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Journal of Chromatography A, 1043 (2004) 149–157
JOURNAL OF CHROMATOGRAPHY A
www.elsevier.com/locate/chroma

Equivalence of the microscopic and macroscopic models of chromatography: stochastic–dispersive versus lumped kinetic model

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Received 4 February 2004; received in revised form 26 May 2004; accepted 28 May 2004

Abstract

The microscopic model of chromatography is a stochastic model that consists of two fundamental processes: (i) the random migration of the molecules in the mobile phase, and (ii) the random adsorption–desorption of molecules on the stationary phase contained in a chromatographic column. The diffusion and drift of the molecules in the mobile phase is described with a simple one-dimensional random walk. The adsorption–desorption process is modeled by a Poisson process that assumes exponential sojourn times of the molecules in both the mobile and the stationary phases. The microscopic, or molecular model of chromatography studied here turns out to be identical to the macroscopic lumped kinetic model of chromatography, whose solution is well known in chromatography. A complete equivalence of the two models is established via the identical expressions they provide for the band profiles.

Keywords: Chromatographic models; Stochastic–dispersive model; Lumped kinetic model; Characteristic function; Adsorption–desorption kinetics

1. Introduction

Chromatographic processes are usually described with *macroscopic* models. Very often this consists in formulating a proper differential mass balance equation that describes the physico-chemical processes of chromatography with a desired detail [1,2]. The chromatographic band profiles are obtained via the integration of the mass balance equations. The mass balance models usually assume instantaneous equilibrium between the mobile and the stationary phases or use kinetic rate constants to characterize the resistance to mass transfer or adsorption–desorption.

The *microscopic*—or stochastic—models, on the other hand, depict the chromatographic processes at a molecular level via the random migration of the molecules along the chromatographic column.

Statistical or stochastic approaches have always offered a successful alternative to model chemical kinetics [3]. The stochastic model of chromatography was introduced by Giddings and Eyring [4]. In their model, they assumed that while migrating along the column, a molecule performs a random number of adsorption and desorption steps characterized by a Poisson distribution. Furthermore, once a molecule is adsorbed on the stationary phase, the time spent until desorption—the sojourn time—is a random variable, too. This latter random variable follows an exponential distribution. A significant effort has been devoted to the extension of the stochastic model to heterogeneous surfaces in the 1960s, but the handling of the problem in time domain resulted in rather complex expressions, inadequate for practical calculations [5,6].

de Clerk et al. [7] and Weiss [8] used the master equation to develop the stochastic model of chromatography. Their models result in an asymmetrical chromatographic elution profile on a finite-length column, with a limiting Gaussian distribution at sufficiently long times.

In the field of chemical engineering, the stochastic approach was used to determine residence time distributions in systems governed by dispersion [9,10].

The characteristic function (CF) approach remarkably facilitates the use of the stochastic model of chromatography [11,12]. The use of CF facilitated the extension of the

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doi:10.1016/j.chroma.2004.05.081

stochastic theory to two-site [13] or to generic multiple-site heterogeneous surfaces [14] that are very complex to handle otherwise [4,15,16]. Thus, the CF approach of the stochastic theory is able to model the band profile that is due to any unimodal or multimodal distribution of sorption energies. The stochastic model was further extended to describe the effect of mobile phase dispersion and size exclusion effects as well [17–19].

By means of the CF method, closed form expressions are obtained in Fourier domain for the band profiles, thus the statistical moments can directly be calculated even if the transformation into time domain is possible numerically only [20].

The stochastic model of nonlinear chromatography was developed via Monte Carlo simulations [21] and it was demonstrated that the Monte Carlo model of nonlinear chromatography is equivalent to the macroscopic kinetic model of Thomas [22].

The dispersion in the mobile phase is very often neglected in the stochastic models. In some studies the contribution of the mobile phase dispersion was modeled simply with a Gaussian distribution [11,23,17] or by first-passage density calculated from the diffusion equation [15].

In this study, we make a distinction between destructive and nondestructive detectors to provide a versatile description of the mobile phase process. The former one is modeled by the first passage distribution, the latter one with the diffusion equation.

There have been some attempts to compare the microscopic and the macroscopic models of chromatography. Usually this is restricted to the comparison of the first and the second moments. Cavazzini et al. showed that the number of theoretical plates calculated by either the microscopic or the macroscopic kinetic models of chromatography agree as long as the mobile phase dispersion is neglected [14]. Felinger et al. considered the mobile phase dispersion by a Gaussian peak and proved that the first and the second moments of the stochastic–dispersive and the lumped kinetic models are identical [17].

In the different fields of science, there is a countless number of cases in which one physical system is modeled in significantly different ways [24]. These models are based on different physical descriptions of the problem (according to the author's preference) and need proper mathematical tools to be handled. When a consistent set of initial hypotheses is assumed, equivalence between different models is evidently expected, even though there may be no apparently immediate or obvious connection between them. Nevertheless, any model has its specific peculiarities that make it a unique tool for the understanding of the described phenomena.

This appears particularly so in the case of chromatography, for which the effort of a unifying description between macroscopic and microscopic models is far from being complete. On the other hand, in our opinion, a microscopic–stochastic description of the chromatographic process will in the future provide a notably powerful tool to interpret the information gathered by new frontiers of chromatographic separations (such as separation at micro and nano level, sensoristic approach, etc. [25–28]).

In this study, we introduce a stochastic–dispersive model of chromatography and compare that model with the lumped kinetic model of chromatography. From a physical–chemical point of view, these models are of very similar complexity. Both models characterize the homogeneous adsorption and desorption processes by rate constants or—what is equivalent—with average residence times. Furthermore, both models describe the mobile phase dispersion with one axial dispersion coefficient. The fundamental difference between the models relies in the modeling approach. The microscopic model is built up by a first passage distribution arising from a 1-D discrete random walk, accompanied by a random sequence of adsorption events (this latter is characterized by a Poisson process). The macroscopic model is obtained by solving a partial differential equation.

The aim of the present manuscript is two-fold:

(i) The mobile phase dispersion is considered by a one-dimensional random walk and by the first passage time distribution arising from the random walk. When combined with the stochastic process of adsorption–desorption, this approach leads to a rather general stochastic representation of the chromatographic process.
(ii) Furthermore, we show that not only the first and the second moments but also the whole peak shape obtained with the microscopic and the macroscopic models studied here are identical. The model developed here is absolutely equivalent to the lumped kinetic model, thus the link between the macroscopic (mass-balance based) model and the microscopic (random walk) model is fully established.

The anonymous referees of the present work do not think that the microscopic and macroscopic models we compare in this study are fundamentally different in nature, because the two models use similar parameters and they model the chromatographic process in the same depth. In our opinion, however, the uniqueness of the microscopic model is not only in the level of the physical detail but also in the exact probabilistic structure of the stochastic process. It is, of course, well known that when 1-D diffusion is modeled at the microscopic level by the independent random movement of the molecules, the solution becomes identical to the Fick equations derived from the macroscopic model [24]. The chromatographic process is much more complicated than diffusion with drift, and the proper modeling of the adsorption–desorption process is essential. It is indeed expected that some equivalence should exist between microscopic and macroscopic models as macroscopic models can be regarded as ensemble averaged microscopic models.

2. Theory and results

We first focus on the mobile phase process and then consider that molecules adsorb on the stationary phase. We assume that molecules diffuse at random in the mobile phase and this random diffusion is accompanied by a drift of constant velocity.

2.1. The random walk model of diffusion with drift

Let us assume that on a one-dimensional grid a particle steps at discrete times between sites. $P_n(k)$ denotes the probability that the particle is at position k after n steps. We assume that the wandering particles have no memory, the steps are uncorrelated and independent. We imagine that the length of one step is one. The probability that the particle steps to the right is p, whereas a step to the left has the probability of $q = 1 - p$. When $p = q = 1/2$, we have a pure diffusion without drift. Otherwise $p \neq q$ implies a convection. $P_n(k)$ can be expressed as:

$$P_n(k) = pP_{n-1}(k-1) + qP_{n-1}(k+1) \tag{1}$$

When the random walk starts, the particle is at the origin, i.e. $P_0(0) = 1$ and $P_0(k) = 0$ for any k. After one step, the probability that the particle is at k is

$$P_1(k) = pP_0(k-1) + qP_0(k+1) \tag{2}$$

Eq. (2) yields $P_1(1) = p$, $P_1(-1) = q$ and $P_1(k) = 0$ for other values of k. The probability $P_n(k)$ is the sum of n random quantities. The sum of random numbers can be conveniently calculated by means of the CF. The CF of the random variable X is the expectation $E\{e^{i\xi X}\}$, where ξ is an auxiliary variable and i is the imaginary unit. The CF of a random variable and the probability density function of the random variable form a Fourier transform pair.

The CF of a unit shift is $e^{i\xi}$, therefore the CF of $P_1(k)$ is:

$$P_1(\xi) = pe^{i\xi} + qe^{-i\xi} \tag{3}$$

The CF of the final probability $P_n(k)$ after n random steps is:

$$P_n(\xi) = (pe^{i\xi} + qe^{-i\xi})^n = e^{-i\xi n}(pe^{2i\xi} + q)^n \tag{4}$$

To calculate the probability density function from $P_n(\xi)$, we recall that the CF of the binomial distribution:

$$P(n,k) = \binom{n}{k} p^k q^{n-k} \tag{5}$$

has the form of

$$P(n,\xi) = (pe^{i\xi} + q)^n \tag{6}$$

Utilizing this property, and recalling the time-shift and scaling theorems of Fourier transform[1] we obtain the following binomial distribution for the position of the wandering particle after n steps:

$$P_n(k) = \frac{1}{2}\binom{n}{(n+k)/2} p^{(n+k)/2} q^{(n-k)/2} \tag{7}$$

The mean and the variance of the binomial distribution of Eq. (5) are np and npq, respectively. The moments of the distribution of Eq. (7) can be calculated from the derivatives of the CF (Eq. (4)). We obtain that the mean and the variance are $n(p-q)$ and $4npq$, respectively. The binomial distribution of Eq. (7) can be approximated by the following Gaussian equation when n is sufficiently large:

$$p_n(k) = \frac{1}{\sqrt{8\pi npq}} e^{-[k-n(p-q)]^2/8npq} \tag{8}$$

We assume that the time between successive steps is τ. Thus, the total time of the random walk is $t = n\tau$. The rate of drift can be calculated as $u = (p-q)/\tau$. We define the diffusion coefficient as one half of the rate of variance increase in time:

$$D = \frac{1}{2}\frac{\mathrm{d}\sigma_x^2}{\mathrm{d}t} \tag{9}$$

where symbol σ_x^2 illuminates the fact that a 1-D model has been used. Since the variance is $\sigma_x^2 = 4npq = 4tpq/\tau$, the diffusion coefficient is $D = 2pq/\tau$. When the distance between neighboring grid points is Δ, the length of one step is also Δ and the distance of point k from the origin is $z = k\Delta$. Introducing all these definitions in Eq. (8), we have the following probability density function:

$$p(z,t) = \frac{1}{\sqrt{4\pi Dt}} \exp\left[-\frac{(z-ut)^2}{4Dt}\right] \tag{10}$$

Eq. (10) gives the probability that a diffusing particle is at z at time t. Although Eq. (10) was derived assuming discrete time and length, the same expression is obtained for the case of a random walk in continuous time and length.

When both the time and the length are continuous variables, the following partial differential equation (PDE) can be written for the probability that a particle is at position z at time t [29,30]:

$$\frac{\partial p(z,t)}{\partial t} = -u\frac{\partial p(z,t)}{\partial z} + D\frac{\partial^2 p(z,t)}{\partial z^2} \tag{11}$$

The solution of this mass balance equation is given in Eq. (10) when assuming the same initial condition, i.e. that the molecule is at the origin at $t = 0$: $p(z,0) = \delta(z)$.

We recall that the distribution in Eq. (10) gives the probability that at time t the particle is at a distance z from the origin. Therefore $p(z,t)$ includes those particles too which wandered to a longer distance than z and diffused backward to z. In chromatography, $p(L,t)$ gives the band profile recorded with a nondestructive detector. For instance, with UV detection in HPLC, a molecule might diffuse back to the detector cell, just after it has left the cell.

[1] The time-shift theorem states that the term frequency-domain term $e^{i\xi n}$ represents a shift by n in the time domain. The scaling property expresses that if $f(t)$ and $F(\omega)$ are a Fourier pair, then $f(at)$ and $F(\omega/a)/|a|$ are also a Fourier pair.

If we want to know when a particle reached position z for the first time, we have to calculate the first passage time distribution. This second scenario will give the band profile with a destructive detector, such as the flame ionization detector. In destructive detectors, the molecule is destroyed as soon as it enters the detector cell, therefore it is not possible that one molecule is detected twice due to backward diffusion. This distinction, in theory, gives different band profiles. In the practice, however, the difference between the band profiles calculated by the two approaches is completely negligible and experimentally cannot be measured.

In Appendix A, the most important peak shape parameters are summarized for nondestructive detectors.

2.2. First passage time

We are interested in calculating the first passage distribution $f(z,t)$, i.e. the probability that the first passage of a particle through a position $z > 0$ will occur between t and $t + \mathrm{d}t$ [31,32]. This position z in chromatography corresponds exactly to the column outlet. The first passage time in a one-dimensional continuum can be calculated with the following convolution integral [29]:

$$p(z,t) = \int_0^t f(z,\tau)p(0,t-\tau)\mathrm{d}\tau \tag{12}$$

In Laplace domain, the above equation simplifies to

$$\tilde{p}(z,s) = \tilde{f}(z,s)\tilde{p}(0,s) \tag{13}$$

where

$$\tilde{p}(z,s) = \int_0^\infty p(z,t)e^{-st}\mathrm{d}t \tag{14}$$

The Laplace transform of $p(z,t)$ (Eq. (10)) is

$$\tilde{p}(z,s) = \frac{1}{\sqrt{4Ds+u^2}}\exp\left[\frac{z}{2D}(u-\sqrt{4Ds+u^2})\right] \tag{15}$$

We can calculate $\tilde{f}(z,s)$ by means of Eq. (13) and we obtain

$$\tilde{f}(z,s) = \exp\left[\frac{z}{2D}(u-\sqrt{4Ds+u^2})\right] \tag{16}$$

For the density function given in Eq. (10) we get the following expression for the first passage time after the inverse Laplace transform of Eq. (16):

$$f(z,t) = \frac{z}{\sqrt{4\pi Dt^3}}\exp\left[-\frac{(z-ut)^2}{4Dt}\right] \tag{17}$$

It is interesting to note that both $p(z,t)$ and $f(z,t)$ are solutions of Eq. (11). We obtain $f(z,t)$ as the solution of Eq. (11) with different boundary conditions: $p(z,0) = 0$ and $p(0,t) = \delta(t)$. Furthermore, when $f(z,t)$ is obtained as the solution of the diffusion equation, the first passage time distribution is also $f(z,t)$ itself. For the column outlet we obtain the following first passage time distribution:

$$f(t) = \frac{L}{\sqrt{4\pi Dt^3}}\exp\left[-\frac{(L-ut)^2}{4Dt}\right] \tag{18}$$

When we introduce $N_d = Lu/(2D)$ to account for the mobile phase dispersion and $t_0 = L/u$ for the dead time of the column, $f(t)$ becomes:

$$f(t) = \sqrt{\frac{N_d t_0}{2\pi t^3}}\exp\left[-\frac{N_d}{2}\frac{(t-t_0)^2}{t_0 t}\right] \tag{19}$$

The CF of $f(t)$ is

$$\phi_m(\omega) = \exp\left[N_d\left(1-\sqrt{1-\frac{2i\omega t_0}{N_d}}\right)\right] \tag{20}$$

2.3. The microscopic kinetic model

We assume that, as it migrates along the column, the molecule adsorbs and desorbs at random. The number of adsorption–desorption steps is given by a Poisson distribution:

$$p_k = \frac{e^{-k}n^k}{k!} \tag{21}$$

where n is the mean number of sorption steps. The CF of the Poisson distribution is:

$$\phi_k(\omega) = \sum_k p_k e^{ik\omega} = e^{n(e^{i\omega}-1)} \tag{22}$$

The sojourn time in the stationary phase during one adsorption step is given by an exponential distribution:

$$f_s(t) = \frac{e^{-t/\tau_s}}{\tau_s} \tag{23}$$

where τ_s is the average sojourn time. The CF of $f_s(t)$ is

$$\phi_s(\omega) = \frac{1}{1-i\omega\tau_s} \tag{24}$$

When the surface of the stationary phase—and thus the adsorption–desorption kinetics—is homogeneous, every adsorption step of each molecule is characterized by $f_s(t)$. The residence time in the stationary phase of a molecule that undergoes k adsorption steps is the sum of k random numbers that follow the exponential distribution of $f_s(t)$. That sum can be calculated as the k-fold convolution of $f_s(t)$, or alternatively as the product of k CFs $\phi_s(\omega)$. The fraction of the molecules that adsorbs k times is p_k.

Thus the CF of the residence time in the stationary phase can be expressed as:

$$\phi_S(\omega) = \sum_k p_k \phi_s^k(\omega) \tag{25}$$

Recalling the identity $x^k = e^{k\ln x}$, we can reexpress Eq. (25) as:

$$\phi_S(\omega) = \sum_k p_k e^{(-i)ik\ln\phi_s(\omega)} \tag{26}$$

Remembering the definition of ϕ_k in Eq. (22), we can write Eq. (26) as:

$$\phi_S(\omega) = \phi_k[-i\ln\phi_s(\omega)] \tag{27}$$

The substitution of Eqs. (22) and (24) into Eq. (27) gives:

$$\phi_S(\omega) = \exp(n[\phi_s(\omega) - 1]) = \exp\left(\frac{n}{1 - i\omega\tau_s} - n\right) \quad (28)$$

This is the CF of the residence time in the stationary phase. For a constant mobile phase velocity, when there is no mobile phase diffusion, the effect of the mobile phase is simply an increase of the elution time by t_0, which is expressed via the CF as:

$$\phi_R(\omega) = \phi_S(\omega)e^{i\omega t_0} = \exp\left[\frac{t_0}{\tau_m}(\phi_s(\omega) - 1) + i\omega t_0\right] \quad (29)$$

Dondi et al. have shown that the effect of the mobile phase dispersion on the retention time can be handled in the same manner as the effect of the nonconstant adsorption–desorption steps on the stationary phase time [33]. On the analogy of Eq. (27), the following expression is written for the CF of the retention times:

$$\phi_R(\omega) = \phi_m[-i \ln \phi_r(\omega)] \quad (30)$$

where ϕ_r is a normalized retention time, such as that $\phi_r^{t_0} = \phi_R$, i.e. recalling Eq. (30) we will have:

$$\phi_r(\omega) = \exp\left\{\frac{1}{\tau_m}[\phi_s(\omega) - 1] + i\omega\right\} \quad (31)$$

When we combine Eqs. (20), (30) and (31), the CF of the total retention time becomes:

$$\phi_R(\omega) = \exp\left[N_d\left(1 - \sqrt{1 - \frac{2}{N_d}(n[\phi_s(\omega) - 1] + i\omega t_0)}\right)\right] \quad (32)$$

and since $\phi_s(\omega) = 1/(1 - i\omega\tau_s)$, ϕ_R (Eq. (24)) is written as

$$\phi_R(\omega) = \exp\left[N_d\left(1 - \sqrt{1 - \frac{2i\omega}{N_d}\left(\frac{n\tau_s}{1 - i\omega\tau_s} + t_0\right)}\right)\right] \quad (33)$$

Eq. (33) is the CF of the probability density function of the elution time of the individual molecules. Thus, the band profile can be obtained directly from Eq. (33) by inverse Fourier transform.

The moments of the band profile are calculated rather simply making use of the moment theorem of the Fourier transform. The first moment of the peak about the origin is:

$$\mu_1 = t_0 + n\tau_s \quad (34)$$

The second central moment is

$$\mu_2' = 2n\tau_s^2 + \frac{(t_0 + n\tau_s)^2}{N_d} \quad (35)$$

Since the stochastic models gives the corrected retention time in the form of $t_R' = n\tau_s$ and the retention time as $t_R = t_0 + n\tau_s$, we can write the second central moment as:

$$\mu_2' = \frac{2(t_R')^2}{n} + \frac{t_R^2}{N_d} \quad (36)$$

By means of the moments we can calculate the inverse of the column efficiency as:

$$\frac{1}{N} = \frac{\mu_2'}{\mu_1^2} = \frac{2}{n}\left(\frac{t_R'}{t_R}\right)^2 + \frac{1}{N_d} \quad (37)$$

or

$$\frac{1}{N} = \frac{2}{n}\left(\frac{k'}{k' + 1}\right)^2 + \frac{1}{N_d} \quad (38)$$

The skew is given by the following equations:

$$S = \frac{3}{\sqrt{nN_d}} \frac{n^2(k' + 1)^3 + 2nN_dk'^2(k' + 1) + 2N_d^2k'^3}{[n(k' + 1)^2 + 2N_dk'^2]^{3/2}} \quad (39)$$

In the above derivation we expressed the moments with the use of conventional chromatographic terms. We can, however, express the moments and other characteristics with the terms of the microscopic process to better reflect how the mean number of adsorption steps and the mean time needed for one step influence the retention time and band broadening:

$$\mu_1 = n\tau_t \quad (40)$$

$$\mu_2' = 2n\tau_s^2 + \frac{n^2\tau_t^2}{N_d} \quad (41)$$

$$\frac{1}{N} = \frac{1}{N_d} + \frac{2}{n}\left(\frac{\tau_s}{\tau_t}\right)^2 \quad (42)$$

where $\tau_t = \tau_s + \tau_m$ is the total mean time of one adsorption–desorption step. The height of a theoretical plate is calculated as:

$$H = \frac{N}{L} = \frac{2D}{u} + \frac{2u}{\tau_m}\left(\frac{1}{\tau_m} + \frac{1}{\tau_s}\right)^{-2} \quad (43)$$

The skew can be expressed as

$$S = \frac{3}{\sqrt{nN_d}} \frac{n^2\tau_t^3 + 2nN_d\tau_s^2\tau_t + 2N_d^2\tau_s^3}{(n\tau_t^2 + 2N_d\tau_s^2)^{3/2}} \quad (44)$$

Eq. (38) suggests that with the here derived stochastic kinetic model of chromatography and with the lumped kinetic model we have very similar expressions for the number of theoretical plates. For this reason, we seek further analogies between the microscopic and the macroscopic models.

2.4. The macroscopic lumped kinetic model

There are several kinetic models of various level of sophistication to model chromatography [1,34–36]. The conventional lumped kinetic model is a well-known, thoroughly investigated model of linear chromatography [37]. We summarize here briefly the solution of the so-called reaction-dispersive lumped kinetic model. This model consists of a mass balance equation and a kinetic rate equation. The mass balance equation is written as:

$$\frac{\partial c(z,t)}{\partial t} + F\frac{\partial q(z,t)}{\partial t} + u\frac{\partial c(z,t)}{\partial z} = D\frac{\partial^2 c(z,t)}{\partial z^2} \quad (45)$$

where $F = (1-\varepsilon)/\varepsilon$ is the phase ratio, ε being the total porosity.

The *reaction-dispersive* model attributes the nonequilibrium state to the slow adsorption desorption process, while the *transport-dispersive* model assumes that the adsorption–desorption is fast, but the mass transfer kinetics is slow. In linear chromatography, these models are equivalent. In the reaction-dispersive model, the mass balance is described by Eq. (45), and the rate of concentration change in the stationary phase is given by the following first-order kinetic equation:

$$\frac{\partial q(z,t)}{\partial t} = k_a c(z,t) - k_d q(z,t) \tag{46}$$

where k_a and k_d are the rate constants for the adsorption and desorption processes, respectively.

The boundary conditions describe an infinitesimally narrow injection of unit area at $z = 0$ and at time $t = 0$: $c(z,0) = 0$ and $c(0,t) = \delta(t)$. The differential equation can conveniently be solved by Laplace transform. The Laplace transform of Eqs. (45) and (46) are, respectively:

$$s\tilde{c}(z,s) + Fs\tilde{q}(z,s) + u\frac{\mathrm{d}\tilde{c}(z,s)}{\mathrm{d}z} = D\frac{\mathrm{d}^2\tilde{c}(z,s)}{\mathrm{d}z^2} \tag{47}$$

and

$$s\tilde{q}(z,s) = k_a\tilde{c}(z,s) - k_d\tilde{q}(z,s) \tag{48}$$

Eqs. (47) and (48) can be combined by eliminating $\tilde{q}(z,s)$ and we arrive at the following ordinary differential equation:

$$s\left(1+\frac{Fk_a}{s+k_d}\right)\tilde{c}(z,s) + u\frac{\mathrm{d}\tilde{c}(z,s)}{\mathrm{d}z} = D\frac{\mathrm{d}^2\tilde{c}(z,s)}{\mathrm{d}z^2} \tag{49}$$

With the boundary condition of an impulse injection, $\tilde{c}(0,s) = 1$, we have the following solution:

$$\tilde{c}(z,s) = \exp\left[\frac{zu}{2D}\left(1-\sqrt{1+\frac{4D_s}{u^2}\left(1+\frac{Fk_a}{k_d+s}\right)}\right)\right] \tag{50}$$

When we set $z = L$, and introduce $N_d = Lu/(2D)$ to account for the mobile phase dispersion and $t_0 = L/u$ for the dead time of the column, we obtain the Laplace transform of the band profile as:

$$\tilde{c}(s) = \exp\left[N_d\left(1-\sqrt{1+\frac{2t_0 s}{N_d}\left(1+\frac{Fk_a}{k_d+s}\right)}\right)\right] \tag{51}$$

We can further modify $\tilde{c}(s)$ by considering the definition of the mass transfer units: $N_m = Fk_a t_0 = k' k_d t_0$:

$$\tilde{c}(s) = \exp\left[N_d\left(1-\sqrt{1+\frac{2s}{N_d}\left(\frac{N_m/k_d}{1+s/k_d}+t_0\right)}\right)\right] \tag{52}$$

The first moment of the band profile is calculated by the differentiation of $\tilde{c}(s)$:

$$\mu_1 = t_0\left(1+\frac{Fk_a}{k_d}\right) = t_0\left(1+k'\right) \tag{53}$$

being $k' = Fk_a/k_d$. The second central moment is:

$$\mu_2' = \frac{2t_0 k'}{k_d} + \frac{t_0^2}{N_d}\left(1+k'\right)^2 \tag{54}$$

which can be reexpressed as

$$\mu_2' = \frac{2(t_R')^2}{N_m} + \frac{t_R^2}{N_d} \tag{55}$$

From the first two moments, we can express the inverse of the plate number:

$$\frac{1}{N} = \frac{2}{N_m}\left(\frac{k'}{k'+1}\right)^2 + \frac{1}{N_d} \tag{56}$$

2.5. Comparison of the microscopic and the macroscopic models

The comparison of Eqs. (38) and (56) demonstrates that the plate numbers calculated by either the microscopic or the macroscopic are identical only if $N_m = n$. Thus we can conclude that the *number of mass transfer units* in the macroscopic and the *average number of adsorption–desorption steps are synonymous expressions*.

Not only the moments of the two models are identical, but also the band profiles calculated by either the microscopic or the macroscopic approach are completely equivalent. To show this, we compare the CF of the microscopic (Eq. (33)) and the Laplace transform of the macroscopic (Eq. (52)) band profiles. The following three points should be considered for $\phi_R(\omega)$ and $\tilde{c}(s)$ to see that they represent totally identical band profiles:

1. The desorption rate constant k_d expresses the probability of one desorption event per unit time, thus it must be the reciprocal of the average adsorption time τ_s, i.e. evidently $1/k_d = \tau_s$.
2. The number of mass transfer units equals the mean number of adsorption steps, i.e. as we have already shown: $N_m = n$.
3. From the definition of the CF and that of the Laplace transform, we can conclude that the $s = -i\omega$ relationship must exist between the arguments of $\tilde{c}$ and ϕ_R.

Recalling these three substitutions, we can state that the microscopic kinetic model of chromatography is completely identical to the well known macroscopic, lumped kinetic model. Eq. (33) derived via the CF and Eq. (52) derived in the Laplace domain give totally identical band profiles.

Note the two models use similar parameters to characterize the kinetics of the adsorption–desorption process and in both models the mobile phase dispersion is modeled with an axial dispersion coefficient. This similarity, however does not guarantee that the band profiles predicted by the two models will be identical. Besides the parameters characterizing the kinetics of the adsorption–desorption process and the axial dispersion coefficient, the structure of the microscopic model is rather unique and the stochastic-dispersive

model is equivalent to the lumped kinetic model only if we assume exponential distribution for the sojourn times (τ_s and τ_m) and Poisson distribution for the number of adsorption events. Without these details, the microscopic model will not be equivalent to the macroscopic lumped kinetic model. If, for instance, we had assumed that every molecule undergoes the same number of adsorption events, we would have obtained a completely different microscopic model that could not be made equivalent to the lumped kinetic model but it could be compared to the Martin–Synge plate model [12].

Therefore, the uniqueness of the microscopic model consists in both the level of the physical detail and the probabilistic structure of the stochastic process.

2.6. Neglecting the contribution of mobile phase

The stochastic model of Giddings and Eyring [4] is a simplified case of the stochastic–dispersive model considered here. In their approach, the contribution of the mobile phase was ignored, the stationary phase process was considered in that model only. The mobile phase process has two effects on the brand profile. It shifts the peak position by t_0 and broadens the band due to the diffusion process, which is characterized by D. The solution by the CF to that model is given as:

$$\phi(\omega) = \exp\left[\frac{n}{1 - i\omega\tau_s} - n\right] = \exp\left[\frac{i\omega n\tau_s}{1 - i\omega\tau_s}\right] \tag{57}$$

The corresponding band profile can simply be calculated by an inverse Fourier transform

$$c(t) = e^{-t/\tau_s - n}\sqrt{\frac{n}{t\tau_s}}I_1\left(\sqrt{\frac{4nt}{\tau_s}}\right) \tag{58}$$

To obtain the solution with the conventional macroscopic model, we write $D = 0$ in Eq. (45) and solve the PDE as before. The solution is:

$$\tilde{c}(s) = \exp\left[-\frac{sN_m}{k_d + s} - st_0\right] \tag{59}$$

In order to compensate for the mobile phase hold-up time, we have to shift the peak by $-t_0$. To do so, we multiply $\tilde{c}(s)$ by e^{st_0} to get:

$$\tilde{c}(s) = \exp\left[-\frac{sN_m}{k_d + s}\right] = \exp\left[\frac{N_m}{1 + s/k_d} - N_m\right] \tag{60}$$

The inverse Laplace transform of this solution is

$$c(t) = e^{-tk_d - N_m}\sqrt{\frac{N_m k_d}{t}}I_1\left(\sqrt{4N_m k_d t}\right) \tag{61}$$

We can see again that the band profiles expressed by the microscopic and macroscopic approaches (Eqs. (58) and (61)) are completely identical since $\tau_s = 1/k_d$ and $n = N_m$.

3. Conclusions

In this study we have reconsidered the stochastic–dispersive model for chromatography, which is a microscopic model established at molecular level. The model is composed in two parts. The migration of the solute molecules in the mobile phase is modeled with a one-dimensional random walk and this random migration is combined with a stochastic adsorption–desorption process.

In Eq. (33) an analytical solution in the Fourier domain is given for band profiles due to the stochastic–dispersive model of chromatography. From that solution all the moments of the peak can be calculated, or by a numerical inverse Fourier transformation, the chromatogram can be obtained. To ease the calculation of the inverse Fourier transform, the real and imaginary parts of the complex function $\phi_R(\omega)$ are reported in Appendix B.

Although the model was developed here for homogeneous adsorption–desorption kinetics, it is rather simple to apply the stochastic–dispersive model to heterogeneous surfaces with any kind of complexity. To achieve that, $\phi_S(\omega)$ (see Eq. (28)) should be replaced by the proper CF of the heterogeneous kinetics. This procedure is described in detail elsewhere [14,17].

Our results show that the band profile calculated by the stochastic–dispersive model for chromatography is completely identical to the one obtained by the conventional lumped kinetic model. Thus, the kinetic models—either microscopic, or macroscopic—are equivalent. Furthermore, other macroscopic kinetic models, such as the general rate model or the lumped pore model are also equivalent in linear chromatography with the lumped kinetic model [38]. Thus, a general correspondence is found among the kinetic models. The modeling of the chromatographic process at molecular level gains importance with the spread of nanoscale separations.

It is discussable whether the equivalence we found is due to the rather similar physical–chemical conditions we have assumed in the two models. It is important to note, however, that—besides the modeling of the mobile phase dispersion with the first passage time distribution—the exponential distribution for the sojourn times and the Poisson distribution for the number of adsorption events are the fine details that make the present microscopic model equivalent to the macroscopic lumped kinetic model.

Acknowledgements

This work was supported in part by grant T034353 from the Hungarian National Science Foundation (OTKA), furthermore by grant MIUR–COFIN 2003039537 and by NATO Collaborative Linkage Grant PST.CLG. 979081.

Appendix A. Nondestructive detector

The band profile in the case of a nondestructive detector is obtained if not the first-passage distribution but the probability distribution of a diffusing molecule used in the present model to describe the mobile phase process. In this instance the following function (obtained as Eq. (10)) is used in the derivation of the model instead the one given in Eq. (18):

$$f(t) = \frac{u}{\sqrt{4\pi D t}} \exp\left[-\frac{(L-ut)^2}{4Dt}\right] \tag{A.1}$$

The CF of this distribution is

$$\phi_m(\omega) = \left(1 - \frac{2i\omega t_0}{N}\right)^{-1/2} \exp\left[N_d\left(1 - \sqrt{1 - \frac{2i\omega t_0}{N_d}}\right)\right] \tag{A.2}$$

Therefore, instead of (33) we obtain the following CF for the elution time distribution

$$\phi_R(\omega) = \frac{\exp[N_d(1-\sqrt{1-(2i\omega/N_d)((n\tau_s/1-i\omega\tau_s)+t_0)})]}{\sqrt{1-(2i\omega/N_d)((n\tau_s/1-i\omega\tau_s)+t_0)}} \tag{A.3}$$

The first moment, the second central moment, and the column efficiency we obtain when nondestructive detector are as follows:

$$\mu_1 = \frac{N_d+1}{N_d} n\tau_t \tag{A.4}$$

$$\mu_2' = 2\frac{N_d+1}{N_d} n\tau_s^2 + \frac{N_d+2}{N_d^2} n^2\tau_t^2 \tag{A.5}$$

$$\frac{1}{N} = \frac{N_d+2}{(N_d+1)^2} + \frac{N_d}{N_d+1}\frac{2}{n}\left(\frac{\tau_s}{\tau_t}\right)^2 \tag{A.6}$$

These expression are slightly different from Eqs. (40) to (42). But since the value of N_d is usually very large ($N_d > 10^4$), practically no difference is seen between Eqs. (40)–(42) and Eqs. (A.4)–(A.6).

Appendix B. The real and imaginary parts of the CF

The real and imaginary parts of the complex function $\phi_R(\omega)$ (see Eq. (33)) are required when one uses a software or programming language that cannot represent complex numbers. The following formulas can be used to evaluate the real and imaginary parts of the CF:

$$\Re\phi_R(\omega) = \exp\left[N_d\left(1 - \frac{\sqrt{p+q}}{2}\right)\right] \cos\frac{N_d\sqrt{p-q}}{2} \tag{B.1}$$

$$\Im\phi_R(\omega) = -\exp\left[N_d\left(1 - \frac{\sqrt{p+q}}{2}\right)\right] \sin\frac{N_d\sqrt{p-q}}{2} \tag{B.2}$$

where

$$p = \sqrt{q^2 + \frac{16\omega^2}{N_d^2}\left(t_0 + \frac{n\tau}{1+\omega^2\tau^2}\right)^2} \tag{B.3}$$

$$q = 2 + \frac{4\omega^2 n\tau^2}{N_d(1+\omega^2\tau^2)} \tag{B.4}$$

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