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A Stochastic Approach to Chromatographic Theory Based on the Master Equation

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Summary

The general requirements, in particular the statistical-mechanical foundations, of a dynamical theory of chromatography have been investigated. A general chromatographic model, representing a special form of the master-equation formalism of nonequilibrium statistical mechanics, has been established. The physical and mathematical nature of dispersion coefficients have been analyzed in some detail and the relation between these parameters and those measured in chromatography are briefly discussed.

Theories of chromatography may be divided into two main categories; those based on the conservation of mass and those following the stochastic (or random-walk) approach. Recently it has become increasingly apparent that these theories suffer from a number of deficiencies. First, the conservation-of-mass approach entails the solution of partial differential equations involving mathematical difficulties which limit its application to practical situations (*1*). Second, current stochastic theories yield inexact results (2) and lack a well-founded and common basis. Third, it is, in both cases, often difficult to clearly interpret the physical significance of the mathematical operations and results.

The present paper presents a critical evaluation of the general requirements of a dynamic theory of chromatography and, in particular, examines the statistical-mechanical foundations of such a theory. A general chromatographic model, representing a special form of the master-equation formalism of nonequilibrium statistical mechanics, is established and the essential equivalence between the two traditional approaches is demonstrated. The physical and mathematical nature of dispersion coefficients is analyzed in some detail and the connection between these parameters and those measured in chromatography is briefly discussed.

The general model combines the basic simplicity of the random-walk approach with the mathematical rigor of nonequilibrium theory. The purpose, at this stage, has been to formulate a general theoretical framework from which specific situations of practical interest can be dealt with in detail; for this reason the formulation presented below is necessarily relatively abstract.

THE THEORY OF PREDICTION

The general requirements of a theory of prediction are most conveniently formulated in abstract vector space. A system is defined in terms of a set of quantities $A_1, A_2, \ldots, A_n$ which is considered as forming a basis for the description space. Any possible state of the system is then represented by a vector $\mathbf{A}^i \equiv (A_1^i, A_2^i, \ldots, A_n^i)$ or, equivalently, by a single point in this space, and all points are assumed to be connected arc-wise. Change in the system is defined as change in the position of the representative point in the space. In order to describe change, a time parameter, t, is introduced and it is assumed that time intervals, Δt, are well defined relative to some independent periodic reference system.

The fundamental structure of the dynamical formalism is determined by requiring the theory to conform to two requirements: that of determinism and that of a 1:1 correspondence between theory and experiment. Determinism implies that, given the state of the system at an initial time t_0, the theory must be able to predict the state of the system uniquely at any subsequent time t. Consider the chromatographic system as an assemblage of N particles acted upon by various forces. If the whole experimental arrangement is isolated, it is well known that the dynamical state of the system may be represented by a single point in the phase space spanned by the $6N$ generalized coordinates $(q_1, \ldots, q_{3N})$ and momenta $(p_1, \ldots, p_{3N})$ of the particles. In this space determinism is satisfied by considering the motion as being generated by means of the Hamilton function $H(q_j, p_j)$ via the canonical equations of motion.

$$\dot{q}_j = \frac{\partial H}{\partial p_j} \quad \dot{p}_j = -\frac{\partial H}{\partial q_j} \qquad (j = 1, 2, \ldots, 3N) \tag{1}$$

However, although these equations are correct in the classical limit, this approach is useless in practice because even the three-particle problem has until now defied solution in closed form. On the other hand, such a solution would contain much more information than is necessary for chromatographic purposes. To remedy this it is necessary to specify the requirements of chromatographic measurement space and to map phase space onto a description space which is in a 1:1 correspondence with the measurement space. Alternatively, one could conceivably reverse the process, i.e., decide first on the requirements and then adapt the measurements accordingly. In the light of the present state of chromatographic experimental technique the first of these approaches is preferred here. For convenience, the discussion below will be restricted to column chromatography; with a few minor changes in notation it also applies to other experimental arrangements.

In general a chromatographic detector measures the number of solute molecules passing an axial plane (usually the column outlet) per unit time. The measurement space is therefore essentially unidimensional. The measured quantity can also be specified in probabilistic terms by numerically equating the fraction of the total number of molecules of the particular species per unit volume to the probability f of finding an arbitrary representative molecule of that species in the volume. This is a necessary requirement for a 1:1 correspondence, because it is assumed that the detector does not distinguish between different molecules of the same chemical species. The description space is therefore also unidimensional, representing the longitudinal displacement of the representative molecule from a fixed origin. The laws of motion in the phase plane corresponding to this description space can now be formulated.

Consider, for example, the projected motion of the total system's representative point on a single (x_j, p_j) phase plane. The Hamilton function generating the motion on this plane has the form $H = H(x_j, p_j, t)$, where the explicit time dependence results from the coupling with the other degrees of freedom. It may be remarked in passing that it is this explicit time dependence which causes the dynamical equations of chromatography to be time-irreversible (3). Since the detector assigns equal weights to all molecules located at x_j^0, one should consider the simultaneous motion of all particles located at x_j^0 at a time t_0 on a representative (x_j, p_j) phase plane. This construction may be thought of as the appropriate ensemble for chromatography, analogous to the Gibbsian ensembles for the total phase space.

The p_j^0 values of the particles will be distributed over a whole range of values as a result of the difference in initial states of the particles and difference in the explicit time dependence of the appropriate Hamilton function. However, it is important to note that this variation will be bounded as a result of the fact that the representative point of the whole system is confined to move on a single energy hypersurface. If the subsequent paths of these molecules are therefore followed during a time interval, Δt, one would find a situation such as that depicted in Fig. 1.

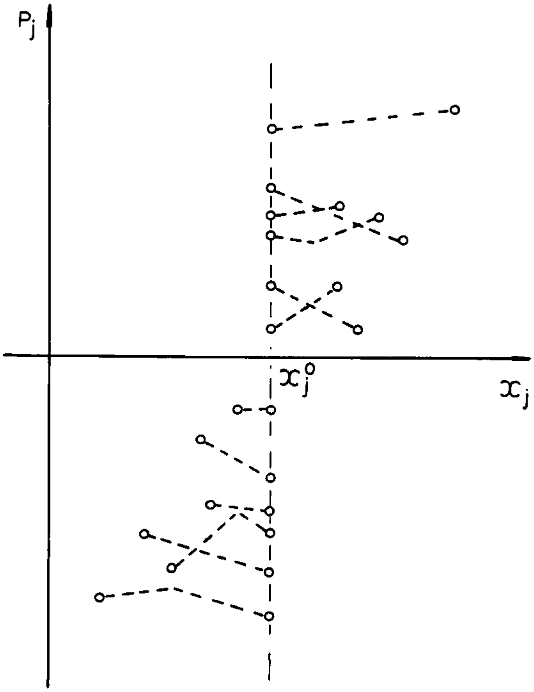

FIG. 1

Consider now that a mathematical net of net width Δx is drawn over the column length. If the probability for a molecule to be in a particular cell is defined as the number of points lying within that cell divided by the total number of points, one obtains, at every instant t, a probability distribution as in Fig. 2. Since all the points in the phase plane move according to the deterministic laws of classical mechanics, it is obvious that the probability distribution's temporal evolution will also be governed by deterministic equations. One may call this a dynamical theory of distributions and proceed as follows to find a suitable formalism in which to cast it.

It is evident from the above that the state of the system, at each time t, can be represented by a vector $\mathrm{f}(t) = (f_1(t), f_2(t), \ldots, f_n(t))$, where $f_i(t)$ is the probability per unit volume of finding a particle in the ith cell. At a time Δt later, this vector will have changed into $\mathrm{f}(t + \Delta t)$ under the action of the classical laws of motion, which can be symbolically represented by an operator Λ_{op}, that is,

$$\mathrm{f}(t + \Delta t) = \Lambda_{\mathrm{op}} f(t) \tag{2}$$

To ensure determinism, this operator must be either explicitly time-independent or its time dependence must be known. It can

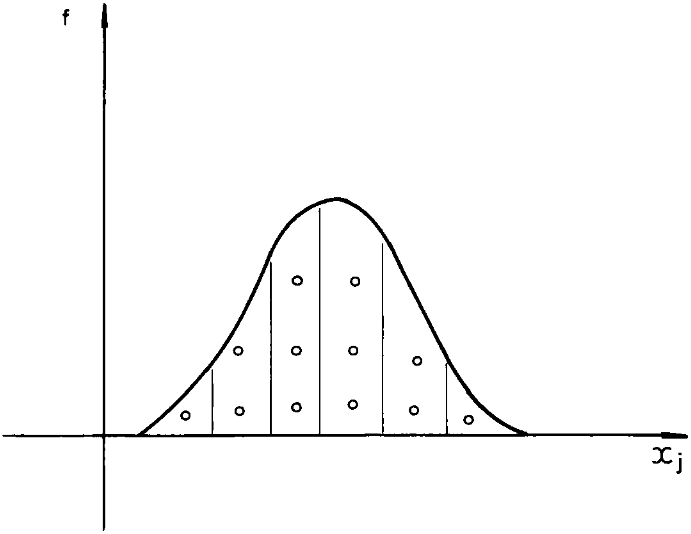

FIG. 2

be shown (*4*) that Λ_{op} can be represented by a matrix the elements of which are defined as transition probabilities from cell *i* to cell *j*. When $\Delta t \to 0$ Eq. (2) may be rewritten as (5)

$$\frac{df_i}{dt} = \sum_j (\Lambda_{ji} f_j - \Lambda_{ij} f_i) \tag{3}$$

where Λ_{ij} are now transition probabilities per unit time. Equation (3) is a particular form of the master equation which has acquired great prominence in recent studies on nonequilibrium statistical mechanics (*6–8*). In the present context Eq. (3) is regarded as expressing the requirement of determinism in the prediction of the temporal change of the probability distribution.

If the transition probabilities Λ_{ij} are known, Eq. (2) can be used to simulate chromatographic processes on an electronic computer. With an arbitrary input function f(0) at time $t = 0$, the chromatogram at a time $t = n\,\Delta t$ is given by (9)

$$\mathrm{f}(t) = \Lambda_{\text{op}}^{n}\,\mathrm{f}(0) \tag{4}$$

where Λ_{op}^{n} is the *n*th power of the matrix Λ_{op}. This approach is implicit in the work of Vink (*10*). Although the method suffers from the disadvantage that it does not lead to analytical expressions, it should, nevertheless, prove useful where the analytical approach, as outlined below, becomes mathematically intractable, and it should also provide a powerful means of assessing the validity of analytical theories.

LIMITING FORMS OF THE MASTER EQUATION APPLICABLE TO CHROMATOGRAPHY

In certain cases where the transition probabilities have simple forms, the master equation may be recast into partial-differential-equation form. Two of these forms are of special importance in chromatography—those corresponding to convection and those to dispersion. We find it convenient, initially, to develop the theory in terms of parameters describing these processes; the transposition to chromatographically more convenient parameters will be dealt with later.

Each term in the master equation represents either a positive or negative contribution to the probability of the cell under consideration and is the product of two conditional probabilities, the first, say f_i, gives the chance of the particle being found in a unit volume of the ith cell, the second Λ_{ij} the probability that, if it is in the cell i at the time t, it will be found in cell j at time $t + \Delta t$. Consider a net of net width Δx spanning the column. Then $\Lambda_{x,x+\Delta x}$ may be defined as

$$\Lambda_{x,x+\Delta x} = \Lambda_c \frac{\overline{\Delta x}'}{\Delta x \, \Delta t'} \tag{5}$$

where Λ_c is a product of other relevant conditional probabilities determined by the physical characteristics of the phenomenon being described. $\overline{\Delta x}'$ is the mean distance traveled in the $+x$ direction in time $\Delta t'$ by the molecules situated in the x cell at time t. Equation (5) may also be rewritten as

$$\Lambda_{x,x+\Delta x} = \frac{\Lambda_c}{\overline{\Delta t}} \tag{6}$$

where $\overline{\Delta t}$ has the definite physical meaning of the mean time taken by the particles in the x cell to traverse the net width Δx.

Convection

Consider a point x in the column with $\Lambda_{x,x+\Delta x} = \Lambda_{x-\Delta x,x} = \Lambda =$ a constant, and all other transition probabilities equal to zero (Fig. 3).

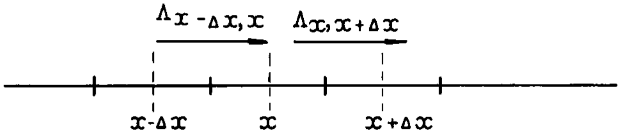

FIG. 3

The master equation for the x cell is then

$$\begin{aligned} \frac{\partial f}{\partial t} &= \Lambda_{x-\Delta x,x} f_{x-\Delta x} - \Lambda_{x,x+\Delta x} f_x \\ &= -\Lambda \, \Delta x (f_x - f_{x-\Delta x})/\Delta x \\ &= -\bar{u} \frac{\partial f}{\partial x} \end{aligned} \tag{7}$$

where Eq. (5) has been used and the limit $\Delta x \rightarrow 0$ has been taken. $\bar{u}$ is physically interpreted as the mean velocity of particles in the x cell.

Diffusion

Let the transition probability scheme be as depicted in Fig. 4. Δx is considered to be the distance between isotropic scattering centers. The master equation then reduces to

$$\frac{\partial f}{\partial t} = \Lambda(\Delta x)^2 \frac{f_{x+\Delta x} + f_{x-\Delta x} - 2f_x}{(\Delta x)^2} \tag{8}$$

It is now important to note that it is not permissible to take the limit $\Delta x \rightarrow 0$ in Eq. (8) because Δx has a definite physical meaning, viz., the distance between the scattering centers. If $\Delta x \ll l$, the length of the column, Taylor's theorem may, however, be used to approximate

$$\frac{f_{x+\Delta x} + f_{x-\Delta x} - 2f_x}{(\Delta x)^2} = \frac{\partial^2 f}{\partial x^2}$$

Equation (6) then becomes

$$\frac{\partial f}{\partial t} = \Lambda(\Delta x)^2 \frac{\partial^2 f}{\partial x^2} \tag{9}$$

Since both Λ and Δx are constants, $\Lambda(\Delta x)^2$ may be equated to a constant coefficient, D, so that the final form is

$$\frac{\partial f}{\partial t} = D \frac{\partial^2 f}{\partial x^2} \tag{10}$$

The above transition-probability scheme corresponds to the classical random walk, so that Eq. (10) is the partial differential equation describing the random-walk process. Equation (10) is usually

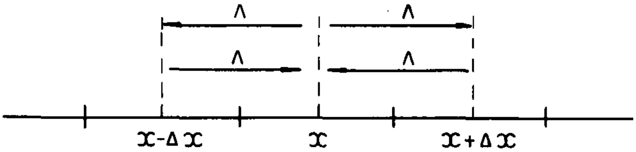

FIG. 4

obtained by the application of conservation of mass and Fick's law of diffusion (*11*). Equation (8) has also been obtained in a different context, but in an analogous manner as above, by Chandrasekhar (*13*) and Ree et al. (*14*).

The coefficient D is of considerable importance in chromatography and may also be computed by considering the netto fractional flux ΔJ of molecules through a cell boundary. From Fig. 4 this follows as

$$\begin{aligned}\Delta J &= \Lambda f_{x+\Delta x}\,\Delta x - \Lambda f_x\,\Delta x\\ &= \Lambda(\Delta x)^2\frac{\partial f}{\partial x}\\ &= D\frac{\partial^2 f}{\partial x^2} \qquad (11)\end{aligned}$$

D may therefore be computed either by means of Eqs. (10) or (11), the latter being the starting point for the generalized nonequilibrium theory (*12*). The basic equivalence of the above theories is therefore established, as they are merely different ways of expressing the information contained in the basic transition-probability scheme.

When both convection and diffusion are operative in the column Eqs. (5) and (8) may be combined to give

$$\frac{\partial f}{\partial t} = -\bar{u}\frac{\partial f}{\partial x} + D\frac{\partial^2 f}{\partial x^2}$$

which is the Fokker-Planck diffusion equation with drift.

THE THEORY OF DISPERSION COEFFICIENTS

The derivation of the Fokker-Planck equation in the previous section was based on a transition scheme which is unnecessarily restrictive. It is the purpose of the present section to show that a generalized diffusion coefficient, the dispersion coefficient, may be defined which, in addition to molecular diffusion, is also able to describe the effects of more than one type of scattering center, anisotropic scattering, and virtual scattering centers.

The motion of a representative particle in a single phase plane is controlled by an explicitly time-dependent potential function resulting from the direct or indirect interaction of the particle with (1) the externally applied pressure gradient, (2) the walls of the column, (3) the column packing, (4) the stationary phase, and (5) the other mobile particles. It is impossible to account exactly for these interactions (this would involve solution of the complete equations of motion), so we are forced to devise simplified models of the processes involved.

It will be assumed that the effect of the pressure gradient and the walls may be inferred from a knowledge of the column-wide velocity distribution. This means that they directly contribute only to the convective term as the mean axial velocity averaged over the column cross section. The other effects manifest themselves as contributions to the total dispersion coefficient. In the present paper only an outline of some of the more general aspects concerning the evaluation of these will be given; detailed calculations for both open and packed tubular columns will be given elsewhere.

The Molecular Diffusion Coefficient (D_m)

Molecular diffusion results from the interaction of the representative particle with the Maxwell-Boltzmann velocity distribution superimposed on the convective flow pattern, the reasonable assumption being made that this equilibrium distribution is not perturbed by the forces causing the convective flow. The mean distance between scattering centers is identified with the mean free path Λ, and since $\Lambda = c\ \Delta\bar{t}$, where c is the molecular speed between collisions, the diffusion coefficient is given, from Eqs. (6), (9), and (10) by

$$D_m = \Lambda_c c\lambda \tag{12}$$

where Λ_c depends on the precise definition of c.

Superimposed Scattering Systems

It frequently happens (e.g., in packed columns) that more than one system of periodically distributed scattering systems operate simultaneously. Consider, for simplicity, two such systems with periodicities Δx_1 and Δx_2. By writing down the master equation for an x cell (Fig. 5) it is easily shown that

$$\frac{\partial f}{\partial t} = (D_1 + D_2)\frac{\partial^2 f}{\partial x^2} \tag{13}$$

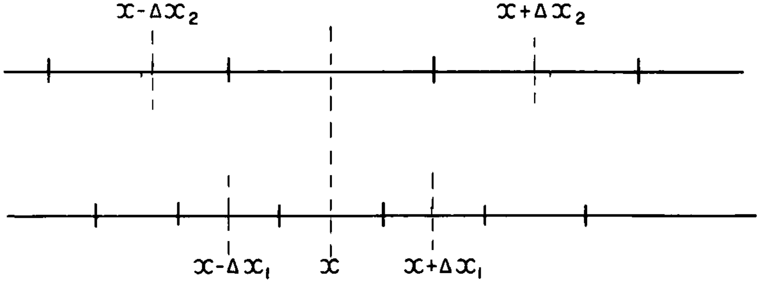

FIG. 5

where $D_1 = \Lambda_1(\Delta x_1)^2$ and $D_2 = \Lambda_2(\Delta x_2)^2$, assuming that both Δx_1 and Δx_2 are so small that Taylor's expansion may be used. It is also required that the total transition probability be written as the sum of Λ_1 and Λ_2. The feasibility of this procedure is a matter of investigation for each specific situation.

Anisotropic Scattering

Consider the transition scheme depicted in Fig. 6. The master equation for the x cell now reads

$$\frac{\partial f}{\partial t} = \Lambda_1 f_{x-\Delta x} + \Lambda_2 f_{x+\Delta x} - \Lambda_1 f_x - \Lambda_2 f_x \tag{14}$$

From Taylor's theorem it follows that

$$\begin{aligned} \Lambda_1 f_{x-\Delta x} &= \Lambda_1\left[f_x - \frac{\partial f}{\partial x}\Delta x + \frac{1}{2}\frac{\partial^2 f}{\partial x^2}(\Delta x)^2\right] \\ \Lambda_2 f_{x+\Delta x} &= \Lambda_2\left[f_x + \frac{\partial f}{\partial x}\Delta x + \frac{1}{2}\frac{\partial^2 f}{\partial x^2}\Delta x)^2\right] \end{aligned} \tag{15}$$

when third- and higher-order terms are neglected. From (14) and

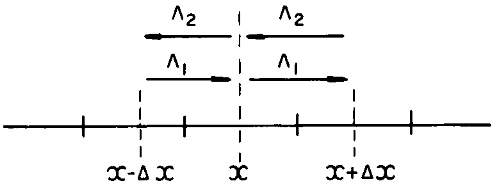

FIG. 6

(15) we have

$$\frac{\partial f}{\partial t} = (\Lambda_2 - \Lambda_1)\,\Delta x\,\frac{\partial f}{\partial x} + \tfrac{1}{2}(\Lambda_1 + \Lambda_2)(\Delta x)^2\,\frac{\partial^2 f}{\partial x^2}$$

$$= (\bar{u}_2 - \bar{u}_1)\,\frac{\partial f}{\partial x} + \tfrac{1}{2}(D_1 + D_2)\,\frac{\partial^2 f}{\partial x^2} \tag{16}$$

This important result shows that anisotropic scattering results in a drift term due to the difference in velocities and an effective dispersion coefficient equal to the mean of the two dispersion coefficients

$$D_1 = (\Delta x)^2\Lambda_1 \quad \text{and} \quad D_2 = (\Delta x)^2\Lambda_2 \tag{17}$$

However, it is not necessary to restrict the theory to second-order terms. If the expansion (15) is extended to include third-order terms, one finds

$$\frac{\partial f}{\partial t} = (\bar{u}_2 - \bar{u}_1)\,\frac{\partial f}{\partial x} + \tfrac{1}{2}(D_1 + D_2)\,\frac{\partial^2 f}{\partial x^2} + \tfrac{1}{6}(S_2 - S_1)\,\frac{\partial^3 f}{\partial x^3} \tag{18}$$

with $S_i = \Lambda_i(\Delta x)^3 = \text{constant}$.

When the theory of isotropic scattering is similarly extended, the coefficient of $\partial^3 f/\partial x^3$ is found to be zero. This result implies that the usual theories of chromatography, which only consider second-order terms, may be inadequate for systems in which anisotropic scattering occurs. The chromatographic significance of these results is discussed below.

Virtual Scattering Centers

These arise as a result of coupling between different rate processes in the column. Examples of these are the coupling between the longitudinal flow profile and lateral diffusion, and the interaction between lateral diffusion and the exchange processes between the stationary and mobile phases. All these processes are characterized by a time which is the time taken by a representative particle to experience the virtual scattering. These will be discussed elsewhere.

INTERPRETATION OF THE CHROMATOGRAM PARAMETERS IN TERMS OF THE DISTRIBUTION-FUNCTION PARAMETERS

In chromatography the chromatogram is usually described in terms of parameters related to the first three moments m_0, m_1, and m_2 of the distribution function. They are found by applying the operator $\int_{-\infty}^{+\infty} (x - \bar{x})^n \, dx$ to the distribution function, where

$$\bar{x} = \int_{-\infty}^{+\infty} xf \, dx$$

That is,

$$m_0 = \int_{-\infty}^{+\infty} f \, dx \tag{19}$$

$$m_1 = \int_{-\infty}^{+\infty} (x - \bar{x}) f \, dx = 0 \tag{20}$$

$$m_2 = \int_{-\infty}^{+\infty} (x - \bar{x})^2 f \, dx \tag{21}$$

m_0 is, by definition of f, equal to unity. m_1 is the mean of the distribution and coincides with the origin in the above case, because all distances are referred to $\bar{x}$. m_2 is the variance and gives an indication of the bandwidth. It is customary (*16*) to express m_2 in terms of the local plate height

$$H_x = \frac{dm_2}{d\bar{x}} \tag{22}$$

which is the increase of the variance per unit distance moved by the mean of the distribution.

Consider now the more general equation governing the evolution of a chromatogram which was proposed in the previous section:

$$\frac{\partial f}{\partial t} = -\bar{u} \frac{\partial f}{\partial x} + D \frac{\partial^2 f}{\partial x^2} - S \frac{\partial^3 f}{\partial x^3} \tag{23}$$

D and S are assumed constant. When use is made of the fact that $\lim x \to \pm\infty \; \partial^n f/\partial x^n = 0$ in the integration by parts, it can be proved that

$$\int_{-\infty}^{+\infty} (x - \bar{x})^n \frac{\partial^m f}{\partial x^m} \, dx = (-1)^m m! \, \delta_{mn} \tag{24}$$

where δ_{mn} is the Kronecker delta. By operating on Eq. (23) with the operator $\int_{-\infty}^{+\infty} (x-\bar{x})^n \, dx$ $(n = 0, 1, 2, 3)$ and by using Eq. (24) we find

$$\frac{dm_0}{dt} = 0 \tag{25}$$

$$\frac{dm_1}{dt} = 0 \tag{26}$$

$$\frac{dm_2}{dt} = 2D \tag{27}$$

$$\frac{dm_3}{dt} = 6S \tag{28}$$

Equation (25) expresses the conservation of mass, while Eq. (26) shows that the distribution mean moves with a velocity $\bar{u}$, i.e., equal to the negative of the coefficient of $\partial f/\partial x$ in Eq. (23). From Eqs. (26), (27), and (22) it follows that the local plate height is given by

$$H_x = \frac{dm_2}{dt}\frac{dt}{d\bar{x}} = \frac{2D}{\bar{u}} \tag{29}$$

Since m_3 is a measure of the skewness of the peak, S is a measure of the rate of increase in this skewness. This result is a generalization of previous theories which predict a tendency toward a gaussian distribution.

For the purpose of chromatography, the third-order partial differential equation [Eq. (23)] may therefore be replaced by the simple set of ordinary first-order differential equations (25) to (28). These require the specification only of the moments of the initial distribution for their complete solution.

The theory outlined above is strictly valid only when $\bar{u}$, D, and S are constant. It may, however, be easily extended (*17*) to the case where these parameters depend on x, provided their variation within the peak width is negligible compared to the variation along the length l of the column.

When D and S are dependent on f (nonlinear chromatography) the operator $\int_{-\infty}^{+\infty} (x-\bar{x})^n \, dx$ is not able to extract the desired chromatographic information directly from Eq. (23). It may ther become necessary first to solve this equation for f before operating on it with the moment generator. Alternatively, it might be possible to construct an operator which will transform Eq. (23) into a form from which the time dependence of the moments may be found more easily.

CONCLUSIONS

The general equation describing the temporal change of the solute distribution in a chromatographic column is the special form, Eq. (3), of the master equation. When the transition probabilities can be written in terms only of x and f, this equation reduces to a partial differential equation of the form

$$\frac{\partial f}{\partial t} = -\bar{u}\,\frac{\partial f}{\partial x} + D\,\frac{\partial^2 f}{\partial x^2} - S\,\frac{\partial^3 f}{\partial x^3} + T\,\frac{\partial^4 f}{\partial x^4} \cdots \tag{30}$$

where the coefficients $\bar{u}$, D, S, and T, etc., are functions of x, f, and other column parameters. These coefficients may all be calculated in terms of transition probabilities, which, in turn, are found by averaging the appropriate chromatographic ensemble.

The order to which Eq. (30) is considered significant is governed by the amount of information required about the peak characteristics. For instance, if retention times and bandwidths are the only factors in which one is interested, third- and higher-order terms may be neglected. However, if peak asymmetry is of importance, it may become necessary to include third-order terms. This will, however, depend on the relative magnitudes of the contributions of S, the concentration dependence of D, and the influence of the initial distribution to the peak skewness.

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