

Adsorbed solution model for prediction of normal-phase chromatography process with varying composition of the mobile phase

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Abstract

The adsorbed solution model has been used to predict competitive adsorption equilibria of the solute and the active component of mobile phase in a normal-phase liquid chromatography system. The inputs to the calculations were the single adsorption isotherms accounting for energetic heterogeneity of the adsorbent surface and non-ideality of the mobile phase solution. The competitive adsorption model has been coupled with a model of the column dynamics and used for simulating of chromatography process at different mobile phase composition. The predictions have been verified by comparing the simulated and experimental chromatograms. The model allowed quantitative prediction of chromatography process on the basis of the pure-species adsorption isotherms.

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1. Introduction

Chromatographic separations are usually realized in isocratic mode, i.e., with constant temperature, pressure or solvent composition of the mobile phase during the process. However, it is well known that the adsorption behaviors of the system can be strongly affected by changes of these operating parameters. Changes of adsorption properties are commonly used for bed regeneration in cyclic adsorption processes such as thermal and pressure swing-adsorption and displacement-purge adsorption [1,2].

In liquid chromatography, the idea of affecting the adsorption behavior by a modulation of the mobile phase composition is often exploited to improve the separation performance in chromatographic processes.

The effect of the mobile phase composition on the retention in normal-phase systems operating under conditions of a linear isotherm has been described using theoretical models of adsorption developed in [3–6]. In these models, the adsorption on a polar adsorbent surface was understood as a competition between the molecules of the solute and the modifier on the adsorption sites. Despite some differences, all the models lead

after simplifications to the same simple equation describing the retention of solute as a function of concentration of a strong solvent (the modifier):

$$k'_0 = k'(c_{\text{mod}})^{-m} \quad (1)$$

where k'_0 is the retention factor of the solute in the pure strong solvent, m is the empirical constant, which is determined by fitting to the set of experimental retention data acquired at different modifier content in the mobile phase. k'_0 is the retention factor correlated with the slope of the isotherm of the solute at $c \rightarrow 0$:

$$k'_0 = F \left. \frac{\partial q^*}{\partial c} \right|_{c \rightarrow 0}, \quad (2)$$

where $F = (1 - \varepsilon_t)/\varepsilon_t$ is the phase ratio.

If the mobile phase composition varies during the process (solvent gradient), the retention of the solute is correlated with the profile of the modifier concentration propagating along the space z and time t co-ordinate, i.e., $c_{\text{mod}}(z, t)$. Various models for retention predictions of the solute under gradient conditions accounting for possible adsorption of the modifier are discussed in [7].

For predictions of non-linear chromatography processes realized at constant mobile phase composition as well as at varying elution strength empirical or semi-empirical approaches dominate. The idea behind these approaches is to measure adsorption

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Nomenclature

c	concentration in mobile phase (mol/cm ³)
D_a	apparent diffusion coefficient (m ² /s)
F	$\frac{1-\varepsilon_t}{\varepsilon_t}$ = phase ratio
h	characterizes heterogeneity of surface in the Unilan isotherm model
k_+	adsorption rate coefficient (1/s)
k_-	desorption rate coefficient (1/s)
K	equilibrium constant
M	molar mass (g/mol)
N	column efficiency
q	amount adsorbed (mol/cm ³)
q^∞	saturation capacity (mol/cm ³)
t	time coordinate (s)
t_r	retention time (s)
t_{r0}	dead time (s)
u	superficial mobile phase velocity (cm/s)
x	mole fraction
z	space coordinate (cm)
<i>Greek letters</i>	
ε_t	total void fraction of the column
Γ	excess adsorption (mol/cm ³)
γ	activity coefficient
π	modified spreading pressure (mol/cm ³), (g/cm ³)
<i>Subscripts</i>	
A	organic component
F	feed
i	component index
mod	eluent modifier
<i>Superscripts</i>	
*	equilibrium conditions
m	mobile phase
s	adsorbed phase

equilibria of the solute at different mobile phase composition and to develop an adsorption model correlating the values of the isotherm coefficients with the mobile phase composition. Typically, in order to describe the dependency of the isotherm coefficients on the modifier concentration, a power-law dependency related to Eq. (1) is used. Such an approach can serve as a base for the process optimization [8,9]. This simplified approach has been extended in [10] by accounting for the adsorption of the modifier and employed for the modeling of gradient elution in continuous chromatography [11]. In this approach, the isotherm coefficients are correlated with local distribution of the modifier concentration calculated by the use of a dynamic model.

Since for a binary chromatographic system “solute-modifier”, the concentration of the modifier both in the solid and the mobile phase is typically much higher compared to that of the solute the perturbation of the modifier equilibrium by the eluting solute is often insignificant. In this case, adsorption of the modifier can be evaluated by the single isotherm equation

and the simplified models discussed above can provide a good description of overloaded profiles. The analysis of the accuracy of such models [12] pointed that in order to describe adsorption under typical for chromatography conditions a complex model accounting for competition is not necessary. However, if concentration of the solute and the modifier in both the mobile and the stationary phase are comparable (i.e., strength of adsorption of both the species is similar) competition between the solute and the modifier leads to marked deformations of band profiles and cannot be neglected.

The simplest competitive model has been suggested in [12]; it assumed the competitive Langmuir isotherm for binary (solute-modifier) adsorption equilibria. If the coefficients of the single isotherm “modifier-weak solvent” are known, the coefficients of the competitive isotherm “solute-modifier” at the specified concentration of the modifier can be determined. A similar model has been adopted in [13] wherein the adsorption of various solvents on a normal as well as reversed stationary phase has been studied. The coefficients of competitive isotherm have been determined for a selected concentration of the modifier in the mobile phase. Such a model offered a good reproduction of the data of competitive adsorption, but solely for the mobile phase composition studied. A change of the mobile phase composition would force identification of a new competitive isotherm.

The adsorption model for predictions of non-linear competitive adsorption equilibria of the solute and the organic solvent in a reversed-phase system has been suggested in [14]. The variations of the adsorption properties of the solute with the mobile phase composition were predicted on the basis of single isotherms of “solute-weak solvent” and “organic solvent-weak solvent”. The model assumed multilayer adsorption mechanism of solvents in the presence of the alkyl-bonded stationary phase. The competitive adsorption mechanism of the solute was dominated by adsorption of the organic solvent, which was present in the mobile phase with relatively high concentration with respect to that of the solute. In this case, the perturbation of adsorption equilibrium of the solvent by the solute was neglected. Moreover, the two-site competitive adsorption on the alkyl chains and on the polar surface has been considered. The adsorption on these separate two-sites was assumed to be homogenous; moreover, their contribution to the overall saturation capacity was assumed to be the same for both the solute and the modifier.

In this work, similar approach has been employed for a normal-phase system. However, the silica surface is strongly heterogeneous and adsorption heterogeneity of the solute and the solvent cannot be approximated to be the same. The single isotherm model proposed accounted for energetic heterogeneity of the adsorbent surface and non-ideality of the mobile phase. The modified bi-Langmuir and the modified Unilan model [15] have been considered. The non-ideality of the mobile phase has been accounted for by introducing activity coefficients calculated by the use the UNIFAC method [16,17]. The non-ideality of the adsorbed phase was neglected for the systems of solvents studied; the molecules were adsorbed in single-layer without additional interactions.

For description of competitive adsorption equilibria, the framework given by the adsorbed solution theory [15] has been

adopted. The thermodynamics of ideal adsorbed solutions (IAS) was established as a method for predicting multicomponent adsorption using solely single-solute adsorption. The method was first proposed for adsorption of gas mixtures [18], and extended to multicomponent adsorption from dilute liquid solutions [19]. The IAS model reduces to the multicomponent competitive isotherm if each single-solute isotherm is a Langmuir with the same saturation capacity. Deviations from the IAS theory due to interactions of the solutes in the adsorbed phase can be accounted for by the real adsorbed solution theory (RAS). The non-idealities of the adsorbed phase are lumped into solid phase activity coefficients [20–24]. However, deviations from the IAS model are often suggested to originate from heterogeneity of adsorbent surface [25].

For heterogeneous surface, the mechanism of multicomponent adsorption is complicated, since it involves the competition between molecules on each type of adsorption site [25,26]. For two-site heterogeneous surface, the multicomponent adsorption can be described by the IAS model for each site separately; the total adsorbed amount is then a sum of amounts adsorbed on each site [25].

In the heterogeneous adsorbed solution model (HIAS) developed in [26], the surface of adsorbent is described as a collection of sites of different adsorption. The competition takes place on each type of site. Such an approach, although correct, requires a number of adjustable parameters accounting for the energy distribution on the adsorbent surface.

In this work, to describe non-linear competitive adsorption of solute in the presence of the modifier, the conventional IAS approach [19] has been extended by taking into account changes of the mobile phase activity according to the variation of the modifier concentration. The binary adsorption equilibria were predicted on the basis of the single-species isotherms. The competitive adsorption model has been coupled with a model of the column dynamics and used to simulate chromatography process at different mobile phase composition.

For experimental verification, two typical systems (mixtures) of solvents have been selected, i.e., system (A) ethyl acetate (modifier)–*n*-hexane (inert) or system (B) 2-propanol (modifier)–*n*-hexane (inert). The solute was cyclopentanone exhibiting heterogeneous mechanism of adsorption on the normal-phase surface. Moreover, cyclopentanone was easily dissolved in *n*-hexane, which allowed measurement the adsorption equilibria at pure weak solvent. The experiment consisted in acquiring of adsorption excess in the single systems, i.e., “modifier–*n*-hexane” and “solute–*n*-hexane”. Additionally, a set of chromatograms of the solute at different contents of the modifier in the mobile phase has been registered. Wide concentration range of the modifier has been analyzed covering low saturation level, for which solute perturbed the adsorption equilibrium of the modifier, as well as high level wherein such a perturbation was not evidenced.

The predictions have been verified by comparing the simulated and experimental chromatograms. The successful experimental verification indicated the adequacy of the model for single-component equilibria and the predictive model for binary equilibria of the solute-modifier.

2. Theory

2.1. Single-solute equilibria

2.1.1. Langmuir model

The adsorption process of a component *A* on an active site “*S*” on the adsorbent surface can be described as follows:



The rate equation corresponding to the above mechanism is expressed by:

$$\begin{aligned} \frac{dx_A^s}{dt} &= k_{+1}x_A^m\gamma_A^m x^s - k_{-1}x_A^s\gamma_A^s \\ &= k_{+1}x_A^m\gamma_A^m(1 - x_A^s) - k_{-1}x_A^s\gamma_A^s \end{aligned} \quad (4)$$

where x_A^m is the mole fraction of *A* in the mobile phase, $x_A^s = q_A/q_A^\infty$ is the mole fraction of *A* in the adsorbed phase, q_A is the amount adsorbed, q_A^∞ is the saturation capacity, x^s is the mole fraction of free sites on the surface, γ_A^m , γ_A^s are the activity coefficients of *A* in the mobile and solid phase, respectively.

If adsorption–desorption kinetics is fast, both the phases can be assumed to be in equilibrium:

$$K = \frac{x_A^s\gamma_A^s}{x_A^m\gamma_A^m x^s} = \frac{x_A^s\gamma_A^s}{x_A^m\gamma_A^m(1 - x_A^s)} \quad (5)$$

where $K = k_{+1}/k_{-1}$ is the temperature dependent equilibrium constant, $K = K_0 \exp(E/RT)$ with K_0 as the pre-exponential coefficient and E the energy of adsorption.

From Eq. (5), the amount adsorbed at the equilibrium q_A^* can be calculated:

$$q_A^* = x_A^s q_A^\infty = \frac{q_A^\infty K x_A^m \gamma_A^m}{\gamma_A^s + K x_A^m \gamma_A^m} \quad (6)$$

Typically, Eq. (6) has an implicit form since the activity coefficients in the solid phase are a function of the fraction of *A* in the adsorbed phase, i.e., $\gamma_A^s = f(x_A^s)$.

Due to relatively low solute concentrations, which are characteristic for chromatography separations, the behavior of adsorbed phase can be usually assumed to be ideal, i.e.:

$$q_A^* = \frac{q_A^\infty K x_A^m \gamma_A^m}{1 + K x_A^m \gamma_A^m} \quad (7)$$

Moreover, for such low concentrations, the activity coefficient of the solute in the mobile phase can be assumed as constant and, provided constant mobile phase composition, can be lumped into the value of the equilibrium constant. Then Eq. (7) converts to the well-known Langmuir isotherm model. If variation of the mobile phase composition is considered, the changes of activity coefficient of the solute with the modifier concentration have to be taken into account.

2.1.2. Surface heterogeneity

2.1.2.1. Two-site heterogeneous surface model–modified bi-Langmuir model. The Eq. (7) can be selected to construct the

two-site model of heterogeneous surface. For the two-sites I and II, the isotherm can be expressed as follows:

$$q_A^* = \frac{q_{AI}^\infty K_I x_A^m \gamma_A^m}{1 + K_I x_A^m \gamma_A^m} + \frac{q_{AII}^\infty K_{II} x_A^m \gamma_A^m}{1 + K_{II} x_A^m \gamma_A^m} \quad (8)$$

2.1.2.2. Modified Unilan model. To account for surface heterogeneity, an energy distribution can be introduced. In the Unilan equation, a patch wise surface is assumed, for each patch the local Langmuir isotherm is applicable [15]. The distribution of energy is assumed uniform and given by:

$$f(E) = \begin{cases} \frac{1}{E_{\max} - E_{\min}} & \text{for } E_{\min} < E < E_{\max} \\ 0 & \text{for } E < E_{\min} \text{ or } E > E_{\max} \end{cases} \quad (9)$$

The modified Unilan equation accounting for non-ideality of the mobile-phase can be obtained from integrating Eq. (7):

$$q_A^* = \int_{-\infty}^{+\infty} \frac{q_A^\infty K x_A^m \gamma_A^m}{1 + K x_A^m \gamma_A^m} f(E) dE \quad (10)$$

$$q_A^* = \frac{q_A^\infty}{(2h)} \ln \left(\frac{1 + \bar{K} x_A^m \gamma_A^m \exp(h)}{1 + \bar{K} x_A^m \gamma_A^m \exp(-h)} \right) \quad (11)$$

where $\bar{K} = K_0 \exp(\bar{E}/RT)$; $\bar{E} = (E_{\min} + E_{\max})/2$; $h = (E_{\max} - E_{\min})/2RT$. The parameter h characterizes heterogeneity of surface, for homogeneous surface, i.e., for $h=0$, Eq. (11) is reduced to Eq. (7).

2.2. Excess adsorption

The excess adsorption for a mixture of a single component and an inert is expressed by the following equation [27]:

$$\Gamma_A^* = q_A^* - q_A^* x_A^m = q_A^* (1 - x_A^m) \quad (12)$$

For low concentrations: $\Gamma_A^* \cong q_A^*$.

The concentration in the adsorbed phase q_A^* is represented by an appropriate isotherm equation, e.g., for the bi-Langmuir model it holds:

$$\Gamma_A^* = \left(\frac{q_{AI}^\infty K_I x_A^m \gamma_A^m}{1 + K_I x_A^m \gamma_A^m} + \frac{q_{AII}^\infty K_{II} x_A^m \gamma_A^m}{1 + K_{II} x_A^m \gamma_A^m} \right) (1 - x_A^m) \quad (13)$$

or for the Unilan model:

$$\Gamma_A^* = \left[\frac{q_A^\infty}{(2h)} \ln \left(\frac{1 + \bar{K} x_A^m \gamma_A^m \exp(h)}{1 + \bar{K} x_A^m \gamma_A^m \exp(-h)} \right) \right] (1 - x_A^m) \quad (14)$$

2.3. Competitive isotherm—(AST) adsorbed solution theory

The AST model assumes that a modified spreading pressure for each of single i -th solute is equal to:

$$\pi_i(a_i^0) = \int_0^{a_i^0} \frac{q_i^*(a_i)}{a_i} da_i \quad (15)$$

where $a_i = x_i \gamma_i$ is the concentration activity, a_i^0 is fictitious activity for the pure components at which these components would

possess the same spreading pressure π_{mix} alone as the mixture:

$$\pi_{\text{mix}} = \pi_i. \quad (16)$$

The equilibrium relationships are written:

$$a_i = x_i^s a_i^0 \quad (17)$$

with:

$$\sum_{i=1}^n \frac{a_i}{a_i^0} = 1 \quad (18)$$

In order to calculate a_i^0 and x_i^s , the set of Eqs. (15)–(18) have to be solved numerically. The competitive equilibrium isotherms can be calculated using the single-component isotherms for total equilibrium loading:

$$\frac{1}{q_{\text{tot}}^*} = \sum_{i=1}^n \frac{x_i^s}{q_i^*(a_i^0)} \quad (19)$$

The stationary concentration of each solute species of the mixture is calculated from:

$$q_i^* = x_i^s q_{\text{tot}}^* \quad (20)$$

To calculate binary equilibrium, the model exploits solely the single-isotherm equations “component-inert” without adjustable parameter accounting for binary adsorption equilibrium [18,19].

2.4. Model of the chromatographic column

For the mathematical modeling, a permanently established equilibrium between the concentration of the component in the mobile and stationary phases has been assumed. The differential mass balance for a single i -th component in the mobile phase can be expressed as follows [28–31]:

$$\frac{\partial c_i^m}{\partial t} + F \frac{\partial \Gamma_i^*}{\partial t} + w \frac{\partial c_i^m}{\partial z} = D_a \frac{\partial^2 c_i^m}{\partial z^2} \quad (21)$$

where $w = u/\varepsilon_t$ is interstitial velocity; ε_t is total column porosity; D_a is apparent dispersion coefficient related to the column efficiency as $N = wL/2D_a$; c_i^m is the concentration of the component in the mobile phase; t, z are time and space co-ordinates, Γ_i^* is the excess adsorption at the equilibrium with c_i^m .

The excess adsorption for a mixture of an adsorbable component of the mobile phase (modifier) and an inert is expressed by Eq. (12).

For the solute, due to its low concentration $\Gamma_i^* \cong q_i^*$.

Introducing mole fractions into Eq. (21), one obtains [14]:

$$\frac{\partial x_i^m}{\partial t} + F \frac{M^m}{\rho^m} \frac{\partial \Gamma_i^*}{\partial t} + w \frac{\partial x_i^m}{\partial z} = D_a \frac{\partial^2 x_i^m}{\partial z^2} \quad (22)$$

where M^m and ρ^m are the equivalent molar mass and the density of the mobile phase; $M^m = f(x_i^m)$, $\rho^m = f(x_i^m)$.

To describe chromatography processes, the Danckwerts-type boundary conditions are usually assumed:

$$t > 0; \quad z = 0$$

$$u(x_{i,F}(t) - x_i^m(t, 0)) = -D_a \frac{\partial x_i^m(t, 0)}{\partial z} \quad (23)$$

where $x_{i,F}(t)$ defines the injection profile of the sample.

For a rectangular pulse injection it holds:

$$x_{i,F}(t) = \begin{cases} x_{i,F} & \text{for } t \in [0, t_p] \\ 0 & \text{for } t > t_p \end{cases} \quad (24)$$

2.5. Determining the excess adsorption

The excess adsorption was determined by the use of the perturbation method. In this method, the column is initially equilibrated at a known concentration level and then a small perturbation is introduced as a rectangular impulse. Since the difference between the equilibrium concentration and the response concentration is small, the column remains in equilibrium. The operation is repeated for different concentration levels and the retention times of the pulses are measured and analyzed. The mathematical analysis is based on the principles of classical equilibrium theory [32,33].

In the equilibrium theory, the chromatographic process is described by the ideal model, which assumes permanent equilibrium between the component concentrations in the mobile and stationary phases and neglects axial dispersion and kinetic effects. The ideal model can be represented by Eq. (22) neglecting the dispersion term. After rearrangement for an i -th single component, it holds:

$$\frac{\partial x_i^m}{\partial t} + \left(\frac{w}{1 + F(d\Gamma_i^*/dx_i^m)(M^m(x_i^m)/\rho^m(x_i^m))} \right) \frac{\partial x_i^m}{\partial z} = 0 \quad (25)$$

The retention time of the pulse is expressed as:

$$t_{ri}(x_i^m) = t_{r0} \left(1 + F \frac{d\Gamma_i^*}{dx_i^m} \frac{M^m(x_i^m)}{\rho^m(x_i^m)} \right) \quad (26)$$

where $t_{r0} = L/w$ is the retention time of a non-retained component (i.e., dead time of the column).

Eq. (26) can be used for calculating the excess adsorption of component $i = A$ defined by Eq. (12):

$$\Gamma_A^* = \int_0^{x_A} \left(\frac{t_r/t_{r0} - 1}{F} \right) \frac{\rho^m(x_i^m)}{M^m(x_i^m)} dx_A \quad (27)$$

or,

$$\Gamma_A^* = \int_1^{x_A} \left(\frac{t_r/t_{r0} - 1}{F} \frac{\rho^m(x_i^m)}{M^m(x_i^m)} dx_A \right) \quad (27a)$$

In Eqs. (27) and (27a), Γ_A^* is the excess adsorption corresponding to the volume of the adsorbent (e.g., mol/(cm³ of adsorbent)).

2.6. Numerical tools

2.6.1. Single isotherm

The parameters of the isotherm model (i.e., Eqs. (13) and (14) have been determined by the use of the random search optimization algorithm (see details in [14]). Random search strategies

often offer higher reliability in locating global optima compared to deterministic methods. Conventional deterministic methods frequently fail, particularly in cases when several model coefficients have to be determined and the optimization becomes trapped in local minima. In the algorithm, the objective function was the sum of the square differences between experimental and the simulated excess adsorption data.

2.6.2. Competitive isotherm

In order to calculate the competitive equilibrium data, the AST model (Eqs. (15)–(18)) was solved by the use of the Marquardt–Levenberg routine, which enabled fast convergence of the solution.

2.6.3. Calculation of the band profiles

The set of partial differential Eqs. (22)–(24) was solved by the use of a fast finite difference method; namely, the forward–backward differential scheme was employed [30]. The local adsorbed amount for the components of binary mixture was calculated by the use of the AST model.

3. Experimental

3.1. Columns and chemicals

3.1.1. Column

Column 250 mm and 4 mm i.d. packed with silica LiChrospher[®] Si 60 with pore diameter 60 Å and particle size 5 μm (Merck, Darmstadt, Germany).

3.1.2. Chemicals

Model compound (solute) was cyclopentanone (C5) (Sigma–Aldrich), which is liquid at ambient conditions. For the mobile phase binary mixtures have been used:

- ethyl acetate (EA)– n -hexane;
- 2-propanol (ISO)– n -hexane;

for HPLC (Merck, Darmstadt, Germany). The water content in these solvents was very small, i.e., max. 0.02 wt% in ethyl acetate and min 0.01 wt% in n -hexane.

All experiments were performed at 25 °C.

3.1.3. Instruments

HPLC instrument LaChrom with autosampler, UV and RI detector and a data station (Merck, Darmstadt). The pulses of the modifiers (EA and ISO) were detected by the use of RI detector, the pulses and band profiles of C5 were detected by the use of UV detector at 280 nm wavelength. The RI detector was found to be more effective for detection of solvents; due to high concentration of solvents in the mobile phase, the dependence of the UV signal versus the concentration is strongly non-linear. Therefore, with an increase of the concentration of the modifier in the mobile phase, the perturbation pulses become not visible. The pulses and band profiles were recorded at the flow-rate of 1 cm³/min, the injection volume was 20 μL.

3.2. Procedures

3.2.1. Initialization and verification of the experiments

The experiment started with the saturation of the column with a polar solvent (i.e., ethyl acetate). Because the solvents were not dried additionally, the stationary phase was saturated irreversibly by traces of water contained in the mobile phase (see Section 3.1.2). Since the concentration of water in solvents did not increase traces of water adsorbed accordingly to its adsorption equilibrium remained unchanged during the whole procedure and did not influence reproducibility of the experiment. In order to verify reproducibility, the selected perturbation measurements were repeated after accomplishing all the experimental trials reported below. All the measurements were found to be fully reproducible apart from retention of the solute C5 and 2-propanol at pure *n*-hexane (see also Section 4), which varied randomly without exhibiting any trends characteristic for deactivation of the surface. These problems resulted from handling such a very volatile solvent as pure *n*-hexane.

3.2.2. Perturbation measurement of single isotherm

In order to determine the adsorption isotherms the column was equilibrated with various concentration of the single compound. For each saturation level corresponding to the adequate concentration of the component in the mobile phase, a pulse with a small excess of concentration with respect to the equilibrium was injected.

For the system solute (C5)–*n*-hexane the concentration of C5 in the mobile phase was varying over the range 0.05–2 wt% (i.e., $x_{C5}^m = 7.35 \times 10^{-4}$ to 0.029).

For the modifiers, the whole concentration range was covered starting from 0 vol.% up to $x_{EA}^m = 1$ for EA and 0.05% to $x_{ISO}^m = 1$ for ISO.

The retention data obtained at a very low C5 and ISO content $x_A^m \rightarrow 0$ (converging to pure *n*-hexane) required a long retention and were not reproducible and uncertain. The stable and reproducible values were recorded above ca. 0.05 vol.%.

Moreover, if the component is strongly retained, the retention for the concentration of $c \rightarrow 0$ can be very long and cannot be determined. In such a case, the perturbation measurements should be started with certain saturation of the stationary phase by the component to be investigated.

3.2.3. Column porosity

In order to determine the column porosity, the dead time of the column (i.e., $t_{r0} = L\varepsilon_t/u$) was evaluated from the constraint: $\Gamma_A^*(x_A^m = 1) = 0$, which forces the integral value in Eq. (27) [14]:

$$\Gamma_A^* = \int_0^1 \left(\frac{t_r/t_{r0} - 1}{F} \right) \frac{\rho^m}{M^m} dx_A^m = 0.$$

For calculations, the set of retention times obtained for the system EA–*n*-hexane, for which the retention data at pure *n*-hexane were reliable. The obtained values of the dead time

were: $t_0 = 2.42$ min, which corresponded to the total porosity $\varepsilon_t = 0.772$.

3.2.4. Competitive equilibrium

The pulses and the overloaded concentration profiles of the solute C5 were recorded at various modifier concentrations. For the ternary system (A): C5–EA–*n*-hexane, the EA concentration was varied between 5 and 100 vol.% ($x_{EA}^m = 0.0067$ –1).

In order to cover similar retention range of C5 for the ternary system (B): C5–ISO–*n*-hexane, the concentration of ISO was changed from 0.05 to 100 vol.% ($x_{ISO}^m = 0.0034$ –1).

3.2.5. Activity coefficients

The activity coefficients were calculated by the use of the UNIFAC method:

- *Binary systems*: EA–*n*-hexane, ISO–*n*-hexane and C5–*n*-hexane.

The activity coefficients for the binary systems:

- for EA–*n*-hexane, the activity coefficients γ_{EA}^m vary from 2.84 (at pure *n*-hexane) to 1 (at pure EA);
- for ISO–*n*-hexane, the activity coefficients γ_{ISO}^m vary from 21.53 (at pure *n*-hexane) to 1 (pure ISO);
- for C5–*n*-hexane due to low solute concentration, activity coefficient remains practically unchanged. Hence, the dependence $\gamma_{C5}^m = f(x_{C5}^m)$ was neglected and constant value of $\gamma_{C5}^m = 3.38$ at $x_{C5}^m \rightarrow 0$ in pure *n*-hexane was assumed for calculations.

- *Ternary systems*: (A) C5–EA–*n*-hexane and (B) C5–ISO–*n*-hexane.

In both the systems, the dependence $\gamma_{C5}^m = f(x_{C5}^m)$ was neglected.

The activity coefficient of C5 $\gamma_{C5}^m = f(x_{mod}^m)$ and of the modifier $\gamma_{mod}^m = f(x_{mod}^m)$ is the function of the mobile phase composition:

- for the system (A) in the range of $x_{EA}^m = (\sim 0$ to $\sim 1)$ γ_{C5}^m varies from 3.38 to 1.32 and γ_{EA}^m varies from 2.76 to 1.26;
- for system (B) in the range of $x_{ISO}^m = (\sim 0$ to $\sim 1)$ γ_{C5}^m varies from 3.38 to 2.42 and γ_{ISO}^m varies from 20.2 to 4.28.

The obtained data of activity coefficients versus the mole fraction of the modifier were approximated by exponential empirical dependencies $\gamma_{C5}^m = f(x_{mod}^m)$ and $\gamma_{mod}^m = f(x_{mod}^m)$ for mod = EA or ISO, e.g.:

- for EA–*n*-hexane the following equation has been used:

$$\begin{aligned} \gamma_{EA}^m &= 0.879 + 2.332 \times \exp\left(-\frac{x_{EA}^m}{0.334}\right) \\ &+ 0.196 \times \exp\left(-\frac{x_{EA}^m}{0.00093}\right) - 0.0938 \\ &\times \exp\left(-\frac{x_{EA}^m}{0.762}\right) \end{aligned}$$

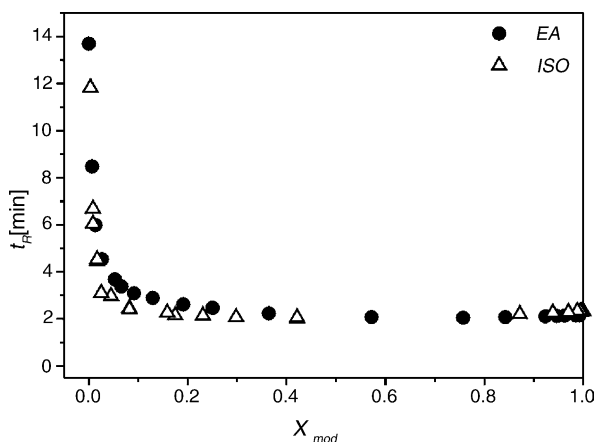


Fig. 1. Results of the pulse analysis for the systems: ethyl acetate (EA)–*n*-hexane and 2-propanol (ISO)–*n*-hexane.

- for ISO–*n*-hexane:

$$\gamma_{\text{ISO}}^m = 11.462 \times \exp\left(-\frac{x_{\text{ISO}}^m}{0.033}\right) + 1.672$$

$$\times \exp\left(-\frac{x_{\text{ISO}}^m}{1.738}\right) + 9.132 \times \exp\left(-\frac{x_{\text{ISO}}^m}{0.128}\right)$$

The coefficients were determined by fitting the UNIFAC data to a function of exponential decay of the second or the third order implemented in the program Microcal Origin ver. 5.0. In fact, any mathematical function can be used for fitting provided that it reproduces correctly the data obtained by the UNIFAC method.

4. Results and discussion

4.1. Single adsorption isotherm

In Fig. 1, the retention time of pulses of the modifier versus its mole fraction in the mobile phase is presented. The corresponding excess adsorption is depicted in Fig. 2a. Since the results of retention measurements at pure *n*-hexane for 2-propanol (ISO) were uncertain, the excess was calculated by the use of Eq. (27a).

The adsorption data depicted in Fig. 2a and b indicate that surface is saturated by the more polar modifier (i.e., ISO) at a relatively low concentration in the mobile phase. Moreover,

due to its high polarity ISO behaviors strongly non-ideally in the mobile phase containing *n*-hexane (see the activity values above), which influences significantly on excess adsorption.

The set of experimental data of the excess adsorption presented in Fig. 2a was used for determining the parameters of the bi-Langmuir and Unilan models (see Eqs. (13) and (14)). The isotherm model was coupled with the adequate dependency $\gamma_A^m = f(x_A^m)$ (A (modifier) = EA or ISO). The set of the parameter for the bi-Langmuir and the Unilan models is presented in Table 1; the simulated excess adsorption is depicted in Fig. 2a. Both the models reproduce the adsorption data for EA with similar accuracy, while the bi-Langmuir model is slightly more accurate for ISO. The adsorption isotherms corresponding to Fig. 2a are depicted in Fig. 2b.

It is evident that for the bi-Langmuir model two energetically different adsorption sites can be distinguished—with low and high equilibrium constant. The two-sites model should be considered as a rough approximation of energetically non-uniform surface and both the K_I and K_{II} constant as average values.

Note that the saturation capacity for EA for low energetic site (site I) is much higher than that for C5 and ISO, which can be rather attributed to the inaccuracy of the two-site model than to real distribution of sites on the surface. For the Unilan model, the saturation capacity for all the components were found to be very similar, hence the value of q_i^∞ giving the best fit to the experimental data for C5 was also used for the modeling of the Unilan isotherm for ISO and EA.

In Fig. 3a, retention of the C5 perturbation pulses versus its mole fraction in the mobile phase is presented. These data were not converted to the excess adsorption; the changes of retention were significant and resulted in strongly non-linear curvature of the retention dependence. Therefore, they could be exploited directly, without additional integration errors, in the optimization procedure on the basis of Eq. (26). The concentration derivatives in Eq. (26) were calculated numerically. The resulting isotherm is depicted in Fig. 3b.

The retention data of the modifiers could not be handled in the same way because the changes of retention versus the concentration were very small over a wide range of concentration (see Fig. 1) and the multi-parameter optimization was not effective.

Note that determining the single isotherm “solute-weak solvent” is possible for solutes with good solubility in a weak solvent. However, in principle, if the non-linear isotherm for

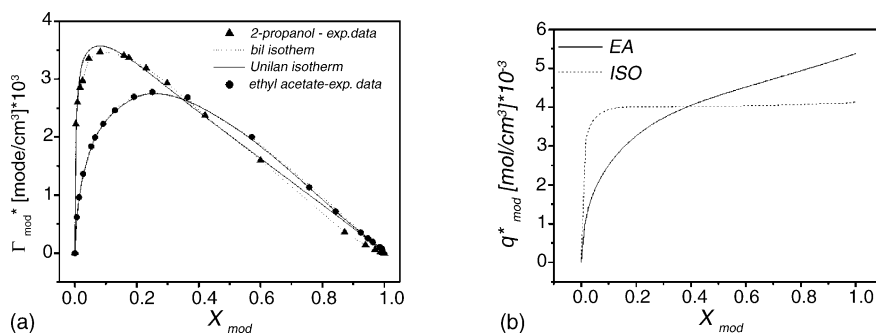


Fig. 2. Adsorption for the systems: EA–*n*-hexane and ISO–*n*-hexane: (a) excess adsorption; (b) corresponding adsorption isotherms.

Table 1
Values of the parameters for the single isotherm model

Component/isotherm	Cyclopentanone C5 (model component)	Ethyl acetate EA (eluent modifier)	2-Propanol ISO (eluent modifier)
biL isotherm—Eq. (13)			
q_{iI}^{∞}	0.0024	0.0133	0.0025
K_{iI}	20.32	0.448	0.504
q_{iII}^{∞}	0.0010	0.00142	0.0034
K_{iII}	548	25.276	16.44
RSS	1.53×10^{-8}	5.85×10^{-8}	3.2×10^{-7}
Unilan isotherm—Eq. (14)			
q_i^{∞}	0.0059	0.0059 ^a	0.0059 ^a
K_i	3.23	3.40	4.366
h_i	5.35	0.873	3.038
RSS	1.47×10^{-8}	3.83×10^{-8}	4.7×10^{-7}

RSS: residual sum of square differences between adsorption excess predicted and experimental.

^a Set the same as for the solute C5.

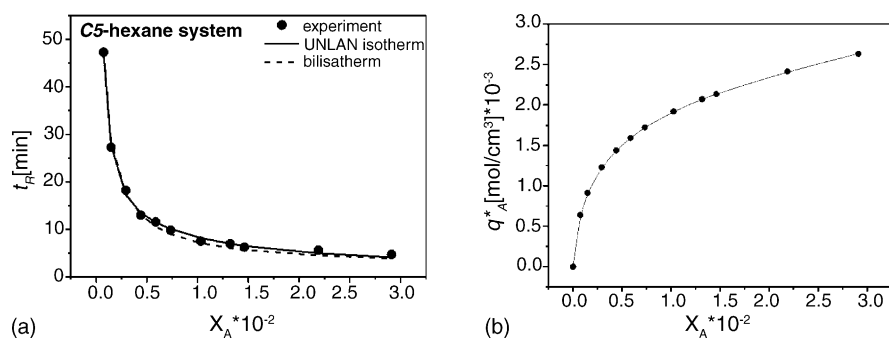


Fig. 3. Results of the perturbation analysis for the system C5–*n*-hexane: (a) retention time of perturbation pulses vs. the concentration of the solute in the mobile phase; (b) corresponding adsorption isotherm.

a selected composition of the mobile phase is determined, the AST model allows estimation of the adsorption behaviour at pure weak solvent.

4.2. Competitive isotherm

4.2.1. Simulating of the pulse retention

The pulses and overloaded profiles of C5 were recorded at different saturation levels of the modifiers. For the simulations, the dynamic model (Eqs. (22)–(24)) was solved, the local solid phase concentrations of C5-modifier (EA or ISO) were calculated by the use of the AST model (Eqs. (15)–(18)).

The AST isotherm model was coupled with the adequate dependencies of activity coefficients in the ternary systems: $\gamma_{C5}^m = f(x_A^m)$ and $\gamma_A^m = f(x_A^m)$ (A (modifier) = EA or ISO).

The variations of retention time of solute pulses versus the modifier concentration determined experimentally and theoretically are presented in Fig. 4 for the system A, i.e., EA–*n*-hexane and in Fig. 5 for the system B, i.e., ISO–*n*-hexane.

Due to low concentration of the solute in pulses, the equilibrium of the modifier is not perturbed during chromatographic elution. The solute occupies the adsorption sites free of the adsorbed modifier. If the saturation capacities for the solute and the modifier are the same, i.e., $q_A^{\infty} = q_{C5}^{\infty}$, and all the adsorption sites are energetically homogenous, the free surface available for the solute, q^s , can be approximated as $q^s = q_A^{\infty} - q_A^*$, where

q_A^* is the amount of the modifier adsorbed according to its adsorption equilibrium $q_A^* = f(x_A^m)$. However, for the silica surface, the energetic heterogeneity of the solute was found to differ markedly from that of the modifier. In this case, the amount of adsorption sites available for the solute in the presence of the modifier can be calculated by the use of AST theory.

For the system (A), a good agreement between simulated and theoretical retention was obtained for the bi-Langmuir model and excellent for the Unilan model over the whole

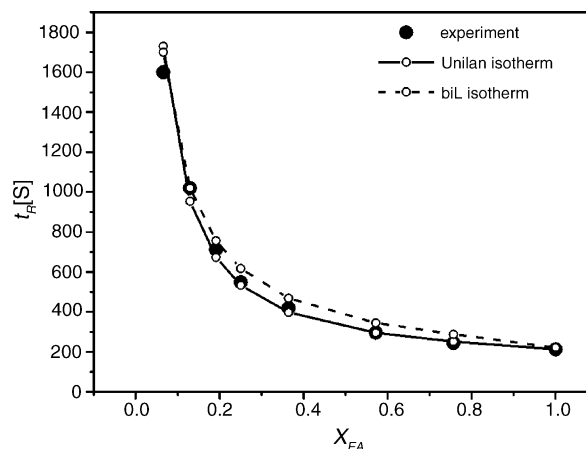


Fig. 4. Variation of the retention time of C5 pulses vs. concentration of EA in *n*-hexane (system A).

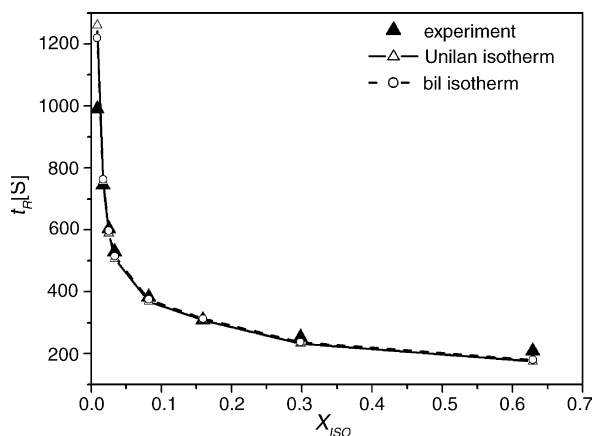


Fig. 5. Variation of the retention time of C5 pulses vs. the concentration of ISO in *n*-hexane (system B).

range of investigated saturation levels for the modifier. The good agreement could be achieved when the same model of energy distribution was assumed for both the component, e.g., simultaneously the bi-Langmuir model for the solute and the modifier or the Unilan for both the components.

The simulated retention in the system (B) was reproduced from above 1 vol.% ($x_{ISO}^m = 0.017$) of the modifier concentration. In this system, the discrepancy between predictions and experimental data was slightly lower for the bi-Langmuir model than for the Unilan model.

In the range of low modifier concentration, significant deviations between experimental data and predictions for both the models are evident (see Fig. 5 the lowest saturation level). These deviations can be expected to originate from few reasons:

- uncertainty of the isotherm data at a low modifier content;
- inaccuracy of the single isotherm model in the range of low solute and modifier concentration. Simulations performed revealed that inaccuracies in prediction of the isotherm slope in the range of low concentration influences significantly on the results of the predictions of the AST model. This phenomenon has been already mentioned in [20];
- inaccuracy of the competition model; in order to describe the binary adsorption more correctly, the energy distribution might be determined following [26]. Unfortunately, due to a number of adjustable parameters, the HIAS model appears to be not adequate for practical purposes, i.e., predicting the chromatographic elution at various mobile phase compositions.

Nevertheless, under typical conditions for chromatography of relatively high concentration excess of the modifier in the stationary phase with respect to the solute the model was found to be very effective.

4.2.2. Simulating of the non-linear profiles

In Fig. 6, the simulations of non-linear chromatographic profiles for the system of ethyl acetate (EA) as a modifier is shown. The Unilan model of isotherm was employed.

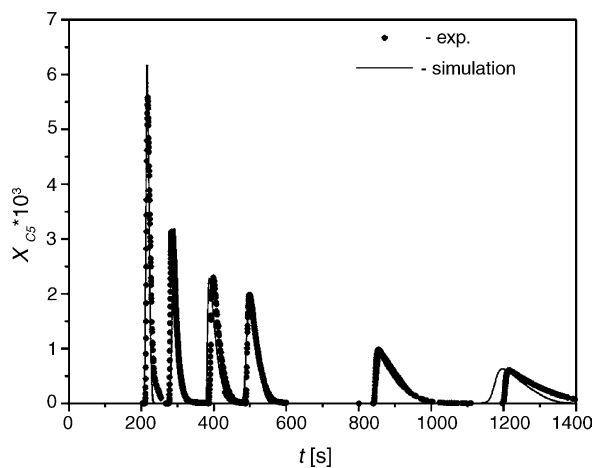


Fig. 6. Concentration profiles registered at different concentration of EA in the mobile phase: $x_{EA}^m = 0.066$; 0.129; 0.25027; 0.364; 0.572; 1, respectively (see corresponding saturation level of the stationary phase in Fig. 2b), the feed concentration of the solute c.a. $x_{C5,F} = 0.053$ for all the chromatograms—the solute was always dissolved in the adequate solvent used as the mobile phase.

The agreement between the simulated and the experimental peak shapes was very good but not perfect. Some discrepancies are evident for the lowest saturation level; moreover, the model predict slightly too symmetrical profiles for high saturation levels. However, taking into account that no adjustment has been made and the predictions are based on the single-species isotherm the agreement is very satisfactory indicating adequacy of the adsorption model developed.

For the system (B), the model bi-Langmuir isotherm model was employed offering slightly better results in the pulse analysis and, thus, better fit between the peak position simulated and recorded experimentally.

In Fig. 7, the comparison between experiment and simulation for the lowest saturation level, for which the experimental retention was reproducible by the model proposed. It is evident that the model was able to predict deformation of the peak shape, resulting from the competition between solute and the modifier, which is present in the mobile phase at relatively low,

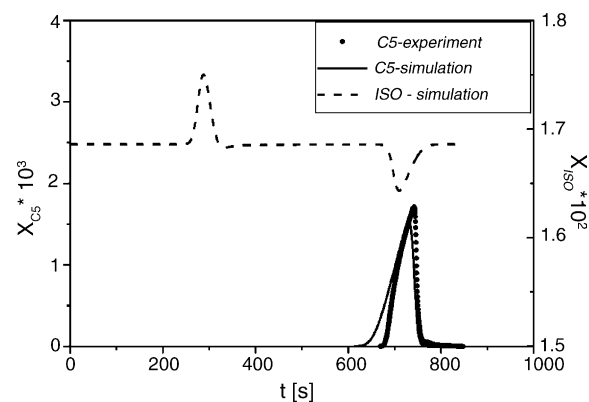


Fig. 7. Concentration profiles registered at the concentration $x_{ISO}^m = 0.0169$ of ISO in the mobile phase (see corresponding saturation level of the stationary phase in Fig. 2b), the feed concentration of the solute $x_{C5,F} = 0.064$.

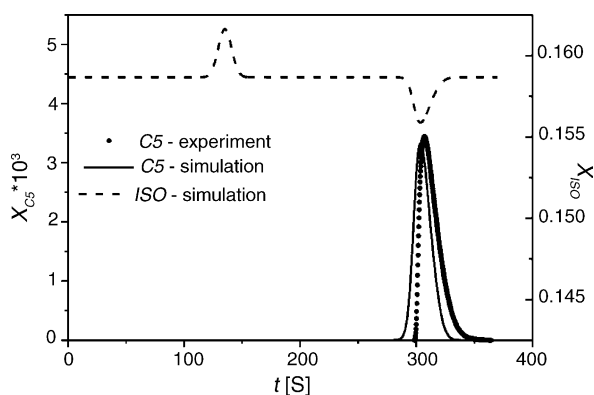


Fig. 8. Concentration profiles registered at the concentration $x_{\text{ISO}}^m = 0.159$ of ISO in the mobile phase (see corresponding saturation level of the stationary phase in Fig. 2b), the feed concentration of the solute $x_{\text{C5,F}} = 0.050$ the solute was dissolved in the solvent used as the mobile phase.

comparable to the solute concentration. In order to illustrate the competition, the concentration profile of the modifier and the solute at the column outlet are superimposed in the same figure.

For higher modifier concentration, the competition of the solute and the modifier become negligible and the peak profile converts to typical Langmuirian shape. This phenomenon can be observed in Fig. 8, wherein it is evident that the concentration level of the modifier is much higher compared to that of the modifier (compare left and right scale of the plot).

The quality of the comparison between simulations and experiment for the system (B) is similar to that achieved for the system (A). For high modifier content, the predicted profiles were too symmetrical comparing to the experiment. Nevertheless, the effectiveness of predictions was satisfactory.

5. Conclusion

The adsorbed solution model has been used for the prediction of competitive adsorption equilibria of the solute and the active component of mobile phase on the basis of single-species adsorption isotherm.

The single adsorption isotherms were determined on the basis of excess adsorption data measured in the system of single component-inert. The isotherm model accounted for energetic heterogeneity of the adsorbent surface and non-ideality of the mobile phase solution.

In order to verify the effectiveness of the model in predicting of chromatography process at varying mobile phase composition, the series of chromatograms registered at different modifier content in the mobile phase were compared to theoretical simulations.

The agreement between simulated and experimental profiles was very good at relatively high modifier content in the mobile phase compared to that of the solute.

In the range of low modifier concentration, significant deviations between experimental data and predictions were evident, which originated from uncertainty of the isotherm data for a low modifier content, inaccuracy of the single isotherm models in

the range of low solute and modifier concentration, inaccuracy of the competitive model.

For typical for chromatography conditions of high concentration, excess of the modifier with respect to the solute the model was found to be very effective; however, perfect agreement between simulated and experimental profiles cannot be expected. The method can be used for evaluation adsorption behaviour of the solute in the presence of different solvents, for which adsorption equilibrium is known. The successful experimental verification indicated the adequacy of the model for single-component equilibria and the predictive model for binary equilibria of the solute-modifier.

Acknowledgments

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