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A THEORETICAL DERIVATION OF THE AXIAL DIFFUSION COEFFICIENT IN CHROMATOGRAPHY*

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SUMMARY

The basic differential equation that describes the passage of exchanging solute through a chromatographic column is derived from a material balance on a differential element of the column by assuming that the size of the differential volume element cannot be made arbitrarily small, due to the non-homogeneity of the system. This approach is used to derive an expression for the axial diffusion coefficient which is equivalent to the experimentally determined form of the axial diffusion coefficient. The model of Fricke for conductivity in suspensions is used to relate the effective molecular diffusivity portion of the axial diffusion coefficient to the solute diffusivities in the mobile and stationary phases. This leads to a labyrinth factor for molecular diffusion in the bed that is solely a function of the void fraction.

INTRODUCTION

The goal of a theoretical approach to chromatography is the development of a system of mathematical relationships which will allow reasonable predictions of chromatographic behavior. Such a mathematical model, in the form of differential equations, is well established[1–8]. The basic differential equation, derived from a material balance on a differential element of the chromatographic bed, describes the concentration of solute in both stationary and mobile phases as a function of distance from column inlet z and time t. It is generally given as (*cf.* ref. 4)

$$\left(\frac{\partial c}{\partial t}\right)_z + \frac{1}{\alpha}\left(\frac{\partial n}{\partial t}\right)_z + U_e\left(\frac{\partial c}{\partial z}\right)_t - D_a\left(\frac{\partial^2 c}{\partial z^2}\right)_t = 0 \qquad (1)$$

where c = concentration of solute in the mobile phase (moles per unit volume of fluid);
n = concentration of solute in the stationary phase (moles per unit volume of packed bed);

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α = void fraction;
U_e = effective linear velocity of fluid through the bed (cm/sec);
D_a = axial diffusion coefficient of solute in the bed (cm²/sec).

Since the system under investigation involves flow in a packed bed, the axial diffusion coefficient D_a depends on two effects: the molecular diffusion of the solute in the mobile and stationary phases; and the convective diffusion of solute as a result of flow through the interstices of the bed. The molecular diffusion coefficient of a solute in a liquid medium is normally reduced when a dispersed phase is introduced into the medium[9-11]. Thus the diffusion coefficient of the solute is modified by a labyrinth factor when a stationary phase is present. The contribution of convective diffusion to the combined diffusional process is directly related to the Peclet number (see ref. 12), which is, in effect, the ratio of convective to molecular diffusivities. Hence the convective diffusion contribution is proportional to the velocity of the fluid and some characteristic length in the system of interest (*e.g.*, the diameter of the dispersed-phase particulates). Consequently, the form of the axial diffusion coefficient is generally given as[5,13]

$$D_a = \gamma D_1 + D_\varepsilon \qquad (2)$$

where D_1 = molecular diffusion coefficient of solute in fluid (cm²/sec);
D_ε = eddy diffusion coefficient of solute due to convective effects (cm²/sec);
γ = labyrinth factor that results from the presence of particulates (in the system) which impede the molecular diffusion of the solute.

Also, from a simplified view of D_ε,

$$D_\varepsilon = \lambda\, d_0\, U_e \qquad (3)$$

where λ = empirical parameter;
d_0 = diameter of particulates.

This form for the axial diffusion coefficient is not predicted by the differential equation; it is merely an assumed and experimentally verified relationship used in the solution of the differential equation. The purpose of this communication is to show that the experimentally determined form for the axial diffusion coefficient does indeed arise during the development of a mathematical model of solute behavior in chromatography. To illustrate this, however, we must re-derive eqn. 1 using a slightly different and essentially neglected approach. The results obtained by this approach will serve to generalize the study on longitudinal diffusion in chromatography, which Glueckauf *et al.*[14] began and Lapidus and Amundson[4] extended.

THEORY

A material balance on a differential section Δz of the chromatographic column shown in Fig. 1 leads to the following equation:

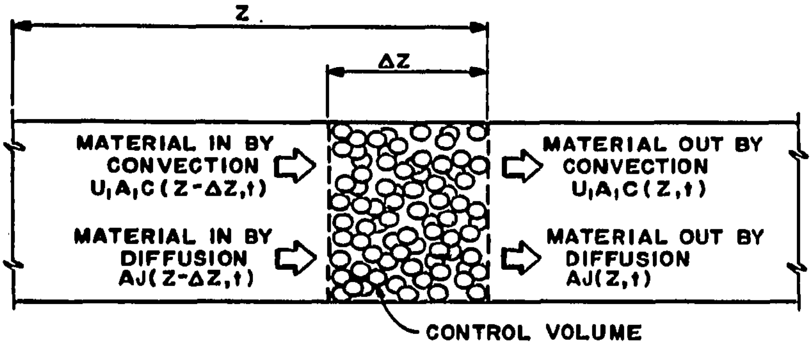

Fig. 1. Material balance on a differential section of a chromatographic column.

$$\underbrace{\alpha \Delta z \cdot A \left(\frac{\partial c}{\partial t}\right)_z + \Delta z \cdot A \left(\frac{\partial n}{\partial t}\right)_z}_{\text{total mass accumulation}} = \underbrace{U_l A_l \{c(z-\Delta z,t) - c(z,t)\}}_{\text{mass accumulation due to convention}} + \underbrace{A\,\{J(z-\Delta z,t) - J(z,t)\}}_{\text{mass accumulation due to molecular diffusion}} \quad (4)$$

where A = cross-sectional area of column (cm^2);
A_l = average cross-sectional area of the void space in the column (cm^2);
J = diffusive flux (molecular) across the whole cross-sectional area A (moles/cm$^2 \cdot$sec);
U_l = actual average linear velocity through the interstices of the bed (cm/sec).

We replace $U_l A_l$, the volumetric flow-rate through the packed bed, with $U_0 A$, where U_0 is the linear velocity of fluid in the tube that would exist if the flow-rate remained the same but the spheres were removed (superficial velocity). Then eqn. 4 becomes

$$\alpha \cdot \Delta z \left(\frac{\partial c}{\partial t}\right)_z + \Delta z \left(\frac{\partial n}{\partial t}\right)_z = U_0 \{c(z-\Delta z,t) - c(z,t)\} + \{J(z-\Delta z,t) - J(z,t)\} \quad (5)$$

We now construct the following Taylor series expansions:

$$c(z-\Delta z,t) = c(z,t) - \left(\frac{\partial c}{\partial z}\right)_t \Delta z + \tfrac{1}{2}\left(\frac{\partial^2 c}{\partial z^2}\right)_t \Delta z^2 + \cdots \quad (6a)$$

and

$$J(z-\Delta z,t) = J(z,t) - \left(\frac{\partial J}{\partial z}\right)_t \Delta z + \tfrac{1}{2}\left(\frac{\partial^2 J}{\partial z^2}\right)_t \Delta z^2 + \cdots \quad (6b)$$

and insist that, because of the non-homogeneity of the medium, we cannot take Δz arbitrarily small but can only reduce it to a thickness on the order of a few sphere diameters (the approach taken by Glueckauf[6]). Thus we include terms of order $(\Delta z)^2$ in eqns. 6a and 6b. We do assume, however, that the spheres are small enough to allow us to neglect terms of order $(\Delta z)^3$ and higher. Using eqns. 6a and 6b in eqn. 5 and eliminating all unnecessary terms, we arrive at the following material balance:

$$\alpha\left(\frac{\partial c}{\partial t}\right)_z + \left(\frac{\partial n}{\partial t}\right)_z + U_0\left\{\left(\frac{\partial c}{\partial z}\right) - \frac{\Delta z}{2}\left(\frac{\partial^2 c}{\partial z^2}\right)\right\}_t + \left\{\left(\frac{\partial J}{\partial z}\right) - \frac{\Delta z}{2}\left(\frac{\partial^2 J}{\partial z^2}\right)\right\}_t = 0 \tag{7}$$

Defining $J = -\bar{D}_m\left(\frac{\partial c}{\partial z}\right)_t$ and neglecting third-order differentials, eqn. 7 becomes:

$$\alpha\left(\frac{\partial c}{\partial t}\right)_z + \left(\frac{\partial n}{\partial t}\right)_z + U_0\left(\frac{\partial c}{\partial z}\right)_t - \left\{\frac{\Delta z\cdot U_0}{2} + \bar{D}_m\right\}\left(\frac{\partial^2 c}{\partial z^2}\right)_t = 0 \tag{8}$$

where $\bar{D}_m$ is the average molecular diffusivity of solute across the total cross-sectional area at z.

Since the magnitude of Δz is determined by the size of the spheres, we can set

$$\Delta z = 2\lambda' d_0 \tag{9}$$

where λ' is some empirical constant. Substituting eqn. 9 into eqn. 8, dividing through by α, and setting

$$U_e = U_0/\alpha, \quad \lambda = \lambda'/\alpha \tag{10}$$

and

$$D_a = \left\{\lambda d_0 U_e + \frac{1}{\alpha}\bar{D}_m\right\} \tag{11}$$

we have

$$\left(\frac{\partial c}{\partial t}\right)_z + \frac{1}{\alpha}\left(\frac{\partial n}{\partial t}\right)_z + U_e\left(\frac{\partial c}{\partial z}\right)_t - D_a\left(\frac{\partial^2 c}{\partial z^2}\right)_t = 0 \tag{12}$$

which is identical to the original differential equation given in eqn. 1. Also, the form for the axial diffusion coefficient, given in eqn. 11, which results from the derivation, is (with the exception of the molecular diffusivity term) in exact agreement with the experimental form given in eqn. 2.

Finally, we desire a relationship between the effective molecular diffusion coefficient $\bar{D}_m$ and the measurable diffusivities in the bed. Since $\bar{D}_m$ is the coefficient of proportionality between the flux and the concentration gradient[12], the flux term J must be carefully defined before $\bar{D}_m$ can be determined. In the present case, J is defined as the diffusional flux across the total cross-sectional area of the column, which includes diffusion in the stationary phase as well as in the mobile phase.

In developing a useful relationship for $\bar{D}_m$, a few prerequisite assumptions are necessary:

(1) The concentration of solute in the adsorbent, n, is composed of two terms: the concentration of solute in the pores of adsorbent, c^*; and an adsorbed concentration, n^*.

(2) At the adsorbent–solution interface, $c = c^*$; *i.e.*, the concentration of free solute is continuous across the boundary.

These two assumptions suggest a relationship between the average diffusivity in the bed and the individual diffusivities in the continuous and dispersed phases which is similar to that developed initially by Maxwell[15] for thermal conductivity in granular media and later used by Fricke[16] for the electrical conductivity in a dispersed phase. This relationship, which has previously been used to predict diffusivities in dispersed phases[17–20], is given by

$$\bar{D}_m = D_1 \left\{\frac{1 + \xi R}{1 - R}\right\} \tag{13}$$

where

$$R = \alpha \left\{\frac{D_2/D_1 - 1}{D_2/D_1 + \xi}\right\} \tag{14}$$

and D_1 = diffusivity of solute in the mobile phase;
D_2 = diffusivity of solute in the stationary phase;
ξ = shape factor (= 2 for spheres).

Since we know that the labyrinth factor in the adsorbent is quite small ($\ll 1$) for diffusion of solute in the pores of ion exchangers[21], we expect

$$D_2 \ll D_1$$

Thus, for the spherical adsorbent particles where $\xi = 2$ (see Fig. 2), eqn. 13 reduces to

$$\bar{D}_m = 2D_1 \left\{\frac{1 - \alpha}{2 + \alpha}\right\} \tag{15}$$

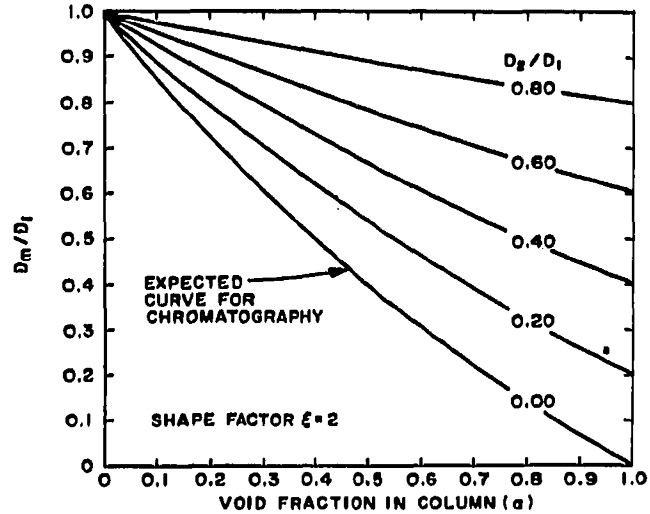

Fig. 2. Effective molecular diffusivity *versus* void fraction for various ratios of stationary to mobile phase solute diffusion coefficients.

and our final expression for the axial diffusion coefficient becomes

$$D_a = \left\{\lambda d_0 U_v + \frac{2}{\alpha}\left(\frac{1-\alpha}{2+\alpha}\right) D_1\right\} \tag{16}$$

where now the labyrinth factor γ (weighted by $1/\alpha$) in eqn. 2 is

$$\gamma = \frac{2}{\alpha}\left(\frac{1-\alpha}{2+\alpha}\right) \tag{17}$$

DISCUSSION

Attempts to solve eqn. 1 analytically have been made by many investigators. Normally, assumptions regarding the size and shape of the input pulse, the nature of the exchange kinetics, etc., that simplify the mathematics are necessary to achieve a closed-form solution of the differential equation. Unfortunately, the peculiar physical characteristics of the particular system under investigation (*e.g.*, non-linear adsorption kinetics[22]) often necessitate assumptions that result in complex mathematical equations. These equations must be solved numerically. In all cases, the attempts begin with the differential equation and proceed toward a solution; rarely is the differential equation itself examined.

The derivation of this partial differential equation begins with a material balance on a differential volume element (disk) of fluid in a chromatographic column. The normal approach taken in a continuous system is to let the size of the differential element approach zero once the material balance has been completed. This procedure results in a bona fide differential equation. However, when the mass balance is performed on a volume element containing both a mobile phase and a stationary phase, the subsequent step of allowing the volume element to approach zero is questionable and, at best, an unjustified approximation.

This problem has been recognized during attempts to model other discontinuous systems. Spaeth and Friedlander[23], studying the convective diffusion of certain gaseous solutes in blood, chose a volume element large enough to give an effective macroscopic continuum. The concentration terms were, therefore, average concentrations of the pseudocontinuous system. However, the basic differential equation used in that work was taken from continuum mechanics[24], and the effect that a volume element of finite size would have on the differential equation was not discussed. Glueckauf[6], on the other hand, took the non-vanishing size of the volume element into account in setting up the material balance. Although he neglected molecular diffusion, he did obtain a dispersion term in the resulting differential equation. This dispersion term resulted specifically from allowing the thickness of the differential element to remain finite. Hamilton *et al.*[13] later showed consistency between Glueckauf's result and the result obtained by Van Deemter *et al.*[5], although they apparently missed the significance of one important aspect of this consonance. For, in the case of the solution of Van Deemter *et al.*, the form of the axial diffusion coefficient was assumed, not derived. On the other hand, the dispersion term that appears in Glueckauf's solution is derived from the basic material balance on the control volume. On equating the two, one finds that Glueckauf's dispersion term is equivalent to the convective diffusion portion of the axial diffusion term that appears in the solution of

Van Deemter *et al.* Since Glueckauf neglected molecular diffusion, this term does not appear in the dispersion term in his basic differential equation (eqn. 3, ref. 6). Thus the convective diffusion portion of the axial diffusion coefficient, which arises experimentally as a result of the presence of the particulates in the system, can be deduced theoretically (apart from the empiricism of eqn. 9) from the basic material balance on the differential control volume in the chromatographic column. This is accomplished by not allowing the thickness of the differential volume element to decrease below the size of the particulates in the system, as shown in the present paper.

The present analysis shows that the axial diffusion coefficient is weighted by the inverse of the void fraction when the partial differential equation is in the form given by eqn. 1. Thus if the experimental labyrinth factor γ in eqn. 2 is greater than the void fraction (Hamilton *et al.*[13] give the range of γ as 0.5 to 1.0, whereas α is normally about 0.4), the effective tortuosity will actually be greater than unity (see Fig. 3).

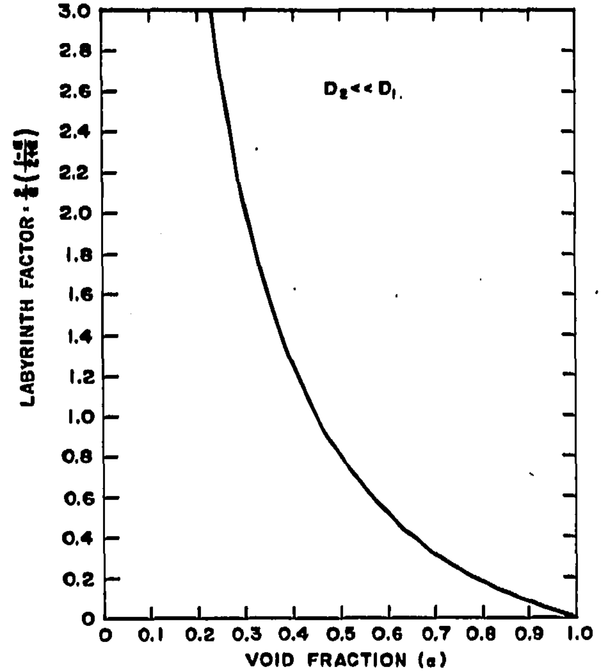

Fig. 3. Labyrinth factor in the chromatographic bed *versus* the void fraction.

Since the diffusive flux J is based on the whole cross-sectional area of the column, the effective molecular diffusion coefficient $\bar{D}_m$ is a function of the solute diffusivities in both the mobile and stationary phases. Thus we desire some functional relationship between the average diffusion coefficient in a non-homogenous medium and the individual diffusivities in the continuous and dispersed phases. Although such a relationship has been derived by Fricke[16], the derivation was based on a non-convective system. However, recent results in flowing blood[19] indicate that the model of diffusion in stationary granular media can be applied to convective systems also.

Consequently, the Fricke model is used in the present analysis to relate the effective molecular diffusivity to measurable quantities.

If the diffusivity of solute in the stationary phase is significantly less than the diffusivity of solute in the mobile phase and the particulates are spherical, the Fricke model for diffusion in heterogeneous media can be greatly simplified. In this case, the average diffusivity is found to be only a function of the void fraction and the diffusivity of the solute in the mobile phase. With this simplification, which should be valid for most chromatographic systems, the form of the effective molecular diffusivity in eqn. 8 is seen to be identical to that in eqn. 2, with the labyrinth factor as a function solely of the void fraction.

CONCLUSION

The basic partial differential equation describing solute behavior in chromatography is derived by setting up the appropriate mass balances on a differential element of the chromatographic column. Unlike the normal procedure when dealing with a continuum, however, the differential element is not allowed to become vanishingly small. The diameter of the particulates is used as a lower limit to the size of the differential volume element. This approach generates an additional dispersion term in the resulting differential equation which is due to the inhomogeneity of the system. This additional term is the convective diffusion part of the axial diffusion coefficient.

The analysis also yields an effective molecular diffusion coefficient for the diffusive flux across the total cross-sectional area of the bed. Thus this average diffusion coefficient is a function of the solute diffusivities in both the mobile and stationary phases. Assuming spherical adsorbent particles, the model of Fricke[16] for conductivity in a non-homogeneous medium is used to relate the average molecular diffusivity in the bed to the void fraction and the individual solute diffusivities in the two phases. Using this model, the labyrinth factor γ is found to depend only on the void fraction α.

NOMENCLATURE

A = cross-sectional area of chromatographic column (cm^2)
A_l = average cross-sectional area of void space in column (cm^2)
c = concentration of solute in the mobile phase (moles/ml)
D_a = axial diffusion coefficient of solute in the bed (cm^2/sec)
D_ε = eddy diffusivity of solute (cm^2/sec)
$\bar{D}_m$ = effective molecular diffusion coefficient of solute in the bed (cm^2/sec)
D_1 = molecular diffusion coefficient of solute in mobile phase (cm^2/sec)
D_2 = molecular diffusion coefficient of solute in stationary phase (cm^2/sec)
d_0 = diameter of adsorbent (cm)
n = concentration of solute in the stationary phase (moles/ml packed bed)
t = time (sec)
U_e = effective linear velocity in chromatographic column (cm/sec)
U_l = actual average linear velocity through interstices in packed column (cm/sec)
U_0 = linear velocity through unpacked column (cm/sec)
z = distance from column inlet (cm)
Δz = width of differential control element (cm)

α = void fraction
ξ = shape factor in Fricke relationship
γ = labyrinth factor for molecular diffusion in packed column
λ = empirical constant in eddy diffusion relationship
λ' = empirical constant in eddy diffusion relationship

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