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Variance of a zone migrating in a non-uniform time-invariant linear medium

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ABSTRACT

A general model describing the evolution (expansion and contraction) of a zone migrating in a non-uniform (coordinate-dependent) chromatographic medium was developed. Equations for the spatial and temporal rates of change of variance of a zone were derived starting from the basic principle of mass balance in convective diffusion in a one-dimensional non-uniform medium. Also, the distinction between local and average values of many important quantities describing the evolution of a zone in a non-uniform medium such as velocity of a zone, plate height, chromatographic efficiency and was re-examined. It was shown that under certain conditions covering all practically important cases the chromatographic efficiency of a non-uniform medium cannot exceed that of a corresponding uniform medium. The study also produced unexpected results. It became apparent that a gradient of diffusivity affected the velocity of migration of an analyte in a column, and part of dispersion-related zone broadening could be recovered. It also became apparent that previous approaches for dealing with non-uniformity depended on unknown implicit conditions. Typically, these conditions were not satisfied in the cases considered. For example, many classical results deemed to be exact values must be viewed only as approximations. Hence, the known pressure correction factor for plate height in capillary gas chromatography with ideal gases is only an approximation to a still unknown correct value.

INTRODUCTION

Existing chromatographic theory has done an admirable job in predicting the performance of capillary columns under uniform and near uniform conditions. However, situations in which chromatographic conditions are not uniform throughout the column have been only partially addressed [*e.g.*, the effect of large pressure drops in gas chromatography (GC) with ideal carrier gases has been explained]. The general approach has been to develop theory for uniform conditions, then apply correction factors to account for non-uniformity. Such an approach is inherently limited to relatively small deviations from non-uniformity. In this paper, a general expression is developed which directly describes zone broadening under time-invariant, non-uniform conditions (zones traversing standing gradients). The intent is to lay a foundation for further work in which the effects of simultaneous time-variant and spatially non-uniform conditions on peak shape can be described.

Physical conditions often change from the inlet to the outlet of the column. A typical example of such a non-uniform (coordinate-dependent) chromatographic medium is the change in density of the carrier gas in GC caused by the pressure drop from the inlet to the outlet. With small-diameter capillary columns, the column inlet pressure can be many times the column outlet pressure. This pressure drop has an impact on chromatographic performance in terms of both speed and efficiency.

Non-uniformity of other conditions along the column can also affect chromatographic performance. Variations in column cross-sectional area, stationary phase film thickness and composition, mobile phase composition, etc., are further examples in GC. Other techniques such as liquid (LC) and supercritical fluid chromatography (SFC) and others are also affected by non-uniform conditions.

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Thus, non-uniform conditions are widely encountered in chromatography.

Analysis of a non-uniform chromatographic medium becomes significantly more complex when non-uniformity of a medium is combined with a sample overloading, a cause of non-linear effects, and/or with time variance of a medium such as in the case of temperature programming in GC or programming of solvent composition in LC and SFC. The scope of this paper is limited to analysis of a linear time-invariant (constant in time) medium.

In analytical chromatography, whenever possible, non-linearity is avoided by measures such as injection of a substantially small amount of a sample. Time variance, on the other hand, is an important component of many analytical techniques. The theory of non-uniformity combined with time variance is a subject of the next paper in this series.

The most widely used approach to the theoretical analysis of chromatography in a non-uniform time-invariant linear medium was outlined by Golay [1] in 1958. Specific results accounting for the compressibility of an ideal carrier gas in GC were published by Giddings and co-workers [2,3] in 1959–60. A more general treatment published by Giddings a few years later [4–6] is widely considered as the basis for the analysis of all types of non-uniformity in a chromatographic medium.

Unfortunately, these known theories have shortcomings. As the starting point, results are derived for a uniform medium, and corrections are applied to accommodate non-uniformity in further derivations. Hence the derivations rely on the implicit assumption of uniformity of chromatographic conditions within a zone of a migrating analyte.

For example, Golay suggested that non-uniformity should be treated in the following way. He wrote (ref. 1, p. 43) that the conclusions in that reference[a] "are applicable to columns of uniform cross-sections in which the input to exit pressure ratio is near unity. When there is a succession of varying cross-sections ..., we should *replace* the second moment [of density] u by the volumetric second moment U, the incremental value of which is: $\mathrm{d}U = S^2\mathrm{d}u$, where S represents the cross-section area of the column *at the point considered*". In a similar manner, Golay considers corrections for pressure drop and for combination of both types of non-uniformity. Substantial in that discussion are two factors: (a) the starting point of $\mathrm{d}u$ (incremental variance of the zone) which was previously derived for *uniform* conditions, and (b) the correction by multiplying $\mathrm{d}u$ by quantities such as S^2 *at the point considered.* If conditions within a zone of a non-zero width are substantially non-uniform it becomes unclear which is "*the point considered*", and the correction of an incremental variance by a single parameter (in this case S) becomes generally inappropriate.

Similarly, analysis developed by Giddings [5] starts by dividing a column into equal small segments. It was then assumed that the local conditions within each segment *approach uniformity*, and are represented with *any required precision* when the number of segments becomes sufficiently large. This is a common mathematical technique. However, in derivations for non-uniform chromatography, the size of a segment could not be meaningfully reduced below the width of a zone of analyte in the vicinity of a given location. Therefore, the logic fails if conditions remain substantially non-uniform *within* the zone. Therefore, for such derivations, the requireme nt of uniformity of conditions within a zone of a non-zero width is implicitly a *de facto* limitation even if not explicitly stated. Obviously, if time-invariant conditions are uniform within a zone at any position in a column, the entire column must be uniform, and analysis of non-uniformity becomes irrelevant. The analysis can and must be expected to yield practically accurate and reliable predictions if conditions within a zone are *almost* uniform. It must be recognized, however, that the predictions based on such an assumption are approximate.

For example, utilizing the aforementioned methodology, Stewart *et al.* [2] in 1959 and Golay [7] in 1963 arrived at the same value for what is now well known as Giddings' correction factor for the plate height in a compressible ideal carrier gas in GC [2]. Although in GC conditions as functions of coordinates typically do not change rapidly, nevertheless, they are not constant within the zone [1]. Therefore, it must be recognized that even in an ideal case, Giddings' correction factor is only an approximation to the still unknown correct value.

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[a] All notations in this paragraph are the same as in the source [1] and are limited to this paragraph only.

Further, when a theory is based on the assumption of near uniformity of chromatographic conditions within a zone while actual conditions are substantially non-uniform, as can be the case in SFC [8], predictions of the theory become unreliable.

Hence non-uniform conditions are only superficially dealt with in chromatographic theory.

The purpose of this paper was to develop a general theory of chromatography in a non-uniform time-invariant linear medium. The topic of the paper was a study of evolution of variance of a zone of analyte migrating in the medium.

The model

It is important to base a general study of the process of a chromatographic separation in a non-uniform medium on a model which reduces all specifics of the process to a minimum set of independent factors.

Giddings [6] treated the process of a velocity-based chromatographic separation in a uniform column as a one-dimensional phenomenon described by the mass-balance equation of convective diffusion [6,9]:

$$\frac{\partial m}{\partial t} = D \cdot \frac{\partial^2 m}{\partial x^2} - v \cdot \frac{\partial m}{\partial x} \qquad (1)$$

where all quantities m, D and v are cross-sectional averages, m is the amount of analyte per unit of column length, which will be referred to as the specific mass of analyte, D is the effective diffusivity (in brief, diffusivity) of analyte in the column, representing the cross-sectional average of all factors causing dispersion [10] of a zone, such as molecular diffusivity in the mobile phase and resistance to mass transfer, and v is the velocity of migration of analyte which could be described through a cross-sectional averaged velocity of the mobile phase, v_m, and a capacity factor of the analyte, k, as

$$v = v_m/(1 + k) \qquad (2)$$

A chromatographic theory based on a mass-balance equation such as eqn. 1 provides a high level of generality, as it allows reduction of all the specifics of a chromatographic process (such as the thermodynamics of all internal interactions in a medium and statistics of migration of a sample [6,11,12] affected by such interactions) to only two parameters: the dispersivity and the velocity of migration of the sample in the medium.

Eqn. 1 and similar equations [13] are widely used for studies of chromatography in uniform media. In a non-uniform medium, both the velocity of the analyte and its dispersion at each specific location are functions of the coordinate of the location. Unfortunately, to adapt eqn. 1 and similar equations to a non-uniform medium, it is not enough simply to assume that both parameters, D and v, are functions of x. With that assumption, eqn. 1 is *not mass conservative*, *i.e.*, it does not represent the balance of mass in a non-uniform medium.

A more general equation of convective diffusion in a one-dimensional medium is

$$\frac{\partial m}{\partial t} = \frac{\partial}{\partial x}\left(D \cdot \frac{\partial m}{\partial x}\right) - \frac{\partial}{\partial x}(vm) \qquad (3)$$

This equation is *mass conservative* even when D and v are functions of x and t (see Appendix). Eqn. 3 represents a one-dimensional version of a more general mass-conservative three-dimensional convective diffusion equation [9]:

$$\frac{\partial \rho}{\partial t} = \mathrm{div}\,(D_m \,\mathrm{grad}\,\rho) - \mathrm{div}\,(\rho \mathbf{v}) \qquad (4)$$

where ρ is the density of the migrating entity, D_m is its molecular diffusivity and $\mathbf{v}$ is a vector of velocity in the medium.

In eqn. 3, all coordinate-dependent properties of a non-uniform medium such as a variation in column diameter, thickness and composition of stationary phase are represented by the two functions of the coordinate, D and v. Obviously, when a medium is uniform, *i.e.*, $\partial D/\partial x = \partial v/\partial x = 0$ for any x, eqn. 3 could be rewritten as eqn. 1.

In this paper, eqn. 3 is the basic model for chromatography in a non-uniform medium.

Limitations within the model

The assumptions limiting the scope of the model in this paper can be summarized as follows.

C1. The medium is time invariant and linear, *i.e.*, the quantities $D = D(x)$ and $v = v(x)$ depend only on x.

Assumption of linearity (no dependence of D and v on m) allows one, among other simplifications, to deal individually with each component of a complex mixture. Thus, only migration of a single-component analyte is studied. The assumption of time invariance (no dependence of D and v on t) avoids complications caused by interaction of variation of chromatographic conditions in space with their variation in time.

It is also assumed that the quantities D and v are finite within any bounded interval of the x-axis, and D is not negative. Further, derivatives $\partial v/\partial x$ and $\partial D/\partial x$ are limited when x approaches infinity. More accurately:

C2. $0 \leqslant D < \infty$ and $|v| < \infty$ when $|x| < \infty$; $|\partial v/\partial x| < \infty$ and $|\partial D/\partial x| < \infty$ when $x \to \pm\infty$.

As for a zone of analyte, it is assumed that its second moment is always limited (limited width of the zone). That, together with the recognition of the fact that the specific mass, $m = m(x,t)$, of the zone is a non-negative function, could be formally expressed as:

$$\text{C3.}\quad \left|\int_{-\infty}^{\infty} x^2 m \mathrm{d}x\right| < \infty; \qquad m \geqslant 0 \tag{5}$$

It is apparent that only condition C1 provides a significant limitation to the scope of the theory. The other two sets of conditions, C2 and C3, are almost unrestrictive.

The last two conditions could be combined for further use as follows. Inequalities 5 imply:

$$x^3 m \to 0 \text{ and } x^4 \cdot \frac{\partial m}{\partial x} \to 0 \text{ when } x \to \pm\infty \tag{6}$$

Combination of these relationships and conditions C2 provides

$$xDm \to 0,\ x^2 vm \to 0,\ x^2 D \cdot \frac{\partial m}{\partial x} \to 0 \text{ and } x^2 m \cdot \frac{\partial D}{\partial x} \to 0 \text{ when } x \to \pm\infty \tag{7}$$

Moments and other relevant relationships

As stated earlier, the purpose of this paper was to account for variations in D and v down the column, in calculations of the variance,

$$\sigma^2 = \int_{-\infty}^{\infty} (x - z)^2 m \mathrm{d}x \tag{8}$$

of specific mass in a zone, the second central moment of m. The variance is mathematically the most convenient representation of the width of a zone.

In eqn. 8, the quantity

$$z = \int_{-\infty}^{\infty} xm\mathrm{d}x \tag{9}$$

is the first moment of m which represents a coordinate of the center of mass of the zone. Both eqns. 8 and 9 assume that m is normalized so that the zone has a unity mass, *i.e.*,

$$\int_{-\infty}^{\infty} m\mathrm{d}x = 1 \tag{10}$$

Such normalization is possible owing to the mass-conservative nature of the model. It is also useful to note that eqn. 9 implies

$$\int_{-\infty}^{\infty} (x - z)m\mathrm{d}x = 0 \tag{11}$$

Several other relationships from the theory of chromatography in a uniform medium are relevant to further discussions.

Giddings [6] has shown that the diffusivity, D, in eqn. 1 could be expressed via the column plate height, H, as

$$D = Hv/2 \tag{12}$$

Relationships between a column plate height and other column parameters are known from the literature [1,6,14,15].

From another perspective, Golay's [1] expressions

$$\mathrm{d}\sigma^2/\mathrm{d}x = H \tag{13}$$

and

$$\mathrm{d}\sigma^2/\mathrm{d}t = Hv \tag{14}$$

allow interpretation of H in eqn. 13 as a spatial rate of dispersion of a zone while the quantity Hv in eqn. 14 and, therefore, the diffusivity, D, in eqn. 12 could be interpreted as a representative of the zone's temporal dispersion rate.

It is also interesting that eqn. 14 is a generalization of Einstein's [16,17] expression $\sigma^2 = 2Dt$ for Brownian motion in a stationary ($v = 0$) medium. In the differential form, the latter can be rewritten as

$$\mathrm{d}\sigma^2/\mathrm{d}t = 2D \tag{15}$$

which, together with eqn. 14, serves as another justification for eqn. 12.

Expressions 13–15 represent spatial and temporal rates of growth of σ^2 in uniform media. Similar equations for the evolution of σ^2 in a non-uniform medium are derived from eqn. 3 in the next section.

THEORY

Aggregate velocity of migration of a zone

As mentioned earlier, the subject of this paper is the derivation of the spatial and temporal rates of change of σ^2 in a non-uniform medium.

If the location of a zone in space is represented by its center of mass, z, then the spatial rate of changes of σ^2 is $\mathrm{d}\sigma^2/\mathrm{d}z$ and the temporal rate is $\mathrm{d}\sigma^2/\mathrm{d}t$. The two relate as

$$\frac{\mathrm{d}\sigma^2}{\mathrm{d}z} = \frac{\mathrm{d}t}{\mathrm{d}z}\cdot\frac{\mathrm{d}\sigma^2}{\mathrm{d}t} = \frac{1}{u_\mathrm{a}}\cdot\frac{\mathrm{d}\sigma^2}{\mathrm{d}t} \qquad (16)$$

where

$$u_\mathrm{a} = \mathrm{d}z/\mathrm{d}t \qquad (17)$$

is a temporal rate of displacement of the center of mass of the zone. This quantity can be viewed as an aggregate velocity of migration of the entire zone. In a non-uniform medium, u_a could be different from local velocities of elements of the zone.

It can be shown (see Appendix) that

$$u_\mathrm{a} = \int_{-\infty}^{\infty}\left(v + \frac{\partial D}{\partial x}\right)m\mathrm{d}x = \int_{-\infty}^{\infty} um\mathrm{d}x \qquad (18)$$

where

$$u = u(x) = v + \frac{\partial D}{\partial x} \qquad (19)$$

The integral on the right-hand side of eqn. 18 represents the momentum of a zone and indicates that it is the quantity u (not v) which represents the net local velocity of migration of analyte in the medium. According to eqn. 19, the net velocity, u, consists of two components. Component $\partial D/\partial x$ represents the migration velocity caused by a gradient of diffusivity and exists *only* in a non-uniform medium. The other component, v, is the convective velocity of the analyte defined for a uniform medium as in eqn. 2 [1,6]. In a non-uniform medium, both v_m and k in eqn. 2 defining v could be functions of x, *i.e.*, $v_\mathrm{m} = v_\mathrm{m}(x)$, $k = k(x)$.

Rearranged equation of convective diffusion

Using the notation in eqn. 19, eqn. 3 can be rewritten (see Appendix) in the form

$$\frac{\partial m}{\partial t} = \frac{\partial^2}{\partial x^2}(Dm) - \frac{\partial}{\partial x}(um) \qquad (20)$$

which is more convenient for analysis of evolution of variance of a zone (see below). Eqn. 20 is similar to what is known in physics as the Fokker–Planck equation [18]. Further developments are based on eqn. 20.

Evolution of variance of a zone

The temporal rate of change of variance of a zone, $\mathrm{d}\sigma^2/\mathrm{d}t$, could be expressed (see Appendix) as

$$\frac{\mathrm{d}\sigma^2}{\mathrm{d}t} = 2\int_{-\infty}^{\infty} Dm\mathrm{d}x + 2\int_{-\infty}^{\infty}(x - z)um\mathrm{d}x \qquad (21)$$

and can be viewed as a generalization of Einstein's eqn. 15 applied to a convective dispersion in a one-dimensional non-uniform medium. Substitution of eqn. 21 in eqn. 16 yields an expression for the spatial rate of change of σ^2:

$$\frac{\mathrm{d}\sigma^2}{\mathrm{d}z} = \frac{2}{u_\mathrm{a}}\int_{-\infty}^{\infty} Dm\mathrm{d}x + \frac{2}{u_\mathrm{a}}\int_{-\infty}^{\infty}(x - z)um\mathrm{d}x \qquad (22)$$

which can be further rewritten as

$$\frac{\mathrm{d}\sigma^2}{\mathrm{d}z} = \frac{1}{u_\mathrm{a}}\int_{-\infty}^{\infty} Hum\mathrm{d}x + \frac{2}{u_\mathrm{a}}\int_{-\infty}^{\infty}(x - z)um\mathrm{d}x \qquad (23)$$

where similarly to eqn. 12,

$$H = H(x) = 2D/u \qquad (24)$$

Eqn. 23 can be viewed as a generalization of Golay's eqn. 13 for non-uniform media with the quantity H playing the role of the local plate height. Further discussion of this topic is postponed until the next section.

Typically in chromatography, the column length rather than the retention time of an analyte is known *a priori*. This makes the spatial rate, $\mathrm{d}\sigma^2/\mathrm{d}z$, more convenient than the temporal rate, $\mathrm{d}\sigma^2/\mathrm{dt}$, for calculation of the variance of a zone at the column outlet. Therefore, greater attention in further developments is given to the former.

Approximation of the spatial rate of zone variance

Eqns. 21–23 describe the evolution of variance of a zone migrating in a one-dimensional linear time-invariant non-uniform medium under practically unrestrictive conditions (C2 and C3). The conditions allow even for a random non-uniformity where the velocity, u, and diffusivity, D, of the analyte can change so rapidly that the gradients, $\partial v/\partial x$ and $\partial D/\partial x$, can change signs several times within the zone.

Chromatographically, this might include variations in conditions such as a completely random variation in the column inside diameter, stationary phase film thickness or particle size of a packing material in a column.

Typically in chromatography, zones of analytes are so narrow relative to the column length that

C4. gradients, $\partial v/\partial x$ and $\partial D/\partial x$, are nearly constant within a zone.

It is important to emphasize that these conditions require no limit on the degree of change of u or D within the zone, or along the entire column. The conditions only limit the degree of the change of gradients of those quantities within the zone. However, even the gradients are allowed to have large changes along the entire column. Examples include locally nearly constant density gradients in GC and SFC.

Except for special cases, eqns. 21–23 are difficult to solve. However, under condition C4, they could be replaced by simplified approximations. Thus, if condition C4 is valid with a required precision, eqn. 23 can be reduced to the ordinary differential equation (see Appendix) for $\sigma^2 = \sigma^2(z)$:

$$(\sigma^2)' = H + 2\sigma^2 \cdot \frac{u'}{u} \text{ or } (\sigma^2)' = H + \sigma^2 \cdot \frac{(u^2)'}{u^2} \quad (25)$$

where the prime serves as an abbreviation for a derivative by z. Obviously, for media with a uniform velocity ($u' = 0$), this equation becomes Golay's eqn. 13.

To solve eqn. 25, one may introduce a quantity

$$\tau^2 = \sigma^2/u^2 \quad (26)$$

which represents a measure of variance of a zone in time units. Eqn. 25 could be rearranged as

$$(\tau^2)' = (\sigma^2/u^2)' = H/u^2 \quad (27)$$

and

$$\tau^2 = \frac{\sigma^2}{u^2} = \frac{\sigma^2(0)}{u^2(0)} + \int_0^z \frac{H}{u^2} \cdot \mathrm{d}x \quad (28)$$

where $\sigma^2(0)$ and $u^2(0)$ are, respectively, the variance and the velocity of the zone at the beginning of its path (column inlet).

If $\sigma^2(0) = 0$, then

$$\tau^2 = \int_0^z \frac{H}{u^2} \cdot \mathrm{d}x \quad \text{and} \quad \sigma^2 = u^2 \int_0^z \frac{H}{u^2} \cdot \mathrm{d}x \quad (29)$$

Further, under typical chromatographic conditions,

C5. $\left|\frac{\partial D}{\partial x}\right| \ll |v|$

In that case, owing to eqn. 19, eqns. 27 and 29 could be reduced respectively to

$$(\tau^2)' = (\sigma^2/v^2)' = H/v^2 \quad (30)$$

and

$$\tau^2 = \int_0^z \frac{H}{v^2} \cdot \mathrm{d}x \quad \text{and} \quad \sigma^2 = v^2 \int_0^z \frac{H}{v^2} \cdot \mathrm{d}x \quad (31)$$

Eqn. 30 reflects Golay's [1] approach to accounting for non-uniformity in a medium. Also, eqns. 30 and 31 reflect Giddings' idea [4,6] of additivity of local $\mathrm{d}\tau^2$ values in their contribution to the total τ^2 value of a zone of analyte at any location along its path. This discussion continues in the next section.

Finally, for a uniform medium, the latter expressions yield

$$\sigma^2 = Hz \quad (32)$$

which, after substitution of eqn. 24 and $z = ut$, takes the form of Einstein's relationship $\sigma^2 = 2Dt$.

DISCUSSION

Local and aggregate plate height and diffusivity

Earlier, a quantity H (eqn. 24) was introduced. Comparison of eqn. 24 with Giddings' eqn. 12 shows that in uniform media, the quantity H in eqn. 24 defines a chromatographic plate height. A similar conclusion follows from comparison of eqns. 14 and 15.

To interpret the quantity H in a non-uniform medium, consider eqn. 23 and an extremely narrow zone with a center of mass z. When the variance of the zone approaches zero, its specific mass, m, as a function of x approaches Dirac's delta-function $\delta(x - z)$. The latter conclusion comes from an examination of eqn. 8. When m converges to the delta-function, the first term in eqn. 23 converges to H and the second term vanishes. Thus, the entire expression converges to $d\sigma^2/dz = H(z)$, which is similar to Golay's eqn. 13 and indicates that in a non-uniform medium, the quantity H is a local plate height. A similar conclusion could be derived from assuming $\sigma^2 = 0$ in eqn. 25.

The concept of a local plate height helps in further interpretation of the first term on the right-hand side of eqn. 23. Note first that the quantity

$$f_u = f_u(x,t) = um \tag{33}$$

represents a local mass flow (in brief, a flow) due to migration of analyte[a]. The zeroth moment, M_0, of f_u is the same as an aggregate velocity of the zone. Indeed, from eqns. 33 and 18:

$$M_0 = \int_{-\infty}^{\infty} f_u dx = \int_{-\infty}^{\infty} um dx = u_a \tag{34}$$

Eqns. 33 and 34 allow the first term on the right-hand side of eqn. 23 to be rewritten as

$$H_a = H_a(z) = \frac{1}{u_a} \int_{-\infty}^{\infty} Hum dx = \frac{1}{M_0} \int_{-\infty}^{\infty} Hf_u dx \tag{35}$$

indicating that H_a is a flow-weighted average plate height, and could be referred to as an aggregate plate height of the zone. Unlike a local plate height, the aggregate plate height is no longer a property of the medium alone, but also depends on spatial distribution of the flow of analyte. Of course, if the plate height is uniform (H is constant), eqn. 35 becomes $H_a = H$. In other words, if the local plate height in a medium is uniform, its aggregate plate height is everywhere the same as the local plate height.

The first term on the right-hand side of eqn. 21 could be interpreted in a similar manner. Indeed, a quantity

$$D_a = D_a(z) = \int_{-\infty}^{\infty} Dm dx \tag{36}$$

could be introduced which is a specific-mass-weighted average of the diffusivity, and can be referred to as an aggregate diffusivity of a zone (a combined property of a medium and a zone).

Comparison of the first terms on the right-hand side of eqns. 22 and 23 with notations 35 and 36 suggests that

$$H_a = 2D_a/u_a \tag{37}$$

a relationship similar to that in eqn. 24 for local quantities.

Further, in a uniform chromatographic medium, a plate height is a spatial rate of growth of variance of a zone (eqn. 13) while the quantity $2D$ can be interpreted as a temporal rate of growth of variance of the zone (eqn. 15). In a non-uniform medium, the analogy remains. A local plate height and a local diffusivity represent, respectively, a local spatial rate and half of a local temporal rate of growth of variance of a zone. Similarly, an aggregate plate height and an aggregate diffusivity represent, respectively, an aggregate spatial rate and half of an aggregate temporal rate of growth of variance of a zone.

In spite of many similarities between the aggregate plate height and diffusivity, there is an important difference. A specific mass, m, and a migration flow, f_u, of an analyte could be viewed as static and dynamic distributions of a zone, respectively. Therefore, an aggregate diffusivity, being a specific-mass-weighted average (eqn. 36), can be viewed as a static average of a local diffusivity. The aggregate plate height, on the other hand, is a flow-weighted average (eqn. 35), and can be viewed as a dynamic average of local plate height.

This discussion could be summarized as follows. It is an accepted practice in the chromatographic literature to view a zone migrating in a non-uniform medium as a lump entity subjected to dispersion with a single spatial dispersion rate equal to a local plate height, H, at the center of mass of the zone. This is a convenient logical concept. However, as the previous discussion suggests, that single spatial dispersion rate is an aggregate plate height, H_a, which is also a function of the coordinate of the center of mass of the zone but might be different from the local plate height there. Similar conclusions are valid for local and aggregate diffusivities in a non-uniform medium.

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[a] This does not include a component, $-\partial/\partial x\,(Dm)$, of a local mass flow due to the zone dispersion in the medium.

Gradient of diffusivity

All the results discussed so far were derived from eqn. 20, which along with notation 19 indicates that the gradient, $\partial D/\partial x$, of the diffusivity behaves as a component of velocity of an analyte. This was not previously known in the chromatographic literature.

The appearance of the quantity $\partial D/\partial x$ as a part of velocity indicates that a positive $\partial D/\partial x$ increases and a negative $\partial D/\partial x$ reduces the velocity of analyte.

Recognition of the fact that the gradient of diffusivity behaves as a component of velocity helped significantly in deriving eqns. 21–23 and in understanding the mechanisms of evolution of a zone in a non-uniform medium.

Comparison with known results

As was mentioned earlier, eqn. 30 reflects Golay's [1] approach to accounting for non-uniformity in a medium. Golay recommended a similar approach as a corrective measure against such sources of non-uniformity as pressure drop in GC with an ideal carrier gas, non-uniformity of column diameter and combinations of both. Here, eqn. 30 has been derived for a combination of any non-uniformities.

It was also mentioned before that eqns. 30 and 31 reflect Giddings' heuristic assumption [4,6] of additivity of local $d\tau^2$ values in their contribution to the total τ^2 value of a zone of analyte at any location along its path.

It must be noted, however, that the treatment of non-uniformity in the aforementioned references relies on the implicit assumption that all chromatographic conditions within the zone are nearly uniform. A more detailed discussion was presented in the Introduction.

Here, eqns. 21–23 for evolution of variance of a zone have been derived under no limits to non-uniformity in a medium.

A simplified version (eqn. 25) and its modifications (eqns. 27, 28 and 29) do impose some limits to non-uniformity, namely both gradients, $\partial v/\partial x$ and $\partial D/\partial x$, must be nearly constant within the zone. Still, no limits to the rate or degree of change of D and/or v is required. In short, eqn. 25 can be applied to a wider class of non-uniform media and allow more relaxed conditions than previous treatments of non-uniformity.

For typical chromatographic conditions, eqn. 25 can be further reduced to eqns. 30 and 31. Special cases of these equations are known from the literature [1,4,6]. However, again, in this paper, eqns. 30 and 31 are shown to be applicable to a wider class of non-uniform media and allow more relaxed conditions than previous treatments.

APPLICATION OF THE THEORY

Erosion of chromatographic efficiency

It can be argued that a positive gradient of velocity of a zone can reduce efficiency as it causes extra expansion of the zone. Alternatively, when a zone of analyte suffers significant deceleration it contracts. It can be argued, therefore, that creating a negative gradient of velocity in a column can improve chromatographic efficiency. Such statements are examined in this section.

To simplify mathematical expressions in this section, a quantity

$$\phi = \phi(x) = 1/u \tag{38}$$

is introduced where ϕ is measured in units of time per unit length and could be interpreted as a spatial rate of delay, or delay rate of an analyte: the greater the delay rate at some coordinate of a medium, the longer the analyte remains in the vicinity of that coordinate. Utilizing the delay rate, the retention time, t_r, at $x = L$ could be expressed as

$$t_r = \int_0^L \phi \mathrm{d}x \tag{39}$$

A chromatographic efficiency, N, is defined as $N = t_r^2/\tau^2(L)$ with $\sigma^2(0) = 0$. Substituting here eqns. 29 and 39, and taking into account notation 38, one has

$$N = \frac{\left(\int_0^L \phi \mathrm{d}x\right)^2}{\int_0^L H\phi^2 \mathrm{d}x} \tag{40}$$

A similar expression for apparent plate height was derived earlier by Giddings [4]. Introducing notations

$$N_\Sigma = \int_0^L \frac{\mathrm{d}x}{H} \quad \text{and} \quad \varepsilon^2 = \frac{\left(\int_0^L H\phi^2 \mathrm{d}x\right)\int_0^L \frac{\mathrm{d}x}{H}}{\left(\int_0^L \phi \mathrm{d}x\right)^2} \tag{41}$$

one has

$$N = N_\Sigma/\varepsilon^2 \tag{42}$$

The quantity $1/H$ in the integrals in eqn. 41 represents a local specific efficiency (efficiency per unit length at a given location) of a medium (a column). Therefore, the quantity N_Σ in eqn. 41 is the sum of all local efficiencies and can be referred to as a cumulative efficiency of a non-uniform medium (a column). If the velocity of a zone was uniform, and only the column plate height was not uniform, the efficiency of the column would have been N_Σ.

For the quantity ε^2, it can be shown (see Appendix) that

$$\varepsilon^2 \geqslant 1 \tag{43}$$

Thus, from eqn. 42, the chromatographic efficiency of a non-uniform medium cannot exceed its cumulative efficiency (standing gradients cannot improve efficiency). Giddings [4] came to the same conclusion for the special case when only the velocity of the analyte could vary along a column while the local plate height remained the same everywhere. The derivation of inequality 43 employed here did not require such a limitation.

Quantities ε^2 and ε represent, respectively, the degree of erosion of efficiency and resolution due to non-uniformity within a medium and can be referred to as erosion factors of those quantities.

Re-examination of the introductory statements of this section provide further interpretation of the erosion factor.

Note first that eqn. 42 gives the same result whether the velocity of analyte (inverse of the delay rate) increases or decreases down its path. This means that both types of non-uniformity are equally damaging to efficiency.

Indeed, when a zone of analyte accelerates down its path owing to the positive velocity gradient and broadens, the loss from the zone expansion is partially compensated for by the accompanying gain from faster migration of the zone. The compensation, however, is not large enough to prevent a net erosion of efficiency. GC represents a typical example of a medium with positive velocity gradients. Similarly, when a zone decelerates down its path due to the negative velocity gradient and narrows, the gain from the zone contraction is smaller than the accompanying loss from the zone's slower migration. The net result is erosion of efficiency. SFC represents a typical example of a medium with the negative velocity gradients [19]. In either case, the net result of non-uniformity is erosion of efficiency and resolution.

Still, there is one favorable aspect from this net unfavorable outcome. As the erosion is a result of two competing effects (such as the gain from a zone contraction and the loss from its deceleration), a large degree of the erosion ($\varepsilon \gg 1$) could be considered as an exception rather than the rule. This observation is confirmed by experimental data [20].

Consider now a medium where the plate height is uniform (H is constant) but the delay rate varies down the column. Examples include cases with a large pressure drop in GC and SFC where local plate height changes not nearly as much as a local velocity of an analyte. In these media, the cumulative efficiency (eqn. 41) has a more familiar form:

$$N_\Sigma = L/H \tag{44}$$

and the eqn. 42 can be reduced to

$$\varepsilon^2 = \frac{L\int_0^L \phi^2 \mathrm{d}x}{\left(\int_0^L \phi \mathrm{d}x\right)^2} = 1 + \frac{L^{-1}\int_0^L \Delta\phi^2 \mathrm{d}x}{\phi_{\mathrm{av}}^2} \tag{45}$$

where (Fig. 1) $\phi_{\mathrm{av}} = L^{-1}\int_0^L \phi \mathrm{d}x$ is a column length averaged delay rate and $\Delta\phi = \phi - \phi_{\mathrm{av}}$ is a local variation of the delay rate (a deviation of a delay rate from its average). Obviously, $\Delta\phi$ has a zero average. The numerator on the right-hand side of eqn. 45 represents an average "energy" of the variation in delay rate. Therefore, the erosion factor, ε^2, deviates from unity by the ratio of the average "energy" of variation of the delay rate to the square of the average delay rate. The above "energy" is always positive as long as the delay rate is not uniform. Therefore, when the delay rate is not uniform the erosion factor is always larger than unity. On the other hand, drastic non-monotonic variations of delay rate down the path might be required in order to cause a significant difference between the "energy" and the square of the area under the function $\phi(x)$. Therefore, monotonic changes in the velocity of the analyte along the column (even orders of magnitude changes) might cause only a slight ero-

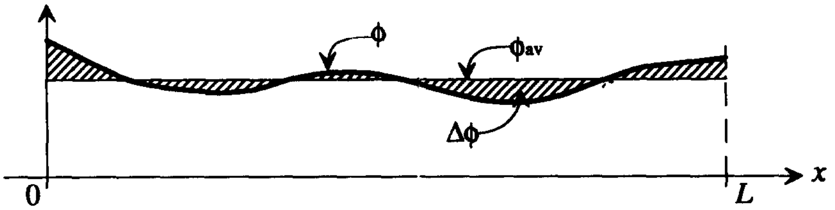

Fig. 1. Non-uniform delay rate. The shaded area represents the variation, $\Delta\phi$, of the delay rate, ϕ, relative to its average, ϕ_{av}. In the case of a uniform plate height, the decrease in chromatographic efficiency due to the non-uniformity of the delay rate is proportional to the ratio of the average "energy" of $\Delta\phi$ to ϕ_{av}^2.

sion of efficiency. This interpretation helps to explain the experimental SFC data [20] where even large deceleration of analytes caused only the small erosion of efficiency.

An example of a weak influence of a zone acceleration on efficiency is GC with compressible carrier gas. It has been shown by Stewart *et al.* [2] and it directly follows from eqn. 45 that for non-retained peaks in GC using an ideal carrier gas

$$\varepsilon^2 = \frac{9(p^4 - 1)(p^2 - 1)}{8(p^3 - 1)^2} \tag{46}$$

where p is the inlet-to-outlet pressure ratio across the column. It also represents an outlet-to-inlet velocity ratio of the analyte. From eqn. 46, it follows that even for large ratios of outlet-to-inlet velocity, the erosion of column efficiency could not exceed 12.5%.

It must be pointed out, however, that eqn. 46 is based on the *approximate* eqn. 25 (conditions C4). Therefore, eqn. 46 *cannot be viewed as the exact expression* for the erosion of efficiency in GC with an ideal carrier gas; it is only the first approximation of that quantity. This important theoretical fact has not been recognized before.

CONCLUSIONS

A general model (eqn. 3) for chromatography based on convective diffusion has been proposed. The model can be applied to a chromatographic medium which can be non-uniform, time-varying and non-linear, or have any combination of these properties. Such a model has not previously been found in the chromatographic literature.

In this paper, the model was utilized for the analysis of non-uniform time-invariant linear media. The main subject of this paper was the derivation of variance of a zone of analyte migrating in such a medium. Results of the derivation are applicable to any type of non-uniformity regardless of its cause, be it variation in the density of an ideal or non-ideal carrier gas, in the column diameter, in the thickness or in the composition of the stationary phase, etc.

It has been found that a special form of the model known as the Fokker–Planck equation is the most convenient for moment analysis in such a medium, and can be used in other moment-based studies of chromatography. The Fokker–Planck equation has not previously been utilized in the chromatographic literature.

Exact eqns. 21, 22 and 23 for temporal and spatial derivatives of variance of a zone have been derived. These are the first exact expressions for the general case of non-uniformity.

The expressions could be further reduced to a first-order ordinary linear differential equation (eqn. 25) if gradients of diffusivity and velocity in the medium are locally nearly constant (changes can be large but nearly linear). Such a general equation for a zone variance in a non-uniform medium was not known before. Further, the conditions under which eqn. 25 was valid are less restrictive than those known from the literature. Previous implicit or explicit conditions were more restrictive yet were developed for narrower cases.

It has been shown that regardless of the type of non-uniformity, chromatographic efficiency cannot be improved. This statement is more general than a similar statement published before. On the other hand, a simple graphical concept based on the newly introduced delay rate in a non-uniform medium has been developed to demonstrate that in many instances even significant non-uniformity can cause only minor decreases in efficiency. Roughly, it is impossible to gain extra efficiency via non-uniformity, but significant losses are unlikely unless the medium becomes very lumpy.

It has also been shown that in a non-uniform medium, a gradient of diffusivity affects the local velocity of migration of the analyte. Although for typical chromatographic conditions the addition is virtually insignificant, recognition of the fact is theoretically important. References to the phenomenon have not been found in the literature. Several new parameters of a non-uniform chromatographic medium were also introduced.

SYMBOLS

D	local effective diffusivity in a medium (length^2/time)
D_a	aggregate diffusivity of a zone of analyte (length^2/time)
D_m	molecular diffusivity (length^2/time)
f_u	local mass flow due to migration of analyte (mass/time)
H	local plate height (length)
H_a	aggregate plate height of a zone of analyte (length)
k	capacity factor
L	length of a path of a zone (length)
m	specific mass of a migrating analyte (mass/length)
N_Σ	cumulative chromatographic efficiency
N	chromatographic efficiency
p	ratio of inlet to outlet pressure on a column
t	time (time)
t_r	retention time of a zone (time)
u	net local velocity of an analyte (length/time)
u_a	aggregate velocity of a zone (length/time)
v	local convective velocity of analyte (length/time)
v_m	local velocity of a mobile phase (length/time)
x	spatial coordinate (length)
z	center of mass (first moment) of a zone (length)
ε	erosion factor
ϕ	delay rate of an analyte (time/length)
ϕ_{av}	average delay rate of an analyte (time/length)
$\Delta\phi$	variation of delay rate (time/length)
ρ	density (mass/length^3)
σ^2	variance (second central moment) of a zone (length^2)
τ^2	time measure of variance of a zone ($\tau^2 = \sigma^2/u^2$) (time^2)

APPENDIX

Mass balance of convective diffusion in a non-uniform medium

The total mass of a zone migrating in a unbounded medium could be expressed as $\int_{-\infty}^{\infty} m\mathrm{d}x$. Its derivative $\frac{\mathrm{d}}{\mathrm{d}t}\int_{-\infty}^{\infty} m\mathrm{d}x$ reflects the variation of the total mass with time, and must be zero if the total mass is to be conserved. Taking account of eqn. 3, one has

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_{-\infty}^{\infty} m\mathrm{d}x = \int_{-\infty}^{\infty} \frac{\partial m}{\partial t}\mathrm{d}x = \int_{-\infty}^{\infty}\left[\frac{\partial}{\partial x}\left(D\cdot\frac{\partial m}{\partial x}\right) - \frac{\partial}{\partial x}(vm)\right]\mathrm{d}x = \left(D\cdot\frac{\partial m}{\partial x} - vm\right)\Bigg|_{-\infty}^{\infty} = 0$$

The last transaction to zero becomes valid under the following practically unrestrictive assumptions (see C2 and C3 in the main text): $m \to 0$, $|\partial D/\partial x| < \infty$ and $|v| < \infty$ when $x \to \pm\infty$.

Derivation of aggregate velocity, $\mathrm{d}z/\mathrm{d}t$, *of a zone*

Taking account of eqns. 17, 9 and 3, then integrating by parts one has

$$u_a = \frac{\mathrm{d}z}{\mathrm{d}t} = \frac{\mathrm{d}}{\mathrm{d}t}\int_{-\infty}^{\infty} xm\mathrm{d}x = \int_{-\infty}^{\infty}\frac{\partial}{\partial t}(xm)\mathrm{d}x = \int_{-\infty}^{\infty} x\cdot\frac{\partial m}{\partial t}\mathrm{d}x = \int_{-\infty}^{\infty} x\left[\frac{\partial}{\partial x}\left(D\cdot\frac{\partial m}{\partial x}\right) - \frac{\partial}{\partial x}(vm)\right]\mathrm{d}x =$$

$$\int_{-\infty}^{\infty} x\mathrm{d}\left(D\cdot\frac{\partial m}{\partial x} - vm\right) = xD\cdot\frac{\partial m}{\partial x}\Bigg|_{-\infty}^{\infty} - \int_{-\infty}^{\infty} D\cdot\frac{\partial m}{\partial x}\mathrm{d}x - xvm\Bigg|_{-\infty}^{\infty} + \int_{-\infty}^{\infty} vm\mathrm{d}x = \int_{-\infty}^{\infty} vm\mathrm{d}x - \int_{-\infty}^{\infty} D\cdot\frac{\partial m}{\partial x}\cdot\mathrm{d}x$$

The last transaction here was based on the properties 7 securing $xD(\partial m/\partial x)\Big|_{-\infty}^{\infty} = 0$, $xvm\Big|_{-\infty}^{\infty} = 0$. When properties 7 are accounted for again, integration by parts for the second integral in the last right-hand side yields

$$u_a = \int_{-\infty}^{\infty} vm\mathrm{d}x - Dm\Big|_{-\infty}^{\infty} + \int_{-\infty}^{\infty} \frac{\partial D}{\partial x} \cdot m\mathrm{d}x = \int_{-\infty}^{\infty} vm\mathrm{d}x + \int_{-\infty}^{\infty} \frac{\partial D}{\partial x} \cdot m\mathrm{d}x = \int_{-\infty}^{\infty} \left(v + \frac{\partial D}{\partial x}\right) m\mathrm{d}x \tag{47}$$

Modification of the equation for convective diffusion

Eqn. 3 can be modified in the following way. After adding a quantity $m(\partial D/\partial x)$ within both derivatives of its right-hand side, one has

$$\frac{\partial m}{\partial t} = \frac{\partial}{\partial x}\left(D \cdot \frac{\partial m}{\partial x} + m \cdot \frac{\partial D}{\partial x}\right) - \frac{\partial}{\partial x}\left(vm + m \cdot \frac{\partial D}{\partial x}\right) = \frac{\partial^2}{\partial x^2}(Dm) - \frac{\partial}{\partial x}\left[\left(v + \frac{\partial D}{\partial x}\right) m\right]$$

After introduction of a variable u by eqn. 19, the last equation becomes

$$\frac{\partial m}{\partial t} = \frac{\partial^2}{\partial x^2}(Dm) - \frac{\partial}{\partial x}(um)$$

Derivation of $\mathrm{d}\sigma^2/\mathrm{d}t$

This derivation is based on the modified equation of convective diffusion derived above. Starting with eqn. 8, and repeating integration by parts similar to that employed for derivation of $\mathrm{d}z/\mathrm{d}t$ above, one has

$$\frac{\mathrm{d}\sigma^2}{\mathrm{d}t} = \frac{\mathrm{d}}{\mathrm{d}t}\int_{-\infty}^{\infty} (x - z)^2 m\mathrm{d}x = -\int_{-\infty}^{\infty} 2z(x - z) \cdot \frac{\mathrm{d}z}{\mathrm{d}t} \cdot m\mathrm{d}x + \int_{-\infty}^{\infty} (x - z)^2 \cdot \frac{\partial m}{\partial t} \cdot \mathrm{d}x = -2u_a z \int_{-\infty}^{\infty} (x - z)m\mathrm{d}x +$$
$$\int_{-\infty}^{\infty} (x - z)^2 \left(\frac{\partial^2}{\partial x^2}(Dm) - \frac{\partial}{\partial x}(um)\right) \mathrm{d}x = -2u_a z \int_{-\infty}^{\infty} (x - z)m\mathrm{d}x + \int_{-\infty}^{\infty} (x - z)^2 \mathrm{d}\left(\frac{\partial}{\partial x}(Dm) - um\right)$$

Owing to eqn. 11, the first integral in the last sum vanishes. Integrating the second integral by parts, one further has

$$\frac{\mathrm{d}\sigma^2}{\mathrm{d}t} = (x - z)^2 \left(\frac{\partial}{\partial x}(D\rho) - um\right)\Bigg|_{-\infty}^{\infty} - 2\int_{-\infty}^{\infty} (x - z)\left(\frac{\partial}{\partial x}(Dm) - um\right)\mathrm{d}x$$

Eqns. 7 nullify the value of $(x - z)^2\left(\frac{\partial}{\partial x}(Dm) - vm\right)\Bigg|_{-\infty}^{\infty}$. Integrating the remaining integral by parts again, one further has

$$\frac{\mathrm{d}\sigma^2}{\mathrm{d}t} = -2\int_{-\infty}^{\infty} (x - z)\left(\frac{\partial}{\partial x}(Dm) - um\right)\mathrm{d}x = -2\int_{-\infty}^{\infty} (x - z)\mathrm{d}(Dm) + 2\int_{-\infty}^{\infty} (x - z)um\mathrm{d}x = -2(x - z)Dm\Big|_{-\infty}^{\infty} +$$
$$2\int_{-\infty}^{\infty} Dm\mathrm{d}x + 2\int_{-\infty}^{\infty} (x - z)um\mathrm{d}x$$

With the first member of the last right-hand side nullified by eqns. 7 again, the entire expression finally becomes

$$\frac{d\sigma^2}{dt} = 2\int_{-\infty}^{\infty} Dm\,dx + 2\int_{-\infty}^{\infty} (x - z)um\,dx$$

Derivation of ordinary differential equation for σ^2

At any x-coordinate of a medium, both u and D could be expressed via their linear terms and the second-order remainders as:

$$u = u(z) + u'(z)(x - z) + O_u; \quad O_u = O_u(x,z)$$

$$D = D(z) + D'(z)(x - z) + O_D; \quad O_D = O_D(x,z)$$

If both the second-order remainders, O_u and O_D, in these expressions are substantially small within a zone of analyte, then the above expressions could be replaced with their respective linear approximations:

$$u = u(z) + u'(z)(x - z) \tag{48}$$

$$D = D(z) + D'(z)(x - z) \tag{49}$$

Owing to eqns. 48 and 11, the aggregate velocity from eqn. 18 becomes

$$u_a = u(z) \tag{50}$$

Finally, recalling eqns. 11, 8 and 24 and substituting eqns. 48, 49 and 50 into eqn. 22, one has

$$\frac{d\sigma^2}{dz} = H(z) + \frac{2\sigma^2}{u(z)} \cdot \frac{du}{dz}$$

Lower bound for the erosion factor

As H is positive, new functions

$$f = \phi\sqrt{H}, \quad g = \frac{1}{\sqrt{H}}$$

could be introduced to rewrite eqn. 41 as

$$\varepsilon^2 = \frac{\left(\int_0^L H\phi^2 dx\right)\int_0^L \frac{dx}{H}}{\left(\int_0^L \phi dx\right)^2} = \frac{\left(\int_0^L f^2 dx\right)\int_0^L g^2 dx}{\left(\int_0^L fg dx\right)^2}$$

According to the Cauchy–Schwarz inequality

$$\varepsilon^2 \geqslant 1.$$

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