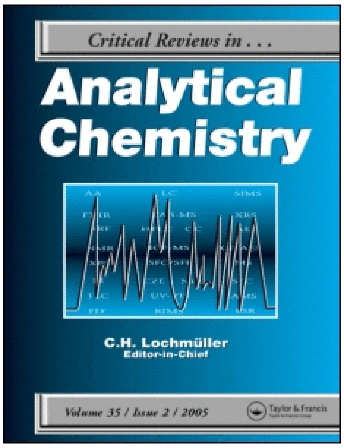

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Considerations on Speed of Separation, Detection, and Identification Limits in Capillary GC and GC/MS

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CONSIDERATION ON SPEED OF SEPARATION, DETECTION, AND IDENTIFICATION LIMITS IN CAPILLARY GC AND GC/MS

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I. INTRODUCTION

The introduction of open tubular columns by Golay[1,2] in 1957/58 initiated a revolution in analytical chemistry. With the simultaneous development of highly sensitive detectors, much progress in capillary gas chromatography (GC) was made during the following years.

Columns of various materials and dimensions were used from the onset. Capillaries with inner diameters between 35 μm[3] and 2 mm,[4] and with lengths up to 1 mi[5] were already used around 1960. Advances in glass capillary column technology[6,7] in the 1960s and 1970s were followed by the introduction of fused silica capillaries in 1979.[8] Today, fused silica has virtually replaced all other column materials in the widely commercialized field of capillary GC.

As a result of these advances, the chromatographer now has a wide-ranging choice of open tubular columns. Commercially available columns have diameters between "narrow-bore" and "wide-bore" (typically 50 and 750 μm, respectively) and the stationary phase film thickness can be anywhere between 0 and 5 μm. These columns can be operated over a wide temperature range at outlet pressures from vacuum up to tens of bars.

The expression "coating efficiency" is often used to compare the performance of columns with different geometry and of actual columns with that which can be theoretically achieved. In reality, coating efficiency has little or nothing to do with the efficiency of the coating process. A preferred expression is "utilization of theoretical efficiency" (UTE).[9a] UTE relates the actual efficiency to the theoretically expected efficiency of a column for a given radius and capacity factor, assuming that the liquid diffusion term and pressure correction factors can be neglected.

For thick-film and/or narrow-bore columns, of course, these assumptions are not true anymore[9b] and so UTE can give only limited information on the column quality. Moreover, in many publications dealing with the speed of analysis obtainable by various columns, the plate numbers are often not kept constant. Therefore, exact equations for various optimum chromatographic conditions, taking all pressure factors and the liquid mass-transfer term into account, have to be considered. Variation of column dimensions and phase ratios also largely affects the minimum detectable amounts and concentrations, as well as the maximum sample capacities. Developments in theoretical insights are evaluated and condensed in state-of-the-art equations and examples are given that illustrate the validity of the theories presented.

II. CHROMATOGRAPHIC BAND BROADENING IN OPEN TUBULAR COLUMNS

Relative band broadening in chromatography is expressed in terms of theoretical plate height, H. The apparent plate height is the measured value, given operationally as:

$$H = L\frac{\sigma^2}{t_R^2} \tag{1a}$$

where L is the column length, t_R is the retention time of a solute, and σ is the standard deviation in elution time. The quotient $(t_R/\sigma)^2$ is called the plate number: $N = L/H$.

The relative band broadening in capillary columns is satisfactorily described by the Golay equation[2], extended to situations of appreciable pressure drop by Giddings et al.[10] Taking gas decompression effects into account, the equation for the measured or apparent plate height of a capillary with uniformly distributed liquid film is

$$H = \left[\frac{B_o}{u_o} + C_{m,o}\,u_o\right] f_1 + C_s u_o f_2 \tag{1b}$$

In this equation, the following symbols are used:

$$B_o = 2\,D_{m,o} \tag{2}$$

$$C_{m,o} = \frac{11k^2 + 6k + 1}{24(k+1)^2}\cdot\frac{r^2}{D_{m,o}} \tag{3}$$

$$C_s = \frac{2k}{3(k+1)^2}\cdot\frac{d_f^2}{D_s} \tag{4}$$

$D_{m,o}$ is the binary gas diffusion coefficient of a component in the mobile gas phase at column outlet pressure, D_s is the diffusion coefficient of the component in the stationary liquid phase, k is the capacity factor of the component, r is the inner column radius, d_f is the film thickness of the stationary liquid phase, and u_o is the linear gas velocity at the column outlet.

Defining $P = p_i/p_o$ as the ratio of column inlet over outlet pressure, the Giddings[10] and James-Martin[11] pressure-drop correction factors are

$$f_1 = \frac{9}{8}\frac{(P^4-1)(P^2-1)}{(P^3-1)^2} \tag{5}$$

$$f_2 = \frac{3}{2}\frac{(P^2-1)}{(P^3-1)} \tag{6}$$

For low pressure-drop columns ($P \rightarrow 1$), both factors approach the value of one. If P approaches infinity, $f_1 \rightarrow 9/8$ and $f_2 \rightarrow 3/(2P)$.

If a pressure gradient exists, decompression of the gas along the column causes its velocity to increase from inlet to outlet. For an ideal gas, both its linear velocity, u, and the binary solute/carrier gas phase diffusion coefficient, D_m, vary inversely with pressure:

$$u\,p = u_i p_i = u_x p_x = u_o p_o \tag{7}$$

$$D_m p = D_{m,i}p_i = D_{m,x}p_x = D_{m,o}p_o \tag{8}$$

with subscripts i and o denoting inlet and outlet and x denoting any position in the column.

Introducing the (time-)average linear gas velocity $\bar{u} = f_2 u_o$,[12] the (length-)average pressure $\bar{p} = p_o/f_2$, the atmospheric pressure p_a (e.g., p_a = 100 kPa = 1 bar), and u_a as the linear gas velocity at unit pressure p_a, Equation 7 can be extended as follows:

$$\Psi = u_i p_i = u_o p_o = \bar{u}\,\bar{p} = u_a p_a \tag{9}$$

Under constant operational conditions Ψ is a constant.

The combination of Equations 8 and 9 shows:

$$\frac{D_{m,o}}{u_o} = \frac{D_{m,a}}{u_a} = \frac{D_{m,a}p_a}{\Psi} \tag{10}$$

with $D_{m,a}$ denoting the binary gas diffusion coefficient at unit pressure p_a. Giving B and C_m the same subscript as the corresponding gas-phase diffusivity, D_m, Equation 1b can be rewritten as:

$$H = \left[\frac{B_a p_a f_1}{\Psi^2} + \frac{C_{m,a} f_1}{p_a} + \frac{C_s}{\bar{p}}\right]\Psi \tag{11}$$

or

$$\Psi = p_a\left[\frac{\dfrac{H\Psi}{p_a} - B_a f_1}{C_{m,a} f_1 + C_s \cdot \dfrac{p_a}{\bar{p}}}\right]^{1/2} \tag{12}$$

Note that the square root term represents u_a, the velocity at atmospheric pressure.

Equation 11 shows that $H = f(\bar{u})$ cannot be straightforwardly evaluated because Ψ, $\bar{p}$, and f_1 cannot be expressed generally as simple functions of $\bar{u}$. However, Equation 11 can be rearranged to:

$$\frac{H}{\bar{u}} = \left[\frac{B_a p_a}{\Psi^2} + \frac{C_{m,a}}{p_a}\right] f_1 \bar{p} + C_s \tag{13}$$

which can be considered to be exclusively pressure dependent because Ψ is given by the Hagen-Poiseuille equation for viscous flow of ideal gases through open tubular columns:

$$\Psi = \frac{r^2 p_o^2}{16\eta L}(P^2 - 1) = \frac{r^2}{16\eta L}(p_i^2 - p_o^2) \tag{14}$$

where η is the dynamic viscosity of the carrier gas.

For a given column operated at constant outlet pressure p_o (and constant temperature), the values of f_1, $\bar{p} = p_o/f_2$ and Ψ are determined by p_i only (see Equations 5, 6, and 14). Therefore, $H/\bar{u} = f(p_i)$ can be evaluated. Subsequently, for any value of p_i, $\bar{u} = \Psi/\bar{p}$ can

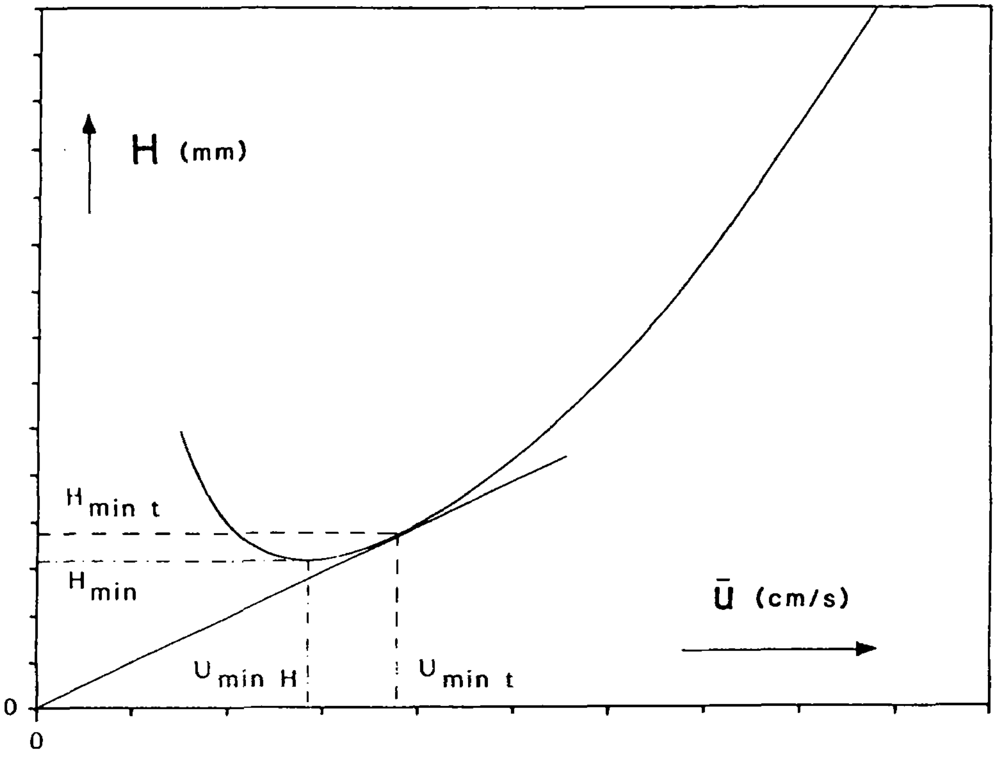

FIGURE 1. Typical shape of a H vs. ū curve showing two optimum conditions for a given column: the maximum plate number per unit of length (min H) and per unit of time (min t).

be calculated from Equation 14. Hence, H = f(ū) can be obtained by multiplying Equation 13 with ū.

Equation 14 can be rearranged to:

$$p_i^2 = \frac{16\eta L}{r^2}\Psi + p_o^2 \tag{15}$$

By combining Equations 11 or 12 with Equations 14 or 15, various optimum conditions can be calculated (see Figure 1).

III. OPTIMUM CHROMATOGRAPHIC CONDITIONS

Cramers et al.[13] derived the minimum of the H vs. u_o function (at constant p_o) by differentiation of Equation 1 with respect to u_o. The derivatives $\delta f_1/\delta u_o$ and $\delta f_2/\delta u_o$ were calculated as $(\delta f/\delta P)(\delta P/\delta u_o)$. [The latter derivative follows from Equation 14: $\delta u_o/\delta P = u_o 2P/(P^2 - 1)$]. The authors found an "optimum" outlet velocity, corresponding with minimum plate height, of:

$$u_{o,\min H} = \left[\frac{B_o(f_1 - y_1)}{C_{m,o}(f_1 + y_1) + C_s(f_2 + y_2)}\right]^{1/2} \tag{16}$$

After elaboration, their y factors appear to equal:

$$y_1 = u_o\delta f_1/\delta u_o = f_1 - f_2P(2f_1 - f_2P) \tag{17}$$

$$y_2 = u_o \delta f_2 / \delta u_o = f_2(1 - f_2P) \tag{18}$$

Note that $f_2P = p_i/\bar{p}$ and $1 < f_2P < 3/2$ for $1 < P < \infty$.

Using Equations 9, 10, 17, and 18, Equation 16 can be rearranged into:

$$\Psi_{\min H} = p_a \left[\frac{B_a f_2 P(2f_1 - f_2P)}{C_{m,a}[2f_1 - f_2P(2f_1 - f_2P)] + C_s \frac{p_a}{\bar{p}}(2 - f_2P)} \right]^{1/2} \tag{19}$$

The same authors showed that $y_1 << f_1$ for all practical purposes, meaning that $f_1 \simeq f_2P(2f_1 - f_2P)$ (see Equation 17). (y_1 reaches a maximum of 3.19% of f_1 at $P = 2.56$.) Equation 19 can, therefore, be simplified as follows:

$$\Psi_{\min H} \simeq p_a \left[\frac{B_a f_1}{C_{m,a} f_1 + C_s \frac{p_a}{\bar{p}}(2 - f_2P)} \right]^{1/2} \tag{20}$$

For a given column (L and r constant) and a given carrier gas/stationary phase/solute system at a given temperature (η, $D_{m,a}$, k, D_s, d_f constant) and outlet pressure (p_o = constant), the optimum inlet pressure can be calculated numerically by iteration from Equation 15, using the optimum Ψ values given by Equation 19 or 20. Using $\bar{p} = p_o/f_2$ and $\bar{u} = \Psi/\bar{p}$, the corresponding H values can then be calculated from Equation 11.

Apart from the maximum number of plates attainable per unit of column length, the minimum time operation of a given column is of interest. In isothermal GC, the retention time, t_R, of a compound can be described by:

$$t_R = \frac{L}{\bar{u}}(1 + k) = N(1 + k)\frac{H}{\bar{u}} \tag{21}$$

While retention times can be reduced at will (by reducing L or k, or increasing $\bar{u}$), the possibilities for increasing the speed of analysis for a given separation problem are limited by the relationship between retention time and column resolution or plate number.

The well-known resolution equation reads:

$$R_s = \frac{1}{4}\frac{k}{k + 1}\frac{\alpha - 1}{\alpha}N^{1/2} \tag{22a}$$

where R_s is the resolution between two subsequently eluting peaks, k is the capacity factor of the last eluting compound, and $\alpha = k_2/k_1$ is the relative retention.

R_s is measured operationally as:

$$R_s = \frac{t_{R,2} - t_{R,1}}{2(\sigma_2 + \sigma_1)} = \frac{\Delta t_R}{4\sigma} \tag{22b}$$

Combining Equations 21 and 22 yields an explicit relationship between analysis time and resolution for a two-component mixture:

$$t_R = 16\frac{(1 + k)^3}{k^2}\frac{\alpha^2}{(\alpha - 1)^2}R_s^2\frac{H}{\bar{u}} \tag{23}$$

Equation 23 was derived as such by Ettre[14] in 1973 and already conceived by Purnell[15] and Giddings[16] in the early 1960s. Equation 23 clearly shows the importance of selectivity and resolution. If minimum analysis time is important, then selectivity and resolution should be optimized, as discussed later in the section concerning speed of analysis.

The retention time can be further minimized by reducing H/ū (see Equation 23). Hence, Equation 13 should be differentiated. For a given column (L = constant), $\delta(H/\bar{u})/\delta\bar{u} = 0$ yields (for p_o = constant):

$$\Psi_{L,\min t} = p_a \left[\frac{B_a}{C_{m,a}} \cdot \frac{2f_1 + f_2P(f_1 - f_2P)}{f_2P(f_2P - f_1)} \right]^{1/2} \tag{24}$$

In deriving this result, $\delta P/\delta\bar{u}$ and $\delta\bar{p}/\delta\bar{u}$ were calculated as the reciprocals of the respective derivatives of Equation 14, using $\delta\bar{p}/\delta P = \bar{p}(f_2P - 1)\cdot 2P/(P^2 - 1)$.

In addition to the maximum plate number and separation speed for a given column, there is a third optimum: the minimum analysis time for a given separation problem requiring N plates.

For this purpose, Equation 15 can be rewritten as:

$$p_i^2 = \frac{16\eta N}{r^2} H\Psi + p_o^2 \tag{25}$$

and, hence, the optimum value of HΨ has to be determined. Combining Equations 11 and 12 yields:

$$\frac{H}{\bar{u}} = \frac{C_{m,a}\bar{p}f_1/p_a + C_s}{1 - B_a p_a f_1/(H\Psi)} = \frac{\text{numerator}}{\text{denominator}} \tag{26}$$

Substitution of HΨ from Equation 25 yields another pressure-dependent plate height equation. Therefore, minimum time conditions for N = constant are best calculated (for p_o = constant) via:

$$\frac{\delta(H/\bar{u})}{\delta P} = \frac{\delta(\text{numerator})/\delta P}{\text{demoninator}} - \frac{\text{numerator}}{\text{denominator}^2} \cdot \frac{\delta(\text{denominator})}{\delta P} \tag{27}$$

Hence, putting the result equal to zero:

$$\frac{H}{\bar{u}} = \frac{\delta(\text{numerator})/\delta P}{\delta(\text{denominator})/\delta P} \tag{28}$$

Equation 28 can be evaluated as:

$$\frac{H}{\bar{u}} = \frac{C_{m,a}\dfrac{p_o}{p_a}\left[\dfrac{(f_2P)^2 + f_1(2 - 2f_2P)}{f_2(2 - f_2P)}\right] + C_s}{1 - \dfrac{B_a p_a}{H\Psi}\left[\dfrac{(f_2P)^2 + f_1(2 - 3f_2P)}{(2 - f_2P)}\right]} \tag{29}$$

Combining Equations 26 and 29 yields:

$$H\Psi = -B_a p_a \frac{f_1^2 C_{m,a} + C_s (2f_1 - f_2P)\, p_a/\bar{p}}{C_{m,a}(f_1 - f_2P)} \tag{30}$$

Using Equation 25, p_i can now be numerically calculated by iteration. Once $p_{i,opt}$ is determined, all pressure factors can be calculated and Ψ is found by substitution of Equation 30 into Equation 12:

$$\Psi_{N,\min t} = p_a \left[\frac{B_a}{C_{m,a}} \cdot \frac{(2f_1 - f_2P)}{(f_2P - f_1)} \right]^{1/2} \tag{31}$$

The resulting set of equations for the optimum H values, corresponding with the various optimum Ψ values, is given by:

$$\left[\frac{H}{\Psi}\right]_{\min H} = 2\frac{C_{m,a}}{p_a} \frac{f_1^2}{f_2P(2f_1 - f_2P)} + \frac{C_s}{\bar{p}} \frac{2f_1 + f_2P(f_1 - f_2P)}{f_2P(2f_1 - f_2P)} \tag{32}$$

$$\left[\frac{H}{\Psi}\right]_{\min H} \simeq 2\frac{C_{m,a}}{p_a} f_1 + \frac{C_s}{\bar{p}} (3 - f_2P) \tag{33}$$

$$\left[\frac{H}{\Psi}\right]_{L,\min t} = 2\frac{C_{m,a}}{p_a} \cdot \frac{f_1^2}{2f_1 + f_2P(f_1 - f_2P)} + \frac{C_s}{\bar{p}} \tag{34}$$

$$\left[\frac{H}{\Psi}\right]_{N,\min t} = \frac{C_{m,a}}{p_a} \cdot \frac{f_1^2}{2f_1 - f_2P} + \frac{C_s}{\bar{p}} \tag{35}$$

From Equations 32 through 35, it can be seen that the H/Ψ equations are complex pressure-dependent relationships. However, the resistance to mass transfer in the stationary phase, C_s, can sometimes be neglected with respect to that in the gas phase, C_m, as is the case with thin-film columns.

For thin-film columns with a low inlet-to-outlet pressure ratio ($P = p_i/p_o \rightarrow 1$), the optimum chromatographic conditions follow from Equations 32 through 35, where Equations 32—33 and 34—35, respectively, lead to identical expressions:

$$\left[\frac{H}{\Psi}\right]_{\min H} = 2\frac{C_{m,a}}{p_a} \tag{36}$$

$$\left[\frac{H}{\Psi}\right]_{\min t} = \frac{C_{m,a}}{p_a} \tag{37}$$

Substitution of Equations 36 or 37 and 3 into Equation 23 yields:

$$t_R = \frac{2n}{3} R_s^2 r^2 \frac{(1 + k)(11k^2 + 6k + 1)}{k^2} \frac{\alpha^2}{(\alpha - 1)^2} \frac{\bar{p}}{p_a D_{m,a}} \tag{38}$$

where n = 1 for minimum time operation and n = 2 for minimum plate height conditions. It can be seen that reduction of the column diameter is a very effective way to increase the speed of analysis. A decrease of the average column pressure, $\bar{p}$, will also shorten analysis times. However, the condition of $P \rightarrow 1$ can no longer be maintained when narrow-bore columns and/or subatmospheric pressures are employed.

IV. VACUUM OUTLET COLUMNS

As shown by Equation 38, vacuum outlet operation ultimately yields the shortest optimum analysis times. Giddings[17] already proved theoretically in 1962 that "minimum-time operation in gas chromatography" can be achieved only, and always, when the column is operated with a vacuum outlet ($p_o \rightarrow 0$). Application of capillary columns at vacuum outlet is, of course, interesting in combined gas chromatography mass spectrometry (GC/MS). The first reports[18-21] in this field, appearing at the same time, showed the validity of this theory. However, confusion about deteriorating effects of vacuum on the separation efficiency (due to comparisons of plate numbers at nonoptimum conditions) prevented widespread application. Since then, few reports[22-25] on vacuum outlet capillary GC appeared until the introduction of fused silica columns.[8] These flexible capillaries are ideally suited for direct insertion into the ion source of a mass spectrometer. The wide use of these columns with vacuum outlet in GC/MS stimulated further research in the underlying theory.[26-31]

The equations derived thus far are generally valid for open tubular columns. For vacuum outlet ($p_o \rightarrow 0$), or high pressure-drop columns ($P \rightarrow \infty$) in general, most equations are greatly simplified. Under $P \rightarrow \infty$ conditions, $f_1 \rightarrow 9/8$, $f_2P \rightarrow 3/2$, $\bar{p} \rightarrow 2p_i/3$, and Equation 14 reduces to:

$$\Psi \rightarrow \frac{r^2}{16\eta L} p_i^2 = \frac{64\eta L}{9r^2} \bar{u}^2 \qquad (39)$$

This equation is valid for viscous flow conditions only. It can be shown that, in vacuum-outlet chromatography, low pressures exist only at the very end of the column. Only a negligible part of the column is working under conditions of molecular flow.[23] Consequently, Equation 39 and all following equations derived from it are valid.

Using Equation 39 and the limiting value of f_1, Equation 11 can be written as follows:

$$H_{P \rightarrow \infty} = \left[\frac{B_a p_a X}{p_i^2} + \frac{C_{m,a}}{p_a X} p_i^2\right] \frac{9}{8} pl \frac{3}{2} C_s p_i X \qquad (40)$$

with $X = 16\eta L/r^2$. Equation 40 was already derived by Myers and Giddings.[32]

As an alternative,

$$H_{P \rightarrow \infty} = \left[\frac{9B_a p_a}{4X\bar{u}^2} + \frac{4C_{m,a}X}{9p_a} \bar{u}^2\right] \frac{9}{8} + C_s\bar{u} \qquad (41)$$

Both the exclusively pressure- or velocity-dependent Equations 40 and 41 are of practical importance for high-pressure or vacuum-outlet chromatography. (Computer) fitting of these expressions to experimental data is preferred over the fitting of Equation 1b because u_o and B_o are extremely large at vacuum outlet, while $C_{m,o}$ and f_2 are extremely small. Moreover, p_i and $\bar{u}$ can always be measured conveniently.

Equations 19, 20, 24, and 31, which give the Ψ expressions for the various optima, reduce to a set of three expressions, with Equations 19 and 20 leading to identical results for $P \rightarrow \infty$:

$$\Psi_{P \rightarrow \infty, \mathrm{min}\ H} = p_a \left[\frac{3B_a}{3C_{m,a} + C_s \frac{p_a}{p_i}}\right]^{1/2} \qquad (42)$$

$$\Psi_{P \rightarrow \infty, L, \mathrm{min}\ t} = p_a \left[\frac{3B_a}{C_{m,a}}\right]^{1/2} \qquad (43)$$

$$\Psi_{P\to\infty,N,\min t} = p_a \left[\frac{2B_a}{C_{m,a}}\right]^{1/2} \tag{44}$$

Equation 30 is simplified to:

$$H\Psi = 3\, B_a p_a \left[\frac{9}{8} + \frac{C_s}{C_{m,a}}\frac{p_a}{p_i}\right] \tag{45}$$

A similar result was already presented in 1962 by Giddings,[17] who introduced the concept of "critical inlet pressure", p_c:

$$p_c^2 = 18\eta N B_a p_a / r^2 = \frac{9}{8} B_a p_a\, X/H \tag{46}$$

The relationship between $H\Psi$ and p_c is given by:

$$H\Psi = \frac{9}{8} B_a p_a \left[\frac{p_i}{p_c}\right]^2 \tag{47}$$

Using Equation 39, Equations 42 through 44 can be rewritten as functions of p_i^2. Neglecting the C_s term in Equation 42, the results are condensed as follows:

$$p_i^2 = p_a X \left[\frac{n \cdot B_a}{C_{m,a}}\right]^{1/2} \tag{48}$$

with n = 1 for minimum plate height conditions, n = 3 for minimum time conditions for a given column (L = constant), and n = 2 for minimum analysis time for a requested plate number (N = constant).

Substitution of Equations 32 through 34 in Equation 11 yields:

$$\left[\frac{H}{\bar{u}}\right]_{\min H} = \frac{3}{2}\frac{p_i}{p_a} C_{m,a} + \frac{3}{2} C_s \tag{49}$$

$$\left[\frac{H}{\bar{u}}\right]_{L,\min t} = \frac{p_i}{p_a} C_{m,a} + C_s \tag{50}$$

$$\left[\frac{H}{\bar{u}}\right]_{N,\min t} = \frac{9}{8}\frac{p_i}{p_a} C_{m,a} + C_s \tag{51}$$

The inlet pressures can be expressed as a function of p_c. Equation 47 can be converted into:

$$p_i^2 = \frac{8}{9} p_c^2 \frac{H}{\Psi} \frac{\Psi^2}{B_a p_a} \tag{52}$$

which, after substitution of Equation 11, yields:

$$p_i^2 = p_c^2 \left[1 + \left\{\frac{C_{m,a}}{p_a} + \frac{4}{3}\frac{C_s}{p_i}\right\} \frac{\Psi^2}{B_a p_a}\right] \tag{53}$$

Insertion of the three Ψ values from Equations 42 through 44 gives:

$$p^2_{i,\min H} = 2\,p_c^2 \cdot \frac{\frac{p_i}{p_a} C_{m,a} + C_s}{\frac{p_i}{p_a} C_{m,a} + \frac{2}{3} C_s} \tag{54}$$

$$p^2_{i,L,\min t} = 4\,p_c^2 \cdot \frac{\frac{p_i}{p_a} C_{m,a} + C_s}{\frac{p_i}{p_a} C_{m,a}} \tag{55}$$

$$p^2_{i,N,\min t} = 3\,p_c^2 \cdot \frac{\frac{p_i}{p_a} C_{m,a} + \frac{8}{9} C_s}{\frac{p_i}{p_a} C_{m,a}} \tag{56}$$

For thin-film columns ($C_s << C_{m,a}$), Equations 54 through 56 reduce to $p_i^2 = n \cdot p_c^2$, with n = 2 (minimum H), n = 4 (minimum t, L constant), and n = 3 (minimum t, N constant). Note that p_c and L are generally not equal in these instances.

Substitution of Equation 49 through 51 in Equation 21 for vacuum outlet operation of thin-film columns, yields:

$$t_{R,\min H} = N(1 + k)\,\frac{3}{2}\sqrt{2}\,\frac{p_c}{p_a}\,C_{m,a} \tag{57}$$

$$t_{R,L,\min t} = N(1 + k)\,2\,\frac{p_c}{p_a}\,C_{m,a} \tag{58}$$

$$t_{R,N,\min t} = N(1 + k)\,\frac{9}{8}\sqrt{3}\,\frac{p_c}{p_a}\,C_{m,a} \tag{59}$$

The factors $3\sqrt{2/2}:2:9\sqrt{3/8}$ are 2.12:2:1.95.

Substitution of Equations 46, 2, and 3 in Equations 57 through 59 gives:

$$t_R = n\,r\,N^{3/2}\,\frac{11k^2 + 6k + 1}{4(k + 1)}\left[\frac{\eta}{p_a D_{m,a}}\right]^{1/2} \tag{60}$$

where n represents the previously mentioned factors from Equations 57 through 59. Combining Equation 60 with resolution Equation 22, thereby eliminating N, yields:

$$t_R = 16n\,R_s^3\,r\,\frac{(k + 1)^2\,(11k^2 + 6k + 1)}{k^3}\,\frac{\alpha^3}{(\alpha - 1)^3}\left[\frac{\eta}{p_a D_{m,a}}\right]^{1/2} \tag{61}$$

Equation 61 had been published earlier by Guiochon[33] and Leclercq et al.[29] The constant 16n equals $24\sqrt{2}$ (= 33.9), 32, and $18\sqrt{3}$ (= 31.2), respectively, for the three optima.

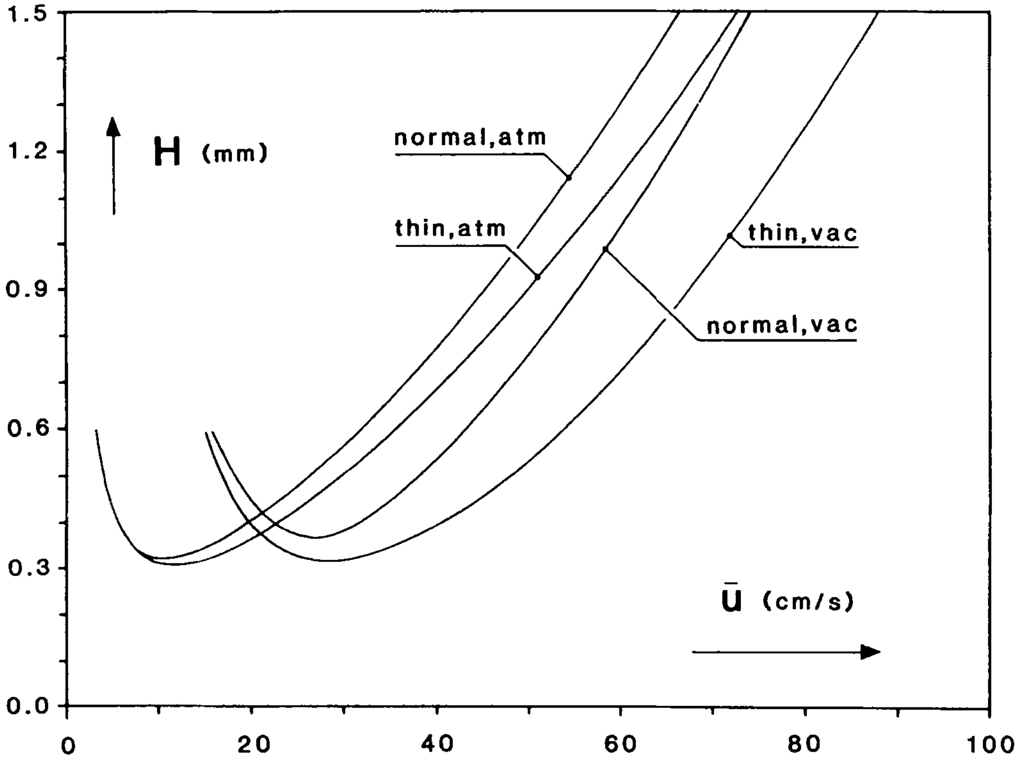

FIGURE 2. Measured H vs. ū curves with nitrogen carrier gas at atmospheric and vacuum outlet (Solute: *n*-dodecane tuned to k = 2 by adjusting T_c. Columns: 0.38-mm I.D. SE-30; "thin" L = 30 m, d_f = 0.4 μm, T_c = 127°C; "normal" L = 34 m, d_f = 1 μm, T_c = 149°C.)

V. SPEED OF ANALYSIS

Equations 38 and 61 clearly show all factors affecting the speed of analysis. If fast chromatographic separations are required, two conditions should be met for any given column. First, vacuum outlet conditions should be employed (see Equation 38). Second, hydrogen or helium should be used as a carrier gas because these gases show the lowest $\eta/D_{m,a}$ ratio.[17,26] Equation 61 indicates that the analysis times in vacuum outlet chromatography, relative to the "best" gas (hydrogen), are hydrogen — 2, helium — 3, and nitrogen — 5, which are not as dramatic as stated by Giddings.[17] Figures 2 and 3 show measured H vs. ū curves for nitrogen and helium, respectively. The gas velocities at the corresponding minima of the curves are higher with helium than with nitrogen, as predicted. The shift of the minima to higher gas velocities by decreasing the column outlet pressure from atmospheric to vacuum is also evident.

Equations 38 and 61 reveal a second- to third-power dependence of the retention time, t_R, on $\alpha/(\alpha - 1)$ and R_s. Hence, the stationary phase should be carefully selected and an unnecessarily large resolution should be avoided. The stationary phase and the separation temperature should be tuned to yield solute capacity factors around k = 1.76, for which the k-containing terms in Equations 38 and 61 approach minimum values,[33] while maximizing the relative retention α.

Once the carrier gas, the capacity factor k, the relative retention α, and the resolution R_s have been selected and the column is operated at vacuum outlet, the separation speed can be further increased by employing linear gas velocities higher than the optimum value.[28]

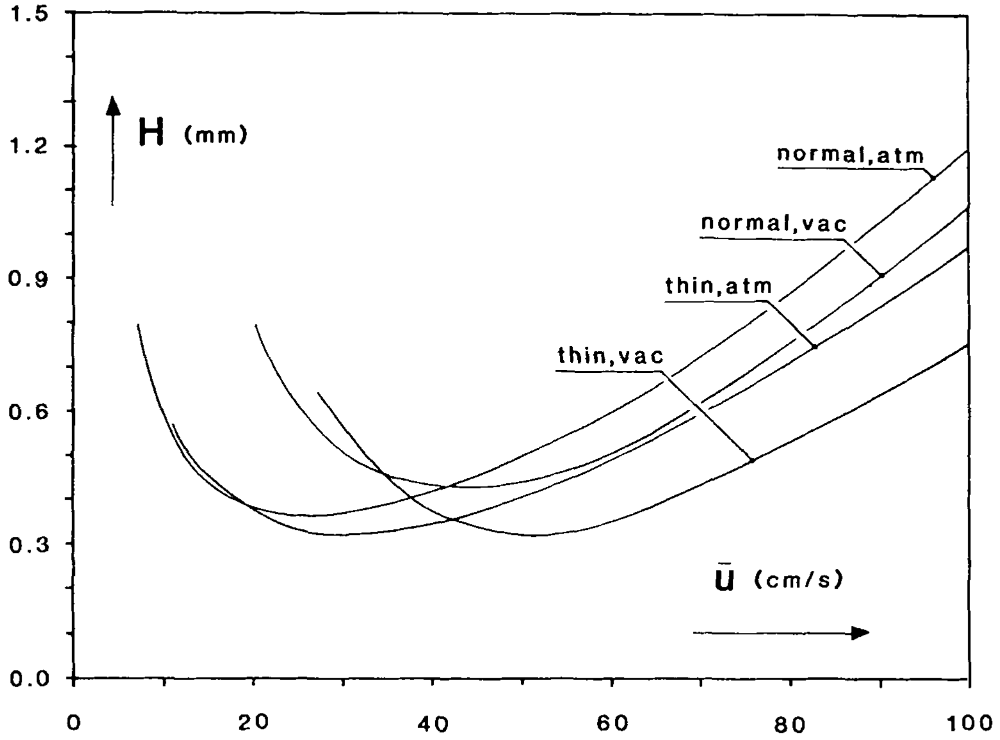

FIGURE 3. Measured H vs. ū curves with helium carrier gas at atmospheric and vacuum outlet (columns and conditions are the same as in Figure 2).

For thin-film columns with vacuum outlet, the inlet pressure required for minimum time operation is $\sqrt{3/2}\,p_{i,\mathrm{min}\,H}$[17,27] (see Equations 54 and 56).

The best possibility to shorten analysis times for a given separation problem is to reduce the column inner diameter 2r (see Equations 38 and 61). Since H is directly proportional to r (for thin-film columns), the column length can be reduced in proportion to r while maintaining the required resolution.[26] For short, low plate number columns working at low pressure drops, the optimum carrier gas velocity is inversely proportional to the column diameter, so that t_R is found to decrease with the square of r. For columns with high plate numbers and, hence, large pressure drops (viz., vacuum outlet), the analysis time is directly proportional to the column diameter, while ū is no longer dependent on r.

Figure 4 is an example of a "fast" chromatogram obtained with a 50-μm I.D. capillary column. This demonstrates that analysis times are, indeed, five times shorter than the 1.5 h needed with conventional 0.25-mm I.D. columns (with the same plate number). Narrow-bore columns can also be used to generate extremely high plate numbers in an affordably reasonable time. Figure 5 is the last part of a chromatogram obtained with a 95 m × 65 μm column having one million theoretical plates.

By operating a given column at vacuum outlet, the maximum attainable plate number is decreased (see Figures 2 and 3) because the C_s term becomes relatively more important and $N{\cdot}f_1$ is constant.[26,34] However, the column can be lengthened to compensate for this loss. If the required plate number, N, for a given separation problem is kept constant, the gain, G_N, in speed of analysis by using a (longer) column at vacuum outlet, compared with the same (but shorter) column operated at atmospheric outlet (all other operational conditions being constant), follows from Equations 21, 33, and 49:

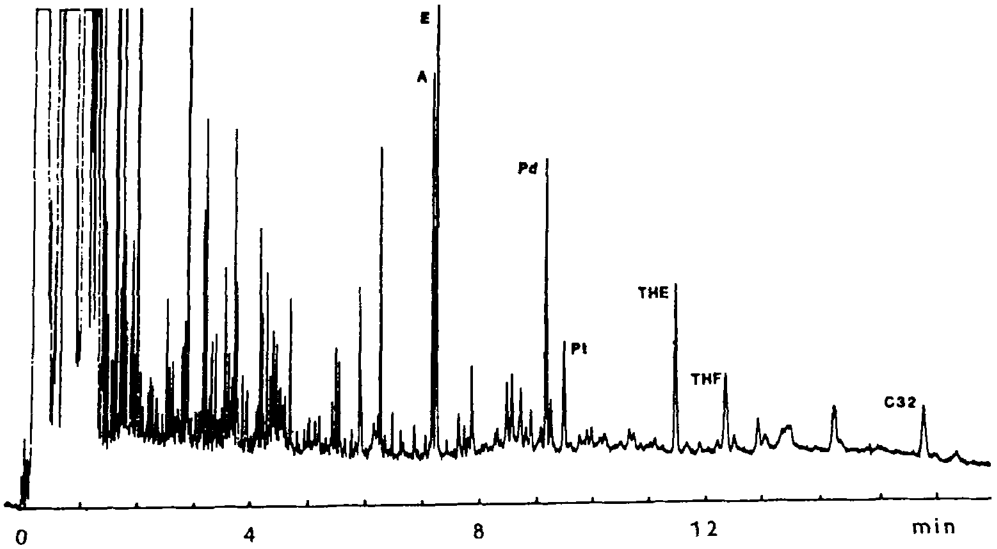

FIGURE 4. Urinary steroid profile of a normal adult female from a 6.7 m × 50 μm I.D. OV-1 column. (Carrier gas helium, inlet pressure 10 bar, splitless injection. Temperature program: 1 min 75°C, 40°C/min to 260°C. Compounds: methoxime trimethylsilyl derivatives of A = androsterone, E = etiocholanolone, Pd = Pregnanediol, Pt = Pregnanetriol, C32 = *n*-dotriacontane.)

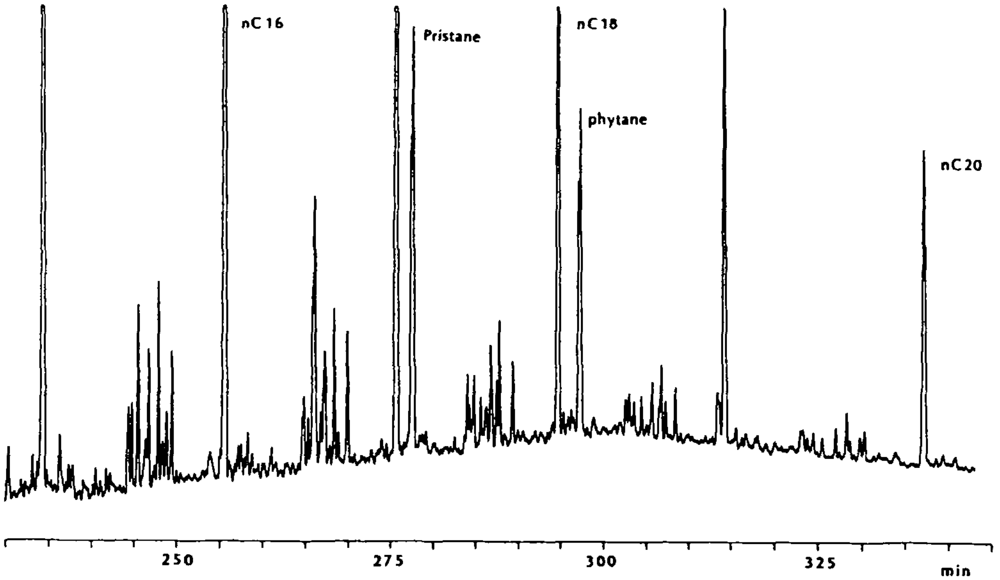

FIGURE 5. Partial gas chromatogram of a Dutch natural gas condensate obtained with a 95 m × 65 μm I.D. OV-1 column having one million theoretical plates. (Carrier gas nitrogen, inlet pressure 19 bar, split injection. Temperature program: 10 min 50°C, 0.6°C/min to 220°C.)

$$G_N = \frac{2\left[2\,C_m \frac{p_o}{p_a}\frac{f_1}{f_2} + C_s\,(3 - f_2P)\right]_{atm}}{3\left[C_m \frac{p_i}{p_a} + C_s\right]_{vac}} \tag{62}$$

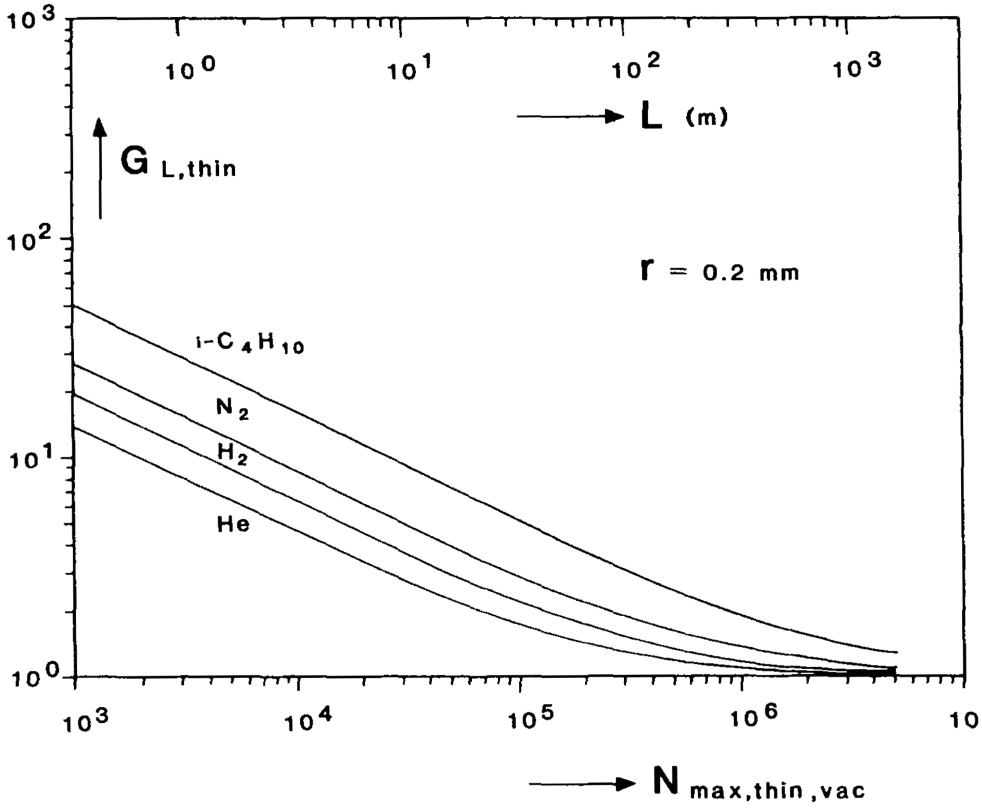

FIGURE 6. Gain in speed of analysis, by operating given thin-film columns at vacuum compared with atmospheric outlet, as a function of the maximum attainable plate number, for selected carrier gases. (r = 0.2 mm, T_c = 127°C, solute: *n*-dodecane. The length axis is valid for k = 2.) (From Leclercq, P. A. and Cramers, C. A., *J. High Resol. Chromatogr. Chromatogr. Commun.*, 10, 269, 1987. With permission.)

Interpretation of this equation is very complicated. Evaluation is possible only in boundary cases, such as for relatively thin-film columns ($p_aC_s << p_iC_m$).

Under minimum plate height conditions, the retention time of a solute in a thin-film open-tubular column is given by a combination of Equations 21, 33, and 3:

$$t_R = \frac{11k^2 + 6k + 1}{12(1 + k)} \frac{f_1\bar{p}}{p_aD_{m,a}} r^2N \tag{63}$$

Vacuum outlet operation of a given thin-film column under minimum plate height conditions yields analysis times as given by Equation 60, with n = $3\sqrt{2}/2$.

The gain, G_L, in analysis time by operating a given thin-film column (length L and r constant) at vacuum outlet instead of atmospheric outlet follows from Equations 63 and 60:

$$G_L = \frac{t_{R,atm}}{t_{R,vac}} = \frac{r\,\bar{p}_{atm}}{4\,(2\eta\, p_aD_{m,a}\, N_{vac})^{1/2}} \tag{64}$$

where use was made of the relation $(N \cdot f_1)_{atm} = 9/8\ N_{vac}$.[26,34]

Equation 64 shows that the gain is proportional to the column diameter and inversely proportional to the square root of the plate number. Therefore, vacuum outlet operation is particularly beneficial for short- and wide-bore columns.[17,26,31] This can also be concluded from Figure 6, where G_L is plotted as a function of the plate number for selected carrier

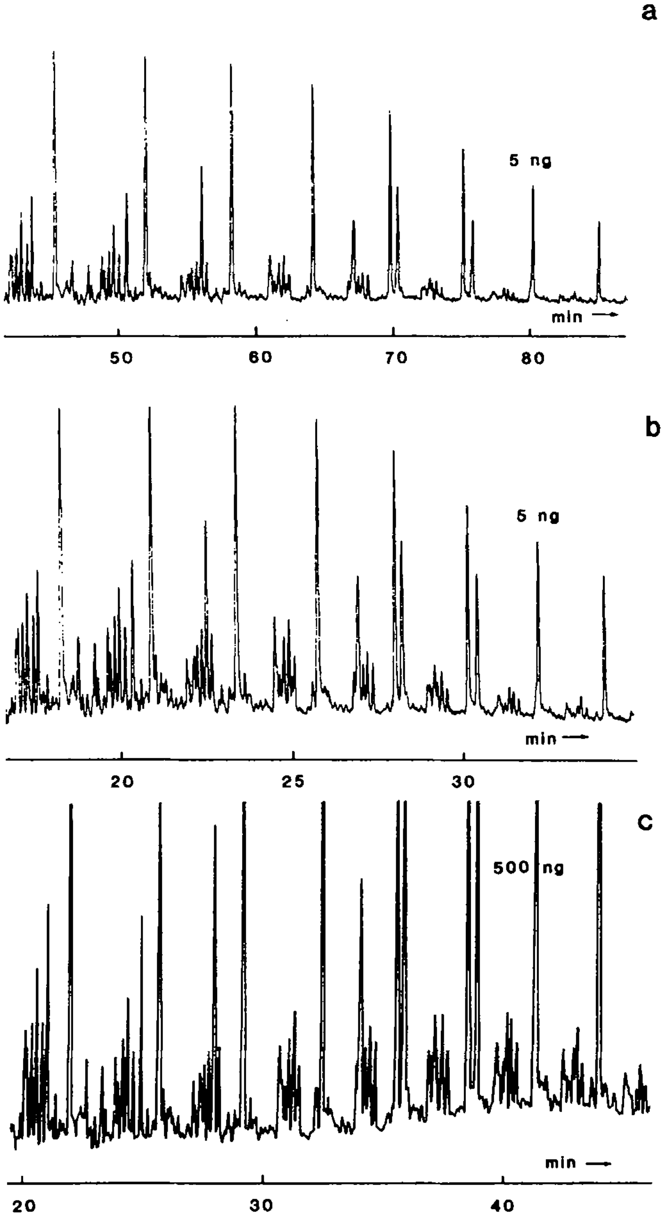

FIGURE 7. Partial chromatograms of a Dutch natural gas condensate obtained with 0.38-mm I.D. SE-30 columns at atmospheric (a) and vacuum outlet (b and c). (Carrier gas nitrogen, split injection. Columns are as in Figure 2; for a and b, $L = 30$ m, $d_f = 0.4$ μm, temperature programmed from 58 to 200°C at 8°C/min; for c, $L = 34$ m, $d_f = 1$ μm, programmed from 80 to 222°C at 8°C/min.)

gases. Figure 7 shows partial chromatograms obtained at minimum plate height conditions at atmospheric and vacuum outlet. Comparison of the lower and upper traces shows that the negative effect of the thicker stationary phase on the optimum analysis time is more that compensated for by the effect of vacuum outlet operation.

Notwithstanding the validity of Equation 64, both Equations 63 and 60 indicate that retention times decrease with smaller column diameters. The question then arises: when are (wide-bore) vacuum outlet columns faster than (narrow-bore) columns operated at atmospheric outlet? When comparing (thin-film) columns with different diameters for a given separation problem ($N_{required} = N_{atm} = N_{vac}$), the capacity factor, k, is kept constant, i.e., the phase ratio of the columns and the separation temperature should be constant. Under these conditions, vacuum outlet is faster than atmospheric outlet operation whenever $t_{R,atm} > t_{R,vac}$ or, using Equations 63 and 60, whenever:

$$(f_1\ \bar{p}\ r^2)_{atm} > \frac{9}{2}(2\eta\ p_a\ D_{m,a}\ N)^{1/2}\ r_{vac} \tag{65}$$

under minimum plate height conditions. This inequality has been evaluated numerically.[31] The conclusions of this recent study are condensed here.

Vacuum outlet columns always yield analysis times shorter than atmospheric-outlet columns, as long as the inner diameter of the former is smaller than, or equal to, that of the latter. The gain in speed of analysis by vacuum outlet operation is reduced by decreasing column diameters and increasing maximum plate numbers.

Vacuum outlet operation of columns with a diameter larger than atmospheric outlet columns can still be beneficial, but only for wide-bore columns with relatively low plate numbers. In these instances, the gain in analysis times is only marginal, the more so because low-pressure-drop (atmospheric outlet) columns can be operated advantageously at gas velocities beyond the optimum ones, while vacuum outlet columns require optimal velocity tuning.[28]

The application of high plate number (long, narrow-bore) columns at vacuum outlet no longer increases the attainable speed of analysis and is advantageous only if secondary factors are important. Apart from trivial advantages as in GC/MS,[29] vacuum outlet is, for example, an excellent way to reduce effective detector dead volumes (hot wire, electron capture,[35] and light pipes for Fourier transform infrared spectrometry [FTIR]).

Obviously, the choice between application of wide-bore or narrow-bore columns can also be governed by considerations other than striving for minimum operation time. Sample capacity and detection limits are also affected by column dimensions, as is elaborated in the next section.

At this point, a few remarks on the practical application of the presented theory are appropriate. As mentioned previously, comparisons of columns of different dimensions, and particularly of columns operated at different pressures, have given rise to much confusion in the literature. The importance of well-defined normalized conditions in these comparisons cannot be stressed enough. For example, theory predicts that vacuum outlet operation of a capillary column cannot be compared with atmospheric outlet operation when the inlet pressure is lowered simply by one bar, as is still common practice.[36] Rather, for thin-film columns, the inlet pressures for minimum plate height conditions relate as follows:[26]

$$p^2_{i,min\ H,vac} = p^2_{i,min\ H,atm} - p_a^2 \tag{66}$$

A practical example is illustrative: suppose a given column, operated at atmospheric outlet under minimum plate height conditions, has an optimum inlet pressure of 1 bar gauge reading, which is 2 bar absolute. Vacuum outlet operation of this column at minimum plate height conditions thus requires an inlet pressure of $p_i = \sqrt{2^2 - 1^2}$ bar $= 1.73$ bar.

A computer program for the calculation of the various optimum conditions for any open tubular column, operated at arbitrarily selectable outlet pressures, has been published.[37] Data on the temperature dependence of carrier gas viscosities and binary solute/phase diffusivities can be found in the literature. For hydrogen, helium, or nitrogen, carrier gas viscosities can best be calculated according to Ettre[38] and gas phase (*n*-alkane/carrier gas) diffusion coefficients according to Fuller et al.[39] Data on solute/stationary phase diffusion coefficients are scarce. Gas/liquid diffusivities for *n*-alkanes in methylsilicone phases have been reported by Hawkes et al.[40,41]

VI. SAMPLE CAPACITY

Thus far, only column characteristics have been considered. Extra-column contributions to peak broadening are important also, especially with respect to column resolution or efficiency.

The sequence, injection — chromatographic separation — detection — signal handling, etc., can be seen as a series of independent unit operations. Hence, the rule of additivity of variances applies:

$$\sigma_t^2 = \sigma_c^2 + \sigma_i^2 + \Sigma(\sigma_o^2) \tag{67}$$

where σ_t^2 is the overall or apparent peak variance, σ_i is the injection bandwidth, σ_c is the chromatographic band broadening, and $\Sigma(\sigma_o^2)$ accounts for the sum of remaining extra-column variances (caused by time constants of the detector and signal amplifier, digitizing sampling frequency, etc.). Assuming that the injection of the sample is the only source of extra-column peak broadening, and expressing the injection bandwidth in proportion to the bandwidth caused purely by the separation process, or $\sigma_i = b{\cdot}\sigma_c$, then:

$$\sigma_t = \sqrt{1 + b^2}\,\sigma_c \tag{68}$$

and so the overall plate number, N_t, is reduced to:

$$N_t = \frac{N_{max}}{1 + b^2} \tag{69}$$

The b factor has an effect on both the apparent peak resolution, R_t, and the detector response, R_d, (see Equation 22b):

$$R_t = \frac{\Delta t_R}{4\sigma_t} = \frac{\Delta t_R}{4\sigma_c\sqrt{1 + b^2}} = \frac{R_s}{\sqrt{1 + b^2}} \tag{70}$$

and

$$R_d = F_cC_i\,S\,\frac{\sigma_i}{\sigma_t} = F_cC_i\,S\,\frac{b}{\sqrt{1 + b^2}} \tag{71}$$

where F_c is the volumetric column flow rate, C_i is the injected solute concentration, and S is the detector sensitivity.

The demands of a sufficiently large resolution and a maximum detector response are incompatible. Maximum detector response requires injection bandwidths much larger than the standard deviation in elution time determined by the chromatographic process. Maximum resolution is obtained only for infinitely small injection bandwidths. Although the optimum compromise very much depends upon the specific analytical problem, in general the product of R_t and R_d should be maximized. This maximum is achieved for $b = 1$.[42] This means that optimum detector response is obtained at 40% extra-column band broadening by the injection, compared with 100% by the chromatographic process. In practice, a 10% reduction of the plate number, i.e., a 5% reduction in resolution (see Equations 69 and 70),[43] is more acceptable. This corresponds to an injection bandwidth of about 50% of the square root of the column variance ($b = 0.5$).

The sample capacity, Q_s, is the maximum amount of a component which can be injected on a column giving a limited (e.g., 10%) increased peak width. In their fundamental paper published in 1956,[44] van Deemter et al. related the sample capacity of a column to the volume of a theoretical plate. This was elaborated by Keulemans,[45] who defined the maximum allowable injection volume of sample vapor, V_{max}, as follows:

$$V_{max} = a \cdot V_{eff} \sqrt{N} \tag{72}$$

where a is a factor, $V_{eff} = V_g (1 + k)/N$ is the effective volume of a plate, and $V_g = \pi (r - d_f)^2 L$ is the volume of the gas phase in the column. Hence,

$$V_{max} = a \cdot \pi (r - d_f)^2 \sqrt{LH} (1 + k) \tag{73}$$

Using this equation, Ettre[43] has extensively discussed the influence of changes of column parameters on the sample capacity.

The injection volume, V_{inj}, also can be expressed as:

$$V_{inj} = \sqrt{K_i} F_c \sigma_i \tag{74}$$

where K_i is the injection profile factor with a value of 12 for plug injections.[46,47]

Elaboration of Equation 74 leads to Equation 73, with $a = b \cdot \sqrt{K_i}$, b being defined as σ_i/σ_c. Given a 10% contribution of the injection bandwidth relative to the overall peak width ($b = 0.5$), $a = \sqrt{3} = 1.73$ for plug injections. This value is 4 to 100 times higher than that found in practice.[45] It has been reported that a depends on the solute and some unspecified parameters.[43] A suitable explanation for this discrepancy has yet to be found.

According to the general gas law:[48]

$$V_{max} = \frac{Q_s}{M} \frac{R\,T_c}{p_s} \tag{75}$$

where R is the universal gas constant, T_c is the column temperature, M is the molecular weight of the solute, and p_s is its saturated vapor pressure at T_c.

Combining Equations 73 and 75 yields:

$$Q_s = a \cdot \pi \frac{p_s M}{R\,T_c} (R - d_f)^2 \sqrt{LH} (1 + k) \tag{76}$$

In Figure 8, this relationship is plotted for 0.5-mm I.D. columns as a function of the film thickness for various plate numbers. The advantage of the use of wide-bore, thick film columns for the sample capacity is directly reflected in Equation 76. Note that $(LH)^{1/2}$ is proportional to the column diameter and, hence, the sample capacity is proportional to the third power of the column radius. Furthermore, k includes the volume of the stationary phase related to the film thickness d_f:

$$k = K/\beta \tag{77}$$

where K is the partition coefficient and β is the phase ratio.

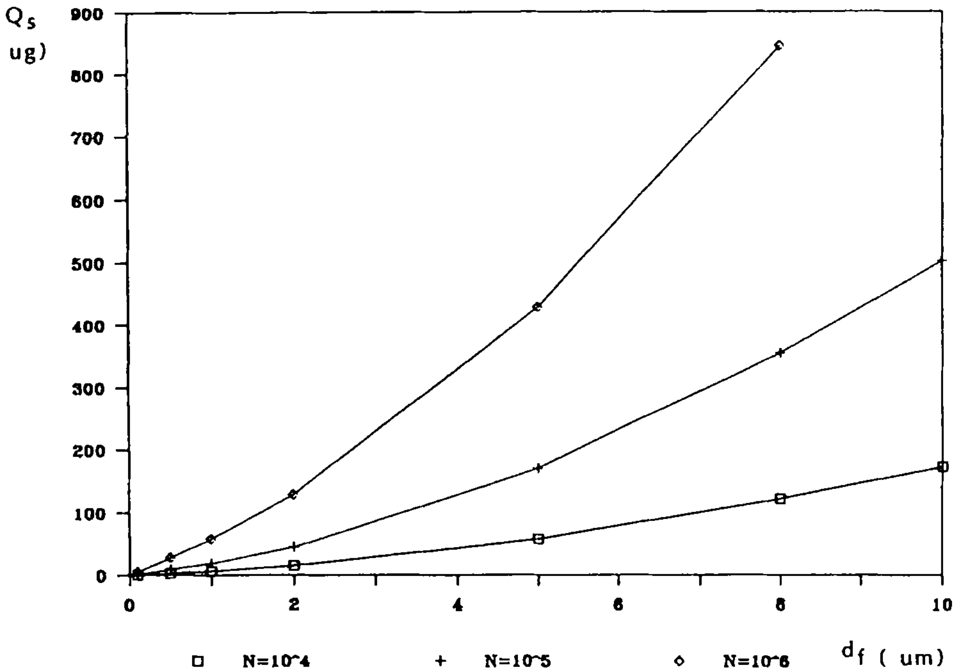

FIGURE 8. Calculated sample capacities (amounts of solute that cause 10% peak broadening by column overloading) for a 0.5-mm I.D. column as a function of the film thickness, for three maximum plate numbers. (Phase system: helium/SE-30; *n*-dodecane as solute with k = 2 by temperature tuning; factor a = 1.)

$$\beta = \frac{V_g}{V_l} = \frac{(r - d_f)^2}{d_f(2r - d_f)} \approx \frac{r}{2d_f} \tag{78}$$

Combining Equations 76 through 78 yields:[49]

$$Q_s = a \cdot \pi \frac{p_s M}{R\,T_c} \sqrt{LH}\, r^2 \left(1 + \frac{2d_f}{r} K\right) \tag{79}$$

The partition coefficient, K, is concentration dependent whenever the distribution isotherms are nonlinear, as encountered normally in practice. Binary solute/stationary phase mixtures are often nonideal solutions and Raoult's law is no longer valid. An additional "Raoult law factor", the activity coefficient of a solute in the stationary liquid phase, plays a role:[48]

$$p_g = \gamma(y)\, y\, p_s \tag{80}$$

where p_g is the vapor pressure of the component in the mobile gas phase, γ is the activity coefficient, and y is the mole fraction of the solute in the liquid phase.

The effect of the solute mole fraction, y, on γ follows a Margules relation:[50,51]

$$\log \gamma = (1 - y^2) \log \gamma^0 \tag{81}$$

where γ^0 is the activity coefficient at infinite dilution. (γ^0 values are listed in handbooks.)

The partition coefficient can, hence, be expressed as:[51]

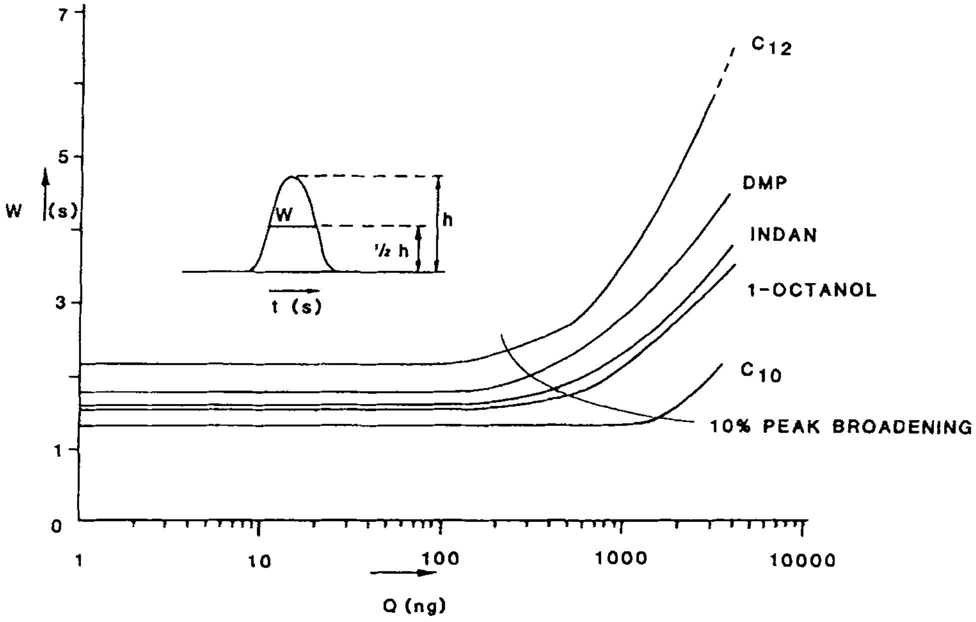

FIGURE 9. Measured peak widths as a function of the injected amounts of several solutes. The 10% peak broadening curve indicates sample capacities. (Column: 25 m × 0.33 mm I.D. × 0.52 μm SE-30, T_c = 140°C. Helium carrier gas, p_i = 1.5 bar, p_o = 1 bar. Split injection. Compounds: C10 = *n*-decane, DMP = dimethylphenol, C12 = *n*-dodecane.)

$$K = \frac{C_l}{C_g} = \frac{y\ m}{p_g/(RT_c)} = \frac{m\ R\ T_c}{\gamma\ p_s} \tag{82}$$

where C_l and C_g are the concentrations of the solute in the liquid and gas phase, respectively, and m is the number of moles of stationary phase per unit volume (or density per mole).

Equations 81, 82, and 79 indicate that high concentrations of solute will influence the partition coefficient and, hence, the sample capacity. Ideally, for a solute/stationary phase system with $\gamma^o = 1$, peak symmetry can be maintained to high solute concentrations. Such systems are rare: only apolar solutes (viz., hydrocarbons) on nonpolar stationary phases approach this ideal situation. Dissimilar solute/solvent systems usually give larger values of γ^o and, hence, strong deviations from linearity even at low mole fractions. When $\gamma^o >> 1$ (e.g., for alcohols on most liquid phases), asymmetric ("overloaded") peaks will result, even at very limited inlet concentrations.

Recent experimental results from the authors' laboratory indicate that the current definitions for sample capacity are not appropriate (see Figures 9 and 10).[52] On nonpolar columns, peak asymmetry by column overloading becomes apparent for sample amounts an order of magnitude less than those causing 10% peak broadening or 5% loss in resolution, even for hydrocarbons. For further elaboration on overloading effects, the reader is referred to the literature.[50,51]

VII. DETECTION AND IDENTIFICATION LIMITS

The detection limits for a component are determined by the column and detector properties. Two types of detectors have to be considered: mass flow-sensitive (e.g., flame ionization) detectors and concentration-sensitive (e.g., hot wire) detectors.

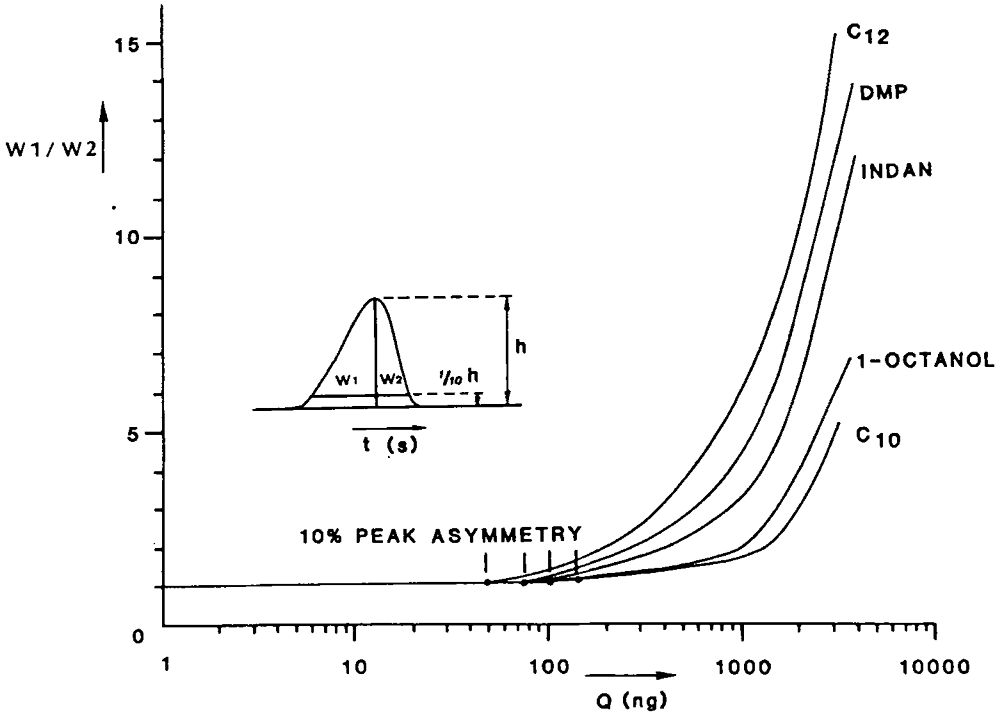

FIGURE 10. Measured peak asymmetries as a function of the injected amount of several solutes. (Conditions and compounds as in Figure 9.)

A. Minimum Detectable Amounts

For a mass flow-sensitive detector, the minimum detectable amount, defined as the mass of a compound to be introduced onto the column in order to give a detector signal of four times the noise level, is given by:

$$Q_o^m = \sqrt{2\pi}\,\frac{4R_n}{S}\,\sigma_t = \sqrt{2\pi}\,\frac{4R_n}{S}\,\sqrt{1 + b^2}\,\frac{t_R}{\sqrt{N}} \qquad (83)$$

and for a concentration-sensitive detector, it is given by:

$$Q_o^c = \sqrt{2\pi}\,\frac{4R_n}{S}\,\sigma_t\,F_d \qquad (84)$$

where R_n is the detector noise, S is the detector sensitivity, σ_t is the actual standard deviation of the Gaussian-shaped peak, and F_d is the volumetric gas flow rate through the detector cell at the detector temperature and pressure.

As can been seen from Equations 83 and 84, Q_o is proportional to the peak width. For a given plate number N, Q_o is proportional to the retention time t_R. Therefore, the minimum detectable amount for a mass flow-sensitive detector increases proportionally with the square of the column diameter if the pressure drop is low (see Equation 63).

For high plate number columns, Q_o^m is linearly dependent on the column radius r (see Equation 60). Very small quantities can be detected on narrow-bore columns, the more so because narrower peaks result in a higher signal and, thus, in a better signal-to-noise ratio when a fixed amount of sample is introduced.

The expressions for the minimum detectable amounts can be rearranged using Equations

68, 1a, 21, and 69. For minimum plate height conditions, incorporation of Equation 33 finally yields:

$$Q_o^m = \sqrt{2\pi}\,\frac{4R_n}{S}\sqrt{N_t}\,(1 + b^2)\,(1 + k)\left[2C_{m,a}\frac{\bar{p}f_1}{p_a} + C_s\,(3 - f_2P)\right] \tag{85}$$

$$Q_o^c = Q_o^m\,F_d \tag{86}$$

Equations 85 and 86 have been evaluated in detail by Noij et al.[42] For low pressure drop (P → 1) thin-film columns, these equations can be simplified. Substitution of Equations 68, 1a, 63, and 69 in Equation 83 gives:[42]

$$Q_o^m = \frac{\sqrt{2\pi}}{3}\,\frac{R_n}{S}\,\frac{11k^2 + 6k + 1}{(k + 1)}\sqrt{N_t}\,(1 + b^2)\,\frac{p_o}{p_aD_{m,a}}\,r^2 \tag{87}$$

When F_d is equal to the column flow ($F_d = F_c = \pi r^2 u_{o,\min H}$) and neglecting the film thickness with respect to the column radius, the combination of Equations 86, 87, and 20 yields:

$$Q_o^c = 4\pi\,\frac{\sqrt{2\pi}}{3}\,\frac{R_n}{S}\sqrt{11k^2 + 6k + 1}\,\sqrt{N_t}\,(1 + b^2)\,r^3 \tag{88}$$

For high pressure drop (P → ∞) thin-film columns, Equation 60 should be used in calculations instead of Equation 63. After inclusion of Equation 69, Equations 85 and 86 finally read:

$$Q_o^m = 3\sqrt{\pi}\,\frac{R_n}{S}\,\frac{11k^2 + 6k + 1}{(k + 1)}\,N_t\,(1 + b^2)^{3/2}\left[\frac{\eta}{p_aD_{m,a}}\right]^{1/2} r \tag{89}$$

$$Q_o^c = 12\pi\sqrt{3\pi}\,\frac{R_n}{S}\sqrt{11k^2 + 6k + 1}\,N_t\,(1 + b^2)^{3/2}\left[\frac{\eta p_aD_{m,a}}{p_o}\right]^{1/2} r^2 \tag{90}$$

B. Minimum Analyte Concentrations

The minimum analyte concentration in the injected sample is related to the minimum detectable amount by:

$$C_o = \frac{Q_o}{V_{inj}} \tag{91}$$

where V_{inj} is the injected sample volume at the same temperature and pressure as C_o. Combining the relationships expressed in Equations 91, 83, 84, 68, and 74 finally yields (for both types of detectors and thin-film columns):

$$C_o^m = \sqrt{\frac{2}{3\pi K_i}\,\frac{R_n}{S}}\,\frac{\sqrt{11k^2 + 6k + 1}}{(k + 1)}\,\frac{\sqrt{1 + b^2}}{b}\,\frac{p_o}{p_ad_{m,a}}\,\frac{1}{r} \tag{92}$$

$$C_o^c = 4\sqrt{\frac{2\pi}{K_i}\,\frac{R_n}{S}}\,\frac{\sqrt{1 + b^2}}{b} \tag{93}$$

C. Detection Limits

A large effect of the column inner diameter on the minimum detectable amount is shown by Equations 87 through 90. A second- to third-power dependence exists for concentration-sensitive detectors, whereas for mass flow-sensitive detectors, Q_o is proportional to r up to r^2. When differently sized columns with equal plate numbers are compared, injection of a fixed amount of a solute will give the highest detector signals for the smallest bore columns.

This does not, however, imply that narrow-bore capillary columns should be used in trace analysis. If a fixed relative contribution of the injection bandwidth to the overall peak variance is allowed, Equation 73 shows that a decreased column radius and a consequently reduced plate height drastically restrict the maximum sample volume to be injected. Therefore, the minimum detectable concentration is not proportional to the minimum detectable amount. Equation 92 shows that the minimum analyte concentration in the injected sample, C_o, is inversely proportional to the column inner diameter when a mass flow-sensitive detector is used. C_o is independent of r for concentration-sensitive detectors (see Equation 93). This means that, unless a sample preconcentration technique is employed, highly diluted samples can best be analyzed using a wide-bore column (in combination with a mass flow-sensitive detector), allowing the introduction of a relatively large sample. It should be noted that a large column inner diameter has the drawback of long analysis times.

When a particular separation problem requires a larger plate number, a longer column should be employed if all the other parameters are kept constant (i.e., r, k, α, and b). The influence of the plate number on the minimum detectable amount and the minimum analyte concentration is similar for both detector types (see Figure 11). Depending upon the pressure drop, Q_o increases proportional to the square root of N_t up to linearly with N_t. Although C_o is not affected by the column length, excessive plate numbers should be avoided because of the needlessly long analysis times (see Equations 60 and 63). Separation of a "critical pair" of components at a small plate number is enabled by the application of a highly selective stationary phase. Furthermore, the peak resolution should not be better than needed for baseline separation because of the undesired effect on t_R and Q_o.

The detectability of trace compounds is unfavorably influenced by large k values. Both Q_o and C_o increase with increasing capacity factor for a mass flow-sensitive detector. When a concentration-sensitive detector is used, the effect on Q_o is less pronounced and C_o is unaffected. The GC oven temperature and the stationary phase film thickness should be selected in such a way that the smallest possible k values are obtained. However, one must realize that the resolution drops rapidly when k is less than one, resulting in a larger plate number required to establish a certain resolution. As discussed previously, this counterbalances the advantage of a small k value.

Detection limits are also influenced by the contribution of the injection bandwidth to the overall peakwidth. Small values of b, defined as σ_i/σ_c, have a disadvantageous effect on C_o, whereas this is favorable for Q_o. Large b values drastically reduce the peak resolution. In general, the injection bandwidth should be 10 to 100% of the chromatographic peak broadening ($b = 0.1 - 1$). When an on-column sample enrichment technique is employed (e.g., cryogenic trapping), detectability is favored by narrow-bore columns because the minimum detectable amount decreases more than proportionally with decreasing column inner diameter. Furthermore, narrow-bore capillary columns have the benefit of short analysis times, although at the cost of high inlet pressures.

So far, the stationary phase film thickness has been left out of consideration because of the complexity of the related theoretical treatment. A complete survey of the implications of an increased stationary phase film thickness (d_f) on the minimum detectable amount, as well as on the minimum analatye concentration, was published recently[53] and is summarized here.

Two approaches were followed to study the effect of increasing film thickness. Either the

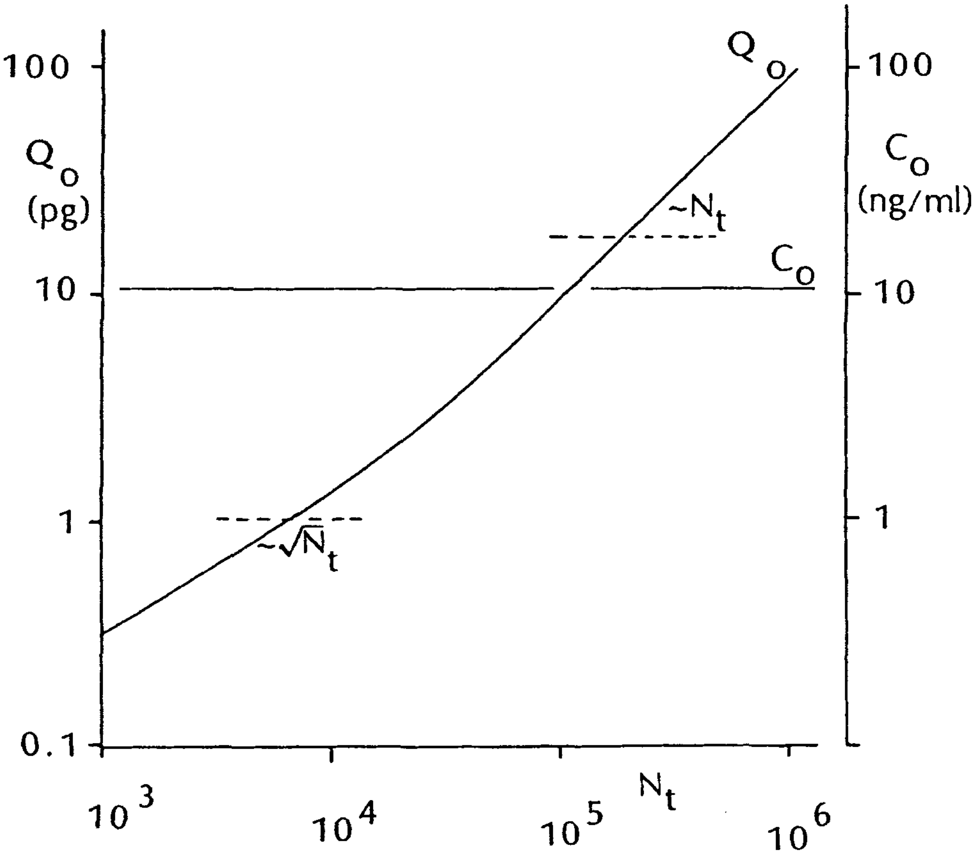

FIGURE 11. Minimum detectable amounts and concentrations as a function of the apparent plate height, for both types of detectors. ($r = 50$ μm, $k = 4$, $b = 0.1$. FID: $S = 10^{-2}$ A.s/g, $R_n = 2 \times 10^{-14}$ A.) (From Noij, Th., Curvers, J., and Cramers, C. A., *J. High Resol. Chromatogr. Chromatogr. Commun.*, 9, 752, 1986. With permission.)

separation temperature was kept constant (option 1), resulting in larger values of the capacity factor, k, or the column temperature was increased to keep k constant (option 2). At constant temperature, C_o always increases with the film thickness for mass flow-sensitive detectors. Wide-bore, thin-film columns offer the lowest value of C_o attainable. For concentration-sensitive detectors, C_o is affected neither by column diameter nor film thickness. The Q_o vs. $1/\beta$ plot (see Figure 12) shows a minimum at constant temperature, suggesting an optimum film thickness for both mass flow- and concentration-sensitive detectors. At elevated temperatures (k constant) in combination with mass flow-sensitive detectors, an optimum film thickness again exists, corresponding with a minimum value of C_o. Q_o always increases with film thickness for both types of detectors.

As indicated previously, in some situations the lowest values of C_o and Q_o are obtained at an increased film thickness, the effect being marginal. As a first guideline for the daily practice of capillary GC with respect to minimum values of C_o and Q_o, the use of thin-film columns is preferred.

D. Identification Limits

In GC/MS, a mass spectrometer can be used in the selected ion monitoring mode, i.e., for recording the ion current at one or more masses. In this mode, the mass spectrometer behaves as a mass flow-sensitive detector.[33] Therefore, the minimum detectable amounts are appropriately described by Equation 89.

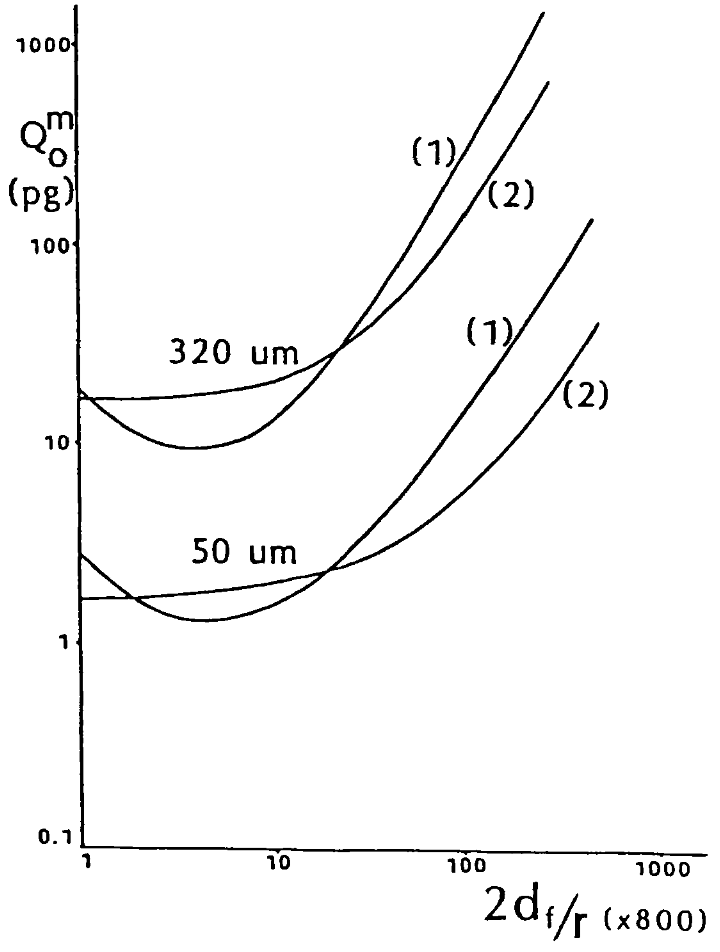

FIGURE 12. Minimum detectable amounts as a function of the relative film thickness for a mass flow-sensitive detector, for narrow- and wide-bore columns. (1) T_c = constant; (2) k = constant. (b = 0.1. Option 1, T_c = 110°C; option 2, k = 4.) (From Noij, Th. and Cramers, C. A., *8th Int. Symp. on Capillary Chromatography*, Vol. 1., Sandra, P., Ed., Huethig, Heidelberg, 1987, 95. With permission.)

In the scanning mode, i.e., recording the ion currents over a certain mass range repetitively, ion statistics become important. Preferably, five to ten mass spectra are acquired during the elution of a chromatographic peak. For this reason, and also to keep mass discrimination effects during one scan within acceptable limits, the scanning speed of the mass spectrometer has to be in proportion to the chromatographic speed of analysis. When the scanning speed is increased in proportion to the separation speed, no effect on the sensitivity is expected. When the amount of sample is kept constant, the number of ions collected during a scan is constant as long as the number of scans per chromatographic peak width is the same. Nevertheless, comparisons of columns with different dimensions, but equal plate numbers, in vacuum outlet GC/MS showed that the observed identification limits are proportional to the analysis time and, hence, to the column diameter (see Equation 60).[29]

Identification limits are defined as the minimal amounts needed to produce interpretable spectra. In conventional capillary column GC/MS, where spectra are acquired at a rate of one per second, identification limits are in the order of 1 ng per compound. The smallest signal that can be detected is a single ion, but statistically such an event is very unreliable when scanning. For this reason, ion statistics dictate that five ions per mass are considered a minimum for reliable detection during scanning at this rate, Hence, requiring a signal-to-noise ratio of 20, the base peak in a scanned mass spectrum should represent at least 100 ions. In order to be interpretable, an average electron impact mass spectrum should, therefore, correspond with at least 10^3 to 10^4 ions collected during one scan. The identification limit thus equals about 10^{-15} C or 10^{-10} to 10^{-9} g of compound per scan, depending on the mass spectral resolution and assuming an ionization efficiency of $1{:}10^6$.

The observed gain in sensitivity of capillary GC/MS by decreasing the column diameter might be explained by a reduction of the noise level by faster scanning. Background ion currents, while varying with mass, are of the order of 10^2 to 10^3 ions per second. Therefore, less background ions are detected in faster scanning experiments. Moreover, the gas flow from narrow-bore columns is much less than from conventional ones (proportional to r^2 for constant plate numbers) and so is the column bleeding mass flow.

VIII. CONCLUSIONS

Recent developments in column technology in capillary GC point in three directions:

1. Improving the selectivity of the phase systems used: synthesis of new polar phases; tuning of polarity by coupled column systems; development of highly specific (e.g., chiral) liquid phases; the use of adsorbants (open tubular columns with porous layers of Al_2O_3, Mol Sieve 5A, or Porapak Q).
2. Narrow-bore, thin-film columns (typically 50- to 100-μm I.D.; 0.05 to 0.1 μm film thickness) having large plate numbers and a high generation speed of plates per unit time — these types of columns emerged from the need for faster and more efficient separations of complex mixtures of organic compounds. Owing to their decreased plate height, extremely narrow peaks are obtained. Detectability is favored as well since narrow peaks result in a better signal-to-noise ratio when a given amount of solute is introduced.
3. Wide-bore, thick-film columns — these columns, with typical dimensions of 0.5-mm I.D. and film thicknesses of 5 μm (bonded phases), have a low generation speed of plates per unit time. However, they offer a large sample capacity and the large carrier gas flows involved enable their use in combination with heat conductivity cells and FTIR techniques.

The working range $W = Q_s/Q_o$ of a column should generally exceed the concentration ratio of the compounds in the sample to be analyzed. If not, the detector response for the trace compounds can only be distinguished from the noise level when the column is overloaded for the main peaks. This may obscure small peaks eluting next to the overloaded peaks. In practice, for high plate number columns, W is proportional to r^2, a distinct advantage of wide-bore columns. The selection of a column inner diameter, therefore, often implies a compromise between speed of analysis and required working range. The largest working range is always obtained with wide-bore, thick-film columns.

Extra-column contributions to peak dispersion should be kept to a minimum. Therefore, the duration of the injection band for a given (high) plate number should be lowered proportionally to the analysis time and, thus, the column radius r. Extremely fast separations (10^4 plates per second) can only be executed with input bandwidths of the order of milliseconds, requiring the use of special sample introduction systems (e.g., fluidic logic sample devices).[54] Split-mode injection allows sample bandwidths between 50 ms and 0.1 s for gases and of the order of 1 s for high-boiling liquid samples.

The time constant τ, of detection/data acquisition should be such that $\tau \leqslant 0.1\sigma_c$. Only for very fast (low plate number) separations does this become critical. Modern instrumentation offers time constants of the order of 0.1 s, allowing the separation of peaks with a σ of the order 1 s. Narrow-bore columns with high plate numbers ($>10^5$) can be exploited without serious difficulties.

SYMBOLS

a = Undefined factor relating theoretically predicted and experimentally observed sample capacities
b = σ_i/σ_c
B_a = $2D_{m,a}$
B_o = $2D_{m,o}$
C_g = Concentration of solute in the gas phase
C_i = Concentration of solute at injection time
C_l = Concentration of solute in the liquid phase
$C_{m,a}$ = Resistance to mass transfer in the mobile gas phase at unit pressure p_a
$C_{m,o}$ = Resistance to mass transfer in the mobile gas phase at column outlet pressure
C_o = Minimum analyte concentration
C_s = Resistance to mass transfer in the stationary liquid phase
d_f = Stationary phase film thickness
$D_{m,a}$ = Solute diffusion coefficient in the mobile phase at unit pressure p_a
$D_{m,o}$ = Solute diffusion coefficient in the mobile phase at column outlet pressure
D_s = Solute diffusion coefficient in the stationary phase
f_1 = Pressure correction factor after Giddings
f_2 = Pressure correction factor after James and Martin
F_c = Volumetric column flow at outlet conditions
F_d = Volumetric detector flow
G_L = Gain in speed of analysis by operating a given column at vacuum instead of atmospheric outlet
G_N = Gain in speed of analysis by operating a lengthened column at vacuum instead of atmospheric outlet (constant N)
h = Peak height at peak apex
H = Plate height
k = Solute capacity factor
k_1 = Capacity factor of the first eluting solute of a "critical pair"
k_2 = Capacity factor of the second eluting solute of a "critical pair"
K = $\beta k = C_l/C_g$ = solute distribution constant (partition coefficient)
K_i = Injection profile factor
L = Column length
m = Number of moles of stationary phase per unit volume
M = Molecular weight of solute
n = Constant
N = Theoretical plate number
N_t = Actual total plate number
p = Pressure
$\bar{p}$ = p_o/f_2 = (length) average column pressure
p_a = Unit pressure (e.g., 1 bar)
p_c = Critical inlet pressure
p_g = Vapor pressure of a solute in the carrier gas
p_i = Column inlet pressure

p_o = Column outlet pressure
p_s = Saturated solute vapor pressure at column temperature
p_x = Local pressure at position x in the column
P = p_i/p_o
Q = Amount of solute introduced in the column
Q_o = Minimum detectable amount
Q_s = Sample capacity = maximum amount of sample that can be injected
R = Gas constant
R_d = Detector response
R_n = Detector noise
R_s = Peak resolution
S = Detector sensitivity
t_R = Solute retention time
$t_{R,1}$ = Retention time of the first eluting solute of a "critical pair"
$t_{R,2}$ = Retention time of the second eluting solute of a "critical pair"
T_c = Column temperature
r = Column inner radius
u = Linear carrier gas velocity
$\bar{u}$ = f_2u_o = (time) average linear carrier gas velocity
u_a = Carrier gas velocity at unit pressure p_a
u_i = Carrier gas velocity at column inlet
u_o = Carrier gas velocity at column outlet conditions
u_x = Local carrier gas velocity at a distance x in the column
V_{eff} = Effective volume of a plate
V_{inj} = Injected sample volume
V_g = Volume of gas phase in the column
V_l = Volume of liquid phase in the column
w = Measured peak width at half height
w_1 = Measured half width of the leading peak edge at one tenth of the peak height
w_2 = Measured half width of the tailing peak edge at one tenth of the peak height
W = Q_s/Q_o = column working range
X = $16\eta L/r^2$
y = Mole fraction of the solute in the liquid phase
y_1 = $f_1 - f_2P(2f_1 - f_2P)$
y_2 = $f_2(1 - f_2P)$
α = k_2/k_1 = relative retention
β = V_g/V_l = column phase ratio
γ = Activity coefficient of the solute in the liquid phase
γ^o = Activity coefficient at infinite dilution
η = Dynamic viscosity of the carrier gas
σ = Standard deviation in elution time of a solute
σ_c = Standard deviation of the chromatographic peak broadening process
σ_i = Standard deviation of the input band
σ_o = Standard deviation of other extra-column peak broadening factors
σ_t = Total (apparent) standard deviation of a peak
σ_1 = Standard deviation of the first eluting peak of a "critical pair"
σ_2 = Standard deviation of second eluting peak of a "critical pair"
τ = Time constant of detector electronics
Ψ = $\bar{p}.\bar{u}$ (see Equation 9 for definition)

SUBSCRIPTS

atm = At atmospheric column outlet conditions
L = For constant column length
max = The maximum value
min H = At minimum plate height conditions
min t = At minimum time conditions
N = For constant plate number
$P \to \infty$ = For high column pressure drops
vac = At vacuum outlet conditions

SUPERSCRIPTS

c = For concentration-sensitive detectors
m = For mass flow-sensitive detectors

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