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Analysis of isotachic patterns in displacement chromatography

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ABSTRACT

Most previous theoretical treatments of displacement chromatography have been confined to systems that follow the competitive Langmuir isotherm. With the assumption of such idealized multi-component adsorption behavior, in a sufficiently long column the final outcome of the process is always expected to be an isotachic displacement train having a series of adjacent separated bands of increasing concentration. Several recent reports, however, suggest that no such train forms when the single-component isotherms of the separands cross. In order to examine the possibility of separation under such conditions, the stability of the isotachic pattern is analyzed and criteria for displacement and for stability of the resulting boundaries are established. The approach requires the knowledge of the multi-component isotherm that governs the adsorption of the separands. As the competitive Langmuir isotherm completely fails to represent such behavior, the pertinent multi-component isotherms are generated from Langmuir single-component isotherms within the framework of the ideal adsorbed solution model. The results obtained with such a multi-component isotherm in binary separations show that three operating regions in displacement chromatography can be identified when the single-component isotherms of the separands cross. In one region at sufficiently low concentrations, the two components separate and appear in the same order as in linear chromatography. In a second region at sufficiently high concentrations, the bands are predicted to separate but appear in the reverse order. In the third region at intermediate concentrations, complete separation is not possible, and the resulting isotachic pattern contains a mixed zone. The stability analysis presented here facilitates the prediction of the outcome of displacement without the need for arduous computation; it is fairly general and may be applied to systems that follow other multi-component isotherms.

INTRODUCTION

Displacement is one of the three operational modes of chromatography identified by Tiselius [1,2]. In it, a feed mixture is followed into the column by a solution containing a substance called the displacer, which binds so strongly to the stationary phase that it drives the feed components ahead of its front. Under favorable conditions, the components eventually separate into adjacent bands that all move at the velocity of the displacer front, thus forming an isotachic pattern known as the displacement train. Displacement is a *non-linear* chromatographic method; the displacer and separand concentrations have to be high enough that the equilibrium relationship governing the simultaneous adsorption of the components, *i.e.*, the multi-component adsorption isotherm, is both competitive and *non-linear*. As a consequence,

migrating molecules interfere strongly with one another as they traverse the column and, under appropriate conditions, the interference facilitates separation. This is in contrast with *linear* elution chromatography, most commonly employed in analytical practice, where concentrations are kept low so that adsorption isotherms are *linear* and components migrate through the column without interference.

The rudiments of the displacement process were already recognized by Tswett in 1906, but it was not until the Tiselius' formal classification and the pioneering work of Glükauf [3] that its principles were placed on a firm footing. Glükauf's theoretical approach was quite general, but, for the sake of mathematical simplicity, he used only the competitive Langmuir isotherm. The subsequent treatment of Helfferich and Klein [4] also hinged upon the use of this isotherm. As a result, the prevalent understanding of non-linear chromatography in general and displacement chromatography in particular was, until recently, restricted to systems that would obey the competitive Langmuirian model.

However, the competitive Langmuir isotherm model is valid only when the saturation capacities of the stationary phase for all the various adsorbing components are identical, and thus it has very limited practical relevance. Another characteristic feature of this model is that the selectivity between any pair of components is constant, independent of concentration. As a consequence, the requirements for a displacement separation would merely be that the displacer be retained more strongly than the feed components and that its concentration be above a certain minimum value [3]. Then, in the absence of axial dispersion and given a suitably long column, a displacement train would eventually be formed, with the components fully separated and arranged in order of increasing initial slopes of their respective single-component isotherms.

Early success [5,6] and the implicit assurance from theory that separation would be achieved upon fulfilling such simple criteria encouraged experimental efforts in the 1940s and 1950s. Displacement chromatography was used for a brief period to separate a variety of compounds, from petroleum products to rare earths and biochemicals (see refs. 7 and 8 for reviews). Thereafter it was overshadowed by the development of linear chromatography and, after a hiatus of more than 20 years, was revived in the early 1980s [9–11]. The efficient columns and sorbents of today's high-performance era have made displacement chromatography practicable, and it has established itself in a number of preparative applications, including the purification of antibiotics, peptides and even proteins (see refs. 8 and 12 for reviews).

On the other hand, when the method has failed, researchers have been perplexed and frustrated. Recent experimental studies, both from this and from other laboratories, have shown that displacement is likely to be unsuccessful if the single-component isotherms cross one another when drawn on the same plane [13–16]. In an adsorption process it is generally true that larger molecules bind more strongly to the sorbent than smaller ones and their individual isotherms therefore have a larger initial slope. However, because the larger molecules may occupy more space on the surface of the sorbent they would be expected to have lower saturation capacities, in molar terms. Isotherms of larger and smaller molecules would therefore often cross. Indeed, from these considerations, crossing isotherms are more likely to be the rule than the exception, and a thorough investigation is necesary to gain insight into the mechanisms that dictate the sucess or failure of displacement processes under such circumstances.

In many instances, the isotherms of the components often individually fit the Langmuir single-component model. However, because of the different saturation capacities of the components, the competitive, or multi-component Langmuir isotherm model is not thermodynamically consistent [17–19] and, even when forced into service despite this limitation, cannot account for the observed behavior. This was noticed in an early qualitatiative study by Tiselius's group [20], where it was found that the selectivity between a feed component and the displacer may actually reach unity and even undergo a reversal, leading to the loss of a sharp front between displacer and feed component.

Evidently, adsorption isotherms other than the competitive Langmuir model are needed to describe such behavior. One means of generating thermodynamically consistent multi-component isotherms from single-component data is provided by the ideal adsorbed solution (IAS) method, introduced first for gas–solid adsorption [21] and later extended to liquid systems [22]. Using the IAS approach, it has been shown that selectivity inversion, *i.e.*, the reversal in the order of band appearance on going from low to high concentration, may occur in systems where the respective single-component isotherms cross [23]. The treatment of Frey [24], which is based on considerations of free energy consumption at concentration discontinuities within the column and requires information only about single-but not multi-component isotherms, also implies selectivity reversal in such systems. What is not clear from either study, however, is whether complete separation always occurs in the final pattern, or if a mixed band, indicative of an adsorption azeotrope, or "adsorbotrope", forms instead.

Here we tackle afresh the issue of selectivity reversal and the formation of azeotropes by analyzing the stability of the displacement train. The approach is general and may be applied also to other multi-component isotherm formalisms. The Langmuir and IAS multi-component isotherms are compared for their ability to predict the observed behavior and their advantages and shortcomings are exposed.

THEORY

In developing our theory, we shall assume that conditions of "ideal" chromatography prevail, *i.e.*, there is no axial dispersion and instantaneous equilibrium is reached everywhere in the column. This allows us to focus on the fundamental characteristic that distinguishes non-linear processes, such as displacement, from linear chromatography, *viz.*, the effect of the competitive adsorption behavior. This assumption has been used in the past and found to provide respectable approximations to observed behavior in non-linear systems [3].

For brevity, single-component adsorption isotherms will be referred to either as "SC" or as "parent" isotherms, and multi-component isotherms as "MC" isotherms. As we are concerned for the most part with liquid chromatography, it is understood that the term "SC isotherm" alludes to the adsorption of a component from a solvent that by definition is assumed to be absent from the adsorbed phase [25,26]. We shall restrict our attention to SC isotherms that can be fitted to the one-component Langmuir model, given for a component i by [27]

$$q_i = \frac{\lambda_i b_i c_i}{1 + b_i c_i} \tag{1}$$

where q_i and c_i are the concentrations of i in the stationary and and mobile phases, respectively, and λ_i and b_i are the pertinent isotherm parameters; λ_i represents the largest possible value of q_i, and is known as the saturation capacity of the stationary phase for component i. The initial slope of this isotherm is $a_i = \lambda_i b_i$. In liquid chromatography, SC isotherms of the separands and displacer can often be fitted successfully to eqn. 1 [28–30]. We use such isotherms for the sake of simplicity; the results of our treatment can be extended to many cases where the SC isotherms are not so well behaved. However, additional factors must be taken into account when the isotherms have features such as inflection points, and these are not addressed here.

We have already referred to the competitive Langmuir model, which is an example of a multi-component or MC isotherm which is constructed to describe the simultaneous adsorption of several components. In general, such an isotherm must be obtained by fitting an appropriate function to equilibrium adsorption data over the composition range of interest. This is a tedious task, however, and only very few such measurements have been made in liquid chromatographic systems [31,32]. For shortage of experimental data multi-component adsorption behavior is usually described by a formalism that uses parameters derived from SC isotherm data. In the past, the competitive Langmuir equation has been widely used in the past for this purpose and is given by [33]

$$q_i = \frac{\lambda_i b_i c_i}{1 + \sum_{j=1}^{n} b_j c_j} \qquad i = 1, 2, \ldots, n \tag{2}$$

where n is the total number of adsorbed components. In eqn. 2, as with all MC isotherms, the stationary phase concentration of a component i is a function of the mobile phase concentrations of all the components the system and it can be represented by an n-dimensional surface in an $(n + 1)$-dimensional space.

One remarkable feature of the competitive Langmuir model is that it predicts a constant selectivity for any two components, regardless of their respective concentrations or that of any additional components. The selectivity, or separation factor, for two species A and B, α_{BA}, is defined as the ratio $q_B c_A / q_A c_B$. Constant selectivity is what makes the competitive Langmuir isotherm attractive for mathematical treatment, but is an artifact which narrowly restricts the applicability of the model.

A property that is common to most MC isotherms is that the isotherm of one component, when measured in the presence of a fixed concentration of another, is "suppressed" compared with its SC isotherm, *i.e.*, it has a lower initial slope and possibly also a lower saturation level as well. This suppression has important consequences in displacement, as we shall see later.

The competitive Langmuir model is valid only in the case where the SC saturation capacities for all n components are equal, *i.e.*, when

$$\lambda_1 = \ldots = \lambda_i = \ldots = \lambda_n = \lambda \tag{3}$$

Nevertheless, because of its mathematical simplicity, eqn. 2 has often been used even when eqn. 3 does not hold. In such cases, however, eqn. 2 fails to satisfy the Gibbs adsorption equation and therefore violates the second law of thermodynamics [17–

19]. Consequently, any predictions about non-linear chromatography obtained by applying eqn. 2 in this manner are of dubious value.

With these preliminary remarks, we now turn our attention to displacement chromatography. The salient feature of displacement, according to the Tiselian concept [1], is that in the process the various feed components separate into a series of successive bands, followed by the displacer, all moving at the same velocity. When the isotachic conditions is achieved, the characteristic velocity of the train is the species velocity of the displacer, u_D, given by [4]

$$u_D = \frac{u_0}{1 + \phi\dfrac{q_D^*}{c_D^*}} \tag{4}$$

where u_0 is the velocity of the bulk mobile phase, q_D^* and c_D^* are the equilibrium concentrations of the displacer in the stationary and mobile phases, respectively, and ϕ is the phase ratio. Under isotachic conditions, the species velocities of all the pure components, A, B, etc., in the displacement train are identical, so that

$$\frac{q_A^*}{c_A^*} = \frac{q_B^*}{c_B^*} = \ldots = \frac{q_D^*}{c_D^*} \equiv \Delta \tag{5}$$

As each band contains a single feed component, their concentrations in the displacement train are determined graphically from the points at which the respective single-component isotherms intersect the so-called "operating line" having slope Δ and intercept zero. It follows that in order for a species to be part of the displacement train, its single-component isotherm must not lie wholly below the operating line. This is Glükauf's condition for displacement [3].

For predicting behavior in displacement chromatography, one consequence of using the competitive Langmuir model given by eqn. 2 is that Glükauf's condition is sufficient to ensure a successful displacement separation. Thus, if the system were to follow the Langmuir MC isotherm, the ultimate outcome of a displacement run can be completely determined from the SC isotherms and the operating line, according to the picture described above.

Whereas this beguilingly simple construction seems wholly adequate in many instances [8,9,34], it appears to break down when the parent isotherms of the separands cross one another. Experimental results under such conditions show only partial, or no, separation even when Glükauf's conditions is met [14–16].

Conditions for establishment of the displacement train

Evidently, in the case of crossing SC isotherms, Glükauf's condition is insufficient, and the model with the Langmuir MC isotherm fails. Consequently, another MC isotherm function is required and new conditions for displacement must be formulated. First, we intend here to derive such conditions from an analysis of the stability of the displacement train; an appropriate MC isotherm is discussed later. The stability analysis is fairly general and applicable to most MC isotherms generated

from monotonically concave downward SC isotherms which have no inflection points. Extension to other more complex SC isotherm shapes may be possible but requires further investigation. The analysis is prefaced with the following comments.

In an ideal chromatographic system with concave downward parent isotherms, as long as Glükauf's conditions is met and an appropriate displacer is chosen, all displacement processes will, in a column of sufficient length, attain the isotachic state. This happens because Glükauf's condition ensures that the individual feed components would, on their own, move slower than the displacer. However, the displacer does not allow any feed components behind its front, and so forces the components to move at its velocity; any differences in local velocity of the feed components eventually disppear. (It suffices for present purposes that the displacer be one whose isotherm completely overlies that of the feed components; a more general idea of an "appropriate" displacer will emerge from the following discussion.) In the terminology of Helfferich and Klein [4], the train reaches a "coherent" state, *i.e.*, all concentration discontinuities in the system propagate at a constant velocity, and the velocities of the bands on either side of these boundaries meet the coherence conditions. In the following discussion it will be assumed that the coherence and Glükauf conditions, together termed the "zeroth" displacement conditions, are satisfied.

Stability of the displacement train

The desired outcome of a displacement experiment is the completely separated coherent pattern predicted by the Tiselian model. However, as seen experimentally in the case of crossing isotherms, it does not appear that this state is always achieved. One may then ask whether there are other possible coherent states and, if so, which of them is the likely result in a given displacement run? The answer to this question will be sought here by carrying out "Gedanken experiments" to examine the stability of the Tiselian train. If the train is found to be stable to small perturbations, there exists by implication a driving force that propels the system towards and maintains it in the separated state. This is not to say that such stability guarantees the formation of the separated state from every previously mixed state, but that there is at least a pathway towards separation from the perturbed state. If the train is not stable, such a driving force is absent and the separation cannot proceed to completion, so that some alternative coherent state containing mixed bands may result.

Consider a displacement train with a pair of successive bands of feed components A and B which are separated by a sharp boundary. The respective concentrations of the pure bands are c_A^* and c_B^* as dictated by the operating line given by eqn. 5. In the first "Gedanken experiment", imagine that a trace amount of the leading component, A, is brought into the domain of the trailing component B without noticeably changing the concentration of either band. For the system to return to the sharply separated state, the velocity of that trace of A must be greater than the characteristic velocity of the displacement train.

The velocity of A under these conditions is given by

$$(u_A)^0_{c_B = c_B^*} = \frac{u_0}{1 + \phi \left(\dfrac{q_A}{c_A} \right)^0_{c_B = c_B^*}} \tag{6}$$

where the superscript 0 and the subscript $c_B = c_B^*$ indicates that the quantities are evaluated as $c_A \to 0$ and at $c_B = c_B^*$. For the system to be stable to the perturbation, it therefore follows that

$$\left(\frac{q_A}{c_A}\right)^0_{c_B = c_B^*} < \Delta \tag{7}$$

where Δ is the ratio q_B^*/c_B^* or q_A^*/c_A^* as determined by the operating line (see eqn. 5).

In a second "Gedanken experiment", let us consider that a trace amount of the trailing component B encroaches into the domain of the leading component A. Following an argument similar to that above the condition for stability in this case is

$$\left(\frac{q_B}{c_B}\right)^0_{c_A = c_A^*} > \Delta \tag{8}$$

Eqns. 7 and 8 will be termed the first and second stability conditions, respectively. Note that in the eqns. 7 and 8, c_A^* and c_B^* depend on Δ.

When both stability conditions are satisfied the boundary between A and B is stable to small perturbations. Unlike Glükauf's condition which is determined solely from the parent single-component isotherms, the terms $(q_A/c_A)^0_{c_B = c_B^*}$ and $(q_B/c_B)^0_{c_A = c_A^*}$ in the stability conditions expressed by eqns. 7 and 8 depend on the multi-component isotherm that describes the simultaneous adsorption of the components. As we shall see later, the stability conditions will be used to determine the result of a displacement run. It ought to have been obvious that the outcome should depend on the MC isotherm, and not just the SC isotherms. In the past, however, this fact has been clouded by the employment of the competitive Langmuir isotherm because only this MC formalism allows the final pattern to be determined from the SC isotherms alone.

A closer examination shows that the first stability condition, eqn. 7, is an affirmation of the driving force for displacement, *i.e.*, the trailing component, B, must suppress the isotherm of the leading component, A, sufficiently so that it is never allowed to fall behind. The second condition, eqn. 8, essentially ensures that the front of B is self-sharpening. In the absence of the leading component the front of B would self-sharpen naturally because of its concave downward isotherm [4]. Since as a rule A also suppresses the isotherm of B, the condition assures that the self-sharpening effect is still operative.

Whereas an SC isotherm is a line on a two-dimensional plot, an MC isotherm of a binary mixture, as mentioned before, is represented by a pair of two-dimensional planes in a three-dimensional space. However, little information can be gained from such illustration of the MC isotherms, and a graphical analysis of displacement is facilitated by projecting certain key features from the three-dimensional space to a two-dimensional plot of c_B *versus* c_A, which is known as a "hodograph". In order to visualize the stability conditions graphically, we consider points on the hodograph at which the stability criteria are just satisfied. For the first conditions this point is

$$\left(\frac{q_A}{c_A}\right)^0_{c_B = c_B^*} = \frac{q_B^*}{c_B^*} \tag{9}$$

and for the second

$$\left(\frac{q_B}{c_B}\right)^0_{c_A = c_A^*} = \frac{q_A^*}{c_A^*} \tag{10}$$

In the hodograph, eqns. 9 and 10 represent points along the c_B and c_A axes, respectively, at which the selectivity, α_{BA}, is unity. The two conditions in eqns. 7 and 8 thus indicate that a final pattern of complete separation in which the bands have the order AB is stable when the selectivities at the points $(0, c_B^*)$ and $(c_A^*, 0)$ in the hodograph both exceed unity. On the other hand, if the selectivities at both of these points are lower than unity, a train with the order BA is predicted to be stable. However, the stability conditions are violated if the respective selectivities at $(0, c_B^*)$ and $(c_A^*, 0)$ are greater and lower than unity, or *vice versa*. As a result, under these conditions the final pattern of complete separation is unstable, and some alternative coherent state will be reached. The problem of determining the stability of the displacement train thus reduces to that of finding the points of unit selectivity, if they exist at all, on the c_B and c_A axes, and ensuring that the lcoations of $(0, c_B^*)$ and $(c_A^*, 0)$, as dictated by the operating line, lie on the appropriate sides of line connecting these points. Graphical illustrations of the analysis are shown later.

Multi-component isotherms generated by the IAS method

The constant selectivity feature of the competitive Langmuir isotherm precludes any possibility of finding in the hodograph points or regions of unit selectivity (except in the degenerate case where the SC isotherms are identical), and thus makes any discusison of stability pointless: with this MC isotherm, as long as the zeroth conditions are satisfied, all displacement trains are stable, and the only final patterns reached are those of complete separation. In practice, constant selectivity is unlikely to be realized, and MC isotherms that allows for variable selectivity are necessary.

As already mentioned, the Langmuir MC isotherm violates the Gibbs adsorption equation unless eqn. 3 is satisfied. The Gibbs equation relates adsorbed amounts to the spreading pressure, defined as the difference of the interfacial tensions between the multi-component solution–sorbent and the pure principal solvent–sorbent systems. The ideal adsorbed solution (IAS) method, so called because it uses an analogue of Raoult's-law ideality to describe the adsorbed phase, provides a framework to generate a multi-component isotherm that satisfies Gibbs equation from any set of single-component isotherms [21,22]. The antecedents of this approach and a useful general result are presented in Appendix A. Our interest here is to use the IAS method to obtain multi-component isotherms from Langmuir parent isotherms. In this case the calculation proceeds in two steps (see Appendix A). First, the reduced spreading pressure, Π, is determined for the given set of Langmuir SC isotherm parameters and concentrations of the components in the mobile phase from the implicit equation (see Appendix A)

$$\sum_{j=1}^{n} \frac{b_j c_j}{\exp(\Pi/\lambda_j) - 1} = 1 \tag{11}$$

The numerical solution of eqn. 11 is greatly facilitated by using as an initial guess the approximation to Π put forward by LeVan and Vermeulen [19]. Next, for a known value of Π, the multi-component isotherm is calculated from

$$q_i = \frac{b_i c_i / [\exp(\Pi/\lambda_i) - 1]}{\displaystyle\sum_{j=1}^{n} b_j c_j \exp(\Pi/\lambda_j) / \{\lambda_j [\exp(\Pi/\lambda_j) - 1]^2\}} \qquad i = 1, 2, ..., n \qquad (12)$$

The relationship given in eqn. 12 is hereinafter termed the IAS/L isotherm. In the case where eqn. 10 is satisfied, eqn. 12 reduces to the competitive Langmuir isoherm (eqn. 9), which is therefore a special case of the IAS/L equation.

Computation of displacement profiles

The stability criteria have been applied to the displacement of a binary mixture in the light of IAS/L isotherms. The results are illustrated by computer simulations of displacement profiles under various conditions. Exact solutions for the ideal case, *i.e.*, without dispersion in the system, cannot be found; instead, the calculations are carried out using the so called "semi-ideal" model [35,36]. The finite difference scheme for the solution of the resulting first-order partial differential equations introduces a numerical error that can be made to approximate the desired amount of dispersion in the system, quantified by a plate number $N (= u_0 L/2\mathscr{D}$, where L is the column length and $\mathscr{D}$ the effective axial dispersion coefficient that accounts for all dispersive processes in the system; N is also equal to L/H, where H is the plate height). The numerical scheme also introduces some additional errors but at sufficiently high values of N these do not significantly effect the calculations [36]. For convenience, in the calculations it is assumed that the phase ratio is unity. In addition, a constant plate height was used, so that the plate number gives an indication of the column length required. The results are presented as plots of the outlet concentration of the components *versus* the column volumes of mobile phase that have passed through the system. Note that with this representation, as long as the plate number is fixed, the actual values employed for the plate height and flow-rate need not be specified.

RESULTS AND DISCUSSION

Our goal here is to use the stability criteria put forward above to examine in detail the deviations from the classical Tiselian displacement picture observed when the parent isotherms of the separands cross. For this purpose, we shall consider the separation of pairs of components A and B, whose single-component isotherms intersect, as depicted in Fig. 1a. The displacement will be driven by a displacer whose isotherm overlies those of the separands. As the stability criteria are general, they ought to be applicable to any displacement system. For simplicity, however, we shall confine our attention to those that obey the IAS/L multi-component isotherm given in eqn. 12. In Appendix B, the treatment is extended to systems obeying another thermodynamically consistent MC isotherm; the results differ only marginally from those obtained with the IAS/L isotherm.
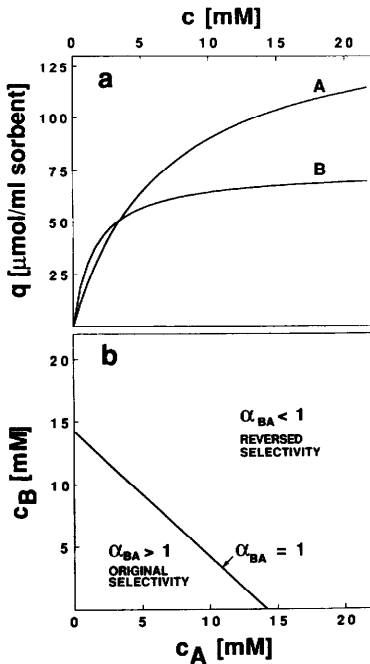
Fig. 1. (a) Plots of crossing single-component isotherms of components A and B and (b) the corresponding line of unit selectivity in a hodograph. The latter was calculated from eqn. 15 with the isotherm parameters λ_A = 150 μmol/ml sorbent, b_A = 0.15 l/mmol, λ_B = 75 μmol/ml sorbent, b_B = 0.62 l/mmol; c_x was obtained as 14.22 mM.

Selectivity inversion

As is evident from eqns. 9 and 10, a stability analysis is necessary only in those systems where the selectivity between the separands becomes unity at some points. In general, for separands A and B, such points define a line that demarcates regions of opposite selectivity in the hodograph space. We must therefore first examine under what conditions such regions exist.

The IAS/L isotherm allows for variable selectivity and can be used in the description of systems where selectivity inversion takes place [23]. It must be noted at the outset that, as with all MC isotherms generated only from SC isotherm data, the predictive power of the IAS/L isotherm is limited to "well behaved" systems. In case of the IAS method, "well behaved" implies that activity coefficients of the components in the moble and adsorbed phases are close to unity (for definition of adsorbed phase activity coefficients, see refs. 37 and 38). Even with this restriction, however, the IAS/L isotherm represents a distinct improvement over the competitive Langmuir isotherm, which cannot describe systems with changing selectivity.

From eqn. 12, the selectivity between two components, α_{BA}, is given by

$$\alpha_{BA} = \frac{b_B[\exp(\Pi/\lambda_A) - 1]}{b_A[\exp(\Pi/\lambda_B) - 1]} \tag{13}$$

where Π is a function of the concentrations c_A and c_B and is determined from eqn. 11. To locate points of unit selectivity, α_{BA} is set to unity in eqn. 13; the result is an implicit equation that can be solved for Π', the reduced spreading pressure that corresponds to all points of unit selectivity:

$$\frac{b_B[\exp(\Pi'/\lambda_A) - 1]}{b_A[\exp(\Pi'/\lambda_B) - 1]} = 1 \tag{14}$$

Introducing Π' into eqn. 11 and multiplying the result by $[\exp(\Pi'/\lambda_A) - 1]/b_A$ yields

$$c_A + c_B = \frac{[\exp(\Pi'/\lambda_A) - 1]}{b_A} \equiv c_x \tag{15}$$

In Appendix A, eqn. 15 is generalized for all MC isotherms generated by the IAS method, regardless of the shape of the parent isotherms. The result expresses an important property of the IAS isotherms: all points of unit selectivity between two components, if they exist at all, are connected by a straight line of slope -1 on a hodograph. The unit selectivity line intersects both the c_A and c_B axes at the value c_x, which is given by $[\exp(\Pi'/\lambda_A) - 1]/b_A$ in the case of the IAS/L isotherm.

An analysis of eqn. 14 shows that it has a real solution for Π' only if $b_B > b_A$, then $\lambda_B < \lambda_A$ and *vice versa*. When the parent isotherms of A and B cross, *i.e.*, $\lambda_B b_B > \lambda_A b_A$, and $\lambda_B < \lambda_A$ or *vice versa*, these criteria for a real solution for Π' are always satisfied. It would appear that they could also be satisfied without requiring the SC isotherms to intersect. However, in order to be physically acceptable, Π' must be positive (see eqn. 15), and this is found to occur *only* when the isotherms cross. Thus, according to the IAS/L isotherm model, selectivity inversion occurs only when the parent isotherms of the two components cross and the two regions of opposite selectivity are demarcated by a line of unit selectivity with slope -1 in the hodograph space.

A pair of crossing single-component isotherms and the corresponding unit selectivity line in a hodograph are shown in Fig. 1a and b, respectively. It is seen that whenever the sum of the concentrations $c_B + c_A$ is less than c_x, the selectivity, α_{BA}, is greater than unity, *i.e.*, $\alpha_{BA} > 1$, and *vice versa*. The two regions will be termed the regions of original and reversed selectivity, respectively. Fig. 1 also shows that the concentrations corresponding to points of unit selectivity along the c_B and c_A axes do not coincide with the intersection point of the parent isotherms. Indeed, this latter intersection point on two-dimensional plots has no physical significance *per se*. Within the hermeneutics of the IAS method the true concentration of unit selectivity, c_x, can be found by numerically solving eqn. 14 for Π' and substituting the result in eqn. 15. The dependence of c_x on the initial selectivity, *i.e.*, the selectivity at infinitesimal concentrations of both components A and B, α^0 ($= \lambda_b b_B/\lambda_A b_A$, or a_B/a_A, the ratio of the Henry's-law constants), is plotted for different values of the ratio of the saturation capacities λ_B/λ_A in Fig. 2. The results indicate that for a fixed saturation capacity ratio, c_x increases with increasing α^0, whereas for fixed α^0, c_x decreases with decreasing λ_B/λ_A. This is the same trend expected for the intersection point of the parent isotherms, and hence one may formulate a crude rule of thumb: if the sum of the
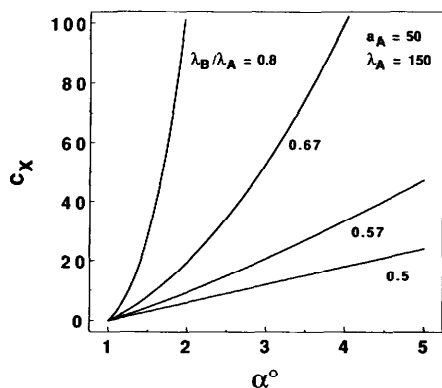
Fig. 2. Plots of the total concentration of unit selectivity, c_x, *versus* the initial selectivity $\alpha^0 = a_A/a_B$, calculated from eqn. 15 for the parameter values shown. The trends predicted in this diagram are independent of the actual parameter values chosen.

concentrations of the two components do not exceed that of the intersection point at any location in the column, selectivity in version is avoided altogether. This is valid for all three modes of frontal, elution or displacement chromatography. Our results show that, within the framework of the IAS/L isotherm, the true selectivity reversal
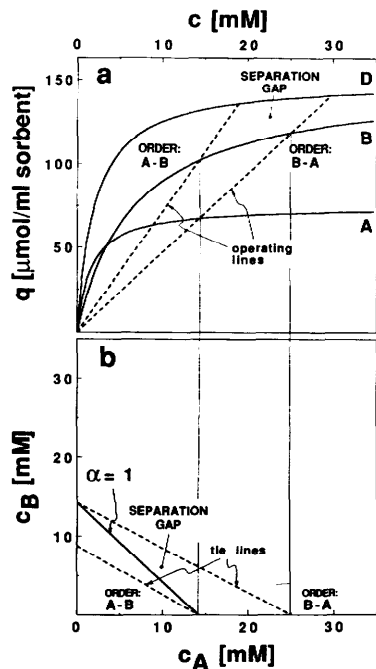

Fig. 3. (a) Crossing SC isotherms of components A and B, and the displacer, along with operating lines, and (b) the corresponding hodograph showing tie lines and the unit selectivity line. The operating and tie lines shown demarcate the space into three operating regions, as discussed in the text. Displacer parameters: $\lambda_D = 150 \ \mu mol/ml$ sorbent, $b_D = 0.5 \ l/mmol$; other parameters as in Fig. 1.

concentration, c_x, is always greater than the apparent crossing point, and the rule of thumb is therefore always conservative.

Displacement chromatography with crossing isotherms

More precise rules for displacement chromatography can be formulated by considering the stability conditions in eqns. 7 and 8. Consider the displacement of a mixture of two components A and B whose SC isotherms cross, and whose multicomponent isotherm follows the IAS/L equation. The isotherms of A, B and that of a displacer are shown in Fig. 3a and a corresponding hodograph of c_A *versus* c_B is depicted in Fig. 3b. Operating lines are drawn on the isotherm plot from the origin to the point on the displacer isotherm corresponding to the displacer concentration. Two such lines are shown in Fig. 3a. The operating lines transformed into the hodograph space are termed here "tie lines" and are shown on the hodograph in Fig. 3b. It is seen that each tie line is constructed from an operating line and connects the concentrations c_A^* and c_B^* determined by the intersection of the operating lines with the respective parent isotherms. A tie line merely serves to highlight the concentrations c_A^* and c_B^* on the axes of the hodograph that are the predicted concentrations of the bands in a completely separated Tiselian displacement train; apart from this it does not appear to have physical significance within the hodograph space. The unit selectivity line, $c_B + c_A = c_x$ is also drawn on the hodograph. The two tie lines and corresponding operating lines shown are for the cases where $c_A^* = c_x$ and $c_B^* = c_x$.

As mentioned in the discussion following eqn. 10, the stability conditions indicate that a separated isotachic sequence AB is stable if the corresponding concentrations c_A^* and c_B^* both lie below the line of unit selectivity, *i.e.*, below the tie line passing through $c_A^* = c_x$. On the other hand, when both c_A^* and c_B^* lie above the unit selectivity line, *i.e.*, when the tie line lies above the one passing through $c_B^* = c_x$, a stable isotachic pattern with the opposite order, in this case BA, is expected. Further, the stability conditions require that when c_A^* and c_B^* lie on opposite sides of the unit selectivity line, *i.e.*, the operating lines and corresponding tie lines lie between those shown in Fig. 3a and b, a completely separated pattern is not obtained. The operating region between these lines will be termed the "separation gap". Operating lines to the left of the gap yield displacement trains with original selectivity and those to the right of it trains with reversed selectivity. In the gap, no complete separation is possible. The construction in Fig. 3 allows us to visualize on a plot of the SC isotherms the separation gap that has been obtained from the stability analysis based on the corresponding MC isotherm.

To illustrate the results of operating in the different regions, simulations of displacement separations were carried out with the IAS/L isotherm as described earlier. With conditions chosen such that the operating line lies to the left of the gap, as shown in Fig. 4a, the calculated displacement profiles in Fig. 4b show that components A and B have separated into individual bands, with order AB. It is interesting to note that, because in this case the operating line lies above the intersection point of the parent isotherms, the concentration reached by A is higher than that of B, unlike in the classical picture of a displacement train [11]. This serves to emphasize that although the crossing of the SC isotherms is indicative of selectivity reversal, the location of their intersection point *per se* does not correspond to the concentration of unit selectivity as might have been inferred from a superficial examination.
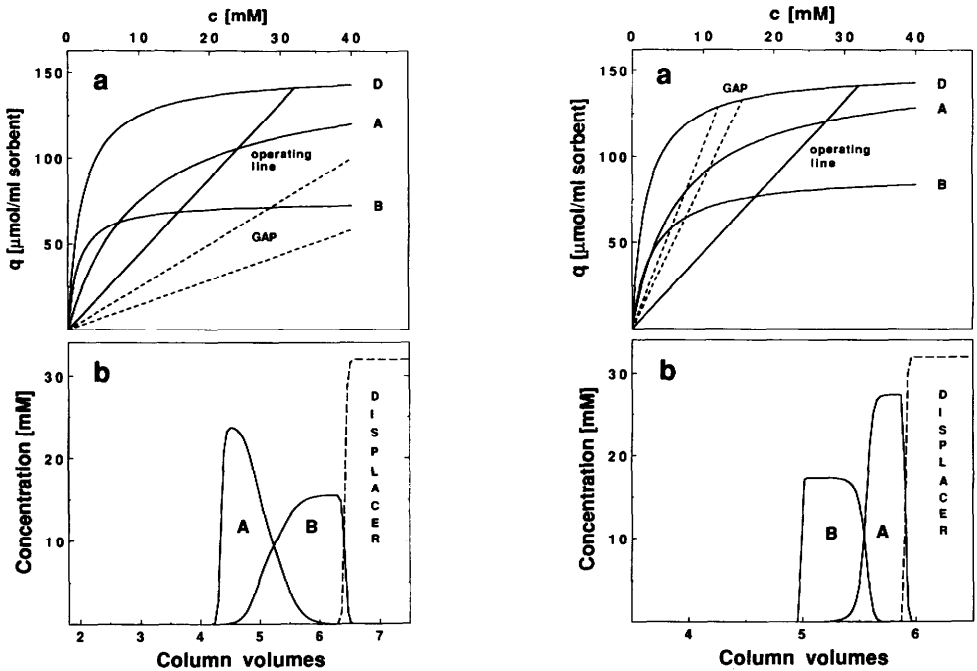
Fig. 4 (a) Crossing SC isotherms of components A and B and isotherm of the displacer showing an operating line lying to the left of the separation gap, and (b) displacement profiles calcualted using the IAS/L isotherm for the same conditions. Plate number, N = 2800; feed, 20 mM A and 20 mM B in one column volume. Isotherm parameters: λ_A = 150 μmol/ml sorbent, b_A = 0.1 l/mmol, λ_B = 75 μmol/ml sorbent, b_B = 0.7 l/mmol; c_x was calculated from eqn. 15 to be 50 mM. Displacer parameters as in Fig. 3; displacer concentration, 32 mM.

Fig. 5. (a) Crossing SC isotherms of components A and B and isotherm of the displacer showing an operating line lying to the right of the separation gap and (b) displacement profiles calculated using the IAS/L isotherm for the same conditions. Plate number, N = 10 000; feed, 5 mM A and 5 mM B in 1.25 column volumes. Isotherm parameters: λ_A = 150 μmol/ml sorbent, b_A = 0.15 l/mmol, λ_B = 90 μmol/ml sorbent, b_B = 0.33 l/mmol; c_x was calculated from eqn. 15 to be 7.34 mM. Displacer parameters and concentrations as in Fig. 4.

With conditions such that the operating line lies to the right of the separation gap, as depicted in Fig. 5a, the calculated displacement profiles shown in Fig. 5b display reversed selectivity, with bands appearing in the order BA as predicted from the above analysis. The plate number, N, chosen for this example was 10 000, indicative of a fairly difficult separation. A high plate number requirement for the calculation translates in practice into the need for a long column.

For the sake of comparison, we also carried out simulations by forcing the SC isotherms into the competitive Langmuir formalism. The results under conditions identical with those in Figs. 4 and 5 are shown in Fig. 6a and b, respectively. The bands in Fig. 6a appear in the same order and at the same concentrations, but are better separated than those in Fig. 4b. This is because the competitive Langmuir isotherm predicts a constant selectivity, $\alpha^0 = a_B/a_A$, at all concentrations, whereas with the IAS/L isotherm the selectivity ranges from α^0, its highest value at very low concentration, to some value close to unity at the higher concentrations of the final
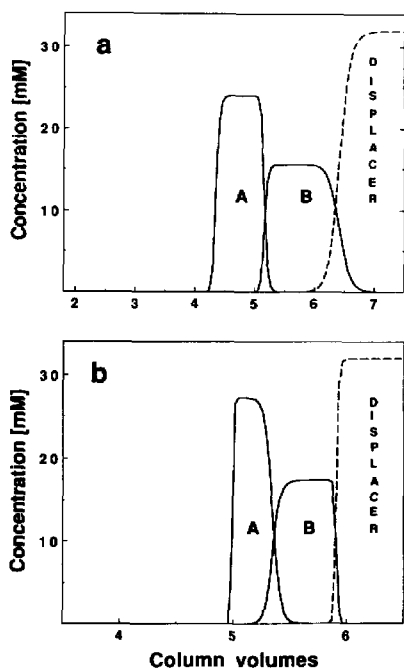
Fig. 6. Displacement profiles calculated with the competitive Langmuir isotherm under conditions given in (a) Fig. 4b and (b) Fig. 5b.
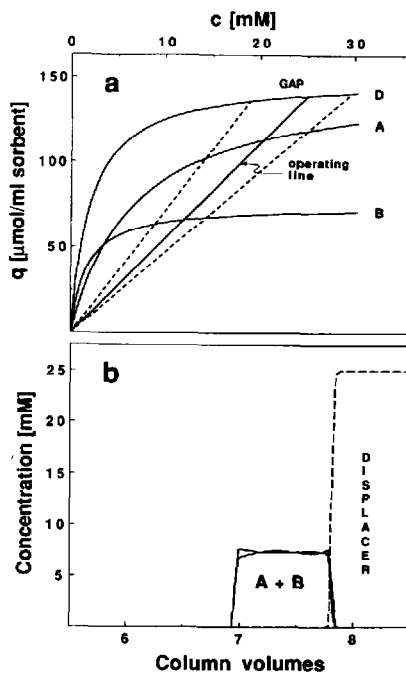
Fig. 7. (a) Crossing SC isotherms of components A and B and isotherm of the displacer showing an operating line lying in the separation gap, and (b) displacement profiles calculated using the IAS/L isotherm under the same conditions. Plate number, $N = 10\,000$; feed, 20 mM A and 20 mM B in 0.5 column volume. Isotherm parameters as in Figs. 1 and 3; displacer concentration, 25 mM.

pattern. Therefore, in the latter instance, the overall selectivity is lower, and the separation is consequently more difficult. Under conditions where a reversed order is predicted by the IAS/L as the final outcome, the calculations with the Langmuir isotherm in Fig. 6b continue to show the bands appearing in the order of original selectivity. Fig. 6 therefore confirms the inadequacy of the competitive Langmuir isotherm for use in dynamic adsorption systems discussed earlier.

A crude estimate of the difficulty of the separation can be determined from the selectivities at the inlet feed concentration and in the final pattern. For example, in the case shown in Fig. 4, the selectivity at the composition of the feed is 1.12, and at $(c_A^*, 0)$ and $(0, c_B^*)$ it is 1.59 and 1.57, respectively. In contrast, the selectivity given by the ratio of Henry's-law constants is 3.5. On the other hand, in the separation shown in Fig. 5, the selectivity, α_{BA}, at the column inlet is 0.933 (i.e., $\alpha_{AB} = 1.07$), at $(c_A^*, 0)$ it is 0.646 ($\alpha_{AB} = 1.55$) and at $(0, c_B^*)$ it is 0.827 ($\alpha_{AB} = 1.21$); however, the ratio of Henry's-law constants, α^0, is 1.33. The long development required for this separation is largely due to the very low initial selectivity. It is interesting that the selectivities at the end points of the tie lines are different from each other; the consequence of this in Fig. 5B is that the tail of B is somewhat sharper than the front of A.

In order to investigate how the feed concentration affects the profiles calculated with the IAS/L isotherm, we have carried out numerous simulations with the same parent isotherms and operating lines as in Figs. 4a and 5a, but with feed concentrations that, in the hodograph space, lie across the line of unit selectivity from the predicted separated pattern. Although higher plate numbers were required to bring about the separation, final patterns of complete separation were always achieved. Thus, at least within the hermeneutics of the IAS/L isotherm, the stability criterion appears to provide a sufficient condition for a given final pattern to eventually prevail.

The separation gap: formation of azeotropes

When the operating line lies in the separation gap, as illustrated in Fig. 7a, according to the stability analysis no completely separated state can be reached because the pattern would be unstable. Indeed, the calculated profiles in Fig. 7b show no sign of any separation. This kind of mixed displacement profile has been reported [16,39].

When operating in the separation gap, the final state eventually reached depends on the composition of the feed. Let us consider a displacement process, with the operating line in the gap, that has reached a coherent state, *i.e.*, with concentration profiles that no longer change as the bands continue to traverse the column. As shown above, the final pattern of complete separation is unstable and hence a mixed zone must form. For the mixed zone to persist at a given composition, it must travel at the velocity of the displacer and the composition of the components must be such that the selectivity is unity (or else there is a tendency for change). Thus the composition of the mixed zone must lie on the line of unit selectivity in the hodograph. If the proportion of the two components in the feed differs from that of such a mixed zone, conservation of mass dictates that there must be at least one other zone. In general, there could be several mixed zones that have the requisite properties; however, when adsorption is governed by the IAS/L isotherm, there is only one such mixed zone. Thus the other zone must be that of a pure substance. Depending on the relative amounts of the separands in the feed with respect to those of the mixed zone, the pure band contains either component A or B.

The mixed zone represents an "azeotropic" composition, *i.e.*, a mixed band that persists in the course of the displacement process. Unlike azeotropes in distillation which form only at one composition, all compositions along the unit selectivity line appear to be potential azeotropic points. Also, unlike in distillation, the azeotrope may be broken, at least in principle, simply by changing the displacer concentration so that the operating line moves out of the gap. Further, the elimination of any potential selectivity inversion or azeotropy by addition of another component may be possible as has been proposed [23,40] and is discussed later.

What order of appearance is expected for the train of mixed and pure zones? Consider the situation where the pure band is component A. As in the "Gedanken experiments" conducted earlier, let us bring a trace of B from the mixed band into the domain of A. The hodograph in Fig. 3b shows that when the operating and tie lines lie in the separation gap, the point $(c_A^*, 0)$ is in the region of reversed selectivity. Thus the trace of B should move more rapidly than A and be pushed ahead. If the pure band were B instead, a trace of A brought into its domain would likewise be pushed ahead because the point $(0, c_B^*)$ is in the region of original selectivity. This forces us to

the conclusion that whether the pure band is of A or B, it must be located behind the mixed band.

In an attempt to confirm these assertions, several simulations were performed with the operating line in the separation gap and with feed concentrations such that either A or B were in excess with respect to the anticipated mixed-zone composition. Under such conditions, the displacement train evolved extremely slowly; *e.g.*, with parameters similar to those in Fig. 7, more than 15 000 plates were typically required before an unequivocal trend towards the expected final state could be discerned. The slow development is not surprising, because at the concentrations in question the selectivity is always close to unity.

In order to circumvent the lengthy calculations, another approach was taken to examine the order of the mixed and pure bands. In the simulations the feed itself was introduced in the anticipated final state, *i.e.*, with a mixed zone at the relevant composition along the unit selectivity line, either preceded or followed by a pure band of A or B. (The anticipated mixed-zone composition was found by searching the unit selectivity line numerically for the point where its velocity is equal to that of the displacer). It was reasoned that if the feed pattern closely resembled the actual final state, the concentration profiles would show very little change, apart from dispersion,
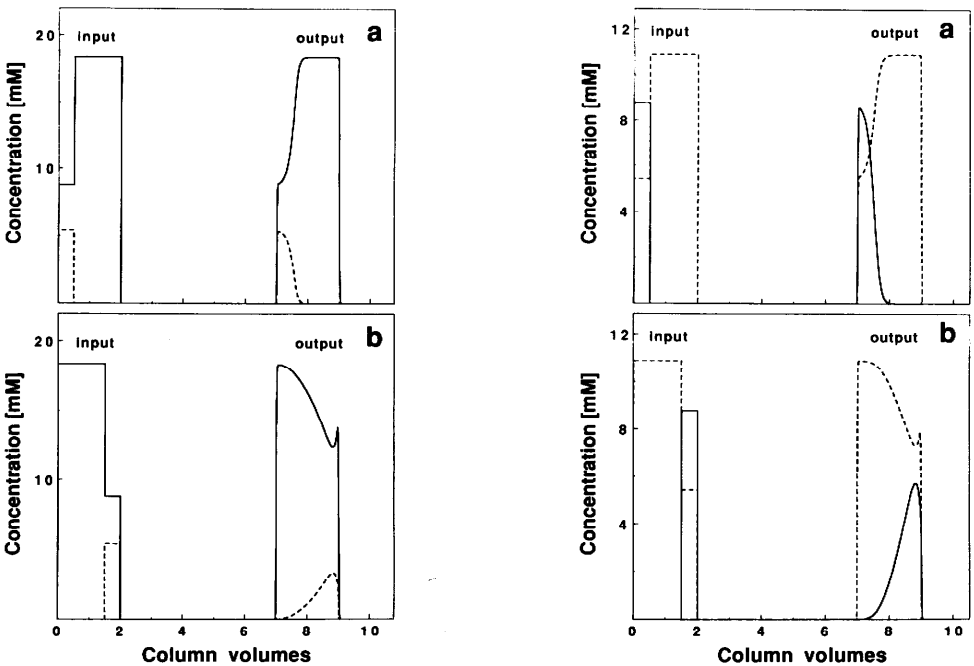

Fig. 8. Displacement profiles calculated with input profiles having a pure zone of component A (———) and a mixed zone containing components A (———) and B(- - - -). In (a) the mixed zone precedes the pure zone into the column and in (b) the inlet order of zones is reversed. Parameters as in Fig. 7 with a displacer concentrations of 23 mM. The mixed zone composition lies along the unit selectivity line in Fig. 3b with $c_A = 8.8$ and $c_B = 5.42$. The displacer profile is not shown.

Fig. 9. Displacement profiles calculated with input profiles composed of a pure zone of B and a mixed zone containing components A and B as shown in the plots. All other conditions as in Fig. 8.

when the displacement proceeds over a significant length of column. The feed and corresponding effluent patterns from a 10 000-plate column when the pure band of A follows and precedes the mixed band are shown in Fig. 8a and b, respectively. The results are in accord with our expectations: when the pure band follows the mixed band, the change in the concentration profiles is minimal when the bands traverse the column. When the order of mixed and pure bands is reversed, however, the concentration profiles in the effluent no longer resemble the input profiles. In Fig. 9a and b, similar results are shown when the pure band is component B.

Azeotropy with non-IAS multi-component isotherms

All systems that display selectivity inversion are not likely to behave as the IAS/L isotherm predicts. In Appendix A, a result is derived that shows that all MC isotherms based on the IAS theory, regardless of the form of the parent isotherms (as long as they do not have points at which $dq/dc \rightarrow \infty$), are constrained in such a way that points of constant selectivity lie on straight lines in hodograph space. Further, it is shown that in such systems, if points of unit selectivity exist, they must lie on a line of slope -1; eqn. 15 is a special case of this for Langmuir parent isotherms. Much as constant selectivity over the entire composition range is an artifact of the competitive Langmuir equation, this constraint is a shortcoming of IAS isotherms. The IAS approached represents a significant improvement over the MC Langmuir isotherm, as it can describe systems with variable selectivity, but it is by no means the only correct MC isotherm. Indeed, to describe real systems, non-idealities must often be incorporated, and the behavior may be considerably different form that predicted by the IAS method [22,37,38]. With this background, a brief discussion of selectivity reversal and azeotropy in non-IAS/L systems is presented here.

With the IAS/L isotherm, the concentration c_x always lies beyond the intersection points of the SC isotherms. As a consequence, the operating lines in the hodograph, *i.e.*, the tie lines, which lie in the separation gap are always less steep than the unit selectivity line, as shown in Fig. 3a. Thus, for tie lines within the gap, the points $(0, c_B^*)$ and $(c_A^*, 0)$ always lie in the region of initial and opposite selectivity and the argument given above for the order of the mixed and pure bands always holds. On the other hand, if the adsorption were governed by some other MC isotherm so that the pertinent tie lines were now steeper than the unit selectivity line (which is not necessarily straight), the point $(c_A^*, 0)$ for a tie line that crosses the unit selectivity line would lie in the region of original selectivity, whereas $(0, c_B^*)$ would now lie in the region of reversed selectivity. The "Gedanken experiment" above would then yield the opposite result, and the pure band would be expected to precede the mixed one. With some MC isotherms the unit selectivity line may coincide with a tie line, and there is no separation gap or azeotropy even though the system exhibits selectivity reversal, as shown in Appendix B for the generalized multi-component Langmuir isotherm.

These are only two examples of departure from the IAS/L MC isotherm. In a study of azeotropy in frontal chromatography, Basmadjian *et al.* [41] have pointed out several further possibilities for azeotropic systems that do not fall within the purview of the IAS method. For example, they consider two cases where the hodograph space is broken up into more than two regions of inverted selectivity. In such a system, if a suitable displacer were to be found, mere meeting of the stability

conditions discussed above may be insufficient to obtain separated displacement pattern from any previously mixed state. There is then no recourse but to search for all points on the concentration axes and the unit selectivity lines that have species velocities equal to that of the displacer, and decide which combinations of such points would eventually evolve as the final state from a given feed composition.

One system that shows simpler behavior than what has just been described, but is unlike that predicted by the IAS approach, is that of benzenesulfonic acid and *p*-nitrophenol adsorbed from aqueous solutions onto activated carbon [41]. Here the unit selectivity line appears to project outward from the origin of the hodograph. If a suitable displacer were chosen for this system, all possible tie lines would be found to intersect the unit selectivity line. It would therefore be impossible to obtain a completely separated displacement train in this system regardless of the displacer concentration. By performing an analysis akin to that mentioned above, one can predict for such systems that the final pattern ought to be one where a pure band of either component, depending on the relevant feed and azeotropic compositions, precedes a mixed band.

Eliminating azeotropes by adding another component

The results of this study show that selectivity reversal is in general detrimental to displacement chromatography, even when stable patterns of complete separation are expected. As suggested in previous studies, the addition of another component can be used to eliminate an possibility of azeotropy [23,40]. As we have not yet found a strategy by using a component merely added to the feed, we are considering here the addition of another component to the carrier. In order to determine the concentration of a component C required to ensure that there are no longer any points of unit selectivity in the c_A–c_B hodograph, we rearrange eqn. 11, written for three components and evaluated at $\Pi = \Pi'$ (see eqn. 14) to obtain

$$c_A + c_B = \frac{\exp(\Pi'/\lambda_A) - 1}{b_A}\left(1 - \frac{b_C c_C}{\exp(\Pi'/\lambda_C) - 1}\right) = c_X(c_C) \qquad (16)$$

The total concentration of unit selectivity, c_x, is now seen to be a function of the concentration of the additive, c_C. This concentration goes to zero at $c_C = [\exp(\Pi'/\lambda_C) - 1]/b_C$; above this the value of Π is always greater than Π', and there will no longer be a unit selectivity line. However, the addition of a third component in such a manner is accompanied by both a reduction in the retention and the sorption capacity of components A and B. When this effect is large it may render the system useless for preparative separations [23,40]. The reduction in retention and the sorption capacity depends on Π', which is determined from the isotherm parameters of A and B alone and is thus largely independent of the particular components C employed. As a consequence, in systems where the reduction in sorption capacity by addition of a particular additive is too severe, it is not likely that the use of another additive will be successful. In such cases, it would be necessary to change other conditions, such as pH, temperature or even the sorbent itself in order to eliminate completely the unwanted selectivity reversal.

APPENDIX A

After presenting an outline of the IAS method an expression is derived for the points of constant selectivity in hodograph space that is generally valid for multi-component isotherms based on the ideal adsorbed solution (IAS) approach and facilitates the analysis of such MC isotherms.

The IAS method

The IAS approach provides a framework to generate thermodynamically consistent multi-component adsorption isotherms from any set of single-component isotherm data [21,22]. The basic hypothesis is that the adsorbed phase is "ideal" in sense corresponding to Raoult's law in liquid–vapor equilibria. That is, the fluid phase concentration, c_i, of a component i in equilibrium with the adsorbed phase is related to a standard state concentration, c_i^s by

$$c_i = z_i c_i^s \qquad i = 1, ..., N \tag{A-1}$$

where z_i is the mole fraction of i in the adsorbed phase and N is the total number of adsorbed components. In adsorption from liquid solutions, the adsorbed phase is defined by the "solvent-not-adsorbed" convention and therefore the mole fraction does not include the principal solvent [22]. The standard state is defined as a system containing only the component i (and the principal solvent) at the same temperature and spreading pressure as the multi-component system being considered. The spreading pressure, π, is the difference between the solution–sorbent interfacial tension and the pure reference solvent–sorbent interfacial tension. A reduced spreading pressure, Π, is defined as $\pi A / RT$, where A is the surface area of the sorbent assumed to be equally accessible to all adsorbates, R is the gas constant and T is the temperature. The standard state concentration c_i^s is not a constant at a given temperature, as is the saturation vapor pressure in Raoult's law, but depends on Π which varies with the composition of the multi-component mixture. The relationship between Π and c_i^s is determined from the Gibbs' adsorption equation and the adsorption isotherm for a single component using the expression [22]

$$\Pi = \int_0^{c_i^s} \frac{q_i(c_i)}{c_i} \cdot dc_i \qquad i = 1, ..., N \tag{A-2}$$

where $q_i(c_i)$ is the pertinent SC isotherm. Note that since q_i and c_i are always positive, in the absence of conditions under which $dq_i/dc_i \to \infty$, Π is a single-valued function of c_i^s and *vice versa*. As the concentrations, c_i, in multi-component solution are

known, and the sum of the mole fractions in the adsorbed phase is unity, Π can be determined in principle form the single equation

$$\sum_{j=1}^{N} \frac{c_j}{c_j^s(\Pi)} = 1 \tag{A-3}$$

This equation can be employed in practice only when an explicit relationship for c_i^s as a function of Π can be found from eqn. A-2. For example, eqn. 11 corresponds to this equation written for the case where the single-component isotherms have the Langmuirian form. If the integral in eqn. A-2 cannot be solved analytically and the function cannot be inverted explicitly, other numerical methods must be employed to determine Π [42]. Once Π and therefore c_i^s are known, then z_i for each component can be found from eqn. A-1.

It can be shown that the total adsorbed amount on the stationary phase, q_T, is given by [22]

$$q_T = \frac{1}{\displaystyle\sum_{j=1}^{N} \frac{z_j}{q_j^s}} \tag{A-4}$$

where q_i^s is the stationary phase concentration of i in equilibrium with c_i^s in the respective single-component system. The adsorbed amounts of each component, q_i, are then simply given by

$$q_i = z_i q_T \tag{A-5}$$

Eqn. 12 is a combination of eqns. A-4 and A-5 written in terms of Π and c_i for the case of SC Langmuir isotherms.

Constant selectivity with IAS isotherms
Here it is shown that the selectivity for any two components, in the case of MC isotherms obtained by the IAS method, is a function of the reduced spreading pressure, Π. Further, it is shown that for nearly all forms of the parent isotherms in a binary system with two components A and B, the locus of constant selectivity, α_{BA}, in a hodograph of c_B *versus* c_A, is a straight line of slope $-1/\alpha_{BA}$. It follows then that, if they exist, points of unit selectivity in any binary IAS isotherm lie on a straight line of slope -1.

Combining eqns. A-1 and A-5 yields

$$q_i = \frac{c_i}{c_i^s(\Pi)} \cdot q_T \tag{A-6}$$

The selectivity for two components, α_{BA}, is defined as $q_B c_A / q_A c_B$; from eqn. A-6 the selectivity is thus seen to be

$$\alpha_{BA} = \frac{c_A^s(\Pi)}{c_B^s(\Pi)} \tag{A-7}$$

which is a function of Π only (besides the parameters of the parent isotherms).

Combining equation A-3 written for a binary system with eqn. A-7 and rearranging the result yields

$$c_B = c_B^s(\Pi) - \frac{c_A}{\alpha_{BA}(\Pi)} \tag{A-8}$$

Thus the loci of constant α_{BA} (or of constant Π) are straight lines of slope $-1/\alpha_{BA}$ in the hodograph space. Eqn. A-8 is meaningful only when c_A^s and c_B^s are single-valued functions of Π, which is always the case as long as there are no points on the SC isotherms at which $dq_i/dc_i \rightarrow \infty$. Note that in general there could be several values of Π for which the selectivity is the same, and consequently several parallel lines in the hodograph having the same selectivity. Eqn. 15 in the text is a special case of eqn. A-8 written for $\alpha_{BA} = 1$ and Langmuir SC isotherms.

APPENDIX B

Generalized multi-component Langmuir isotherm with selectivity inversion
        Here another thermodynamically consistent MC isotherm is presented that can account for cases where the individual components have different saturation capacities. The derivation is essentially a simple extension of the equilibrium arguments that lead to the competitive Langmuir isotherm, and it is therefore called the generalized multi-component Langmuir (GML) isotherm. (The isotherm may well have been described before, but we could not find any reference to it. It is formally similar to the multivalent ion-exchange isotherm [43], with the exception that no electroneutrality condition must be satisfied at the sorbent surface). This isotherm formalism will then be used in the same way as he IAS/L isotherm was in the main body of the text, to examine the different operating regions of displacement chromatography.

The generalized multi-component Langmuir isotherm
        Consider the set of binding reactions

$$i + v_i \Theta \Leftrightarrow \overline{i\Theta_{v_i}} \qquad i = 1, ..., N \tag{B-1}$$

where i is one of N species in the liquid phase, Θ is a free binding site on the sorbent, v_i is a stoichiometric coefficient and $\overline{i\Theta_{v_i}}$ represents i in the adsorbed state on the stationary phase. The equilibrium constants, K_i, for the process are represented by

$$K_i = \frac{q_i}{c_i[\Theta]^{v_i}} \qquad i = 1, ..., N \tag{B-2}$$

where q_i and c_i are the respective concentrations of i in the stationary and mobile phases and $[\Theta]$ represent the concentration of free binding sites. If the total concentration of binding sites is Λ, one can write

$$[\Theta] + \sum_{j=1}^{N} v_j q_j = \Lambda \tag{B-3}$$

Substitution of eqn. B-2 into eqn. B-3 yields

$$[\Theta] + \sum_{j=1}^{N} v_j K_j c_j [\Theta]^{v_j} = \Lambda \tag{B-4}$$

Although eqn. B-4 can in general have multiple solutions, it has only one solution that lies in the range $0 < [\Theta] < \Lambda$, as more than one stationary phase composition in equilibrium with a given mobile phase condition is excluded from this treatment. When this solution is found for $[\Theta]$, the concentrations of the N species in the stationary phase are obtained on rearranging eqn. B-2 as

$$q_i = K_i c_i [\Theta]^{v_i} \qquad i = 1, \dots, N \tag{B-5}$$

It is noted that eqns. B-5 and B-4 reduce to the competitive Langmuir equation when all the stoichiometric coefficients, v_i, are unity.

The corresponding parent isotherm for component i is given by the implicit expression

$$q_i = K_i c_i (\Lambda - v_i q_i)^{v_i} \qquad i = 1, \dots, N \tag{B-6}$$

This isotherm has the initial slope $K_i \Lambda^{v_i}$ and saturation capacity Λ/v_i. Fitting of experimental single-component isotherm data to this equation is a non-trivial exercise because, in order to ensure a unique value of Λ, all the isotherms involved must be fit simultaneously. These difficulties are not germane here, however, as the concern is how a set of components that follow such an isotherm would behave in displacement chromatography.

Selectivity inversion

The selectivity, α_{BA} when eqn. B-5 holds is given by

$$\alpha_{BA} = \frac{q_B c_A}{q_A c_B} = \frac{K_B [\Theta]^{v_B}}{K_A [\Theta]^{v_A}} \tag{B-7}$$

Thus, when α_{BA} is unity, the corresponding concentration of free sites, $[\Theta]'$, is

$$[\Theta]' = \left(\frac{K_A}{K_B}\right)^{\frac{1}{v_B - v_A}} \tag{B-8}$$

As mentioned above, $[\Theta]'$ must lie between 0 and Λ. Thus, with the GML isotherm, selectivity inversion will occur only when

$$\Lambda > \left(\frac{K_A}{K_B}\right)^{\frac{1}{\nu_B - \nu_A}} \tag{B-9}$$

This condition is satisfied for $\nu_B > \nu_A$ when $K_B\Lambda^{\nu_B} > K_A\Lambda^{\nu_A}$, and *vice versa, i.e.,* whenever the parent isotherms cross.

On substituting eqn. B-8 into eqn. B-4 we find that the locus of unit selectivity in c_A-c_B hodograph space is a straight line given by

$$c_B = c_B' - \frac{\nu_A}{\nu_B} \cdot c_A \tag{B-10a}$$

This line has slope $-\nu_A/\nu_B$, and intercept c_B' given by

$$c_B' = \left[\Lambda - \left(\frac{K_A}{K_B}\right)^{\frac{1}{\nu_B - \nu_A}}\right] \Big/ \left[\nu_B K_B \left(\frac{K_A}{K_B}\right)^{\frac{\nu_B}{\nu_B - \nu_A}}\right] \tag{B-10b}$$

Operating regimes for displacement chromatography

To determine the different operating regimes in the case of crossing isotherms for the multi-component isotherm formalism given by eqn. B-5, we examine first the equation of the tie line that connects those points on the c_A and c_B axes in the hodograph which correspond to the intersections of the respective parent isotherms with an operating line of slope Λ. The intersection points with the parent isotherms can be found from eqn. B-6 to be

$$c_i^* = \left[\Lambda - \left(\frac{\Lambda}{K_i}\right)^{\frac{1}{\nu_i}}\right] \Big/ \nu_i\Lambda \qquad i = A, B \tag{B-11}$$

The tie line that connects $(0, c_B^*)$ and $(c_A^*, 0)$ in the hodograph is given by the equation $c_B = c_B^* - (c_B^*/c_A^*)c_A$. Expressing the pertinent concentrations from eqn. B-11 we obtain that the slope of this tie line, m_T, is given by

$$m_T = - \left[\frac{\Lambda - \left(\frac{\Lambda}{K_B}\right)^{\frac{1}{\nu_B}}}{\Lambda - \left(\frac{\Lambda}{K_A}\right)^{\frac{1}{\nu_A}}}\right]^{\frac{\nu_A}{\nu_B}} \tag{B-12}$$

The term in square brackets on the right-hand side of eqn. B-12 becomes unity at

$$\Lambda = \left(K_B^{\frac{1}{\nu_B}} / K_B^{\frac{1}{\nu_B}}\right)^{\frac{\nu_A \nu_B}{\nu_B - \nu_A}} \equiv \Lambda^* \tag{B-13}$$

After some algebraic manipulation, it can be shown that at this value of Λ, $c_B^* = c_B'$. Thus the tie line passing through c_B' has the same slope, $-v_A/v_B$, as the unit selectivity line. Additionally, one can show that no tie line actually crosses the unit selectivity line. Thus, within the framework of the GML isotherm, when the parent isotherms of A and B cross there are two operating regions, separated from each other by an operating line of slope Δ^*. These regions correspond to final patterns of complete separation with different order of the components: for operating lines of slope greater than Δ^* the order is AB, and for those with slope lower than Δ^* it is BA.

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