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Use of the LeVan–Vermeulen isotherm model for the calculation of elution band profiles in non-linear chromatography

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ABSTRACT

The two-term LeVan–Vermeulen isotherm is the simplest competitive isotherm based on the ideal adsorbed solution model. It applies when both components follow individually the single-component Langmuir isotherm model. It takes into account the influence of the difference in the column saturation capacity for these two components. Individual band profiles calculated with this isotherm are in qualitative agreement with experimental results. They exhibit a stronger displacement effect, a weaker tag-along effect and a higher degree of band separation than predicted by the Langmuir competitive isotherm when the column saturation capacity is larger for the second component than for the first. Conversely, when the column saturation capacity is larger for the first component than for the second, the displacement effect is less intense and the tag-along effect is stronger than with the competitive Langmuir isotherm and the separation deteriorates. When the sample size is increased, a reversal of the elution order is observed.

INTRODUCTION

As we have previously reported, there is excellent agreement between the band profiles measured experimentally and those calculated in the case of single-component or binary mixture samples when the equilibrium isotherms of the compounds involved can be accounted for exactly [1–6]. With most single-component samples, adsorption data in normal- and reversed-phase chromatography are well accounted for by a Langmuir [1,2] or a bi-Langmuir isotherm [4]. This is in agreement with results reported by others [7,8]. On the other hand, with binary mixtures, the adsorption data could be fitted correctly on a bi-Langmuir isotherm only for enantiomers [4]. In other instances [3,5], no Langmuir-type competitive isotherm could account accurately for the data, although the single-component Langmuir isotherm accounted well for the data corresponding to the two single-component samples.

These results are in agreement with the assumptions of the Langmuir model, essentially that the solution and the adsorbed phase behave ideally and that there are no molecular interactions. With enantiomers, the chiral selective sites which have the highest interaction energy and a low saturation capacity are filled first and their

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saturation is reached at low concentrations in the mobile phase, so deviations from ideal behavior in the solution are small [4,6]. As the density of chiral selective sites on the surface of the stationary phase is low, molecular interactions between adsorbate molecules are insignificant and deviations from ideal behavior in the adsorbed phase remain small. Finally, the column saturation capacities for the two enantiomers are nearly equal [4,6]. All these favorable circumstances are absent in the other instances, where isomers or less closely related compounds were studied [3,5].

Another fundamental assumption made in the competitive Langmuir model is that the column saturation capacity is the same for the components involved. Otherwise, the Langmuir competitive isotherm does not satisfy the Gibbs adsorption isotherm equation and, consequently, is thermodynamically inconsistent [9]. This restriction is of great practical importance because in most instances the more retained component of a pair has the larger molecule, which interacts more strongly with the stationary phase but also which occupies the larger surface area on the adsorbent surface, and hence has the lower saturation capacity. In such a case, the single-component isotherms intersect. In the converse case, when the column saturation capacity for the more strongly retained component is larger than that of the less retained component, the single-component isotherms diverge. In both instances, however, the Langmuir competitive isotherm predicts that the selectivity, $(q_2/C_2)/(q_1/C_1)$ (where q_i and C_i are the concentrations of component i in the stationary and mobile phase, respectively), remains constant and equal to the relative retention under linear (*i.e.*, analytical) conditions, $\alpha = k'_{0,2}/k'_{0,1}$. This is a basic characteristic of the competitive Langmuir isotherm model that the selectivity is constant, independent of the concentrations of the two compounds. Its consequences are important.

We have shown that in overloaded elution chromatography, if the Langmuir competitive isotherm model is valid, the ideal model predicts that the intensity of the displacement effect is increased and at the same time the separation deteriorates if the column saturation capacity of the second component is decreased (and isotherm intersection takes place) at a constant column saturation capacity for the first component and constant sample size [10]. This is explained by the resulting increase in the loading factor for the second component ($L_{f,2} = n_2/W_2$, where n_2 is the amount of component 2 and W_2 is the column saturation capacity). If the sample size is reduced to keep constant the loading factor for the second component at the same time as the column saturation capacity for the second component is reduced, the displacement effect is increased and the separation is improved. Conversely, if the column saturation capacity of the second component is increased at constant column saturation capacity for the first component and constant sample size (and isotherm divergence takes place), the intensity of the tag-along effect increases and the intensity of the displacement effect decreases, but at the same time the separation is improved because the loading factor corresponding to a given sample size is decreased [10]. Restoring the initial value of the loading factor by increasing also the sample size gives a chromatogram in which the displacement effect is less intense, the tag-along effect more intense and the degree of separation degraded.

These results are confirmed by the chromatograms calculated using the semi-ideal model and competitive Langmuir isotherms with various ratios of the column saturation capacities for the two components [11]. Calculations also show that the formation of an isotachic train is not affected by the intersection of the single-component isotherms of the two components of a binary mixture, as long as the competitive Langmuir model is valid. The conditions under which the isotachic train forms depend essentially on the value of the loading factors and on the column efficiency [12]. The only consequence of the isotherm intersection is that the height of the concentration plateau of the second band is lower than that of the concentration plateau of the first band.

These theoretical consequences of the Langmuir competitive isotherm model are in direct contradiction with many experimental observations. Cox and Snyder [13] reported that when the more retained component of a binary mixture has the lower column saturation capacity, the intensity of the displacement effect of the first component by the second is minimal, the broadening of the second component band is important, extensive band overlap takes place and poor separation is achieved. Conversely, when the two single-component isotherms diverge, the intensity of the displacement effect is enhanced, the tailing of the first component band behind the front of the second band is reduced and the separation is improved. Similarly, Horváth [14] and Subramanian and Cramer [15] reported that it is impossible (or at least very difficult) to obtain an isotachic train in displacement chromatography when the single-component isotherms of the mixture components intersect. Displacement can be achieved only by changing the mobile phase composition [14], which alters the isotherms.

This contradiction between experimental and theoretical results suggests that the competitive Langmuir model is not satisfactory, at least when the column saturation capacities of the two components are significantly different. This conclusion also agrees with our experimental results [1–6]. It is also supported by theoretical considerations. As mentioned above, the competitive Langmuir isotherm is not consistent with the Gibbs adsorption isotherm equation unless the column saturation capacities of the mixture components are equal, at least when the adsorption of the solvent is ignored [9]. In fact, the Langmuir competitive isotherm is justified only on the basis of very simple kinetic considerations [16]. Its popularity stems from the convenience with which the parameters of the competitive isotherms are derived from the single-component isotherms. More sophisticated isotherms, however, enjoy also this property. The models derived from the ideal adsorbed solution (IAS) theory belong to this group.

The IAS theory was developed by Myers and Prausnitz [17], precisely to allow the prediction of multi-component isotherms using data obtained from single-component measurements. The IAS theory is essentially a procedure permitting the derivation of a competitive isotherm consistent with a given set of single-component isotherms (*e.g.*, Langmuir or Freundlich isotherms) and consistent with the basic thermodynamic requirements (*i.e.*, the Gibbs adsorption isotherm equation). The IAS theory is based on the same assumptions as the Langmuir isotherm, an ideal adsorbed solution for both the stationary and the mobile phases. However, as the IAS theory based its interpretation of the deviation of the adsorption behavior from the Langmuir competitive model on the Gibbs adsorption isotherm, the IAS isotherm obtained is always consistent with thermodynamics, regardless of the relative values of the column saturation capacities.

Henson and Kabel [18] showed that the IAS theory predicts competitive gas–solid adsorption isotherms of gases which are accurate at low surface coverages but deviate systematically from experimental data at high coverages. Later, the IAS theory was extended to competitive liquid–solid adsorption in the case of dilute solutions [19]. It was also used in combination with a trial-and-error procedure for the prediction of competitive binary gas–solid isotherms for species obeying the single-component Langmuir isotherm [20] or the Freundlich isotherm [21].

Using the IAS theory, LeVan and Vermeulen [22] derived gas–solid competitive binary isotherms in the form of a rapidly converging series expansion, provided that the single-component isotherms are either Langmuir or Freundlich isotherms. The competitive isotherm reduces to the single-component isotherm when the concentration of the other component approaches zero. The LeVan–Vermeulen isotherm, based on single-component Langmuir isotherms, reduces to the classical competitive Langmuir isotherm when the specific saturation capacities of the two components are equal. When these capacities are unequal, the isotherms satisfy the Gibbs adsorption isotherm equation and hence they are thermodynamically consistent. Extension of these IAS isotherms to liquid–solid isotherms is straightforward, provided that we assume that the solution is dilute and the adsorption of the solvent can be neglected.

The aim of this paper is to examine the implications of using the LeVan–Vermeulen isotherm in preparative chromatography and the influence of the ratio of the column saturation capacities on the intensity of the displacement and the tag-along effects.

THEORY

A most important problem in the thermodynamics of phase equilibria is whether we can predict the competitive equilibrium behavior of two components knowing only their single-component isotherms. In principle, this should not be possible since it is tantamount to neglecting the difference $E_{1,2} - (E_{1,1} + E_{2,2})/2$ between the molecular interaction energy of the unsymmetrical pair, $E_{1,2}$ and the average of the molecular interaction energies of the symmetrical pairs of molecules, $E_{1,1}$ and $E_{2,2}$. In many applications in the separation sciences, however, we are interested in pairs of closely related compounds which have similar properties. In such cases, deviations from this assumption may be expected to be small, so the problem can be rephrased as follows. Can we predict the competitive isotherms of a binary mixture from the single-component isotherms with an accuracy compatible with the accuracy we require for the prediction of the individual band profiles in chromatography and the need for a reasonably accurate calculation of the influence of experimental parameters on the production rate and recovery yield.

We assume in the following that the single-component equilibrium isotherms of the two components of the mixture follow the Langmuir isotherm model:

$$q_i = \frac{b_i q_{s,i} C_i}{1 + b_i C_i} \tag{1}$$

where q_i and C_i are the stationary and mobile phase concentrations of component i at equilibrium, a_i and b_i are numerical coefficients characteristic of the component i and $q_{s,i}$ is the specific column saturation capacity, reported as the amount of component i needed to form a monolayer per unit volume of packing material. Eqn. 1 is equivalent to the conventional Langmuir isotherm, with $a_i = b_i q_{s,i}$.

Based on the IAS theory, LeVan and Vermeulen [22] derived an isotherm for mixtures of gases and vapors which follow the single-component Langmuir model. Extended to the case of solutions, this isotherm can be written as

$$q_i = \frac{b_i q_s C_i}{1 + b_1 C_1 + b_2 C_2} + C_i \cdot \frac{\partial q_s}{\partial C_i} \ln (1 + b_1 C_1 + b_2 C_2) \tag{2}$$

In eqn. 2, q_s can be considered as a weighted average monolayer capacity. Depending on the number of terms which are considered in the Taylor series expansion giving q_s, a family of isotherms can be derived. We consider here the first three members of this family.

Formally, the classical competitive Langmuir isotherm could be obtained by writing that $q_s = q'_s = (q_{s,1} + q_{s,2})/2$. We obtain

$$q_i = \frac{q'_s b_i C_i}{1 + b_1 C_1 + b_2 C_2} \tag{3a}$$

Eqn. 3a is a correct competitive Langmuir isotherm only if $q_{s,1} = q_{s,2}$. Then, it is the first-term expansion of the LeVan–Vermeulen isotherm. The classical competitive Langmuir isotherm, where q'_s in eqn. 3a is replaced with $q_{s,i}$:

$$q_i = \frac{q_{s,i} b_i C_i}{1 + b_1 C_1 + b_2 C_2} \tag{3b}$$

is not an IAS isotherm if $q_{s,1} \neq q_{s,2}$.

For the two-term expansion of the LeVan–Vermeulen isotherm, the value of q_s is given by

$$q_s = \frac{q_{s,1} b_1 C_1 + q_{s,2} b_2 C_2}{b_1 C_1 + b_2 C_2} \tag{4}$$

Hence the two-term expansion of the LeVan–Vermeulen isotherm is obtained by combining eqns. 2 and 4:

$$q_1 = \frac{q_s b_1 C_1}{1 + b_1 C_1 + b_2 C_2} + \Delta_{1,2} \tag{5}$$

and

$$q_2 = \frac{q_s b_2 C_2}{1 + b_1 C_1 + b_2 C_2} - \Delta_{1,2} \tag{6}$$

with

$$\Delta_{1,2} = (q_{s,1} - q_{s,2}) \frac{b_1 b_2 C_1 C_2}{(b_1 C_1 + b_2 C_2)^2} \ln (1 + b_1 C_1 + b_2 C_2) \tag{7}$$

For the three-term expansion of the LeVan–Vermeulen isotherm, the value of q_s, denoted q_s^* for the sake of clarity, is written as

$$q_s^* = \frac{q_{s,1}b_1C_1 + q_{s,2}b_2C_2}{b_1C_1 + b_2C_2} + 2\frac{(q_{s,1} - q_{s,2})^2}{(q_{s,1} + q_{s,2})} \cdot \frac{b_1b_2C_1C_2}{(b_1C_1 + b_2C_2)^2} \cdot \left[\left(\frac{1}{b_1C_1 + b_2C_2} + 1/2\right) \ln(1 + b_1C_1 + b_2C_2) - 1\right] \quad (8)$$

Hence the three-term expansion of the LeVan–Vermeulen isotherm becomes

$$q_1 = \frac{q_s^* b_1C_1}{1 + b_1C_1 + b_2C_2} + \triangle_{1,2}(1 + \triangle_{1,3}) \quad (9)$$

and

$$q_2 = \frac{q_s^* b_2C_2}{1 + b_1C_1 + b_2C_2} - \triangle_{1,2}(1 + \triangle_{2,3}) \quad (10)$$

In eqns. 9 and 10, $\triangle_{1,2}$ is given by eqn. 7 and

$$\triangle_{1,3} = \frac{q_{s,1} - q_{s,2}}{q_{s,1} + q_{s,2}} \cdot \frac{1}{b_1C_1 + b_2C_2}\left[\frac{(b_2C_2)^2 + 2b_2C_2 - 4b_1C_1 - (b_1C_1)^2}{b_1C_1 + b_2C_2} \cdot \ln(1 + b_1C_1 + b_2C_2) + \frac{3(b_1C_1)^2 + 4b_1C_1 + b_1b_2C_1C_2 - 2b_2C_2 - 2(b_2C_2)^2}{1 + b_1C_1 + b_2C_2}\right] \quad (11)$$

$$\triangle_{2,3} = \frac{q_{s,2} - q_{s,1}}{q_{s,1} + q_{s,2}} \cdot \frac{1}{b_1C_1 + b_2C_2}\left[\frac{(b_1C_1)^2 + 2b_1C_1 - 4b_2C_2 - (b_2C_2)^2}{b_1C_1 + b_2C_2} \cdot \ln(1 + b_1C_1 + b_2C_2) + \frac{3(b_2C_2)^2 + 4b_2C_2 + b_1b_2C_1C_2 - 2b_1C_1 - 2(b_1C_1)^2}{1 + b_1C_1 + b_2C_2}\right] \quad (12)$$

Although complex, these isotherm equations depend on only four parameters, the two specific column saturation capacities, $q_{s,i}$ and the two coefficients b_i which are respectively equal to the ratios $a_i/q_{s,i} = k'_{i,0}/Fq_{s,i}$, where F is the phase ratio of the column and $k'_{i,0}$ is the retention factor under linear (*i.e.*, analytical) conditions. These four parameters can be derived simply from the single-component isotherms, provided that these isotherms are accounted for by a simple Langmuir isotherm.

Examination of these equations shows that when the column saturation capacity for the first-eluted component is smaller than that for the second component (diverging isotherms), the amount of first component adsorbed at equilibrium is lower than that predicted by the simple Langmuir competitive model and the amount of the second component adsorbed at equilibrium is larger than that predicted by this model. The converse is true when the column saturation capacity for the first component is the larger (isotherm intersection). When the two column saturation capacities are equal

($q_{s,1} = q_{s,2} = q_s$), eqns. 5 and 6 or 9 and 10 are reduced to the classical Langmuir competitive isotherm, eqn. 3b.

We have used the three series of equations, eqns. 3b, 5 and 6, and 9 and 10, for simulation purposes, using the semi-ideal model of chromatography described previously [23–25]. The results are reported and compared in the next section.

RESULTS AND DISCUSSION

We have studied the influence of the ratio of the column saturation capacities for the two components and the influence of the composition ratio of the feed.

Influence of the ratio of the column saturation capacities

Figs. 1–5 were calculated for the same mixture composition (concentration ratio

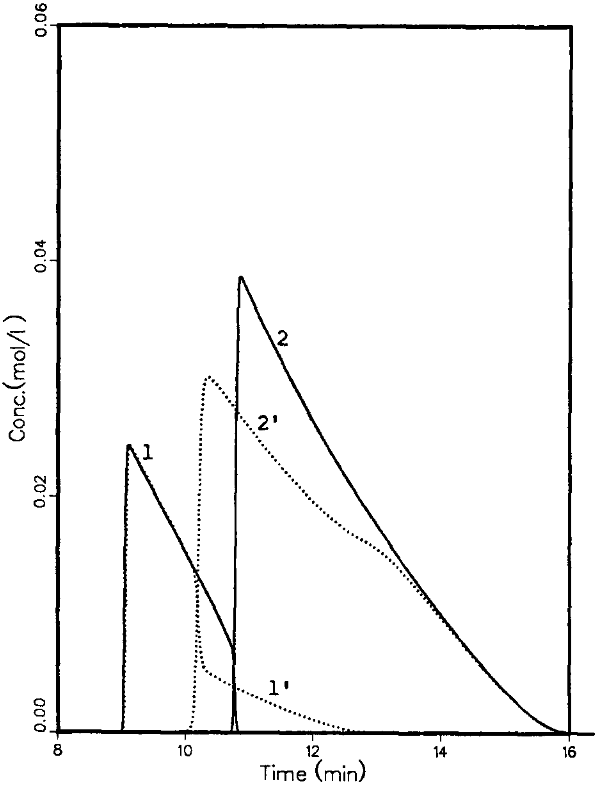


Fig. 1. Overloaded elution of a binary mixture. Comparison between the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions: (I) column, phase ratio $F = 0.25$; flow velocity, 0.125 cm/s; column length, 25 cm; column efficiency, $N = 5000$; (II) isotherm, limiting retention factor of the first component, $k'_{0,1} = 3$; relative retention, $\alpha = k'_{0,2}/k'_{0,1} = 1.2$; $b_i = a_i/q_{s,i} = k_i/Fq_{s,i}$; specific column saturation capacities, $q_{s,2} = 2$ mmol/ml, $q_{s,1} = 1$ mmol/ml; (III) sample, feed composition, 1:3; sample size, $n_1 + n_2 = 0.166$ mmol; injection time, $t_p = 10$ s; concentrations in the feed, $C_1^0 = 0.25$ M, $C_2^0 = 0.75$ M; loading factor for the first component, $L_{f,1} = 0.05$, and for the second component, $L_{f,2} = 0.075$.

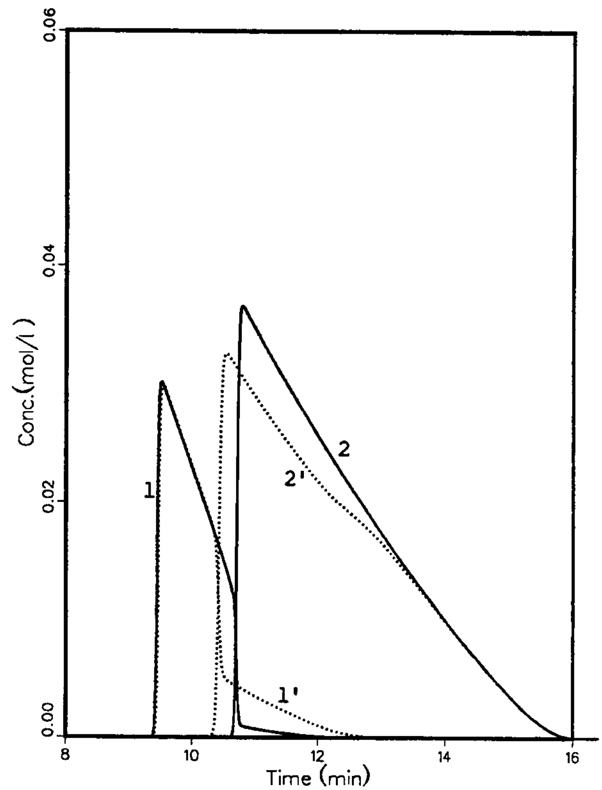


Fig. 2. Overloaded elution of a binary mixture. Comparison between the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 1, except $q_{s,1}$ = 1.5 mmol/ml and $L_{f,1}$ = 0.033.

of the first and second components = 1:3), the same sample size and the same column saturation capacity for the second component ($q_{s,2}$ = 2), and hence for the same loading factor for the second component ($L_{f,2}$ = 7.5%). The specific column saturation capacity for the second component increases from 1 (Fig. 1) to 1.5 (Fig. 2), 2 (Fig. 3), 3 (Fig. 4) and 4 (Fig. 5). The loading factor for the first component decreases in proportion to the reverse of the column saturation capacity. In each figure, the profiles calculated with the Langmuir competitive isotherm (dotted lines) and with the two-term expansion of the LeVan–Vermeulen isotherm (solid lines) are superimposed.

As expected, when the column saturation capacities for the two components are the same (Fig. 3), the LeVan–Vermeulen isotherm reduces to the Langmuir competitive isotherm and the band profiles calculated with the two isotherms are identical. When the column saturation capacity of the first component is lower than that of the second component (Figs. 1 and 2), the LeVan–Vermeulen isotherm predicts a better separation of the two components, a much narrower mixed zone, a weak tag-along effect and a very strong displacement effect. This is especially noticeable in Fig. 1, where the separation predicted by the LeVan–Vermeulen isotherm is nearly total, which is far from the case for the separation predicted by the Langmuir

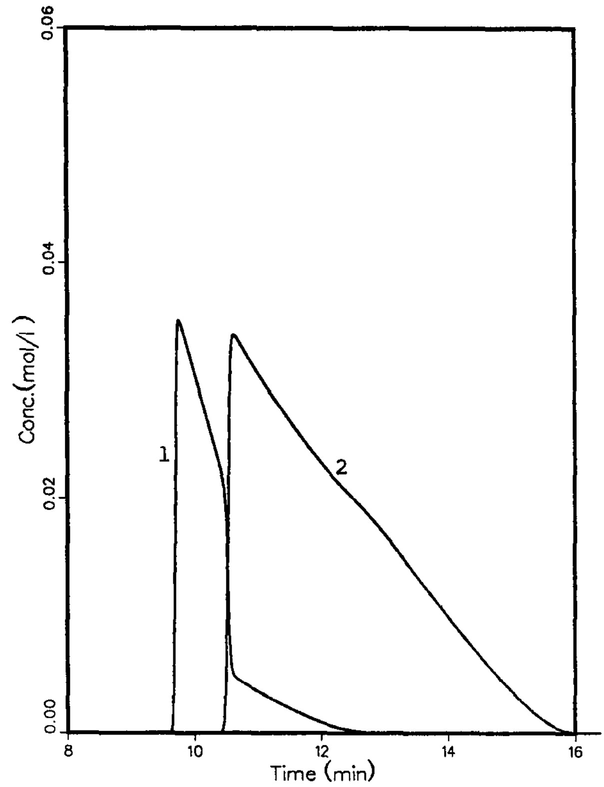


Fig. 3. Overloaded elution of a binary mixture. Comparison between the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). In this case, solid and dotted lines are superimposed and cannot be distinguished. Experimental conditions as in Fig. 1, except $q_{s,1}$ = 2 mmol/ml and $L_{f,1}$ = 0.025.

competitive isotherm. In this case (Fig. 1), the band profile for the second component is nearly identical whether the component is injected pure or in a mixture with the first component. This result is in agreement with experimental observations reported previously [13,26]. Its consequence is a production rate that is higher than that predicted with the competitive Langmuir isotherm.

In contrast, when the column saturation capacity of the first component is larger than that of the second (Figs. 4 and 5), the chromatograms calculated with the LeVan–Vermeulen isotherms exhibit an enhanced tag-along effect and a weak (Fig. 4) or very reduced (Fig. 5) displacement effect. In the latter instance, the mixed zone is very important. With the sample load used ($L_{f,2}$ = 7.5%), a negligible amount of the first component can be recovered pure and the production rate for the second component is abnormally low. This means that a smaller sample size should be used for preparative applications and the production rate is much decreased compared with the prediction based on calculations carried out with the competitive Langmuir isotherm model.

In summary, in agreement with the experimental results and in contrast with the

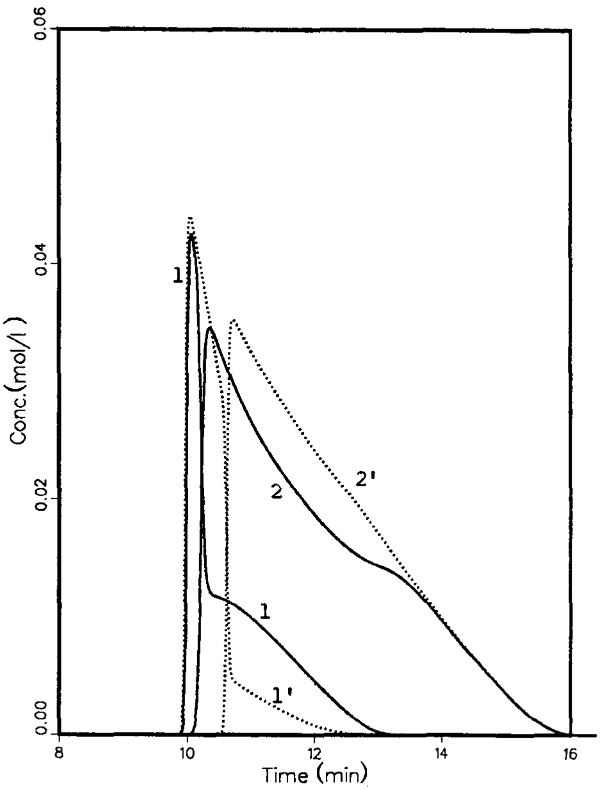


Fig. 4. Overloaded elution of a binary mixture. Comparison between the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 1, except $q_{s,1}$ = 3 mmol/ml and $L_{f,1}$ = 0.0166.

Langmuir competitive isotherm, the LeVan–Vermeulen isotherm predicts that the displacement effect is enhanced and the tag-along effect depressed when the column saturation capacity ratio, $q_{s,1}/q_{s,2}$, is smaller than unity and the maximum production rate is larger, while the opposite is true when the ratio $q_{s,1}/q_{s,2}$ is larger than unity.

Influence of the feed composition on band interference

Ratio of the column saturation capacities, $q_{s,1}/q_{s,2}$, smaller than unity. In this case, we assume that the specific saturation capacities for the first and second components are 1 and 2, respectively ($q_{s,1}/q_{s,2} = 0.5$). Figs. 6–8 compare the two-term expansion (solid lines) and the three-term expansion (dotted lines) of the LeVan–Vermeulen isotherm with the competitive Langmuir isotherm (dashed lines), as plots of the stationary phase concentrations, q_1 and q_2, *versus* the sum $C = C_1 + C_2$ for three relative compositions, C_1/C_2, equal to 1:9, 1:1 and 9:1. These figures represent the three intersections of the isotherm surface by the vertical planes through the origin having slopes of 1/9, 1 and 9.

In none of the three cases is there any significant difference between the solid and

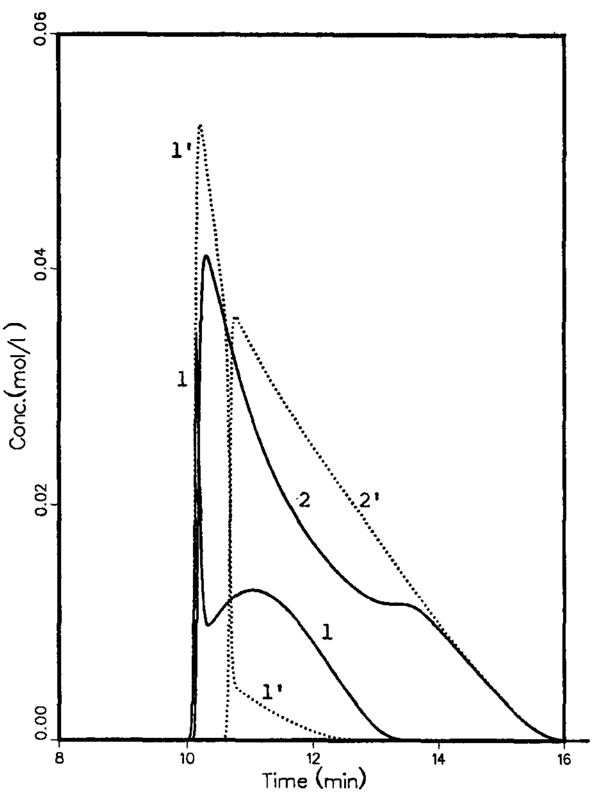


Fig. 5. Overloaded elution of a binary mixture. Comparison between the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 1, except $q_{s,1}$ = 4 mmol/ml and $L_{f,1}$ = 0.0125.

the dotted lines. This shows that in the concentration range investigated here the correction introduced by the third term of the expansion in eqns. 9 and 10 is negligible. This concentration range (0–200 mM) includes those typically used in preparative liquid chromatography. This result is important because the third-term correction is needed as a matter of principle to give physical sense to the isotherm and avoid the existence of a maximum of the stationary phase concentration for some intermediate mobile phase concentration. On the other hand, significant differences are observed between the predictions of the LeVan–Vermeulen and the Langmuir competitive isotherms, especially in the intermediate range of relative concentrations (see Fig. 7).

One of the characteristic features of the Langmuir isotherm is that the separation factor, $(q_2/C_2)/(q_1/C_1) = a_2/a_1 = \alpha$, is independent of the concentrations C_1 and C_2. This result is obtained directly from the isotherm eqn. 3b. Thus, the ratio $r_q = q_2/q_1$ is constant for the Langmuir competitive isotherms in each of Figs. 6–8, and equal to $\alpha C_2/C_1$. This ratio r_q is equal to 9α in Fig. 6, to α in Fig. 7 and to $\alpha/9$ in Fig 8. We observe in these figures that the LeVan–Vermeulen isotherms of the two components are further apart than predicted by the Langmuir competitive model. With the

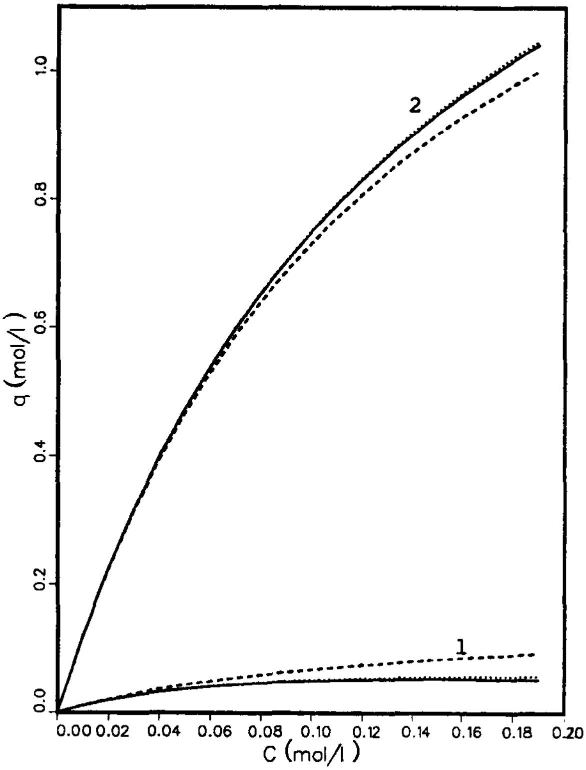
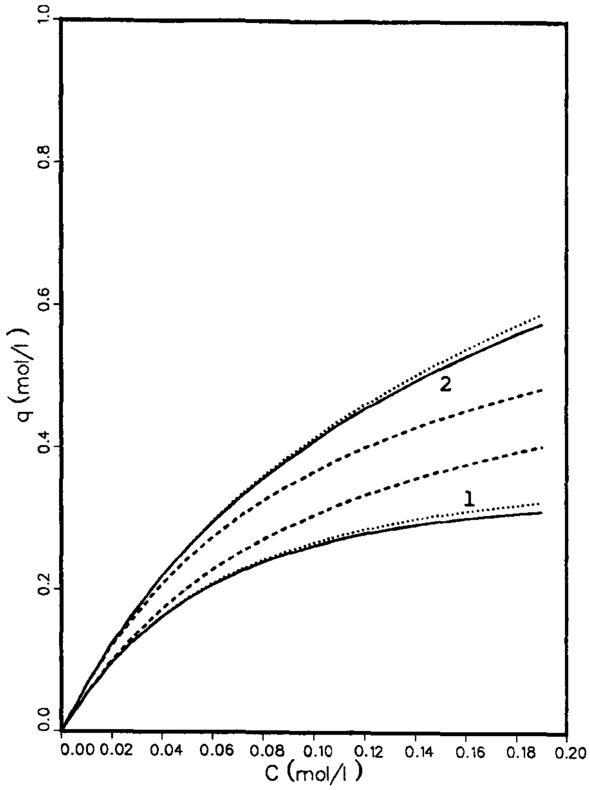


Fig. 6. Equilibrium isotherms. Comparison between the two-term (solid lines) and the three-term (dotted lines) expansions of the LeVan–Vermeulen isotherm and the Langmuir (dashed lines) competitive isotherm. Plots of (1) q_1 and (2) q_2 *versus* the total mobile phase concentration, $C = C_1 + C_2$. Experimental conditions: (I) column, column phase ratio $F = 0.25$; (II) isotherm, specific column saturation capacity $q_{s,1} = 1$ mmol/ml; $q_{s,2} = 2$ mmol/ml; $k'_{0,1} = 3$; $\alpha = k'_{0,2}/k'_{0,1} = 1.2$; $b_i = a_i/q_{s,i} = k_i/Fq_{s,i}$; (III) sample, feed composition, 1:9.

LeVan–Vermeulen model, the separation factor is not constant. It increases with increasing total concentration when the column saturation capacity of the first component is smaller than that of the second component. This can be seen in eqn. 9, where the correction term $\Delta_{1,2}$ is negative in this instance. Accordingly, the stationary phase concentration of the first component at equilibrium, q_1, is smaller with the LeVan–Vermeulen isotherm than with the Langmuir competitive isotherm and, conversely, q_2 calculated with the LeVan–Vermeulen isotherm is greater than that derived from the Langmuir competitive isotherm. The difference between the values predicted by the two isotherm equations increase with increasing mobile phase concentration.

Figs. 9–12 illustrate the influence of the composition of the feed on the individual elution band profiles of the two components at constant total sample size ($n_1 + n_2 = 0.166$ mmol) and with values of the specific saturation capacities of 1 and 2 mmol/ml for the first and second components, respectively. Because the column saturation



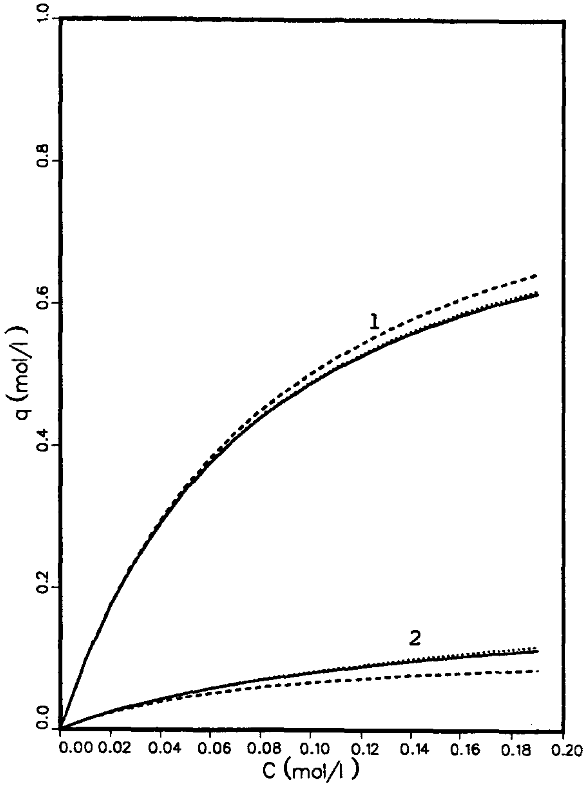
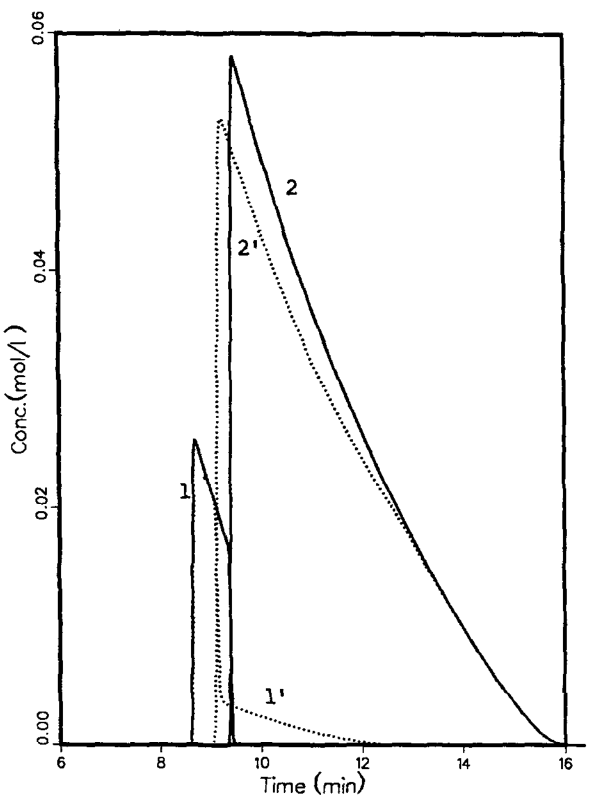


Fig. 7. Equilibrium isotherms. Same as Fig. 6. Experimental conditions as in Fig. 6, except feed composition = 1:1.

Fig. 8. Equilibrium isotherms. Same as Fig. 6. Experimental conditions as in Fig. 6, except feed composition = 9:1.



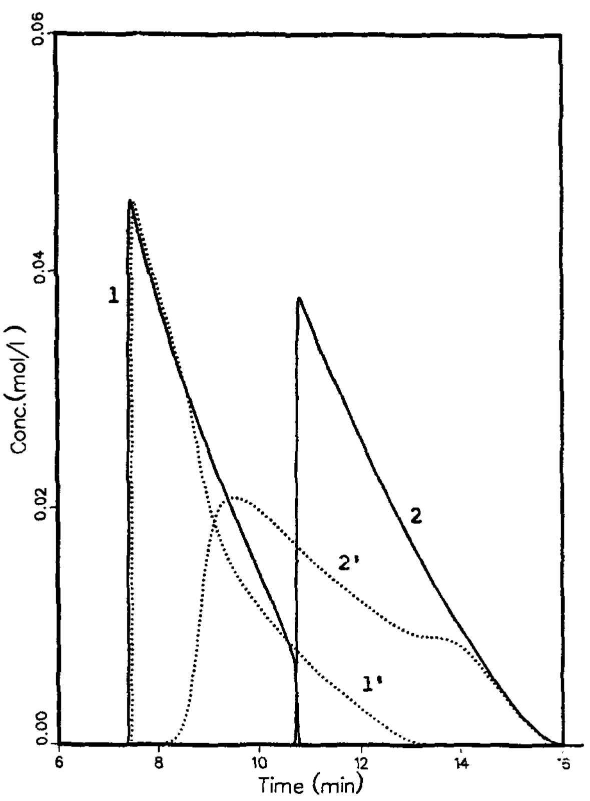
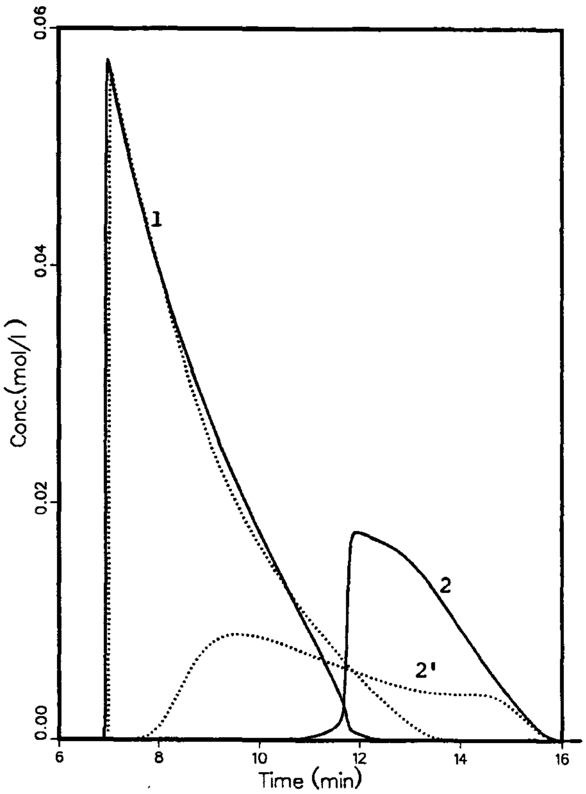


Fig. 9. Overloaded elution of a binary mixture. Influence of feed composition on the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 1, except feed composition = 1:9.

Fig. 10. Overloaded elution of a binary mixture. Influence of feed composition on the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 1, except feed composition = 1:1.



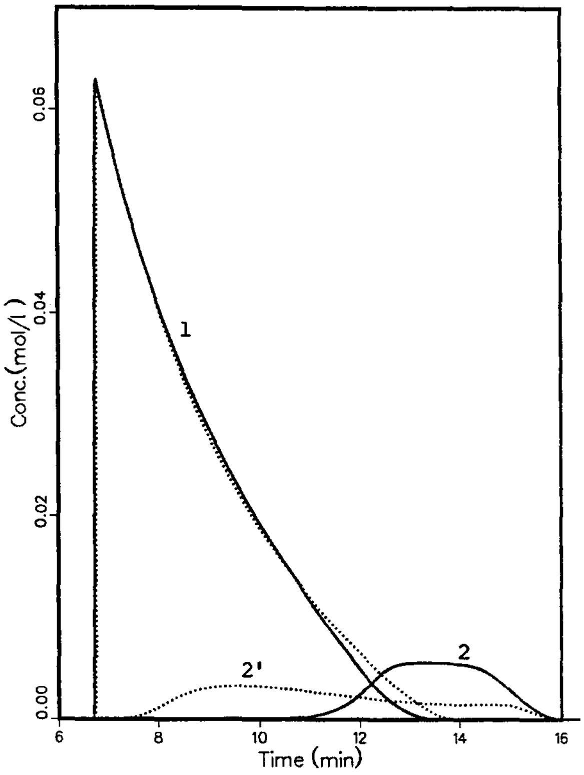


Fig. 11. Overloaded elution of a binary mixture. Influence of feed composition on the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 1, except feed composition = 3:1.

Fig. 12. Overloaded elution of a binary mixture. Influence of feed composition on the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 1, except feed composition = 9:1.

capacities for the two components are different, however, the total loading factor is not constant. As above (Figs. 1–5), the solid lines give the profiles calculated with the LeVan–Vermeulen isotherm and the dotted lines those calculated with the Langmuir competitive isotherm. The differences are profound, much larger than the relatively modest differences between the isotherms (Figs. 6–8) would lead one to expect. The chromatogram in Fig. 9 (feed composition = 1:9) is similar to that in Fig. 1 (feed composition = 1:3). The displacement effect is much enhanced compared with the prediction of the Langmuir competitive isotherm; the band profile of the second component is nearly identical with the profile obtained for the same amount of pure component; the separation is nearly total. A similar result is also obtained for the chromatogram in Fig. 10 (feed composition = 1:1). Again, the displacement effect is very strong and the separation is nearly total. The tag-along effect predicted on the basis of the use of the Langmuir competitive isotherm is absent.

As with the Langmuir isotherm, a further decrease in the feed concentration of the second component reduces the intensity of the displacement effect (Fig. 11, feed composition = 3:1) and eventually makes it vanish (Fig. 12, feed composition = 9:1). In contrast to what takes place with the Langmuir competitive isotherm, the separation calculated with the LeVan–Vermeulen isotherm remains satisfactory for a 3:1 mixture, in spite of the large sample size used, and even for a 9:1 mixture the recovery yields in preparative chromatography remain large. This is due to a reduced tailing of the first band and to a considerably depressed tag-along effect. Only a weak tag-along effect is seen in Fig. 11 for the profiles calculated with the LeVan–Vermeulen isotherm. The top of the second component band is flattened whereas its profile becomes wider and shorter than would be observed for the same amount of pure second component. Nevertheless, no concentration plateau is recorded at this feed composition. Even for a 9:1 feed composition (Fig. 12), the concentration plateau of the second component band (solid line) is narrow. The band is much taller and narrower than predicted by the Langmuir competitive isotherm, and it interferes to a much lesser degree with the first component band.

In summary, when the ratio of the column saturation capacities, $q_{s,1}/q_{s,2}$, is smaller than unity, the displacement effect is enhanced at all feed compositions, the tag-along effect is depressed and the separation between the two bands is markedly improved, allowing a large increase in the production rate, especially under recovery yield constraints.

Ratio of the column saturation capacities, $q_{s,1}/q_{s,2}$, greater than unity. In this case we have assumed $q_{s,1} = 4$ and $q_{s,2} = 2$. Figs. 13–15 show the competitive isotherms calculated using the two-term expansion (solid lines) and the three-term expansion (dotted lines) of the LeVan–Vermeulen isotherm and the Langmuir competitive model (dashed lines). In all instances, the equilibrium concentrations in the stationary phase are plotted *versus* the total mobile phase concentration, as in Figs. 6–8. As in the previous instance, there is little difference between the two- and the three-term expansions of the LeVan–Vermeulen isotherm, even for the 1:1 mixture (Fig. 14) for which the isotherms of the two components intersect.

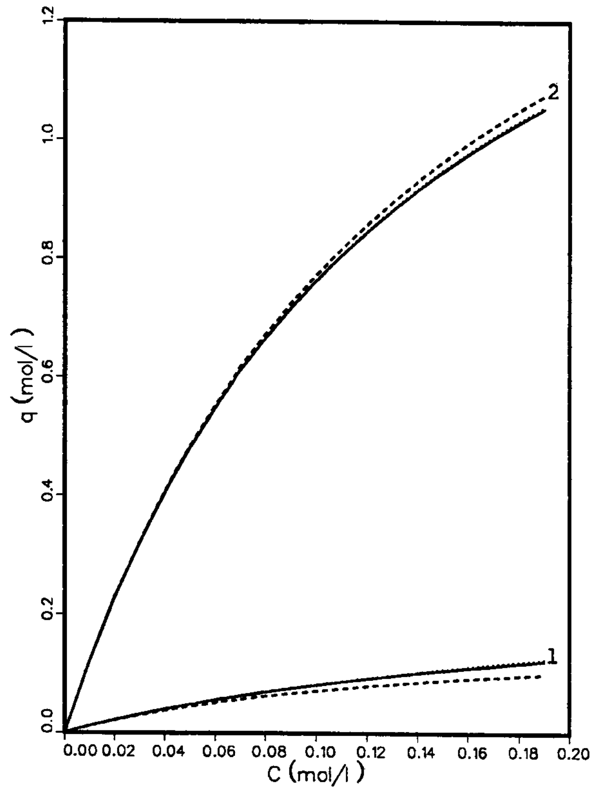
In contrast, there are marked differences between the LeVan–Vermeulen and the Langmuir competitive isotherms. As in this instance $\Delta_{1,2}$ is positive, the LeVan–Vermeulen isotherm predicts values of q_1 which are larger and values of q_2 which are smaller than those calculated by the Langmuir competitive isotherm. The first component appears to be more retained and the second component less retained with the LeVan–Vermeulen model than with the Langmuir model. In the three figures, the ratio q_2/q_1 remains constant for the Langmuir competitive isotherms, as was observed in the previous instance (Figs. 6–8, $q_{s,1}/q_{s,2} < 1$). The separation factor is constant with the Langmuir competitive model, whereas it is not with the LeVan–Vermeulen model; the separation factor may even become smaller than unity and the competitive isotherms intersect (Fig. 14). As a consequence of these effects, the calculated band profiles are very different, depending on which isotherm model is used.

Figs. 16–20 illustrate the influence of the feed composition on the individual band profiles. The five chromatograms have been calculated for the same total sample size ($n_1 + n_2 = 0.05$ mmol, 0.3 times the amount used for Figs. 9–12). The feed composition is changed from 1:9 (Fig. 16) to 9:1 (Fig. 20). When the relative concentration of the second component decreases, we always observe a progressive decrease in the intensity of the displacement effect and a correlative increase in the intensity of the tag-along effect. This was already noted with the Langmuir competitive isotherm [10]. This was also observed in the previous section (Figs. 9–12). This is seen again in Figs. 16–20. However, the displacement effect was extremely strong when $q_{s,1}/q_{s,2} = 0.5$ and disappeared only at very low values of C_2/C_1, whereas the tag-along effect was weak in the best cases. The situation is reversed in the present case.

The displacement effect is already weak for the 1:9 mixture (Fig. 16). It becomes negligible as soon as the concentration of the first component exceeds that of the second (Figs. 19 and 20). In all chromatograms, the first component band tails severely beyond the front of the second component band. In contrast, the tag-along effect is important for all values of the relative feed composition. It appears noticeable in Fig. 16 (feed composition = 1:9), whereas it is not seen on the profiles calculated with the Langmuir competitive isotherm in Figs. 16–18. The chromatograms derived from the Langmuir competitive model in Figs. 16–20 correspond to nearly touching bands. In contrast, the band interference is important for the chromatograms calculated with the LeVan–Vermeulen isotherm. In Figs. 18–20 the profile of the second component calculated with the LeVan–Vermeulen isotherm exhibits two maxima, especially noticeable in Fig. 19 (feed composition = 3:1).

Figs. 21–24 show the band profiles calculated for a larger sample size ($n_1 + n_2 =$ 0.166 mmol, the same amount as for Figs. 1–5 and 9–12). The values used for the feed composition are 1:9 (Fig. 21), 1:1 (Fig. 22), 3:1 (Fig. 23) and 9:1 (Fig. 24). The chromatogram for a feed composition of 1:3 was shown in Fig. 5. The effects of the sample size and of the nature of the isotherm used for the calculations are striking. With the Langmuir competitive isotherm, increasing the sample size from 0.05 to 0.166 mmol changes the chromatogram from a touching bands to an overlapping bands case. The intensity of both the displacement and tag-along effects increases with increasing sample size, whereas the resolution between the two bands decreases [10].

With the LeVan–Vermeulen isotherms, the influence of the sample size on the chromatograms is more important. For all feed compositions, the two band fronts are eluted simultaneously. The band profile of the first component exhibits two maxima. The first is very sharp and is eluted at the common front, coincidental with the first band front as calculated with the Langmuir competitive isotherm. The second maximum of the first band is eluted well after the maximum of the second component band. The rear profile of the second band is depressed by the presence of the first band



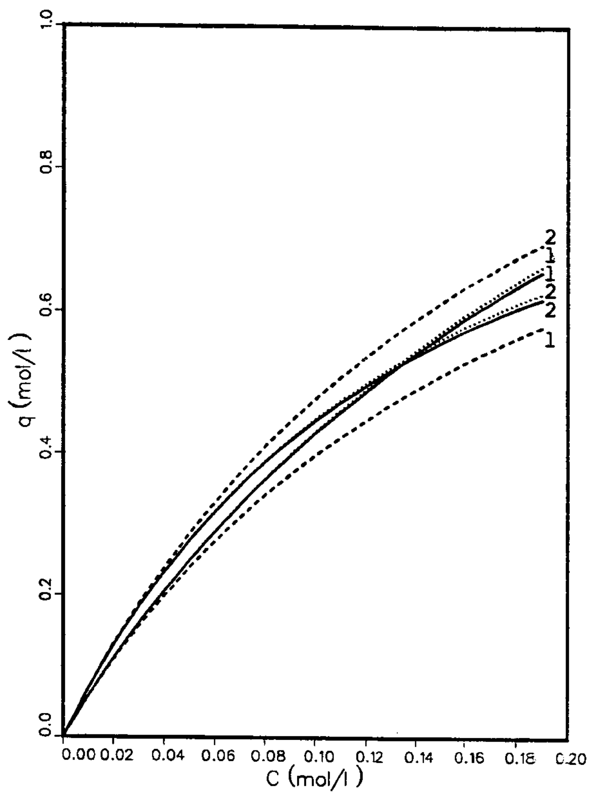
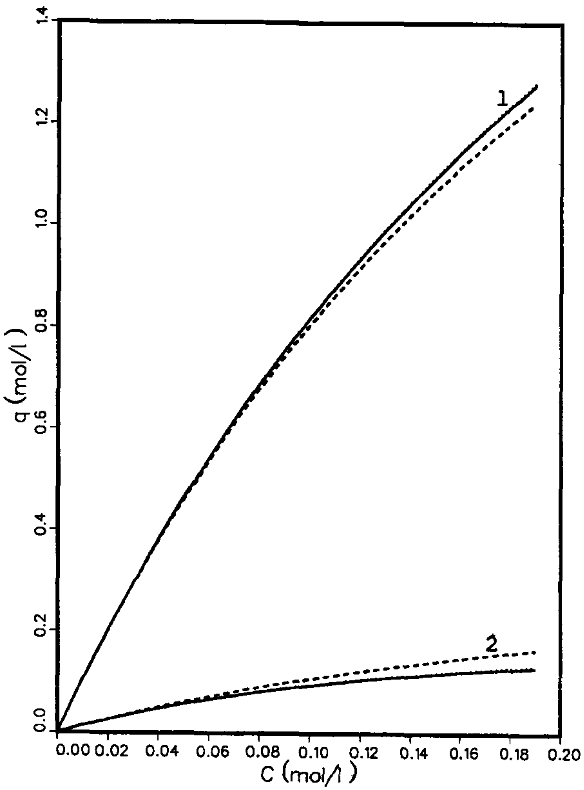


Fig. 13. Equilibrium isotherms. Comparison between the two-term (solid lines) and the three-term (dotted lines) expansion of the LeVan–Vermeulen isotherm and the Langmuir (dashed lines) competitive isotherm. Plots of (1) q_1 and (2) q_2 *versus* the total mobile phase concentration, $C = C_1 + C_2$. Experimental conditions as in Fig. 6, except $q_{s,1} = 4$ mmol/ml.

Fig. 14. Equilibrium isotherms. Same as Figs. 6 and 13. Experimental conditions as in Fig. 6, except $q_{s,1} = 4$ mmol/ml and feed composition = 1:1.



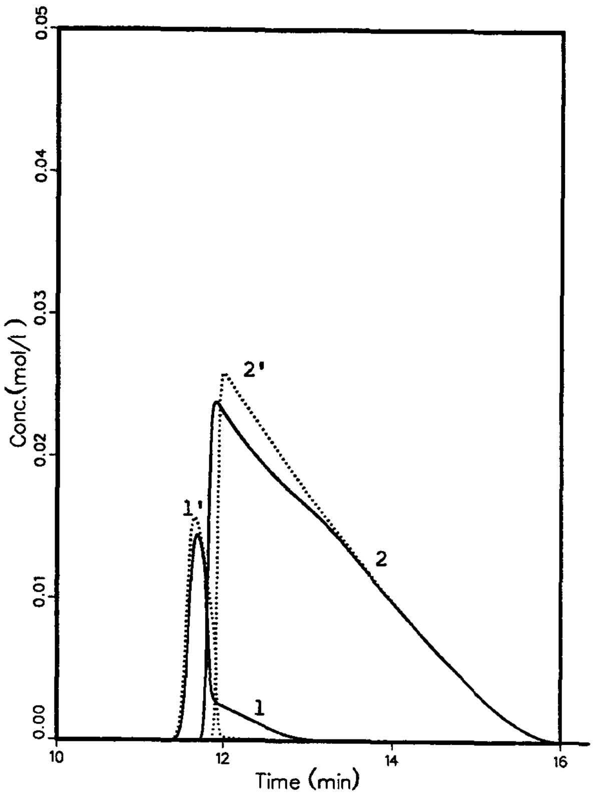


Fig. 15. Equilibrium isotherms. Same as Figs. 6 and 13. Experimental conditions as in Fig. 6, except $q_{s,1}$ = 4 mmol/ml and feed composition = 9:1.

Fig. 16. Overloaded elution of a binary mixture. Influence of feed composition on the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 1, except $q_{s,1}$ = 4 mmol/ml, sample size = 0.05 mmol and feed composition = 1:9.

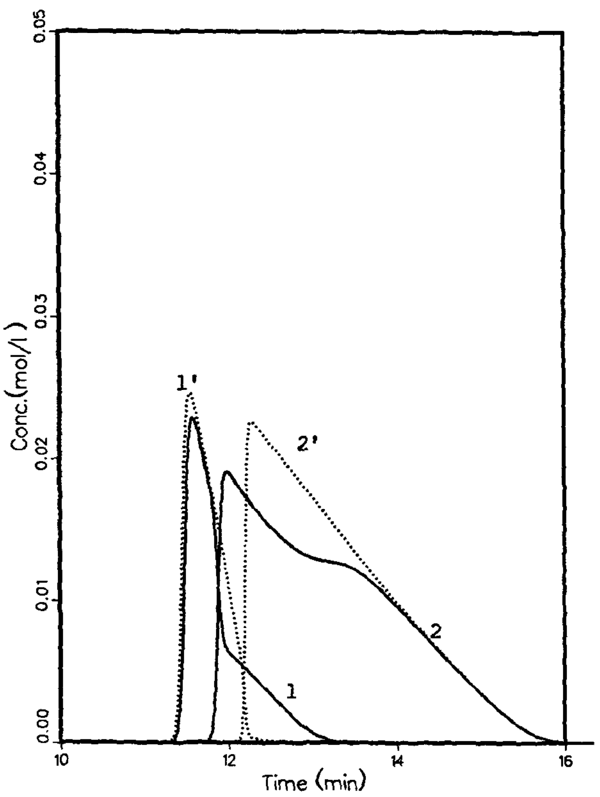


Fig. 17. Overloaded elution of a binary mixture. Influence of feed composition on the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 16, except feed composition = 1:3.

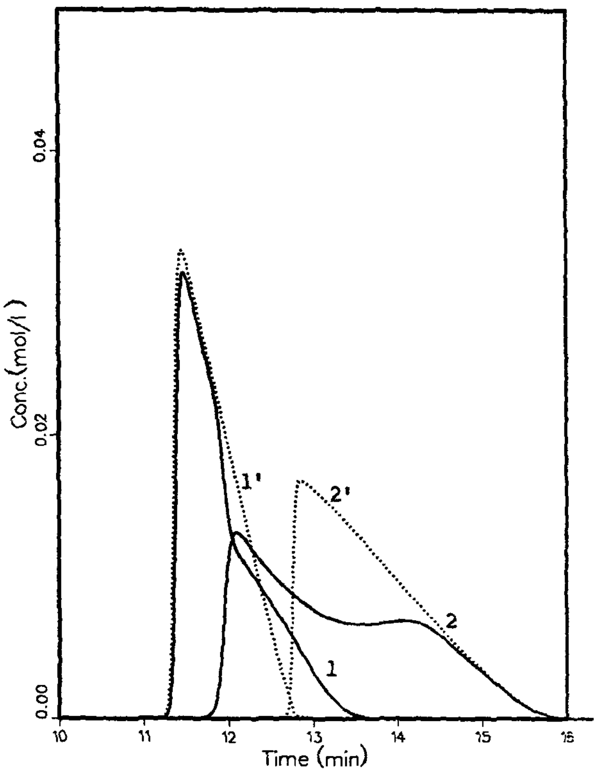


Fig. 18. Overloaded elution of a binary mixture. Influence of feed composition on the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 16, except feed composition = 1:1.

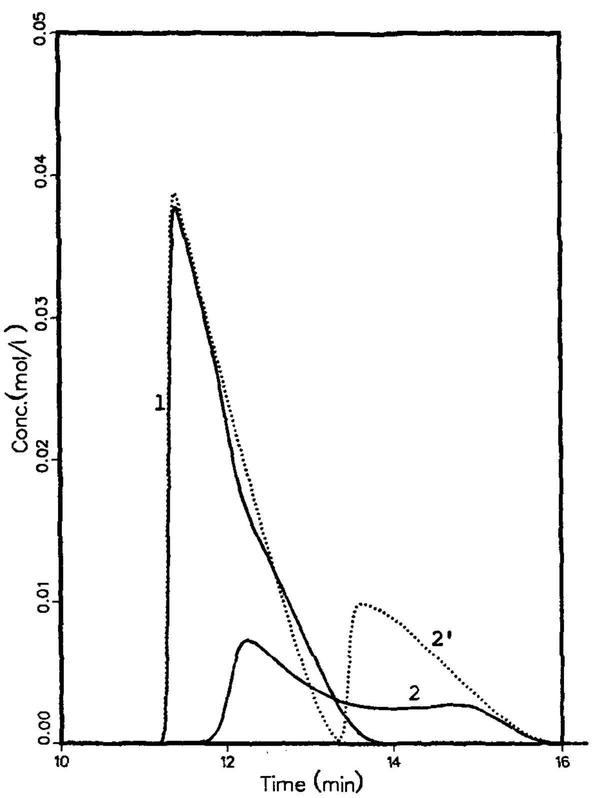


Fig. 19. Overloaded elution of a binary mixture. Influence of feed composition on the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 16, except feed composition = 3:1.

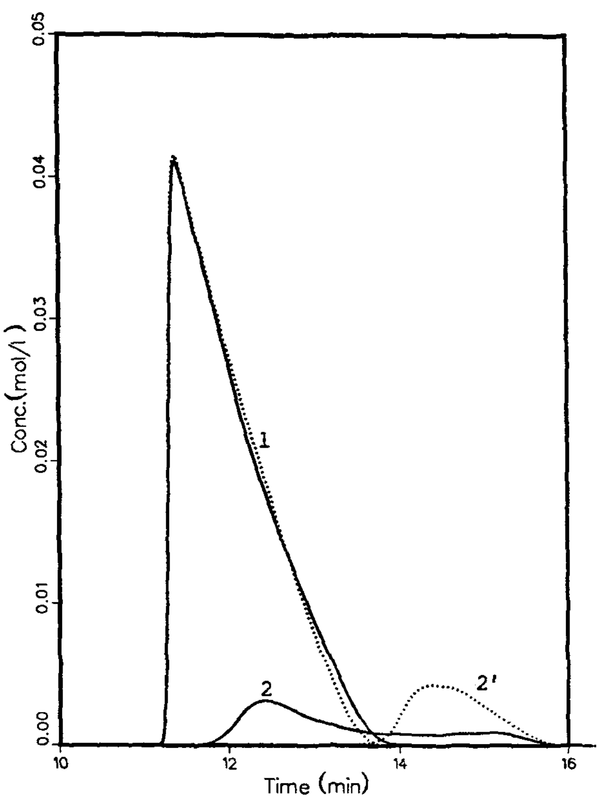
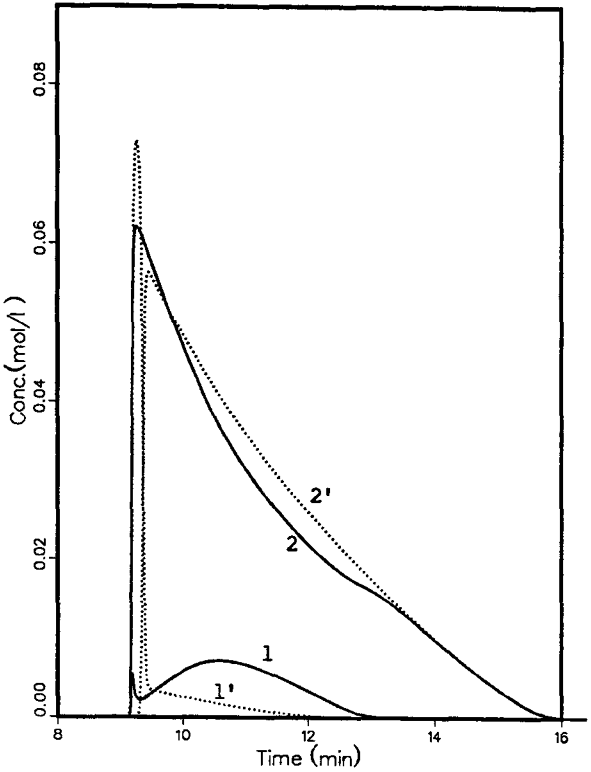


Fig. 20. Overloaded elution of a binary mixture. Influence of feed composition on the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 16, except feed composition = 9:1.



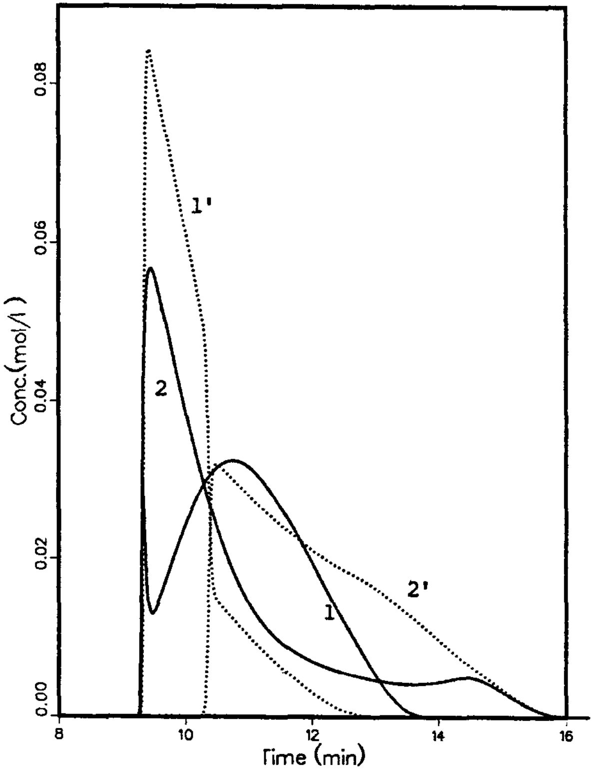
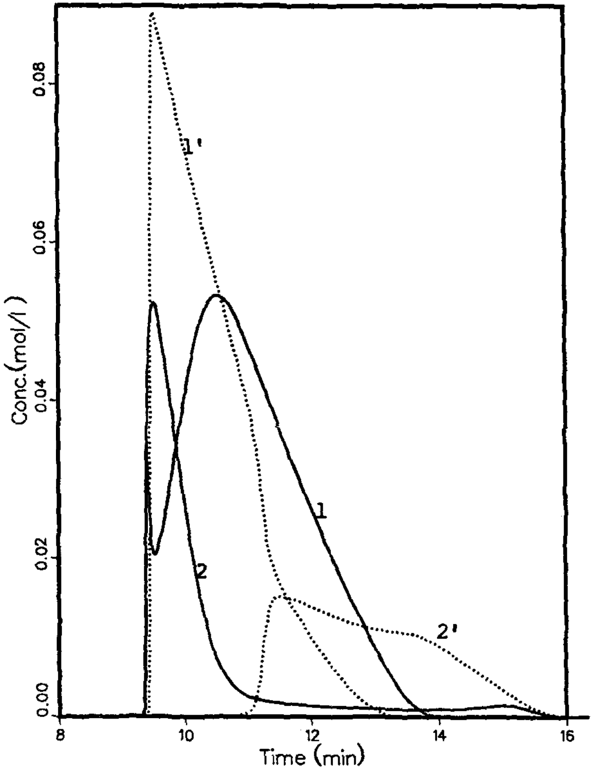


Fig. 21. Overloaded elution of a binary mixture. Influence of feed composition on the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 16, except sample size = 0.166 mmol.

Fig. 22. Overloaded elution of a binary mixture. Influence of feed composition on the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 21, except feed composition = 1:1.



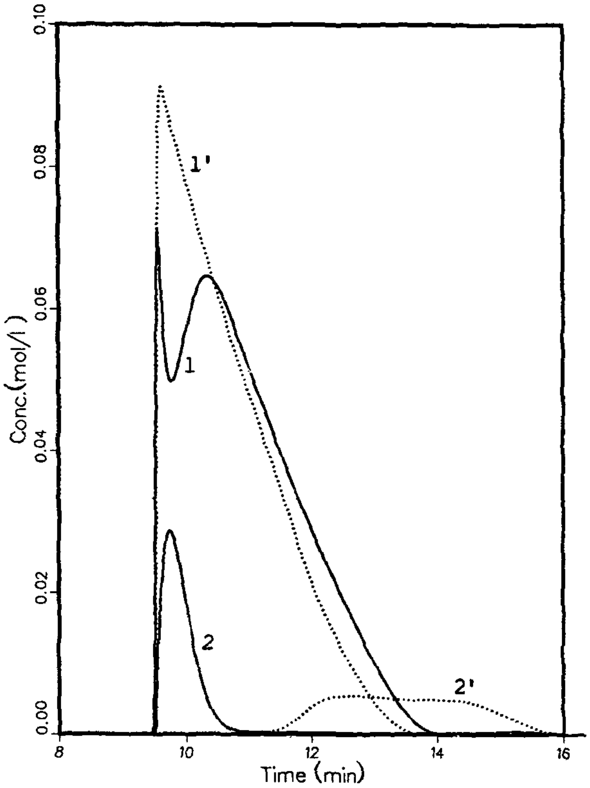
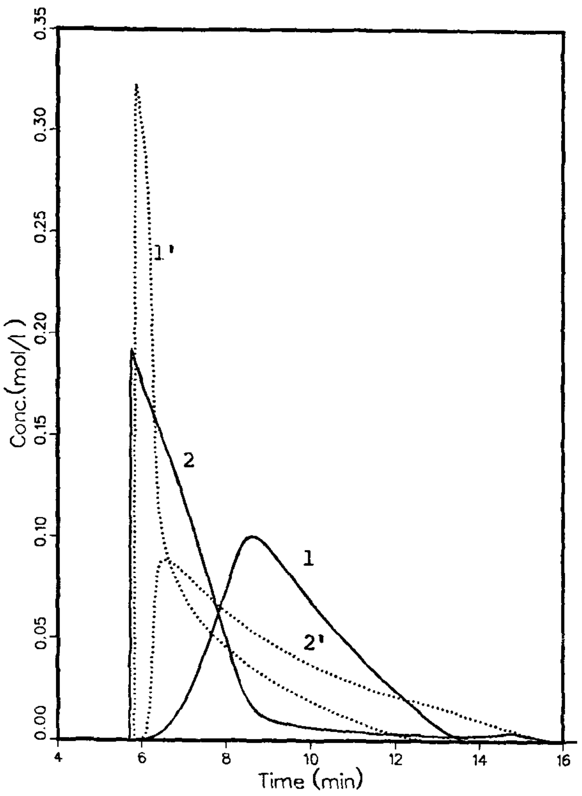


Fig. 23. Overloaded elution of a binary mixture. Influence of feed composition on the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 21, except feed composition = 3:1.

Fig. 24. Overloaded elution of a binary mixture. Influence of feed composition on the band profiles calculated using the two-term expansion of the LeVan–Vermeulen isotherm (eqns. 4—7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 21, except feed composition = 9:1.



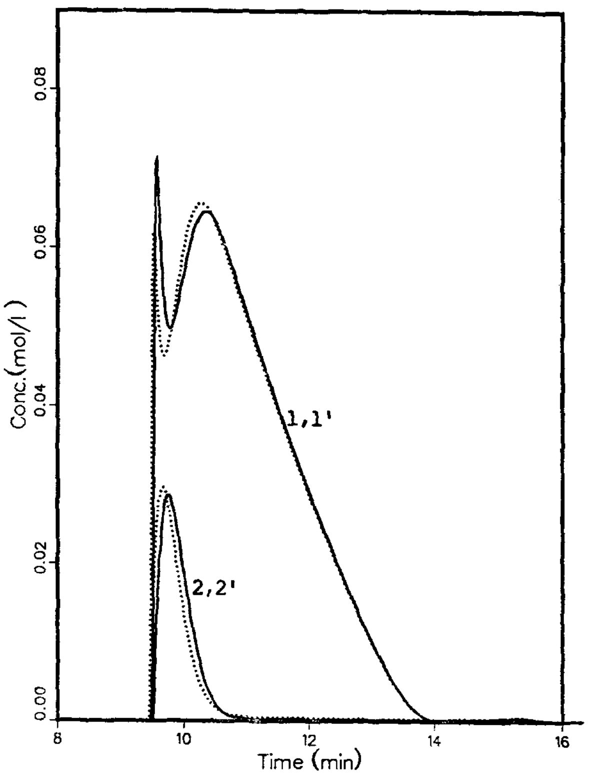


Fig. 25. Overloaded elution of a binary mixture. *Influence of feed composition on the band profiles calculated using the two-term expansion of the* LeVan–Vermeulen isotherm (eqns. 4–7, solid lines) and the conventional Langmuir competitive isotherm (eqn. 3b, dotted lines). Experimental conditions as in Fig. 1, except $q_{s,1}$ = 4 mmol/ml, sample size = 0.664 mmol and feed composition = 1:1 (also, same conditions as in Fig. 18, except sample size). The Langmuir isotherm elution order is the reverse of the order predicted by the LeVan–Vermeulen isotherm.

Fig. 26. Overloaded elution of a binary mixture. Comparison between the band profiles calculated using the two-term expansion (eqns. 4–7, solid lines) and the three-term expansion of the LeVan–Vermeulen isotherm (eqns. 8–12, dotted lines). Experimental conditions as in Fig. 24.

(see Figs. 5, 21 and 22) and ends in a long tail (Figs. 22 and 23). This same tail exists in the second-component profile in the chromatogram in Fig. 24, but is barely visible.

Compared with the chromatograms in Figs. 16–20, those in Figs. 5 and 21–24 are intermediates in the reversal of the elution order which takes place when the sample size increases. This is illustrated by Fig. 25, which shows the individual profiles calculated for a sample size of 0.664 mmol (feed composition = 1:1). Even in this instance, however, the second-component band exhibits a long, low tail which ends only at the limiting retention time of the second-component under linear conditions. In all instances, the LeVan–Vermeulen iostherm predicts a separation between the two bands which is much worse than that predicted by the Langmuir competitive isotherm. It is not possible to recover any pure fraction of the first-component under any of the conditions simulated in Figs. 5 and 21–25. The amounts of 98% pure first- or second-component which can be recovered with these chromatograms is very low, much lower than with the chromatograms obtained with the Langmuir competitive isotherms.

Fig. 25 demonstrates that the LeVan–Vermeulen isotherm predicts the inversion of the elution order of the components of a binary mixture at large sample sizes when their equilibrium isotherms intersect. A similar result has been described previously in displacement chromatography [27]. The elution order of the two-component bands in the isotachic train depends on the displacer concentration. The Langmuir competitive isotherm model is unable to explain this effect.

Finally, Fig. 26 compares the chromatograms calculated with the two-term (solid lines) and the three-term (dotted lines) expansions of the LeVan–Vermeulen isotherm. Although the sample size is large (0.166 mmol), the differences between these chromatograms are hardly significant. This demonstrates that the LeVan–Vermeulen series converges very rapidly.

CONCLUSIONS

The LeVan–Vermeulen isotherm offers several practical advantages over the Langmuir competitive isotherm, in addition to the theoretical advantage of being consistent with the Gibbs adsorption isotherm equation. In agreement with experimental results, it predicts an enhanced displacement effect, a decreased tag-along effect, a better separation and a higher production rate when the column saturation capacity of the first-component is smaller than that of the second. Conversely, it also predicts a reduced displacement effect, a larger tag-along effect and a degraded separation, with considerable band interference, in the opposite case, when the column saturation capacity is larger for the first-component than for the second.

The reversal of the elution order of *cis*- and *trans*-androsterone with increasing sample size has been previously observed [28]. It has remained unexplained so far and is in contradiction with the Langmuir competitive model. It is accounted for by the LeVan–Vermeulen isotherm. By the same token, it would also explain the unexpected difficulties reported in the separation of some mixtures by preparative chromatography, where the recovery of pure fractions was impossible. This phenomenon is the elution equivalent of the difficulties encountered in the development of separations by displacement chromatography in the case of compounds exhibiting the isotherm intersection effect [27].

In spite of these advantages, the LeVan–Vermeulen isotherm is still unable to permit the quantitative prediction of the individual band profiles for multi-component samples in chromatography. Like the Langmuir isotherm, this model assumed ideal behavior of the mobile and stationary phases. These assumptions restrict the validity of the model to cases where the mobile phase concentrations of the compounds studied are low, of the order of a few millimolar.

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