

## GC/MS and the chromatographic challenge

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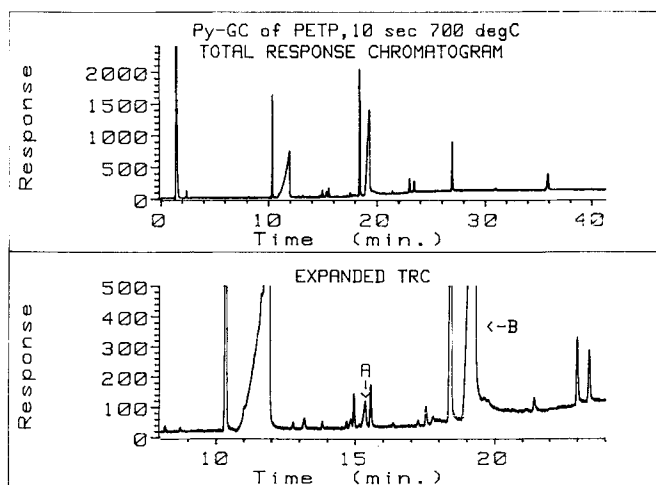


Figure 2

Total response chromatogram of Py-GC-FTIR analysis of polyethylene terephthalate and expanded TRC (ret. time 8-24 min).

Pyrolysis: 10 s, 700°C. OV-1 cap. column  $d_f = 0.4 \times 10^{-6}$  m;  $l = 25$  m; i.d. = 0.28 mm. Oven temp.: 40°C → 240°C, 5°/min. Carrier gas: N<sub>2</sub>.

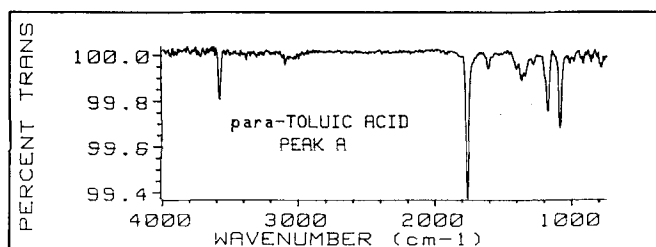


Figure 3

IR spectrum of peak A, as indicated in Figure 2.

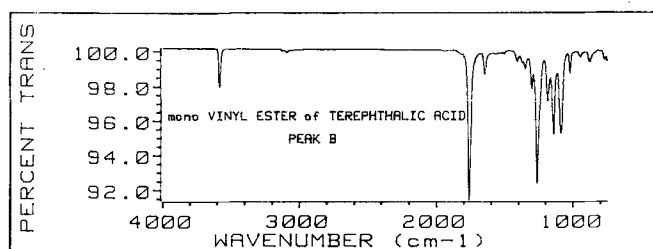


Figure 4

IR spectrum of peak B, as indicated in Figure 2.

into the capillary column. The characteristics of the column were:  $l = 25$  m; i.d. = 0.28 mm; coating OV-1,  $d_f = 0.4 \times 10^{-6}$  m. The IR spectra obtained for peak A and B (see expanded TRC in Fig. 2) are shown in Figures 3 and 4.

Even for the very small peak A a high quality IR spectrum could be obtained. A library search identified the peak to be *p*-toluic acid (hit factor 945).

In conclusion, the results demonstrate that this IR system is indeed capable of producing good quality IR spectra, even from a few ng sample, without sacrificing the chromatographic performance of a standard capillary GC-system.

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# GC/MS and the Chromatographic Challenge

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## Key Words:

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Theory

Separation speed

Detection limits

Identification limits

## 1 Introduction

Minimal time operation in gas chromatography (GC) has been a research topic ever since the introduction of open tubular columns 30 years ago. As early as 1962, Giddings [1] proved theoretically and Desty *et al.* [2] demonstrated experimentally that fast separations can be achieved by vacuum-outlet operation

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and by applying narrow-bore columns, respectively. Subsequent practical applications were, however, limited to a few instances, until the advent of fused silica capillaries since 1979 [3]. Nowadays, these flexible columns have virtually replaced all other open tubular columns. Commercial availability of these columns, with diameters between 100-750  $\mu$ m and a variety of stationary phases, has revolutionized the field of gas chromatography. Fused

silica columns can easily be mounted in an oven, and coupling to a mass spectrometer can simply be achieved by direct insertion of the column end into the ion source. These developments have triggered a renewed interest in studying the influence of pressure drops and column characteristics on chromatographic performance in general, and on separation speed and sample size working ranges in particular [4].

The continuing trend towards faster GC separations of ever decreasing sample amounts is a real challenge to mass spectrometry (MS) as a superdetection technique. The application of narrow-bore (50  $\mu\text{m}$  i.d.) columns in on-line GC/MS has been reported [5]. In the present contribution, considerations on speed of separation, detection and identification limits in high speed GC/MS are further elaborated.

## 2 Theory

### 2.1 Speed of Analysis

The relation between analysis time and column resolution for a two-component mixture is [6]:

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

where

- $t_R$  = retention time of the last eluting compound.
- $k$  = capacity factor of the last eluting compound.
- $\alpha$  =  $k_2/k_1$  = relative retention of the two solutes.
- $R$  =  $(t_{R,2} - t_{R,1}) / (4\bar{\sigma})$  = column resolution.
- $\bar{\sigma}$  = average standard deviation of the two peaks.
- $H$  =  $L \cdot \bar{\sigma}^2 / t_R^2 = L/N$  = theoretical plate height.
- $L$  = column length
- $N$  = theoretical column plate number
- $\bar{u}$  = average linear carrier gas velocity.

Evaluation of eq. (1) is not simple, because  $H/\bar{u}$  is a rather complex pressure-dependent function of  $k$ , column dimensions, and solute diffusion coefficients. This function can be simplified appreciably by neglecting the stationary phase contribution to peak dispersion, which is a reasonable assumption in many instances (i.e., whenever the film thickness is less than one percent of the inner column radius). For thin film columns, operated at optimum chromatographic conditions, eq. (1) can be expressed in more basic column parameters [4]:

$$t_R = C \cdot \underbrace{\left[ \frac{(2\eta)^{x-1}}{D_{m,a}} \frac{(\bar{p})^{2-x}}{p_a} \right]^{1/x}}_{\text{gas phase (nature, temp., pressure)}} \cdot \underbrace{\frac{(11k^2 + 6k + 1)}{3(k+1)}}_{\text{liquid phase (nature, temperature)}} \cdot \underbrace{\left[ 6 \frac{k+1}{k} \frac{\alpha}{\alpha-1} R \right]^{x+1} \cdot \left[ \frac{r}{3} \right]^{3-x}}_{\text{column dimensions}} \quad (2)$$

with:

- $C = 1$  for minimum plate height conditions, and
- $C = \frac{1}{2} \left( \frac{4}{3} \sqrt{2} \right)^{x-1}$  for minimum time conditions [4].

In eq. (2) the following symbols are used:

- $x$  = pressure drop dependent constant ( $1 \leq x \leq 2$ ).
- $x \rightarrow 1$  for low pressure drop columns ( $P \rightarrow 1$ ).
- $x \rightarrow 2$  for high pressure drop columns ( $P \rightarrow \infty$ ).
- $P$  =  $p_i / p_o$  = ratio of inlet-to-outlet pressure.
- $\bar{p}$  = average column pressure.
- $p_a$  = atmospheric pressure.
- $\eta$  = dynamic viscosity of the carrier gas.
- $D_{m,a}$  = diffusion coefficient of the solute in the carrier gas at atmospheric pressure.
- $r$  = inner column radius.

Eq. (2) is a generalized form of the high-pressure-drop equations published by Guiochon [7] and Cramers and Leclercq [4,5]. Eq. (2) clearly shows all factors affecting the speed of analysis. For multicomponent mixtures, as encountered in practice, this equation is still largely valid [7], since the "critical pair" of peaks to be separated is similar to the "two-component mixture" to be resolved.

If fast chromatographic separations are required, the following conditions should be met [4,5].

The gas phase term in eq. (2) dictates that hydrogen is the carrier gas of choice, with helium as second best (about 40% slower). Other gases are at least 2.5 times slower.

The liquid phase term shows a minimum between  $k=0.91$  ( $x \rightarrow 1$ , or  $P \rightarrow 1$ ) and  $k=1.76$  [ $x \rightarrow 2, P \rightarrow \infty$ ] for low and high pressure drop columns, respectively. This means that the last eluting peak should have a capacity factor of less than two, corresponding with a retention time of less than three times the column hold-up (dead) time. This can be effected by polarity tuning and by raising the column temperature  $k \sim \exp(1/T)$ . Increasing the temperature also affects the gas phase term positively. The temperature dependent viscosity and diffusivity make the gas phase term proportional with  $T^{-0.5}$  to  $T^{-1.75}$ , for high and low pressure drop columns, respectively.

The appearance of the chromatogram is largely determined by the selectivity of the stationary phase, and hence by  $\alpha$  and  $R$ . The factor  $\alpha/(\alpha-1)$  approaches a minimum value of one for large values of  $\alpha$ . An  $\alpha < 5$  will cause analysis times to be less than twice the theoretically achievable minimum time. For a capillary column with  $10^5$  theoretical plates, the capacity factors of two successive peaks,  $k_1 \cong k_2 \cong 2$ , must differ only by 2% for complete separation ( $R = 1$ ).

The value of  $R$  can be selected by choosing the stationary phase and the separation temperature, but also by choosing column dimensions. For minimum analysis times,  $R$  should be minimized:  $R = 1$ .

Once  $k$ ,  $\alpha$ , and  $R$  have been selected, the number  $N$  of theoretical plates required for the separation can be calculated:

$$N = \left[ 4R \frac{k+1}{k} \frac{\alpha}{\alpha-1} \right]^2 \quad (3)$$

This efficiency can be achieved with various column dimensions ( $N = L/H$ ) at arbitrary average pressures. *E.g.*, a  $5\text{ m} \times 50\text{ }\mu\text{m}$  i.d. column has about the same theoretical plate number as a  $25\text{ m} \times 0.25\text{ mm}$  i.d. column [8]. For minimum analysis times, however, eq. (2) shows that the smallest possible column diameter should be used. Reduction of the diameter is more efficient than lowering the average pressure [8]. Vacuum-outlet operation is always the ultimate optimum in high speed chromatography, but its effect is rapidly decreased by the application of higher pressure drop (narrower bore) columns.

The prices to pay when reducing column dimensions are the increasing inlet pressure and the decreasing injection band widths required. Current research indicates that  $10\text{ }\mu\text{m}$  i.d. columns might be the limit in practice.

## 2.2 Detection and Identification Limits

For a constant plate number, the minimum detectable amount of a solute is proportional to its retention time [4]. Reduction of the column inner diameter is advantageous for both concentration- and mass-flow sensitive detectors [9,10]. Decreased peak broadening, and a resulting higher signal-to-noise ratio for fixed amounts of a solute injected, also ensure a lower detection limit in the "selected-ion-monitoring" mode in GC/MS.

In vacuum-outlet GC/MS ( $P \rightarrow \infty$ ), detectability is improved in proportion to the decrease in analysis time, and hence in column diameter (see eq. (2)).

In the scanning mode of GC/MS, the sensitivity topic needs further elaboration. If the scan rate of the mass spectrometer, *i.e.* the rate at which full mass spectra are acquired repetitively, is increased proportionally to the decreased column diameter, no effects on identification limits are expected (**Figure 1**). Identification limits are defined as the minimal amounts needed to produce interpretable spectra.

In considerations on mass spectral acquisition rates, ion statistics always play a role [5,11]. For a fixed amount of injected solute, however, a "slow" column, yielding a broad peak, produces the same overall number of ions as a "fast" column, generating a sharp peak. Therefore, the number of ions collected during one scan, *i.e.* the chance to collect ions of any particular mass while scanning, remains unchanged.

It was found experimentally, however, that a reduction of the column diameter in vacuum-outlet GC/MS results in a better detection limit, proportional to the analysis time and diameter (constant  $N$  and injected amount) [5].

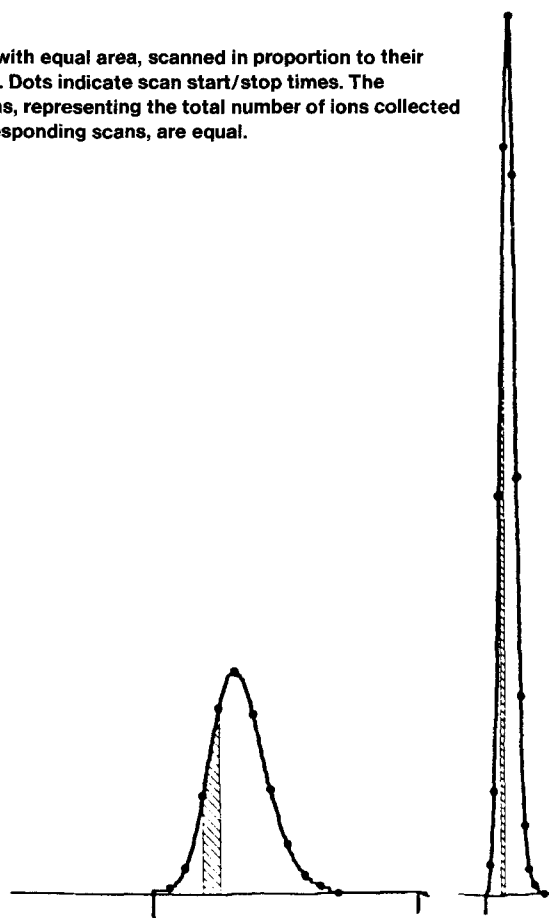
The tentative explanation is again an increased signal-to-noise ratio, for two-fold reasons. Firstly, less spectrometric (detector) "dark" or background current ( $10^3$  ions/s) is detected when scanning faster. Secondly, the chemical noise is reduced, because the column gas flow ( $\sim r^2$ ), and hence the stationary phase bleeding, is lower.

## 2.3 Sample Capacity and Column Working Range

Narrow-bore, thin-film columns contain only a very small amount of liquid phase and are therefore easily overloaded. The sample capacity of a column is proportional to the third power of the column diameter [4], which is of distinct advantage for wide-bore columns.

**Figure 1**

Two peaks with equal area, scanned in proportion to their widths (1:4). Dots indicate scan start/stop times. The shaded areas, representing the total number of ions collected during corresponding scans, are equal.



The ratio of sample capacity to minimum detectable amount determines the column working range. For high-plate-number or vacuum-outlet columns, the working range is proportional to  $r^2$ , again in favor of wide-bore columns.

## 3 Discussion

In GC/MS, at least five to ten mass spectra should be acquired during the elution of a chromatographic peak. This is necessary in order to guarantee mass spectral integrity, *i.e.* to minimize changes in sample concentration in the ion source during one scan, thus preventing unacceptable distortion of relative peak intensities in a single spectrum. Relatively high scan rates are also needed to warrant chromatographic integrity, *i.e.* to enable separation of overlapping peaks and reconstruction of the chromatogram from consecutive recorded spectra.

On-going developments in the direction of faster (and more sensitive) chromatographic separations are especially challenging for GC/MS. Despite the commercial availability of low-cost mass spectrometers, a simple GC/MS set-up still has a price tag of five-to-ten times the costs of a gas chromatograph. An increased sample throughput is therefore of appreciable economic interest.

The limits in scanning speeds of various types of mass spectrometers have been discussed in detail by *Holland et al.* [11]. Their analysis of ion transmit times, *i.e.* the times it takes an ion to traverse the distance through the mass analyzer between ion

source and detector, resulted in a predicted maximum scan repetition limit of 4-8 Hz, achievable only with recent quadrupole instruments (magnetic sector instruments being two times slower). Their estimates seem conservative, however, in the light of our results [5].

Nevertheless, scan rates in excess of 5000 mass units/second, over a mass range of e.g. 500 daltons, seem to be unattainable as these are directly limited by ion transit times (10-100  $\mu$ s, proportional to mass).

Contrary to wide-spread opinions, ion statistics do not impose limitations to minimum detectable amounts. As long as  $10^3$ - $10^4$  ions can be collected during one scan, the absolute acquisition speed is not important [5].

Mass spectral techniques that avoid the scanning process all together will be the solution for high-speed GC/MS in the future. These techniques, by which the ion currents of an array of masses can be measured simultaneously without scanning, are placed within our reach by recent developments in micro-electronics and huge, high-speed computer memories.

Three basic types of mass analyzers are suited for simultaneous ion collection [11]. One type is the double-focusing mass spectrometer in the Mattauch-Herzog geometry, in which the photoplate is replaced by an array of microchannel electron multipliers. A second type is the time-of-flight mass spectrometer with "time-array detection" following each ionization pulse. The third type is the Fourier transform implementation of ion cyclotron resonance mass spectrometry, also based on pulsed ionization.

Whatever technique will win in practice, the future of high-speed GC/MS seems secured. In addition to faster and more sensitive analyses, high-speed GC/MS also enables analysis of many underivatized compounds.

Results with soft-ionization methods in MS and MS/MS indicate that very-high-molecular-weight compounds can be volatilized to stable ions on a short time scale. Similar effects are observed in high-speed gas chromatography [12]. One might speculate that GC, "the poor man's mass spectrometer" of the 1950's, once again might replace MS in MS/MS in the future.

#### 4 Conclusions

Vacuum outlet gas chromatography is of particular interest for columns with a high permeability (due to a large internal diameter or a short length).

Vacuum outlet gas chromatography should be considered when short analysis times and large sample capacities are required simultaneously.

Narrow-bore columns always generate the highest plate number per time unit. Vacuum outlet operation of these columns does not produce any practical advantages [8]. In practice, the use of 100  $\mu$ m i.d. columns is recommended. These columns are commercially available, and do not require excessive inlet pressures, or unrealistic injection bandwidths.

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