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Evaluation of time-of-flight mass spectrometric detection for fast gas chromatography

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Abstract

Separations below 1 s of a mixture of organic compounds ranging from C_5 to C_8 have been performed to investigate the performance of a time-of-flight mass spectrometer in fast gas chromatography. The gaseous samples were focussed on a cold trap, and then injected after thermal desorption to obtain the required narrow input band-widths. Also, to obtain a very fast separation, a short narrow bore column was used, operated at above-optimum inlet pressures. With this system, it was possible to identify ten compounds within 500 ms, showing peak-widths (2.354σ) as narrow as 12 ms. The spectral acquisition rate used for these analyses was 500 Hz. The quality of the recorded spectra and the comparison with library spectra was very high. Deconvolution algorithms offer the possibility of identifying overlapping peaks. It is shown that the spectral scan speed of the time-of-flight mass spectrometer is high enough for very fast separations.

Keywords: Gas chromatography, fast; Mass spectrometry; Alkanes; Benzene; Toluene

1. Introduction

The combination of a chromatographic separation technique with mass spectrometric detection is a very powerful tool for the study and identification of organic compounds in complex samples. Also, in case the identity of a compound is known, it can be advantageous to use mass spectrometric detection. With MS detection, target peaks can readily be identified in crowded chromatograms. By using extracted ion traces, non-separated peaks can even be quantified. Finally, MS detection greatly simplifies method development as compounds of interest can easily be identified in groups of interfering peaks. In gas chromatography (GC), mass spectrometry is nowadays widely used as a detection device. Several types of mass spectrometer are available for coupling to GC systems. These systems differ in the way that the ion-fragments, formed from the molecules eluting from the GC column, are separated according to their mass. Important mass analyzers are the ion trap, the sector instrument, the quadrupole and the time-of-flight mass spectrometer. The performances of each of the resulting mass spectrometers show

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[1]We regret we have to report the death of Piet A. Leclercq on March 22, 2000.

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differences in terms of acquisition rates, detection limits, mass spectrometric resolution and quality of the mass spectra obtained. The choice of the most suitable mass spectrometer is very much dependent on the composition of the sample, the detection limits and the speed of separation. Currently, there is a clear trend towards faster methods for analysis. Several methods for faster GC have been described in the literature [1–7]. Other important trends in GC are the ever increasing need for positive identification and the need for more flexible systems that allow the analysis of a wide variety of samples on one system. These last two trends clearly result in a strong requirement for mass spectrometric detection. Combination of fast GC with mass spectrometric detection is by no means trivial.

For an accurate description of a chromatographic peak in a chromatogram, at least 15–20 datapoints across a peak are required [8–9]. Typical acquisition rates of scanning mass spectrometers like the ion trap, the quadrupole and the sector instrument, range from ten to twenty spectra per second in the full scan mode. Hence, only chromatographic peaks with a width of 0.5 s or more can be accurately represented.

The most important method to achieve fast GC is the use of columns with a reduced inner diameter (50–150 μm) [1–2]. Unless very short columns are used, the peak-widths obtained from such columns are usually slightly above 1 s. Scanning mass spectrometers are hence capable of offering the speed required for MS detection. In Table 1, peak-widths are calculated for analyses on a standard column, a narrow bore column and two extremely short columns. Here, the influence on band broadening of only the column itself is taken into account. From this table, it is clear that for very fast separations on short columns, the spectral acquisition rate of scanning mass spectrometers is too low.

The use of an MS system compared to using an atmospheric outlet like a flame ionization detector will significantly increase the speed of analysis [10]. The highest gain in speed is obtained when using short wide bore columns. Very short columns in combination with MS can provide separations in the seconds- or even sub-second range, yielding peak-widths of 5–15 ms. For these separations, an extremely fast spectral acquisition rate is required. Time-of-flight mass spectrometers can provide up to 500 full spectra per second. In this work, separations in the sub-second range were performed using a very short narrow bore column. The primary goal of this work was to investigate the performance of the time-of-flight (TOF) mass spectrometer in high-speed separations and to explore the limits of TOF-MS detection.

The terms fast GC, very fast GC and ultra fast GC are often used in literature, but until now they have not been well defined with regard to analysis times and peak-widths. Dagan and Amirav [11] defined a speed enhancement factor to divide analyses in the three fast GC categories. This factor is the increase in speed that can be obtained by using a shorter

Table 1
Comparison of calculated plate number, retention-time and peak-width at half-height for a standard, fast, very fast and ultra fast separation[a]

Type of analysis	Inner diameter of column (μm)	Length (m)	Plate number	Retention time (s)	Peak-width at half-height (s)
P_{out} = 100 kPa					
Standard	320	25	90 000	160	1
Fast	50	10	26 0000	60	0.2
Very fast	50	1	25 000	2.0	0.03
Ultra fast	50	0.3	7000	0.40	0.01
P_{out} = 0 kPa					
Standard	320	25	75 000	100	0.7
Fast	50	10	26 0000	60	0.2
Very fast	50	1	24 000	2.0	0.03
Ultra fast	50	0.3	6500	0.30	0.01

[a] Calculations are performed using the Golay–Giddings equation, incorporated in the computer program developed by Leclercq [15]. Conditions for these calculations are: $\beta = 62.5$, compound = hexane, $T = 330$ K, carrier gas = helium, peak-width at half-height (2.354σ).

column and a higher carrier gas velocity in comparison to the same analysis on a conventional GC column under optimum carrier gas velocity conditions.

In this paper, a classification is made based on peak-widths (2.354σ) and total analysis-times. This is shown in Table 1.

1. Fast GC: separation in the minutes range; peak-width, several seconds.
2. Very fast GC: separation in the seconds range; peak-width, 30–200 ms.
3. Ultra fast GC: separation in the sub-second range; peak-width, 5–30 ms.

As already mentioned, fast separations typically can be obtained from columns with an inner diameter of 50–150 μm. Very fast separations can be obtained by using short columns of about 1 m with inner diameters ranging from 50 to 320 μm. Typical analyses are shown in the work of Dagan and Amirav [11] and of Davis et al. [12]. Typical ultra fast analyses are separations in the milliseconds range, with peak-widths ranging from a few to 10 ms. Jonker and Poppe [13] obtained ultra fast separations on a very short packed column with very small particle diameters. In their paper, ultra fast separations were shown with peak-widths of 4 ms and a separation time of 150 ms for the separation of four compounds. In the present paper, an example will be shown of a separation of ten compounds in 500 ms, and the applicability of TOF-MS for GC separations in the 0.01 to 1 s range is investigated.

2. Theory

In 1981, Cramers et al. [10] derived an equation describing the gain in speed of analysis using a vacuum outlet compared to an atmospheric outlet operation. This equation reads:

$$G = \frac{\bar{v}_{\mathrm{opt,vac}}}{\bar{v}_{\mathrm{opt,atm}}} = \frac{\bar{P}_{\mathrm{opt,atm}}}{\bar{P}_{\mathrm{opt,vac}}} = \frac{(P^3_{i,\mathrm{opt,atm}} - P^3_{\mathrm{atm}})}{(P^2_{i,\mathrm{opt,atm}} - P^2_{\mathrm{atm}})^{3/2}} \qquad (1)$$

where: $\bar{v}_{\mathrm{opt},vac}$ and $\bar{v}_{\mathrm{opt,atm}}$ are the average optimum gas velocities through a capillary column at vacuum outlet and atmospheric outlet conditions, respectively; $\bar{P}_{\mathrm{opt},vac}$ and $\bar{P}_{\mathrm{opt,atm}}$ are the average optimum column pressure at vacuum outlet and atmospheric outlet conditions; $P_{i,\mathrm{opt,atm}}$ is the optimum inlet pressure at atmospheric outlet conditions; P_{atm} is the atmospheric pressure.

From this equation, it is clear that for short wide bore columns, the gain in speed is much higher than for long narrow bore columns. For the short wide bore column, the pressure inside the column is low over its entire length. The resulting high diffusion coefficients result in a high speed of analysis, as is shown in Fig. 1. A complication factor when using a short wide bore column with MS detection, is the high resulting column outlet flow. This flow can easily be higher than 10 ml/min, which is too high for the pumps to maintain the vacuum in the system at an acceptable level. Summarizing, there are various options for fast GC separations. For the present purpose, assessing the limits of TOF-MS detection, we opted for the use of short 50 μm columns operated at above-optimum inlet pressures to achieve the highest separation speed possible.

3. Experimental

The GC system used in this work was an HP6890 (Hewlett-Packard, Wilmington, DE, USA) equipped with a Gerstel PTV CIS-4 injector (Gerstel, Mülheim an der Ruhr, Germany). Injections were performed in the hot split mode, at an injection temperature of 250°C. The system was operated in the constant pressure mode with an inlet-pressure of 450 kPa. The injections took place at a split-ratio of 1:100. The analyses were performed isothermally at 75°C, unless stated otherwise. The column used was a 30 cm×50 μm capillary column with a 0.17-μm film of a non-polar OV-1 stationary phase (MEGA, Fisons, Milan, Italy). Helium was used as the carrier-gas.

The time-of-flight mass spectrometer used was the Pegasus II MS (LECO, St. Joseph, MI, USA). This is a reflectron-type TOF-MS system equipped with an electron impact ionization (EI) source. Ions are created using EI ionization. After ionization, the fragments are pushed into the flight tube by a push pulse electrode, at a rate of 5000 pulses per second. The maximum possible data-rate obtainable with the TOF-MS system is 500 spectra per second, which means that a single acquired spectrum consists of a sum of ten transients. The total length of the flight

Figure 1

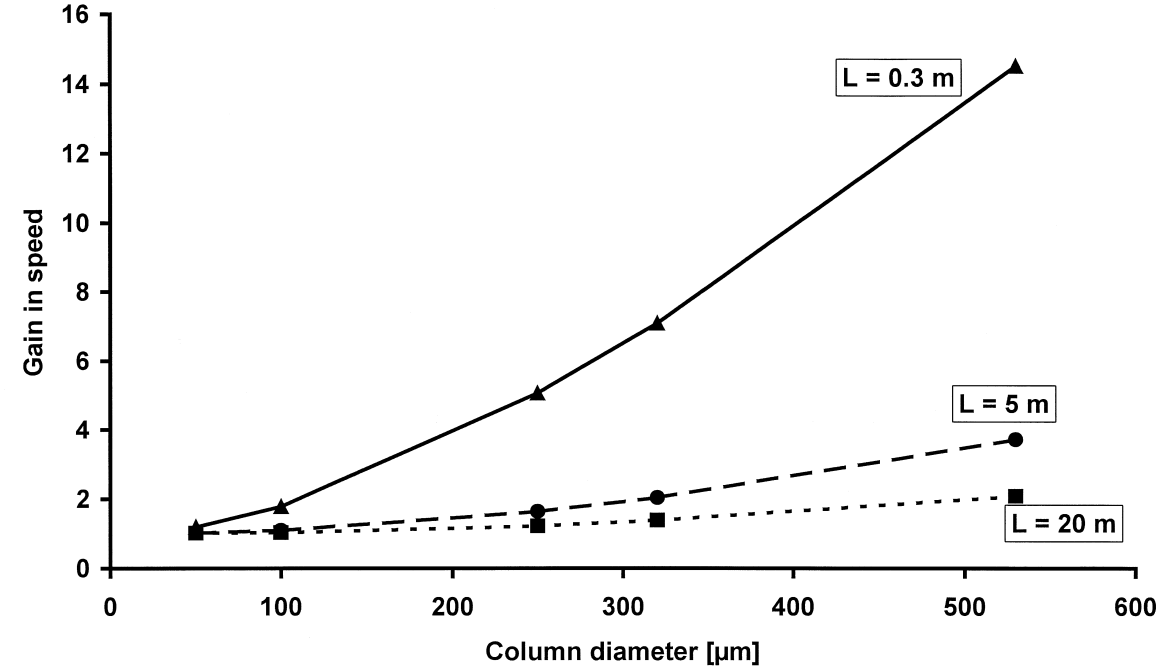

Fig. 1. Influence of column diameter and column length on gain in speed using a vacuum outlet compared to an atmospheric outlet.

path of the ions is more than 1 m. The upper mass range for detection in the Pegasus TOF-MS system is $m/z = 1000$. The flight time of this ion will be approximately 170 μs. The temperature of the transfer-line between the GC and the MS was maintained at 275°C. The ion source temperature was 200°C. The pressure in the system was 10^{-8}–10^{-7} Torr, which was achieved using two turbo-molecular pumps, one located at the ion-source and the other one at the reflectron side of the flight tube (1 Torr = 133.322 Pa). Data processing was performed using LECO Pegasus II software, version 1.10.

Headspace samples (1 μl) were injected manually with a 10-μl syringe. After injection, the compounds were trapped and cryofocussed on the head of the column by using a cold-trap, similar to the system described previously [14]. Helium, cooled to about −70°C by passing it through liquid nitrogen, was used as a cooling medium. Re-injection of the trapped sample took place by flash-heating a metal capillary surrounding the fused-silica column using a pulsed resistive heating device made in the laboratory. By putting a voltage of about 11 V across the metal capillary, heating rates of 4000°C/s could be reached [14]. The final temperature of the trap was approximately 165°C. The flow of cooling gas was not interrupted during the heating step.

3.1. Reagents

Pentane, hexane and heptane were purchased from Merck (Darmstadt, Germany), octane, 2,3-dimethylbutane, 1,4-dimethylcyclohexane (*cis*-+*trans*-) and methylcyclohexane were from Fluka (Buchs, Switzerland), and toluene and benzene were from Polyscience (Niles, IL, USA). All had purities higher than 99%, except for pentane, which had a purity of 95%.

4. Results and discussion

4.1. Cryogenic focussing inlet system

In previous work, we have described a cryogenic focussing inlet system that is capable of generating

input band-widths in the milliseconds range [14]. An example of a very fast analysis is shown in Fig. 2. This chromatogram shows the separation of ten compounds in 500 ms. The column used here was 0.3 m long and had an inner diameter of 50 μm. The plate number was approximately 3500, which is close to the theoretical value. This chromatogram was recorded from mass 40 to mass 200 at 500 spectra per second, which is the maximum scan speed of the TOF-MS system. Peak-widths obtained in this chromatogram are approximately 12 ms. Peak-widths were obtained of 10 to 20 ms, for compounds ranging from C_6 to C_8, which is comparable to the values obtained with the mass spectrometer. In Table 2, the peaks (Fig. 2) are identified and the similarity with library spectra is shown. From this table, it is clear that even for such extremely fast separations, identification of the compounds can take place with an excellent library similarity for most of the compounds. This means that the quality of the collected spectra is very high. An example of the good spectral quality of the TOF-MS system is shown in Fig. 3. This figure shows a comparison between a recorded spectrum and the library spectrum. The injected amount was approximately 1 ng for each compound.

Table 2
Library search results from the analysis shown in Fig. 2

Peak number	Name	Similarity
1	Pentane	939
2	Butane,2,3-dimethyl-	910
3	Hexane	927
4	Benzene	957
5	Heptane	921
6	Cyclohexane, methyl-	927
7	Toluene	890
8	Cyclohexane, 1,4-dimethyl-(*trans*)	898
9	Octane	907
10	Cyclohexane, 1,4-dimethyl-(*cis*)	798

In Table 3, the experimental plate heights, optimal velocities etc. for the 0.3 m×50 μm column are compared to theoretical values. The data for the 50

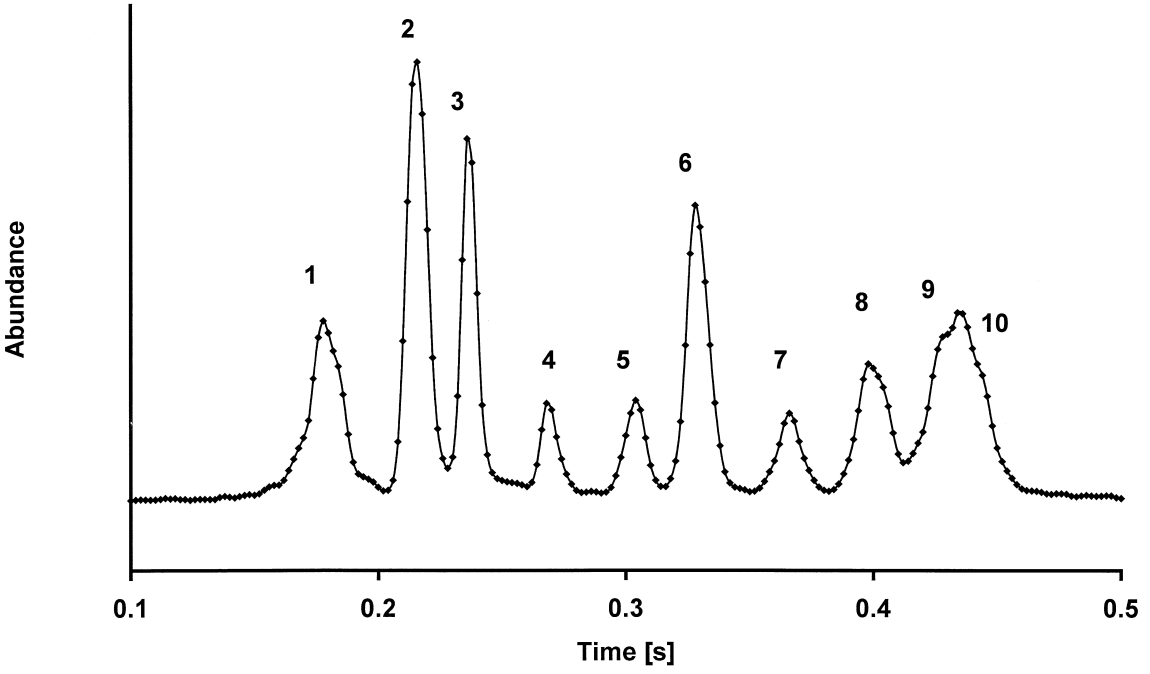

Fig. 2. Ultra fast analysis of ten compounds within 500 ms on a 0.3 m×50 μm column with a 0.17-μm thickness non-polar OV-1 phase, using a cryogenic focussing inlet system. Inlet pressure, 450 kPa; carrier gas, helium; split flow, 400 ml/min; $T_{injector}$, 250°C; T_{oven}, 75°C. Injection and sampling: 1 μl; headspace (≈1 ng/compound). Detection, time-of-flight mass spectrometer; $T_{transfer\ line}$, 275°C; T_{source}, 200°C; scan rate, 500 spectra/s, from mass 40 to 200. Compounds: (1) pentane; (2) 2,3-dimethylbutane; (3) hexane; (4) benzene; (5) heptane; (6) methylcyclohexane; (7) toluene; (8) *trans*-1,4-dimethylcyclohexane; (9) octane and (10) *cis*-1,4-dimethylcyclohexane.

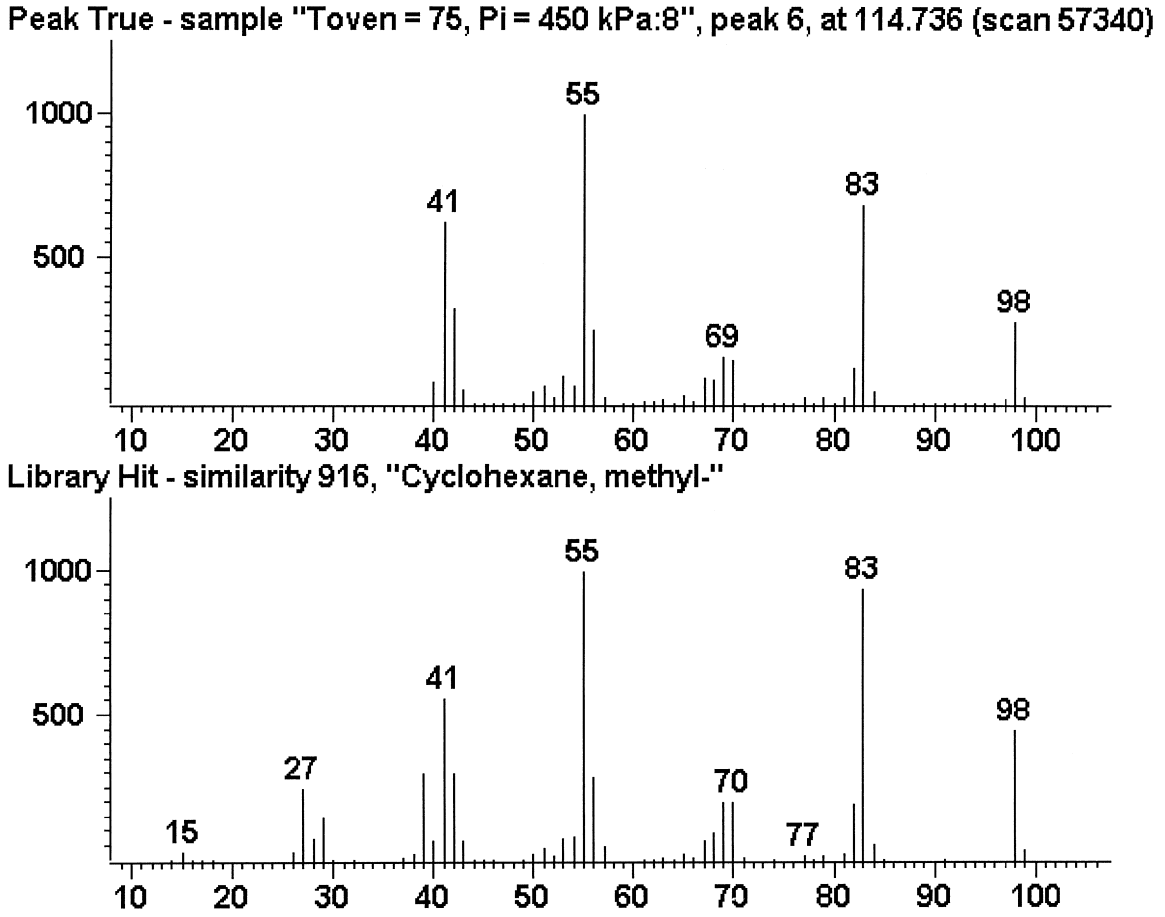

Fig. 3. Example of a measured spectrum compared to a NIST-library spectrum, taken from the ultra fast analysis shown in Fig. 2.

μm column are compared to calculated values for a 320-μm column. Calculations were performed using a computer program developed by Leclercq and Cramers [15]. In the experimental work, the column was operated at an inlet pressure of 550 kPa. From Table 3, it can be seen that this is significantly above the optimum pressure of 270 kPa. A pressure exceeding the optimum value was selected for speed reasons. The low plate number (3600 compared to 9000) is also a consequence of operating the column

Table 3
Comparison of experimental data and calculated values, for a short 50 μm column and a short 320 μm column

	d_c=50 μm, l=0.3 m		d_c=320 μm, l=0.3 m
	Experimental	Optimum calculated	Optimum calculated
Absolute inlet pressure (kPa)	550	270	55
Average gas velocity (cm/s)	200	150	600
Number of plates	3600	9000	2400
Column flow (ml/min)	0.8	0.3	10

at above-optimum velocities. The column outlet-flow, reduced to atmospheric pressure, was calculated using Eqs. (2) and (3):

$$Q = \pi r^2 \bar{u}(\bar{P}/P_{atm}) \quad (2)$$

$$\bar{P} = \frac{P_o}{f_2} \quad (3)$$

where: Q is the column outlet flow; r is the column radius; P is the average column pressure; f_2 is the pressure correction factor ($=3/2P$ for $P \rightarrow \infty$ at vacuum outlet), with $P = P_i/P_o$ as the ratio of inlet to outlet pressure.

From the flow calculations, it can be concluded that a very short 320 μm column can only be coupled to a mass spectrometer when using a narrow bore restriction. Recently, it was shown that optimum performance is obtained if this restrictor is mounted at the column inlet [16]. Another possibility would be to split the column flow before entering the mass spectrometer, but this will decrease sensitivity.

The use of mass spectrometric detection in chromatography offers an additional means of distinguishing different solutes. Non-separated peaks can be 'separated' on the basis of mass spectral differences. Mass spectrometry hence offers an alternative route towards faster analysis. Spectral deconvolution of the Leco Pegasus II software offers the possibility of deconvoluting and identifying overlapping peaks. Some chromatographic separation is however required for the deconvolution algorithm to recognize the presence of two or more compounds in one peak [17,18]. Fig. 4 shows the identification of the coeluting compounds octane and *cis*-1,4-dimethylcyclohexane (see Fig. 2). The separation here amounts to 10 ms or five spectra (rectangle). Fig. 5 shows the influence of the spectral collection rate on the peak resolution and the deconvolution performance of the software. The sample analyzed is the

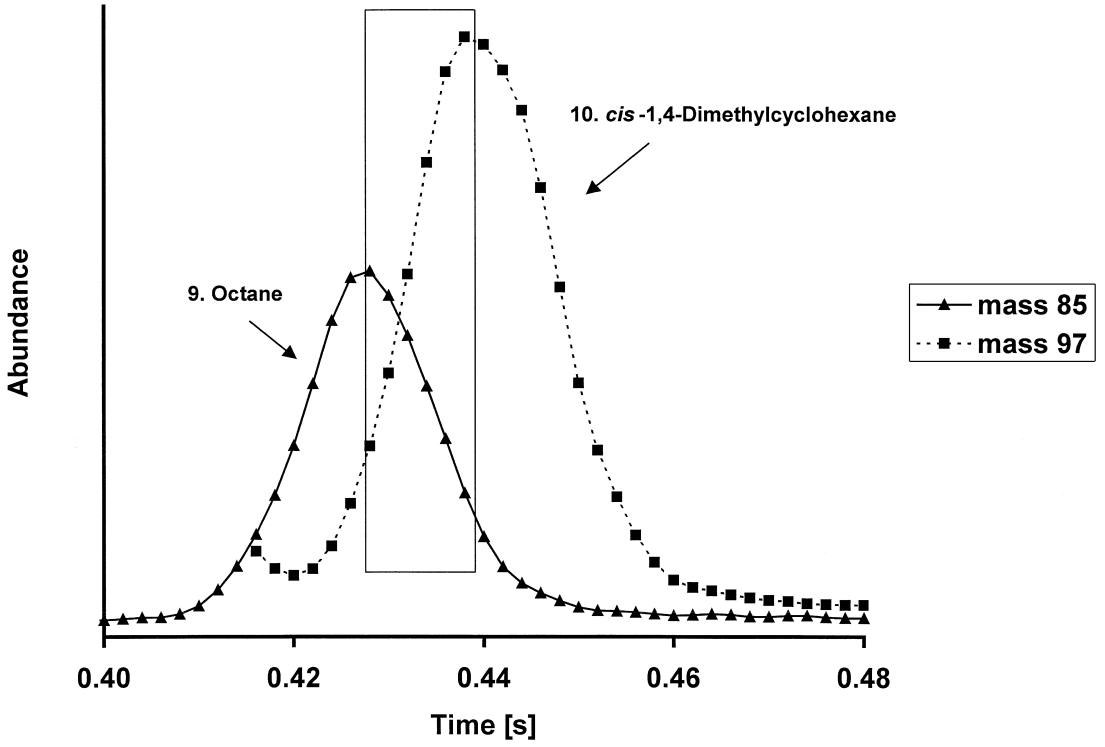

Fig. 4. Deconvolution of octane and *cis*-1,4-dimethylcyclohexane, peaks 9 and 10 of the ultra fast separation shown in Fig. 2. In this graph, the unique masses 85 and 97 are plotted, which are specific for the two compounds.

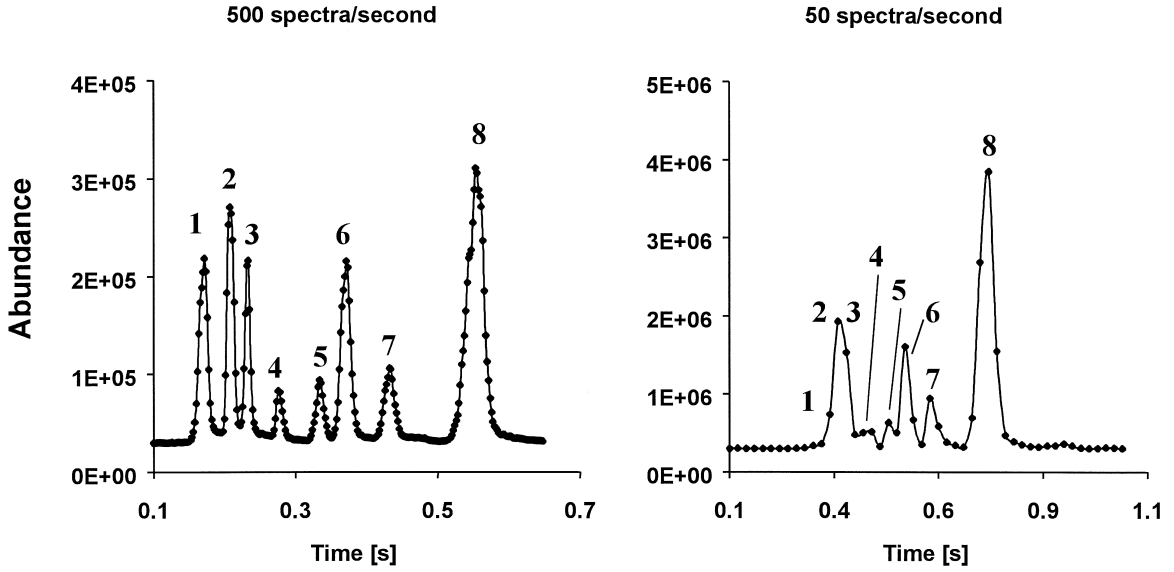

Fig. 5. Comparison of chromatograms recorded at 500 and 50 spectra per second, respectively. Analysis conditions: see Fig. 2; T_{oven}, 60°C. Compounds: (1) pentane; (2) 2,3-dimethylbutane; (3) hexane; (4) benzene; (5) heptane; (6) methylcyclohexane; (7) toluene and (8) octane.

same as shown in Fig. 2. At 500 spectra per second, the first three peaks are baseline separated. If the same separation is repeated at a scan rate of only 50 spectra per second, these three peaks can no longer be distinguished. In Table 3, the similarity index of the experimentally obtained spectra collected at 500 spectra per second is compared to that of spectra recorded at 50 spectra per second. At 50 spectra per second, only three–five spectra are collected over the peak. This means that it is no longer possible to identify or deconvolute overlapping peaks. At 50 spectra per second, all the compounds could be identified, but for 50% of the compounds, this had to be done manually (Table 4). Deconvolution certainly is a helpful tool in the separation of complex samples and for the identification of coeluting peaks. Spectral deconvolution methods however should be applied with some care.

Table 4
Similarity of library spectra for analyses recorded at 500 and 50 spectra per second. Analyses are shown in Fig. 5

	Name	500 spectra/s	50 spectra/s
1	Pentane	941	851 (manually)
2	Butane, 2,3-dimethyl-	919	920 (library)
3	Hexane	938	942 (manually)
4	Benzene	962	949 (library)
5	Heptane	935	899 (manually)
6	Cyclohexane, methyl-	927	926 (library)
7	Toluene	904	849 (manually)
8	Octane	922	926 (library)

From Fig. 5 it can be seen that the sensitivity increases at decreasing scan rate. When scanning at a scan speed of 500 spectra per second, only ten transients are summed. At a scan rate of 50 spectra per second, 100 transients are summed. Signal theory states that this results in a gain in the signal to noise ratio of $\sqrt{10}$. In conclusion, the optimum scan rate is a compromise between preserving resolution and maximizing sensitivity.

5. Conclusions

From the results presented here, it can be concluded that TOF-MS is very suitable as a detection method for very fast separations. With TOF-MS, it is possible to accurately detect peaks with peak-widths in the milliseconds range. Even for peaks as narrow as 12 ms, the quality of the spectra is very high. Deconvolution techniques can be used to advantage, but, nevertheless, some cautiousness has to be taken into account.

The limits of the system have been explored and, at even faster separations, more than 500 spectra are required. Such fast analyses are not yet performed on a daily routine base, but might become of more interest in the future.

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