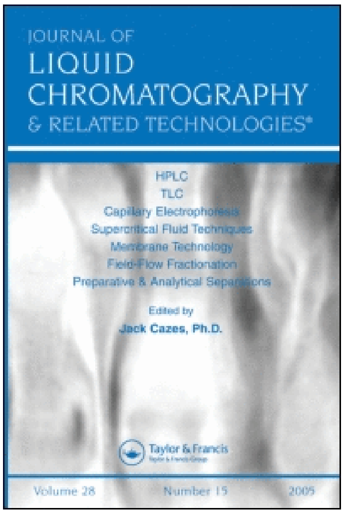

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# Molecular Theory of Liquid Adsorption Chromatography

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# MOLECULAR THEORY OF LIQUID ADSORPTION CHROMATOGRAPHY

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## ABSTRACT

A statistical-mechanical theory, based on a lattice model, has been developed to address the molecular mechanism of retention and selectivity in both normal-phase and reversed-phase liquid adsorption chromatography. The model is a natural "competitive-equilibrium" one, where possible contributions from solvent-solvent and solute-solvent interactions, and, hence, from solution nonideality, are not neglected. Homogeneous and heterogeneous adsorbent surfaces, single-solvent and binary mixed-solvent mobile phases, and solute molecules of different size and shape are treated. Practical applications of the theory are presented to demonstrate its utility and significance.

For homogeneous adsorbents and neat solvents, the molecular energetics of retention and selectivity are examined, with special emphasis on the effects of solute size and shape, and, relatedly, the modes of solute adsorption. Separations of geometrical isomers and homologous series in real and simulated chromatographic processes are investigated, confirming predictions of the theory and the important role of solvent-solvent and solute-solvent interactions in reversed-phase systems. The implications of a more general retention equation for microscopically heterogeneous adsorbents are discussed. The dependence of capacity ratio on mobile-phase composition for binary solvents is analyzed in some detail. An often important contribution arising from solution nonideality is predicted theoretically. This is shown to be consistent with experimental results on normal-phase and reversed-phase systems.

## INTRODUCTION

The impetus for this study was the perceived need of a general, rigorous, yet tractable, molecular theory of liquid adsorption chromatography (LAC), applicable to both normal-phase (NP) and reversed-phase (RP) modes, and potentially extendible to such highly modified adsorbents as chemically bonded phases. Phenomenological and semi-theoretic models have been proposed for LAC, particularly in the NP mode with the polar adsorbents silica gel and alumina (1-14). From them have come useful correlative equations and practical guides such as "solvent strength" or eluotropic series. However, there remain unsettled questions such as realistic modelling of adsorbent heterogeneity, the effects of solute (sample) molecular shape and size, and the explicit functional dependence of retention on mobile-phase (eluent) composition for mixed-solvent systems. Therefore, a statistical-mechanical model has been developed from first principles (15), to provide: a) a more rigorous theoretical foundation for LAC (column and thin-layer chromatography), b) an interpretive framework capable of bringing more coherence to the vast amount of reported data, c) further insight into the molecular mechanism of solute retention and selectivity, and the respective roles of the mobile and stationary phases in NP and RP separations, and d) theoretical resolution of the unsettled issues.

Here, we summarize the salient features of our model and the derived equations. Practical applications and interesting implications of the theory are then presented for NP and RP processes. Effectively planar homogeneous and heterogeneous adsorbent surfaces, single-solvent and binary mixed-solvent mobile phases, and solute molecules of different size and shape are considered.

## THEORY

The focus of the theoretical treatment is on equilibrium properties, viz., infinite-dilution (16) distribution constants and capacity ratios for nonelectrolytic solutes with nonelectrolytic solvents under isochratic elution conditions. Of ultimate interest is the distribution of solute between a bulk-solvent mobile phase and a stationary phase formed by the adsorption of a monolayer (17) of solvent on a planar surface. The statistical-mechanical analysis is based on a lattice model and utilizes the Bragg-Williams method to construct the canonical partition functions for the solute and the solvent(s) in both the mobile and stationary phases (15). The two phases are linked by the usual equilibrium condition, i.e., equality of the chemical potential of the solute in the two phases and, for a binary solvent mixture, equality of the chemical potential for each solvent component in the two phases. Entropy effects are automatically included, and cancellation of solute-solvent and solvent-solvent interactions between the two phases is not assumed. Thus, the model is a natural "competitive-equilibrium" model where possible contributions from solution nonideality are not ignored.

In the most general form of the model, we consider a heterogeneous planar surface containing $\omega$ types of energetically and/or chemically different adsorption sites, each of arbitrary unit area ($A_j = 1$, for all j). The "monomeric" solvent molecules (components 1 and 2 for binary mixed solvents) are taken to be cubic in shape, with the area of any given face equal to the area of an adsorption site, i.e., $A_1 = A_2 = A_j = 1$ (17). The shape of the solute molecule (component 3) is approximated by either a regular or irregular rectangular prism possessing six faces (a to f) capable of making full and direct contact with the adsorbent surface. (For example, the solute may be cubic, rodlike, platelike, L-shaped, U-shaped, etc; see later.) The area of the i-th face, relative to that of an adsorption site, is designated by $A_{3_i}$.

Considering a single solvent (component 1 only) and letting $y_3$ and $x_3$ be the equilibrium mole fractions of solute in the stationary and mobile phases, respectively, we obtain the following expression for the infinite-dilution mole-fraction distribution constant $K_{3(1)}$ (15);

$$K_{3(1)} = \frac{y_3}{x_3} = \frac{1}{6}\sum_{i=a}^{f}\left(\sum_{j=\alpha}^{\omega}\left[g_j \exp\{-\beta\Delta w_{j,i}\}\right]^{A_{3_i}}\right), \qquad (1)$$

where $g_j$ is the fraction of adsorption sites that are of type j and $\beta = (k_B T)^{-1}$, where $k_B$ is the Boltzmann constant and T is the temperature in Kelvin. Also:

$$\Delta w_{j,i} = w_{3_i j} - w_{1j} + w_{11} - w_{13_i}, \qquad (2)$$

where the w's are <u>negative</u> quantities and refer to attractive-interaction free energies (18) per unit area. (For example, $w_{3_i j}$ represents the interaction between a surface adsorption site of type j and a unit area of the i-th face of a solute molecule.) The term $\Delta w_{j,i}$, which may be negative or positive, is then the interchange free energy per unit area for the process:

$$1\text{-}j(\text{stat.}) + 1\text{-}3_i(\text{mob.}) = 3_i\text{-}j(\text{stat.}) + 1\text{-}1(\text{mob.}), \qquad (3)$$

which corresponds to the transfer of solute from the mobile to the stationary phase and the concomitant reversed transfer of solvent. This involves the breaking of $1\text{-}3_i$ and 1-j interactions and the formation of 1-1 and $3_i\text{-}j$ interactions.

For "monomeric" solute molecules (i.e., $A_{3_i} = 1$, for all i) and a homogeneous surface (one type of adsorption site only), we obtain the following expression for the distribution constant $K_{3(1+2)}$ with a binary mixed-solvent system (15,19):

$$\frac{1}{K_{3(1+2)}} = \frac{x_1}{K_{3(1)}}\exp[C\beta(\delta_{12}+\delta_{13}-\delta_{23})] + \frac{x_2}{K_{3(2)}}\exp[D\beta(\delta_{12}+\delta_{23}-\delta_{13})], \qquad (4)$$

where $K_{3(1)}$ and $K_{3(2)}$ are the distribution constants with neat solvents 1 and 2, respectively, $x_1$ and $x_2$ are the mobile-phase mole fractions of 1 and 2 in the mixed-solvent system, and C and D are given by:

$$\left.\begin{aligned} C &= 6x_2 - 5y_2 = 1 + 5y_1 - 6x_1 \\ D &= 6x_1 - 5y_1 = 1 + 5y_2 - 6x_2 \end{aligned}\right\} , \tag{5}$$

where $y_1$ and $y_2$ are the stationary-phase mole fractions of 1 and 2 in the mixed-solvent system. The $\delta$'s refer to interchange free energies:

$$\delta_{mn} = \delta_{nm} = w_{mn} - (w_{mm} + w_{nn})/2 . \tag{6}$$

They reflect contributions from solution nonideality and, hence, can be phrased in terms of activity coefficients (see later.)

The mobile and stationary-phase solvent compositions are related through (15):

$$\frac{(y_2)(1-x_2)}{(1-y_2)(x_2)} \exp[(12x_2-10y_2)\cdot\beta\delta_{12}] = \frac{K_{3(1)}}{K_{3(2)}} \exp[\beta(\delta_{12}+\delta_{23}-\delta_{13})] . \tag{7}$$

Combining equations (4) and (7), the following useful relations are derived:

$$K_{3(1+2)} = K_{3(1)}(y_1/x_1) \exp[(6x_1-5y_1-1)\cdot\beta(\delta_{12}+\delta_{13}-\delta_{23})] , \tag{8}$$

$$K_{3(1+2)} = K_{3(2)}(y_2/x_2) \exp[(6x_2-5y_2-1)\cdot\beta(\delta_{12}+\delta_{23}-\delta_{13})] . \tag{9}$$

Although the above equations may appear to be formidable at first glance, their application to actual and simulated chromatographic cases will permit their simplification and demonstrate their utility and significance.

In comparing the retention of solutes with a given solvent and on a given column or TLC plate, it is apparent that relative K values will be equivalent to relative capacity-ratio (k') values. Similarly, since the present theoretical analysis deals only with solvent molecules of the same size, relative K values may be regarded as relative k' values when assessing the effect of varying the nature or composition of the eluent.

## HOMOGENEOUS ADSORBENT AND NEAT SOLVENT

In this section we consider a homogeneous surface (type s adsorption sites only) and a single-component solvent. The relevant form of equation (1) is:

$$K_{3(1)} = (1/6)\sum_{i=a}^{f} [\exp(-\beta\Delta w_{s,i})]^{A_{3i}} \quad , \qquad (10)$$

where $\Delta w_{s,i} = w_{3_is} - w_{1s} + w_{11} - w_{13_i}$ .

### Monomeric Solutes

With a chemically homogeneous monomeric solute, $A_{3_i} = 1$ for all i and the six faces are energetically equivalent. Hence:

$K_{3(1)} = \exp(-\beta\Delta w_s)$, where $\Delta w_s = w_{3s} - w_{1s} + w_{11} - w_{13}$.

Clearly, strong solute-adsorbent and solvent-solvent interactions promote negative $\Delta w_s$ values and act to prolong retention, while strong solvent-adsorbent and solvent-solute interactions promote positive $\Delta w_s$ values and favor more rapid elution. Absolute retention is thus governed by the balance or "competition" among these four interaction terms. For two such solutes (u and v), the relative retention or separation factor $F_{uv}$ is:

$$F_{uv} = K_{v(1)}/K_{u(1)} = k'_{v(1)}/k'_{u(1)} = \exp\{-\beta\Delta(\Delta w_s)\},$$

where $\Delta(\Delta w_s) = (w_{vs} - w_{us}) - (w_{1v} - w_{1u})$.

Therefore, the separation is determined by the relative strengths of solute-adsorbent <u>and</u> solute-solvent interactions.

From equation (10), for a chemically heterogeneous monomeric solute where one of the six faces (denoted by a star) is energetically different than the other five, the absolute retention is a sum of two contributions:

$$K_{3(1)} = (1/6)\exp(-\beta\Delta w_s^{*}) + (5/6)\exp(-\beta\Delta w_s),$$

where $\Delta w_s^{(*)} = w_{3s}^{(*)} - w_{1s} + w_{11} - w_{13}^{(*)}$.

However, if the unique face (representing, perhaps, a polar functional group) experiences especially strong interactions with the surface or especially weak intereactions with the solvent, so that $-\beta\Delta w_s^* >> -\beta\Delta w_s$, then its retention contribution would dominate despite the smaller pre-exponential or "degeneracy" factor. The separation factor of two such solutes (u and v) differing only in the chemical nature of the unique face is:

$$F_{uv} = \frac{k'_{v(1)}}{k'_{u(1)}} = \frac{\exp(-\beta\Delta w_{s(v)}^*) + 5\exp(-\beta\Delta w_s)}{\exp(-\beta\Delta w_{s(u)}^*) + 5\exp(-\beta\Delta w_s)} .$$

For convenience, consider the case $-\beta\Delta w_{s(v)}^* > -\beta\Delta w_{s(u)}^*$, so that $F_{uv} > 1$. The maximization of $F_{uv}$ is achieved when $\Delta w_s$ is as positive as possible. This would minimize the retention contribution associated with the five common faces (representing, perhaps, nonpolar groups) and would reduce their interference with the separation. Under these conditions,

$$F_{uv} \simeq \exp\{-\beta\Delta(\Delta w_s^*)\}, \text{ where } \Delta(\Delta w_s^*) = \Delta w_{s(v)}^* - \Delta w_{s(u)}^* .$$

As is well known, such "chemical-type" separations can be accomplished in a NP system with a polar adsorbent and a solvent of moderate polarity. That is, the solvent should be polar enough to produce a positive $\Delta w_s$ and to elute the solutes in a resonable period of time, but not so polar as to inhibit access of the polar functional group of the solute to the adsorbent surface.

## Nonmonomeric Solutes

The above analysis was based solely on energetic considerations. Let us now examine the additional effects of solute geometry, i.e., size and shape, on retention and selectivity.

For two chemically homogeneous solutes, a 1 x 1 x p rod and a 1 x m x n plate, equation (10) yields:

$$K_{3(1)}^{rod} = (1/3)\exp(-\beta\Delta w_s) + (2/3)\exp(-\beta\Delta w_s p)$$

$$K_{3(1)}^{plate} = (1/3)\exp(-\beta\Delta w_s m) + (1/3)\exp(-\beta\Delta w_s n) + (1/3)\exp(-\beta\Delta w_s mn).$$

Note that each contribution to $K_{3(1)}$ consists of the product of the fraction of ways a particular solute adsorption mode can be achieved and the Boltzmann factor involving the interchange free energy for that mode. In $K_{3(1)}^{rod}$, the first term represents the vertical-adsorption contribution and the second, the horizontal-adsorption contribution. As with monomeric solutes, absolute retention increases as $\Delta w_s$ becomes more negative and decreases as $\Delta w_s$ becomes more positive.

The foregoing expressions may be used to illustrate selectivity on the basis of solute shape. Consider, for example, the separation of two geometrical isomers of comparable molecular volume, a 1 x 1 x 6 rod and a 1 x 2 x 3 plate. Letting $F = K_{3(1)}^{rod}/K_{3(1)}^{plate}$, it is clear that when $\Delta w_s = 0$, $K_{3(1)}^{rod} = K_{3(1)}^{plate}$ and $F = 1$. In this case, each of the six solute faces has the same probability of adsorbing on the surface. The effective adsorption cross-sectional area $<A_3>$, relative to that of the solvent, is then 13/3 for the rodlike solute and 11/3 for the platelike one. When $\Delta w_s \neq 0$, $F > 1$ and separation becomes possible. For $\beta\Delta w_s = +0.5$ (solute prefers the mobile phase), $F = 1.10$ and the tendency for both solutes is to adsorb on the surface through their smallest-area faces. With increasing $\beta\Delta w_s$, $<A_3> \rightarrow 1$ for the rods and $<A_3> \rightarrow 2$ for the plates. For $\beta\Delta w_s = -0.5$ (solute prefers the stationary phase), $F = 1.53$ and adsorption via the largest-area faces is favored. This tendency becomes more pronounced as $\beta\Delta w_s$ becomes more negative, leading to an optimum F value of 2.00, with $<A_3> \rightarrow 6$ for both solutes. It would appear, therefore, that this separation could be achieved using a nonpolar adsorbent (20-22) and a solvent of greater polarity than the solutes, as in a RP system. Since the main interaction between the solute or solvent and the adsorbent would then involve dispersion forces, the desired negative $\beta\Delta w_s$ would stem primarily from stronger solvent-solvent interactions relative to unit-area solute-solvent interactions.

It is possible to treat other solute shapes within the framework of the model. Consider, for example, U-shaped and Z-shaped hexamers of unit thickness, representing, perhaps, _cis_ and _trans_ isomers, respectively:

$$K^{Z}_{3(1)} = (1/3)\exp(-\beta\Delta w_s) + (1/3)\exp(-2\beta\Delta w_s) + (1/3)\exp(-6\beta\Delta w_s)$$

$$K^{U}_{3(1)} = (1/2)\exp(-2\beta\Delta w_s) + (1/6)\exp(-4\beta\Delta w_s) + (1/3)\exp(-6\beta\Delta w_s)$$

$$F = K^{Z}_{3(1)}/K^{U}_{3(1)}.$$

It can be shown that, provided $\beta\Delta w_s$ is sufficiently positive, a respectable separation is attainable (e.g., $F = 1.53$ when $\beta\Delta w_s = +0.5$). This indicates that the solvent/adsorbent system should be selected to produce somewhat stronger 1-s interactions relative to unit-area 3-s interactions and/or somewhat stronger unit-area 1-3 interactions relative to 1-1 interactions. As discussed earlier, this is feasible with a well-chosen NP system.

Turning now to a direct application of the theory, let us examine homologous series separations. It is well known that NP systems with polar adsorbents are not effective in separating, for example, a homologous series of _n_-alkyl alcohols, whereas RP systems with carbon adsorbents are (20,21). The theory affords an interpretation of this and affirms the important role of strong solvent-solvent interactions in the RP separations.

Regarding the solute molecules in question as chemically heterogeneous rods of length p and unit-area base, each consisting of an energetically unique face (denoted by a star) of unit area and five energetically equivalent faces (one of unit area and the remaining four of area p), we have from equation (10):

$$K_{3(1)} = (1/6)\exp(-\beta\Delta w^{*}_{s}) + (1/6)\exp(-\beta\Delta w_s) + (2/3)\exp(-\beta\Delta w_s p),$$

where $\Delta w^{*}_{s}$ and $\Delta w_s$ are the unit-area interchange free energies relating to the unique face (the polar functional group) and the other five faces (the alkyl portion of the molecule), respectively. Of interest is the variation of $\ell n\ K_{3(1)}$ with solute chain length p (roughly, solute carbon number):

$$S_p = \frac{d\ell nK_{3(1)}}{dp} = \frac{d\ell nk'_{3(1)}}{dp} = \frac{-4\beta\Delta w_s}{4+\exp(-\beta\Delta w_s^{*}+\beta\Delta w_s p)+\exp(-\beta\Delta w_s+\beta\Delta w_s p)} \qquad (11)$$

where the magnitude of $S_p$ is thus a measure of the goodness of a homologous series separation. In general, $S_p$ varies with solute carbon number and its direction is determined by the sign of $\beta\Delta w_s$.

If $\beta\Delta w_s$ is positive, $S_p$ will be negative and will rapidly approach zero with increasing p. To simulate a typical NP system with a silica-gel adsorbent and a solvent which, as before, is of modest polarity, consider the combination $\beta\Delta w_s^{*} = -0.50$ and $\beta\Delta w_s = +0.50$. From equation (11), one calculates that $S_p = -0.21$ at $p = 1$, diminishing to $S_p = -0.03$ at $p = 6$. Such a system would not be effective for separating homologs in the vicinity of n-$C_6$. Indeed, in this p range the $\beta\Delta w_s^{*}$ contribution controls both the $k'_{3(1)}$ and $S_p$ values, and the predominant mode of solute adsorption is vertical adsorption through the unique face.

On the other hand, in an RP system with a carbonaceous adsorbent and a polar solvent, one would expect $\beta\Delta w_s$ to be negative because of strong solvent-solvent interactions, as discussed earlier. Further, since $-w_{13}^{*} > -w_{13}$, the inequality $-\beta\Delta w_s > -\beta\Delta w_s^{*}$ would hold. For illustrative purposes, consider the combination $\beta\Delta w_s^{*} = -0.40$ and $\beta\Delta w_s = -0.60$. One calculates that $S_p = 0.43$ at $p = 1$, increasing to $S_p = 0.59$ to $p = 6$, and reaching $S_p = -\beta\Delta w_s = 0.60$ at higher $S_p$. Hence, excellent homologous-series separation is predicted over the entire p range, and $S_p$ in the vicinity of n-$C_6$ is essentially equal to the limiting $S_p$ value. (This would obtain for any realistic value of $\beta\Delta w_s^{*}$.) Here, the $\beta\Delta w_s p$ contribution controls both $k'_{3(1)}$ and $S_p$, and the horizontal mode of solute adsorption dominates. The theory thus predicts that, for sufficiently large p, $S_p$ should be independent of the chemical nature of the polar functional group and should be approximately equal to $-\beta\Delta w_s$.

To test the theory, the results of Guiochon et al (20,23) are analyzed. Shown in Figure 2 of ref. 20 are linear plots of $\log_{10}k'_{3(1)}$ vs. solute carbon number for n-alkyl benzenes, bromides, chlorides and alcohols. In this RP system, the adsorbent used was a modified carbon black and the solvent was acetonitrile (ACN). Analysis of the data gives $S_p = 0.56$, independent of solute functionality, as predicted. Also, the alcohols have the smallest k' values. This follows from the theory in that the alcohols are expected to have the most negative $w^*_{13}$, the highest $\Delta w^*_s$ and, hence, the shortest retention. Guiochon's group also determined k''s using pyrocarbon coated on silica as the adsorbent (21-23). The solute series studied were n-alkanes and n-alkyl benzenes and methyl esters; the solvents were ACN and a 50/50 (v/v) mixture of ACN and $H_2O$ (23). For sufficiently large carbon number, the plots are again virtually linear, yielding $S_p$ values of +0.49 and +0.71 with the former and latter solvent, respectively, independent of solute functionality. Moreover, in the light of the theory, both the larger $S_p$ and higher k' values found with the latter solvent must be due to stronger solvent-solvent interactions (more negative $w_{11}$, hence, more negative $\Delta w_s$). Clearly, unlike many NP processes, the mechanism of retention and selectivity cannot be reasonably addressed in RP-LAC without accounting for solvent-solvent interactions.

## HETEROGENEOUS ADSORBENT AND NEAT SOLVENT

For a chemically and/or energetically heterogeneous adsorbent and a single-component solvent, it is usually assumed (1,10,14) that:

$$K_{3(1)} = \sum_j g_j K_{3(1),j} \tag{12}$$

where $g_j$ is the fraction of type-j adsorption sites and $K_{3(1),j}$ is the distribution constant with a homogeneous adsorbent of type j. (A similar expression may be written for $k'_{3(1)}$.) We note from equation (1) that equation (12) is strictly valid only for monomeric solutes ($A_{3_i} = 1$ for all i).

Consider, for example, a chemically homogeneous rodlike solute and a heterogeneous adsorbent consisting of two types of sites (s and t). From equation (1):

$$K_{3(1)} = \frac{1}{3}[g_s\exp(-\beta\Delta w_s) + (1-g_s)\exp(-\beta\Delta w_t)] + \frac{2}{3}[g_s\exp(-\beta\Delta w_s) + (1-g_s)\exp(-\beta\Delta w_t)]^p, \quad (13)$$

where $\Delta w_s = w_{3s} - w_{1s} + w_{11} - w_{13}$, and $\Delta w_t = w_{3t} - w_{1t} + w_{11} - w_{13}$. Equation (13) reveals that the equilibrium distribution constant consists of a sum of two contributions: the first term corresponds to retention by vertical adsorption of solute on either an s or t type site, while the second term corresponds to horizontal adsorption on p contiguous and <u>randomly distributed</u> s or t type sites. Clearly, only if p = 1 can equation (13) be written in the form of equation (12):

$$K_{3(1)} = g_sK_{3(1),s} + (1-g_s)K_{3(1),t} \;. \quad (14)$$

However, in the special case where vertical adsorption dominates (sufficiently positive Δw's and large p), equation (14) represents a reasonable approximation (24).

## HOMOGENEOUS ADSORBENT AND BINARY SOLVENT MIXTURE

The treatments and discussion in this section are based on equations (4) to (9), which specifically deal with homogeneous adsorbents and monomeric solutes and solvents. In many cases the component molecules of the experimental systems to be examined differ in size and shape, therefore precluding fully quantitative analysis of the data via the present model. Nevertheless, the general validity of these equations will be demonstrated, as will the importance of solution-nonideality effects.

In principle, the δ's in this model can be determined from experimentally accessible solution-phase activity coefficients of 2 in 1 ($\gamma_{2(1)}$) and of 3 at infinite dilution in a mixture of 1 + 2 ($\gamma^{\infty}_{3(1+2)}$):

$$\ln \gamma_{2(1)} = 6\beta\delta_{12}z_1^2$$

$$\ln \gamma^{\infty}_{3(1+2)} = 6\beta\,\delta_{13}z_1 + 6\beta\delta_{23}z_2 - 6\beta\delta_{12}z_1z_2,$$

where $\gamma$ measures the deviation from Raoult's law, and $z$ refers to the mole fraction. Again, however, the above equations are only approximate when applied to mixtures consisting of molecules of disparate size and shape (25).

In the subsequent analysis, the K's will be replaced by k''s in equations (4) to (9), as justified earlier. Also, 1 and 2 will will refer to, respectively, the less and more polar components of the binary solvent mixture. The monomeric solute will be formally regarded as being chemically homogeneous. This is not as restrictive as might appear, because the relevant interchange free energy may be viewed as an effective or averaged quantity, $<\Delta w_s>$. For instance, setting $A_{3_i} = 1$ in equation (10), we obtain:

$$<\Delta w_s> = \frac{\sum_{i=a}^{f} \Delta w_{s,i} \exp(-\beta\Delta w_{s,i})}{\sum_{i=a}^{f} \exp(-\beta\Delta w_{s,i})} \quad ,$$

where we have averaged over the six faces of the solute molecule, which, in general, may be chemically heterogeneous.

## Reversed-Phase Systems

From equations (6) and (10), the relative retention of a particular solute with neat solvents 1 and 2 is given by:

$$k'_{3(2)}/k'_{3(1)} = \exp[\beta(w_{2s} - w_{1s} + \frac{w_{11}}{2} - \frac{w_{22}}{2} + \delta_{23} - \delta_{13})]. \qquad (15)$$

If the homogeneous adsorbent is a nonpolar carbonaceous one, so that $w_{2s}$ and $w_{1s}$ are determined primarily by dispersion forces, then solvent-solvent and solvent-solute interactions will govern the magnitude of the relative capacity ratios. Furthermore, if component 2 is highly polar (e.g., $H_2O$), one would expect $-w_{22}$ to be much greater than $-w_{11}$ and, except for solutes much more polar than component 1, $\delta_{23}$ to be greater than $\delta_{13}$. Thus, $k'_{3(2)} >> k'_{3(1)}$ in the usual RP system.

With a binary mixed-solvent system, the stationary-phase composition ($y_2$) can be determined for a given mobile-phase composition ($x_2$) through equation (7). Using various realistic sets of values for $k'_{3(2)}/k'_{3(1)}$, $\delta_{12}$, $\delta_{13}$ and $\delta_{23}$, it can be shown that, in a typical aqueous RP system, $y_2$ should remain quite small until rather high $x_2$ values are reached. For example, with $k'_{3(2)}/k'_{3(1)} = 50, \beta\delta_{12} = \beta\delta_{13} = 1/3$ and $\beta\delta_{23} = 2/3$, one calculates that $y_2 \simeq 0.005$ at $x_2 = 0.50$, $y_2 \simeq 0.01$ at $x_2 = 0.90$, and $y_2 \simeq 0.09$ at $x_2 = 0.99$. (Note that the condition $\beta\delta_{12} > 1/3$ corresponds to phase separation, i.e., a region of solvent immiscibility). In other words, for $x_2 < 0.90$, it is reasonable to assume that $y_2 \simeq 0$ ($y_1 \simeq 1$). Clearly, solvent component 2 prefers to stay in the mobile phase to take better advantage of strong 2-2 interactions, thereby "driving" the less polar solvent component into the stationary-phase layer.

Accordingly, setting $y_1 = 1$ in equation (8), we have:

$$\ell n\, k'_{3(1+2)} = \ell n\, k'_{3(1)} - \ell n\,(1-x_2) - 6x_2(\delta_{12}+\delta_{13}-\delta_{23})\beta. \quad (16)$$

Neglecting the solution-nonideality contribution in equation (16), one would predict that, independent of the nature of the solute:

$$S_x = d\ell n\, k'_{3(1+2)}/dx_2 = (1-x_2)^{-1}, \quad (17)$$

where $S_x$ is the slope of a $\ell n$ k' vs. $x_2$ plot. Including this contribution, we obtain:

$$S_x = (1-x_2)^{-1} - 6(\delta_{12} + \delta_{13} - \delta_{23})\beta. \quad (18)$$

Experimental results for various solutes with a pyrocarbon-on-silica adsorbent and a methanol-water solvent mixture do not conform to equation (17). (See Figure 9b of ref. 21.) Indeed, the $\ell n$ k' vs. solvent composition plots for most of the solutes are virtually linear, displaying positive $S_x$ values much greater than unity. Equation (18) can account for this behavior if $\delta_{12} + \delta_{13} - \delta_{23}$ is sufficiently negative. Choosing a typical solute, the results for nitrobenzene are analyzed in more detail.

With $\beta(\delta_{12} + \delta_{13} - \delta_{23}) = -0.88$, equation (16) furnishes an excellent fit, and the observed average slope ($S_x \approx 6.5$) and slight curvature are faithfully reproduced. This value most likely reflects a very positive $\delta_{23}$ value which, in turn, stems from the relative weakness of 2-3 interactions compared to the strength of 2-2 interactions. It is consistent with the low solubility and high activity coefficient of nitrobenzene in water.

It is also possible to rationalize the relative $k'_{3(1)}$'s: nitrobenzene>chlorobenzene≈pyridine>toluene>phenol>benzene>aniline. According to our model, this order should follow the combined ranking of the strength of 3-s and the weakness of 1-3 interactions. Finally, the average $S_x$ values go as follows: chlorobenzene≈toluene>benzene>aniline≈nitrobenzene≈phenol>pyridine. This descending order may follow $\delta_{23}$, which becomes less positive with increasing strength of 2-3 interactions, leading to smaller $S_x$ values and increased curvature (equation (18)). This could explain the observed behavior of pyridine, which is the solute best accommodated by $H_2O$ (21).

### Normal-Phase Systems

In typical NP-LAC systems with a polar adsorbent and a mixed solvent containing a fairly polar moderator (component 2), it generally holds that $k'_{3(1)} >> k'_{3(2)}$. This is usually rationalized in terms of the relative strengths of 1-s and 2-s interactions. While this may be largely so, equation (15) suggests that solvent-solvent and solute-solvent interactions could also play a role. This is borne out in the following analysis.

Employing realistic values of $k'_{3(2)}/k'_{3(1)}$, $\delta_{12}$ and $\delta_{12} + \delta_{23} - \delta_{13}$, application of equation (7) reveals that the usual situation in mixed-solvent NP processes is that $y_2 >> x_2$ for small $x_2$. For example, letting $k'_{3(2)}/k'_{3(1)} = 0.01, \beta\delta_{12} = 1/3$ and $\beta(\delta_{12} + \delta_{23} - \delta_{13}) = 1/3$, we find that at an $x_2$ of less than 0.03, $y_2 = 0.99$. (Note that the calculation is particularly sensitive to the value of $\beta\delta_{12}$.) Accordingly, for sufficiently large $x_2$ (i.e., a few mole percent), it is generally reasonable to let $y_2 \approx 1$ in equation (9), yielding:

$$\ell n\ k'_{3(1+2)} = \ell n\ k'_{3(2)} - \ell n\ x_2 - 6x_1(\delta_{12} + \delta_{23} - \delta_{13})\beta. \qquad (19)$$

Neglecting the solution-nonideality contribution, one would predict that, independent of the nature of the solute:

$$S_{\ell n\ x} = d\ \ell n\ k'_{3(1+2)}/d\ \ell n\ x_2 = -1, \qquad (20)$$

where $S_{\ell n\ x}$ is the slope of a $\ell n$ k' vs. $\ell n\ x_2$ plot. Including this contribution, we obtain:

$$S_{\ell n\ x} = -1 + 6x_2(\delta_{12} + \delta_{23} - \delta_{13})\beta, \qquad (21)$$

where we note that $S_{\ell n\ x}$ may increase or decrease with increasing $\ell n\ x_2$, depending on the sign of the $\delta$ term. Equations (19) to (21) are strictly valid for $x_2 > x_2'$, where $x_2'$ is the mobile-phase composition at which $y_2$ becomes sufficiently close to unity (say, $y_2 \approx 0.99$). In this composition region the solute is essentially "competing" with the polar moderator for a surface adsorption site.

Many NP systems conform at least approximately to equation (20), indicating that solution-nonideality effects are often unimportant (2,8,26). In other cases, however, pronounced curvature is observed in $\ell n$ k' vs. $\ell n\ x_2$ plots (6,7,11,27,28), consistent with equation (21).

Slaats et al (7) have carried out studies with silica as the absorbent, n-heptane as the nonpolar solvent component, 2-propanol and ethyl acetate as moderators, and 1-phenylethanol (PE), benzyl acetate (BA) and nitrobenzene (NB) as the solutes. With 2-propanol, the plot for PE is found to be virtually linear ($S_{\ell n\ x} \approx -0.9$), while those for BA and NB display slopes which (roughly) become less negative with increasing $x_2$. This suggests that the solution-nonideality term in equation (21) is a small positive quantity for PE and a larger positive quantity for the other solutes. [With $\beta \cdot (\delta_{12} + \delta_{23} - \delta_{13}) \approx +0.2$, we obtain the observed $S_{\ln x}$ for PE.] This may be interpreted as follows. Because of the functional similarity between PE and 2-propanol, one would expect $\delta_{12}$ to be close to $\delta_{13}$, and $\delta_{23}$ to be close to zero. For the less "polar" BA and NB, one would anticipate the inequalities $\delta_{12}>\delta_{13}$ and $\delta_{23}>0$. This is in qualitative accord with the published activity coefficient data (7,25). Similar arguments may be presented in analyzing the results with the less polar moderator ethyl acetate. Here, though, the plot for BA most closely follows equation (20), as expected, while those for PE and NB exhibit slopes which become more negative with increasing $x_2$, indicating that $\delta_{12} + \delta_{23} - \delta_{13}$ is negative.

### Comparison With Previous Models

Multiplying both sides of equation (8) by $x_1$ and equation (9) by $x_2$ and adding, we find:

$$\ln k'_{3(1+2)} = y_1 k'_{3(1)} \exp[(6x_1-5y_1-1)\cdot\beta(\delta_{12}+\delta_{13}-\delta_{23})]$$

$$+ y_2 k'_{3(2)} \exp[(6x_2-5y_2-1)\cdot\beta(\delta_{12}+\delta_{23}-\delta_{13})]. \tag{22}$$

*Only if* we then assume *ideal-solution* behavior (i.e., $\delta_{mn} = 0$), do we obtain the expression commonly used to treat binary mixed-solvent systems (1,8,9,13):

$$k'_{3(1+2)} = y_1 k'_{3(1)} + y_2 k'_{3(2)} \ . \tag{23}$$

In terms of mobile-phase composition, the ideal-solution counterpart of equation (23) is a special case of equation (14):

$$(1/k'_{3(1+2)}) = (x_1/k'_{3(1)}) + (x_2/k'_{3(2)}), \tag{24}$$

which is of the same general form as the expression proposed by Scott and Kucera (3,4,8). For $x_2/k'_{3(2)} >> x_1/k'_{3(1)}$, as is the case in most NP systems for sufficiently large $x_2$, equation (24) may be approximated by:

$$\ln k'_{3(1+2)} = \ln k'_{3(2)} - \ln x_2 \ , \tag{25}$$

a result derived previously by others (8). (Note that equation (19) reduces to equation (25) when $\delta_{mn} = 0$.)

It can also be shown that the useful NP equations developed by Snyder (1,2) represent a special case of our general theory. If we assume ideal-solution behavior and consider a nonmonomeric solute for which one mode of surface adsorption is dominant, the modified form of equation (15) is:

$$\ell n\ (k'_{3(2)}/k'_{3(1)}) = A_3 \cdot \beta(w_{2s} - w_{1s} + \frac{w_{11}}{2} - \frac{w_{22}}{2}),$$

where $A_3$ is the relative area of that face of the solute molecule corresponding to the dominant mode. Keeping in mind that w is a negative quantity and assuming that the strength of solvent-adsorbent interactions is proportional to that of solvent-solvent interactions (proportionality constant of $\alpha$), we obtain Snyder's well-known expression:

$$\ell n\ (k'_{3(2)}/k'_{3(1)}) = \alpha'_s A_3(\varepsilon_1 - \varepsilon_2), \tag{26}$$

where $\alpha'_s = \alpha-(1/2)$, $\varepsilon_1 = -\beta w_{11}$ and $\varepsilon_2 = -\beta w_{22}$. Also, $\alpha'_s$ is referred to as the adsorbent-activity parameter and $\varepsilon$ as the solvent strength parameter.

With a binary ideal mixed-solvent system, equation (24) may be rearranged to give:

$$\ell n\ (k'_{3(1)}/k'_{3(1+2)}) = \ell n\ [1 + x_2(\frac{k'_{3(1)}}{k'_{3(2)}} - 1)]. \tag{27}$$

According to Snyder, by analogy to equation (26):

$$\ell n\ (k'_{3(1)}/k'_{3(1+2)}) = \alpha'_s A_3(\bar{\varepsilon} - \varepsilon_1), \tag{28}$$

where $\bar{\varepsilon}$ is the effective solvent strength of the binary mixture. Substituting $k'_{3(1)}/k'_{3(2)}$ from equation (26) into the r.h.s. of equation (27), and comparing the result with the r.h.s. of equation (28), we obtain:

$$\bar{\varepsilon} = \varepsilon_1 + \frac{\ell n\ [x_2(\exp\{\alpha'_s A_3(\varepsilon_2 - \varepsilon_1)\}) + 1 - x_2]}{\alpha'_s A_3} \tag{29}$$

which is Snyder's familiar equation.

It should be emphasized that equations (23) to (29) are all based on the assumption of solution ideality. In the previous parts of this section, evidence was presented that this assumption is often not justifiable.

## CONCLUDING REMARKS

In this study we have demonstrated the utility and significance of a new molecular theory of LAC. The theoretical model itself is consistent with the commonly held view that the stationary phase is formed by the adsorption of a monolayer of solvent on the adsorbent surface. Recently, however, Scott and Kucera (29) executed careful measurements, the results of which were interpreted as indicative of bilayer formation in certain cases (high concentration of polar or hydrogen-bonding solvents on silica-gel surfaces). It was also suggested that some solutes may interact only with the primary layer, displacing solvent in the second layer, but not interacting directly with the adsorbent surface itself. Should this view prevail, the current model would have to be adapted to allow for the possibility of multilayer adsorption (17).

It must be pointed out, however, that deviation from the Langmuir isotherm for monolayer adsorption does not necessarily imply multilayer adsorption. The deviation might simply be due to solution-nonideality effects (30). Indeed, a remarkable variety of isotherm shapes can be generated from equation (7), depending on the values of the molecular parameters (15). Only for ideal solutions ($\delta_{mn} = 0$), does equation (7) produce the expected Langmuir form:

$$y_2 = \eta_{12}x_2/[1 + (\eta_{12} - 1)x_2],$$

where $\eta_{12} = K_{3(1)}/K_{3(2)}$.

Finally, we mention that, in an attempt to simulate chromatographic behavior with chemically bonded phases, our model is currently being extended to include highly modified adsorbents.

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16. In ref. 15 we treat the more general, but experimentally rarer case of finite solute concentration.

17. Note that the model can be extended to allow for the possibility of multilayer adsorption (see Concluding Remarks). It is also possible to treat "nomonomeric" solvent molecules, such as rodlike ones.

18. Each w may be written in the form $w = \varepsilon - k_B T \ell n\ q$, where $\varepsilon$ is an interaction energy and q is a molecular partition function (15). Therefore, w is a temperature-dependent free-energy term.

19. In ref. 15 we also consider binary solvent mixtures with heterogeneous adsorbents and with solutes of different size and shape.

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24. Equation (14) would be valid for macroscopically heterogeneous adsorbent surface consisting of very large clusters of s-type sites separated from very large clusters of t-type sites. In that case, horizontal adsorption of the solute would essentially take place on p continguous s-type sites or p contiguous t-type sites, rather than on p contiguous and randomly distributed (i.e., heterogeneous on a molecular level) s or t type sites.

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27. Although their model is different than ours, Slaats et al (7) have properly identified solution nonideality, in the mobile phase and in the stationary phase, as a major source of such curvature.

28. In some cases (3,4), too small an $x_2$ range has been studied to establish the definite presence or absence of curvature.

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