Separation Science and Technology
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

The M3C Process: A New Multicolumn Chromatographic Process Integrating a Concentration Step. I—The Equilibrium Model

Souhir Abdelmoumen[a]; Laurence Muhr[a]; Michel Bailly[a]; Olivier Ludemann-Hombourger[b]
[a] Laboratoire des Sciences du Génie Chimique, Nancy, France [b] Novasep SAS, Boulevard de la Moselle, Pompey, France

To cite this Article Abdelmoumen, Souhir , Muhr, Laurence , Bailly, Michel and Ludemann-Hombourger, Olivier(2006) 'The M3C Process: A New Multicolumn Chromatographic Process Integrating a Concentration Step. I—The Equilibrium Model', Separation Science and Technology, 41: 12, 2639 — 2663

To link to this Article: DOI: 10.1080/01496390600829992

URL: http://dx.doi.org/10.1080/01496390600829992

Separation Science and Technology, 41: 2639–2663, 2006

ISSN 0149-6395 print/1520-5754 online
DOI: 10.1080/01496390600829992

The M3C Process: A New Multicolumn Chromatographic Process Integrating a Concentration Step. I—The Equilibrium Model

Souhir Abdelmoumen, Laurence Muhr, and Michel Bailly
Laboratoire des Sciences du Génie Chimique, Nancy, France

Olivier Ludemann-Hombourger
Novasep SAS, Boulevard de la Moselle, Pompey, France

Abstract: A new Multicolumn Chromatographic process, called M3C, is introduced. The originality of this process relies on the integration of a concentration loop at the extract level on the recycling stream of a Multicolumn Continuous Process (Simulated Moving Bed, Varicol…). Thanks to the tools of the equilibrium theory applied to an equivalent True Moving Bed integrating a concentration step, the working parameters of this new process are estimated in the case of multicomponent competitive Langmuir adsorption isotherms. The performances of this process are compared to those of the classical True Moving Bed in terms of productivity and eluent consumption, and exhibit significant improvement.

Keywords: Multicolumn continuous chromatography, M3C process, preparative chromatography, displacement effect, equilibrium theory

INTRODUCTION

For several decades preparative liquid phase chromatography has got an increasing field of applications, especially with the introduction of the

Received 13 March 2006, Accepted 10 May 2006
Address correspondence to Michel Bailly, Laboratoire des Sciences du Génie Chimique, CNRS-ENSIC BP 20451, F-54001, Nancy, France. E-mail: michel.bailly@ensic.inpl-nancy.fr

concept of True Moving Beds (TMB). The basic idea consists of the realization of a separation using a real counter-current between the solid and the liquid phase, by analogy with other unit operations such as distillation or extraction. However, this countercurrent process gives rise to technological difficulties. At the end of the 50's, the replacement of the real movement of the solid phase by a simulated one allowed to overcome this difficulty. Therefore, the invention of the Simulated Moving Bed (SMB) in 1960 by the UOP company (1) strongly contributed to the development of the preparative chromatography in different fields of industry such as petrochemical and sugar industries. In the 90's, this operating mode was applied in the field of fine chemistry, mainly for the purification of chiral molecules. Other Multicolumn Continuous processes (MCC) were later introduced such as the VariCol (2), the Modicon (3), and the Powerfeed processes (4).

Besides, the major difficulty to implement these processes lies in the determination of adequate operating parameters to carry out a given separation with optimal performances. The equilibrium theory developed by Glueckauf (5), Rhee et al. (6), Tondeur (7), and Helfferich (8) allows to describe the dynamics of a chromatographic column in view of an adsorption equilibrium; this theory was developed in both cases of a fixed (6) and a moving bed single column (9). Many studies were then carried out in the case of MCC, in order to estimate operating conditions for binary mixtures separations (10–12), for ternary separations (13), and for multi-components systems (14–16). It can be noticed that, although the studied MCC are not True Moving Beds, TMB tools are used, considering architectures which enable transposition rules.

The aim of the present work is to extend this analysis in order to estimate the different parameters required for a separation of a binary mixture on a True Moving Bed integrating a concentration step in the recycling loop at the extract position. The approach is based on the equilibrium theory. This theory is used to focus on the process thermodynamics to fully explore and understand the process dynamics. The performances of this new process will be compared to those of the classical TMB to illustrate the benefits of adding a concentration step in the process.

PRINCIPLE OF THE MULTICOLUMN CONTINUOUS PROCESSES

The True Moving Bed

A True Moving Bed consists of a single chromatographic column within which the liquid and the solid phases move counter-currently. The principle of the separation of a binary mixture (1+2), for which species 2 is more retained on the solid phase than species 1, is illustrated in Fig. 1. Injection and collection points delimit four zones: feed and eluent are injected respectively between zones II and III and between zones IV and I, whereas the extract and the raffinate are collected respectively between zones I and II and between zones III and IV.

Each of the four zones of the TMB insures a special function:

- Zone I: desorption of species 2
- Zone II: desorption of species 1
- Zone III: adsorption of species 2
- Zone IV: adsorption of species 1, recovery of a part of the eluent before re-circulation.

To obtain concentrated final pure products, the extract and the raffinate are evaporated and the eluent can be recycled to minimize the solvent consumption of the process. In an industrial unit, MCC processes are thus coupled with two evaporators, on the extract and raffinate collection lines.

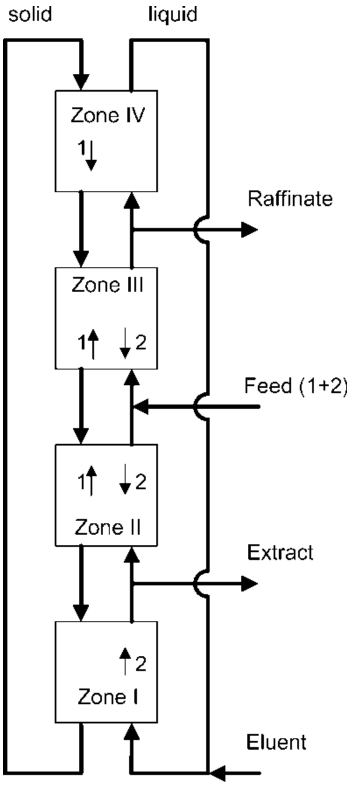

Figure 1. Classical four zones True Moving Bed.

The True Moving Bed Integrating a Concentration Loop

The peculiarity of this process with regard to the classical TMB is based on the integration of a concentration step located at the extract level (17). The fraction of the solution recycled from zone I to zone II is concentrated before reinjection.

The basic concept of the new M3C process is to reduce the required flow rate in zone II and therefore to increase the feed flow rate by a modification of the retention of the species 1 in zone II. As depicted in the previous section, zone II is aimed at desorbing the less retained compound 1. Integrating a concentration step at the inlet of zone II creates an increase of the concentration of the more retained compound. Under certain circumstances, a high concentration of the most retained compound creates a displacement effect on the less retained compound and eases its desorption. This process is therefore particularly interesting for non-linear systems, where competitive effects occur between the separated species.

The application of the equilibrium theory is justified, considering that the desired displacement effect is purely based on the process thermodynamics characterized by the competitive adsorption of the two species on the stationary phase. This theory will be applied to better understand the process dynamics and to characterize the expected benefits compared to the classical MCC processes.

This concentration step can be realized, as illustrated in Fig. 2, through the mixing of a fraction of the outlet of zone I with the required amount of the highly concentrated product obtained at the outlet of the extract evaporator. The concentration of the injected stream in zone II must be controlled, it adds a complementary operating parameter compared to the TMB process. A procedure of calculation of the adequate flow rates allowing to realize separations on this process, considering a non-linear equilibrium adsorption, will be clarified in the following section. The influence of the concentration factor between zone I and II will be highlighted.

APPLICATION OF THE EQUILIBRIUM THEORY

Mass Balance

Before dealing with the case of a four zones Moving Bed, we consider the case of a binary separation on a single ideal column within which the liquid and the solid phase are circulating in a counter-current movement (9). The term “ideal” requires that:

- The system is one-dimensional in the direction of the liquid stream.
- The volumetric flow rate of each phase as well as the packing porosity ε are constant.

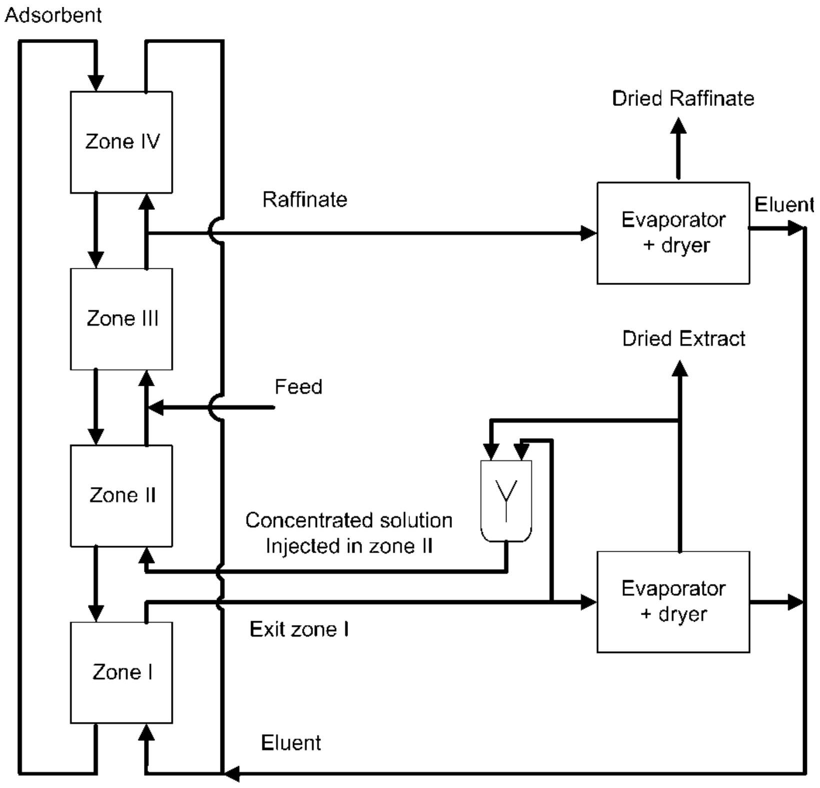

Figure 2. The concentration loop.

- Local equilibrium is established between both phases.
- The axial dispersion is negligible compared to the convective transport.
- The adsorption is isothermal and isochoric

The differential mass balance of a component *i* can be written as:

$$u_e \frac{\partial C_i}{\partial z} - v_e \frac{1-\varepsilon}{\varepsilon}\frac{\partial n_i}{\partial z} + \frac{\partial C_i}{\partial t} + \frac{1-\varepsilon}{\varepsilon}\frac{\partial n_i}{\partial t} = 0; \quad \forall i \in [1,2]. \tag{1}$$

If the coherence condition is fulfilled (see Equation (11)), Equation (1) can be rearranged and the following relation is obtained:

$$\frac{\partial C_i}{\partial t} + u_{C_i}\frac{\partial C_i}{\partial z} = 0. \tag{2}$$

Where u_{C_i} is the migration velocity of the concentration C_i defined by:

$$u_{C_i} = \left(\frac{\partial z}{\partial t}\right)_{C_i} = \frac{u_e[1-(1/q)(\partial n_i/\partial C_i)]}{1+[(1-\varepsilon)/\varepsilon]/(\partial n_i/\partial C_i)}. \tag{3}$$

Where q is the reduced liquid flow rate, defined as the ratio of the liquid flow rate to the solid one. The relation (2) has the form of a simple kinematic wave (18). This relation corresponds to the propagation of a wave of concentration with the velocity u_{C_i}, which is the velocity of a concentration when the equilibrium between phases is reached. According to relation (3), this parameter depends on the slope of the equilibrium adsorption isotherm. It can be noted that the migration velocity of a concentration must be differentiated from the molecule velocity which is the velocity of a fraction of molecules contained in the mobile phase and which move at the velocity of this one (19).

Equilibrium Adsorption Isotherm

In the following part of this paper, the separation of a binary mixture (1+2), for which the species 2 is the most retained on the solid phase, is considered. The adsorption equilibrium is governed by a competitive Langmuir type isotherm.

The concentration in the solid phase of each of the species is given by the relation (4):

$$n_i = \frac{N_i K_i C_i}{1 + \sum_j K_j C_j} = \frac{a_i C_i}{1 + \sum_j K_j C_j}. \tag{4}$$

The solvent is assumed to behave as an inert component, without any affinity for the adsorbent, and both components are classified in order of affinity such as:

$$N_1 K_1 < N_2 K_2. \tag{5}$$

The Characteristic Equation

Given that n_i depends on C_i through the adsorption isotherm relation, Equation (1) describes the interdependence between the different species' mass balances. In order to make these equations become independent, a change of base (6) is carried out: the space of concentrations C_i is replaced by the space of parameters ω_i. These one are the roots of the characteristic equation, which constitutes the bijection relation between C_i and ω_i:

$$\omega \sum_i \frac{K_i C_i}{N_i K_i - \omega} = 1. \tag{6}$$

Otherwise, according to the concentration in solid phase:

$$\sum_i \frac{K_i n_i}{N_i K_i - \omega} = 1. \tag{7}$$

The roots ω_i verify the following relation:

$$0 \leq \omega_1 \leq N_1K_1 \leq \omega_2 \leq N_2K_2. \tag{8}$$

Conversely, knowing the roots ω_i we can calculate C_i or n_i using the Equations (9) and (10):

$$C_i = \frac{\prod_{j=1}^{2}(N_iK_i/\omega_j - 1)}{K_i(N_iK_i/N_jK_j - 1)_{j \neq i}}. \tag{9}$$

$$n_i = \frac{\prod_{j=1}^{2}(N_iK_i - \omega_j)}{K_i(N_iK_i - N_jK_j)_{j \neq i}}. \tag{10}$$

And the denominator D of the Langmuir equation verifies:

$$D_i = \prod_i \frac{N_iK_i}{\omega_i} = 1 + \sum_i K_iC_i.$$

The parameters ω_i, although without evident physical meaning, allow to derive analytical expressions characterizing the dynamics of the chromatographic column (plate composition, wave velocity), as will be done in the following sections.

Waves Generation

The equilibrium theory shows that in the case of a Langmuir type isotherm:

- The saturation of a clean bed by a mixture of 2 species generates 2 compressive waves, which separate 3 states of concentrations in the column.
- On the other hand, if a column, initially saturated by a mixture of 2 species, is regenerated with a pure eluent, 2 dispersive waves, separating 3 states of concentration, are obtained.

The Coherence Condition

In a multi-component system, a wave can be coherent or not coherent. For a position and a given time, when a concentration of a species moves together with the concentration of the other species, the whole moves at the same speed; all the concentrations are thus in phase and so form a coherent wave (8). The condition of coherence is described by the equality of the migration velocity of the various concentrations, which can be expressed by:

$$\left(\frac{\partial n_i}{\partial C_i}\right)_z = \left(\frac{\partial n_j}{\partial C_j}\right)_z. \tag{11}$$

This differential condition of coherence expresses the equality of the partial derivative along a given direction. It can be noted that this condition must be fulfilled to obtain the Equation (3) given previously.

The Hodograph Space

The variations of compositions which verify the differential condition of coherence can be represented in the space (C_1, C_2). The construction of the solution of Equation (11) in this space is called state diagram and the transformation from the physical space (z, t) to the space (C_1, C_2) is called hodograph transformation. This construction neither depends on z and t, nor on the operating conditions, and is only intrinsic to the adsorption isotherm type. In the case of a Langmuir type isotherm, two families of straight-lines, called characteristics, are obtained. One characteristic represents a wave, dispersive or compressive, obeying the coherence condition: this condition is verified only along these characteristics.

Figure 3 illustrates an example of state diagram. Coordinates are the concentrations of both components in the mobile phase (a representation using the solid phase concentrations can also be considered). C_2 is, in the present study, the concentration of the most retained species. The plane contains an infinity of straight lines of two different trajectories. The

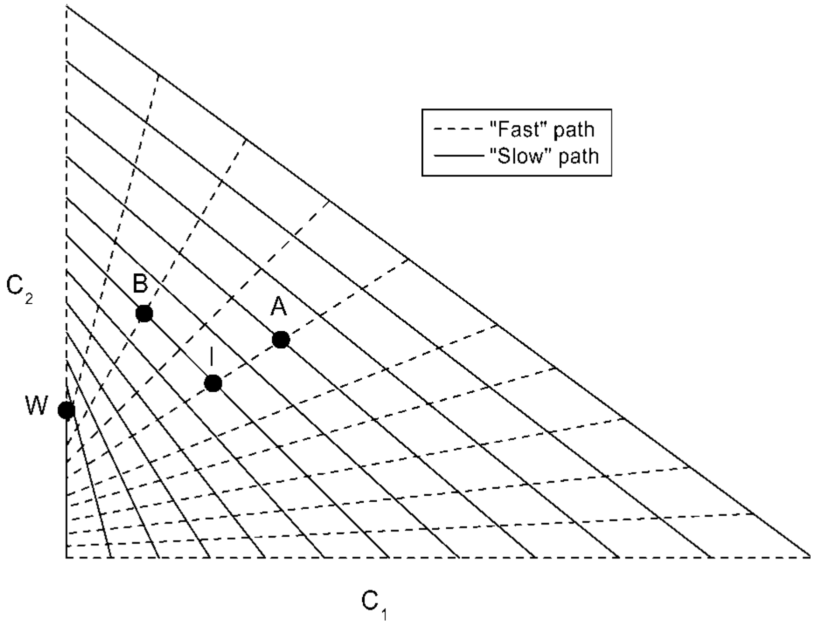

Figure 3. Example of state diagram.

continuous lines correspond to the characteristics having a low migration velocity whereas the dashed ones correspond to a higher migration velocity. These waves are respectively called "slow" and "fast". Every composition of the diagram is at the intersection of two characteristics, a "slow" and a "fast" one.

It can be shown (6) that the hodograph is orthogonal in the ω space: the smallest ω value varies along the fast path, while the highest remains constant. Conversely, the highest ω value varies along the slow path, while the lowest remains constant.

This representation involves a particular point, W (Watershed Point) for which the characteristic Equation (6) has a double root equal to N_1K_1 (20). The W point coordinates are $(0, N_2/N_1K_1 - 1/K_2)$.

It can be noted that axes also represent characteristics: the C_1 axis is a fast characteristic and the C_2 axis is divided into two types of trajectories on both sides of the W point. A characteristic which leaves a "slow" axis is a "fast" characteristic and vice versa. Therefore, every composition of one of both axes is also at the intersection of two characteristics of different natures: slow and fast.

This type of construction allows to predict the response of a chromatographic column by drawing the path followed to go from a given composition to another one. This path is represented by a succession of segments, one for each wave, arranged in the direction of the fluid movement. It indicates the sequence of compositions met within the column between the inlet and the outlet of this one at a given time.

An example is illustrated in Fig. 3. If the initial composition of a column corresponds for instance to point A, and this column is fed with composition B, two waves are generated. The first one to breakthrough is the fast one, corresponding to the A-I path. Along this path, the most retained species concentration is decreasing, resulting in a dispersive wave. The second wave corresponds to the I-B path on the slow characteristic. As C_2 increases along this path, a compressive wave is generated.

FLOW RATE DETERMINATION PROCEDURE

The Case of the Classical TMB

Let us consider the case of a binary mixture (1+2), where species 2 is the most retained by the solid phase. The basic idea is to look for the conditions which enable the required migration direction of each species, in each zone, to be obtained. These directions are indicated on Fig. 1. For a given zone, a species i has to move either in the direction of the liquid phase or in that of the solid phase in order to be collected at the right place.

Then, by estimating the migration velocity in each of the TMB zones and by taking into account the interconnection of these zones, it is possible to determine the flow rate intervals leading to a feasible separation.

The interface of the feed injection, which is presented in Fig. 4a, separates two sections of the TMB, namely:

- a section S1 in which 2 dispersive waves are generated, as it is fed by the eluent which regenerates the solid containing 2 adsorbed species.
- a section S2 in which 2 compressive waves are generated as it is fed by a binary mixture which saturates the regenerated bed.

The separation is complete if the flux of species 1 is null at section S1 inlet and the flux of species 2 is null at section S2 outlet.

To evaluate the flow rates allowing this separation, one may stabilize either a compressive wave, or a composition of a dispersive wave, or an intermediate state. This evaluation requires the knowledge of the parameters ω^S and ω^L, corresponding respectively to the solid phase composition S entering section 1, and to the liquid phase composition L entering section 2. The corresponding limit reduced flow rates are then given in the general case (Figure 4a), for a state k, by the following relations (9):

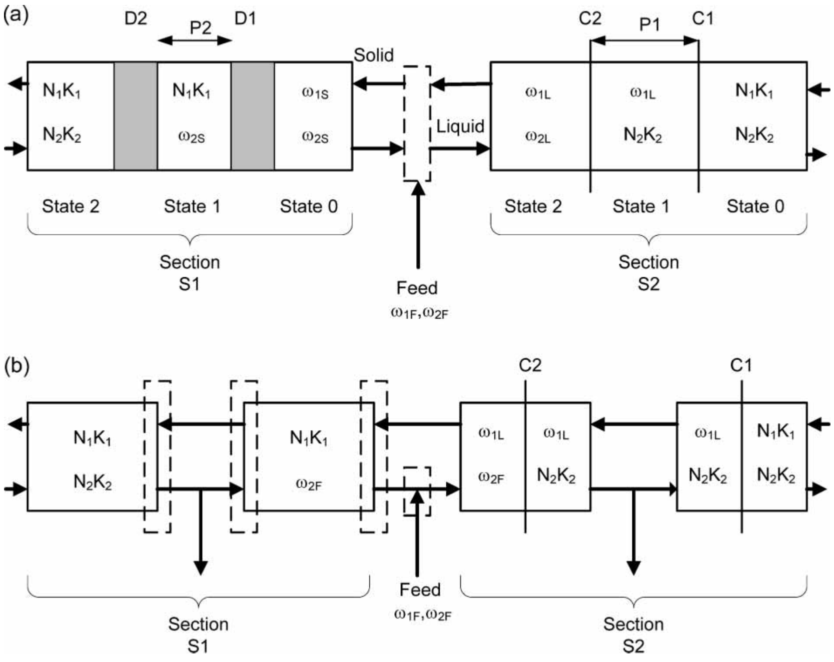

Figure 4. States of concentration and waves generated around the feed for a classical TMB – (a) The general case – (b) The maximum feed flow rate case.

Case of a compressive wave:

$$q_k = \frac{N_k K_k}{\prod_{j=1}^{k} N_j K_j / \omega_j^L}. \tag{12}$$

Case of a dispersive wave:

$$q_k^* = \frac{\omega_k^S}{\prod_{j=k}^{2} N_j K_j / \omega_j^S} \quad \text{and} \quad q_*^k = \frac{N_k K_k}{\prod_{j=k+1}^{2} N_j K_j / \omega_j^S}. \tag{13}$$

Where q^* corresponds to the higher value of the reduced flowrate, whereas q_* corresponds to the lower one. This methodology, which allows to determine the operating flowrates, is therefore based upon the choice of the waves to stabilize, and upon the mass balance at the interface, which takes into account the relation between *L*, *S*, and the *Feed* stream.

The Maximum Feed Flow Rate

The conditions of the maximum feed flow rate correspond to the maximum flow rate in zone III and the minimum flow rate in zone II which enable to obtain pure products. The corresponding flow rates of the various zones of the TMB were previously determined (10), in the case of a binary Langmuir equilibrium, and are reminded in Table 1. The corresponding states are presented in Fig. 4b. It can be noted that the conditions of the maximum feed flow rate lead to the formation of discontinuities at the extremities of zones I and II. These discontinuities are represented using dashed boxes on Fig. 4b.

The Case of the M3C

Compared with the classical TMB, this process integrates a concentration step between zone I outlet and zone II inlet. As already explained previously, this operation can be carried out as illustrated in Fig. 2. Hence, the system can be

Table 1. Reduced flow rates of the four zones of the TMB

Feed	$q_F = \dfrac{(a_2 - a_1)^2}{D_F(a_2 - \omega_{1F})}$
Zone I	$q_I = a_2$
Zone II	$q_{II} = \dfrac{a_1 \omega_{2F}}{a_2}$
Zone III	$q_{III} = q_{II} + q_F$
Zone IV	$q_{IV} = \omega_{1L} = \omega_{1F} + \dfrac{(a_1 - \omega_{1F})^2}{a_2 - \omega_{1F}}$

divided into three sections, which are illustrated in Fig. 5. Section S2 is rigorously similar to the one obtained in the TMB. On the other hand, a compressive wave is formed in section S1.

Hodograph

In the following part of this paper, ketoprofen separation, which is a racemate mixture of two enantiomers S(+) and R(−), will be considered. This separation has been previously studied by Charton (21), as a test system. The enantiomer S(+) is the most active biologically and it is the most retained species on the solid phase, thus recovered at the extract point. The parameters of the equilibrium adsorption isotherm which will be used are gathered in Table 2.

Figure 6 represents the hodograph calculated using these data. The *W* point coordinates are in that case (0,1.76).

The paths followed on this graph are drawn respectively:

- in the case of a classical TMB
- in the case of a TMB integrating a concentration step. Two concentration factors $\alpha = 1.75$ and 2, have for instance been chosen, where α is defined as:

$$\alpha = \frac{\text{Total concentration at zone II inlet}}{\text{Total concentration at zone I outlet}} = \frac{C_2^{II}}{C_2^{I}}.$$

In these three cases, the total ketoprofen feed concentration is 5 g/L.

In the case of the classical TMB, it can be observed that, for a given feed and eluent, the composition is delimited by a quadrilateral space, which makes it impossible to obtain more concentrated products.

It is therefore worth studying as to how to get out of this confined zone.

1. It can be observed that, if a concentrated solution corresponding to point *A* composition (on the C_{S+} axis, below the *W* point on Fig. 6) is injected

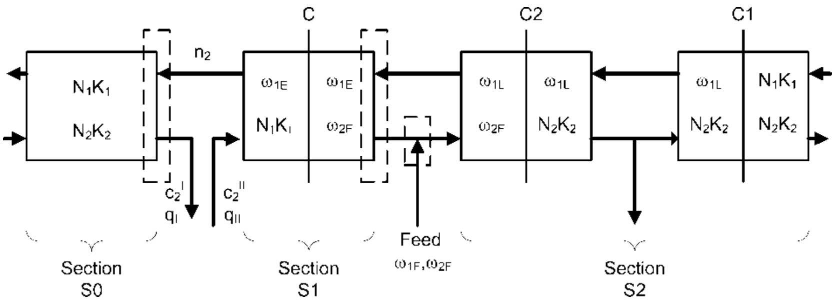

Figure 5. States of concentration and waves generated around the feed – TMB integrating a concentration loop.

Table 2. Isotherms of adsorption equilibrium of the ketoprofen enantiomers (21)

	R(−) Enantiomer	S(+) Enantiomer
a	7.326	9.287
K (L/g)	0.115	0.152
N (g/L)	63.7	61.1
ε	0.674	
Adsorbent	Daicel Chiralcel OJ	
Eluent	Hexane/2-propanol/AcOH	

after the extract collection point (section S1 inlet in Fig. 5), the path *AE* (slow characteristic) is first followed. The paths which are then followed are the same ones as those in the TMB case. It is therefore useless carrying this concentration step.

2. On the other hand, let us consider point *B* in Fig. 6, intercept of the slow path between the feed composition and the C_{S+} axis. If a concentration B_1, higher than *W* but lower than *B*, is injected at the inlet of section II, it can be observed that there will successively be the formation of a compressive wave and a dispersive wave in zone II. If a concentration B_2 higher than *B* is injected at the inlet of section II, two compressive waves develop in zone II. In both cases, a compressive wave appears in

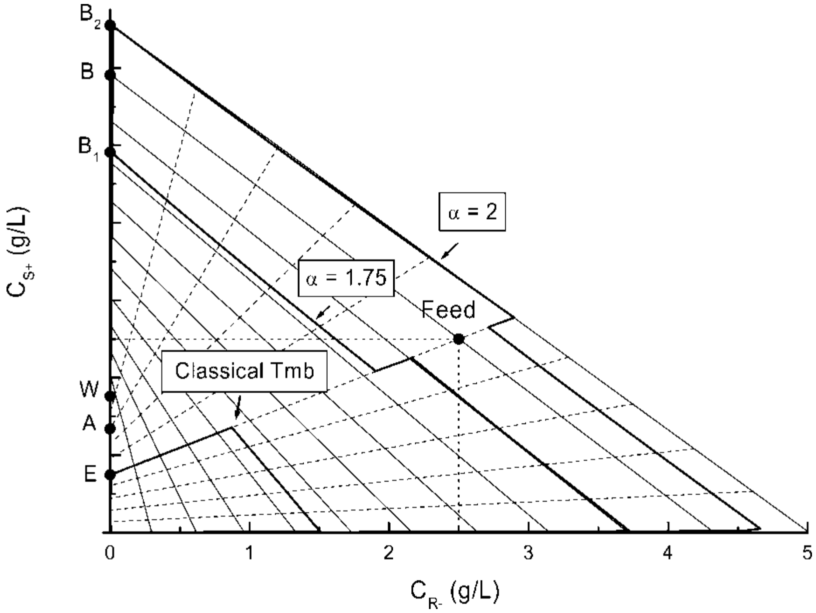

Figure 6. Hodographs: classical TMB and M3C processes.

zone III. The determination of zone II flow rate (see q_{II} expression in Table 3 and relation (20)) demonstrates that it leads to the decreasing of zone II flow rate (see q_{II} expression in Table 1).

The interest of the concentration step appears therefore only if the concentration C_{S+} exceeds that of the W point. It must be noticed that this crucial point of the study can clearly be understood thanks to the hodograph tool. This result can hardly be obtained by a simple intuitive approach.

Calculation of the Reduced Flow Rates

The aim of this section is to determine the reduced feed flow rates of the four sections of the M3C. We will use an approach analogous to the one developed for the classical TMB (10), considering again the case of the maximum feed flow rate. Comparing Figs 4b and 5, it must be underlined that the main specificity of the present M3C case relies on section S1: the aim is to stabilize the compressive wave C, in order to obtain pure species 2 in the outlet solid phase. Moreover, we will make the hypothesis that the compressive wave C2, through which species 2 vanishes, can be stabilized in the first zone of section S2 without violation of a coherence or mass balance rule. This assumption, which must be verified, allows using the "ω rule," demonstrated in (10), establishing the following relationship between the highest ω value of the feed solution, the liquid entering section S2 and the solid entering section S1:

$$\omega_{2S} = \omega_{2L} = \omega_{2F}$$

- Under these assumptions, consider first the extract section:

  The zone II reduced flow rate which allows stabilizing the compressive wave C is given by:

$$q_{II} = \frac{\omega_{2F}\omega_{1E}}{N_2K_2}. \tag{14}$$

Table 3. Reduced flow rates of the four zones of a M3C process

Feed	$q_F = \frac{(a_2-\omega_{1E})(a_2-a_1)}{D_F(a_2-\omega_{1F})}$ with $\omega_{1E} = a_2/\alpha$
Zone I	$q_I = a_2$
Zone II	$q_{II} = \omega_{2F}/\alpha$
Zone III	$q_{III} = q_{II} + q_F$
Zone IV	$q_{IV} = \frac{\omega_{1F}(a_2-a_1)+(a_2/\alpha)(a_1-\omega_{1F})}{a_2-\omega_{1F}}$

Besides, a reduced mass balance on the extracted quantity Φ_2 of species 2 leads to:

$$\Phi_2 = n_2 - q_{II} C_2^{II}$$

A substitution thanks to relations (9) and (10) leads to:

$$\Phi_2 = \left(1 - \frac{q_{II}}{\omega_{1E}}\right)\left(N_2 - \frac{\omega_{1E}}{K_2}\right) = \left(1 - \frac{\omega_{2F}}{N_2 K_2}\right)\left(N_2 - \frac{\omega_{1E}}{K_2}\right)$$

As this quantity must be compensated by the feed flux, the following expression of the feed flow rate can be derived:

$$q_F = \frac{\Phi_2}{C_{2F}} = \frac{(N_2 K_2 - \omega_{1E})(N_2 K_2 - N_1 K_1)}{D_F (N_2 K_2 - \omega_{1F})}. \tag{15}$$

- Consider now the raffinate section:

The zone III reduced flow rate which allows stabilizing the compressive wave C2 is given by:

$$q_{III} = \frac{\omega_{1L}\omega_{2F}}{N_1 K_1}$$

The reduced mass balance Φ_1 on the collected amount of species 1 is:

$$\Phi_1 = \left(\frac{\omega_{2F}}{N_1 K_1} - 1\right)\left(N_1 - \frac{\omega_{1L}}{K_1}\right)$$

Two mass balances must be fulfilled: the feed flux of species 1 compensates the collected amount, and the flow rate in zone III is the sum of the flow rate in zone II and the feed flow rate:

$$\Phi_1 = q_F C_{1F}$$
$$q_{III} = q_{II} + q_F$$

Substituting Φ_1, and q_{II}, q_F and q_{III} by their expressions leads to Equations (16) and (17) in one unknown ω_{II}:

$$\left(N_1 - \frac{\omega_{1L}}{K_1}\right)\left(\frac{\omega_{2F}}{N_1 K_1} - 1\right) = \left(\frac{N_1}{\omega_{1F}} - \frac{1}{K_1}\right)\frac{(N_1 K_1/\omega_{2F} - 1)}{(N_1 K_1/N_2 K_2 - 1)} \times \left(\frac{\omega_{1L}\omega_{2F}}{N_1 K_1} - \frac{\omega_{2F}\omega_{1E}}{N_2 K_2}\right). \tag{16}$$

$$\frac{\omega_{1L}\omega_{2F}}{N_1K_1} = \frac{\omega_{1E}\omega_{2F}}{N_2K_2} + \frac{(N_2K_2 - \omega_{1E})(N_2K_2 - N_1K_1)}{D_F(N_2K_2 - \omega_{1F})}. \tag{17}$$

It can be checked that Equations (16) and (17) allow to obtain the same expression of ω_{1L}

$$\omega_{1L} = \frac{\omega_{1F}(N_2K_2 - N_1K_1) + \omega_{1E}(N_1K_1 - \omega_{1F})}{N_2K_2 - \omega_{1F}}. \tag{18}$$

This result validates the initial assumption on the choice of the flow rates.

It can easily be checked that the feed flow rate given by Equation (15) is higher than that of the classical TMB given in Table 1, for $\omega_{1E} = N_1K_1$ (Equation (8)).

Besides, at the withdrawal point of the extract between section S0 and S1, we have:

$$\begin{aligned} n_2 &= q_I C_2^I \\ q_I &= N_2K_2 \\ C_2^{II} &= \alpha C_2^I \end{aligned}$$

Where the concentration factor α, defined previously, is greater than unity.

Substituting n_2 with $n_2 = N_2K_2C_2^{II}/(1 + K_2C_2^{II})$ and introducing ω_{1E} through $1 + K_2C_2^{II} = N_2K_2/\omega_{1E}$ allows to obtain:

$$\begin{aligned} \omega_{1E} &= N_2K_2/\alpha \\ C_2^{II} &= \frac{\alpha - 1}{K_2} \end{aligned} \quad . \tag{19}$$

So, knowing the invariant ω_{1E}, the flow rates of the various zones of the process can be determined. The expressions of these reduced flow rates are gathered in Table 3.

The Minimum Concentration Factor

It was seen previously that to be able to generate a compressive wave in zone II and therefore decrease the flow rate in this zone, one must inject a minimal concentration of species 2 equal to that of *W* point. This value of concentration allows to define a minimum concentration factor, below which the integration of a loop of concentration is of no interest. The concentration of S(+) at zone II inlet is given by relation (19): this allows to calculate a minimum concentration factor whose expression is

$$\alpha_{\min} = \frac{N_2 K_2}{N_1 K_1} = \frac{a_2}{a_1}. \tag{20}$$

The value of the minimum concentration factor is 1.26 in the case of the present study (Table 2).

PERFORMANCES OF THE MCC PROCESSES: TMB AND M3C

The performance of a purification process is usually formulated in terms of two criteria, the productivity and the eluent consumption, whose combination with economical data allows to estimate the cost of the purification of a mass unit of key product (22).

Considering the species * of interest, the production rate m of the purification unit is defined by:

$$m = Rr^* \cdot C_F^* \cdot Q_F \quad \text{(kg /hour)}$$

where Rr represents the recovery rate. The production rate allows to define two criteria:

- The productivity, which is the production rate per volume unit of column, and which can be related to an investment cost:

  $$Pr^* = Rr^*. \frac{C_F^*.Q_F}{V_{col}} \text{(kg/m}^3\text{/hour)}$$

  where V_{col} corresponds to the volume of all the columns.
- The eluent consumption, which is the evaporated flowrate per production rate unit, and which can be related to an operating cost (22):

  $$EC = \frac{\dot{V}_{evap}}{m} \text{(m}^3\text{/kg)}$$

The flow rates are usually deduced from the reduced flow rates q_i and the solid flow rate Q_S, which in turn is limited by a maximum pressure drop constraint, related to the column lengths.

In the scope of the equilibrium model, the column length cannot be estimated, and the recovery rate equals unity for the calculated reduced flow-rates. This model limitation leads to the definition of a modified productivity criteria, which will only allow to compare the performance of the two processes characterized by the equilibrium model, but in no case to evaluate the real productivity. In the present study, S+ is the species of interest and this modified productivity criteria is defined by:

$$Pr'(S+) = \frac{q_F C_{(S+)F}}{\sum N_{coli}(q_i + (\varepsilon/(1-\varepsilon))}. \tag{21}$$

Where N_{coli} is the number of columns by zone and q_i is the reduced liquid flow rate of the considered zone.

In the opposite, the definition of the eluent consumption is unaffected by this model limitation. The volume of solvent per unit of time $\dot{V}_{evap}$, which has to be evaporated to obtain dried products can be obtained, considering the configuration presented in Fig. 2; it leads to the following eluent consumption expression:

$$EC = \frac{q_{eluent} + q_F}{q_F C_{(S+)F}} = \frac{q_I - q_{II} + q_{Raff}}{q_F C_{(S+)F}} \tag{22}$$

In the following part of this work, these two parameters will be calculated considering a configuration 1/2/2/1, including one column in zones I and IV and two columns in zones II and III.

Evaluation of the TMB Performances

As a preliminary study, the influence of the feed concentration on the two criteria defined previously can be investigated.

Productivity

In Fig. 7 the modified productivity is given as a function of the feed concentration, in the case of the classical TMB. It can be observed that the productivity increases with feed concentration and tends towards an asymptotic value. A feed concentration of 5 g/L enables to reach 80% of the maximum productivity. It must be noted that the choice of feed concentration also depends on ketoprofen solubility in the solvent used, as well as on the feed flow rate range the pump can deliver.

Eluent Consumption

A similar approach can be carried out for eluent consumption, which is given in Fig. 8 as a function of feed concentration, in the case of the classical TMB. It can be observed that the eluent consumption rapidly decreases when the feed concentration increases and tends towards an asymptotic value at infinite feed concentration.

This first study leads to conclude that increasing feed concentration enables to improve both productivity and eluent consumption, up to asymptotic values.

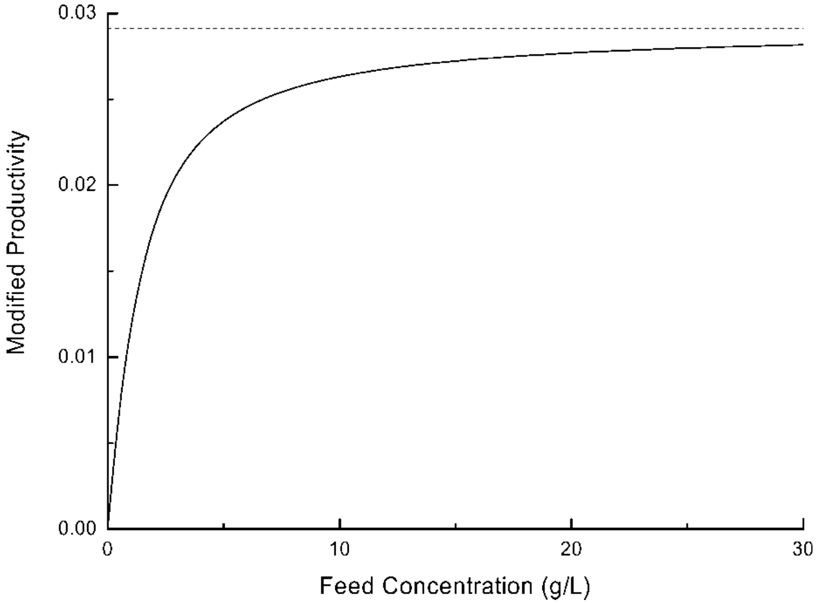

Figure 7. Modified productivity as a function of the feed concentration – classical TMB.

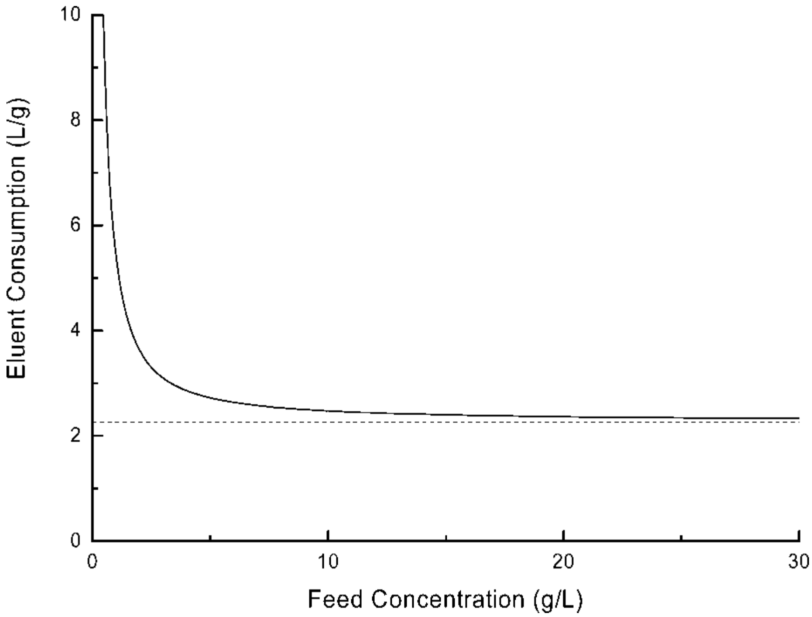

Figure 8. Eluent consumption as a function of the feed concentration – classical TMB.

Evaluation of the M3C Performances

The objective is now to evaluate the influence of M3C concentration factor on the performances of this process. A four zones and six columns system will again be considered.

Productivity

In Fig. 9, the modified productivity is given as a function of feed concentration for concentration factors varying in the range 1 (case of classical TMB) to 6. Figure 10 gives another representation of the same data, considering the particular case of 5 g/L feed concentration. For that specific case, productivity is given as a function of the concentration factor.

It can be observed that, as long as the concentration factor is below the minimal value of 1.26, no improvement of productivity is obtained with the M3C; the productivity remains the same as the one obtained with a classical TMB. However, as soon as the concentration factor is up to 1.26, productivity increases, demonstrating the interest of the introduction of a concentration step.

The productivity then increases with the concentration factor. This is due to the fact that it enables to increase feed flow rate q_F, which is proportional to the productivity. It must be noted that there is also a decrease of the pressure drop.

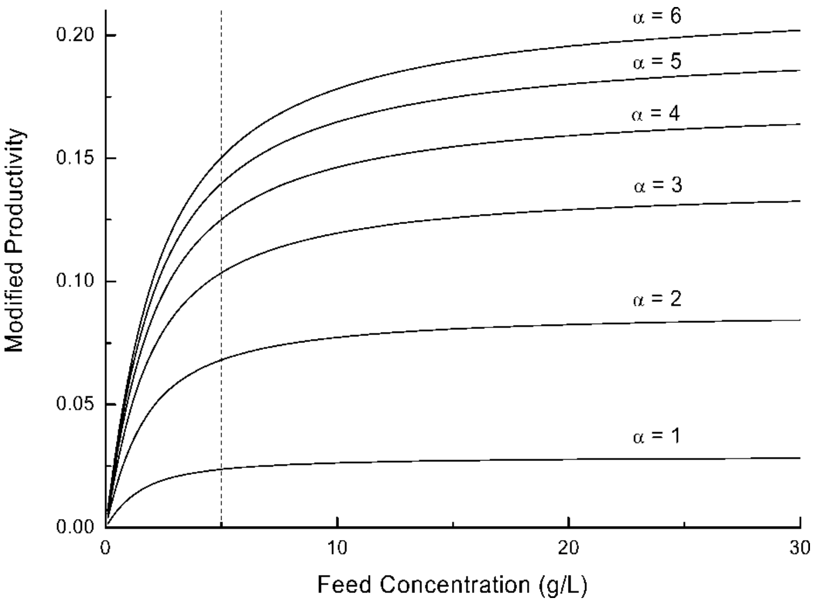

Figure 9. Modified productivity as a function of the feed concentration and the concentration factor.

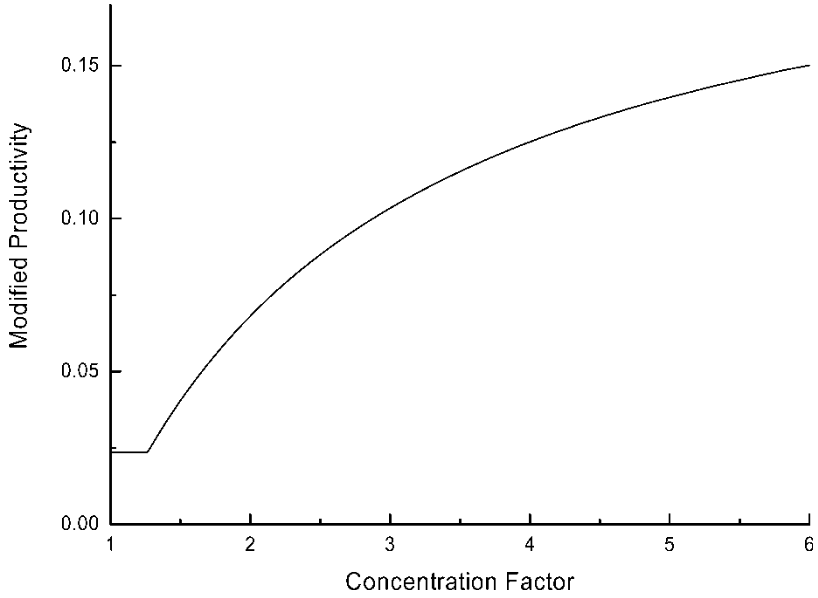

Figure 10. Modified productivity as a function of the concentration factor–feed concentration = 5 g/L.

We can show from the relations giving the feed flow rates presented in Tables 1 and 3:

$$\frac{q_F \text{ with concentration}}{q_F \text{ without concentration}} = \frac{1 - 1/\alpha}{1 - N_1 K_1 / N_2 K_2}$$

In the present case of ketoprofen optical isomers separation, this ratio is equal to 2.36 for a concentration factor of 2.

Moreover, the pressure drop decrease also contributes to the overall effect which finally results in the productivity multiplied by nearly 3 when using a concentration factor of 2, in the case of 5 g/L feed concentration.

Eluent Consumption

In Fig. 11, the eluent consumption is given as a function of feed concentration for concentration factors varying in the range 1 (case of classical TMB) to 6. It can be observed that these curves seem to tend towards an asymptotic one when the concentration factor increases.

Figure 12 gives another representation of the same data, considering the particular case of 5 g/L feed concentration. For that specific case, the eluent consumption is given as a function of the concentration factor. It can be observed that the eluent consumption decreases when the concentration

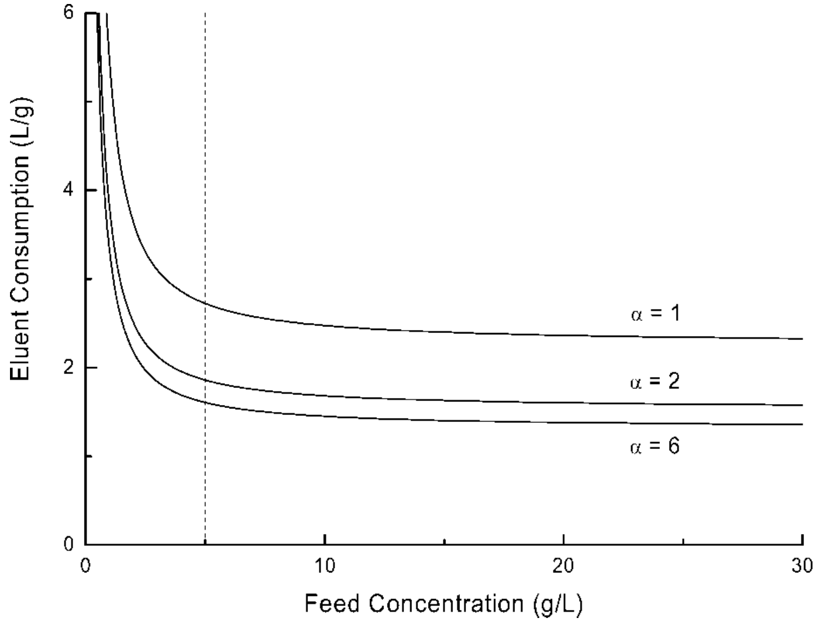

Figure 11. Eluent consumption as a function of the feed concentration and the concentration factor.

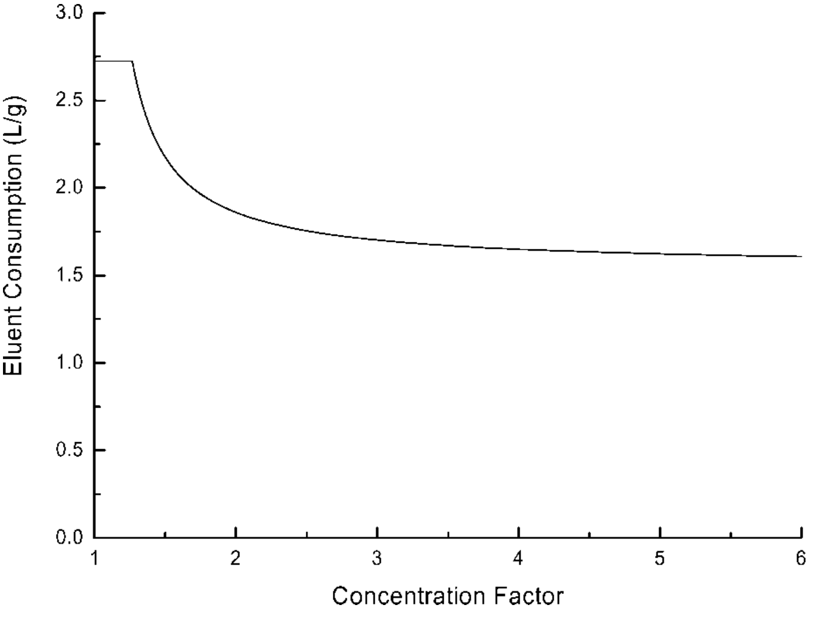

Figure 12. Eluent consumption as a function of the concentration factor–feed concentration = 5 g/L.

factor increases: this value is always lower than that obtained with $\alpha = 1$ (TMB case), demonstrating again the interest of the concentration loop introduction.

CONCLUSION

In the first part of this work, the equilibrium theory was used to determine the TMB flow rates which enable to carry out the separation of a binary mixture into two pure fractions, with and without a step of concentration. This work was realized in the case of an adsorption governed by multicomponent competitive Langmuir isotherms.

The knowledge of these flow rates allows to compare the performances of these processes; it turns out that the productivity increases with the concentration factor and that the eluent consumption is significantly reduced. The limit of this operation is linked to the considered products solubility.

It must be pointed out that these theoretical results have been experimentally validated (23). The experimental procedure, as well as the corresponding results, will be presented in a second publication.

NOTATIONS

a	slope at the origin of the Langmuir isotherm
c	compressive
C	concentration of a species in the liquid phase (g/L)
d	dispersive
K	constant of the Langmuir isotherm
m	production rate of collected product (kg/h)
n	concentration of a species in the solid phase (g/L)
N	total capacity of adsorption of a species (g/L)
p	intermediate state
$\bar{Q}$	volumetric flow rate of the solid (mL/min)
Q	volumetric flow rate of the liquid (mL/min)
q	reduced liquid flow rate $q = Q/\bar{Q}$
S	column section
t	time (s)
u_e	interstitial velocity of the liquid in the column (cm/s)$u_e = Q/\varepsilon S$
v_e	interstitial velocity of the solid in the column (cm/s)$v_e = \bar{Q}/(1 - \varepsilon)S$
$\dot{V}$	liquid flow rate (m^3/hour)
W	watershed point
z	abscissa (m or cm)

Greek Letters

ε	external porosity of the column
ω	root of the characteristic equation
Φ	molar flux
α	concentration factor

Subscripts

Col	column
Extr	extract
Evap	evaporated solvent
F	feed
i, j	species
k	state
L	liquid
Raff	raffinate
S	solid
T,tot	total

List of the Abbreviations

EC	Eluent Consumption
SMB	Simulated Moving Bed
TMB	True Moving Bed
MCC	Multi-Column Continuous
M3C	Multi-Column Continuous + Concentration
Rr	Recovery Rate
Pr	Productivity

REFERENCES

1. Broughton, D.B., Gerhold, C.G. (May 23, 1961) Continuous sorption process employing fixed bed of sorbent and moving inlets and outlets. U.S. Patent 2,985,589.
2. Ludemann-Hombourger, O., Nicoud, R.M., and Bailly, M. (2000) The VARICOL Process: A New Multicolumn Continuous Chromatographic Process. *Sep. Sci. and Technol.*, 35: 1829.
3. Schramm, H., Kienle, A., Kaspereit, M., and Seidel-Morgenstern, A. (2003) Improved operation of simulated moving bed processes through cyclic modulation of feed flow and feed concentration. *Chem. Eng. Sci.*, 58 (23–24): 5217.
4. Kloppenburg, E. and Gilles, E.D. (1999) A new concept for operating simulated moving-bed processes. *Chem. Eng. Technol.*, 22 (10): 813.
5. Glueckauf, E. (1949) Theory of chromatography. VII. The general theory of two solutes following nonlinear isotherms. *Disc. Farad. Soc. Lond.*, 7: 12.

6. Rhee, H-K., Aris, R., and Amundson, N.R. (1970) On the theory of multicomponent chromatography. *Phil. Trans. Roy. Soc. Lond.*, 296 A: 1182, 419.
7. Tondeur, D. (1969) Théorie des colonnes d'échange d'ions. PhD Thesis, Nancy, France.
8. Helfferich, F.G. and Klein, G. (1970) *Multicomponent Chromatography*; Marcel Dekker, Inc.: New York.
9. Rhee, H-K., Aris, R., and Amundson, N.R. (1971) Multicomponent adsorption in continuous countercurrent exchangers. *Phil. Trans. Roy. Soc. Lond.*, 269 A (1194): 187.
10. Storti, S., Mazzotti, M., Morbidelli, M., and Carrà, S. (1993) Robust design of binary countercurrent adsorption separation processes. *AIChE J.*, 39 (3): 471.
11. Nicoud, R.M.; Bailly, M. (June 19, 1997) Méthode pour optimiser le fonctionnement d'un système de séparation des constituants d'un mélange. French Patent 2,764,822.
12. Pais, L.S. and Rodrigues, A.E. (2003) Design of simulated moving bed and Varicol processes for preparative separations with a low number of columns. *J. Chromatogr. A*, 1006 (1–2): 33.
13. Nicolaos, A., Muhr, L., Gotteland, P., Nicoud, R.M., and Bailly, M. (2001) Application of the equilibrium theory to ternary moving bed configurations (4+4, 5+4, 8 and 9 zones): II. Langmuir case. *J. Chromatogr. A*, 908 (1–2): 87.
14. Storti, G., Masi, M., Carra, S., and Morbidelli, M. (1989) Optimal design of multicomponent countercurrent adsorption separation processes involving nonlinear equilibria. *Chem. Eng. Sci.*, 44 (6): 1329.
15. Mazzotti, M., Storti, G., and Morbidelli, M. (1994) Robust design of countercurrent adsorption separation processes: 2. Multicomponent systems. *AIChE J.*, 40 (11): 1825.
16. Migliorini, M., Mazzotti, M., and Morbidelli, M. (2000) Design of simulated moving bed multicomponent separations: Langmuir systems. *Sep. & Purif. Technol.*, 20 (1): 79.
17. Bailly, M., Nicoud, R.M., Adam, P., and Ludemann-Hombourger, O., (April 30, 2004) Procede et dispositif de chromatographie integrant une etape de concentration. French Patent 2,846,252.
18. Tondeur, D. and Bailly, M. (1987) Unifying concepts in non-linear unsteady processes part II: Multicomponent waves, competition and diffusion. *Chem. Eng. Process*, 22 (2): 91.
19. Helfferich, F.G. and Carr, P.W. (1993) Non-linear waves in chromatography: I. Waves, shocks, and shapes. *J. Chromatogr. A*, 629 (2): 97.
20. Helfferich, F.G. (1997) Non-linear waves in chromatography III. Multicomponent Langmuir and Langmuir-like systems. *J. Chromatogr. A*, 768 (2): 169.
21. Charton, F. (1995) Optimisation des coupes et recyclages en chromatographie préparative industrielle. Thesis, INPL-ENSIC, Nancy, France.
22. Charton, F. and Nicoud, R.M. (1995) Complete design of a simulated moving bed. *J. Chromatogr. A*, 702 (1–2): 97.
23. Abdelmoumen, S. (2005) Etude théorique et expérimentale d'un nouveau procédé multicolonnes continu de chromatographie preparative integrant une étape de concentration. Thesis, INPL-ENSIC, Nancy, France.