

Improved model of multicomponent adsorption in reversed-phase liquid chromatography

Jorge E. Garcia-Galdo^a, José Cobas-Rodríguez^a,
Ulises J. Jáuregui-Haza^a, Georges Guiochon^{b,c,*}

^a *Departamento de Desarrollo Tecnológico, Centro de Química Farmacéutica (CQF), Calle 200 y 21, Apdo. 16042, Atabey, Playa, La Habana, Cuba*

^b *Department of Chemistry, The University of Tennessee, Buehler Hall, Knoxville, TN 37996-1600, USA*

^c *Chemical Sciences Division, Oak Ridge National Laboratory, Oak Ridge, TN 37831-6120, USA*

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Abstract

This work presents a modification to the real adsorbed solution model using a Flory–Huggins type of expression that was reported previously. This modification consists in replacing the Flory–Huggins activity coefficient by the spreading pressure dependent approach. This new model takes into account explicitly the adsorbate–adsorbate interactions taking place in the adsorbed phase. It provides an excellent prediction of the competitive, ternary adsorption equilibrium of benzyl alcohol, 2-phenylethanol and 2-methyl benzyl alcohol observed in a reversed-phase liquid chromatographic system using information merely derived from the single-component adsorption experimental data.

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1. Introduction

Preparative chromatography is now widely used in the pharmaceutical industry for the large-scale purification and/or separation of drugs or drug intermediates. The development of a new chromatographic method and particularly its scale-up is a complex operation due to the number of parameters involved, to the fact that the process is almost always conducted under nonlinear conditions, and that the optimization of nonlinear processes is still a very difficult task [1].

Mathematical models for nonlinear chromatography combined with the proper model of adsorption isotherm allow the accurate prediction of elution band profiles under a wide range of operating conditions, hence the optimization of the separation process. The knowledge of the adsorption isotherm is an important prerequisite for any reliable predictive calculation of a chromatographic process. There are many reports discussing single-component adsorption. Few such reports deal with binary adsorption because the experi-

mental determination of competitive adsorption equilibrium data is a difficult, time consuming, and costly task [1–6].

The few sets of experimental data available have been used to develop and validate predictive models of multicomponent adsorption isotherms. These models attempt to estimate competitive adsorption equilibria using only parameters that can be derived from single-component isotherms [7,8]. Different models of this type have been used to correlate single-component adsorption data and to predict binary equilibria, for instance the models of Langmuir [9], Le Van and Vermeulen [10], Fowler and Guggenheim [11], Moreau et al. [12], Ruthven [7], Kiselev [13], Langmuir–Freundlich [14], Jovanovic–Freundlich [8], Fowler–Guggenheim/Langmuir–Freundlich (FGLF) [15], Fowler–Guggenheim–Jovanovic–Freundlich (FGJF) [8] as well as various models derived from the adsorbed solution theory (AST) and based on different assumptions [16]. In almost all cases, the results obtained are not completely satisfactory.

Very few chemists have ever studied the competitive adsorption of ternary mixtures and, among them, Quiñones et al. [17] were the first to report on the determination of actual ternary adsorption data in a chromatographic system (benzyl alcohol, 2-methyl benzyl alcohol and

* Corresponding author. Tel.: +1-865-974-0733,

fax: +1-865-974-2667.

E-mail address: guiochon@utk.edu (G. Guiochon).

2-phenylethanol on C₁₈-silica with aqueous solutions of methanol) and to attempt a prediction of the ternary adsorption isotherms of such mixtures from the parameters of the corresponding single-component isotherms [17]. In their work, they used frontal analysis for the determination of the adsorption data which they modeled using the real adsorbed solution theory (RAST) and applying the Flory–Huggins activity coefficient equation [18] to account for the non-ideal behavior of the compounds in the adsorbed phase. The Flory–Huggins activity equation takes into account the size difference of the molecules [19]. The model derived by Quiñones et al. [17] provides a good prediction of the ternary equilibrium studied, using only numerical parameters derived from the analysis of the three sets of single-component adsorption data. Earlier, Minka and Meyers [20] had determined the excess isotherms of benzene, ethyl acetate and cyclohexane on activated carbon, using a batch method and measuring the solute concentrations before and after immersion of the adsorbent in known solutions. Later, Lisec et al. [21] measured the ternary isotherms of phenol, 2-phenylethanol, and 3-phenyl-1-propanol on a similar C₁₈-silica column with a 1:1 mixture of water and methanol and found that a ternary Langmuir model approximately accounts for the adsorption behavior of this system. Recently, Siperstein and Myers [22] reported competitive adsorption data for mixtures of CO₂, C₂H₄, and C₂H₆ on zeolites.

In this paper, we describe the results obtained when using an alternative approach, the spreading pressure dependent (SPD) activity-coefficient equation [23,24], in order to account for the nonideal behavior of the adsorbate, using the same RAST model as the one derived by Quiñones et al. [17]. This new model, which accounts for the lateral interactions between the adsorbed components, has a better predictive capability for the ternary mixture studied.

2. Theory

Myers and Praustnitz [16] developed the ideal adsorbed solution theory (IAST) in 1965, for gas–solid systems. This same concept was later extended to liquid–solid adsorption systems [25]. Generally, at low concentrations, the IAST model gives an accurate prediction of the behavior of multicomponent equilibria, even in the case of the complex, nonideal systems that describe the adsorption equilibrium of some basic drugs [3]. However, from a theoretical point of view, the applicability of IAST models is restricted to the case of dilute solutions. This thermodynamical approach can be extended to high concentrations systems by including the corresponding activity coefficients into real adsorption solution theory (RAST) models that apply when the adsorbed phase exhibits significant deviations from ideal behavior [26]. Other significant contributions to the thermodynamics of multicomponent adsorption equilibrium include models based on AST and that take into account the heterogeneity of the adsorbent surface [27].

2.1. RAST model using a Flory–Huggins-type expression (RAST-FH)

Recently, Quiñones et al. [17] proposed the following RAST model:

$$\frac{\gamma_i^a \theta_i}{\gamma_s^a (1 - \sum_{k=1}^{N_s} \theta_k)} \frac{n^\infty \gamma_i^{b,\infty}}{\rho_b K_i \gamma_i^{a,\infty}} = \gamma_i^b x_i^b \quad (1)$$

In this equation, the superscripts a and b stand for the adsorbed and the liquid phase, respectively, ρ_b is the molar density of the liquid phase, $\rho_b = C_i/x_i$, x_i is the mole fraction of compound i , C_i is its molar concentration, $\theta_i = q_i/n^\infty$, n^∞ is the saturation capacity of the adsorbed layer, γ_i^b and γ_i^a are the activity coefficients in the bulk liquid and in the stationary phase, respectively, N_s is the number of solutes in the system and K_i is the Henry constant.

Eq. (1) allows the calculation of the mole fraction of solute i in the adsorbed phase. The mole fraction of solute i in the adsorbed phase is:

$$x_i^a = \theta_i = \frac{q_i}{n^\infty} \quad (2)$$

The nonideal behavior of the solute in the liquid phase was estimated using the UNIFAC method [28]. The nonideal behavior of the adsorbate molecules in the adsorbed phase was accounted for using a Flory–Huggins expression:

$$\ln \gamma_i^a = 1 - \ln \sum_{j=1}^N \frac{\alpha_j}{\alpha_i} x_j^a - \frac{1}{\sum_{j=1}^N (\alpha_j/\alpha_i) x_j^a} \quad (3)$$

where α_i and α_j are model parameters and N is the total number of components, including the solvent. It was assumed that, for the solvent present in the adsorbed phase, $\alpha_s = 1$.

Quiñones et al. [17] fitted the single component experimental adsorption data obtained for benzyl alcohol, 2-phenylethanol and 2-methyl benzyl alcohol on their RP-18/water:methanol chromatographic system to their nonideal model (Eq. (1)), using the Wilson model [29] to account for the nonideal behavior in the adsorbed phase. This model provided an excellent correlation of the single component data. The Wilson model represents explicitly the solute–solute interactions using binary parameters. It could not be used for the predictive calculation of the multicomponent equilibria due to the unavailability of the Wilson parameters for solute–solute interactions.

2.2. RAST model using a SPD-type expression (RAST-SPD)

For nonideal multicomponent systems, it is necessary to find an expression of the activity coefficient that accounts for the nonideal behavior of the adsorbed phase. In order to evaluate expressions that allow an accurate prediction of multicomponent equilibria, the spreading-pressure dependent (SPD) activity coefficient model was selected. The theory of the SPD model was adapted for the adsorbate

phase and used by Talu and Zwiebel [23] in order to describe competitive gas adsorption. This model is known as the SPD-nonideal adsorbed solution (SPD-NAS) model. Not only does the SPD-NAS account for the combined effects of the adsorbate–adsorbate interactions, it also allows us to account empirically for the surface heterogeneity of the adsorbent by lumping together these two effects into the single adsorbed phase activity coefficient of each compound [24]. The model can be used in a predictive fashion for the calculation of multicomponent equilibria for gas–solid adsorption systems [23,24]. As indicated earlier, the model explicitly accounts for the lateral interactions between the adsorbed components:

$$\ln \gamma_i = -q_i \ln \left(\sum_{j=1}^N \beta_j \tau_{ji} \right) + q_i - q_i \sum_{k=1}^N \frac{\beta_k \tau_{kj}}{\sum_{k=1}^N \beta_k \tau_{kj}} \quad (4)$$

with

$$\beta_i = \frac{q_i x_i}{\sum_{k=1}^N q_k x_k} \quad (5)$$

$$\tau_{ij} = \exp \left(\frac{z(E_i - E_{ij})}{2RT} \right) \quad (6)$$

In these equations, q_i is a shape factor, E_i is the single component lateral interaction potential, and E_{ij} is the cross-lateral interaction potential, z is the coordination number. The summation is performed over all species, including the solvent adsorbed on the stationary phase.

Usually, the dependence of the activity coefficients on the spreading pressure is related to the lateral interaction potential through the following equation [23]:

$$E_i = \frac{Q_{j\pi}^{\text{st}} - Q_{j0}^{\text{st}}}{(1/2)zM} \quad (7)$$

In this expression, $Q_{j\pi}^{\text{st}}$ is the isosteric heat of adsorption of the single component j under the same spreading pressure as the mixture, Q_{j0}^{st} is the limit isosteric heat of adsorption at zero surface coverage, and M is the Avogadro number.

If the molecules have similar sizes and adsorptive properties, the cross-lateral interaction parameters can be calculated using the following mixture rule [30]:

$$E_{ij} = (E_i E_j)^{1/2} \quad (8)$$

When there are appreciable differences between the properties (size and adsorption energy), of the molecules studied, the right hand side of Eq. (8) should be modified using a correction factor δ_{ij} [30]:

$$E_{ij} = (E_i E_j)^{1/2} (1 - \delta_{ij}) \quad (9)$$

The parameters δ_{ij} are derived from the multicomponent adsorption data. Therefore, the prediction of the behavior of a ternary equilibrium could be made from the parameters derived from the three corresponding sets of binary equilibrium data.

Replacing in Eq. (6) the term $zE_i/2RT$ by a single-component lateral interaction parameter, χ_i , and the term $zE_{ij}/2RT$ by a cross-lateral interaction parameter, χ_{ij} , gives:

$$\tau_{ij} = \exp(\chi_i - \chi_{ij}) \quad (10)$$

The parameters χ_i and χ_{ij} account for the molecular interactions of component i and for the cross-interactions between components i and j , respectively. Note that the lateral interaction potentials are included into the lateral interaction parameters. Therefore, the dependency of the activity coefficient on the spreading pressure is taken into account in these parameters.

The parameter χ_i can be obtained from the analysis of single component data. An estimate of the cross-lateral interaction parameters can be derived from the geometric mean of the single component parameters following the classical mixture rule in Eq. (8):

$$\chi_{ij} = \chi_{ji} = (\chi_i \chi_j)^{0.5} \quad (11)$$

The RAST-SPD model used in this study is defined by the set of equations 1, 4, 5, 10 and 11. We assumed that the shape factors of all components, including the solvent, are 1. We also assumed that, in the system under study, the most important interactions in the adsorbed phase are the solute–solute interactions. Since the mole fractions of all the solutes are less than 0.01, the solvent activity is close to unity and will be assumed always to remain equal to unity. The solute–solvent lateral interactions in the adsorbed phase were neglected (i.e., $\chi_{is} = \chi_{si} = 0$) because the solvent molecules are much smaller and have a much lower polarizability than the solute molecules. The solutes (benzyl alcohol, 2-phenylethanol and 2-methylbenzyl alcohol) have all very nearly the same size, so it is reasonable to assume that the saturation capacities are the same for all three molecules and that they can fit as well in a lattice site.

3. Experimental

The experimental data used in this study were reported previously [17]. They report under tabular form the experimental adsorption data for the three single-components, the three possible binary, and the ternary mixtures of benzyl alcohol, 2-phenylethanol and 2-methyl benzyl alcohol, on a 3.9 mm × 150 mm Symmetry C₁₈ (Waters, Milford, MA, USA) bonded silica column with a methanol–water solution (50:50, v/v) as the mobile phase, at 30 °C. These adsorption data were measured at 1 ml/min by frontal analysis [1,14] using an 1100 HP liquid chromatograph (Agilent Technologies, Palo Alto, CA, USA).

The models used are implicit with respect to the surface coverage. The numerical inversion of each model with respect to the adsorbed concentration was made using a Gauss–Jacobi numerical method [31]. Regressions of the experimental data were performed using a corrected Newton

method. When fitting the single-component data, the best coefficients were obtained by minimizing the residual sum of squares (RSS) combined for the three components:

$$\text{RSS} = \sum_{i=1}^n (q_{\text{ex},i} - q_{t,i})^2 \quad (12)$$

where $q_{\text{ex},i}$ and $q_{t,i}$ are the experimental and calculated values for each data point, respectively.

We used a Fisher's test to compare the Flory–Huggins and the SPD-RAST models that have different numbers of parameters. The best model is the one that exhibits the highest value of the following Fisher parameter [32]:

$$F = \frac{(n-l)\sum_{i=1}^n (q_{\text{ex},i} - \bar{q}_{\text{ex}})^2}{(n-1)\sum_{i=1}^n (q_{\text{ex},i} - q_{t,i})^2} \quad (13)$$

where l is the total number of adjusted parameters of the model and \bar{q}_{ex} is the mean value of the experimental adsorbed phase concentration. As clearly seen in Eq. (13), everything else being equal, F decreases with increasing number of parameters of the model tested. Thus, the comparison of the ability of two models to account for a set of, e.g., adsorption data can be made on the basis of the values of the corresponding F factors. The fact that the two models may have different numbers of adjustable parameters is accounted for in the definition of F .

4. Results and discussion

The experimental single-component adsorption data were fitted to the RAST model (Eq. (1)), using either the Flory–Huggins or the SPD activity coefficient equation to account for the nonideal behavior in the adsorbed phase. Using the parameters derived from these single-component adsorption data, the ternary equilibrium was predicted. Table 1 summarizes the results obtained.

The numerical algorithm and the optimization routines used in this work were different from those used by Quiñones et al. [17]. This suffices to explain why the values obtained for the parameters of the Flory–Huggins model obtained are different from those reported previously by these authors (see Table 1). Note that, the sums of residuals calculated by us are lower than those obtained in the previous study.

Both models give an excellent representation of the single-component adsorption data. However, the correlation of the single-component data using the RAST-SPD model (RSS = 1.0078) is slightly better than the correlation obtained using the RAST-FH model (RSS = 1.4467). The prediction of the ternary adsorption equilibrium given by the RAST-SPD model was better than that of the RAST-FH model, as confirmed by the F -values presented in Table 1. The RAST-SPD model predicts more accurately the adsorption behavior of BA and PE than the RAST-FH model. Conversely, however, the prediction of the adsorption behavior

Table 1
Fit of the single-component adsorption data and prediction of the ternary equilibrium data

Model	Parameters	RSS ^a single component	RSS ternary system	Global RSS	F
RAST-FH					
Reported by Quiñones et al. [17]					
	$K_{\text{BA}} = 2.015$				
	$K_{\text{PE}} = 3.574$				
	$K_{\text{MBA}} = 3.674$		RSS(BA) = 25.21		
	$\alpha_{\text{BA}} = 1.876$		RSS(PE) = 17.19		
	$\alpha_{\text{PE}} = 2.246$		RSS(MBA) = 25.21		
	$\alpha_{\text{MBA}} = 1.787$		$\sum \text{RSS} = 67.61$		
	$n^{\infty} = 2.277$				
Recalculated in this work					
	$K_{\text{BA}} = 1.997$				
	$K_{\text{PE}} = 3.648$	RSS(BA) = 0.22	RSS(BA) = 28.84		
	$K_{\text{MBA}} = 3.659$	RSS(PE) = 0.78	RSS(PE) = 28.58		
	$\alpha_{\text{BA}} = 2.041$	RSS(MBA) = 0.44	RSS(MBA) = 6.81	65.67	794.82
	$\alpha_{\text{PE}} = 2.550$	$\sum \text{RSS} = 1.44$	$\sum \text{RSS} = 64.23$		
	$\alpha_{\text{MBA}} = 2.042$				
	$n^{\infty} = 3.078$				
RAST-SPD					
	$\chi_s = 0.557$				
	$\chi_{\text{BA}} = 0.399$	RSS(BA) = 0.23	RSS(BA) = 21.09		
	$\chi_{\text{PE}} = 14.637$	RSS(PE) = 0.40	RSS(PE) = 22.49		
	$\chi_{\text{MBA}} = 0.403$	RSS(MBA) = 0.38	RSS(MBA) = 17.24	61.83	838.21
	$K_{\text{BA}} = 1.997$	$\sum \text{RSS} = 1.01$	$\sum \text{RSS} = 60.82$		
	$K_{\text{PE}} = 3.533$				
	$K_{\text{MBA}} = 3.658$				
	$n^{\infty} = 5.532$				

^a RSS: residual sum of squares.

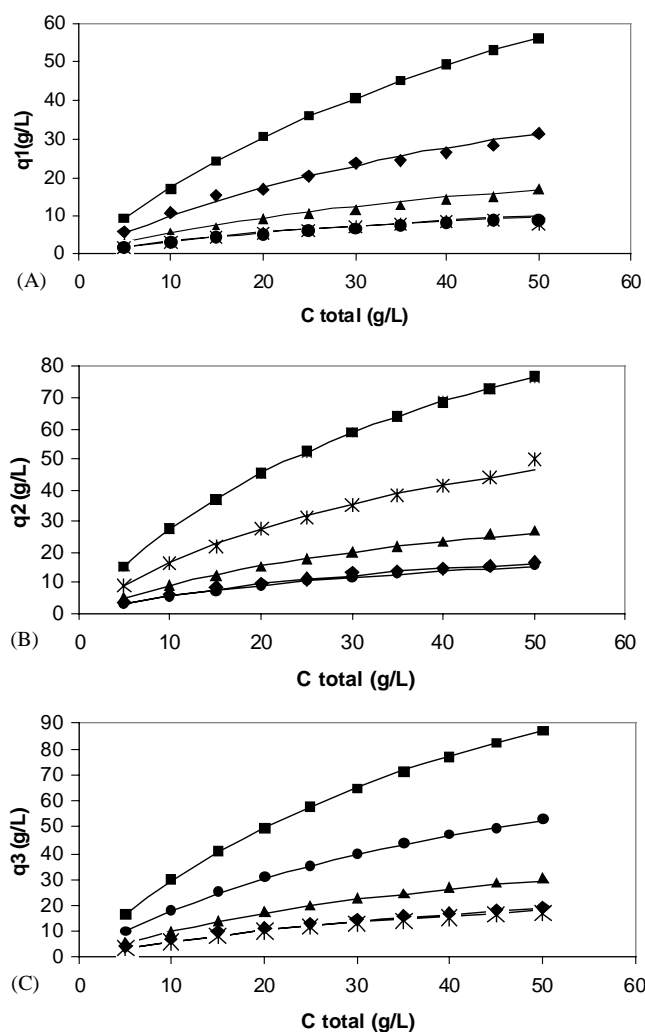


Fig. 1. Adsorption isotherms of BA (A), PE (B), and MBA (C). Symbols, adsorption data determined by frontal analysis. These experimental data are represented with the following symbols: data for single-component (■); data for 1:1:1 mixtures (▲); data for 3:1:1 mixtures (◆); data for 1:3:1 mixtures (✱); data for 1:1:3 mixtures (●). The solid lines are the adsorption isotherms calculated using the RAST-SPD model.

of MBA given by the RAST-FH model is the better one. The graphs in Fig. 1 illustrate the excellent agreement between the experimental adsorption isotherm data and the adsorption isotherms calculated using the new RAST-SPD model.

The lateral interaction parameter is higher for PE (χ_{PE}) than for BA and MBA. This result is unexpected if we consider the important similarities in size and structure of the three solutes studied. However, it is common that predictive models lead to such apparent contradictions and that they exhibit this kind of inconvenience [7,8]. Sometimes, the values of parameters are in contradiction with the physical sense given to them when they were previously defined in the construction of the model. For example, the lateral interactions parameters derived from the Fowler model are very different for homologous compounds such as 2-phenylethanol

and 3-phenylpropanol, even though, in this case, there were no reasons to think that the adsorbate–adsorbate interactions of these compounds should be very different [7]. It is quite frequent that models that are widely applied, such as the quadratic, the Jovanovic, the Langmuir–Freundlich, the Jovanovic–Freundlich, the FGLF and the FGJF models give, in some cases, questionable values for their different parameters [7,8,33]. This may be caused by the semi-empirical nature of these models and also to the different simplifications introduced during the derivation procedure of these models, with the only aim of representing simply and satisfactorily the system under study.

5. Conclusions

The RAST model was initially presented by Quiñones et al. [17] in order to account for the adsorption behavior of the components of a ternary system. We modified this model by replacing the Flory–Huggins equation that these authors had used with the SPD approach. This modification results in a slightly better fit of their single-component experimental data and predicts markedly better the adsorption behavior of their ternary system than did their initial RAST model. The advantage offered by our new model arises from the fact that it takes into account the lateral interactions taking place in the adsorbed phase.

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