}^{\text{ISO}}$  by 1.7 and 2.1%, respectively. Therefore, in the following we use Eq. (13) to evaluate the retention time of a solute in the column, thus neglecting the correction term due to the pressurization effect described above.

### 3.3. The equivalent TMB unit

Let us now identify the conversion rules that determine the flow-rates in the SF-TMB unit, which is equivalent to the SF-SMB unit described above. When these conversion rules are complied with, the SF-TMB can be used to design the operating conditions of the SF-SMB, since the two units achieve in principle the same separation performance.

Let us consider the four sections of the SF-SMB unit and a reference point located at the beginning of the first column of each section (see Ref. [12] for a similar analysis of the TMB/SMB equivalence problem). The fluid flow-rate of the equivalent counter-current SF-TMB unit is given by two contributions: a positive one corresponding to the average SF-SMB flow-rate given by Eq. (8) and a negative one caused by the discrete shift of the entire column in the same direction of the fluid flow, occurring at the switching of the port positions and corresponding to an amount in mass equal to  $V\varepsilon\rho_j$ . The latter quantity must also be averaged over the whole period  $t^*$ , thus yielding:

$$G_j^{\text{TMB}} = G_j^{\text{SMB}} + \frac{V\varepsilon(\rho_j - \rho_4)}{t^*} - \frac{V\varepsilon\rho_j}{t^*} \quad (j = 1, \dots, 4) \quad (14)$$

which can be simplified to:

$$G_j^{\text{TMB}} = G_j^{\text{SMB}} - \frac{V\varepsilon\rho_4}{t^*} \quad (j = 1, \dots, 4) \quad (15)$$

The continuous solid volume flow-rate of the SF-TMB is obtained by calculating the average solid flow-rate in the SF-SMB with respect to the same fixed reference point used before, that is:

$$Q_s = \frac{V(1 - \varepsilon)}{t^*} \quad (16)$$

where  $Q_s$  is the TMB solid flow-rate [13]. Eqs. (15) and (16) define the SF-TMB unit equivalent to the SF-SMB, i.e. a unit that achieves the same separation performance of the SF-SMB unit of interest [14].

#### 4. Design of complete separation operating conditions

Let us consider a binary separation in a SF-TMB unit and assume that there are no mass transfer limitations and no axial dispersion (i.e. we apply the equilibrium theory model) and that the pressure drop in the columns is negligible, i.e. the density is constant through each section. Pressure as well as density may change from section to section in the case of pressure gradient operation mode.

The mass balance for the  $i$ th component in the  $j$ th section can be written as:

$$\frac{\partial(\varepsilon\rho_j w_{i,j} + (1 - \varepsilon)n_{i,j})}{\partial t} + \frac{\partial(G_j^{\text{TMB}} w_{i,j} - Q_s n_{i,j})}{S\partial z} = 0 \quad (17)$$

where  $t$  is time and  $z$  the axial coordinate. In Eq. (17) the adsorbed phase concentration,  $n_{i,j}$  is given in terms of the fluid phase compositions through one of the adsorption isotherms discussed above. It is worth noting that the solid particles are assumed to be non-porous.

The steady state solution of Eq. (17) depends on the adsorption isotherm and on the flow-rate ratios  $G_j^{\text{TMB}}/Q_s$  [7], which can also be expressed in terms of the SMB operating parameters using Eq. (15):

$$m_j = \frac{G_j^{\text{TMB}}}{Q_s} = \frac{G_j^{\text{SMB}} t^* - V\varepsilon\rho_4}{V(1 - \varepsilon)} \quad (j = 1, \dots, 4) \quad (18)$$

The SMB design strategy adopted in the following is the same as in the case of liquid phase SMBs [7]: first, optimal operating conditions to achieve the desired separation performance, i.e. complete separation of A and B, for the SF-TMB unit are determined in terms of  $m_j$  values; then, these are converted into SMB operating parameters using Eq. (18). In the case of an existing SF-SMB operated in pressure gradient mode nine parameters have to be selected, i.e.  $G_j^{\text{SMB}}$ ,  $\rho_j$ , with  $j=1, \dots, 4$ , and  $t^*$ . The switch time is in general selected based on column efficiency considerations, which are omitted here since they have already been discussed elsewhere [15,16].

##### 4.1. Separation of systems described by a linear adsorption isotherm

Substituting Eqs. (5) and (18) into Eq. (17), this reduces to:

$$(\varepsilon\rho_j + (1 - \varepsilon)H_{i,j}^*) \frac{\partial w_{i,j}}{\partial t} + Q_s(m_j - H_{i,j}^*) \frac{\partial w_{i,j}}{S\partial z} = 0 \quad (19)$$

In order to achieve complete separation in a TMB or an SMB unit the following necessary and sufficient conditions must be fulfilled:

$$\begin{aligned} H_{A,1}^* &< m_1 \\ H_{B,2}^* &< m_2 < H_{A,2}^* \\ H_{B,3}^* &< m_3 < H_{A,3}^* \\ m_4 &< H_{B,4}^* \end{aligned} \quad (20)$$

Let us focus on the two central sections of the unit. When the SF-SMB is operated in the pressure gradient mode, two qualitatively different situations may occur, depending on whether  $H_{A,2}^* > H_{B,3}^*$  or  $H_{A,2}^* < H_{B,3}^*$ . The regions of separation for the former case are shown in Fig. 4, while the corresponding diagram for the latter case has been reported elsewhere [8].

Operating points in region 1 of Fig. 4 allow

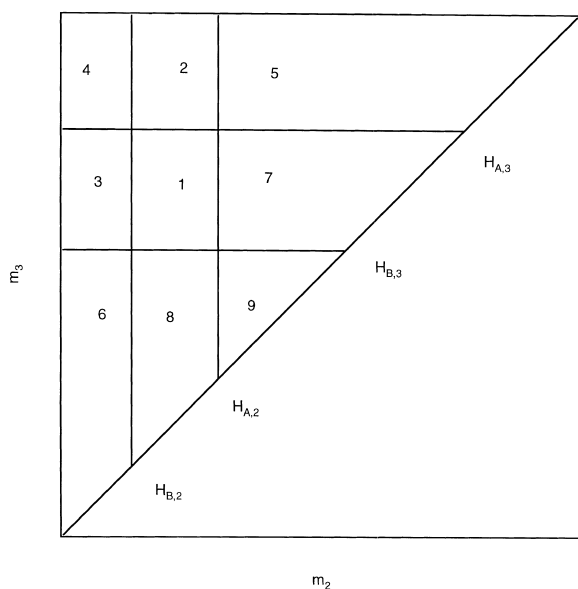


Fig. 4. SF-SMB pressure gradient mode under linear conditions ( $H_{A,2}^* > H_{B,3}^*$ ).

complete separation to be achieved, whereas only the extract is pure in region 2 and only the raffinate is pure in region 3. The two components to be separated distribute in the two outlet streams in region 4, whereas they flood the raffinate and the extract in region 5 or 6, respectively. Finally, regions 7, 8 and 9 are not compatible with adsorption under linear conditions as shown elsewhere [8].

#### 4.2. Separation of systems described by a nonlinear Langmuir isotherm

Let us consider the general case where a nonlinear adsorption equilibrium described by the Langmuir isotherm (7) is established between the adsorbed and the fluid phase.

The constraint on the flow-rate ratio  $m_1$  is the same as in the linear case, i.e.  $m_1 > H_{A,1}^*$ , whereas that on  $m_4$  is a function of  $m_2$  and  $m_3$  [7]. When the complete regeneration of  $\text{CO}_2$  in section 4 is difficult, the SMB unit can be operated in two ways. In the first configuration, only three sections are used, thus collecting the whole stream from section 3 as raffinate, separating all the solute by depressurization

and then recycling  $\text{CO}_2$  to section 1 after recompression. In the second configuration, a different regeneration unit (e.g. activated carbon) is introduced after section 4 to complete the removal of component B without changing the  $\text{CO}_2$  pressure before recycling it to section 1. Both solutions are particularly convenient when using a supercritical eluent.

In the following we focus on sections 2 and 3 of the unit and assume that the proper constraints on  $m_1$  and  $m_4$  are fulfilled, which, with reference to Figs. 1 and 2, implies no component A is adsorbed on the stationary phase after regeneration in section 1 and no component B is present in the mobile phase at the outlet of section 4. The following material balances for the components to be separated apply, provided that complete separation is achieved:

$$\begin{aligned} G_F w_{A,F} + G_2^{\text{TMB}} w_{A,2} - Q_s n_{A,2} &= 0 \\ G_F w_{B,F} - G_3^{\text{TMB}} w_{B,3} + Q_s n_{B,3} &= 0 \end{aligned} \quad (21)$$

where  $G_F$  is the feed flow-rate, i.e.:

$$G_F = G_3^{\text{TMB}} - G_2^{\text{TMB}} \quad (22)$$

Substituting Eq. (18), Eq. (21) yields:

$$\begin{aligned} (m_3 - m_2) w_{A,F} + m_2 w_{A,2} - n_{A,2} &= 0 \\ (m_3 - m_2) w_{B,F} - m_3 w_{B,3} + n_{B,3} &= 0 \end{aligned} \quad (23)$$

which when coupled with Eq. (7), becomes formally identical to the corresponding relations obtained for a liquid SMB [14]. Actually, for the isocratic case, they are indeed identical, while for the pressure gradient case, different equilibrium isotherms in the different sections of the unit, as given by Eq. (7), must be used. It is worth noting that the derivation of these relationships are more complex although conceptually similar to the case of liquid phase SMB [7]. For the sake of brevity we do not report here the mathematical details, which can be found elsewhere [9]. Following such a procedure, the complete separation region for a binary system in the pressure gradient mode is obtained as a function of the isotherm parameters, of the pressure values in sections 2 and 3 and of the feed composition.

In Fig. 5 the complete separation region for the model system under examination is shown for differ-



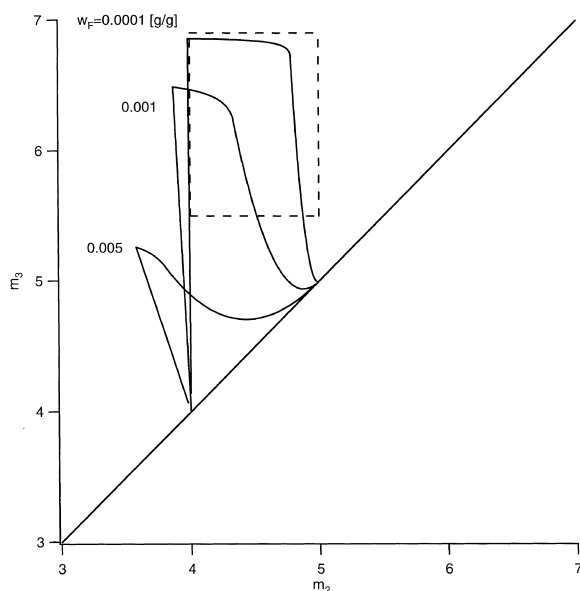


Fig. 5. SF-SMB pressure gradient mode under nonlinear conditions: effect of the feed concentration on the complete separation region. The rectangle drawn with a dotted line represents the complete separation region under linear conditions. Thermodynamic parameters in Eq. (7):  $H_{A2} = 5$ ,  $H_{B2} = 4$ ,  $b = 3$ ,  $N_A = N_B = 0.5$  [g/l],  $\rho_2 = 880$ ,  $\rho_3 = 750$ .

ent values of the overall feed weight fraction. It is worth noting that as in the case of liquid operation, the complete separation region becomes sharper as the feed concentration increases. A peculiar feature of the SF-SMB operating in the pressure gradient mode that does not apply to the liquid SMB is that the linear and nonlinear complete separation regions have different intersections with the diagonal. Operating points close to the diagonal imply, in fact, small feed flow-rates, compared to the flow-rates inside the unit. In liquid SMBs, this implies that the concentrations of the components to be separated within the unit are very small whatever the feed concentration. Therefore, the conditions to achieve complete separation become always the same as in the case of infinitely diluted linear systems. On the contrary, in a SF-SMB unit operating in the pressure gradient mode in region 8 of Fig. 4, the concentration of component B builds up in section 3 and the linear conditions are never achieved, even for small feed flow-rate [9].

## 5. Analysis and optimisation of the separation performance

The classical parameters used to evaluate the performance of SMB units are the desorbent requirement and the productivity per unit mass of stationary phase. Let us discuss these performance parameters as a function of the density levels in the unit and the modifier concentration.

### 5.1. Desorbent requirement

In an SF-SMB unit, the feed of the desorbent implies to cool down the carbon dioxide, pump it at low temperature to a certain pressure and then heat it up to a supercritical state [6]. The operating cost is therefore almost independent of the final pressure, since this is reached by pumping  $\text{CO}_2$  in a liquid state. Therefore, the maximum pressure is established by the technical specifications of the plant and not by the operating costs. As a consequence the cost associated to the desorbent requirement, DR, is simply proportional to the amount of carbon dioxide fed per unit time to section 1,  $G_1$ , and this is the quantity to be minimized in the following. Using condition (20) for the minimum value of  $m_1$ , the minimum flow-rate  $G_1$  can be obtained, which when substituted in Eq. (8) gives:

$$\overline{G_{1,\min}} = \frac{V\rho_1}{t^*}(\varepsilon + (1 - \varepsilon)H_{A1}) \quad (24)$$

Substituting Eq. (4) into the last equation, one obtains:

$$\overline{G_{1,\min}} = \frac{V\rho_1}{t^*} \left( \varepsilon + \frac{1 - \varepsilon}{a_A c_m + d_A} \left( \frac{\rho^0}{\rho_1} \right)^{b_A} \right) \quad (25)$$

For values of the parameters typical of supercritical chromatography where  $b > 1$ , this function is monotonically decreasing with  $\rho_1$ . Therefore, unless other considerations apply, it is convenient to operate at the maximum allowable pressure in section 1 in order to minimize the  $\text{CO}_2$  flow-rate entering section 1.

On the other hand, Eq. (25) indicates that increasing the modifier concentration  $c_m$  has a positive effect on the desorbent requirement. However, this is

counterbalanced by the necessity of recovering the modifier from the collected product streams.

## 5.2. Productivity

The productivity can be defined as following:

$$PR = \frac{w_F F}{M_{sp}} \quad (26)$$

where  $w_F$  is the overall weight fraction of the solutes in the feed,  $M_{sp}$  is the total mass of stationary phase and  $F$  the feed flow-rate, given by  $F = G_3^{SMB} - G_2^{SMB}$ . Substituting Eq. (18) into the last equation yields:

$$PR = \frac{w_F V(1 - \varepsilon)}{t^* M_{sp}} (m_3 - m_2) \quad (27)$$

This relation shows that for a given switch time  $t^*$  productivity is maximum on the vertex of the complete separation region where the distance from the diagonal is maximum. In the linear case, assuming  $b_A = b_B = b$ , and defining the selectivity  $S = H_A^0 / H_B^0$ , Eq. (27) can be recast as:

$$\begin{aligned} PR^{opt} &= \frac{w_F V(1 - \varepsilon) H_{B,3}^*}{t^* M_{sp}} \left( S - \left( \frac{\rho_3}{\rho_2} \right)^{b-1} \right) \\ &= \frac{w_F V(1 - \varepsilon) H_{B,2}^*}{t^* M_{sp}} \left( S \left( \frac{\rho_2}{\rho_3} \right)^{b-1} - 1 \right) \end{aligned} \quad (28)$$

Assuming  $b > 1$ , the productivity is minimum in the isocratic mode, where  $\rho_2 = \rho_3$  and increases for  $\rho_2 > \rho_3$  as the pressure difference between the two central sections of the unit increases. The pressure gradient mode improvement is larger for systems with low selectivity, as it can be seen in Fig. 6, where the ratio:

$$\frac{PR_{PG}^{opt}}{PR_{ISO}^{opt}} = \frac{S - \left( \frac{\rho_3}{\rho_2} \right)^{b-1}}{S - 1} \quad (29)$$

is shown as a function of the system selectivity, assuming that the isocratic density is equal to  $\rho_3$ .

Let us now consider the effect of the modifier concentration on productivity. Since no experimental data on the effect of the modifier concentration on the nonlinear equilibrium of a solute in supercritical carbon dioxide are available, we focus on an SF-

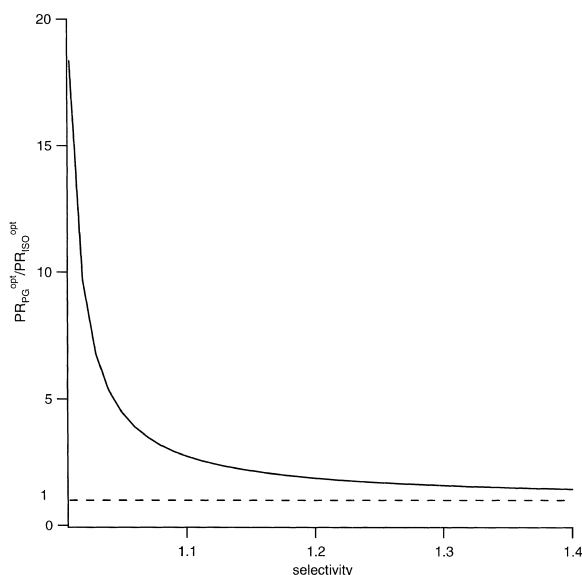


Fig. 6. Performance parameters as a function of the system selectivity:  $\rho_1 = 900$  [g/l],  $\rho_2 = 880$ ,  $\rho_3 = 800$ ,  $\rho_4 = 780$ ,  $b = 3$ .

SMB unit operating under linear conditions. In general, the addition of a modifier has two effects: first the Henry constants become smaller, secondly density changes less with pressure, i.e. the curve  $\rho(P)$  is less steep. Therefore, the productivity in both isocratic and pressure gradient mode decreases and the beneficial effect of a pressure change between sections 2 and 3 becomes less evident.

Let us consider as an example the separation of chrysene and 1-methoxy-naphthalene on silica carried out at a density equal to 0.6 g/cc [11]. Let us assume  $b_A = b_B = 3$ , to describe the decrease of the Henry constants with density. Since the productivity is proportional to the distance from the diagonal of the operating point in the  $(m_2, m_3)$  plane, we can see from Fig. 7 that the maximum productivity in the pressure gradient mode is always larger than in the isocratic mode, but it decreases for increasing modifier concentrations. It follows that optimizing productivity and desorbent requirement leads to low and high modifier concentration, respectively; these opposing trends call for a compromise. Therefore, the best choice of modifier concentration will be based on a rather accurate characterization of the retention behavior of the components to be separated as a

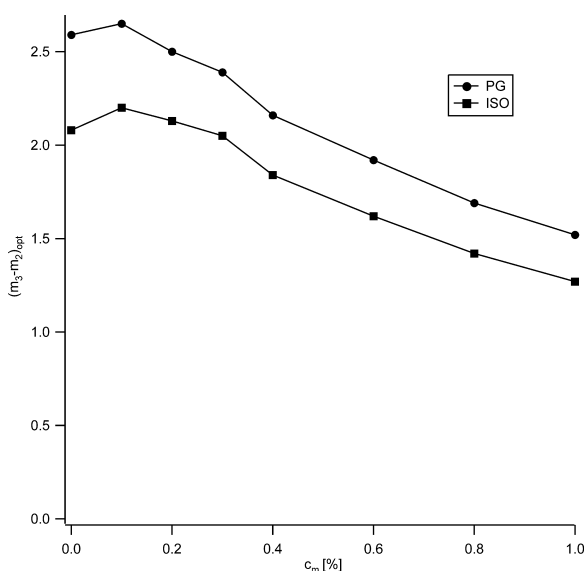


Fig. 7. Distance from the diagonal of the optimal operating point in isocratic and pressure gradient mode as a function of the modifier concentration for the system chrysene and 1-methoxynaphthalene on silica (Whatman Partisil-10) [11].

function of supercritical fluid density and modifier concentration.

## 6. Conclusion

The operation of the SF-SMB unit has been analyzed and, based on suitable simplifying assumptions, the relationships that define the equivalent SF-TMB unit have been derived. This has allowed the “triangle theory” ([7,8]) to be extended to the SF-SMB operating in pressure gradient mode under nonlinear adsorption equilibria. This result provides, in the frame of the equilibrium theory, a rather useful tool for the prediction of the separation performance and the choice of the operating conditions of SF-SMBs. In particular, the separation performance of the unit has been analyzed in terms of desorbent requirement and productivity, and analytical expressions for the optimal operating conditions have been derived. It has been shown that the pressure gradient operating mode yields always better performance

than the isocratic, mode, particularly at low selectivities. It has been demonstrated that a compromise in the choice of the modifier concentration is usually needed in order to match both productivity and desorbent requirements.

## 7. Nomenclature

$a_i$	empirical coefficient in Eq. (3)
$b_i$	exponent in Eq. (2)
$c_i$	fluid phase concentration [g/l]
$d_i$	empirical coefficient in Eq. (3)
$F$	mass feed flow-rate [g/min]
$G_j^{SMB}$	nominal mass flow-rate in section $j$ of the SMB unit [g/min]
$\bar{G}_j$	average mass flow-rate in section $j$ of the SMB unit [g/min]
$G_j^{TMB}$	mass flow-rate in section $j$ of the TMB unit [g/min]
$H_i$	dimensionless Henry constant of component $i$
$H_i^*$	modified Henry constant defined by Eq. (6) [g/l]
$K_i$	Langmuir equilibrium constant defined by Eq. (7) [l/g]
$K_i^*$	modified Langmuir equilibrium constant defined by Eq. (7) [g/g]
$L$	column length [cm]
$m_j$	flow-rate ratio in section $j$ [g/l]
$M_{sp}$	overall amount of stationary phase loaded in the SMB unit [g]
$n_i$	adsorbed phase mass concentration [g/l]
$N_i$	saturation loading capacity of component $i$ [g/l]
$PR$	productivity, defined by Eq. (27) [g/g/min]
$Q_s$	solid flow-rate [l/min]
$S$	column section [cm <sup>2</sup> ]
$S_{AB}$	selectivity, defined by $H_A/H_B$
$t$	time [min]
$t_R$	retention time [min]
$t^*$	switch time [min]
$t_{eq}$	equilibration time [min]
$V$	volume of a single SMB column [l]
$w_i$	fluid phase weight fraction
$z$	axial coordinate [cm]

*Greek*

$\varepsilon$	bed void fraction
$\rho$	fluid phase density [g/l]

*Subscript and superscripts*

A	more retained species
B	less retained species
F	feed
ISO	isocratic operating mode
$i$	component index, $i = A, B$
$j$	section index, $j = 1, \dots, 4$
$m$	modifier
PG	pressure gradient operating mode
0	reference value

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