Modernization of the van Deemter Equation for Chromatographic Zone Dispersion

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In the mid-1950's, a group of Dutch chemical engineers undertook a study of zone dispersion in chromatography. Starting with the equations of Lapidus and Amundson (*1*) they made some approximations and assumptions and arrived at the equation (*2*)

$$h = 2\lambda d_p + \frac{2\gamma D_m}{v} + \frac{8}{\pi^2}\frac{k}{(1+k)^2}\frac{d_f^2}{D_l}v \qquad (1)$$

This has come to be known as the "van Deemter equation." While this title involves some injustice to previous workers (see the review by Giddings) (*3a*), the naming was inevitable since the equation was produced during the early development of gas chromatography and was seized upon, used, and quoted in that dramatic period of chromatographic history. The van Deemter equation was the basis of the many improvements in column design that were realized as the various parameters were optimized. It is now quoted in sophomore texts and physico-chemical research papers as the definitive equation. Often it is given in the simplified form

$$h = A + B/v + Cv \qquad (2)$$

It is unfortunate that it has become fossilized in this way. The equation represented the best that could be said in 1956, but the ensuing decades have shown that chromatographic dispersion is better represented as

$$h = B/v + Cv \qquad (3)$$

$$= B/v + (C_s + C_m)v \qquad (4)$$

$$= \frac{2\gamma D_m}{v} + q\frac{k}{(1+k)^2}\frac{d_f^2}{D_l}v + \frac{\mathrm{fn}(d_p^2, d_c^2, end, v)}{D_m}v \qquad (5)$$

This form is as rigorously correct as current theory allows, is no more complex than van Deemter's form, and lends itself to discussion of the geometrical parameters in the last ($C_m v$) term. It also avoids fossilizing a precise form of the $C_m v$ term which is still poorly understood. The van Deemter equation omitted the $C_m v$ term because the columns of the period contained so much stationary liquid that $C_m v$ was negligible compared to the first ($C_s v$) term. However, once the equation was widely understood and more sensitive detectors became available, it became customary to use less stationary phase so as to reduce d_f and hence C_l so that C_m became relatively more important. From that period in the early 1960's it has been necessary to include $C_m v$ in discussions of zone dispersion.

Usefulness of the Equation

Values of the parameters in eqn. (5) are seldom known with any precision. Its main usefulness is therefore in qualitative discussions of the effect of various parameters on column dispersivity, h, and the compromises that must be made in column design and in controlling temperature and flow rate.

Equation (5) can also be manipulated to give equations for resolution or analysis time. Column design, temperature, and flow rate may then be chosen to optimize the desired performance.

The van Deemter equation has also been used to measure D_l and D_m, quite often by naively using eqn. (1). The use of eqn. (5) makes the problems in experimental design much clearer and shows that such measurements are unlikely to be reliable.

The Meaning of *h*

The use of h was introduced into chromatographic theory by Martin and Synge (*3*). They used a model involving successive equilibrations in a series of "theoretical plates" representing successive segments of the column and called h the "height equivalent to a theoretical plate" or "HETP." This was a logical development of Martin's previous work on multiple liquid-liquid extraction, and the theory of distillation. They used the model to show that peaks should be Gaussian in the limit of a large number of plates, derived a relation between the number of plates and resolution, and

Symbols Used

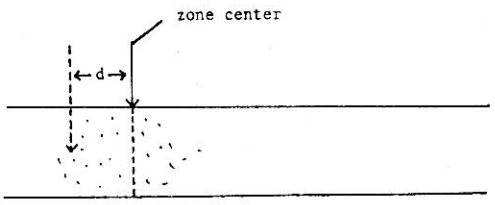
A = eddy diffusion or anastomosis term
B = coefficient of longitudinal diffusion
c = concentration
C = coefficient of mass transfer
d = diameter, or depth
D = coefficient of molecular diffusion
end = end-effects
f = Giddings compressibility factor $9(p_i^4/p_o^4 - 1)(p_i^2/p_o^2 - 1)/8(p_i^3/p_o^3 - 1)^2$
fn = function of
h = column dispersivity ("plate height")
j = James-Martin compressibility factor
k = column capacity ratio $t_s/t_m = Kv_s/v_m$
K = partition coefficient, c_s/c_m
l = length of empty tube containing sample before injection
L = column length
p = pressure
q = factor describing shape of liquid phase
t = time
v = linear velocity, cm of column traversed per second
$\bar{v}$ = average linear velocity = L/t_m
v = volume

Subscripts

ads = adsorbed
c = column
f = film
i = at inlet of column
l = liquid stationary phase
m = mobile phase
o = at outlet of column
p = particle
s = stationary phase

Greek Symbols

γ = obstruction factor
η = viscosity
λ = proportionality factor $A/2d_p$
ϕ = fraction of the mobile phase that is outside the porous particles
σ = standard deviation of distances of molecules of a component from zone center
ω = proportionality constant $C_m D_m/d_p^2$



The variance, σ^2, of the distribution of the molecules of a single substance about their mean position in the column is Σd^2/number of molecules.

showed that resolution varied with the square root of the column length.

This was about the limit of usefulness of this model. It has given us the term "plate height" symbolized by h. This is a most unfortunate inheritance because later models have proved more tractable, easier to comprehend, and less deceptive.

The danger of the model is in the mental concept that it conjures. If a column consisted of a series of plates, then joining two columns together would produce a number of plates equal to the sum of the plates in the separate columns. An analyst using this concept and joining an efficient column to an inefficient one is disappointed to find that the number of plates is reduced and the resolution is worse.

Klinkenburg and Sjenitzer introduced a better model in 1956 when they showed that

$$h = \sigma^2/L$$

where σ^2 is the variance of the distribution of the molecules of a single substance about their mean position in the column or thin layer plate (i.e., Σd^2/number of molecules, in the figure), and L is the distance the zone of substance has moved. In column chromatography, L is usually the column length.

This definition is more useful than the plate height in every way and has rendered the plate concept obsolete. Pedagogically it is superior because σ^2 is directly related to the important experimental phenomena it describes, viz., the spreading of the zone, the width of the chromatographic peak and hence the resolution. Theoretical plates relate to these phenomena only indirectly in a manner needing mathematical treatment. Theoretically it is superior because it relates directly to the underlying physical processes through the Einstein equation (*38*), $\sigma^2 = 2Dt$, where D is the dispersion coefficient and t is the elapsed time. This has formed the basis of the random walk and the nonequilibrium treatments of chromatography.

The use of $h = \sigma^2/L$ as a definition of h eliminates the conceptual error of additive plate numbers described above, but the name "plate height" or "height equivalent to a theoretical plate" or "HETP" perpetuate the error. The term "plate" should now be dropped. For the remainder of this paper h will be referred to as the "column dispersivity." Unfortunately, no such neat name has occurred to the author to replace the popular "plate number"

$$N = L^2/\sigma^2$$

In default of a better name, I have used the name "plate number" in class and indicated that the name has no conceptual significance but is an accident of history.

For the future then, the plate concept should be discarded and replaced by $h = \sigma^2/L$ or in non-uniform columns by $h = d\sigma^2/dL$.

Detailed Treatment

The remainder of this paper will be devoted to a discussion of the reasons that eqn. (1) should no longer be taught and that eqns. (3)–(5) should be preferred and to a discussion of the underlying phenomena in terms that can be transmitted to sophomores. There are some aspects of zone broadening which have practical significance but are not represented in eqn. (5) and it is a matter of pedagogical judgment whether they are better discussed in terms of a more detailed and complex equation or simply as qualitative variations of eqn. (5). The full equation would be

$$h = \frac{2\gamma D_{mo} f}{\bar{v}} + \frac{q d_f^2 k\ \mathrm{fn}(c_{ads}/c_l) f_l}{(1+k)^2 D_l}\bar{v} + \frac{\mathrm{fn}(d_p^2, d_c^2, end) f}{j D_{mo}}\bar{v} \qquad (6)$$

The *A* Term, "Eddy Diffusion"

Much discussion and research has eventually shown that the A term is not useful in discussion of modern chromatography. The confusion surrounding it arises from several causes including conflicting definitions of the phenomena it represents, the ill-defined effect of diffusion on its magnitude, and the fact that in one of its definitions the effect is real at very high velocities.

The term "eddy diffusion" is used by chemical engineers to describe a phenomenon related to turbulence, but turbulence is a type of flow that probably never occurs in chromatographic practice. Van Deemter et al. (*2*) used the term to describe a process occurring in pockets of mobile fluid between particles acting as mixing cells. Later workers used the term to describe the broadening of a chromatographic zone by the variety of short, long, fast, and slow paths by which molecules could migrate through the packing.

Increasingly precise measurements of h showed that there was no measurable additive A term. Hence, the turbulence and the mixing cell models became untenable. The effect of the variety of flow paths remained and became known as the "multipath term" or as "anastomosis" (a term borrowed from physiology where it refers to the complicated interconnections of blood capillaries (*4*)).

The multipath model is necessarily correct. A variety of paths must spread out the molecules and increase h. However, Giddings showed in a series of papers (*5–7*) that the effect is offset by diffusion and is therefore flow-dependent. Most students find this concept difficult so it is explained more fully as follows.

In the absence of diffusion a molecule entering the column is locked into a single meandering flow path through the packing. Any other molecule entering at the same point will follow the same path and all such molecules will take exactly the same time to reach the end of the column. Molecules entering at a different point in the column cross-section will follow a different path and take a longer or shorter time to leave the column. This variety of paths causes the molecules to disperse over a length of column which is independent of the mobile phase velocity. However when there is diffusion in the mobile phase, a molecule migrates from one flow path to another, spending only a short time in each. When the flow rate is very slow, every molecule samples every flow path a large number of times so that every molecule has a similar pattern of flow, and the molecules are not significantly dispersed by this multipath effect. Thus, the multipath term tends to zero as velocity tends to zero. At very fast flow rates there is too little time for this effect so that the multipath term tends to a constant A as velocity tends to infinity. This has been represented by the equation

$$h = \frac{1}{1/A + 1/C_m v} \qquad (7)$$

often called the "coupling equation," a term suggested by Giddings. (*5*) This has often been reproduced in textbooks but *it should not be.* The equation gives presumably correct values at $v = 0$ and $v = \infty$ but there is much experimental data to show that it does not do so at any point between these two extremes. Even the extreme values cannot be confirmed experimentally because the equation is based on the assumption of laminar flow whereas at high velocities turbulence becomes important. Moreover, the unpredictable dependence (*12, 13*) of longitudinal diffusion on velocity makes low-velocity data

uninterpretable. Thus, eqn. (7) gives no more information than the qualitative explanation that precedes it but is deceptive because it seems to do so. There have been many attempts to provide better equations than (7) by Giddings (*3b*), by Knox and his co-workers (*8–10*), and by numerous chemical engineers whose work is reviewed by Cluff and Hawkes (*11*). Knox was able to get good correlation between theory and experiment for unretained samples, but no equation serves for realistic samples with realistic retention times.

This work will not be reviewed here because the thesis of this section is that *no quantitative treatment of this concept should be presented* to students of analytical chemistry. It is of relevance to chemical engineers working with high velocity fluid streams through reactor beds but it makes no significant contribution to zone broadening at the velocities used in chromatography. It was hoped during the 1960's that high velocities would be used in liquid chromatography to obtain fast results, and the discovery that $h \rightarrow A$ as $v \rightarrow \infty$ prepared the way for such work. However, the 1970's have shown that it is more productive to concentrate on short, very efficient columns operated at velocities that produce minimum h.

The multipath effect should be presented qualitatively with no supporting equations to deceive by oversimplification. It should be incorporated in the vague last term of eqn. (5), and will account for the variation of mobile phase mass transfer C_m (discussed later) with velocity. It can, in fact, be discussed under C_m rather than as a separate effect.

The *B*/*v* Term, Longitudinal Diffusion

The van Deemter (*2*) expression $2\gamma D_m/v$ or its abbreviation B/v is essentially correct. There is both theoretical (*3c*) and experimental (*12*) evidence that the obstruction factor γ decreases at very low velocities, but the experimental evidence is contradictory (*13*). Since this term is well explained in textbooks, it will not be discussed here in further detail.

The *Cv* Term, Mass Transfer

The mass transfer term arises because equilibrium between the stationary and mobile phases is not reached instantaneously. Consequently, material in the mobile phase tends to be swept forward ahead of the average position of the zone while material in the stationary phase lags behind. Similarly, material in fast flow paths is swept ahead of material in slow paths.

The more quickly a system tends toward equilibrium the smaller this effect will be. Specifically, the effect is reduced by fast diffusion in the mobile phase moving material from one flow path to another and to the stationary phase, and by fast diffusion in a liquid stationary phase moving material to the interface with the mobile phase. If these processes were infinitely fast, the material in the stationary phase would not lag behind that in the mobile phase and there would be no spreading from this cause.

The faster the mobile phase moves the worse this effect becomes, so the effect is proportional to the velocity and the term is usually written as Cv. The discussion of the multipath term above suggests that this strict proportionality will cease at high velocities in packed columns because the part of Cv that is due to a variety of flow paths will be reduced to the constant term A. This deviation is probably negligible over the range of velocities in which chromatography is actually practiced and should be ignored in elementary treatments.

It is usual to divide the C term into two parts representing mass transfer in the stationary and mobile phases thus

$$C = C_s + C_m \tag{8}$$

The stationary phase mass transfer C_s may be on an adsorbent or in a liquid stationary phase, but as simple adsorption-desorption kinetics are very fast. They make a negligible contribution to C_s. We shall therefore discuss only mass transfer in the liquid phase, C_l.

Liquid Stationary Phase Mass Transfer, C_l

Van Deemter et al. (*2*) derived the expression

$$C_l = \frac{8}{\pi^2}\frac{k}{(1+k)^2}\frac{d_f^2}{D_l} \tag{9}$$

The form of this expression is correct but the factor $8/\pi^2$ is wrong. Moreover, C_l increases when the liquid is coated on an adsorbent support.

Van Deemter's explanation for the $8/\pi^2$ was incomplete. It started with the equation

$$dc/dt = (\pi^2/4)(D_l/d_f^2)(c_g - Kc_l)$$

where c_g and c_l were the concentrations in the gaseous and the liquid phases, and K was the partition coefficient. The equation was said to be derived from "the simplified solution of the general equation for diffusion into a layer" apparently assuming that "the average concentration (in the layer) does not differ too much from the concentration at the surface." No reference was supplied. Diffusion into a layer is discussed at length by Crank (*14*) and the equations he supplies do involve π^2, but they do not obviously lead to the above equation. Even so, there would be no reason to distrust the $8/\pi^2$ had not two separate workers, Giddings (*3d*) and Golay (*15*) both derived the constant as $2/3$. Giddings derived the $2/3$ from nonequilibrium theory, and Golay derived it from an electrical analog using the telegraphers equation. They both obtained the constant $2/3$. As both derivations are complete and comprehensible, the $2/3$ must be accepted as a correction of van Deemter's $8/\pi^2$ (unless a full derivation of eqn. (9) is ever published). For a uniform film then

$$C_l = \frac{2kd_f^2}{3(1+k)^2D_l} \tag{10}$$

However, the liquid film is never uniform. It is held in the pores of supports or on the very irregular surfaces of capillaries. The beautiful electron micrograph of these by Drew and Bens (*16*) clearly show that a uniform film is impossible. Furthermore, even if the support surface were uniform it would support only a few monolayers of uniform film and the rest would run out of the column. Giddings has allowed for the non-uniformity of the liquid layer by replacing the $2/3$ with a "shape factor" q; thus (*3e*),

$$C_l = \frac{qkd_f^2}{(1+k)^2D_l} \tag{11}$$

where d_f is now the depth of the non-uniform film at its deepest point. The shape factor q is an averaging function for d_f^2 such that $(3q/2)d_f^2$ is a suitably weighted average of d_f^2 for the non-uniform film. It normally varies from $2/15$ for spherical particles (as in a bead of resin where d_f is the radius) to $2/3$ for a uniform film. It is possible (*3f*) to conceive shapes that give q outside the range $2/15$ to $2/3$. When the liquid is coated on smooth glass beads and accumulates at the contact points, then $q = 1/12$, and if it were held in pores that were wide at the bottom and narrow at the opening, q would be greater than $2/3$. However, there seems little point in introducing students to these unlikely circumstances.

When there is a variety of different shapes of pores, then q is the mean of the individual values of q for the various types of pore, weighted by the volume of liquid in each type of pore (*3e*)

$$q = \sum_j \frac{v_j}{v_l} q_j \tag{12}$$

where v_j is the volume of stationary phase in pores with shape q_j, and v_l is the total volume of stationary phase. Thus if a small fraction of the liquid accumulates in badly shaped blobs, the effect on h is small.

However, there is yet another complication. A surface supporting a stationary liquid must necessarily be adsorbent (otherwise the liquid will not wet it). Sample molecules may

diffuse through the liquid and be adsorbed at the bottom of it on the support surface. The liquid phase nonequilibrium is then very much increased over simple solution in the liquid. Giddings has derived a correction factor (*3g*) to allow for adsorption below a uniform film, but there is no suitable expression for non-uniform films. It is evident from his derivation that a multiplying factor that is a function of the ratio of adsorbed to dissolved sample c_{ads}/c_l must be used. For a uniform film the multiplying factor is $1 + 2/(1 + c_l/c_{ads}) + 3(c_{ads}/c_l)/(1 + c_l/c_{ads})$. This function approaches $3c_{ads}/c_l$ when $c_{ads} \gg c_l$ so the effect can be dramatic. The important practical consequence is that support surfaces should be no more adsorbent than is necessary to allow the stationary phase to wet them.

A final complication is that all the above equations are derived assuming that the liquid surface is in direct contact with flowing mobile phase. When it is held in the pores of particles, the sample must pass through stagnant mobile phase in these pores before it reaches the stationary phase. In this case, C_l is increased (*17*) by a factor f_l

$$f_l = \frac{\text{mass of sample dissolved (or adsorbed)}}{\text{total mass dissolved (or adsorbed) and in stagnant mobile phase}}$$

This correction factor is usually close to unity and it can be omitted from elementary discussions.

Mobile Phase Mass Transfer, C_m

The complexities of the mobile phase in a packed column have so far defied exact analysis. By contrast, the causes of zone broadening in the mobile phase are qualitatively well understood and the understanding has led to dramatic improvements in column performance in all branches of chromatography. Briefly, h increases with the square of the particle diameter d_p^2, the square of the column diameter d_c^2, the ratio of d_c to the diameter of the coil of a coiled column, and is affected by the geometry of the column, the uniformity of the packing, and the efficiency of the connections from the column to the injection system and the detector.

Particle Diameter, d_p

There are several reasons why the particle diameter is important; these are related to stagnant mobile phase within the particle and to the flow pattern between the particles.

At equilibrium the concentration of sample in the flowing mobile phase would be the same as the concentration in the stagnant mobile phase held in the pores of the particles. In a real column this equilibrium cannot be achieved. Molecules in the pores lag behind those in the flow stream for a time that depends on the distance they must diffuse to leave the particle. This distance is proportional to the particle diameter d_p and thus $C_m \propto d_p^2$. For spherical particles the dependence is given (*3h*) by

$$C_m = \frac{(1 + k - \phi)^2 d_p^2}{30(1 - \phi)\gamma_p(1 + k)^2 D_m} \quad (13)$$

In non-spherical particles the factor 1/30 would change (*18*). It is doubtful whether this equation should be introduced to any but the most advanced students since this term is only one of several C_m terms, most of which cannot be analyzed exactly. However, the qualitative concept $C_m \propto d_p^2$ has practical importance and should be taught at all levels.

The particle must be reached by diffusion from the flow stream. The greater the distance between the particles, the greater is the width of the flow stream through which the sample must diffuse. This distance is proportional to the diameter of the particles and hence C_m is again proportional to d_p^2. In this case there is no convincing equation for C_m and it is often written

$$C_m = \omega d_p^2/D_m \quad (14)$$

where ω is an ill-defined constant.

This same logic shows that in an open tubular column $C_m \propto d_c^2$ and Golay (*15*) and Giddings (*3h*) have shown by different approaches that for a round column

$$C_m = \frac{(1 + 6k + 11k^2)d_c^2}{96(1 + k)^2 D_m} \quad (15)$$

This probably does deserve to be passed on to students because it is rigorously based on a sound model, is consistent with experimental data (*19, 20*), and can be used confidently for calculations. However, it must not be pushed too far. It assumes a parabolic flow profile which is true only with perfectly smooth walls and will be wildly inaccurate for 0.005-in. steel columns, judging from Drew and Bens' micrograph (*16*).

The various flow paths in a column are inevitably out of equilibrium with each other, having different concentrations in each flow stream. The disequilibrium is offset by diffusion between the flow streams, and C_m is, therefore, proportional to the square of the distance between them. The distance is usually a few particle diameters and is assumed to be proportional to d_p. This is again written

$$C_m = \omega d_p^2/D_m \quad (16)$$

However, the assumption is only approximate. It assumes that as the particle diameter is reduced, the arrangement of the particles (the "packing structure") remains unaltered. This is not realistic. Even identical tubes and particles can be packed only moderately reproducibly. Changes in particle diameter will make further changes in the structure. Moreover, the very small particles now used in HPLC are packed by a different technique ("slurry packing") from larger particles with the intention of producing more uniform packing. To complicate matters further, the packing structure changes radically near the wall of the column so that to maintain a uniform packing structure as d_p changes, the column diameter d_c must change in direct proportion. This does not happen in practice so C_m depends in a complex and poorly understood manner on d_p and d_c. Knox's group has done much to elucidate this problem (*8–10*) but the resulting equations fail when applied to retained solutes.

The packing structure is also strongly dependent on the uniformity of the particle diameters so that meticulously size-graded particles give lower C_g than packings with a wider range of particle sizes (*21*).

Column Diameter, d_c

The column diameter confuses the effect of d_p as discussed above, but it also has a direct effect. Littlewood has shown (*22*) experimentally that in a column packed with the light diatomaceous earth "Celite" there is a velocity gradient across the column, i.e., the gas velocity is faster on one side of the column than on the other and varies uniformly across the column. Using this model he showed that C_m varied with d_c^4 and with the square of the slope of the velocity profile. He further showed that a great deal of previously published data was compatible with this model. Other workers have found different flow profiles. Huyten et al. (*23*) found a symmetrical profile in a 3-in. diameter column with fastest flow at the wall. This gives $C_m \propto d_c^2$. The parabolic flow profile in open tubular columns also leads to $C_m \propto d_c^2$ as shown above. It is unlikely that trans-column variations are so important in modern HPLC columns with the advanced packing technology now used. Indeed, it is common experience that 1/4-in. diameter columns give better efficiency than 1/8-in. in HPLC making the exponent of d_c negative.

Coil Diameter

When a column is coiled, the flow path on the inside of the coil is shorter than on the outside; as both have the same pressure drop the flow is faster on the inside and gives rise to trans-column nonequilibrium. It is for this reason that liquid chromatography columns are usually straight. The quanti-

tative effect increases with the column diameter, d_c^2, and decreases with the coil diameter, d_{coil}^2. Giddings has derived the equation (*24*)

$$C_m = \frac{7v^2 d_c^4}{192 d_{coil}^2 D_m} \quad (17)$$

where in this case v and d_{coil} are measured at the column center. Littlewood (*22*) has confirmed the dependence on d_c^4/d_{coil}^2 using a different derivation. This useful equation may be quoted with some confidence although it has not been verified experimentally. It is useful in column design so long as the following warning is added.

When the coil diameter is very small the curvature directs the flow stream across the column. This phenomenon is called "secondary flow," and it reduces C_m in the same way as molecular diffusion across the column, and thus, improves column efficiency. Moulijn et al. (*25*) quote the condition for this phenomenon to occur in an empty tube as

$$v d_c^{3/2}/(\eta D d_{coil})^{1/2} > 10 \quad (18)$$

when η is the kinematic viscosity of the mobile phase. It may be assumed that this phenomenon never occurs in regular chromatographic practice, but very tightly coiled open tubular columns have been shown to give improved efficiency (*25*), and it is possible that it may become chromatographic practice in the future.

"Infinite Diameter Columns"

The zone broadening caused by the change in packing structure near the column wall can be avoided if the sample is not permitted to reach the wall of the column. This can be arranged by injecting the sample into the center of the column cross-section and having the column sufficiently wide that the sample will not be carried to the walls (by diffusion or by the flow pattern) by the time it reaches the end of the column. The outlet system is arranged so that mobile phase near the walls does not enter the detector.

Since the sample does not reach the wall region it experiences the same flow profile as it would in a column of infinite diameter. Knox and Saleem (*9*) first investigated this kind of column in 1969, named it the "infinite diameter column", and demonstrated reductions in plate height up to twofold at high velocities. This has been confirmed by DeStefano and Beachell (*26, 27*). However, there is no data in regular journals on such columns for velocities near those giving minimum h such as are now most used in liquid chromatography. Extrapolation of Knox and Saleem's data (*9*) suggests that they may be worse than regular columns at these lower velocities. However, such columns have been sold commercially so there is presumably evidence of their practical value.

End-effects

Zone spreading also occurs in the injection system and to a lesser extent in the connections from the column to the detector. "End-effects" occurring in these regions have been discussed by many authors of which the most thorough is probably Sternberg (*28*) whose mathematical treatment is beyond the training of most chemists. Even more complex treatments have been offered by Gill and his coworkers, e.g., in reference (*29*).

The principal cause of the broadening is the flow profile across the various tubes through which the sample must flow to and from the column. This is usually more uneven than in the column itself and so causes significant contribution to the C_m term. The longer the column, the less important this becomes, so the contribution to C_m is inversely proportional to the column length. A practical consequence of this is that connecting tubes should be as narrow as possible or, if the design of the instrument prevents this, they should be packed with fine glass beads of about the same diameter as the particles of column packing.

In gas chromatography the sample is often evaporated in the injection system and a finite rate of evaporation spreads the zone into an exponential distribution. The extent of this distribution in space increases with gas velocity so it appears in the C term. However, it is not reduced by diffusion, so it is not part of the C_m term but contributes to C_s. As well as broadening the peak, it also gives it an exponential tail.

If a valve system is used so that the sample is confined in an empty tube before injection, then the C_m term resulting from that empty tube may be overlaid with a contribution due to the finite volume of the sample. If h is defined as σ^2/L and if the distribution due to injection of a finite volume of length l is given by $\sigma^2 = l^2/12$, then the contribution to h is $l^2/12L$. If the sample tube has a smaller cross-section than the fraction of the sectional area of the column that is occupied by mobile phase, then this term must be corrected by a factor equal to the ratio of the two areas.

This could appear as an additive term in the equation for h since it is unaffected by velocity or diffusion and could be considered as a justification for the historical A term as in eqn. (2). There are four reasons for not doing this:

(1) It would continue the present confusion over the A term, which would continue to be attributed to "eddy diffusion."
(2) The equation is usually used to describe phenomena in the column, which this is not.
(3) In a well-designed apparatus it is negligible and the equation would give an unrealistic impression of the dependence of h on v. This would be the more serious because it complicates the algebra when the equation for h is used to predict optima or to evaluate conditions at optima.
(4) The interaction of this term with the C_m term produced by nonequilibrium in the sample tube is not known, and it is conceivable that the overall phenomenon may be better represented as a contribution to C_m.

It seems better to make a break with a term that is mired in confusion and to present $l^2/12L$ in a separate discussion.

Corrections for Gas Compressibility

In gas chromatography the mobile phase expands as it moves through the column and encounters lower pressures. This results in a continuous increase in linear velocity v through the column. It also results in a continuous increase in diffusivity D_g. As both are inversely proportional to pressure, D_g/v remains contant along the column, at least for an ideal gas.

The effect of these variations was elucidated by Giddings (*31*). An elementary exercise in calculus yields

$$h = \frac{B_o j f}{\bar{v}} + \frac{C_{go} f \bar{v}}{j} + C_s \bar{v} \quad (19)$$

where

B_o, C_{go} are B and C_g at the column outlet

$\bar{v}$ = average gas velocity
= column length/elution time of unretained sample

$j = 3(p_i^2/p_o^2 - 1)/2(p_i^3/p_o^3 - 1)$

$f = 9(p_i^4/p_o^4 - 1)(p_i^2/p_o^2 - 1)/8(p_i^3/p_o^3 - 1)^2$
$= j^2(p_i^2/p_o^2 + 1)/2$

This is a less detailed version of eqn. (6). Expressions have also been derived for non-ideal gases by Schettler et al. (*32*).

Summary Equations

To simplify the algebra used in optimization schemes a number of simplified equations have been used. Equations (3) and (4) are the simplest and in the opinion of the writer are also the best. For the higher velocities that characterized liquid chromatography a decade ago, the equation

$$h = Ev^x \quad (20)$$

was often used where x varied from 0.3 to 0.7. This ignored the B/v term which probably was negligible. Now that liquid chromatography is most often carried out at velocities close to the velocity giving minimum h, this form is no longer useful.

Some theoreticians have extended this by adding a term to account for those mass transfer terms that are simply proportional to v to give the equation

$$h = B/v + Cv + Ev^{1/3} \quad (21)$$

The origins of this equation are rather obscure. The earliest use seems to be by Done, Kennedy, and Knox in 1972 (*33*). They give the last term as Ev^n and suggest that $n = 0.33$ is the best value for velocities such that $vd_p/D_m = 10$ to 100. This is much higher than the minimum of the h/v plot that represents velocities that are now usual in modern liquid chromatography, so higher values than $\frac{1}{3}$ can now be expected. The value of $n = 0.33$ comes from an earlier paper by Knox and Parcher (*9*), but reference to the paper shows that it refers to a form of the coupling equation

$$h = 1(1/A + 1/Cv^n) \quad (22)$$

which requires some simplification to reduce to eqn. (20). In any case, eqn. (22) refers only to unretained solutes, and the later work of Knox and Saleem (*10*) shows that it fails for retained solutes. The origin of eqn. (22) is also somewhat obscure but it seems to be a descendant of a similar equation by Hiby (*34*) using an exponent of 0.5 (instead of n or 0.33) to correlate engineering data involving both laminar and turbulent flow. This was first used in chromatography by Huber (*35*).

An equation similar to eqn. (22) was derived theoretically for unretained solutes by Horvath and Lin (*39*) that reduces to the form

$$h = A/v + B/(1 + Cv^{-1/3}) + Dv^{2/3} + Ev$$

This was shown to provide a better fit to experimental data for unretained solutes in packings of glass beads than other published equations. While this was a real step toward understanding zone dispersion, it is improbable that it will represent the real world of retained solutes. Moreover, it was based on Pfeffer and Happel's model (*40*) which showed that the mass transfer coefficient is proportional to $v^{1/3}$ at values of the Peclet number vd_p/D_m (known in chromatographic nomenclature as the reduced plate height) greater than 30 and a porosity of 0.4. Values of vd_p/D_m are seldom that high in chromatographic practice, although they would occur at the very high velocities at which simple versions of the van Deemter equation break down.

It would be unwise to introduce most students to semi-empirical equations such as these. There may be occasion in graduate courses dealing with optimization schemes that are based on these equations, such as the work of Guiochon's group in optimization of thin-layer chromatography (*36*). Otherwise, eqns. (3) and (4) are to be preferred, perhaps supplemented with a qualitative description of the deviations to be expected at higher velocities and the uncertain effect of these deviations at lower velocities. Unfortunately, they have begun to appear in textbooks without any explanation of their origin or their very limited usefulness.

Limitations of the van Deemter Equation

Whatever form of the van Deemter equation is used, it is strictly applicable only to infinitely long columns. The approximations involved in its derivation become progressively more important as the plate number N defined by

$$N \equiv L^2/\sigma^2 \equiv L/h$$

becomes smaller. Giddings (*3j*) has defined this condition approximately as

$$\sqrt{N} \gg 1$$

so that the equation is certainly inapplicable when $N < 100$ and doubtful when $N < 1000$.

Moreover, the flow pattern in the regions near the two ends of the column is different from that in the main body of the column. This has been theoretically elucidated by Gill and Sankasubramanian (*29*) for empty tubes, but there is no guidance, of which the author is aware, to suggest what length of a packed column has unrepresentative flow profiles. On the basis of the work on empty tubes, however, it would seem unwise to apply the van Deemter equation to columns that are less than 50 times as long as they are wide.

These limitations do not affect the qualitative usefulness of the dispersion equation, but unfortunately, a number of workers have attempted to use it to derive kinetic constants using columns that were too short to justify its use. It is therefore important to make students aware of these limitations and prevent future errors of this kind.

Literature Cited

(1) Lapidus, L., and Amundson, N. R., *J. Phys. Chem.*, **56**, 984 (1952).
(2) Van Deemter, J. J., Zuiderweg, F. J., and Klinkenberg, A., *Chem. Eng. Sci.*, **5**, 271 (1956).
(3) Giddings, J. C., "Dynamics of Chromatography," Marcel Dekker, New York, **1965**, (a) pp. 14–18; (b) pp. 53–61; (c) pp. 245–247; (d) Ch. 4; (e) pp. 141–142; (f) pp. 146–147; (g) pp. 163–166; (h) p. 158; (i) pp. 153–4; (j) p. 174.
(4) Littlewood, A. B., "Gas Chromatography," Academic Press, London, **1962**, p. 147.
(5) Giddings, J. C., *Nature*, **187**, 1023 (1959).
(6) Giddings, J. C., *J. Chromatog.*, **5**, 61 (1961).
(7) Giddings, J. C., Robison, R. A., *Anal. Chem.*, **34**, 885 (1962).
(8) Knox, J. H., *Anal. Chem.*, **38**, 253 (1966).
(9) Knox, J. H., and Parcher, J. F., *Anal. Chem.*, **41**, 1599 (1969).
(10) Knox, J. H., and Saleem, M., *J. Chromatog. Sci.*, **7**, 745 (1969).
(11) Cluff, J. R., and Hawkes, S. J., *J. Chromatog. Sci.*, **14**, 248 (1976).
(12) Hawkes, S. J., *Anal. Chem.*, **44**, 1296 (1972).
(13) Bowers, W., and Hawkes, S., *J. Chromatog.*, **134**, 166 (1977).
(14) Crank, J., "The Mathematics of Diffusion," Clarendon Press, Oxford, **1956**. (a) Sec. 2:21; (b) Ch. 4.
(15) Golay, M. J. E., "Gas Chromatography 1958," D. H. Desty (*Editor*) Academic Press, New York, **1958**, p. 36.
(16) Drew, C. M., and Bens, E. M., "Gas Chromatography 1968," C. L. A. Harbourn (*Editor*) Institute of Petroleum, London, **1969**, pp. 3–21.
(17) Hawkes, S. J., *J. Chromatog.*, **68**, 1 (1972).
(18) Kucera, E., *J. Chromatog.*, **19**, 237 (1965).
(19) Scott, R. P. W., and Hazeldean, G. S. F., "Gas Chromatography 1960," R. P. W. Scott (*Editor*) Butterworths, London, **1960**, p. 144.
(20) Desty, D. H., and Goldup, A., "Gas Chromatography 1960," R. P. W. Scott (*Editor*) Butterworths, London, **1960**, p. 162.
(21) Bohemen, J., and Purnell, J. H., "Gas Chromatography 1958," D. H. Desty (*Editor*) Butterworths, London, **1958**, p. 6.
(22) Littlewood, A. B., "Gas Chromatography 1964," A. Goldup (*Editor*) Institute of Petroleum, London, **1965**, p. 77.
(23) Huyten, F. H., van Beersum, W., and Rijnders, G. W. A., "Gas Chromatography 1960," R. P. W. Scott (*Editor*) Butterworths, London, **1960**, p. 224.
(24) Giddings, J. C., *J. Chromatog.*, **3**, 520 (1960).
(25) Moulijn, J. A., Spijker, R., and Kolk, J. F. M., *J. Chromatog.*, **142**, 155 (1977).
(26) DeStefano, J. J., and Beachell, H. C., *J. Chromatog. Sci.*, **8**, 434 (1970).
(27) DeStefano, J. J., and Beachell, H. C., *J. Chromatog. Sci.*, **10**, 658 (1972).
(28) Sternberg, J. C., "Advances in Chromatography," Giddings, J. C., and Keller, R. A. (*Editors*) Marcel Dekker, New York, **2**, 205 (1966).
(29) Gill, W. N., and Sankasubramanian, R., *Proc. Roy. Soc. Lond.*, **A316**, 341 (1970).
(30) Littlewood, A. B., "Gas Chromatography 1958," D. H. Desty (*Editor*) Butterworths, London, **1958**, p. 23.
(31) Giddings, J. C., Seager, S. L., Stucki, L. R., and Stewart, G. H., *Anal. Chem.*, **32**, 867 (1960).
(32) Schettler, P. D., Eikelberger, M., and Giddings, J. C., *Anal. Chem.*, **39**, 146 (1967).
(33) Done, J. N., Kennedy, G. J., and Knox, J. H., "Gas Chromatography 1972," S. G. Perry (*Editor*) Applied Science, London, **1973**, p. 145–155.
(34) Hiby, J. W., "Proceedings of the Symposium on the Interaction between Fluids and Particles, London, 20–22 June 1968," Rottenburg, P. A. (*Editor*) Institute of Chemical Engineers, London, **1968**, p. 317.
(35) Huber, J. F. K., *J. Chromatog. Sci.*, **7**, 85 (1969).
(36) Guiochon, G., Bressolle, F., and Siouffi, A., *J. Chromatog. Sci.*, **17**, 368 (1979).
(37) Martin, A. J. P., and Synge, R. L. M., *Biochem. J.*, **35**, 1358 (1941).
(38) Einstein, A., *Ann. der Physik*, **17**, 549 (1905).
(39) Horvath, C., and Lin, H., *J. Chromatog.*, **126**, 401 (1976).
(40) Pfeffer, R., and Happel, J., *A. I. Ch. E. J.*, **10**, 605 (1964).