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Optimal operation of simulated moving-bed units for non-linear chromatographic separations

II. Bi-Langmuir isotherm¹

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Abstract

Several important theoretical results have been previously obtained to predict the behaviour of continuous chromatographic separation units in the case of Langmuirian type of isotherms. Concerning separation of binary mixtures in a non-adsorbable carrier with SMB units, stoichiometric and non-stoichiometric Langmuir and modified Langmuir have been considered in the frame of equilibrium theory. For these isotherms explicit constraints on the operating parameters have been found to achieve complete separation (M. Mazzotti, G. Storti, M. Morbidelli, *J. Chromatogr. A* 769 (1997) 3; M. Mazzotti, G. Storti, M. Morbidelli, *AIChE J.* 42 (1996) 2784; M. Mazzotti, M. Pedferri, M. Morbidelli, in: *Chiral Europe '96 Symposium*, Spring Innovations Limited, Stockport, UK, 1996); the design of the SMB unit was then reduced to the analysis of the so-called region of complete separation for the operating parameters. In this paper, the same result is presented for the bi-Langmuir case, which can avoid the constant selectivity limit of the Langmuir isotherms. Langmuir and bi-Langmuir isotherms fitting the same set of data taken from the literature were then used here to show the difference in the prediction of the region of complete separation. Finally an analysis of non-linearity effects on performance parameters is presented as a useful criterion for optimization of the separation performances. © 1998 Elsevier Science B.V.

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1. Introduction and background

In the realm of preparative and industrial chromatography, simulated moving-bed (SMB) units have received a continuously increasing attention since their introduction in the early 1960s [4]. A detailed discussion of the basic principles of SMB technology has been reported in Ref. [5]: the main point is that

these are continuous units which simulate a counter current chromatographic separation process by switching the inlet and outlet ports to a closed loop of fixed-bed chromatographic columns, as illustrated in Fig. 1. The SMB technology was originally developed for very large-scale applications in the petrochemical industry, such as the separation of *para*-xylene from the alkyl aromatic C₈ fraction [6]. Only recently several interesting applications in the fine chemical industry have been proposed, in particular for the resolution of racemates [7–18]. Many

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¹Part I of this series is Mazzotti et al., 1997 [1].

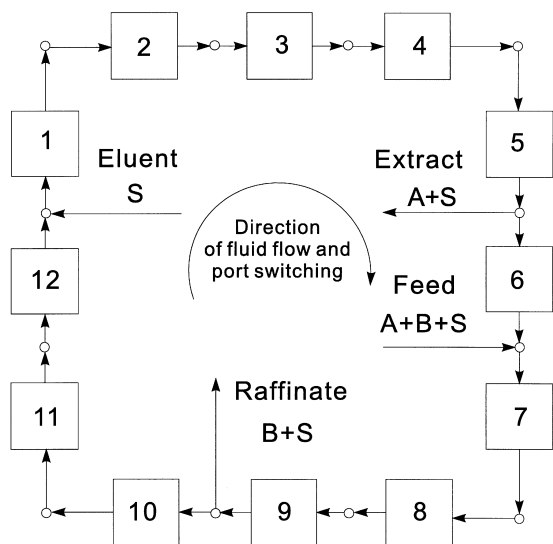


Fig. 1. Scheme of a simulated moving-bed unit for continuous chromatographic separations, with port configuration 5–1–3–3.

examples prove that the SMB technique exhibits interesting advantages over the classical batch chromatographic techniques, in terms of solvent consumption and productivity per unit mass of stationary phase.

With regard to the simulation of those units through mathematical models, it is often convenient to take advantage of the equivalence of their steady-state performance with the four-section true counter current unit (TCC) illustrated in Fig. 2 [5]. Note that, while the TCC unit achieves a steady-state regime, the SMB unit reaches a cyclic transient behaviour exhibiting periodical concentration profiles, with the period equal to the time interval between two successive switches of the ports. In the frame of equilibrium theory the dimensionless mass balance equation for the i -th species in the j -th section of the TCC unit can be written as follows:

$$\frac{\partial}{\partial \tau} [\varepsilon^* c_i^j + (1 - \varepsilon^*) n_i^j] + (1 - \varepsilon_p) \frac{\partial}{\partial x} (m_j c_i^j - n_i^j) = 0 \quad (1)$$

In the previous equation we neglected axial dispersion and mass transfer resistance, thus assuming local equilibrium conditions characterized by the following relationship:

$$n_i = n_i(c) \quad (2)$$

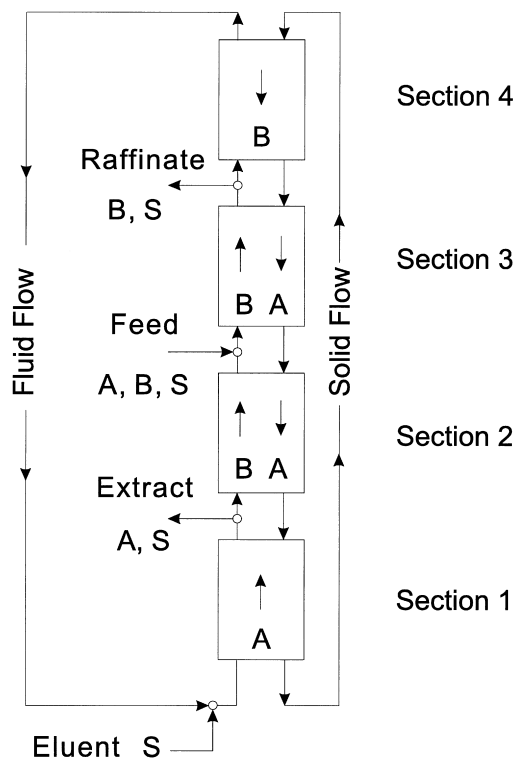


Fig. 2. Scheme of a four-section true counter current unit for continuous chromatographic separations.

It follows that the steady-state profiles in each section, hence the steady-state performances of the SMB unit, as a whole, depend on the following dimensionless parameters

$$m_j = \frac{Q_j^{\text{TCC}} - \varepsilon_p Q_s}{Q_s(1 - \varepsilon_p)} \quad (j = 1, \dots, 4) \quad (3)$$

as well as on the adsorption isotherm (Eq. (2)). Let us consider a binary mixture in a non-adsorbable carrier where we define A and B as the more- and less-retained component, respectively. In order to collect pure outlet streams the net fluxes of species A and B must have opposite directions in sections 2 and 3 (see Fig. 2), while on the other hand sections 1 and 4 have to regenerate the stationary and the mobile phase before recycling, respectively. The problem is to determine the operating conditions, i.e. the values of m_j , which allow to fulfill these requirements. A set of criteria have been derived which allow to define the complete separation region in the

operating parameter space spanned by the four coordinates m_1 , m_2 , m_3 and m_4 for several equilibrium isotherms of applicative interest [1–3,19]. In particular, analytical expressions for the boundaries of the complete separation region in the case of a binary separation have been obtained for the following isotherms:

1.1. Linear isotherm [19]

$$n_i = H_i c_i \quad (i = A, B) \quad (4)$$

The linear case represents a limit behaviour when concentrations in the unit are very low. However this is not the case of production-scale SMB units, which usually operate under overload conditions, leading to non-linear competitive adsorption behaviour.

1.2. Langmuir isotherm [1,2]

$$n_i = \frac{\gamma_i c_i}{1 + \sum_{j=A,B} k_j c_j} \quad (i = A, B) \quad (5)$$

Many chromatographic systems are described through this equilibrium model, which implies constant selectivity:

$$S_{A,B} = \frac{n_A/c_A}{n_B/c_B} = \frac{\gamma_A}{\gamma_B} \quad (6)$$

This assumption is not valid in several cases of applicative interest [20].

1.3. Modified Langmuir isotherm [1]

$$n_i = h c_i + \frac{\gamma_i c_i}{1 + \sum_{j=A,B} k_j c_j} \quad (i = A, B) \quad (7)$$

This isotherm is derived from Eq. (5) by adding a linear term which is the same for both components. Selectivity is not constant as in the Langmuir case, but is constrained to be larger than one for all the composition values, hence selectivity reversal cannot be described. It is worth pointing out that this model cannot take into account stationary phase saturation because of the diverging linear term.

The objective of this work is to present the results obtained by extending the criteria summarized above to the more rich and complex bi-Langmuir isotherm:

$$n_i = \frac{\gamma_i c_i}{1 + \sum_{j=A,B} a_j c_j} + \frac{\delta_i c_i}{1 + \sum_{j=A,B} b_j c_j} \quad (i = A, B) \quad (8)$$

The method adopted to determine the complete separation region in the bi-Langmuir case exploits a more general procedure, which has been derived based on the method of characteristics applied to Eq. (1) and Eq. (2) [21]. The description of this procedure is beyond the scope of this work and is presented elsewhere [22].

The bi-Langmuir isotherm is well-known in chromatography [23], and it is used to describe adsorption behaviour whenever the existence of two types of interacting sites is observed, which is often the case of enantiomeric separation [13,24,25]. Some examples are provided by the stationary phases constituted of a protein having chiral recognition properties which is immobilized on a solid support, such as silica gel [24,26–28] or an anion exchanger [29]. For the racemic mixtures studied in the works cited above, the bi-Langmuir model always gave the best fit interpolation of the experimental data, because it describes the adsorption of the species on the two independent sites; one term of Eq. (8) accounts for selective interactions with the chiral stationary phase, while the other for the non-selective interactions with the support; hence it is the same for both enantiomers [20]. Moreover, the bi-Langmuir isotherm provides a number of parameters high enough to fit experimental data for systems whose adsorption mechanism cannot be described by the simpler isotherms Eq. (4), Eq. (5) and Eq. (7). It is worth noticing that the linear, Langmuir and modified Langmuir isotherms can be regarded as special cases of the bi-Langmuir isotherm. In fact Eq. (4) is obtained by letting $\gamma_i = H_i$ and $a_i = b_i = \delta_i = 0$ in Eq. (8); Eq. (5) by letting $b_i = \delta_i = 0$, and finally Eq. (7) by letting $\delta_i = h$ and $b_i = 0$.

2. Design of operating conditions

Following the approach mentioned above, the

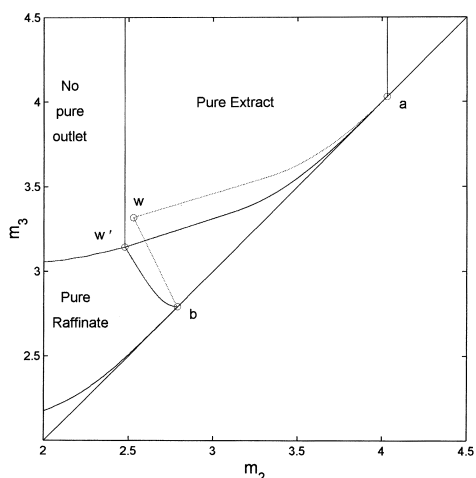


Fig. 3. Plot of the regions of separation in the (m_2, m_3) plane for the bi-Langmuir (---) and Langmuir (···) models respectively; the parameters of the isotherms according to Eq. (5) and Eq. (8) are: Langmuir, $\gamma_A = 4.028$, $k_A = 0.0503$ l/g, $\gamma_B = 2.788$, $k_B = 0.0348$; bi-Langmuir, $\gamma_A = 3.728$, $\delta_A = 0.3$, $a_A = 0.0466$ l/g, $b_A = 3$ l/g, $\gamma_B = 2.688$, $\delta_B = 0.1$, $a_B = 0.0336$ l/g, $b_B = 1$ l/g. Both regions of separation intersect the diagonal of the operating plane at points a, b of coordinates (H_A, H_A) , (H_B, H_B) respectively; w and w' are the optimal points in the Langmuir and bi-Langmuir cases, respectively. The composition of the feed mixture is $c_A^F = c_B^F = 2.9$ g/l.

operating parameter space can be divided into four separation regions, each corresponding to a different separation regime. This is illustrated in Fig. 3, where the projection of the region of separation onto the plane (m_2, m_3) is shown. The calculation has been performed using the bi-Langmuir isotherm characterizing the adsorption behaviour of the enantiomers of 1,1'-bi-2-naphtol on a stationary phase consisting of a protein bonded to a silica gel support [13]. The triangle-shaped region identifies the operating conditions achieving complete separation, i.e. 100% purity in both extract and raffinate. The three regions surrounding it correspond to operating conditions for which one or both outlets are not pure (purity less than 100%). The exact shape and position of these regions depend on the parameters of the bi-Langmuir isotherm and on the feed composition, c_A^F and c_B^F . The above conclusions about the regions of separation in the (m_2, m_3) plane apply only if the relevant constraints on the flow-rate ratios in sections 1 and 4, i.e. m_1 and m_4 , are fulfilled; this is the case in all the examples discussed in this work.

For a comparison, in Fig. 3 the separation region computed with a Langmuir isotherm is shown with dashed boundaries [1]. Its parameters are determined such that the Langmuir isotherm describes as accurately as possible the equilibrium data obtained through the bi-Langmuir isotherm that was used to calculate the separation region with solid boundaries in Fig. 3. The single-component bi-Langmuir isotherms for the pure bi-naphtol enantiomers are compared in Fig. 4 with the single-component Langmuir isotherms. Note that in order to better illustrate the comparison between the two isotherms, concentration values well beyond the solubility of the two enantiomers, which is about 7 g/l (R.M. Nicoud, private communication), are considered in this figure. The parameters of the latter have been chosen by imposing the same initial slopes and saturation loading capacities for the two enantiomers, thus letting $(\gamma_i)^L = (\gamma_i + \delta_i)^{\text{bi-L}}$ and $(\gamma_i/k_i)^L = (\gamma_i/a_i + \delta_i/b_i)^{\text{bi-L}}$, respectively. It is seen that, even though the isotherms in Fig. 4 are very close, the corresponding complete separation regions in Fig. 3 are rather different. In more quantitative terms, at a feed concentration of 2.9 g/l, the adsorbed phase concentrations predicted by the two isotherms differ by less than 6%. Such a difference has rather strong consequences on the separation regions. In particular the boundary wb is curved in the case of the bi-Langmuir isotherm, whereas it is straight in the case

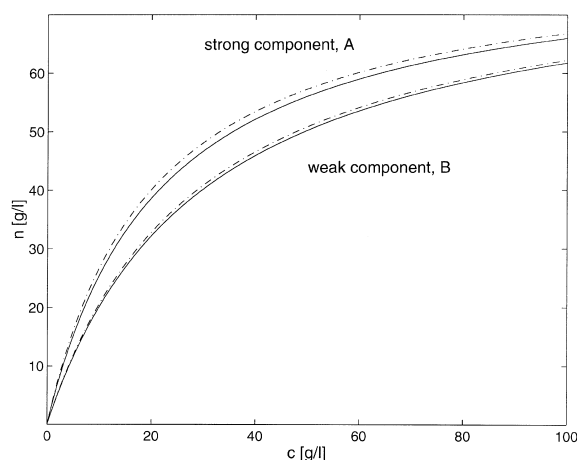


Fig. 4. Single component bi-Langmuir (---) and Langmuir (- · -) adsorption isotherms of both enantiomers. Isotherm parameters as in Fig. 3.

of the Langmuir isotherm. Moreover, although the two complete separation regions share the same base points *a* and *b*, they are far away from each other in the proximity of the points *w* and *w'*. This is a rather serious problem since point *w* corresponds to optimal separation performance and there is therefore a need for a good prediction of its location [1]. This observation provides a good motivation for calculating the complete separation region for the accurate bi-Langmuir isotherm.

3. Non-linear behaviour of SMB units

SMB units typically operate in overload conditions, thus exhibiting non-linear competitive adsorption behaviour. This effect is fully accounted for by the criteria developed in this and in previous works [1,3]. In order to show it, we analyze how the shape and position of the complete separation region change as a function of the feed composition. Several effects can be shown and discussed: we focus in the following on the role of the overall feed concentration and of the concentration of each component in the binary feed mixture.

3.1. Effect of overall feed concentration

First, let us determine the changes in the complete separation region produced by changes of the overall feed concentration c_T^F , while the relative composition of the two components to be separated remains constant. The latter constraint is typical of enantiomers separations, where in particular $c_A^F = c_B^F = c_T^F/2$. At low concentration bi-Langmuir isotherms exhibit linear behaviour (cf. Fig. 4):

$$n_i \approx H_i c_i = (\gamma_i + \delta_i) c_i \quad (i = A, B) \quad (9)$$

Small concentration values in the SMB unit are obtained when the feed concentration, c_T^F , is small, while on the other hand higher feed concentrations imply a higher degree of non-linearity in the separation. These considerations are confirmed by the results shown in Fig. 5, where five different regions of complete separation are drawn and compared with the corresponding linear complete separation region, which is calculated using Eq. (4) and drawn with

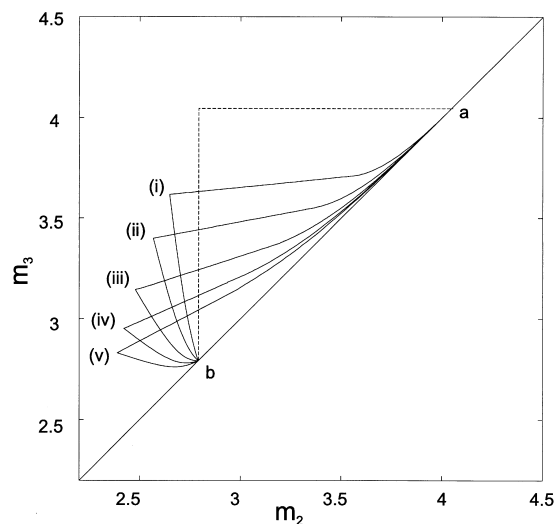


Fig. 5. Effect of the total feed concentration on the region of complete separation in the (m_2, m_3) plane for a system described by the bi-Langmuir adsorption isotherm. Isotherms parameters as in Fig. 3; $c_A^F = c_B^F = c_T^F/2$ g/l; (i) $c_T^F = 1.4$ g/l; (ii) $c_T^F = 3$ g/l; (iii) $c_T^F = 5.8$ g/l; (iv) $c_T^F = 9$ g/l; (v) $c_T^F = 12$ g/l; (- - -) region of separation in the linear case, i.e. when $c_T^F \rightarrow 0$.

dashed boundaries. These refer to the same mixture to be separated, but with different values of the overall feed concentration, c_T^F , which increases from 1.4 g/l in the case of region (i) to 12 g/l in the case of region (v). Note that in reality the overall feed concentration should not overcome the value of 7 g/l due to solubility limitations. It is seen that the triangles tend to converge rapidly to the linear solution if the overall concentration of the feed is decreased. Furthermore the segment *ab*, i.e. the portion of the boundary of the region of complete separation belonging to the diagonal, is the same in all cases, and coincides with that of the linear complete separation region. This is consistent with the property that points close to the diagonal correspond to operating conditions where the feed flow-rate [which according to Eq. (3) is proportional to $(m_3 - m_2)$] is very small and the components to be separated are soon diluted in the unit, thus letting the SMB operate in the linear equilibrium region. On the other hand, in going from the linear region to region (i) and to region (v), the complete separation region becomes smaller and smaller and sharper and sharper, while the optimal operating point, i.e. the

vertex w , moves downwards to the left. This implies that the separation becomes less and less robust (the basis for the discussion is reported in Ref. [1]). These remarks indicate that the behaviour of the SMB units separating systems characterized by the bi-Langmuir isotherm is similar to the case of Langmuir isotherms [1]. Therefore similar conclusions can be drawn, as far as the optimization of the operating conditions is concerned, in terms of productivity, solvent consumption and robustness [1].

3.2. Effect of feed composition

Let us analyze the effect of changing the feed concentration of one species, while keeping the other constant. The effect of changing c_B^F at constant c_A^F is illustrated in Fig. 6, whereas the opposite effect is shown in Fig. 7. With reference to Fig. 6, it can be seen that the portion of the boundary wb of the complete separation region is determined by the value of c_A^F , while increasing the value of c_B^F has only the effect of reducing the size of the complete separation region. On the other hand, Fig. 7 indicates that the effect of the feed concentration of the strong component is similar to the effect of the overall feed

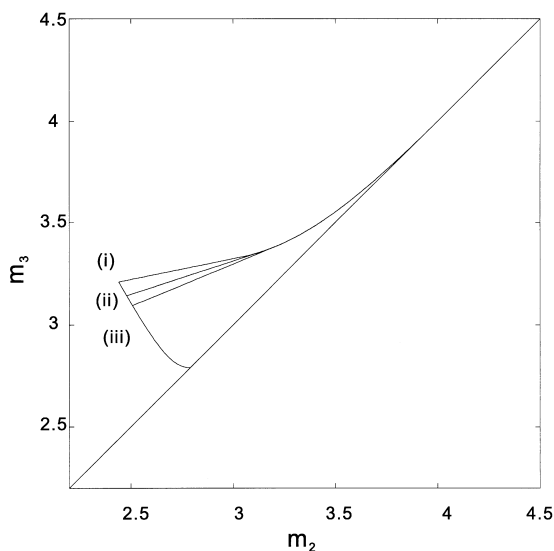


Fig. 6. Effect of c_B^F on the region of complete separation in the (m_2, m_3) plane for the bi-Langmuir isotherm when c_A^F is held constant. Isotherm parameters as in Fig. 3; $c_A^F = 2.9$ g/l; (i) $c_B^F = 1.45$ g/l; (ii) $c_B^F = 2.9$ g/l; (iii) $c_B^F = 4.35$ g/l.

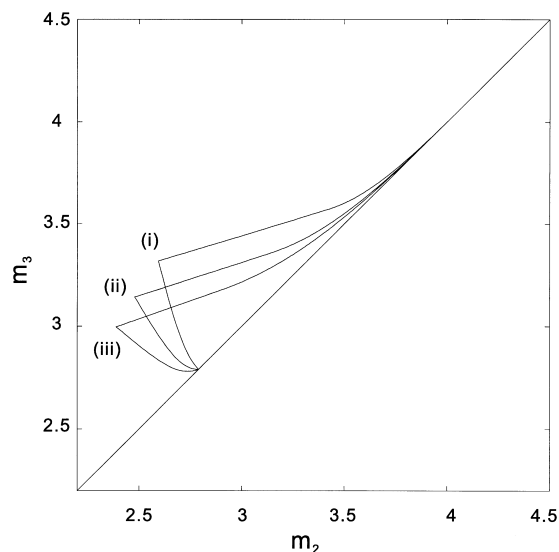


Fig. 7. Effect of c_A^F on the region of complete separation in the (m_2, m_3) plane for the bi-Langmuir isotherm when c_B^F is held constant. Isotherm parameters as in Fig. 3; $c_B^F = 2.9$ g/l; (i) $c_A^F = 1.45$ g/l; (ii) $c_A^F = 2.9$ g/l; (iii) $c_A^F = 4.35$ g/l.

concentration. Since the Langmuir isotherm (Eq. (5)) and the modified Langmuir isotherm (Eq. (7)) are special cases of the bi-Langmuir isotherm, they exhibit qualitatively the same behaviour illustrated in Figs. 6 and 7.

4. Concluding remarks

The application of continuous chromatographic separations based on the SMB technology is gaining more and more interest in the fine chemical and pharmaceutical industries. The design of SMB units and their operating conditions is not straightforward and is made easier through the application of some recently developed criteria, which apply to the set of powerful though simple Langmuir isotherms. In this work the result of application of such criteria to the bi-Langmuir isotherm is presented. This isotherm has a rather large range of applicability due to its physical significance and its flexibility. The results obtained demonstrate on the one hand that the behaviour of SMB units when using a bi-Langmuir isotherm is significantly different from what predicted using a Langmuir isotherm. On the other hand

the qualitative features of the non-linear behaviour of SMB units are the same as those demonstrated for the Langmuir isotherm; therefore it is possible to extend to the bi-Langmuir isotherm all the conclusions for the choice of optimal and robust operating conditions previously drawn in the case of Langmuir isotherm [1]. It is worth noticing that the adopted approach to determine the optimal conditions for a SMB unit is rather efficient.

5. Notation

a_i	bi-Langmuir parameter of component i
b_i	bi-Langmuir parameter of component i
c_i	fluid phase concentration of component i
h	constant linear term in the modified Langmuir isotherm
H_i	Henry constant of species i
k_i	Langmuir parameter of component i
m_j	flow-rate ratio in section j , defined by Eq. (3)
n_i	adsorbed phase concentration of component i
Q_j	volumetric fluid flow-rate in section j
Q_s	volumetric solid flow-rate
x	dimensionless axial coordinate
V	volume of a single adsorption column

5.1. Greek letters

γ_i	Langmuir and bi-Langmuir parameter of component i
δ_i	Langmuir and bi-Langmuir parameter of component i
ε^*	overall void fraction of the bed, defined as $\varepsilon^* = \varepsilon_b + (1 - \varepsilon_b)\varepsilon_p$
ε_b	bed or interparticle void fraction
ε_p	intraparticle void fraction
τ	dimensionless time, tQ_s/V

5.2. Subscripts and superscripts

A	more retained species in the feed
B	less retained species in the feed

E	extract
F	feed
i	component index, $i = A, B$
j	section index, $j = 1, \dots, 4$
R	raffinate
S	eluent

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