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Plate height theory for compressible mobile phase fluids and its application to gas, liquid and supercritical fluid chromatography

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ABSTRACT

General expressions for apparent plate height are derived in terms of temporal and spatial average values of local plate height, solute capacity factor and mobile phase density. The general expressions are applied to the appropriate expressions for gas chromatography, liquid chromatography and supercritical fluid chromatography with open tubular and packed columns. For gas chromatography, the equations reduce to the equations presented earlier by Giddings. For liquid chromatography, the equations reduce to those for local plate height. Predicted results for supercritical fluid chromatography are compared to experimental results reported in the literature.

INTRODUCTION

The deleterious effect of large pressure gradients on column efficiency in chromatography with compressible mobile phase fluids has been a long-recognized problem. The effect is associated with the fact that, as a solute band traverses a chromatographic column, it experiences varying conditions of mobile phase pressure and velocity, and the apparent plate height at the outlet may be significantly greater than the local plate height at any point in the column. In near-ideal gas chromatography (GC) (He or N_2 mobile phase and pressures less than 10 atm) this effect may be measurable but it is never very great. Giddings *et al.*[1] provided the fundamental theoretical treatment of this effect for gas chromatography, showing that the effect was due entirely to expansion of the mobile phase fluid. They showed that, assuming ideal gas behavior, the ratio of apparent plate height to local plate height reaches a maximum value of 9/8 as the ratio of inlet to outlet pressures approaches infinity. In liquid chromatography (LC), the compressibility of the mobile phase is so small that the effect of pressure drop on column efficiency is negligible.

The situation for supercritical fluid chromatography (SFC) is quite different. Density gradients associated with large pressure drops may cause excessive band broadening, especially for strongly retained solutes. For example, in one study[2] the peak widths for some aromatic hydrocarbons were 2–4 times greater for a packed column operated under a large density gradient ($\Delta\rho = 0.18$ g/cm^3) than for the same column operated under a smaller density gradient ($\Delta\rho = 0.06$ g/cm^3). This dependence of column efficiency on density gradients can place significant limits on the resolving power of packed columns when high density gradients are produced. There have been a few detailed studies of this effect in packed column SFC[2,3] as well as in SFC with open tubular columns[4,5], but so far a rigorous theoretical treatment of the phenomenon has been lacking. It is our intention to provide such a treatment with this paper.

Subsequent to the initial investigations by Giddings *et al.*[1], Giddings[6,7] developed the theory into a more general form represented by the relation

$$\hat{H} = L\int(H/u_s^2)dz/[\int(1/u_s)dz]^2 \tag{1}$$

where $\hat{H}$ is the apparent plate height measured at the column outlet, L the column length, and H and u_s are the local values of plate height and solute zone velocity, respectively. Under conditions of near-ideal gas chromatography, where the capacity factor is virtually constant, eqn. 1 can be evaluated as a function of the pressure drop[6]. If however the capacity factor varies with the position in the column, as is commonly the case in SFC, the situation is more complex. Capacity factor is not a simple function of pressure. Recent advances in retention theory suggest that mobile phase density (or more specifically, reduced density) is a fundamental property affecting retention in gas chromatography (GC), LC and SFC[8]. Moreover, Martire[9] has recently derived general equations for the spatial and temporal density distribution functions, average densities and column profiles of the mobile phase fluid, as well as for the apparent capacity factors and column profiles of the solute components. It appears desirable then to rewrite eqn. 1 in terms of mobile phase density and density-dependent terms. Such an expression would be generally applicable to GC, LC and SFC, but would find its primary application in the area of SFC.

FLOW-RELATED QUANTITIES IN SFC

Because of the high compressibility and non-ideal behavior of supercritical fluids, careful definition of flow-rates and related quantities is extremely important to successful treatment of plate theory in SFC. Martire[9] has presented a general treatment of spatial and temporal aspects of column parameters applicable to GC, LC and SFC. Here we extend that treatment primarily to provide the specific tools needed for treatment of plate height theory. Throughout the following discussion we shall assume isothermal conditions and constant mass flow-rate of the mobile phase during a given separation experiment. This is achieved in practice by maintaining fixed pressures at the inlet and outlet of the column. With these restrictions a steady-state condition will be achieved so that the mass flow-rate, $\dot{m}$, remains constant along the length of the column. Radial variations, which may be significant under certain conditions[10], are ignored.

Superficial velocity and flow-rate

The volumetric flow-rate, $\dot{V}$, which is commonly measured experimentally, is related to mass flow-rate $\dot{m}$ by the simple relation

$$\dot{m} = \dot{V}\rho$$

where ρ is the density of the mobile phase. Horváth and Lin[11] define the superficial velocity u_0 as

$$u_0 = (1/A)\dot{V}$$

where A is the cross-sectional area of the tube. This is the velocity calculated from the volumetric flow-rate assuming a tube with no packing. The superficial specific mass flow-rate is then

$$F_0 = \dot{m}/A$$

F_0 is thus the mass flow-rate per unit area assuming no packing is present. It follows from the preceding equations that

$$F_0 = u_0\rho$$

Mobile zone (excluded) velocity and flow-rate

The mobile zone, or excluded, velocity u_e is

$$u_e = u_0/\varepsilon_e$$

where $\varepsilon_e = V_e/V$ is the interparticle porosity and V_e and V are the interparticle volume and empty column volume, respectively. The excluded velocity is taken as the actual linear velocity along the column axis of the moving mobile phase between the particles, or the mobile zone. When microporous packings such as porous silica are used, the intraparticulate mobile phase is assumed to be stagnant. Likewise, the excluded specific mass flow-rate F_e may be defined as

$$F_e = F_0/\varepsilon_e$$

and it follows that

$$F_e = u_e\rho$$

The solute velocity u_s is related to the mobile zone velocity and zone capacity factor k'' by the equation

$$u_s = u_e/(1 + k'') = F_e/(1 + k'')\rho$$

where k'' is the ratio of moles of solute in the stationary zone (stagnant mobile phase plus stationary phase) to moles of solute in the mobile zone (excluded mobile phase).

Mobile phase velocity and flow-rate

The mobile phase velocity u_m, which is the average linear velocity of a mobile phase molecule or of a fully permeating, unsorbed solute, is

$$u_m = u_0/\varepsilon_t$$

where $\varepsilon_t = (V_e + V_i)/V$ is the total porosity and V_i is the intraparticle volume. This is the velocity which is typically measured experimentally. The corresponding mobile phase specific mass flow-rate F_m is then

$$F_m = F_0/\varepsilon_t = u_m\rho$$

and the solute velocity is

$$u_s = u_m/(1 + k') = F_m/(1 + k')\rho$$

where k' is the phase capacity factor, which is the ratio of moles of solute in the stationary phase to moles of solute in mobile phase.

Reduced flow-rates

In order to facilitate the use of reduced densities in the treatment which follows, two reduced mass flow-rate terms are introduced. The reduced superficial specific mass flow-rate F_{0R} is defined

$$F_{0R} = F_0/\rho_{ref} = u_0\rho_R$$

where ρ_{ref} is the reference density of the mobile phase fluid, and $\rho_R = \rho/\rho_{ref}$ is the reduced density. In GC and LC, the mobile phase density at 1 bar or 1 atm is used as the reference density. In SFC, we shall use the critical density of the mobile phase fluid as the reference density. Likewise, the reduced excluded specific mass flow-rate F_{eR} is defined

$$F_{eR} = F_e/\rho_{ref} = u_e\rho_R$$

and the reduced mobile phase specific mass flow-rate F_{mR} is

$$F_{mR} = F_m/\rho_{ref} = u_m\rho_R$$

For a column of fixed diameter and porosity, F_{0R}, F_{eR} and F_{mR} are constant under isothermal, steady state conditions, and represent the linear velocity which the mobile phase or mobile zone would have at the specified mass flow-rate if it were at its reference density.

Retention time for an unretained, excluded solute

For a packed column, the mass of excluded mobile phase m_e (that which is moving) is

$$m_e = V_e <\rho>_z = \varepsilon_e V <\rho>_z$$

where $<\rho>_z$ is the spatial average density[9]. The time to elute one column volume t_u is

$$t_u = m_e/\dot{m} = \varepsilon_e V <\rho>_z/\dot{m}$$

Incorporating the relations $\dot{m} = F_0 A$ and $F_0 = F_e \varepsilon_e$, we obtain

$$t_u = L<\rho>_z/F_e = L<\rho_R>_z/F_{eR}$$

where L is the length of the column.

For an open tubular column

$$t_u = V<\rho>_z/\dot{m} = L<\rho>_z/F_0 = L<\rho_R>_z/F_{0R}$$

Average linear velocity

In some cases the average linear velocity of the mobile phase may be impossible to measure experimentally due to lack of a suitable unretained solute. The above equations for t_u allow for its calculation. For a packed column, the average excluded velocity $<u_e>$ is

$$<u_e> = L/t_u = \dot{m}/(\varepsilon_e A <\rho>_z) = F_e/<\rho>_z = F_{eR}/<\rho_R>_z$$

For an open tubular column, $u = u_0 = u_e$, and

$$<u> = \dot{m}/(A<\rho>_z) = F_0/<\rho>_z = F_{0R}/<\rho_R>_z$$

Noting that $D_t(\rho) = \rho D_z(\rho)$, it can be shown that $<1/\rho>_t = 1/<\rho>_z$, and

$$<u>_t = <F/\rho>_t = F/<\rho>_z$$

Thus it is seen that the average velocity which is usually reported as L/t_u is the temporal average velocity.

Reduced velocity

For efficiency studies involving packed columns, reduced velocity is best defined in terms of the excluded reduced velocity, v_e, that is,

$$v_e = u_e d_p/D_m$$

where d_p is the particle diameter and D_m is the diffusion coefficient of the solute in the mobile phase. Therefore, for a packed column,

$$v_e = F_e d_p/(\rho D_m) = F_{eR} d_p/(\rho_R D_m)$$

For an open-tubular column of diameter d_c,

$$v = u d_c/D_m = F_0 d_c/(\rho D_m) = F_{0R} d_c/(\rho_R D_m)$$

To the extent that the product of density times diffusion coefficient for gases and supercritical fluids is roughly constant[12], so is then the reduced velocity also approximately constant. While this product is constant in gas mixtures at low pressures, some variation is observed at high pressures. Studies on the behavior of the ratio $\rho D/\rho_0 D_0$, where the subscript 0 refers to low pressure values, show that at high pressures (in or near the supercritical region) the value of $\rho D/\rho_0 D_0$ changes in a fashion that is not accurately predicted by Enskog–Thorne theory for dense gas mixtures[13,14]. The product of ρD_m for benzene and some alkylbenzenes in supercritical carbon dioxide[13] at 40°C is less than unity at low density ($0.1 < \rho < 0.6$ g/cm^3) and increases to approximately unity at a CO_2 density of about 0.6 g/cm^3, above which it remains nearly constant. Similar behavior is observed for naphthalene under the same conditions[15], with ρD_m changing from 0.00072 to 0.00097 g cm^{-1} s^{-1} for CO_2 densities from 0.28–0.60 g/cm^3. Therefore the variation in reduced velocity with density can be significant at low densities. This variation notwithstanding, the assumption that v is constant can greatly simplify the equations for apparent plate height (*vide infra*). The question of whether this assumption leads to significant errors will be addressed later in this paper.

PLATE HEIGHT THEORY

The fundamental theory for relating apparent plate height to local plate height for non-uniform columns has been developed by Giddings[6,7]. The apparent (not local) plate height at any point in the column is defined as $\hat{H} = z(\tau^2/t^2)$, where z is distance travelled, τ is the standard deviation of the band in time units, and t is elapsed time. Normally $\hat{H}$ is measured at the outlet, where L, τ and t refer to column length, standard deviation of the eluting band and retention time, respectively. If the column is divided into infinitesimally small segments, the local plate height for each segment is $H_i = L_i\tau_i^2/t_i^2$, where L_i is the length of the segment, τ_i^2 the contribution to variance within that segment, and t_i the time required for the solute band to traverse that segment. Noting that the addition rules for τ and t differ ($\tau^2 = \Sigma\tau_i^2$ and $t = \Sigma t_i$), Giddings showed that

$$\hat{H} = L\Sigma\tau_i^2/(\Sigma t_i)^2$$

and performing the appropriate transformations, obtained the general relation presented above in eqn. 1.

Under usual conditions the column is assumed to be uniform with respect to tube diameter, stationary film thickness, particle diameter, packing structure and other stationary phase parameters. For compressible mobile phases, however, a pressure or density gradient is inevitably present, which results in variations in both the solute zone velocity and local plate height. As noted above, we desire the equivalent expression to eqn. 1 expressed in terms of density.

We begin by recalling that $u_s = F/(1 + k)\rho$, where F and k represent either F_e and k'', or F_m and k'. Under isothermal conditions and constant mass flow-rate, eqn. 1 can therefore be written as

$$\hat{H} = L[\int_0^L H(1 + k)^2\rho^2 dz]/[\int_0^L (1 + k)\rho dz]^2 \tag{2}$$

The variable terms in H can all be expressed as functions of mobile phase density. The final step then in achieving the desired equation requires a transformation of variable from z to ρ, for which we invoke the relation $dz = D_z(\rho)d\rho$, where $D_z(\rho) = (\rho/\eta)(\delta P/\delta\rho)_T$ is the spatial distribution function relating z and ρ for the mobile phase fluid[9] (η, P and T represent viscosity, pressure and temperature, respectively). Dividing numerator and denominator in eqn. 2 by $L^2 = [\int dz]^2$, and substituting $dz = D_z(\rho)d\rho$, we obtain

$$\hat{H} = <H(1 + k)^2\rho^2>_z/<(1 + k)\rho>_z^2 \tag{3a}$$

which is the desired expression, where, once again, k represents either k' or k'', and the brackets $< >_z$ represent the spatial average of the enclosed terms. An expression which is equivalent to eqn. 3a involving both temporal and spatial average quantities is

$$\hat{H} = <H(1 + k)^2\rho>_t/<1 + k>_t^2<\rho>_z \tag{3b}$$

which is arrived at by an alternative approach in the Appendix.

Dividing eqns. 3a and 3b by d_c (column diameter) or d_p (particle diameter) yields the equivalent expressions for apparent reduced plate height $\hat{h}$,

$$\hat{h} = <h(1 + k)^2\rho^2>_z/<1 + k)\rho>_z^2 \tag{4a}$$

and

$$\hat{h} = <h(1 + k)^2\rho>_t/<1 + k>_t^2<\rho>_z \tag{4b}$$

The significant contribution of these equations is that they provide a usable form of Giddings' general expression which is directly applicable to GC, LC and SFC.

APPLICATIONS AND DISCUSSION

In the following discussion we will demonstrate how eqns. 3 and 4 may be used to predict the impact of solute zone velocity gradients in GC, LC and SFC. Because the most significant area of application is expected to be in SFC, that case will be treated in greatest detail.

Plate height equations

For chromatography with open tubular columns, the Golay equation[16] describes plate height exactly under conditions of laminar flow. For packed columns numerous variations of the van Deemter equation have been proposed[11,17-19]. For LC and SFC in columns packed with microparticulate porous silica stationary phases, we employ the equations developed by Knox and Scott[17] and by Horváth and Lin[18]. For GC, in which the stationary phase is a distinct liquid phase on a solid support, we employ the coupled form of the equation proposed by Giddings[19]. We shall refer to these as the Golay, Knox, Horváth–Lin and Giddings equations, respectively. These four equations may be written in general form as follows.
The Golay equation:

$$H = (A/F)f_1(\rho) + Bd_c^2Ff_2(\rho) + CFf_3(\rho) \tag{5a}$$

TABLE I

TERMS IN EQUATIONS FOR LOCAL PLATE HEIGHT

Equation	Constant terms[a]			Density-dependent terms[a]		
	A	B	C	$f_1(\rho)$	$f_2(\rho)$	$f_3(\rho)$
Golay	2	1/96	2/3	$D_m\rho$	$(1 + 6k' + 11k'^2)/[(1 + k')^2 D_m\rho]$	$d_f^2 k'/[(1 + k')^2 D_s\rho]$
Knox[b]	2γ	Constant	$(1 - \phi_\kappa)/(30\gamma_{sm}\phi_\kappa)$	$D_m\rho$	$(D_m\rho)^{-1/3}$	$k''^2/[(1 + k'')^2 D_m\rho]$
Simplified Horváth–Lin	2γ	$2\lambda/\omega$	$\theta/[30\phi(1 + \phi^2)]$	$D_m\rho$	$(D_m\rho)^{-1/3}$	$(\phi + k' + \phi k')^2/[(1 + k')^2 D_m\rho]$
Horváth–Lin[c]	2γ	2λ	$\theta/[30\phi(1 + \phi)^2]$	$D_m\rho$	$(D_m\rho)^{-1/3}$	$(\phi + k' + \phi k')^2/[(1 + k')^2 D_m\rho]$
Giddings	2γ	2λ	q	$D_m\rho$	$(D_m\rho)^{-1}$	$d_f^2 k'/[(1 + k')^2 D_s\rho]$

[a] See glossary of symbols for definitions of terms.

[b] This is a simplified form of the Knox equation. See text.

[c] In Horváth–Lin equation: $D = \kappa/(1 + \phi)^2$; $f_4(\rho) = (\phi + k' + \phi k')^2/[(1 + k')^2 (D_m\rho)^{2/3}]$.

The Knox (or simplified Horváth–Lin) equation:

$$H = (A/F_e)f_1(\rho) + Bd_p^{4/3}F_e^{1/3}f_2(\rho) + Cd_p^2 F_e f_3(\rho) \qquad (5b)$$

The Horváth–Lin equation:

$$H = (A/F_e)f_1(\rho) + Bd_p/[1 + \omega/(d_p F_e)^{1/3}f_2(\rho)] +$$

$$+ Cd_p^2 F_e f_3(\rho) + Dd_p^{5/3}F_e^{2/3}f_4(\rho) \quad (5c)$$

The Giddings equation:

$$H = (A/F_e)f_1(\rho) + Bd_p/\{1 + B/[\omega d_p F_e f_2(\rho)]\} + CF_e f_3(\rho) \qquad (5d)$$

The factors A–D contain constant column parameters, while $f_i(\rho)$ contain terms which may show some dependence on mobile phase density, including D_m, k, d_f (stationary phase film thickness) and D_s (solute diffusion coefficient in the stationary phase). The expressions for the various parameters are given in Table I. Note in particular that the product $D_m\rho$ or $D_s\rho$ appears in each expression for $f_i(\rho)$. γ, λ, κ, q, ω, θ, ϕ and ϕ_K are column constants as defined in refs. 7, 17 and 18 (see Symbols section). We have neglected terms involving adsorption kinetics.

The terms in the Knox equation given in Table I represent a simplified form of the equation. The complete A term given by Knox and Scott is

$$2(\gamma_m + k'\gamma_s D_s/D_m)\rho D_m/F_e$$

where γ_m and γ_s are the obstruction factors to solute diffusion in the mobile and stationary phases. Likewise, the more general form of the C term is

$$(F_e d_p^2/30)\{k''/[(1 + k'')^2 \rho D_{sz}]\}$$

where D_{sz} is the diffusion coefficient of the solute in the stationary zone, and is a complex function of k'', ϕ_K, γ_{sm}, D_m, γ_s and D_s, where γ_{sm} is the obstruction factor in the stagnant mobile phase[17]. If we assume that $D_s/D_m \ll 1$, the A and C terms in the Knox equation simplify to the expressions given in Table I. This assumption is reasonable for GC, and probably for SFC, where diffusivities in the mobile phase are relatively large. In LC, where D_s/D_m may be closer to unity[17,20], the more general form of the Knox equation may provide a better description of band spreading processes.

At sufficiently low reduced velocities, which are of practical interest, the B term of the Horváth–Lin equation is simplified and the D term becomes negligible[18], so that the Horváth–Lin equation reduces to a form similar to the Knox equation, both represented by eqn. 5b. The A and B terms in the Knox and simplified Horváth–Lin equations are identical with the minor difference that Horváth and Lin have provided an explicit expression for the constant B. The major difference appears to be in the C term, given by the expressions

Knox: $(1/30\gamma_{sm}\phi_K)[k''/(1 + k'')]^2(1 - \phi_K)v_e$
Horváth–Lin: $[\theta/30\phi(1 + \phi)^2][(\phi + k' + \phi k')/(1 + k')]^2 v_e$

The apparent difference between these terms arises from the definition of the ϕ and ϕ_K terms. Knox's $\phi_K = V_{sm}/V_m$, whereas Horváth and Lin's $\phi = \phi_{sm}V_{sm}/V_{mz}$, where V_{sm}, V_{mz} and V_m are the volumes of stagnant mobile phase, excluded mobile phase or mobile zone and total mobile phase, respectively. ϕ_{sm} is the fraction of the stagnant mobile phase which is accessible to the solute. For a fully permeating solute ($\phi_{sm} = 1$), $\phi_K = \phi/(1 + \phi)$, and given that[17] $k'' = (k' + \phi_K)/(1 - \phi_K)$, it can be shown that

$$[k''/(1 + k'')]^2(1 - \phi_K)/\gamma_{sm}\phi_K = [\theta/\varepsilon_i\phi(1 + \phi)^2][(\phi + k' + \phi k')/(1 + k')]^2$$

The tortuosity factor used by Horváth and Lin is $\theta = \varepsilon_i/\gamma_{sm}$, where ε_i is the intraparticle porosity[11]. Thus for the conditions, (1) the solute is fully permeating, and (2) $D_s/D_m \approx 0$, the Knox equation is essentially identical to the simplified form of the Horváth–Lin equation, the C term differing only by the constant factor ε_i.

The corresponding expressions for apparent plate height are obtained by application of eqn. 3 or 4 to eqns. 5a–d for local plate height. We prefer to use the form involving temporal averages because certain chromatographic parameters, including capacity factor, are typically measured as temporal average quantities.

For the Golay equation:

$$\hat{H} = (1/G4)[(A/F)<g_3(\rho) \cdot f_1(\rho)>_t + Bd_cF<g_3(\rho) \cdot f_2(\rho)>_t +$$

$$+ CF<g_3(\rho) \cdot f_3(\rho)>_t] \quad (6a)$$

The Knox (or simplified Horváth–Lin) equation:

$$\hat{H} = (1/G4)[(A/F_e)<g_3(\rho) \cdot f_1(\rho)>_t + (Bd_p^{4/3}/F_e^{1/3})<g_3(\rho) \cdot f_2(\rho)>_t +$$

$$+ Cd_p^2F_e<g_3(\rho) \cdot f_3(\rho)>_t] \quad (6b)$$

The Horváth–Lin equation:

$$\hat{H} = (1/G4)\{(A/F_e)<g_3(\rho) \cdot f_1(\rho)>_t + Bd_p<g_3(\rho)/[1 + \omega/(d_pF_ef_2(\rho))^{1/3}]>_t +$$

$$+ Cd_p^2F_e<g_3(\rho) \cdot f_3(\rho)>_t + Dd_p^{5/3}F_e^{2/3}<g_3(\rho) \cdot f_4(\rho)>_t\} \quad (6c)$$

The Giddings equation:

$$\hat{H} = (1/G4)\{(A/F_e)<g_3(\rho) \cdot f_1(\rho)>_t + Bd_p<g_3(\rho)/[1 + B/(\omega d_pF_ef_2(\rho))]>_t +$$

$$+ CF_e<g_3(\rho) \cdot f_3(\rho)>_t\} \quad (6d)$$

where $G4 = <1 + k>_t^2<\rho>_z$ and $g_3(\rho) = (1 + k)^2\rho$. In general, $k = k'$ except in the Knox version of eqn. 6b, where $k = k''$.

We will show that in many situations the above expressions can be greatly simplified to yield more familiar results. In near-ideal gas chromatography, k is nearly independent of density and may be treated as a constant. At high mobile phase densities, the product $D_m\rho$ is approximately constant. Finally, although there is

evidence that high mobile phase densities may cause swelling of the stationary phase[21], we shall assume that d_f and D_s remain constant for the purpose of generating approximate expressions for apparent plate height.

Gas–liquid chromatography

GC is most commonly performed under near-ideal conditions with inlet pressures not exceeding 5 atm and an outlet pressure at ambient atmospheric pressure. Based on a review of available data on diffusivity of moderately large organic solutes in gases such as He and N_2, Giddings[22] concluded that $D_m\rho$ remains constant at pressures up to about 20 atm, consistent with the prediction of Chapman–Enskog theory[23]. The capacity factor varies only slightly with mobile phase density at these low pressures. Data for isooctane and several other compounds on squalane show that for N_2 as carrier gas at an inlet pressure of 5 bar and an outlet pressure of 1 bar, the variation in k' from inlet to outlet is about 5% compared to a five-fold change in density[24]. With this rather small variation in k', eqn. 3a may be approximated by

$$\hat{H} = <H\rho^2>_z/<\rho>_z^2 \tag{7}$$

which upon application to eqn. 5a or 5d, assuming that k', d_f, D_s and $D_m\rho$ are constant, yields

$$\hat{H} = (<\rho^2>_z/<\rho>_z^2)(H_L + H_M) + C'F_e<\rho>_z^{-1} \tag{8}$$

where H_L and H_M represent the longitudinal diffusion (A) term and mobile phase mixing (B) term, respectively, as they appear in eqns. 5a and 5d and $C' = Cf_3(\rho)\rho$, which is constant. For an ideal gas it can be shown that

$$<\rho^2>_z/<\rho>_z^2 = J_2^4(\rho)/[J_2^3(\rho)]^2 = (9/8)(\Gamma^4 - 1)(\Gamma^2 - 1)/(\Gamma^3 - 1)^2$$

and

$$1/<\rho>_z = J_3^2(\rho) = (3/2)[(\Gamma^2 - 1)/(\Gamma^3 - 1)](\rho_{out})^{-1}$$

where $\Gamma = \rho_{in}/\rho_{out}$, and, in general, $J_n^m(\rho) = (n/m)(\Gamma^m - 1)/(\Gamma^n - 1)$. Noting that for an ideal gas $\rho_{in}/\rho_{out} = P_{in}/P_{out}$, eqn. 8 is identical to the expression reported by Giddings *et al.*[1]. At higher pressures and with non-ideal carrier gases, where the variation in capacity factor can be quite large, it may be necessary to invoke eqn. 6. This situation is treated in the section on SFC.

Liquid chromatography

Because of the low compressibility of liquids, the case for liquid chromatography appears to be trivial, *i.e.*, the large pressure drops which are common in high-performance liquid chromatography (HPLC) provide little if any contribution to band spreading. In this section we provide general arguments as to why this should be the case for HPLC with packed columns, and estimate the effect under extreme conditions.

Under ordinary HPLC operating conditions with high-pressure pumps and

microparticulate packings, the inlet and outlet densities will differ no more than about 5%, and under these circumstances[9]

$$<\rho>_t \approx <\rho>_z \approx (\rho_{in} + \rho_{out})/2 \tag{9}$$

Likewise, the capacity factor in LC is nearly independent of the operating pressure[25]. For the moment let us also assume that $D_m\rho$ is constant. Therefore eqn. 7 is appropriate, which when applied to eqn. 5 for columns with porous silica packings, yields

$$\hat{H} \approx (<\rho^2>_z/<\rho>_z^2)H \tag{10}$$

where H represents the entire right-hand side of eqn. 5b or 5c. Now it can be shown that

$$<\rho^2>_z/<\rho>_z^2 = <\rho>_t/<\rho>_z$$

which, based on earlier observations[9], is approximately unity under normal LC conditions. Thus it appears that in LC the apparent plate height may be adequately described by the equation for local plate height using simple averages for density and related quantities.

The conclusion just reached is in agreement with the observation that there has been no general concern raised about the effect of pressure drop on resolution in liquid chromatography. A further test of this conclusion is provided by evaluating the effect of pressure drop in an extreme situation. For this purpose we use published data for the elution of benzyl acetate in a mobile phase of 5% ethyl acetate in n-hexane in a 25 × 0.46 cm I.D. column packed with silica gel (Partisil 10 with a 7.8 μm particle diameter)[26]. This solvent system was chosen by the authors of the cited study in part because of the relatively high compressibility of n-hexane, a property which should also contribute to gradient-induced band spreading. Based on data provided in Table II of ref. 26, this system would yield a flow-rate of approximately 25 ml/min at an inlet pressure of 40 MPa (400 bar). Assuming an interparticle porosity of 0.4 and based on $\rho_{ref} = \rho_{out} = 0.6603$ g cm^{-3} for n-hexane (density at 1 bar, ignoring the presence of ethyl acetate) at 25°C, this flow-rate corresponds to $F_{eR} = 6.52$ cm s^{-1}, which is equal to the excluded linear velocity at the outlet. The local and apparent plate heights under these conditions were estimated from the simplified Horváth–Lin version of eqns. 5b and 6b, respectively. This required the estimation of various pressure-dependent parameters as described below. For a more precise treatment of the pressure dependence of density and viscosity, the reader is referred to other published work[12,25].

(1) Approximate expressions for the spatial and temporal distribution functions, which are $D_z(\rho) = (1/\eta)(\rho^{-1}\delta\rho/\delta P)_T^{-1}$ and $D_t(\rho) = (\rho/\eta)(\rho^{-1}\delta\rho/\delta P)_T^{-1}$, were obtained by assuming that viscosity and compressibility are independent of pressure, yielding $D_z(\rho) = \rho$ and $D_t(\rho) = \rho^2$, the same expressions as for an ideal gas.

(2) The isothermal compressibility for n-hexane was assumed to remain constant at the handbook value[27] of $1.67 \cdot 10^{-3}$ MPa^{-1}, the value at 1 atm. In fact, the compressibility decreases by about 25% at 40 MPa. Our calculation would therefore predict a slightly greater change in density than would actually occur, which would in

turn exaggerate the effect of pressure drop on plate height. Defining the reference density ρ_{ref} as the density at 1 bar, $\rho_{R,out} = 1$, an inlet pressure of 40 MPa corresponds to $\rho_{R,in} = 1.0651$, or $\Delta\rho_R = \rho_{R,in} - \rho_{R,out} = 0.0651$.

(3) The effect of density on capacity factor was estimated from the k' vs. P_{in} data provided in Table VI of ref. 26 and the isothermal compressibility of n-hexane, yielding the following relation for pressures from 0.1 to 40 MPa:

$$k' = k'^0 - 2[0.00343 \text{ MPa}^{-1}/(\rho^{-1}\delta\rho/\delta P)]\Delta\rho_R$$
$$= k'^0 - 4.11\Delta\rho_R$$

where $k'^0 = 1.526$ is the value at 1 bar. The factor 0.00343 MPa^{-1} is the slope for the dependence of k' on P_{in}. This factor is doubled because the average column pressure would be about one-half of P_{in}. Thus the average column pressures studied in ref. 26 never exceeded 20 MPa, and the above relation represents àn extrapolation to 40 MPa. At an inlet pressure of 40 MPa, then, $k' = 1.295$ at the inlet, and the column-averaged value is 1.410, which is consistent with the value of 1.389 calculated from the regression equation given by Katz et al.[26]. Note that the change in k' from inlet to outlet is about 18%. Katz et al.[26] attributed this to an increase in column temperature at higher pressures, even for a thermostated column. Thus one extreme is to assume that k' remains constant throughout the column (i.e., it is independent of density), which would contribute nothing to gradient-induced band spreading. The other extreme, which we have adopted here, is to assume that the column is efficiently thermostated, and that the change in k' is due to the density gradient in the column. The truth probably lies between these two extremes, so that our assumption again has the result of exaggerating the effect of pressure drop on band spreading.

(4) The effect of mobile phase density on the diffusion coefficient (D_m) of ethyl acetate was estimated from D_m vs. P data[28] to yield the expression

$$D_m = D_m^0 - [2.14 \cdot 10^{-7} \text{ cm}^2 \text{ s}^{-1} \text{ Pa}^{-1}/(\rho^{-1}\delta\rho/\delta P)_T]\Delta\rho_R$$
$$= D_m^0 - (1.28 \cdot 10^{-4})\Delta\rho_R$$

where $D_m^0 = 3.097 \cdot 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ is the value at 1 bar.

Based on the approximations outlined above, the spatial averages of the expressions in the equation obtained by application of eqn. 3a to eqn. 5b (i.e., the spatial average analogue to eqn. 6b) were evaluated by numerical integration to a precision of 1 part in 10^5, and a value for $\hat{H}$ was obtained for the conditions stated above ($P_{in} = 40$ MPa) using the values of the column constants stated earlier. A corresponding value for local plate height was calculated from eqn. 5b using spatial average values for ρ_R, k' and D_m, which are the simple average values that would be routinely observed or calculated. The resulting values were $\hat{H} = 7.274 \cdot 10^{-3}$ cm and $H = 7.256 \cdot 10^{-3}$ cm, a difference of less than 0.3%. This calculation was based on rather extreme operating conditions; results for lower inlet pressures and flow-rates produced even smaller differences between $\hat{H}$ and H. Thus the theory correctly predicts what is generally observed in practice, that for an LC column operated isothermally at a constant mass flow-rate, the effect of pressure drop on plate height is insignificant.

TABLE II

SELECTED DATA FOR NAPHTHALENE MODEL

For CO_2 mobile phase at 40°C on 5.0-μm reversed-phase silica, 15 × 0.46 cm I.D. column. Ln $k' = 6.34 - 9.49\rho_R + 2.35\rho_R^2$. See eqn. 12 and related discussion for definitions of $\hat{h}_{est}$, $\bar{h}_{est}$, $G3$, $G4$ and $F2$.

$\langle\rho_R\rangle_t$	F_{eR} cm/s	$\langle v_e\rangle_t$	ΔP bar	P_{avg} bar	P_{out} bar	$\langle k'\rangle_t$	k'_{out}	$\hat{h}$	$\hat{h}/\hat{h}_{est}$	$\bar{h}/\bar{h}_{est}$	$\langle\rho\rangle_t/\langle\rho\rangle_z$	$G3/G4$	$F2/G4$
1.20	0.50	1.24	4.0	94.0	92.0	0.191	0.257	2.93	1.00	1.00	1.00	1.00	0.92
1.20	1.00	2.49	8.1	94.0	90.0	0.203	0.394	2.68	1.00	1.00	1.00	1.00	0.94
1.20	1.50	3.74	12.4	94.2	87.9	0.224	0.660	2.70	1.00	1.00	1.01	1.00	0.97
1.20	2.00	5.01	16.8	94.3	85.9	0.262	1.183	2.79	1.01	1.00	1.02	1.00	1.04
1.20	3.00	7.60	25.7	94.3	81.5	0.405	3.284	3.17	1.06	1.01	1.05	1.03	1.39
1.20	4.00	10.26	34.9	93.9	76.5	0.671	7.306	4.11	1.26	1.05	1.08	1.15	2.14
1.20	5.00	12.98	44.7	92.9	70.5	1.066	14.070	5.78	1.61	1.11	1.12	1.35	3.17
1.20	6.00	15.76	55.5	91.0	63.3	1.681	26.358	8.32	2.10	1.20	1.16	1.61	4.37
1.20	7.01	18.59	67.9	88.0	54.0	2.594	49.874	11.79	2.70	1.32	1.21	1.88	5.53
1.20	8.00	21.43	83.7	82.9	41.1	3.914	101.403	16.51	3.45	1.52	1.27	2.11	6.49
1.30	0.50	1.23	4.0	97.8	95.8	0.132	0.156	2.93	1.00	1.00	1.00	1.00	0.84
1.30	1.00	2.47	8.0	97.9	93.9	0.134	0.193	2.67	1.00	1.00	1.00	1.00	0.84
1.30	1.50	3.70	12.1	98.2	92.2	0.139	0.258	2.68	1.00	1.00	1.00	1.00	0.85
1.30	2.00	4.95	16.3	98.6	90.4	0.146	0.376	2.75	1.00	1.00	1.01	1.00	0.86
1.30	3.00	7.47	25.3	99.2	86.6	0.182	1.025	2.92	1.00	1.00	1.02	1.00	0.92
1.30	4.00	10.04	34.4	99.7	82.5	0.261	2.683	3.20	1.03	1.01	1.04	1.01	1.12
1.30	5.00	12.67	43.7	100.0	78.2	0.417	5.893	3.88	1.17	1.03	1.06	1.08	1.63
1.30	6.00	15.34	53.4	99.8	73.1	0.657	11.148	5.25	1.45	1.09	1.09	1.24	2.47
1.30	7.00	18.07	64.0	98.8	66.8	1.026	20.218	7.59	1.92	1.17	1.12	1.48	3.62
1.30	8.01	20.86	75.5	96.8	59.0	1.571	36.474	11.05	2.55	1.28	1.16	1.77	4.91

1.40	0.50	1.23	4.2	104.1	102.0	0.097	0.105	2.92	1.00	1.00	1.00	1.00	0.79
1.40	1.00	2.47	8.4	104.2	100.1	0.096	0.115	2.66	1.00	1.00	1.00	1.00	0.79
1.40	1.50	3.70	12.6	104.6	98.3	0.097	0.130	2.67	1.00	1.00	1.00	1.00	0.79
1.40	2.00	4.94	16.7	104.6	96.3	0.098	0.150	2.73	1.00	1.00	1.00	1.00	0.79
1.40	3.00	7.42	25.2	105.6	93.0	0.103	0.232	2.88	1.00	1.00	1.01	1.00	0.80
1.40	4.00	9.93	34.1	106.7	89.7	0.113	0.464	3.02	1.00	1.00	1.01	1.00	0.81
1.40	5.00	12.47	43.5	107.8	86.0	0.139	1.207	3.18	1.01	1.00	1.02	1.00	0.86
1.40	6.00	15.06	52.8	108.7	82.2	0.200	3.032	3.45	1.04	1.01	1.04	1.01	1.03
1.40	7.00	17.70	62.4	109.4	78.2	0.305	6.137	4.08	1.15	1.03	1.06	1.07	1.42
1.40	8.00	20.37	72.4	109.5	73.3	0.474	11.245	5.43	1.43	1.09	1.08	1.20	2.14
1.60	0.50	1.26	4.7	132.1	129.7	0.059	0.060	2.91	1.00	1.00	1.00	1.00	0.73
1.60	1.00	2.52	9.5	132.2	127.5	0.059	0.062	2.66	1.00	1.00	1.00	1.00	0.73
1.60	1.50	3.78	14.2	132.5	125.4	0.059	0.063	2.67	1.00	1.00	1.00	1.00	0.73
1.60	2.00	5.03	18.9	132.9	123.5	0.059	0.064	2.72	1.00	1.00	1.00	1.00	0.73
1.60	3.00	7.55	28.4	133.3	119.1	0.059	0.068	2.86	1.00	1.00	1.00	1.00	0.73
1.60	4.00	10.08	37.8	133.8	114.9	0.059	0.073	3.00	1.00	1.00	1.00	1.00	0.73
1.60	5.00	12.59	47.1	133.8	110.2	0.060	0.080	3.12	1.00	1.00	1.00	1.00	0.73
1.60	6.00	15.09	56.5	134.6	106.4	0.061	0.089	3.24	1.00	1.00	1.00	1.00	0.74
1.60	7.00	17.62	65.9	135.7	102.8	0.061	0.101	3.35	1.00	1.00	1.00	1.00	0.74
1.60	7.99	20.14	75.2	137.2	99.6	0.062	0.117	3.45	1.00	1.00	1.00	1.00	0.74

Supercritical fluid chromatography

In SFC we commonly find significant variations in both solute capacity factor and mobile phase density, especially with packed columns, so it is here that eqns. 3 and 4 should be most useful. While it is possible to generate rather large pressure drops in SFC with open tubular columns, the pressure drops under typical conditions are quite small, and the equations for apparent plate height essentially reduce to those for local plate height. Therefore we will focus our attention on results for packed columns. The effects of pressure drop in capillary SFC will be the subject of a future investigation.

To evaluate the effects of solute velocity gradients in packed columns, we employ retention data for the elution of naphthalene at 40°C with CO_2 on porous silica (reversed-phase, Perisorb RP-8)[29]. A fit of ln k' *vs.* reduced density for the reported data yields the relation

$$\ln k' = 6.34 - 9.49\rho_R + 2.35\rho_R^2$$

Values of apparent plate height were calculated using the Horváth–Lin equation (eqn. 6c) and a BASIC program written in Microsoft QuickBASIC 4.0 on a personal computer. Not all of the parameters required for the calculation of plate height were known, so for the constant column parameters we chose the values suggested in ref. 18; $\varepsilon_e = 0.4, \gamma = 0.7, \lambda = 2.5, \phi = 0.8, \theta = 2, \omega = 2$ and $\kappa = 1/15$. Unless otherwise noted, all calculations correspond to CO_2 mobile phase at 40°C with 15-cm column packed with porous silica with a particle diameter of 5 μm. Values of inlet and outlet densities coresponding to selected combinations of temporal average reduced density and reduced excluded mass flow-rate (F_{eR}) were determined based on solutions to the integrated form of Darcy's Law (eqn. A3, Appendix). Inlet and outlet pressures and values of $\eta_R^{-1}(\delta P_R/\delta \rho_R)_T$ were calculated using the Jacobsen–Stewart modification of the Benedict–Webb–Rubin equation[30–32]. The Kozeny–Carman equation was used to calculate specific permeability, and the Reynolds number at the outlet was not allowed
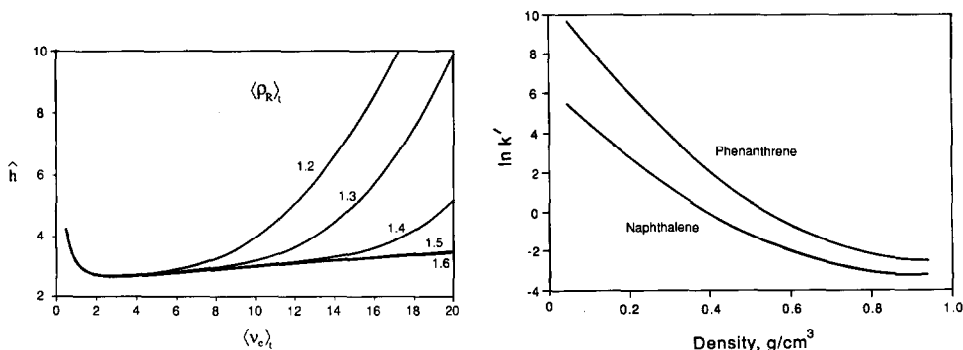

Fig. 1. Predicted effect of reduced velocity on efficiency at various average mobile phase densities for elution of naphthalene. Data calculated from eqn. 6c. Mobile phase: CO_2 at 40°C. Stationary phase: reversed-phase (octyl) porous silica, $d_p = 5$ μm. Column: 15 × 0.46 cm I.D. Solute retention: ln $k' = 6.34 - 9.49\rho_R + 2.35\rho_R^2$. See text for other solute and stationary phase parameters.

Fig. 2. Effect of mobile phase density on capacity factor for naphthalene and phenanthrene on reversed-phase (octyl) silica at 40°C. Data for naphthalene from van Wasen *et al.*[29]. Data for phenanthrene is predicted using Martire–Boehm equation[8].

to exceed 20. Reduced values of viscosity, pressure and density were employed to simplify the numerical calculations. Diffusion coefficient data for naphthalene in CO_2 at 40°C from ref. 15 were fit to a second order polynomial to yield the relation

$$D_m \cdot 10^4 \text{ cm}^2/\text{s} = 3.69 - 2.11\rho_R + 0.361\rho_R^2$$

Viscosity values were calculated from a fourth order polynomial fit to published data[30,33].

Predicted results for the effect of average operating density on efficiency with naphthalene as solute are shown in Fig. 1; selected data corresponding to these plots are presented in Table II. It is seen that the effect of pressure drop is most severe at low average column density. This is consistent with the experimental results of earlier studies[2,34]. This behavior is quite reasonable considering that at low densities $d\rho/dP$ can be quite large, leading to large changes in density and significant expansion of the mobile phase. The effect of this expansion, ignoring effects on k', is represented by $<\rho>_i/<\rho>_z$. For the data shown in Table II, values of this ratio are largest at $<\rho_R>_t = 1.20$, but they are, in general, not large enough to induce effects of the magnitude shown in Fig. 1. Second, we note that the effect of density changes on capacity factor are greatest at low carrier density (Fig. 2). A result of the latter effect is that at $<\rho_R>_t = 1.20$, $<k'>_t$ increases as v_e increases due to the lower densities and therefore higher values of k' experienced near the column outlet. The combined effects of mobile phase expansion, as measured by $<\rho>_i/<\rho>_z$, and the significant changes in capacity factor at low average carrier density, result in the very rapid rise in the h vs. v_e curve beyond the optimum velocity at low average carrier densities. At $<\rho_R>_t = 1.40$, the changes in the ratio $<\rho_R>_i/<\rho_R>_z$ and values of $<k'>_t$ are significantly smaller. For $<\rho_R>_t = 1.60$, where $d\rho/dP$ is relatively small, $<\rho_R>_i/<\rho_R>_z \approx 1.00$ even at high velocities, and $<k'>_t$ remains approximately equal to the value for constant density, so that the gradient-induced band broadening is negligible (Fig. 1).

A family of curves similar to those in Fig. 1 has been reported for the elution of phenanthrene at 50°C at much higher average pressures[2]. We were able to reproduce this behavior at higher pressures also by (1) adjusting the parameters in our equations for capacity factor and diffusion coefficient to yield the values reported in ref. 2 for phenanthrene at 50°C, and (2) using a particle size of 2 μm in a 15-cm column. One effect of raising the temperature is that the maximum compressibility of CO_2 occurs at higher pressure. The smaller particle size results in a larger pressure drop. The combined effect (higher temperature, smaller particle size) is to induce significant changes in k' at higher average operating pressures. Thus our equations are consistent with expected and observed behavior in this respect.

To evaluate the effect of k' on efficiency, we made an estimate of the parameters for phenanthrene in the equation

$$\ln k' = \ln k'^0 - a\rho_R + b\rho_R^2$$

where k'^0 is the capacity factor under ideal GC conditions. Although the theory behind this equation strictly applies to *absorption* chromatography[9], it should serve as a reasonable basis for estimating the effect of solute properties on coefficients a and b, since these are largely mobile phase parameters. Accordingly, estimates of a and b were

TABLE III

SELECTED DATA FOR PHENANTHRENE MODEL

For CO_2 mobile phase at 40°C on 5.0-μm reversed-phase silica, 15 × 0.46 cm I.D. column. $\ln k' = 11 - 13.32\rho_R + 3.30\rho_R^2$. See eqn. 12 and related discussion for definitions of h_{est}, h_{est}, G3, G4 and F2.

$\langle\rho_R\rangle_t$	F_{eR} cm/s	$\langle v_e\rangle_t$	ΔP bar	P_{avg} bar	P_{out} bar	$\langle k'\rangle_t$	k'_{out}	$\hat{h}$	$\hat{h}/h_{est}$	$\hat{h}/h_{est}$	$\langle\rho\rangle_{tl}/\langle\rho\rangle_z$	G3/G4	F2/G4
1.20	0.50	1.50	4.0	94.0	92.0	0.811	1.218	2.87	1.00	1.00	1.00	1.00	1.58
1.20	1.00	3.01	8.1	94.0	90.0	0.903	2.219	2.84	1.03	1.00	1.00	1.03	1.73
1.20	1.50	4.53	12.4	94.2	87.9	1.087	4.572	3.21	1.12	1.00	1.01	1.10	2.13
1.20	2.00	6.07	16.8	94.3	85.9	1.479	10.353	4.24	1.39	1.01	1.02	1.33	3.14
1.20	3.00	9.20	25.7	94.3	81.5	3.390	43.378	9.49	2.70	1.05	1.05	2.44	7.33
1.20	4.00	12.42	34.9	93.9	76.5	8.164	133.224	16.08	3.99	1.11	1.08	3.49	11.06
1.20	5.00	15.72	44.7	92.9	70.5	17.415	334.158	21.35	4.75	1.18	1.12	3.96	12.72
1.20	6.00	19.08	55.5	91.0	63.3	35.638	806.290	26.17	5.30	1.27	1.16	4.12	13.32
1.20	7.01	22.51	67.9	88.0	54.0	70.070	1973.225	31.94	5.96	1.41	1.21	4.20	13.57
1.20	8.00	25.94	83.7	82.9	41.1	134.705	5341.630	40.95	7.11	1.66	1.27	4.27	13.81
1.30	0.50	1.49	4.0	97.8	95.8	0.479	0.602	2.84	1.00	1.00	1.00	1.00	1.27
1.30	1.00	2.99	8.0	97.9	93.9	0.494	0.815	2.72	1.00	1.00	1.00	1.00	1.29
1.30	1.50	4.48	12.1	98.2	92.2	0.525	1.227	2.82	1.01	1.00	1.00	1.01	1.35
1.30	2.00	5.99	16.3	98.6	90.4	0.581	2.076	3.00	1.03	1.00	1.01	1.02	1.47
1.30	3.00	9.04	25.3	99.2	86.6	0.898	8.469	4.23	1.31	1.01	1.02	1.25	2.53
1.30	4.00	12.15	34.4	99.7	82.5	1.866	32.667	9.63	2.62	1.05	1.04	2.30	6.54
1.30	5.00	15.34	43.7	100.0	78.2	4.404	98.529	18.92	4.48	1.11	1.06	3.80	11.90
1.30	6.00	18.58	53.4	99.8	73.1	9.446	241.036	26.74	5.65	1.17	1.09	4.64	14.86
1.30	7.00	21.87	64.0	98.8	66.8	19.246	555.762	33.02	6.35	1.26	1.12	4.95	15.97
1.30	8.01	25.26	75.5	96.8	59.0	37.439	1271.932	39.39	7.00	1.37	1.16	5.04	16.28

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1.40	0.50	1.49	4.2	104.1	102.0	0.309	0.347	2.83	1.00	1.00	1.00	1.00	1.07
1.40	1.00	2.99	8.4	104.2	100.1	0.308	0.394	2.69	1.00	1.00	1.00	1.00	1.07
1.40	1.50	4.48	12.6	104.6	98.3	0.314	0.469	2.76	1.00	1.00	1.00	1.00	1.08
1.40	2.00	5.98	16.7	104.6	96.3	0.320	0.571	2.86	1.00	1.00	1.00	1.00	1.09
1.40	3.00	8.99	25.2	105.6	93.0	0.350	1.051	3.08	1.01	1.00	1.01	1.00	1.15
1.40	4.00	12.02	34.1	106.7	89.7	0.422	2.787	3.44	1.04	1.00	1.01	1.03	1.35
1.40	5.00	15.10	43.5	107.8	86.0	0.656	10.658	5.05	1.41	1.02	1.02	1.29	2.51
1.40	6.00	18.24	52.8	108.7	82.2	1.406	38.783	12.82	3.13	1.07	1.04	2.58	7.33
1.40	7.00	21.42	62.4	109.4	78.2	3.128	104.300	25.91	5.52	1.13	1.06	4.43	13.84
1.40	8.00	24.66	72.4	109.5	73.3	6.636	243.970	37.72	7.15	1.20	1.08	5.63	18.01
1.60	0.50	1.52	4.7	132.1	129.7	0.155	0.160	2.80	1.00	1.00	1.00	1.00	0.87
1.60	1.00	3.05	9.5	132.2	127.5	0.155	0.165	2.67	1.00	1.00	1.00	1.00	0.87
1.60	1.50	4.57	14.2	132.5	125.4	0.155	0.170	2.73	1.00	1.00	1.00	1.00	0.87
1.60	2.00	6.09	18.9	132.9	123.5	0.154	0.175	2.81	1.00	1.00	1.00	1.00	0.87
1.60	3.00	9.14	28.4	133.3	119.1	0.155	0.190	2.99	1.00	1.00	1.00	1.00	0.87
1.60	4.00	12.20	37.8	133.8	114.9	0.157	0.209	3.16	1.00	1.00	1.00	1.00	0.87
1.60	5.00	15.24	47.1	133.8	110.2	0.160	0.238	3.32	1.00	1.00	1.00	1.00	0.88
1.60	6.00	18.26	56.5	134.6	106.4	0.162	0.275	3.46	1.00	1.00	1.00	1.00	0.88
1.60	7.00	21.33	65.9	135.7	102.8	0.165	0.327	3.60	1.00	1.00	1.00	1.00	0.89
1.60	7.99	24.39	75.2	137.2	99.6	0.169	0.405	3.73	1.00	1.00	1.00	1.00	0.89
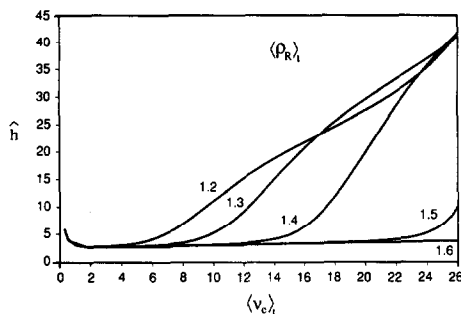
Fig. 3. Predicted effect of reduced velocity on efficiency at various average mobile phase densities for elution of phenanthrene. Ln $k' = 11 - 13.32\rho_R + 3.30\rho_R^2$. Other conditions as in Fig. 1.
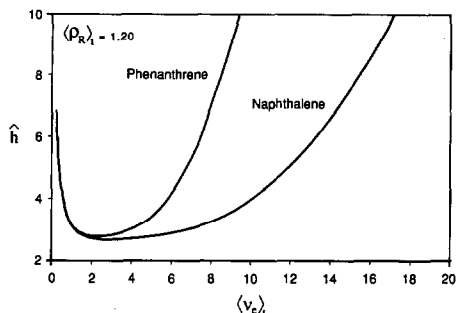
Fig. 4. Predicted effect of solute on efficiency at $<\rho_R> = 1.2$. Conditions as in Fig. 1.

made by multiplying each by the ratio of the Van der Waals volume of phenanthrene to that of naphthalene, yielding $a = 13.32$ and $b = 3.30$. The value of ln k'^0 was then increased to 11, the smallest integral value for which the ln k' vs. ρ_R curve for phenanthrene does not intersect that for naphthalene (Fig. 2). The diffusion coefficient for phenanthrene was estimated by applying a factor of 0.826 to the values for naphthalene, which is the ratio of D_m values for phenanthrene to naphthalene at 240 bar and 50°C[2]. Plots of $\hat{h}$ vs. $<v_e>_t$ are shown in Fig. 3, with corresponding data presented in Table III. Two aspects about these curves are immediately obvious. First is that, at a given average density, $\hat{h}$ for phenanthrene rises much more rapidly than it does for naphthalene (Fig. 4). This is expected because of the larger values of capacity factor. On the basis of the approximate expressions

$$\hat{H} \approx H<(1 + k')^2\rho_R^2>_z/<(1 + k')\rho_R>_z^2 =$$

$$= H<1 + k')^2\rho_R>_t/(<1 + k'>_t^2<\rho_R>_z) \quad (11)$$

which we examine below, $\hat{H}$ should increase with k', since the expression has the form of the average of the square divided by the square of the average. This is consistent with the experimental results obtained by Schoenmakers and Uunk[34], who observed much greater losses in efficiency with pressure drop for naphthalene (average $k' \approx 1.3$) and biphenyl (average $k' \approx 1.1$) than for ethylbenzene (average $k' \approx 0.3$) under identical conditions.

The second interesting aspect of the curves for phenanthrene in Fig. 3 is that, for large values of $<v_e>_t$, they change in curvature, and even intersect one another. These results are predictions based on the model and remain to be verified experimentally.

It is important to emphasize that the data presented in all of the tables and figures are based for the most part on models rather than experimental data, and as such depend on the assumptions made. This distinction is especially important with respect to the effect of solute size on mass transfer in the stationary phase. Experimental results[2] have shown that, at high average densities where gradient-induced band spreading should be insignificant, the reduced plate height curve rises more rapidly for naphthalene than for phenanthrene at reduced velocities above the

optimum. This was attributed to a combination of factors involving the effects of solute size and capacity factor on the magnitude of the C term. These factors are not taken into account in the present treatment.

We now investigate the possibility of simplifying eqn. 6c by assuming that $D_m\rho_R$, and therefore v, can be assumed to remain constant. This results in the attractively simple expression

$$\hat{h}_{est} = (G3/G4)[A/v_e + B/(1 + \omega v_e^{-1/3})] + (F2/G4)[Cv_e + Dv_e^{2/3}] \qquad (12)$$

where $F2 = <(\phi + k' + \phi k')^2 \rho_R>_t$
$\qquad G3 = <(1 + k')^2 \rho_R>_t$
$\qquad G4 = <1 + k'>_t^2 <\rho_R>_z$

The same treatment applied to eqn. 6b results in even simpler expressions. The ratios $\hat{h}/h_{est}$ and $\hat{h}/h_{est}$ are listed in Tables II and III along with other parameters including $G3/G4$ and $F2/G4$. h_{est} is a simple estimate of the reduced plate height calculated from the local plate height equation, using $<k'>_t$ in place of k', and $<D_m\rho_R>_t$ for $D_m\rho_R$. Thus $\hat{h}/h_{est}$ is a measure of the overall effect of solute velocity gradients on efficiency. The data in Tables II and III show that h_{est} is a good approximation of $\hat{h}$ except for the combination of high velocities and low average density. Considering that the evaluation of h_{est} requires evaluation of spatial and temporal averages just as does $\hat{h}$, there appears to be little advantage in utilizing this estimate in actual calculations. However, the expression for h_{est} may serve some purpose as an aid in understanding the impact of solute velocity gradients on the different band-broadening processes.

Considering eqns. 11 and 12, and that the C and D terms in eqn. 12 should be significant only at high velocities, the ratio $G3/G4$ should provide a reasonable indicator of the onset of departure of $\hat{h}$ from the corresponding value assuming no density drop (h_{est}). In fact, we find that the departure of $G3/G4$ from unity parallels that of $\hat{h}/h_{est}$, although the latter increases more rapidly. It is useful to note that as long as $G3/G4 = 1.00$, there is no significant loss of efficiency due to solute velocity gradients. The rapid increase in $\hat{h}/h_{est}$ at higher velocities appears to be related to the relative values of the ratios $G3/G4$ and $F2/G4$. At low velocities, where only the A and B terms are important, $\hat{h}/h_{est} \approx G3/G4$. At higher velocities the C and D terms become significant, and these are multiplied by the ratio $F2/G4$. This ratio increases much more rapidly than does $G3/G4$, resulting in an additional increase in $\hat{h}/h_{est}$. Another possible indicator of the loss of efficiency might be the ratio $<\rho_R>_t/<\rho_R>_z$. In the absence of changes in k' as in near-ideal GC, this would be the case (see eqn. 8). In SFC, however, the added effect of changes in k' make this ratio a rather poor indicator of the onset of loss of resolution. Data for phenanthrene in Table III show that rather large values of $\hat{h}/h_{est}$ are attained before $<\rho_R>_t/<\rho_R>_z$ increases appreciably.

Upon further examination of the data for the naphthalene and phenanthrene models in Tables II and III, the outlet pressure appears to be a simple, reliable indicator of the onset of loss of efficiency, regardless of the average density. Loss of efficiency is experienced at $P_{out} \le 82$ bar for the naphthalene model, and at $P_{out} \lessgtr 90$ bar for the phenanthrene model. The use of outlet pressure or density as a guide to avoid loss of resolution has been noted earlier[3,34].

Figs. 5 and 6 show the effect of particle size for two columns operated at the same temporal average density and keeping all other parameters constant. Fig. 5 shows that
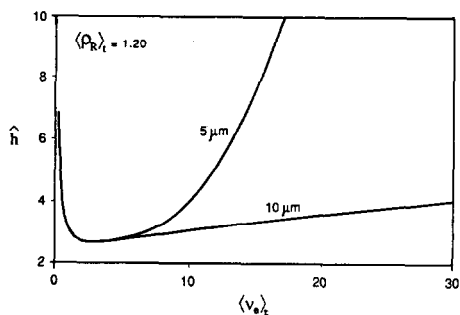
Fig. 5. Predicted effect of particle size on reduced plate height *vs.* reduced velocity curves for elution of naphthalene. Other conditions as in Fig. 1.
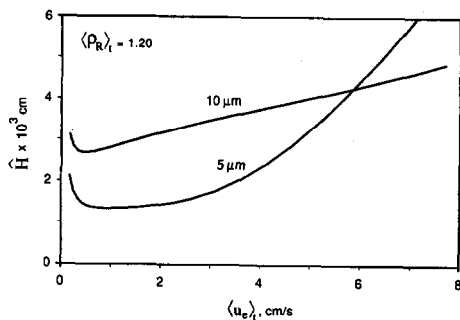
Fig. 6. Predicted effect of particle size on plate height *vs.* linear velocity curves for elution of naphthalene. Other conditions as in Fig. 1.

at high reduced velocities the column packed with smaller particles loses efficiency much more rapidly than the column packed with larger particles. This is due to the larger pressure drop required to operate the column with smaller particles at the same reduced velocity. Fig. 6 shows the variation in actual plate height *versus* average linear velocity. At high linear velocity, the column packed with larger particles becomes more efficient, suggesting that for fast separations it may be desirable to use larger diameter particles. These effects have also been observed experimentally[3,34].

CONCLUSIONS

We have presented a rigorous treatment which accounts for the effect of pressure drop on efficiency in column chromatography for steady state, isothermal operation, and have shown that the results predicted by theory agree in general with experiment. The band broadening which is observed when compressible mobile phase fluids experience large pressure drops in a chromatographic column is a direct result of the solute velocity gradients which are thereby induced. Accurate prediction of the gradient-induced band broadening requires a knowledge of the equation of state for the mobile phase fluid, the dependence of the solute capacity factor on mobile phase density and an explicit expression for local plate height. The dependence of solute diffusion coefficients in the mobile and stationary phases on mobile phase density must also be known. Excluding the possibility of adsorption phenomena, the major limitation to accurate prediction of plate height at this time seems to be a lack of information on the effect of mobile phase density on solute diffusion coefficients in the stationary phase or stationary zone. This limitation notwithstanding, this treatment provides the foundation for prediction of the effects of basic operating parameters such as particle or tube diameter, column length and mobile phase conditions on resolution. As such, it should prove useful for column design and optimization procedures in SFC.

APPENDIX

Alternative derivation of the apparent plate height equation
    The basic approach taken here is similar to that used by Giddings *et al.*[1] for the effect of pressure drop on plate height in gas chromatography, but with consideration of non-ideal behavior of the mobile phase fluid, as well as the effect of mobile phase density on solute capacity factors. It is applicable to gas, liquid and supercritical fluid chromatography under conditions of constant temperature and constant mass flow-rate.
    Let us define a solute zone as a region containing a fixed mass of solute. At a constant mobile phase specific mass flow-rate F_m, the width w of the solute zone, and therefore its velocity, will vary as a result of changes in mobile phase density and solute capacity factor. The velocity of the mobile phase u_m is inversely proportional to its density through the relation

$$u_m = F_m/\rho$$

The velocity of the solute is some fraction of the mobile phase velocity and is related to the capacity factor k' by the relation

$$u_s = u_m/(1 + k')$$

At any point in the column then

$$u_s = F_m/(1 + k')\rho \qquad (A1)$$

Let us divide the column into increments of variable width w which correspond to the widths of a solute zone as it traverses the column. Let Δt be the average time required for a solute molecule to pass through increment j of width w_j, so that

$$w_j = u_{s,j}\Delta t$$

where $u_{s,j}$ is the velocity of the solute in increment j. During the subsequent and equal time period Δt, the solute traverses increment $j + 1$ of width w_{j+1}, and

$$w_{j+1} = (u_{s,j+1})\Delta t$$

Invoking eqn. A1,

$$w_{j+1}/w_j = u_{s,j+1}/u_{s,j} = (1 + k_j')\rho_j/[(1 + k_{j+1}')\rho_{j+1}]$$

We now define σ_j as the *contribution* to solute zone width which occurs *within* segment j. As the solute zone moves through increment $j + 1$, the contribution σ_j to solute zone width which occurred in segment j becomes

$$\sigma_{j+1} = \sigma_j(w_{j+1}/w_j) = \sigma_j(1 + k_j')\rho_j/[(1 + k_{j+1}')\rho_{j+1}]$$

In the absence of a velocity gradient, the variance at the outlet is

$$\sigma_{out}^2 = \Sigma\sigma_j^2$$

In the presence of a gradient, noting that we can replace w_{j+1} with the width of the solute zone at the outlet, the variance becomes

$$\sigma_{out}^2 = \Sigma[\sigma_j^2(1 + k_j')^2\rho_j^2/(1 + k_{out}')^2\rho_{out}^2]$$

Letting z equal the distance travelled by the solute band, substituting $\sigma^2 = Hz$, and summing over a column of length L in the limit of infinitesimally small increments, we obtain

$$\sigma_{out}^2 = \int_0^L \{(H(1 + k')^2\rho^2)/[(1 + k_{out}')^2\rho_{out}^2]\}dz$$

The standard deviation of an eluting peak in elution time-τ is

$$\tau = \sigma_{out}/u_{s,out} = \sigma_{out}(1 + k_{out}')/u_{out}$$

The apparent or measured plate height $\hat{H}$ is then

$$\hat{H} = L(\tau/t_r)^2 = L\sigma_{out}^2(1 + k_{out}')^2/(u_{out}^2t_r^2) =$$

$$= [L/(u_{out}\rho_{out}t_r)^2]\int_0^L H(1 + k')^2\rho^2dz \tag{A2}$$

A change in variable from z to ρ is possible using Darcy's law;

$$u_m = F_m/\rho = -(B^0/\eta)(dP/dz) = -(B^0/\eta)(\delta P/\delta\rho)_T(d\rho/dz)$$

where B^0 is specific permeability, η is viscosity and P is pressure. Rearranging, we obtain

$$dz = -(B^0\rho/F_m\eta)(\delta P/\delta\rho)_T d\rho = -(B^0/F_m)D_z(\rho)d\rho \tag{A3}$$

where $D_z(\rho)$ is the spatial distribution function for the mobile phase fluid[9]. Substituting for dz in eqn. A2,

$$\hat{H} = (B^0 L / F_m^3 t_r^2) \int H(1 + k')^2 \rho^2 D_z(\rho) d\rho \qquad (A4)$$

where the integration limits are from $\rho = \rho_{out}$ at $z = L$ to $\rho = \rho_{in}$ at $z = 0$.

Also noting that dt is related to the temporal distribution function[9] $D_t(\rho)$ by the relation

$$dt = -(B^0 / F_m^2) D_t(\rho) d\rho$$

and that the solute retention time $t_r = (1 + k')t_u$, where t_u is the time required to elute an unretained solute, we obtain

$$dt_r = -(B^0 / F_m^2)(1 + k') D_t(\rho) d\rho$$

and

$$t_r = (B^0 / F_m^2) \int (1 + k') D_t(\rho) d\rho \qquad (A5)$$

Combining eqns. A4 and A5,

$$\hat{H} = (L F_m / B^0)[\int H(1 + k')^2 \rho^2 D_z(\rho) d\rho] / [\int (1 + k') D_t(\rho) d\rho]^2 \qquad (A6)$$

where the integration limits are ρ_{in} to ρ_{out}. Also noting that

$$L = \int dz = (B^0 / F_m) \int D_z(\rho) d\rho$$

and that $\rho D_z(\rho) = D_t(\rho)$, making the appropriate substitutions in eqn. A6, we obtain

$$\hat{H} = <H(1 + k')^2 \rho>_t / (<1 + k'>_t^2 \cdot <\rho>_z) \qquad (A7)$$

or in reduced parameters

$$\hat{h} = \hat{H}/d = <h(1 + k')^2 \rho>_t / (<1 + k'>_t^2 \cdot <\rho>_z) \qquad (A8)$$

where $< >_t$ and $< >_z$ represent the temporal and spatial averages, respectively, of the enclosed functions, and d is the column diameter (d_c) for open tubular columns or the particle diameter (d_p) for packed columns.

SYMBOLS

A	Area
A, B, C, D	Constants in plate height equation
B^0	Specific permeability of a packed bed
D_m, D_s, D_{sz}	Diffusion coefficient of solute, cm^2 s^{-1}: in mobile phase; in stationary phase; in stationary zone

d_c, d_p	Diameter: of column; of particle
d_f	Stationary phase film thickness
$D_t(\rho)$, $D_z(\rho)$	Density distribution function: temporal; spatial
ε_e, ε_i, ε_t	Porosity: interparticle; intraparticle; total
F, F_e, F_m, F_0	Specific mass flow-rate, g cm^{-2} s^{-1}; specific mass flow-rate: of mobile zone; of mobile phase; superficial
F_R, F_{eR}, F_{mR}, F_{0R}	Reduced specific mass flow-rate, cm/s; reduced specific mass flow-rate: of mobile zone; of mobile phase; superficial
γ, γ_m, γ_s, γ_{sm}	Obstruction factor: for longitudinal diffusion; in mobile phase; in stationary phase; in stagnant mobile phase
Γ	Ratio of inlet to outlet density
H, $\hat{H}$	Local plate height; apparent plate height
h, $\hat{h}$, $\hat{h}_{est}$, h_{est}	Reduced plate height: local; apparent; estimated apparent assuming v is constant; simple estimate of local plate height
η, η_R	Viscosity; reduced viscosity
θ	Tortuosity factor for porous particles
k', k'', k	Phase capacity factor; zone capacity factor; k' or k''
k'^0	Phase capacity factor at stated reference conditions
κ, λ, q, ω	Packing parameters
L	Length of column
m_e	Mass of excluded mobile phase
$\dot{m}$	Mass flow-rate, g/s
P, P_{in}, P_{out}	Pressure; inlet pressure; outlet pressure
v, v_e	Reduced velocity; reduced excluded velocity
ρ, ρ_{in}, ρ_{out}, ρ_{ref}	Density; inlet density; outlet density; reference density
ρ_R	Reduced density
σ, τ	Standard deviation of a solute zone: in length units; in time units
t	Time
t_r, t_u	Retention time: of a solute; of an unretained solute
T	Temperature
u_e, u_m, u_0, u_s	Linear velocity: of mobile zone; of mobile phase; superficial; of solute
V, V_e, V_i	Volume: total; interparticle; intraparticle
$\dot{V}$	Volumetric flow-rate, cm^3/s
ϕ	Ratio of intraparticle volume accessible to solute over interstitial void volume
ϕ_{sm}	Fraction of stagnant mobile phase which is accessible to solute
ϕ_K	Ratio of stagnant mobile phase volume to mobile phase volume
w	Width of a solute zone
z	Axial position in column
$< >_t$	Temporal average of function enclosed in brackets
$< >_z$	Spatial average of function enclosed in brackets

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