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Modelling counter-current chromatography: a chemical engineering perspective

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Abstract

In conventional chromatography, a solute is usually viewed to be longitudinally transported only in the mobile phase, remaining longitudinally motionless in the stationary phase. In counter-current chromatography, both phases undergo intense mixing in the variable force field of a coil planet centrifuge and longitudinal dispersion of matter in the stationary phase is not to be excluded. To take into account longitudinal mixing in both phases, a cell model of chromatographic process is proposed in which the number of perfectly mixed cells n is determined by the rates of mixing in stationary (D_S) and mobile (D_m) phases by the equation $n = LF/(2A_cD_m)/(1 + S_f(\lambda - 1))$ with $\lambda = K_DD_S/D_m$ (F, L, A_c and K_D are the mobile phase flow-rate, column length, column cross-section and distribution ratio, respectively). This equation has been derived by comparing the discontinuous cell model with continuous diffusion assuming equilibrium conditions. Parameter determination and their relationships are discussed.

Keywords: Counter-current chromatography; Longitudinal dispersion; Mathematical modelling

1. Introduction

Counter-current chromatography (CCC) is a new technology for analytical and preparative scale separations of chemical and pharmaceutical substances; it combines the features of liquid–liquid extraction and partition chromatography [1,2]. For scaling up, optimisation of device design and operation parameters, it is necessary to describe the chromatographic column hydrodynamics and non-steady state mass transfer between the stationary and mobile phases.

This paper is an attempt to apply approaches used in chemical engineering for modelling of mass transfer processes [3,4], in particular solvent extraction columns [5], to simulate and scale-up the chromatographic process.

The chromatographic column is considered to be a very high (long) extraction column with an extremely high length L to diameter d ratio ($L/d \gg 100$), operating under special conditions: one of the contacting phases is held stationary and mass transfer takes place under non-steady state conditions. In extraction columns, light and heavy phases move countercurrently through a vertical apparatus and they operate under steady-state conditions.

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In conventional chromatography, it is assumed that a solute is transported along the column only while it is in the mobile phase and remains longitudinally motionless in the stationary phase. In CCC, because of the lack of a solid support, both liquids undergo intense mixing in the variable force field of a coil planet centrifuge (mixing and settling zones in the coils [6] and wave mixing [1,7] have been observed) and the axial transport of a solute in the stationary phase cannot be ignored. Thus, in CCC the chromatographic behaviour is influenced by longitudinal mixing in stationary and mobile phases and mass transfer between them. In the modelling and scale up of CCC there is a need for treating as separate phenomena the contributions of dispersion of matter in stationary and mobile phases.

To predict residence time (or the elution profile) of a solute in a chromatographic column, it is essential for there to be a quantitative analysis (or mathematical model) of longitudinal mixing and mass transfer. Furthermore, dispersion phenomenon must be represented by means of a set of equations. A large number of empirical functions have been proposed and used for the description and interpretation of chromatographic peaks. Recently, about 90 of these functions have been reviewed [8]. Since the parameters of these mathematical models are not directly related to the characteristic features of a real chromatographic process, their practical application in the process simulation and scale up is problematic. It is well known that for the reliable simulation and scale up of a mass transfer process the mathematical model applied is to be able to reflect the actual physical (or physical-chemical) picture of the process. If the model replicates, even in the simplified form, the mechanism of the phenomenon, it can be used to simulate the process and analyse the effects of different process variables. In our case, as mentioned above, the spreading of the injected solute in the chromatographic column is caused by the axial mixing in the phases and the mass transfer between them; in addition, extremely high ratio of column length to diameter allows one-dimensional models to be used.

2. Description of the models

Longitudinal dispersion takes place by a complicated interaction of different mechanisms: non-uniform velocity profile of mobile phase flow, turbulence and molecular diffusion in both phases. Two simplified model schemas: 1—discrete (staged)-cell model (a cascade of well mixed equal-size vessels) and, 2—continuous-diffusion model, are shown in Figs. 1 and 2. According to the first model, the axial mixing in the chromatographic column is characterised by one parameter—number of perfectly (ideally) mixed cells n, whereas the second model has two parameters and takes into account separately the rate of mixing in the phases in the form of effective longitudinal diffusion coefficients (D_m in mobile phase, and D_S in stationary phase) defined to involve the effects of non-uniform velocity profile, turbulence and molecular diffusion. Thus, the second model formally relies on the laws of one-dimensional convective diffusion adapted to the flow in the chromatographic column. In the cell model, uniform properties in all parts of the enclosure of each cell are assumed which means that: (1) both phases are uniformly distributed in a cell volume; (2) the concentration of a solute within each phase in a cell is uniform; (3) the distribution of a solute between the phases in a cell is determined by the distribution ratio (partition coefficient) K_D, interphase mass transfer rate and the ratio of phase volumes; (4) the mobile phase flows continuously through a cascade of cells and its residence time distribution in each cell is described by an exponential function (like for any ideally mixed tank). It is important to stress that when the rate of longitudinal mixing is low (and that is the case, for $L/d \gg 100$), simulations based on

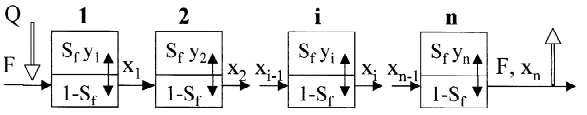

Fig. 1. Schematic diagram of the ideally mixed cells model.

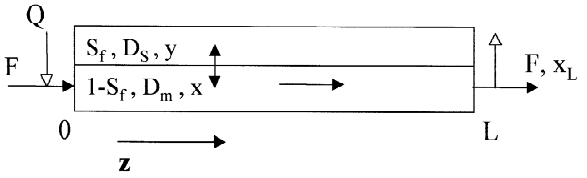

Fig. 2. The schema of the diffusion longitudinal mixing model.

discrete and continuous models give practically identical results, supposed correct relationship between models parameters is used [3–5].

In this paper, we consider the equilibrium assumption: the equilibrium distribution of the passing component between the phases is reached in perfectly mixed cells of a staged model and in any cross-section of a continuous model. This assumption means that the mass transfer is fast enough compared to the other changes occurring so that the process is governed only by the axial dispersion of solute in the stationary and mobile phases and the distribution ratio in the solvent system employed.

Further assumptions: the distribution ratio

$$K_D = y/x = \text{constant}$$

where x and y are concentrations in mobile and stationary phases, respectively.

The retained volume of stationary phase V_S is constant in any cross-section of the column, or when it is expressed as a fraction of column volume S_f:

$$S_f = V_S/(V_S + V_m) = V_S/V_c = \text{constant}$$

where V_m and V_S are the volumes of mobile and stationary phases in the chromatographic column, respectively, and $V_c = V_S + V_m$ is the column volume.

3. Analysis of the models

3.1. Cell model

Mass balance equation for the current i–cell is:

$$\frac{V_m}{n}\frac{dx_i}{d\tau} + \frac{V_S}{n}\frac{dy_i}{d\tau} = F(x_{i-1} - x_i) \quad (1)$$

with $i = 1, 2, \ldots, n$, and where F is the volumetric flow-rate of mobile phase and τ is the time.

The solution of the set of n equations (1) with boundary and initial conditions (2):

$$x_0 = 0. \quad \tau = 0: x_1 = \frac{nQ}{V_c(1 - S_f + S_f K_D)}; x_2 = x_3 = \cdots = x_n = 0 \quad (2)$$

(the inlet concentration of the mobile phase flow is zero; at $\tau = 0$, the amount Q of the solute in the sample is impulsively injected into the first ideally mixed cell) for any i-cell is obtained as:

$$\frac{x_i}{\bar{x}} = \frac{n^i}{(i-1)!} p^i t^{i-1} \exp(-npt) \quad (3)$$

for the last cell ($i = n$):

$$\frac{x_n}{\bar{x}} = \frac{n^n}{(n-1)!} p^n t^{n-1} \exp(-npt) \quad (4)$$

with

$$p = \frac{1}{1 - S_f + S_f K_D} \quad (5)$$

where $\bar{x} = Q/V_c$ is the mean concentration in the column, $t = \tau F/V_c = \tau/\tau_c$ is the dimensionless time, $\tau_c = V_c/F$ is the mean residence time of the mobile phase in the column when it is filled with only mobile phase ($S_f = 0$).

Eq. (4) represents the residence (in chromatographic terms—retention) time distribution of a solute in chromatographic column on the basis of cell model under equilibrium conditions. Let us analyse this distribution (Eq. (4)).

From Eq. (4), the position of the peak maximum on the time axis can be established: In non-dimensional form:

$$t_{max} = \frac{n-1}{np} \quad (6)$$

or in real time

$$\tau_{max} = \frac{V_c}{F}\frac{n-1}{np} = \frac{n-1}{n}\frac{V_c}{F}(1 - S_f + S_f K_D) = \tau_R \quad (7)$$

For $K_D = 0$

$$\tau_{max}(K_D = 0) = \tau_m = \frac{n-1}{n}\frac{V_c}{F}(1 - S_f) \quad (8)$$

In terms of chromatography, τ_R is the total retention time, and τ_m is the time spent in the mobile phase. Eqs. (7) and (8) differ from equations usually used in chromatography by factor $(n-1)/n$. For $n \to \infty$, the considered equations become absolutely identical.

From Eqs. (7) and (8) follows the common relationship between the total time spent in the column and the times spent in individual phases:

$$\tau_R = \tau_m + \tau_m K_D \frac{S_f}{1 - S_f} = \tau_m + \tau_S \quad (9)$$

Rewriting Eq. (7) in terms of volume gives:

$$V_R = \frac{n-1}{n}(V_c - V_S + V_S K_D) = \frac{n-1}{n}(V_m + K_D V_S) \quad (10)$$

For $n \to \infty$, this equation reduces to the fundamental equation of partition chromatography:

$$V_R = V_m + K_D V_S \quad (11)$$

For $K_D = 1$, Eq. (7) reduces to

$$\tau_{max}(K_D = 1) = \tau_R(K_D = 1) = \frac{n-1}{n}\frac{V_c}{F} \quad (12)$$

It must be pointed out that the time of peak maximum, τ_{max}, and the mean residence (or retention) time of a solute in the column (define it as $\bar{\tau}$) are in general different quantities. The mean residence time can be calculated from the chromatographic curve as its first moment. The kth moment of the distribution function (4) in dimensionless (normalised), M_k, and dimensional, m_k form is defined as:

$$M_k = \int_0^\infty t^k \frac{x_n}{\bar{x}}\,dt \quad \text{and} \quad m_k = \int_0^\infty \tau^k x_n\,d\tau$$

The expressions for the moments can be evaluated by integration either of distribution function (4) or the equations (1). The second way is easier: term-by-term integration over $0 \le \tau \le \infty$ by taking into account conditions (2) transforms the set of differential equations (4) to the set of algebraic equations containing the moments instead of concentrations. This set of algebraic equations is easy to solve to find the moments of outlet distributing function. The following expressions for the moments have been obtained:

$$M_0 = \int_0^\infty \frac{x_n}{\bar{x}}\,dt = 1, \quad m_0 = \int_0^\infty x_n\,d\tau = \frac{Q}{F} = \frac{Q}{F}\frac{V_c}{V_c} = \bar{x}\bar{\tau}_c \quad (14)$$

$$M_1 = \bar{t} = \int_0^\infty t\frac{x_n}{\bar{x}}\,dt = \frac{1}{p}, \quad m_1 = \int_0^\infty \tau x_n\,d\tau = \bar{x}\frac{V_c^2}{F^2}(1 - S_f + K_D S_f) = \bar{x}\frac{\tau_c^2}{p} \quad (15)$$

$$M_2 = \int_0^\infty t^2\frac{x_n}{\bar{x}}\,dt = \frac{1+n}{np^2}, \quad m_2 = \bar{x}\frac{(1+n)\tau_c^3}{np^2} \quad (16)$$

$$M_3 = \frac{(n+1)(n+2)}{n^2p^3}, \quad m_3 = \frac{\bar{x}\tau_c^4(n+1)(n+2)}{n^2p^3} \quad (17)$$

First moment defines the mean residence time: in non-dimensional form, $\bar{t} = 1/p$, and in real time units:

$$\bar{\tau} = \frac{m_1}{m_0} = \frac{V_c}{F}(1 - S_f + K_D S_f) = \frac{\tau_c}{p} \quad (18)$$

As can be seen from Eqs. (7) and (18) for $n \to \infty$, $\tau_R = \bar{\tau}$.

The shape of the distribution curve can be characterised by central moments: the distribution width is defined by second central moment, variance σ^2, the asymmetry—by third central moment η. From Eqs. (14)–(18), we obtain the expressions for these quantities as follows in real time:

$$\sigma_n^2 = \frac{1}{m_0}\int_0^\infty (\tau - \bar{\tau})^2 x_n\,d\tau = \frac{m_2}{m_0} - \left(\frac{m_1}{m_0}\right)^2 = \frac{V_c^2}{nF^2}(1 - S_f + K_D S_f)^2 \quad (19)$$

$$\eta_n = \frac{1}{m_0}\int_0^\infty (\tau - \bar{\tau})^3 x_n\,d\tau = \frac{m_3}{m_0} - 3\frac{m_2}{m_0}\frac{m_1}{m_0} + 2\left(\frac{m_1}{m_0}\right)^3 = \frac{2V_c^3}{n^2F^3}(1 - S_f + K_D S_f)^3 \quad (20)$$

and in non-dimensional form

$$\sigma^2 = \frac{\sigma_n^2}{(V_c/F)^2} = \frac{1}{n}(1 - S_f + K_D S_f)^2 = \frac{1}{np^2} \quad (21)$$

$$\eta = \frac{\eta_n}{(V_c/F)^3} = \frac{2}{n^2}(1 - S_f + K_D S_f)^3 = \frac{2}{n^2p^3} \quad (22)$$

For a large number of cells n (low degree of axial mixing) the distribution function (4) can be approximated by a normal distribution:

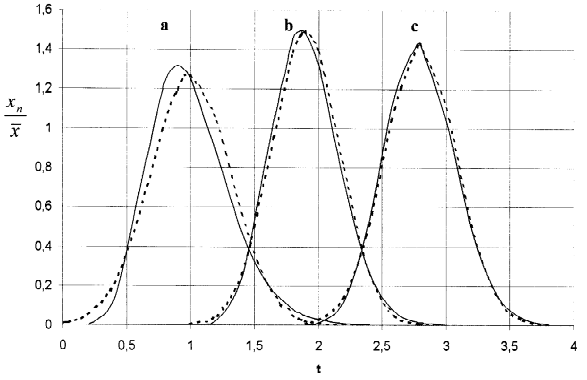

Fig. 3. Chromatographic curves calculated using Eq. (4)—solid lines and Eq. (23)—dotted lines: (a) $n=10$, $K_D=1$; (b) $n=50$, $K_D=2$; (c) $n=100$, $K_D=3$.

$$\frac{x_i}{\bar{x}} = \frac{p}{\sqrt{2\pi/n}} \exp\left[-\frac{(1-pt)^2 n}{2} \right] \tag{23}$$

Fig. 3 shows chromatographic curves calculated for some values of mixing parameter n using Eqs. (4) and (23). As can be seen, the response curves become more identical with growing n.

For the normal (Gauss) distribution (23):

$$t_{max} = \bar{t}, \quad \text{or} \quad \tau_R = \bar{\tau} = \tau_{max} \tag{24}$$

and the distribution curve is always symmetric:

$$\eta = 0 \tag{25}$$

This distribution is often used in chromatography.

For the distribution function (4), expressions (24) and (25) become valid only for $n \to \infty$. For both distributions for $n \to \infty$, $\sigma^2 \to 0$.

The cell model is simple to use, but in the form as presently considered, it is not appropriate for describing the axial dispersion in both phases. For $K_D = 0$ the model reduces to the conventional cell model applied in chemical engineering to describe the effect of axial mixing on reaction and countercurrent mass exchange processes [3–5].

3.2. Diffusion model

The model schema is shown in Fig. 2, the corresponding mathematical model has the following form:

$$A_c(1-S_f)D_m\frac{\partial^2 x}{\partial z^2} - F\frac{\partial x}{\partial z} + A_c S_f D_S \frac{\partial^2 y}{\partial z^2} = A_c(1-S_f)\frac{\partial x}{\partial \tau} + A_c S_f \frac{\partial y}{\partial \tau} \tag{26}$$

$$A_c(1-S_f)D_m\left(\frac{\partial x}{\partial z}\right)_0 + A_c S_f D_S\left(\frac{\partial y}{\partial z}\right)_0 - Fx(z=0) = 0 \tag{27}$$

$$\left(\frac{\partial x}{\partial z}\right)_L = 0 \tag{28}$$

$$x(z,0) = \begin{cases} \dfrac{Q}{\Delta z\, A_c(1-S_f+K_D S_f)}, \ldots\ldots 0 \le z \le \Delta z \\ \ldots\ldots\ldots\ldots 0, \ldots\ldots\ldots\ldots\ldots\ldots \Delta z < z \le L \end{cases} \quad \ldots . \Delta z \to 0 \tag{29}$$

where A_c is column cross-section and z is longitudinal coordinate along the flow tube.

Eq. (26) describes the unsteady-state longitudinal transport of a solute in a chromatographic tubing on the basis of one-dimensional diffusion. Eqs. (27) and (28) represent the boundary conditions for a closed channel, they can be obtained from the material balances at the both ends of the tubing. Expression (29) describes initial conditions.

From Eqs. (26–29), the expressions for the moments of residence time distribution have been found:

$$M_1 = \bar{t} = 1/p = 1 - S_f + K_D S_f \tag{30}$$

$$\sigma^2 = \frac{2}{p^2}\left(\frac{1}{Pe} - \frac{1}{Pe^2} + \frac{1}{Pe^2}\exp(-Pe)\right) \tag{31}$$

$$\eta = \frac{12}{p^3 Pe^2}\left(1 + \exp(-Pe) - \frac{2}{Pe} + \frac{2}{Pe}\exp(-Pe)\right) \tag{32}$$

with

$$Pe = \frac{LF/A_c}{(1-S_f)D_m + K_D S_f D_S} \tag{33}$$

Here Pe is the modified Peclet number, it defines the overall axial mixing rate in a chromatographic column.

As in the case of cell model, for $Pe \to \infty$, $\sigma^2 \to 0$ and $\eta \to 0$. For both models with decreasing rate of longitudinal mixing (with increasing n and Pe), the

rate of approach to zero for η is much greater than for σ^2. This enables the exact solutions for both models to be approximated by a normal distribution.

By comparing Eqs. (15) or (18) and (30), we see that the mean residence time (we can call it the exact retention time) is the same for cell and diffusion models. Furthermore, it can be shown that the expression for mean residence time: in dimensional form—Eq. (18), in non-dimensional form—Eq. (15) or (30), is valid for the non-equilibrium assumption too.

As noted above, for low degree of longitudinal mixing, the solution of the diffusion model equation can be approximated by a normal distribution:

$$\frac{x_L}{\bar{x}} = \frac{p}{2\sqrt{\pi/\mathrm{Pe}}} \exp\left[-\frac{(1-pt)^2 \mathrm{Pe}}{4} \right] \tag{34}$$

3.3. Parameter relationships

By comparative analysis of cell and diffusion models (in particular, Eqs. (21) and (31)), the following relationship between their parameters has been derived:

$$n = \mathrm{Pe}/2$$

This formula can be rewritten as:

$$n = \frac{n_c}{1 + S_f(\lambda - 1)} \tag{35}$$

where

$$n_c = \frac{LF/A_c}{2D_m}$$

is the number of perfectly mixed cells in mobile phase for the case $S_f = 0$;

$$\lambda = \frac{K_D D_S}{D_m} = \frac{D_S y}{D_m x}$$

is a dimensionless number, characterising the ratio of matter dispersion in stationary phase to that in mobile phase.

Formula (35) defines the relationship between the process efficiency (number of theoretical plates, n) and thermodynamic (distribution ratio K_D) and hydrodynamic (longitudinal mixing rates in stationary D_S and mobile D_m phases and S_f) parameters. This relationship demonstrates that the number of theoretical plates (more exact it were to be called the number of ideally mixed cells under equilibrium conditions) may be different for two solutes contained in a sample.

The analysis of formula (35) shows that increase in S_f can oppositely influence the efficiency, depending on λ: the increase in S_f can increase or decrease n.

When a solute has a low distribution ratio and/or the rate of axial mixing in the stationary phase is low and/or the D_m is high, $\lambda < 1$, and $n > n_c$, an increase in S_f (for all other variables being constant) increases n. For an opposite case $\lambda > 1$ and $n < n_c$, an increase in S_f can decrease n.

When $K_D = D_S/D_m$, $\lambda = 1$ and $n = n_c$. When $K_D = 0$ or when the axial mixing in the stationary phase is negligible $\lambda = 0$ and $n = n_c/(1 - S_f) = n_m$ (here n_m is the number of perfectly mixed cells in the mobile phase).

The separation of two solutes is commonly defined by the resolution R_S:

$$R_S = \frac{2(\bar{\tau}_2 - \bar{\tau}_1)}{W_{b1} + W_{b2}} \tag{36}$$

where W_{b1} and W_{b2} are the 4σ base widths of the corresponding output curves.

Replacing W_b in Eq. (36) with the expression $W_b = 4\bar{\tau}/\sqrt{n}$ obtained from Eqs. (18) and (19) provides:

$$R_S = \frac{2(\bar{\tau}_2 - \bar{\tau}_1)}{4\left(\frac{\bar{\tau}_1}{\sqrt{n_1}} + \frac{\bar{\tau}_2}{\sqrt{n_2}}\right)} \tag{37}$$

Substituting the values for $\bar{\tau}$ from Eq. (18) and n from Eq. (35) after rearrangement gives:

$$R_S = \frac{1}{4}(\alpha - 1)\sqrt{n_c} \times \frac{K_{D1}}{\frac{1 - S_f}{2S_f}\left[\sqrt{1 + S_f(\lambda_1 - 1)} + \sqrt{1 + S_f(\lambda_2 - 1)}\right] + \frac{K_{D1}}{2}\left[\sqrt{1 + S_f(\lambda_1 - 1)} + \alpha\sqrt{1 + S_f(\lambda_2 - 1)}\right]} \tag{38}$$

where α is the separation factor commonly defined as the ratio of the distribution ratios of two solutes $\alpha = K_{D2}/K_{D1}$.

Eq. (38) expresses the contribution of separation factor and longitudinal mixing in the phases to resolution. The factor α is influenced by the solvent system selected. Longitudinal mixing in the phases is

mainly determined by the energy input through a force field set up by a coil planet centrifuge, by tubing diameter and by mobile phase flow-rate.

Eq. (38) shows that increasing S_f (for all other variables being constant) can increase or decrease resolution, depending on whether $\lambda<1$, or $\lambda>1$. When $\lambda_1$and λ_2 approach 1, Eq. (38) reduces to:

$$R_S = \frac{1}{4}(\alpha-1)\sqrt{n_c}\frac{K_{D1}}{\frac{1-S_f}{S_f}+\frac{K_{D1}(1+\alpha)}{2}} \quad (39)$$

This equation has the same form as the equation, derived by Conway and Ito [1]; the only difference is in the plate (cell) number term: n_c in Eq. (39) determines the number of ideally mixed cells in the mobile phase for $S_f=0$ and is defined as $n_c = LF/A_c/2D_m$, whereas by Conway and Ito, this term represents the number of theoretical plates.

For preparative and production scale separations it is appropriate to estimate separation efficiency by direct calculation of solute content for each eluting peak. From Eqs. (1)–(3), the relationship between the amount of a solute eluted by the time t, $Q(t)$, and process parameters can be derived as follows:

$$\frac{Q(t)}{Q} = 1-\exp(-npt)\sum_1^n \frac{(npt)^{i-1}}{(i-1)!} \quad (40)$$

Using this equation, one can calculate the time-dependent composition of an eluting sample.

4. Parameter determination from chromatograms

The rates of mixing in the phases can be calculated using Eq. (35) from known retained volume fraction of stationary phase S_f and from measurements of n_1 and n_2, K_{D1} and K_{D2} taken directly from chromatograms:

$$\frac{D_S}{D_m} = \left(\frac{1-S_f}{S_f}\right)\frac{n_1-n_2}{n_2K_{D2}-n_1K_{D1}} \quad D_m = \frac{LF/A_c}{2\,n_1(1-S_f+\lambda_1 S_f)} \quad (41)$$

For experimental estimation of the distribution ratio, it is appropriate to determine K_D from the whole chromatographic curve using Eq. (18) and the relationship:

$$m_k = \int_0^\infty \tau^k x_n \, d\tau \approx \Delta\tau \sum_1^m x_i \tau_i^k \quad (42)$$

The main advantage of this way of measuring distribution ratio is it that the expression for mean residence time—Eq. (18), as mentioned above, is valid for the non-equilibrium assumption too.

To estimate n_1 and n_2, the peak height can be recommended. From Eqs. (4) and (6), we have the peak height as follows:

$$\left(\frac{x_n}{\bar{x}}\right)_{max} = \frac{np}{(n-1)!}(n-1)^{n-1}\exp(1-n) \quad (43)$$

Considering for large n the relationship for factorial

$$(n-1)! \approx \sqrt{2\pi(n-1)}(n-1)^{n-1}\exp(1-n)$$

Eq. (43) can be simplified to

$$\left(\frac{x_n}{\bar{x}}\right)_{max} = \frac{np}{\sqrt{2\pi(n-1)}} \approx \frac{p\sqrt{n}}{\sqrt{2\pi}} \quad (44)$$

This expression is identical to the peak height of the Gauss distribution, Eq. (23). Using Eq. (44), the cell number can be calculated from the measured peak height $(x_n/\bar{x})_{max}$ and mean residence time $\bar{t}$:

$$n = 2\pi\left[\bar{t}\left(\frac{x_n}{\bar{x}}\right)_{max}\right]^2 \quad (45)$$

5. Conclusion

The chromatographic process is appropriate to describe on the modified cell model basis using n determined by Eq. (35). Thus, the process model involves eight dimensional parameters: distribution ratio K_D, longitudinal mixing rates in stationary D_S and mobile D_m phases, column length L, mobile phase flow-rate F, column volume V_c, stationary phase volume V_S and the amount of the solute introduced Q. These eight parameters are reduced to four: two dimensional $\tau_c = V_c/F$, $\bar{x} = Q/V_c$, and two dimensionless p and n defined by Eqs. (5) and (35). The first two dimensional parameters can be calculated from operating data p and n can be taken from chromatograms or calculated from known (ex-

perimentally determined or theoretically predicted) other process parameters. Eq. (35) enables us to estimate the contribution of longitudinal mixing in both phases to overall dispersion of a solute in the column. This approach allows these two phenomena (longitudinal mixing in mobile and stationary phases) to be examined separately, to see their individual effects on the chromatographic process.

The model developed can be applied for CCC process simulation when the mass transfer rate between the phases is large enough to be ignored. In general, it is applicable to symmetrical chromatographic peaks. For low mass transfer, the presented model must be extended to include the mass transfer rate. Then it will be able to describe the asymmetrical peaks as well.

6. Nomenclature

A_c	column cross-section, cm^2
d	column diameter, cm
D_m, D_S	axial dispersion coefficient, cm^2/s
F	flow-rate of mobile phase, ml/s
K_D	distribution ratio (partition coefficient), dimensionless
i	current cell number, dimensionless
L	column length, cm
m_k	kth moment of distribution function, s^{k+1} g/ml
M_k	kth moment of normalised distribution function, dimensionless
n	number of perfectly (ideally) mixed cells, dimensionless
n_c	number of perfectly mixed cells in the case, when the column is filled with mobile phase only, dimensionless
n_m	number of perfectly mixed cells in mobile phase, dimensionless
p	parameter defined by Eq. (5), dimensionless
Pe	Peclet number defined by Eq. (33), dimensionless
Q	total mass of solute injected, g
S_f	fractional volume of column occupied by stationary phase, dimensionless
t	time ($t = \tau F/V_c$), dimensionless
$\bar{t}$	mean residence (retention) time of solute in a column, dimensionless
V_c	column volume, ml
V_m	volume of mobile phase in a column, ml
V_S	volume of stationary phase retained in a column, ml
V_R	total retention volume, ml
W_b	4σ base width of a chromatographic peak, s
x, y	concentration of solute in mobile and stationary phases, g/ml
z	longitudinal coordinate along a flow tube, cm
τ	time, s
$\bar{\tau}$	mean residence (retention) time of solute in a column, s
τ_c	mean residence time of mobile phase in a column, when it is filled with mobile phase only, s

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