High-speed narrow-bore capillary gas chromatography in combination with a fast and double-focusing mass spectrometer

High-Speed Narrow-Bore Capillary Gas Chromatography in Combination with a Fast Double-Focusing Mass Spectrometer

Peter G. Van Ysacker[1], Jeff Brown[2], Hans-Gerd Janssen[1], Piet A. Leclercq[1], and Andy Phillips[2]

[1] Laboratory of Instrumental Analysis, Eindhoven University of Technology, P.O. Box 513, 5600 MB Eindhoven, The Netherlands

[2] Fisons Instruments, VG Analytical, Floats Road, Wythenshawe, Manchester M23 9LE, UK

Key Words:

GC/MS
Scan speed
Detection limits
High-speed GC
Narrow-bore columns
High-resolution MS
Sector mass spectrometers

Summary

In this work the application of high-speed narrow-bore capillary GC in combination with a fast scanning double focusing magnetic sector mass spectrometer is evaluated. Special emphasis is placed upon detection limits and scan speed in the full scan mode and in the selected ion monitoring mode (SIM). In the full scan mode, up to 20 scans per second could be obtained. The detection limits are in the low picogram range in the full scan mode and improve even to 5 to 50 fg in the SIM mode, depending on the sample complexity and mass resolving power. It will be illustrated that by increasing the resolution in the SIM mode, interferences from ions of the same nominal mass-to-charge ratio as the ions of interest are significantly reduced. Chemical background noise can therefore be largely eliminated, thus enhancing the signal-to-noise ratio.

1 Introduction

High-speed GC using open-tubular columns is well known and has been used in research laboratories for many years. As long ago as 1961, Desty *et al.* demonstrated the advantages of the use of narrow-bore columns (i.d. < 100 μm) [1]. These columns offer a high separation efficiency in a short time. It was proved by Schutjes *et al.* that the retention time is reduced proportionally to the column inner diameter in the case of a high pressure drop over the column [2]. The retention time is even decreased proportionally to the square of the column diameter for small pressure drops. An additional advantage of the use of these narrow-bore columns was demonstrated by Noij *et al.* He proved theoretically and experimentally that the minimum detectable amount is favored by the reduction of the column inner diameter [3]. Despite these advantages, the practical use of high-speed GC with narrow-bore columns has been rather limited until now because of the lack of compatible instrumentation. First, the sample capacity of these narrow-bore columns is limited to a few nanograms per compound. This means that very sensitive detection devices are required in order to preserve an acceptable working range. Moreover, the instrumental band broadening becomes more critical the smaller the inside diameter. The injection and detection band broadening have to be very small for being compatible with the small chromatographic band broadening. Sample inlet systems suitable for these narrow-bore columns are for example the cold trap with rapid thermal desorption [4–6], the pneumatically actuated switching valve [7–8], and fluidic logics [9–11]. Considerable effort has also been invested in detection devices. During the last ten years, the combination of high-speed GC with the following detectors has been evaluated: combination with flame ionization [12–13], thermal conductivity [14], photoionization [14], and electron capture detectors [15–17] has been reported, as well as coupling with ion trap [18] and time-of-flight mass spectrometers [19].

The on-line combination of gas chromatography with mass spectrometry is without any doubt the most powerful hyphenated technique for the separation of unknown samples with subsequent identification of the constituents. Modern magnetic sector instruments have several advantages over quadrupole instruments and appear highly promising for coupling to narrow-bore columns. Double focusing magnetic sector instruments are capable of higher mass resolution, and greater sensitivity and specificity than quadrupole instruments. Quadrupole instruments are limited in scan speed because ions are of low energy [20]. The scan speed must be slow enough for mass separation and to allow the ions of interest to traverse the mass analyzer before being rejected as the mass selection changes. Magnetic instruments use ions of higher energy and are not limited in this respect.

In this paper, the use of 50 μm inner diameter GC columns in combination with a sector instrument is reported. We evaluated the scan speed in the full scan mode, and in the selected ion monitoring mode, by using both voltage and magnetic field switching. Conventional magnetic sector instruments are limited to 3 to 5 scans per second. However, with the instrument used, higher scan speeds were anticipated, because the instrument has a smaller, faster, fully laminated, low inductance magnet. At

elevated scan speeds the spectral quality was evaluated. Special attention was also paid to the detection limits in the full scan mode and in the SIM mode. An important advantage of sector instruments is the capability of higher selectivity by using the high resolving power of the mass spectrometer. For complex mixtures, detection levels are limited by interferences from other compounds in the sample. A comparison was made between a mass spectral resolving power of 2000 and unit mass resolution, such as available with quadrupole instruments. The performance of high-speed GC/MS will be illustrated by the analysis of various samples from industrial and environmental origin.

2 Experimental

The system used consisted of a Fisons GC 8000 (Fisons Instruments, Milan, Italy) in combination with a MasSpec double focusing magnetic mass spectrometer (Fisons Instruments, Manchester, England). The mass spectrometer has an EBE tri-sector geometry (**Figure 1**). The ion beam from the ion source has angular and energy divergence [21]. The energy divergence, resulting from the difference of position at which various ions are formed in the ion chamber and from the kinetic motion of the ions, is corrected by the combined energy dispersion of all three sectors. Ions are also focused spatially at the detector. Mass dispersion is achieved by the magnetic sector. Because of this "double focusing" it is possible to perform high resolution MS.

A Tescom 44-1100 high pressure regulator (Tescom Inc., Minnesota, USA) was used to enable high inlet pressures for the carrier gas. The chromatographic system was operated in the constant pressure control mode. High pressures are required in order to obtain maximum separation efficiency. The optimum inlet pressure for the 5 m × 50 µm i.d. column used was 10 bar overpressure. The inlet pressure was monitored by a custom-made digital pressure indicator. Because high split ratios were used to obtain small input band widths, it was difficult to get quantitatively reproducible results. To overcome this problem, a Carlo Erba A200S autosampler (Carlo Erba, Milan, Italy) was used. The SSL71 split/splitless injector was operated at 250 °C. The sample volume was 0.5 µl and a split ratio of about 1/1200 was used. The column temperature was 100 °C and the transfer line from the GC to the MS was operated at 250 °C. For all the experiments a 5 m × 50 µm i.d. DB-1 column (J&W Scientific, Folsom, USA) with a 0.17 µm film thickness was used.

In the full scan mode, the scan range was 40 to 200 Da operating the MS at mass resolving power 400. In the SIM mode, the detection limits of dichlorobenzene were evaluated by monitoring the ions of *m/z* 111.00, 145.97, and 147.97 at mass spectrometric resolving powers of 300 and 2000 at 10% valley, respectively. The data processing was performed using the VG Opus software.

3 Results

In a scanning quadrupole mass spectrometer, ions of different masses are detected sequentially. For quadrupole instruments, the scan speed is limited because of the relatively slow traveling velocity of the ions in the mass analyzer. The velocity of the ions has to be small in order to allow enough oscillations in the mass analyzer for separation. If the quadrupole is scanning too fast, spectral quality is lost and the resolution is reduced drastically. At too high scan rates, no ion can pass trough the mass analyzer.

Normally, with conventional sector instruments, the ion velocity is typically up to 100 times higher. Scan speed is limited on magnetic instruments by the ability to change rapidly the magnetic field without causing eddy currents which distort the field shape and slow the scan down. This problem can be overcome by the use of smaller, faster, fully laminated, low inductance magnets with powerful current supplies. Also in the SIM mode, the use of a small magnet combined with the high dynamic accuracy of a multi-point hall probe (to control the magnet field) enables the mass spectrometer to jump from peak top to peak top at medium resolution in approximately 25 ms. Reducing the switch time allows more dwell time (measuring time) per selected ion. In this way a higher sensitivity could be obtained because the time spent monitoring the ions per unit time is higher or higher sampling frequencies can be applied without loosing sensitivity.

Additionally, for a sector instrument, the mass resolving power (10% valley) $R = m/\Delta m$ is constant over the entire mass range.

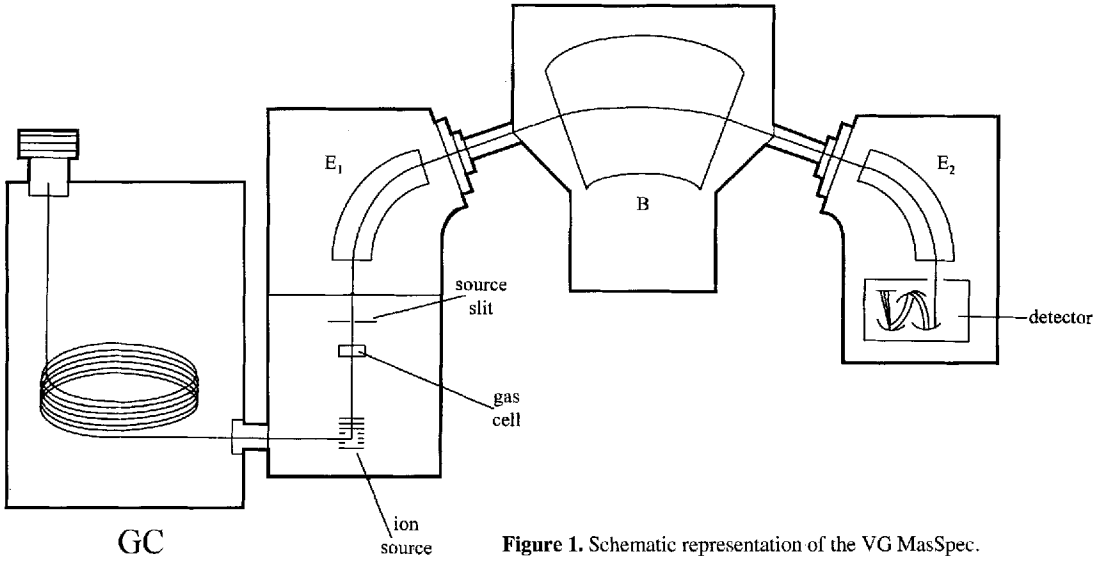

Figure 1. Schematic representation of the VG MasSpec.

For a quadrupole, the peak width is constant which means that the resolution depends on the transmitted m/z value. For quadrupole instruments, a peak width value of 0.5 Da is quite common, hence the resolution is $R = 2m$. In the lower mass range (40–300 Da), which is of interest for high speed GC separations, the peak width for a sector instrument operating at resolution 300 is smaller than the peak width obtained with a quadrupole instrument. In this respect, higher selectivity is obtained and the use of a sector instrument is favored. Extra selectivity could be obtained by operating the mass spectrometer at high resolving power. Higher scan speeds and lower detection limits make the combination of high-speed narrow-bore capillaries to sector instruments highly promising.

3.1 Scan Speed

The most common form of magnetic scan is the exponential one, either upward or downward in mass. It has the advantage of producing mass spectral peaks of constant width. With the MasSpec, the magnet is scanning from high to low masses. The cycle time for completing one spectral scan depends on scan time and resetting time. The cycle time is a function of the scan speed of the magnet and the mass range selected. A small reset time for the magnet is essential because otherwise measuring time, and thus sensitivity, will be reduced. By the use of a fast switching magnet, higher scan speeds can be obtained. In **Table 1**, an overview of the scan time, reset time and the resulting scan speed as a function of differing mass ranges and resolving powers is presented. The scan speed varies from 10 to 20 scans per second, depending on the mass range for a resolving power of 300, and decreases to about 3 to 7 scans per second for a medium resolving power of 2000. By the use of an extra power supply, the reset time might be decreased and the scan speed could be increased up to 30 scans per second at low resolving power.

Table 1. Maximum scan speed in the full scan mode for different mass ranges and dynamic mass resolving powers (at 10% valley).

Mass range (Da)		50–200	50–500
$R = 300$	t_{scan} (ms)	30	50
	t_{reset} (ms)	20	50
	scan speed (scans/s)	20	10
$R = 2000$	t_{scan} (ms)	120	300
	t_{reset} (ms)	20	50
	scan speed (scans/s)	7.14	2.86

It should be noted that at higher scan speeds, the dynamic resolution (when actually scanning a given mass range at a certain scan speed) is different than the static resolution (as determined by adjusting the slit width when sitting on a reference peak). This is illustrated in **Table 2**. From this table it is clear that the dynamic resolution in SIM or at low scan speeds in the full scan mode is hardly affected below resolution 5000. At higher scan speeds in the full scan mode, however, the resolving power reduces very quickly.

Table 2. Comparison of static and dynamic resolving power at different scanning modes and scan speeds.

Static resolving power	Dynamic resolving power		
	Full scan 3 scans/s	Full Scan 20 scans/s	SIM 20 cycles/s
300	300	300	300
2000	2000	300	2000
10000 (ultimate)	3000	300	> 5000

It is easy to compare the scanning possibilities of a quadrupole to the possibilities for a sector machine at the same scan speed, reset time and mass range as shown in Table 2. Assuming a length of 10 cm for the quadrupole rods and an extraction voltage of 5 V, depending on the mass range, reset time and scan speed, it is possible to calculate the time spent per ion in the full scan mode and to calculate the time required for the heaviest ion to travel along the mass separation section of the quadrupole. The results are shown in **Table 3**. From this table it is clear that for scanning the mass range from 50 to 200 Da at 20 scans/s, only part of the ions of $m/z = 200$ will reach the multiplier. This results in very bad mass spectra. Even if the mass range is extended to 500 Da, almost no ion with $m/z = 500$ can reach the multiplier during the time this ion is monitored.

Table 3. Calculation of the time spend per ion in the full scan mode and the time required to cross the mass separation section for the heaviest ion of interest for a quadrupole instrument (length of the quadrupole: 10 cm, extraction voltage: 5eV).

Mass range (Da)	50–200	50–500
Reset time (ms)	20	50
Scan speed (scans/s)	20	10
Time spent per ion (µs)	200	111.1
Time required for the heaviest ion to traverse the quadrupole (µs)	64.6	102

Often, the compounds of interest are present at low levels and hence selected ion recording techniques are preferred in order to obtain better sensitivity. Because the detection limit is dependent on the dwell time per ion, it is important that the reset time for jumping from one ion to another is minimized.

For a sector instrument it can be derived [21] that the mass to charge ratio (m/z) monitored by the detector, at a fixed radius r, is proportional to the square of the strength of the magnetic field (B) and inversely proportional to the accelerating voltage (U) [see Eq. (1)].

$$\frac{m}{z} = \frac{B^2 r^2}{2U} \quad (1)$$

From this equation it can be seen that there are two ways for jumping from one ion mass to the other. In the first situation the

magnet is jumped while the accelerating voltage is kept constant. The other way is to keep the magnetic field constant and vary the accelerating voltage. For most applications it is preferable to vary the magnetic field. For conventional sector instruments, relatively long reset times are required when scanning the magnet. This restriction is of no consequence for conventional GC because of the broader peaks. It becomes, however, more critical for high-speed separations. The scan speed should be compatible with the separation speed to match the chromatographic resolution. This means that for high-speed GC high sampling frequencies are required. Additionally, the measurement time per ion should be as high as possible in order to maximize sensitivity. Because the MasSpec has a small magnet, the switch time can be reduced to 15 to 25 ms. For voltage sweeping, a switch time of only 5 to 10 ms is required but in this situation the ions may be monitored only over a restricted mass range, limited to a 2:1 mass ratio. This can be explained by a difference in the efficiency of ion transmission [21].

In **Table 4** the switch times for voltage and magnetic SIM for going from mass to mass are shown. The measure time per ion per cycle is illustrated in **Figure 2.** For these calculations, we assumed that the reset time (time required for switching from the last peak top of a cycle to the first peak top of the next cycle) is twice the switch time. From Figure 2, it can be concluded that the sensitivity, which is proportional to the square of the dwell time per ion per cycle, decreases drastically when the number of selected ions is increased. For 5 cycles per second (Figure 2A), it is possible to perform SIM by jumping the magnet or by sweeping voltages while relative good sensitivity is obtained. Only for high resolution SIM jumping the magnet, the number of ions recorded is limited to approximately seven. Even with 10 cycles per second, it is possible to perform magnetic SIM with a few ions (Figure 2B). If the number of cycles is increased up to 20 (Figure 2C), it is no longer possible to perform SIM by jumping the magnet. In the same figure it can be seen that only a few ions can be recorded by jumping voltages.

Table 4. Switch times in the SIM mode from peaktop to peaktop in magnetic SIM, respectively voltage SIM, as a function of the mass resolution.

Mass resolving power (at 10% valley)	Switch time(ms) in magnetic SIM	Switch time(ms) in voltage SIM
300	15	5
2000	25	5

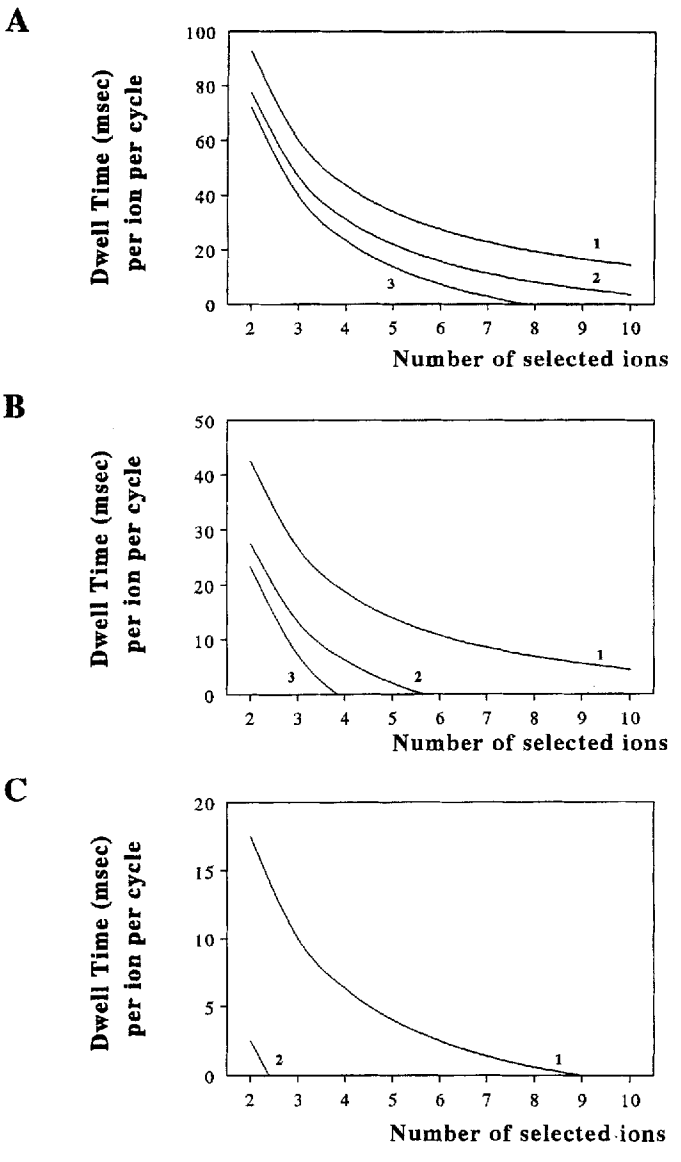

Figure 2. Dwell time per selected ion per scan as a function of the number of selected ions at 5 cycles per second (Figure 2A), 10 cycles per second (Figure 2B) and 20 cycles per second (Figure 2C) jumping voltages and magnetic field in SIM at low and medium resolution MS; voltage SIM (1), magnetic SIM at low resolution (2) and magnetic SIM at medium resolution (3).

3.2 Sensitivity, Dynamic Range, and Detection Limits

The detection limits were calculated according to Eq. (2):

$$Q_0^m = \sqrt{2\pi}\frac{2R_n}{S}\sigma_t \qquad (2)$$

where Q_0^m (g) is the minimum detectable amount (MDA) for a mass flow sensitive detector, R_n (mV) the noise level, *i.e.* the amplitude of the envelope of the baseline which includes all random variations of the detector signal, and S (mV . s/g) is the sensitivity for the GC/MS system. σ_t (s) is the peak width standard deviation. Because the chromatographic peak broadening is small for narrow-bore columns, it is obvious from equation (2) that the detection limit is improved by using 50 µm i.d. columns. To evaluate the sensitivity, a series of mixtures with increasing sample concentrations were injected. The sensitivity is the slope of plotting the area response *vs.* the amount injected onto the column.

In the full scan mode, the detection limits were in the range of 1 to 4 pg (see **Table 5**). The detection limits in the SIM mode depend on the mass resolving power of the mass spectrometer, the sample complexity and the time an ion is recorded per time unit. In **Table 6**, the detection limits of the most intensive ions of 1,4-dichlorobenzene are shown. As can be seen from this table, the sensitivity of the system improves when the resolving power is decreased. When performing higher resolution MS, the source

Table 5. Detection limits of the combined high-speed GC-MS setup in the full scan mode.

Compound	Detection limit (pg)
decane	1.3
2,2,3,3-tetramethylhexane	1.7
1-chlorooctane	2.5
undecane	1.8
2-dodecanone	3.4

Table 6. Detection limits in the SIM mode for some selected ions and the sum of the selected ion currents of 1,4-dichlorobenzene obtained for resolution 300 and 2000 switching the magnet.

Ion of *m/z*	Detection limit limit (fg) with $R = 300$	Detection limit (fg) with $R = 2000$
111.00	6.2	28.5
145.97	2.0	10.0
147.97	5.6	39.2
sum of selected ion currents	2.6	13.4

and collector slits are adjusted to accept a narrower ion beam. In this way ion transmission is reduced and the sensitivity is decreased. The difference in detection limits for selected masses is influenced by the relative intensity of the selected ions in the spectrum and the background noise level. For example, considering the isotopic pattern with two chlorine atoms, the theoretical abundance ratio of the ions at m/z = 147.97 and 145.97 should be close to 1.5. At low resolving power, however, the ratio for the detection limits was found to be about 2.5 and increased even up to 4 at high resolution. This difference is caused by the difference in noise level at these masses. The cycle with switching time and dwell time for the selected ions is presented in **Table 7**. When performing SIM at high resolution it is necessary to monitor at least one reference mass of the calibration gas. For this reason the calibration gas valve is opened during the chromatographic run. By the use of a lock-mass check channel it is possible to ensure the elimination of drift and hysteresis effects allowing the mass spectrometer to switch accurately to the peak tops by checking the reference mass and adjusting mass calibration during the acquisition.

For clean samples the detection limits are lower and hence better, when low resolution is used. At low resolution, the sensitivity is maximized because the mass window is broader and almost all ions can reach the detector. Lower detection limits are only obtained with low resolution if the sample is not complex. SIM data acquired via quadrupole GC/MS systems can be misleading due to interferences from other eluting compounds (chemical noise) within the sample that can mask the compounds of interest. For more complex mixtures and in instances where the concentration of the compounds of interest is particularly low, chemical background signals become a significant problem that hinder both identification and quantitation. These problems have in the past been overcome by pre-concentrating or isolating these compounds prior to GC/MS. This, however, often involves complicated and lengthy chemical and chromatographic separation techniques and can often produce misleading results. By increasing the resolution in the SIM mode, extra selectivity can be obtained. The advantage of sector instruments is the possibility to operate at higher resolving power. This is illustrated by the analysis of PCBs spiked in a waste oil sample. **Table 8** gives a list of the ions monitored together with their elemental composition, switch and dwell times in one cycle. In two instances the second isotope and even for the for the highest selected mass the third isotope has been monitored due to greater intensity.

In **Figure 3** the result of monitoring the ions at mass values of m/z 222.00, 255.96, 291.92, and 325.88 at low resolving power (at the left side) and medium resolving power (at the right side)

Table 7. Switch time and dwell time for the selected ions of 1,4-dichlorobenzene for the determination of the detection limits at low (300) and medium (2000) mass spectrometric resolution.

Ion of *m/z* (Da)	low resolution switch time (ms)	low resolution dwell time (ms)	medium resolution switch time (ms)	medium resolution dwell time (ms)
147.97	30	10	40	10
145.97	20	10	30	10
143.00	–	–	30	20
111.00	25	10	30	10

Table 8. Elemental composition, switch time, and dwell time for the selected ions in the analyses of PCBs in an oil at low (300) and medium (2000) mass spectrometric resolution.

m/z (Da)	elemental composition	low resolution ($R = 300$) switch time (ms)	low resolution ($R = 300$) dwell time (ms)	medium resolution ($R = 2000$) switch time (ms)	medium resolution ($R = 2000$) dwell time (ms)
222.00	$C_{12}H_8{}^{35}Cl_2$	40	10	50	10
255.96	$C_{12}H_7{}^{35}Cl_3$	25	10	25	10
291.92	$C_{12}H_6{}^{35}Cl_3{}^{37}Cl$	25	10	25	10
325.88	$C_{12}H_5{}^{35}Cl_4{}^{37}Cl$	25	10	25	10
359.99	$C_{12}H_4{}^{35}Cl_4{}^{37}Cl_2$	25	10	25	10
218.99	Reference mass	–	–	25	20

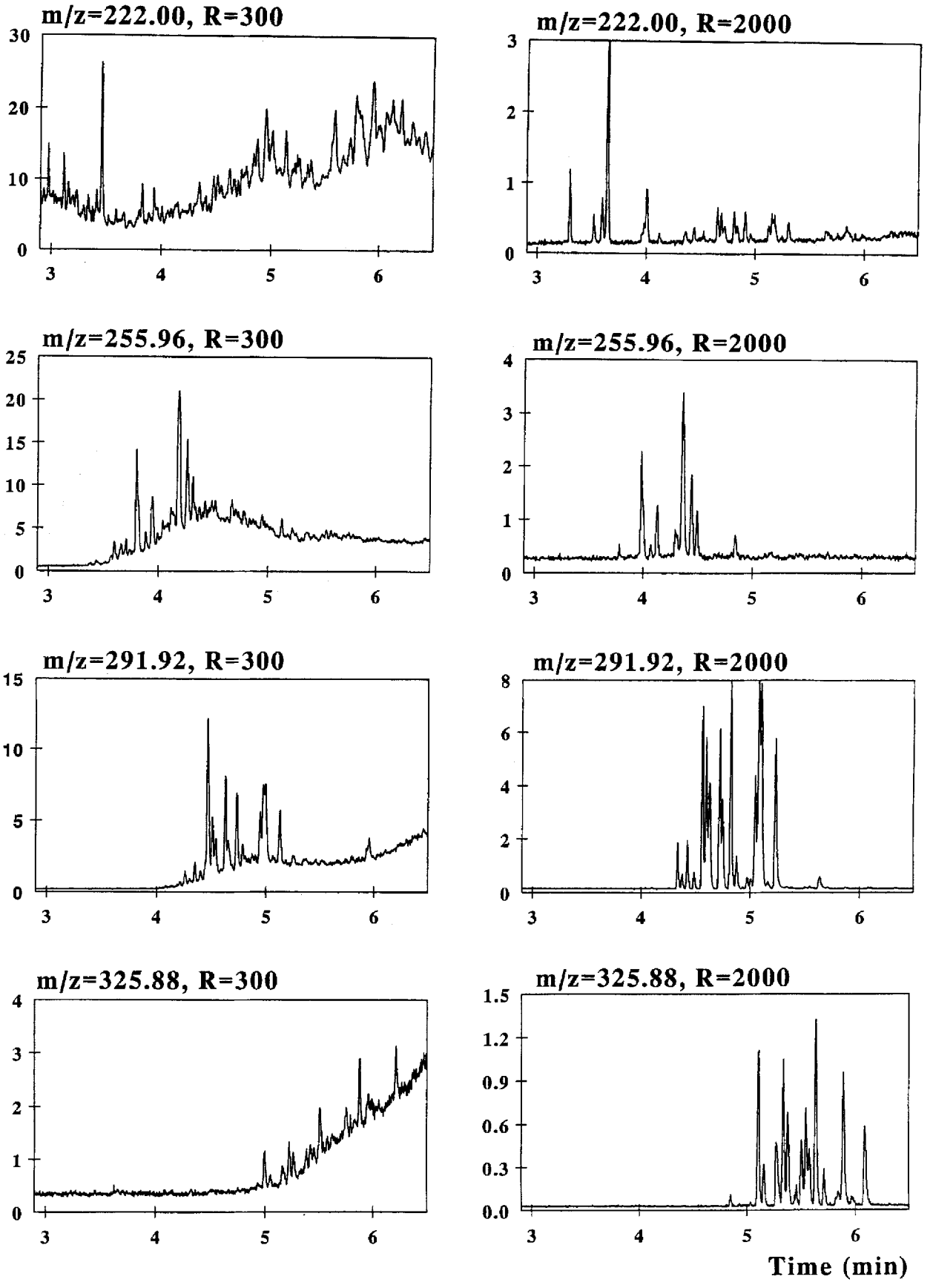

Figure 3. High-speed separation of a waste oil spiked with PCBs (Arochlor 1242). Ion current of 222.00, 255.96, 291.92, and 325.88 at low and medium resolution MS. GC conditions: 50 °C ballistically heated to 280 °C, p_i= 11 atm.

are shown. The responses obtained with low resolution exhibit severe interference. Improvements in the quality of data are seen in all traces. In the *m/z* 325.88 trace the rising baseline towards the end of the run in the low resolution mode suggests the presence of column bleed. Interferences limit the detectability of compounds in the lower concentration range at low mass spectrometric resolution. By the use of high resolution MS, an appreciable decrease in interferences is observed. If the ion intensity of the different chromatograms is examined, it can be seen that the intensity of the ion currents registered with medium resolution MS is decreased by at least a factor of ten. This can be explained by the small mass window (0.16 Da) by which many of the ions of the same nominal mass were discarded. Although the sensitivity for the compounds of interest is reduced, the interferences from ions at the same nominal *m/z* value are reduced even more, thereby enhancing the signal-to-noise ratio.

To evaluate the linearity of the mass spectrometric detection, various samples with increasing concentration were injected. At injected amounts (on the column) exceeding a few ng, ill-shaped peaks were observed, caused by overloading of the separation column. It was found that the mass spectrometer behaves perfectly linearly over the entire range from the detection limits of approximately 1 pg in the full scan mode, respectively 5 to 50 fg in the SIM mode up to a few ng. Additionally, the quality of the mass spectra in the full scan mode was very good over the entire range. Library search gave good results. Even in the low pg range it is possible to identify the compounds. In this way an acceptable working range was obtained to perform high speed GC separations. This working range can even be extended by a factor 20 to 100 by operating the mass spectrometer in the SIM mode.

3.3 Applications

The combination of narrow-bore columns with a fast double focusing mass spectrometer is an attractive hyphenated technique for a large number of high-speed GC analyses.

In **Figure 4** a fast separation of a reference alkylate standard mixture (No. 4-8267, Supelco, Bellafonte, USA) is shown. The separation is carried out in less than 90 s. To obtain the same separation efficiency with a 320 µm column, 10 to 15 min are required. Comparing with reference chromatograms, the most volatile compounds were not observed because of vaporization of these compounds from the sample vial.

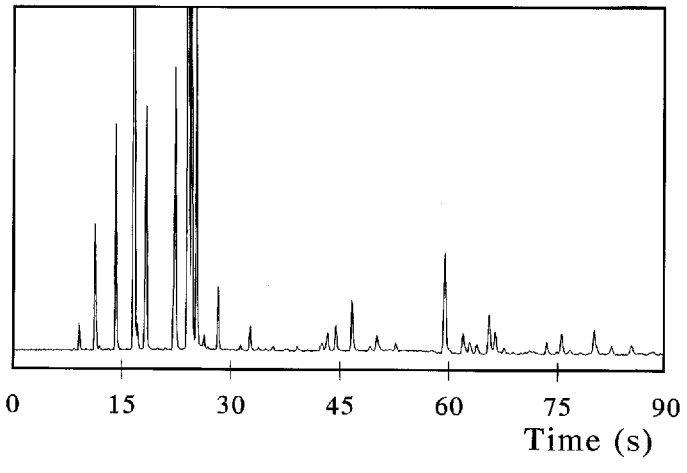

Figure 4. High speed separation of reference alkylate standard: GC conditions: 40 °C → 40 °C/min → 100 °C, p_i = 11 atm. MS conditions: EI, scan speed 12.2 scans/s, mass range 60–200, mass resolution 300.

Another interesting application, shown in **Figure 5**, is the separation of the EPA 610 PAH mixture with splitless injection. The separation is performed within 12 min. A comparison of an experimental mass spectrum and library spectrum is shown in **Figure 6**. Library search gives good peak matching and all compounds could readily be identified.

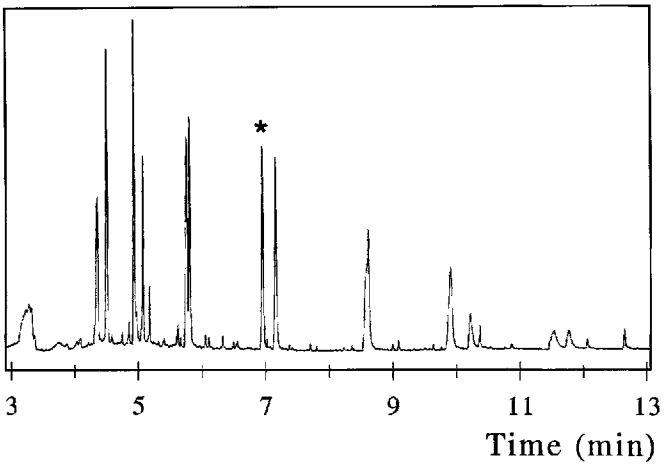

Figure 5. High speed separation of EPA 610 PAH standard: GC conditions: 50 °C (2 min) ballistically heated to 300 °C, splitless time 2 min, V_{inj} = 0.3 µl, p_i = 11 atm. MS conditions: EI, scan speed 9.55 scans/s, mass range 50–500, mass resolution 300.

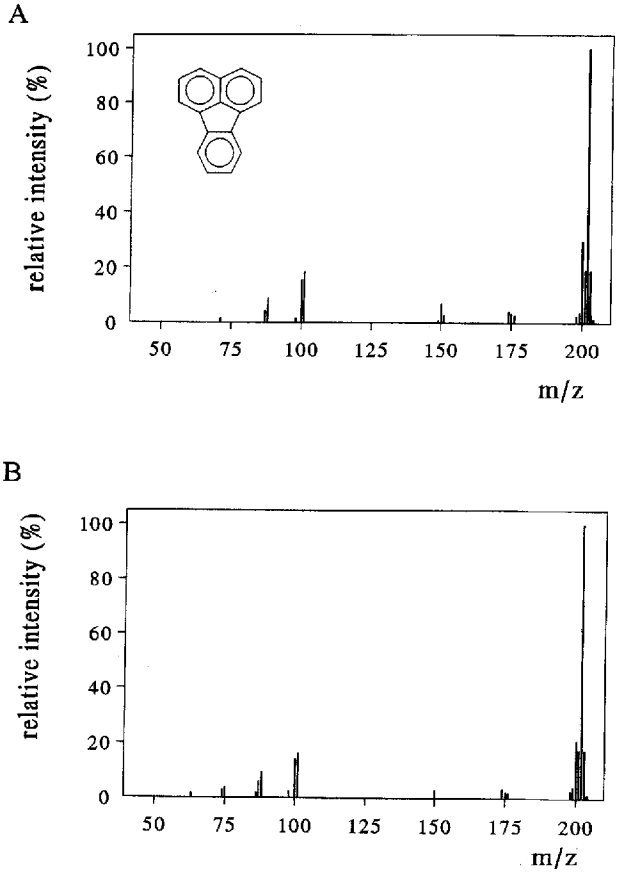

Figure 6. Experimental mass spectrum (Figure 6A) of fluoranthene (peak indicated by * in Figure 5) and the librarary mass spectrum (Figure 6B).

4 Conclusions

It has been demonstrated that the EBE sector instrument operating in the full scan mode is compatible with chromatographic separations in the minute range. In the full scan mode, the scan speed varies from 10 to 20 scans per second, depending on the mass range for low resolving power and decreases to about 3 to 7 scans per second for a medium resolving power. 5 to 10 cycles per second could be obtained with magnetic SIM. Fast multiple ion detection can only be applied using a fast electric jump. The detection limits obtained in the full scan mode are in the low pg range. In the SIM mode, detection limits as low as 5 to 50 fg are obtained, depending on the sample complexity and mass spectrometric resolving power. It was illustrated that for complex mixtures the best signal-to-noise ratio is obtained by operating the MS in the magnetic SIM mode at medium resolving power because there is only a small mass range in the voltage SIM mode.

Acknowledgments

The authors would like to thank the Netherlands Organization for Scientific Research (NWO) for supporting this work by a grant.

References

[1] D.H. Desty, A. Goldup, and W.T. Swanton, "Gas Chromatography", N. Brenner, J.E. Callen, and M.D. Weiss, Eds., Academic Press, New York, 1962, (1961 Lansing Symposium), 105–135.

[2] C.P.M. Schutjes, E.A. Vermeer, J.A. Rijks, and C.A. Cramers, J. Chromatogr. 253 (1982) 1.

[3] T. Noij, J. Curvers, and C.A. Cramers, J. High Resol. Chromatogr. Chromatogr. Commun. 9 (1986) 752.

[4] B.A. Ewels and R.D. Sacks, Anal. Chem. 57 (1985) 2774–2779.

[5] A. van Es, J. Janssen, C.A. Cramers, and J. Rijks, J. High Resol. Chromatogr. Chromatogr. Commun. 11 (1988) 852.

[6] A. Peters, M. Klemp, L. Puig, C. Rankin, and S. Sacks, Analyst 116 (1991) 187.

[7] A. van Es, J. Janssen, R. Bally, C. Cramers, and J. Rijks, J. High Resol. Chromatogr. Chromatogr. Commun. 10 (1987) 273.

[8] H.M. Snijders, H.-G. Janssen, R.M.G. Straatman, and C.A. Cramers, Proc. 15th International Symposium on Capillary Chromatography, Riva del Garda (1993), Huethig, Heidelberg, (1993), 391.

[9] R.L. Wade and S.P. Cram, Anal. Chem. 44 (1972), 131.

[10] G. Gaspar, P. Arpino, and G. Guiochon, J. Chromatogr. Sci. 15 (1977) 256.

[11] C.P.M. Schutjes, C.A. Cramers, C. Vidal-Madjar, and G. Guiochon, J. Chromatogr. 279 (1983), 269.

[12] C.P.M. Schutjes, Thesis, Eindhoven University of Technology, 1985.

[13] A. van Es, Thesis, Eindhoven University of Technology, 1989.

[14] A. van Es, J. Rijks, and C.A. Cramers, J. High Resol. Chromatogr. Chromatogr. Commun. 12 (1989), 303.

[15] H. Ke, S.P. Levine, R.F. Mouradian, and R. Berkley, Am. Ind. Hyg. Assoc. J. 53(2) (1992) 130-137.

[16] C.P.M. Schutjes, E.A. Vermeer, G.J. Scherpenzeel, R.W. Bally, and C.A. Cramers, J. Chromatogr. 289 (1984) 157.

[17] P.G. Van Ysacker, H.-G. Janssen, H.M.J. Snijders, and C.A. Cramers, J. High Resol. Chromatogr. 18 (1995) 397.

[18] P.G. Van Ysacker, H.-G. Janssen, H.M.J. Snijders, P.A. Leclercq, and H.J.M. van Cruchten, C.A. Cramers, J. Microcol. Sep. 5 (1993) 414.

[19] H. Wollnik, R. Becker, H. Götz, A. Kraft, H. Jung, C.-C. Chen, P.G. Van Ysacker, H.G. Janssen, H.M.J. Snijders, P.A. Leclercq, and C.A. Cramers, Int. J. Mass. Spec. Ion Phys. 130 (1994) L7.

[20] C.C. Grimm and S.W. Lloyd, Proceedings of the 42nd ASMS Conference on Mass Spectrometry and Allied Topics, Chicago, Illinois (1994), p 492.

[21] W. McFadden, in "Techniques of combined gas chromatography/mass spectrometry: Applications in organic analysis", J. Wiley & Sons, New York, 1973, p 36.

Ms received: April 10, 1995
Accepted: August 20, 1995