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COMPUTATIONAL ALGORITHM TO PREDICT PEAK PROFILES IN PREPARATIVE HIGH-PERFORMANCE CHROMATOGRAPHY

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Abstract—The computational algorithm and the Prep-LEAR program have been performed on the basis of the LEA model of chromatography. This program intends for calculation of peak profiles in non-linear high-performance chromatography and uses unsimplified adsorption isotherm equations. The computational algorithm and program have been tested by applying these to experimental data of thymine adsorption under conditions of reversed-phase high-performance liquid chromatography. The results of numerical calculations for different sample size introduced agree satisfactorily with experimental data and show the characteristic properties of high-performance chromatography. The usefulness of the Prep-LEAR program was confirmed by predicting peak profiles in preparative adsorption chromatographic processes.

Key words: *Peak Profiles, Preparative Chromatography, Non-linear Adsorption Isotherm, LEA Model, Computational Algorithm, Prep-LEAR Program*

INTRODUCTION

The theory of ideal chromatography in which the instant establishment of adsorption equilibrium is assumed, has been widely used [Wilson, 1940; de Vault, 1943]. This theory has been used for solutions of the inverse chromatographic problems, i.e. for the calculation of adsorption isotherms from experimental peak profiles [de Vault, 1943; Gluekauf, 1947; Belakova et al., 1967; Larin, 1987; Row et al., 1990]. The modeling of chromatography theory can be formulated as the determination of the distribution functions of concentration in mobile phase c(L,t), and adsorption on stationary phase a(L,t) along the adsorbent layer L with time t on the basis of the adsorption isotherm, the mass transfer and axial dispersion coefficients, and the experimental conditions. Usually the peak profile (elution curve) c(L,t) can be measured along the column length L. To simulate the peak profiles in the case of high-performance chromatography it is possible to use only the theory of ideal chromatography [Larin, 1989]. Nevertheless a number of scientists [Smit et al., 1980; Rouchon et al., 1985; Snyder and Cox, 1991; Row and Lee, 1992] prefer to use the other theories, methodologies, and their own computational algorithms that permit to calculate peak profiles in high-performance chromatography by numerical methods taking into account any additional details.

The LEA model was proposed [Larin, 1983a]. This model is quite suitable for design calculations employing arbitrary initial conditions and adsorption isotherms. The basic assumptions of the LEA model are confirmed by experimental data. Before this time the LEA model had been advantageously used to predict the behavior of peak profiles in high-performance chromatography [Larin, 1989], or to calculate peak profiles for columns of the short length [Larin, 1983b].

The purpose of this study is to work out the LEA model's computational algorithm for calculation and prediction of peak profiles in preparative (non-linear) high-performance chromatography.

METHODOLOGY

In our study, the model of a layer of equilibrium adsorption [LEA model, Larin, 1983a] was used to work out the computational algorithm for calculation of peak profiles in preparative high-performance chromatography. This model uses an first order ordinary differential equation which may be written as

$$d\bar{a}/dt + d\bar{c}/dt = (v/L_e)\ [c_B - f^{-1}(\bar{a})] \tag{1}$$

where $\bar{a}$ and $\bar{c}$ are the average solute concentrations in the stationary and mobile phases of a column of length L_e respectively, v is the mobile phase flow rate, a layer of equilibrium adsorption L_e is the effective kinetic constant of the LEA model, c_B is concentration entering to the layer L_e, $f^{-1}(\bar{a})$ is concentration issuing from this layer L_e and also the analytical expression of the adsorption isotherm, when concentration c is a function of adsorption a, and t is time.

Such an approach reduces the initial system of equations to a first order differential equation. It also appears possible to describe chromatographic processes on the basis of the real adsorption isotherms and an effective kinetic constant.

In the LEA model the adsorption values $\bar{a}$ are determined together with the values of the concentrations $f^{-1}(\bar{a})$ issuing from each successive layer L_e at a time. Apart from the layer-by-layer method [Cowan et al., 1986], the LEA model presupposes that over the whole column (and within each L_e layer as well) a continuous distribution of adsorption and concentration is observed.

Eq. (1) is correct for any position of the layer L_e along the column length L. If the total case is considered, Eq. (1) can be written as follows:

$$d\bar{a}_i/dt + d\bar{c}_i/dt = (v/L_e)\ [c_{i-1} - f^{-1}(\bar{a}_i)] \tag{2}$$

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where i denotes the i-th equilibrium adsorption layer, c_{i-1} is the concentration entering to the i-th layer L_e from the previous, (i−1)−th layer L_e.

The application of the LEA model involves the solution of a set of N equations of (2), where $N=L/L_e$ is the total number of layers, and L is the absolute column length. The analytical solution for a linear adsorption isotherm under the plate theory approach was analyzed previously [Ha et al., 1987; Row, 1988]. The analytical solutions in non-linear chromatography are extremely cumbersome. Therefore numerical methods are preferred for solution of a set of N Eq. (2) in the case of arbitrary adsorption isotherms.

The numerical (computational) method involves successive integration of Eq. (2) and is carried out by the finite difference method under assumption $d\bar{c}/dt \ll d\bar{a}/dt$. First, one determined the amounts of solute adsorbed on all the sequential equilibrium adsorption layers, $\Delta\bar{a}=(c_B v \Delta t)/L_e$, for the first given time step, Δt. In the case considered (elution mode of chromatography), the decrease in the amount of solute adsorbed in the first layer, L_e, is calculated at $c_B=0$ ($c_{i=1-1}=0$) and for subsequent layers c_B or c_{i-1} are determined by the concentration that is in equilibrium with the value of $\bar{a}$ for the previous layer L_e using the given adsorption isotherm. The adsorption increment $\Delta\bar{a}$ is then estimated from Eq. (2), and the total value of $\bar{a}$ is calculated by a corresponding algebraic summation of $\Delta\bar{a}$ in each layer. Thus in the second and subsequent layers a successive accumulation of the adsorbed material occurs. In the initial condition for the elution mode of chromatography, the solute sample on the first layer L_e or on a few of the first layers L_e is introduced.

The optimum interval for numerical integration, Δt, is fixed by calculations with various Δt. This interval is chosen such that the computed distribution functions coincide with each other within a given accuracy. It should be stressed that the integration interval, Δt, in the computational algorithm worked out, is just the step in numerical integration. On the basis of methodology presented above and on the basis of the programs LEACH and LEADS [Larin, 1983b], the Prep-LEAR program using Fortran 77 version was developed. This program permits to calculate peak profiles in preparative high-performance liquid chromatography, and on authors opinion it can be used to predict solute peak profiles in preparative scales, realizing in industrial adsorption processes of purification and separation. The usefulness of program Prep-LEAR will be analyzed in the next part.

APPLICATION OF PREP-LEAR PROGRAM TO EXPERIMENTAL DATA

To test the computational algorithm, the previous experimental data of the article [Row et al., 1990] were used. It has been studied the preparative reversed-phase high-performance liquid chromatography of thymine from water as mobile phase on Alltech (250×4.6 mm) C18 HS column [Row et al., 1990]. An adsorption isotherm is the major factor affecting the liquid-solid preparative process under conditions of high-performance chromatography. The adsorption isotherm of thymine from water on the reversed-phase packing material was measured by method of ideal chromatography [de Vault, 1943] and was approximated in [Row et al., 1990] by Langmuir equation:

$$a=a_1c/(1+bc) \tag{3}$$

where a is adsorption on the stationary phase, mg of solute/ml

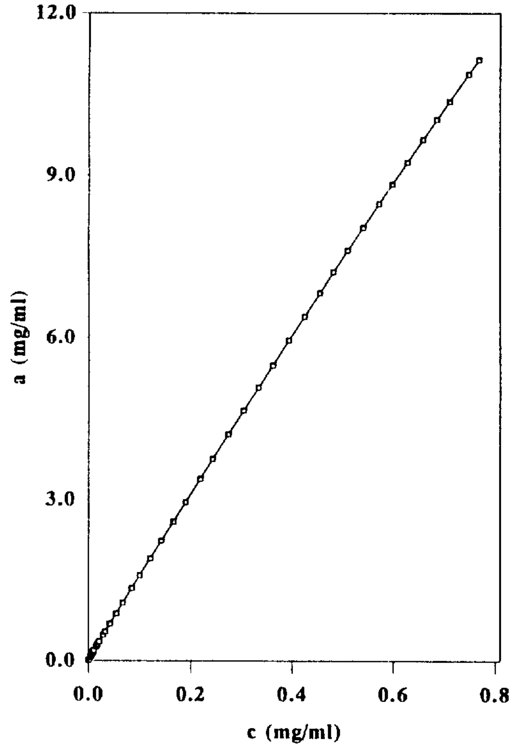

Fig. 1. Adsorption isotherm of thymine from water on reversed-phase material.

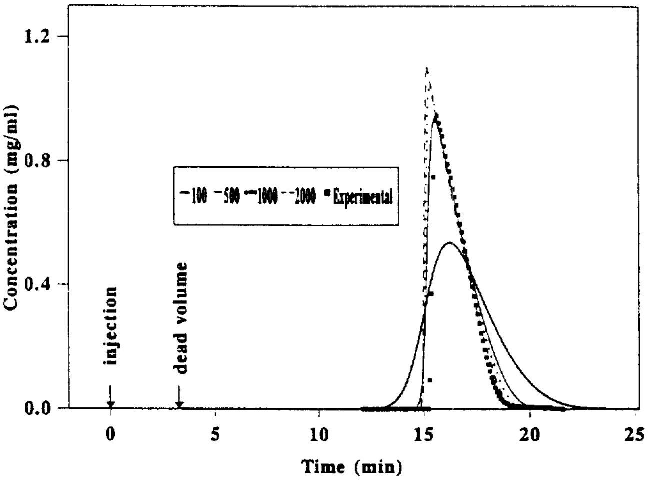

Fig. 2. Comparison of experimental and calculated thymine peak profiles.

(Points-experimental data from [Row et al., 1990]. The numbers of layers N, that was used to calculate peak profiles are shown in a central part of figure. The sample size introduced equals to 2 mg, mobile phase rate equals to 1 ml/min)

of stationary phase, and c is concentration in the mobile phase, mg of solute /ml of mobile phase. a_1 and b are Langmuir adsorption isotherm parameters.

This adsorption isotherm (Fig. 1) has a slightly convex form and is characterized by the next Langmuir adsorption isotherm parameters: $a_1=15.83$ ml/ml and $b=0.12$ ml/mg.

The experimental elution peak profile with the injection volume of 1.0 ml (2 mg/ml thymine concentration) is shown in Fig. 2

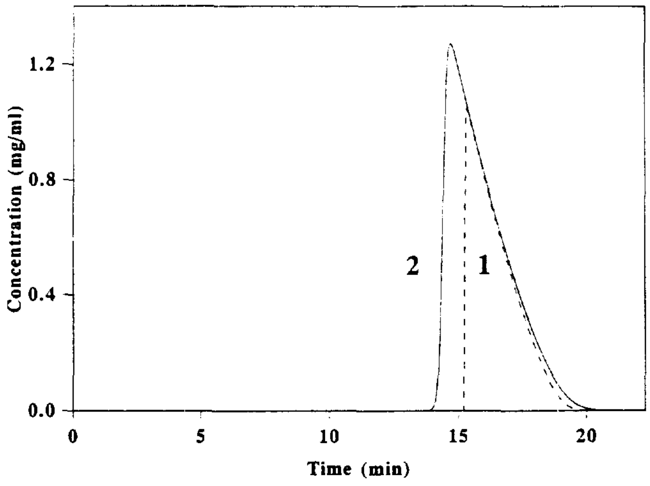

Fig. 3. Peak profiles calculated applying to conditions of Fig. 2. [sample size: 2 mg (curve 1) and 3 mg (curve 2). N=500]

in comparing with the peak profiles calculated for different values of the relative column length N. To calculate peak profiles it was used the integration interval $\Delta t=0.05$ sec. For the value of Δt less than 0.05 sec, a solution of Eq. (2) is stable and the peak profiles calculated are identical. To simulate the way of sample injection the initial quantity of solute was distributed on a few of the first layers L_e. In all cases, the Langmuir adsorption isotherm was used and all conditions (flow rate of mobile phase and a quantity of sample introduced) were corresponded to experimental ones. Final results simulated were corrected on the value of dead volume of 3.2 ml.

From the result of these calculations (Fig. 2), it is known that the peak profile calculated for the value of relative column length $N=100$ do not coincide with the experimental peak. The calculated peak profile for $N=500$ agrees closely with experimental data in the whole. However, peak profiles calculated for $N=1000$ and 2000 show a good coincidence for a tailing part of the experimental peak profile. So, depending on the purposes of preparative chromatographic optimization, it is possible to choice the preferable conditions for simulating peak profiles by Prep-LEAR program.

The numerical results for different sample size introduced (Fig. 3) agree with experimental data as in the previous case of 2 mg injection for N of 500, and show the characteristic properties of high-performance chromatographic behaviour of peak profiles. Namely, when the sample size introduced is increased the back (tailing) parts of peak profiles coincide with each other, and the front parts of peak profiles change their position along time axis remaining sharp form. This result confirms the usefulness of the Prep-LEAR program in calculating and predicting peak profiles in preparative (non-linear) high-performance chromatography.

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NOMENCLATURE

a : adsorption on stationary phase [mg/ml]
$\bar{a}$: average adsorption value on a layer L_e
a_1 and b : coefficients of Langmuir adsorption isotherm equation
c : concentration in mobile phase [mg/ml]
$\bar{c}$: average concentration value on a layer L_e [mg/ml]
c_B : concentration entering to the layer L_e [mg/ml]
c_{i-1} : concentration entering to the i-th layer L_e [mg/ml]
$f^{-1}(a)$: function representing adsorption isotherms
i : number of layer L_e
L : absolute column length [cm]
L_e : effective kinetic constant, a layer of equilibrium adsorption
$N=L/L_e$: relative column length and total number of layers L_e in the column
t : time [min]
v : mobile phase rate [ml/min]

Greek Letters

Δa : adsorption increment used for numerical calculations
Δt : interval of numerical integration in the LEA model

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