

CHROM. 7039

THE ELUTION PROFILE IN A LINEAR CHROMATOGRAPHIC SYSTEM

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(First received January 16th, 1973; revised manuscript received September 10th, 1973)

SUMMARY

A solution of the phenomenological equations that govern a linear chromatographic system is found using the complex Fourier transformation. Only terms with powers less than three in the Fourier "frequency" ω are retained, *i.e.*, the solution corresponds to an asymptotic solution, valid for large times. The velocity of the centre of mass is unaffected by any deviation from quasi-equilibrium conditions, but an additional term appears in the expression for the apparent diffusion coefficient, in accordance with an earlier result obtained by Bak. A definite skewness is also predicted for the instantaneous concentration profile within the second-order approximation, when the distribution coefficient between the mobile and the stationary phase differs from unity. Therefore, in general the asymptotic distribution is not simply a migrating Gaussian distribution. The random-walk theory of Giddings and Eyring yields, in the asymptotic limit, the same centre of mass velocity and an expression for the apparent diffusion coefficient identical with the term for deviation from quasi-equilibrium in the present theory. Their calculations of individual rate constants for adsorption and desorption from experimental elution profiles are considered to be in error because of the neglect of the quasi-equilibrium term due to eddy diffusion in the column.

INTRODUCTION

The problem of the form of the elution profile from a chromatographic column seems to have received serious attention in only very few theoretical treatments. I consider two approaches to be especially important because of their mathematical level, and because they partially lead to the same results. One approach is the random-walk theory of Giddings and Eyring¹. The stochastic reasoning appeared later in a somewhat changed form in another paper by Giddings². This theory neglects the axial eddy diffusion in the column and ascribes the broadening of the chromatographic peak solely to the probability distribution of different sequences of adsorption to and desorption from the stationary phase.

Another approach is the phenomenological one based upon Fourier transformation of the linearized kinetical equations as suggested by Bak³ in a study primarily centred on electrodiffusion phenomena. This treatment includes eddy diffusion, but

the approximations involved are neither very obvious nor very explicitly presented. Two other important approaches that should be mentioned are the Laplace transform solutions given by Lapidus and Amundson⁴ and Kučera⁵. The solutions they give do not, however, appear to be very tractable.

In this paper, Bak's method is followed in principle. His result for the apparent diffusion coefficient is verified in a second-order approximation, but the asymptotic profile in this approximation is *not* simply a uniformly migrating Gaussian distribution as anticipated by Bak³. It is a curve with a definite measure of skewness, if the distribution coefficient between the stationary and the mobile phase differs from unity.

The discussion may be clarified by first demonstrating how far a simple quasi-equilibrium calculation may carry us towards an understanding of the dynamics of peak migration and broadening.

THE QUASI-EQUILIBRIUM SOLUTION

The starting point is the two simultaneous, partial differential equations describing a general chromatographic system:

$$\begin{aligned}\partial c(o)/\partial t &= D \cdot \partial^2 c(o)/\partial x^2 - u \cdot \partial c(o)/\partial x - J_{os} \\ \partial c(s)/\partial t &= + J_{os}\end{aligned}\quad (1)$$

In these equations, c represents the concentrations of the substances subjected to chromatography in moles per unit of total column volume in a slice of column centred at x with thickness dx . The (o) refers to the mobile phase and the (s) to the stationary phase. D is a concentration-independent eddy diffusion coefficient describing the spreading out of the zone due to the many possible routes by which the molecules can pass through the mobile phase. The mean velocity of the mobile phase is u , and D may be a function of u . The flux J_{os} is the number of moles passing from the mobile to the stationary phase per unit of total column volume in the slice. By addition of these two equations, we obtain

$$\partial c(\text{tot})/\partial t = D \cdot \partial^2 c(o)/\partial x^2 - u \cdot \partial c(o)/\partial x \quad (2)$$

In the case of quasi-equilibrium, that is

$$c(s)_{x,t}/c(o)_{x,t} \approx K = k_1/k_2 \quad (3)$$

where K is the adsorption (absorption) coefficient, k_1 the rate constant of adsorption (absorption) and k_2 that of desorption, eqn. 2 reduces to a single partial differential equation:

$$\partial c(\text{tot})/\partial t = (D/1 + K) \cdot \partial^2 c(\text{tot})/\partial x^2 - (u/1 + K) \cdot \partial c(\text{tot})/\partial x \quad (4)$$

From the form of eqn. 4, it is evident that the problem is now an ordinary diffusion-convection problem with an apparent diffusion coefficient given by

$$D_{\text{app}} = D/1 + K \quad (5)$$

and a centre of mass velocity

$$u_{cm} = u/l + K \tag{6}$$

It is in fact possible to proceed a little further without explicitly solving the simultaneous equations (1). Fig. 1 shows a situation in which the quasi-equilibrium assumption fails. The “mobile peak” is here leading and the “stationary peak” is

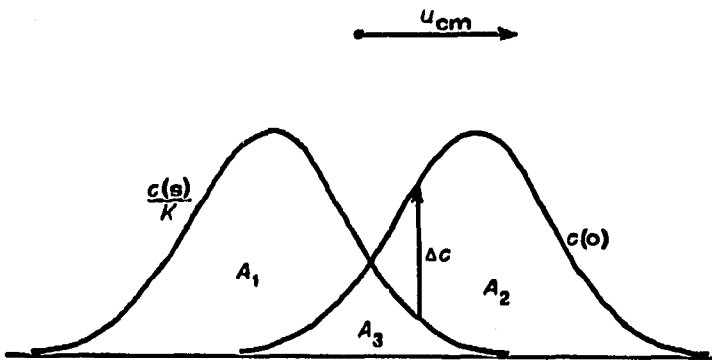


Fig. 1. The two moving peaks of a linear chromatographic system.

lagging behind (of course, both peaks are actually moving). In principle, this must always be the case, also in quasi-equilibrium, but in the latter case the difference between the peaks may be neglected. Thus, in quasi-equilibrium $c(o)$ and $c(s)/K$ as a function of x at a given t can be represented by the same curve. Defining

$$\Delta c = c(o) - \frac{c(s)}{K} \tag{7}$$

we have for a linear or linearized chromatographic system (that is, a chromatographic system in which linear exchange kinetics apply)

$$J_{os} = k_1 \cdot \Delta c \tag{8}$$

When a stationary distribution between the two phases has been reached, then

$$\int_{-\infty}^{+\infty} J_{os} \, dx = k_1 \cdot \int_{-\infty}^{+\infty} \Delta c \cdot dx = 0 \tag{9}$$

Thus, the area A_1 in Fig. 1 equals the area A_2 , and have we $A_1 + A_3 = A_2 + A_3$ or

$$\int_{-\infty}^{+\infty} c(s) \cdot dx / \int_{-\infty}^{+\infty} c(o) \cdot dx = K \tag{10}$$

Therefore, in spite of local deviations from quasi-equilibrium, the overall distribution between the stationary and the mobile phase is not affected, and the centre of mass

velocity will still be given by eqn. 6. The apparent diffusion coefficient will be affected, however, as will be shown in the next section.

THE SECOND-ORDER FOURIER TRANSFORM SOLUTION

Both the "mobile" and the "stationary" concentration profiles have the property that the concentrations and their derivatives vanish at infinity. Therefore, if $U(\omega, t)$ is the Fourier transform of one of the profiles with respect to x

$$U(\omega, t) = (1/\sqrt{2\pi}) \int_{-\infty}^{+\infty} c(x, t) \cdot \exp(i \cdot \omega \cdot x) \cdot dx \quad (11)$$

Then, by the theorem of partial integration:

$$U(\partial c/\partial x) = -i \cdot \omega \cdot U(\omega, t) \quad (12)$$

and

$$U(\partial^2 c/\partial x^2) = -\omega^2 \cdot U(\omega, t) \quad (13)$$

Furthermore, by Leibnitz's rule for the differentiation of specific integrals:

$$U(\partial c/\partial t) = \dot{U}(\omega, t) \quad (14)$$

a dot denoting differentiation with respect to time. The equations (1) can therefore be reduced to two ordinary, simultaneous differential equations by Fourier transforming both sides of the equations. The result is the linear equations

$$\begin{pmatrix} \dot{U}_o \\ \dot{U}_s \end{pmatrix} = K \cdot \begin{pmatrix} U_o \\ U_s \end{pmatrix} \quad (15)$$

with the coefficient matrix

$$K = \begin{pmatrix} -D\omega^2 - k_1 + i \cdot u \cdot \omega & k_2 \\ k_1 & -k_2 \end{pmatrix} \quad (16)$$

Eqn. 15 can be solved for each value of the "frequency" ω for suitable initial conditions, and the solution $c_k(x, t)$, with $k = o, s$, is found by back-transformation:

$$c(x, t) = (1/\sqrt{2\pi}) \int_{-\infty}^{+\infty} U(\omega, t) \cdot \exp(-i \cdot \omega \cdot x) d\omega \quad (17)$$

As in the preceding section, we shall be interested only in the total concentration, $c_{tot}(x, t)$. The explanation is that both the "mobile" and the "stationary" peak are eluted, when the peaks suddenly reach the end of the bed of stationary phase, *i.e.*, the end of the chromatographic column. The elution profile is therefore the sum of the two peaks. Also, in a chromatographic experiment in which the elution flow is suddenly stopped and longitudinal movement (apart from slow thermic diffusion)

ceases, it will be the total concentration profile that characterizes the chromatographic spot. To meet our desire, the variables in eqn. 15 are transformed by

$$\begin{pmatrix} \Sigma \\ \Delta \end{pmatrix} = M^{-1} \cdot \begin{pmatrix} U_o \\ U_s \end{pmatrix} \quad (18)$$

with the transformation matrix

$$M^{-1} = \begin{pmatrix} 1 & 1 \\ 1 & -1 \end{pmatrix} \quad (19)$$

The new kinetic coefficient matrix is given by the similarity transformation

$$K' = M^{-1} K M \quad (20)$$

As will be seen later in this section, we shall only use the 1,1-element:

$$K'_{11} = \frac{1}{2} \cdot (-D\omega^2 + i \cdot u \cdot \omega) \quad (21)$$

The kinetic behaviour is now determined by the eigenvalues of K' , but since eigenvalues are invariant in a similarity transformation, they may just as well be determined from the characteristic equation of K :

$$\lambda^2 + (D \cdot \omega^2 + k_1 + k_2 - i \cdot u \cdot \omega) \cdot \lambda + (D \cdot \omega^2 - i \cdot u \cdot \omega) \cdot k_2 = 0 \quad (22)$$

As λ is complex:

$$\lambda = a + i \cdot b \quad (23)$$

eqn. 22 actually represents two simultaneous equations of second order in a and b :

$$a^2 - b^2 + (D \cdot \omega^2 + k_1 + k_2) \cdot a + u \cdot \omega \cdot b + k_2 \cdot D \cdot \omega^2 = 0 \quad (24)$$

$$2ab + (D \cdot \omega^2 + k_1 + k_2) \cdot b - u \cdot \omega \cdot a - u \cdot \omega \cdot k_2 = 0 \quad (25)$$

For reasons that will be clear at the end of the procedure, we shall be interested in solutions to these equations, which are correct for small frequencies ω . For this purpose, we write

$$a = a_0 + a_1 \cdot \omega + a_2 \cdot \omega^2 + O(\omega^3) \quad (26)$$

$$b = b_0 + b_1 \cdot \omega + b_2 \cdot \omega^2 + O(\omega^3) \quad (27)$$

If we put $\omega = 0$ in eqns. 24 and 25, we obtain for $b_0 \neq 0$ from the second equation

$$a_0 = -(k_1 + k_2)/2$$

which yields, by insertion in the first equation,

$$b_0^2 = -(k_1 + k_2)^2/4$$

with no real solution $\neq 0$. That is,

$$a_0 = b_0 = 0 \quad (28)$$

We insert this result in eqn. 24, and because the coefficient of the first power in ω has to be zero separately, then

$$(k_1 + k_2) \cdot a_1 = 0$$

and

$$a_1 = 0 \quad (29)$$

Since the least power in a is therefore ≥ 2 and the least in b is ≥ 1 , we can drop the terms a^2 , $a \cdot \omega$, $a \cdot \omega^2$ and $a \cdot b$ in eqns. 24 and 25 in a second-order approximation. Eqn. 25 yields

$$b = \frac{u \cdot k_2 \cdot \omega}{D \cdot \omega^2 + k_1 + k_2} = \frac{k_2}{k_1 + k_2} \cdot u \cdot \omega + O(\omega^3) \quad (30)$$

Similarly, eqn. 24 yields

$$a = (b^2 - u \cdot b \cdot \omega - k_2 \cdot D \cdot \omega^2) / (k_1 + k_2) = -D_{\text{app}} \cdot \omega^2 + O(\omega^3) \quad (31)$$

with the definition

$$D_{\text{app}} = \frac{k_2}{k_1 + k_2} \cdot D + \frac{k_1 k_2}{(k_1 + k_2)^3} \cdot u^2 \quad (32)$$

This quantity really turns out later to be the apparent diffusion coefficient. Compare the first term with the quasi-equilibrium expression in eqn. 5. The second eigenvalue $\lambda' = a' + i \cdot b'$ corresponding to the one found above is easily found from the characteristic equation, because

$$\lambda + \lambda' = -(D \cdot \omega^2 + k_1 + k_2) + i \cdot u \cdot \omega$$

that is

$$\lambda' = -\frac{k_1}{k_1 + k_2} \cdot D \cdot \omega^2 + \frac{k_1 k_2}{(k_1 + k_2)^3} \cdot u^2 \cdot \omega^2 - (k_1 + k_2) + i \cdot \frac{k_1}{k_1 + k_2} \cdot u \cdot \omega \quad (33)$$

The solution to the (Σ, Δ) equations are formally

$$\begin{pmatrix} \Sigma(t) \\ \Delta(t) \end{pmatrix} = \exp(K' \cdot t) \cdot \begin{pmatrix} \Sigma(t=0) \\ \Delta(t=0) \end{pmatrix} \quad (34)$$

wherein the matrix exponential function (defined by the same power series as the scalar one) may be simplified by means of Sylvester's theorem, which again is a direct

consequence of the Hamilton–Cayley theorem that every matrix satisfies its own characteristic equation⁶. Especially in the present case, we have

$$\exp(K' \cdot t) = (\lambda - \lambda')^{-1} \cdot [(K' - \lambda' \cdot J) \cdot \exp(\lambda \cdot t) - (K' - \lambda \cdot J) \cdot \exp(\lambda' \cdot t)] \quad (35)$$

Because we are interested only in the stationary solution, we can choose any suitable initial conditions provided that they conform to the criteria underlying eqns. 12 and 13. In addition, we want to focus upon the situation where the peak has become much broader than the initial peak. Therefore, we choose

$$\left. \begin{aligned} c(0) &= (s/2) \cdot \delta(x) \\ c(s) &= (s/2) \cdot \delta(x) \end{aligned} \right\} t = 0 \quad (36)$$

where $\delta(x)$ is Dirac's δ -function and s is the total number of moles in the two peaks. From eqn. 36, we have

$$\Sigma(t=0) = s/\sqrt{2\pi} \text{ and } \Delta(t=0) = 0 \quad (37)$$

It should be noticed that λ' has a contribution $-(k_1 + k_2)$ in its real part, and this eigenvalue apparently refers to the equilibration of stationarity. In this treatment, we shall concern ourselves only with times much greater than that relaxation time:

$$t \gg (k_1 + k_2)^{-1} \quad (38)$$

and neglect the corresponding term in eqn. 35. Therefore,

$$\Sigma(t) = \exp(1, 1) \cdot (s/\sqrt{2\pi}) = \frac{s}{\sqrt{2\pi} \cdot (\lambda - \lambda')} \cdot (K'_{11} - \lambda') \cdot \exp(\lambda \cdot t) \quad (39)$$

The total concentration profile is given by the back-transformation in eqn. 17 with U replaced by Σ . Insertion of eqns. 21, 30, 31 and 33 in eqn. 39 yields

$$\Sigma(\omega, t) = \frac{s}{\sqrt{2\pi}} \cdot \frac{1 - A \omega^2 - i \cdot B \omega}{1 - 2A \omega^2 - 2i \cdot B \omega} \cdot \exp(-D_{app} \omega^2 \cdot t) \exp\left(\frac{k_2}{k_1 + k_2} \cdot t \cdot u \cdot \omega \cdot t\right) \quad (40)$$

with

$$A = -\frac{1}{2} \cdot D \cdot \frac{k_1 - k_2}{(k_1 + k_2)^2} + \frac{k_1 k_2}{(k_1 + k_2)^4} \cdot u^2 \quad (41)$$

and

$$B = \frac{k_1 - k_2}{2(k_1 + k_2)^2} \cdot u \quad (42)$$

The pre-exponential factor in eqn. 40 is now expanded in a power series in ω . Consider the diagram in a complex plane given in Fig. 2. The ratio $r_1:r_2$ is given by

$$r_1 : r_2 = \sqrt{\frac{1 + (B^2 - 2A) \omega^2 + A^2 \omega^4}{1 + 4(B^2 - A) \omega^2 + 4A^2 \omega^4}} = 1 + (A - \frac{3}{2} \cdot B^2) \omega^2 + O(\omega^3)$$

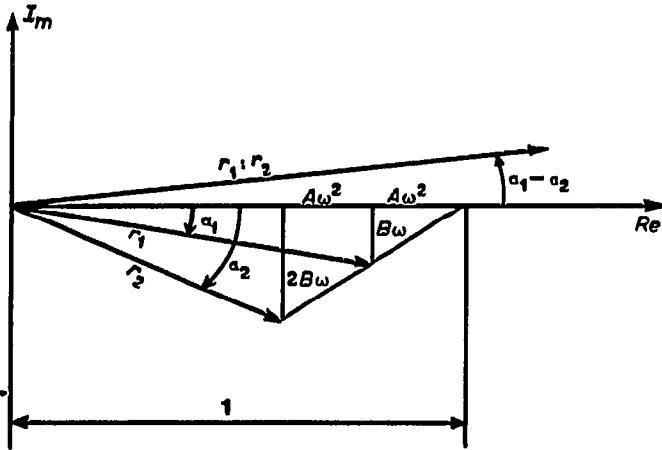


Fig. 2. Diagram in a complex plane for the power expansion in eqn. 43.

For the angles α_1 and α_2 , we have

$$\alpha_1 = \arctan (-B \omega / 1 - A \omega^2) = -B \omega / (1 - A \omega^2) + O [B^3 \omega^3 / (1 - A \omega^2)^3] = -B \omega + O (\omega^3)$$

and

$$\alpha_2 = -2B \omega + O (\omega^3)$$

Therefore

$$\cos (\alpha_1 - \alpha_2) = 1 - \frac{1}{2} (\alpha_1 - \alpha_2)^2 + O [(\alpha_1 - \alpha_2)^4] = 1 - \frac{1}{2} B^2 \omega^2 + O (\omega^3)$$

$$\sin (\alpha_1 - \alpha_2) = (\alpha_1 - \alpha_2) + O [(\alpha_1 - \alpha_2)^3] = B \omega + O (\omega^3)$$

Finally,

$$\frac{1 - A \omega^2 - i \cdot B \omega}{1 - 2A \omega^2 - 2i \cdot B \omega} = 1 + (A - 2B^2) \omega^2 + i B \omega + O (\omega^3) \tag{43}$$

When eqn. 43 is inserted into eqn. 40 and the back-transformation performed, we obtain

$$c_{tot}(x, t) = \frac{s}{2\pi} [I_1 - B \cdot I_2 + (A - 2B^2) \cdot I_3] \tag{44}$$

with the definite integrals

$$I_1 = \int_{-\infty}^{+\infty} \exp (-D_{app} \omega^2 \cdot t) \cdot \cos (-x' \cdot \omega) d\omega \tag{45}$$

$$I_2 = \int_{-\infty}^{+\infty} \omega \cdot \exp (-D_{app} \omega^2 \cdot t) \sin (-x' \cdot \omega) d\omega \tag{46}$$

$$I_3 = \int_{-\infty}^{+\infty} \omega^2 \cdot \exp(-D_{app} \omega^2 \cdot t) \cos(-x' \cdot \omega) d\omega \quad (47)$$

In eqns. 45–47, we have introduced the Galilei-transformed co-ordinate

$$x' = x - \frac{k_2}{k_1 + k_2} \cdot u \cdot t \quad (48)$$

The integral in eqn. 45 is the well known Gauss-integral, which value is found by contour integration to be

$$I_1 = \sqrt{\pi/D_{app} \cdot t} \cdot \exp(-x'^2/4D_{app} \cdot t) \quad (49)$$

The other two integrals can be expressed by the first by means of eqn. 49 with application of the Leibnitz formula:

$$\frac{d}{dy} \int_a^b f(x, y) dx = \int_a^b \partial f / \partial y \cdot dx \quad (50)$$

Differentiation of I_1 (given by eqn. 49) and the integral on the right-hand side of eqn. 45 by $-x'$ yields

$$I_2 = -x' \cdot I_1 / 2D_{app} \cdot t \quad (51)$$

Similarly, differentiation of both sides of eqn. 45 with respect to $D_{app} \cdot t$ and subsequent application of the result in eqn. 51 yields

$$I_3 = (I_1 / 2D_{app} \cdot t) \cdot \left(1 - \frac{x'^2}{2D_{app} \cdot t}\right) \quad (52)$$

Therefore, the final expression for the total concentration profile is

$$c_{tot}(x, t) = \frac{s}{(\sqrt{2\pi}) \sigma} \cdot \exp(-x'^2/2 \sigma^2) \cdot \left[\left(1 + \frac{A - 2B^2}{\sigma^2}\right) + \frac{B}{\sigma^2} \cdot x' - \frac{A - 2B^2}{\sigma^4} \cdot x'^2 \right] \quad (53)$$

The measure of peak width σ is given by the usual "Einstein formula":

$$\sigma = \sqrt{2D_{app} \cdot t} \quad (54)$$

To the solution in eqn. 53, the following comments can be made.

(1) The physical reason for seeking solutions for small ω is that the Fourier-transformed profile contains the factor $\exp(-D_{app} \cdot \omega^2 \cdot t)$, so that the contribution to the back-transformation stems from the smaller ω the larger the values of t .

(2) Eqn. 53 may just as well be regarded as a distribution of times of arrival to a certain point x_0 . If x_0 is the end of the column, eqn. 53 is the elution profile. For this purpose, we may rewrite eqn. 53 as a time function:

$$c_{\text{tot}}(x_0, t) = \frac{s}{\sqrt{4\pi D_{\text{app}} \cdot t}} \cdot \exp \left[-\left(x_0 - \frac{1}{1+K} \cdot u \cdot t\right)^2 / 4D_{\text{app}} \cdot t \right] \cdot \sum_{i=0}^2 L_i \cdot t^{-i}$$

with

$$L_0 = 1 + \frac{k_2^2}{(k_1 + k_2)^2} \cdot u^2 - \frac{B}{2D_{\text{app}}} \cdot \frac{k_2}{k_1 + k_2} \cdot u$$

$$L_1 = (1/2D_{\text{app}}) \cdot (A - 2B^2 + Bx_0 + \frac{A - 2B^2}{D_{\text{app}}} \cdot \frac{k_2}{k_1 + k_2} \cdot u \cdot x_0)$$

$$L_2 = -\frac{A - 2B^2}{4D_{\text{app}}^2} \cdot x_0^2$$

(3) Eqn. 53 shows that the migrating peak will be unsymmetrical. With the definition of B (eqn. 42) taken into consideration, it is apparent that the skewness will be the more significant the greater the value of u and the difference between k_1 and k_2 . It can be seen that:

(a) the front of the instantaneous profile is steeper than the back when $K < 1$;

(b) the back of the instantaneous profile is steeper than the front when $K > 1$.

The front of the migrating peak is defined as the limb where $\partial c/\partial x < 0$, when x is chosen in the direction of the movement of the peak. It is possible to give a qualitative argument for the direction of skewness found. If K is less than unity, the mass contained in the "stationary peak" is less than the mass in the "mobile peak" (eqn. 10) and we therefore have a leading peak followed by a smaller lagging peak, so that the sum of the two peaks will be tailing in the above-mentioned direction.

(4) In an experiment in which the sample is applied as a circular spot (idealized as a two-dimensional Gaussian distribution with the same standard deviation in the x and y directions), as is the case in thin-layer chromatography, the B -effect will result in comet-shaped spots with the tail directed forwards in the case of $K > 1$ and backwards for $K < 1$. For $K = 1$, the iso-concentration profiles will be ellipses with the major axis in the direction of movement when u is large enough for the perturbation term in eqn. 32 to become significant. For the smaller elution velocities, the spots will remain as circles, provided that the eddy diffusion coefficient is independent of direction.

(5) The B -effect will cause all uneven x' moments of the instantaneous profile to be different from zero. The first four moments are

$$M_0 = \int_{-\infty}^{+\infty} c_{\text{tot}} dx' = s \quad (\text{total number of moles}) \quad (55)$$

$$M_1 = \int_{-\infty}^{+\infty} x' \cdot c_{\text{tot}} dx' = s \cdot B \quad (\text{the Galilei co-ordinate of the centre of mass}) \quad (56)$$

$$M_2 = \int_{-\infty}^{+\infty} x'^2 \cdot c_{\text{tot}} dx' = s \cdot [\sigma^2 - 2(A - 2B^2)] \quad (\text{variance}) \quad (57)$$

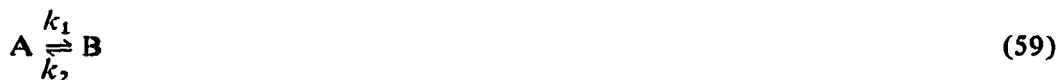
$$M_3 = \int_{-\infty}^{+\infty} x'^3 \cdot c_{\text{tot}} dx' = 3s \cdot B \cdot \sigma^2 \quad (58)$$

It is important to note that M_1 is independent of time, *i.e.*, the peak will remain skewed for $t \rightarrow \infty$. The Gaussian distribution is therefore not the asymptotic stable solution to the chromatographic problem, when the elution velocity is large and K differs from unity. Also, the fact that the Galilei co-ordinate of the centre of mass is independent of time is in accordance with the previously stated result that deviations from quasi-equilibrium will not affect the velocity of the centre of mass.

(6) The "instantaneous skewness" due to the B -effect must be sharply distinguished from the "elution skewness" observed in the elution profile. Eqn. 53a shows that even in the case when $A = B = 0$, *i.e.*, the migrating peak is Gaussian, the elution profile will be unsymmetrical. During the elution, the Gaussian profile will broaden and level out, so that the ascending limb of the elution curve will be steeper than the descending limb. This form of the elution curve is also, in fact, the normal form when the sample is applied as a small zone in comparison with the extension of the peak during elution and the column is long enough for the peak to stabilize. Note that it is the median and not the maximum of the elution curve which corresponds to the centre of mass of the peak.

COMPARISON WITH RANDOM-WALK THEORY

It is also possible to treat the problem of chromatography stochastically from a random-walk point of view, as done by Giddings and Eyring¹ and Giddings². They assumed linear adsorption kinetics as we have in the preceding sections. They generally considered a molecule which can be exchanged between two states A and B:



and question for the probability $P_{AA}(t_1, t_2)$ for a molecule starting in state A and ending in the same state after a specific time t to have spend the time t_1 in state A and $t_2 = t - t_1$ in state B. By summing over the different adsorption-desorption histories of the molecule, they found that

$$P_{AA}(t_1, t_2) = \exp(-k_1 t_1 - k_2 t_2) \cdot \sqrt{k_1 k_2 t_1 / t_2} \cdot I_1(\sqrt{4k_1 k_2 t_1 t_2}) \quad (60)$$

$I_1(x)$ is a modified Bessel function of the first kind of order one. By definition⁷

$$I_\nu(x) = \sum_{k=0}^{\infty} \frac{x^{\nu+2k}}{2^{\nu+2k} \cdot k! \cdot \Gamma(\nu + k + 1)} \quad (61)$$

Similarly, for a molecule starting in A and ending in B:

$$P_{AB}(t_1, t_2) = \exp(-k_1 t_1 - k_2 t_2) \cdot k_1 \cdot J_0(\sqrt{4k_1 k_2 t_1 t_2}) \quad (62)$$

P_{BB} and P_{BA} are found by symmetry considerations. When the number of exchanges (*e.g.*, adsorptions and desorptions) is large, the arguments of the Bessel functions will be so large that the asymptotic expansion⁸ applies:

$$I_\nu(x) \rightarrow \exp(x) / \sqrt{2\pi x}, \quad x \rightarrow \infty \quad (63)$$

so that eqns. 60 and 62 reduce to

$$P_{AA}(t_1, t_2) = \frac{(k_1 k_2 t_1 t_2)^{\frac{1}{2}}}{\sqrt{4\pi} t_2} \cdot \exp [- (\sqrt{k_1 t_1} - \sqrt{k_2 t_2})^2] \quad (64)$$

$$P_{AB}(t_1, t_2) = \frac{k_1}{\sqrt{4\pi} (k_1 k_2 t_1 t_2)^{\frac{1}{2}}} \cdot \exp [- (\sqrt{k_1 t_1} - \sqrt{k_2 t_2})^2] \quad (65)$$

These expressions may be regarded as the distribution of t_1 for a given t . With A representing the molecule in the mobile phase and B the molecule in the stationary phase, this t_1 distribution will also be a representation of the instantaneous profile ($x = u \cdot t_1$). The expressions may also, however, be regarded as the t_2 distribution for fixed t_1 corresponding to the elution profiles with a column length $l = u \cdot t_1$. At first, eqns. 64 and 65 appear to be very different from our previous results in eqns. 53 and 53a. However, at least in one respect there is correspondence. If, for large times, we neglect the weak pre-exponential time dependence in eqns. 64 and 65, we have

$$P(t_1) = C \cdot \exp [- (\sqrt{k_1 t_1} - \sqrt{k_2 (t - t_1)})^2]$$

where C is a normalizing factor and $P(t_1)$ is now the t_1 distribution of the molecule regardless of its initial and final states. With $t_1 = x/u$, we have

$$P(x) = C' \exp [- (\sqrt{k_1 x} - \sqrt{k_2 u \cdot t - k_2 x})^2 / u]$$

If we Taylor-expand the argument of the exponential function about the maximum value x_m , including only second-order deviations, we find the Gaussian profile⁹:

$$P(x) = C' \exp [-(x - x_m)^2 / 4D_{app} \cdot t]$$

with

$$x_m = \frac{k_2}{k_1 + k_2} \cdot u \cdot t$$

and

$$D_{app} = \frac{k_1 k_2}{(k_1 + k_2)^3} \cdot u^2$$

It can be seen that in this approximation the centre of mass velocity is the usual quasi-equilibrium expression, and the apparent diffusion coefficient is identical with the perturbation term in eqn. 32.

Giddings and Eyring¹ have used their expressions to calculate the individual rate constants of adsorption and desorption by fitting these parameters to experimental elution curves. As an example, they calculated k_1 and k_2 for a diazo dye (Brilliant Scarlet 3R) in a column packed with a mixture of Magnesol and Celite adsorbents and similarly for complexed praseodymium ions under conditions described by some other workers. Two years later, Giddings² wrote, however: "Experimental data suitable for comparison with eqns. 16 and 17 (his numbering for eqns. 64 and 65 in

the present paper) have not been found". I would like to close the present theoretical contribution by stressing that in my opinion the above calculations are not correct. As we have seen, the reason for peak broadening in the Giddings-Eyring theory is solely the statistical distribution over different histories of adsorption-desorption sequences. The theory neglects the important contribution from eddy diffusion, which for example is reflected in the fact that species which do not adsorb at all also spread out in time. In a subsequent paper concerning the elution curves from a Sephadex G-25 column, it will be seen that both effects contribute to peak broadening, and we shall calculate individual rate constants that can be shown independently to be of the correct order of magnitude.

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