CHAPTER 6

Advanced Gas Chromatography/Mass Spectrometry Methods

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6.1 FAST GAS CHROMATOGRAPHY/MASS SPECTROMETRY MODE

Gas chromatography (GC)/mass spectrometry (MS) has become a gold standard in many environmental applications, such as monitoring of pollutants (Chapter 2). Most of the priority pollutants are semi-volatile compounds ideally suited for GC separation followed by MS detection in the gas phase.

The natural desire of any researcher dealing with a GC/MS method involves reducing the analysis time. The decreased analysis time readily leads to decreased cost since less input in terms of human resources is needed to produce the same analytic output. If a high sample throughput is a task of an analytical laboratory, fewer instruments are needed to do the same amount of work. Commercially, it is a good way to increase the number of customer samples to be processed in the same amount of time. Conventional GC/MS methods use capillary columns (note that the term 'GC column' used later in this chapter always implies capillary columns rather than packed columns), which are typically 30 m long with a 0.25 mm internal diameter (i.d.). These well-established methods produce adequate results. However, speed is their limitation, as satisfactory separations of complex samples may take an hour or more. In any case, any reduction of time in GC/MS analysis should be in harmony with the quality of produced data, which must remain satisfactory. Thus the primary aim of the fast GC/MS regime is to maintain sufficient resolving power in a shorter time. Nowadays, classic serial analyses (e.g. priority pollutants) can be shortened easily by 3–10 times without sacrificing data quality. The fast GC/MS regime can be achieved by improvement of both GC and MS hardware dedicated to fast GC/MS analysis. It is theoretically possible to speed GC separation, maintaining the same chromatographic resolution to some extent. Afterwards it is possible to shorten the separation time further by sacrificing GC separation. However, the overlapped chromatographic peaks may be resolved by means of processing the data recorded by the MS analyser. Hence, the GC/MS combination enables faster analysis compared to the GC/flame ionisation detector (FID) or any other detectors.

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6.1.1 How can the GC separation be optimised for a fast GC/MS approach?

It is evident that the use of shorter columns reduces the analysis time. Analytes simply spend less time in the column and the total GC run time decreases. However, the separation efficiency, namely peak sharpness and analyte resolution, could be badly affected unless other parameters of the analysis are adjusted. The efficiency of the GC separation is commonly measured as a number of theoretical plates (*N*). The same number of theoretical plates for different column lengths (*L*) means the same resolving power of these columns. The height equivalent to theoretical plate (*H*) is defined as $H = L/N$. If a shorter column is going to be used, the smaller *H* has to be achieved by changing other column characteristics. The *H* parameter is dependent on carrier gas velocity *u*, the inner diameter *d* of a capillary column, diffusion coefficient of the solute in the carrier gas *D* and thermodynamic properties of the solute/phase system, expressed by constant *K*. The height equivalent to theoretical plate (*H*) can be described by the simplified Golay equation (Gonnord *et al*., 1983)

$$H = \frac{2D}{u} + \frac{d^2 \cdot K^2}{96D} \cdot u$$

This equation can be differentiated to calculate the minimal *H*, $H_{\mathrm{min}} = (d/2) \cdot K$ is directly proportional to the i.d. of the capillary column; therefore, to minimise *H*, narrow-bore columns should be used (Figure 6.1).

Another obvious way to decrease the GC run time is to reduce the film thickness of the capillary column used for the analysis. It is clear that analyte should spend less time for an absorption/desorption act in a column with thinner coating. This is indeed observed in practice. Figure 6.1 demonstrates the combined effect of film thickness and column i.d. on retention times of the separated components. It is worth mentioning that peak shape and the potential for quantitative analysis are also better in the case of fast GC separation.

It is obvious that further shortening of GC analysis times can be achieved by increasing carrier gas velocity. In GC, linear velocity (measured in cm/s) refers to the speed at which the carrier gas travels through the column. Analytes are dissolved in and thereby transported through the column by the carrier gas. Thus faster carrier gas speed means faster elution of the components, resulting in shorter run times. As mentioned above, the height of equivalent theoretical plate and the gas velocity are related to each other by the Golay equation. The dependence is non-linear (Figure 6.2), and so-called optimal velocity can be calculated at the point where *H* is minimal, that is where the column efficiency is greatest. As linear velocity deviates from optimal $u_{\mathrm{opt}} = 8D/Kd$, peak shape and chromatographic resolution decrease. At a linear velocity less than optimal, analytes spend too much time in the stationary phase, resulting in great resolution but poor peak shapes and long run times. If the linear velocity is greater than optimal, analytes do not spend enough time in the stationary phase, which results in short analysis times but inadequate GC resolution. Interestingly, narrow columns allow for faster linear velocity. The latter becomes clear when the linear velocity is plotted against *H*. In other words, the Golay equation can be presented graphically in the so-called Golay curve (Figure 6.2).

As previously mentioned, optimal linear velocity is achieved at the lowest point of the curve (points A). According to Figure 6.2, optimal carrier gas velocity increases as column i.d. decreases; for instance, the optimal velocity is 12 (point $A_{0.75}$) and 40 (point $A_{0.10}$) cm/s with 0.75 and 0.10 mm i.d. columns respectively. Narrow columns should be operated at a higher carrier gas velocity, which will comply with the fast GC/MS idea. What is more important, narrow columns

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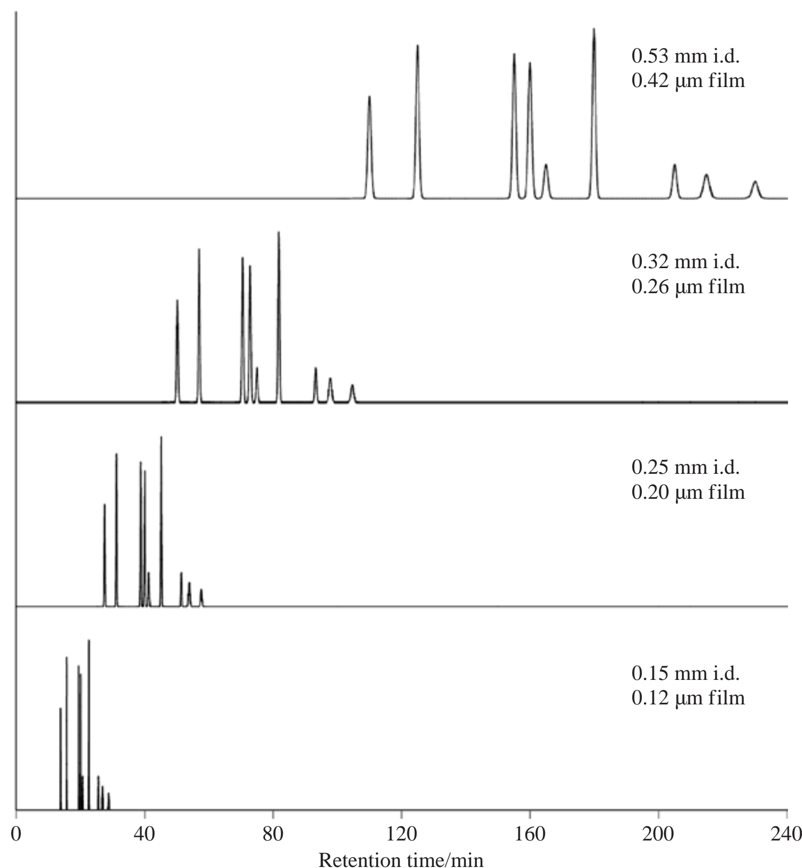
Figure 6.1: Effect of film thickness and column i.d. on the retention times of the components. (Source: Hübschmann, H.-J.: *Handbook of GC/MS: Fundamentals and Applications*, p. 130, 2008. Copyright Wiley-VCH Verlag GmbH & Co. KgaA. Reproduced with permission.)



possess flatter Golay curves. This fact allows the carrier gas velocity to be increased above optimal with negligible decrease in column efficiency.

The flatter Golay curves with lower minimal H can also be obtained by replacing the standard carrier gas helium (He) by hydrogen (Hail and Yost, 1989). However, the high flammability of the latter is a significant restriction for its application in GC/MS.

It is hard to ignore the fact that the faster temperature ramp provided by the GC system helps analytes to be rapidly eluted from the column. Indeed, it works, but the capabilities of the system are limited by the hardware, namely the GC ovens. An elegant way to permit very fast temperature ramps was developed by Thermo Corporation. A special unit consisting of a wire heater, a temperature sensor and a narrow-bore short column wrapped together in ceramic fibre enables a linear temperature ramp of up to 1200°C/min to be achieved. This approach is known as ultra-fast GC and allows GC run times to be less than 3 min. Table 6.1 summarises all the approaches discussed to achieve short GC run times.

In practice, a fast GC/MS column is from 0.10 to 0.18 mm in diameter and 20 m or shorter (see the caption to Figure 6.3). Short columns allow shorter run times, but these are at the expense

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Figure 6.2: Calculated Golay curves corresponding to different column diameters.

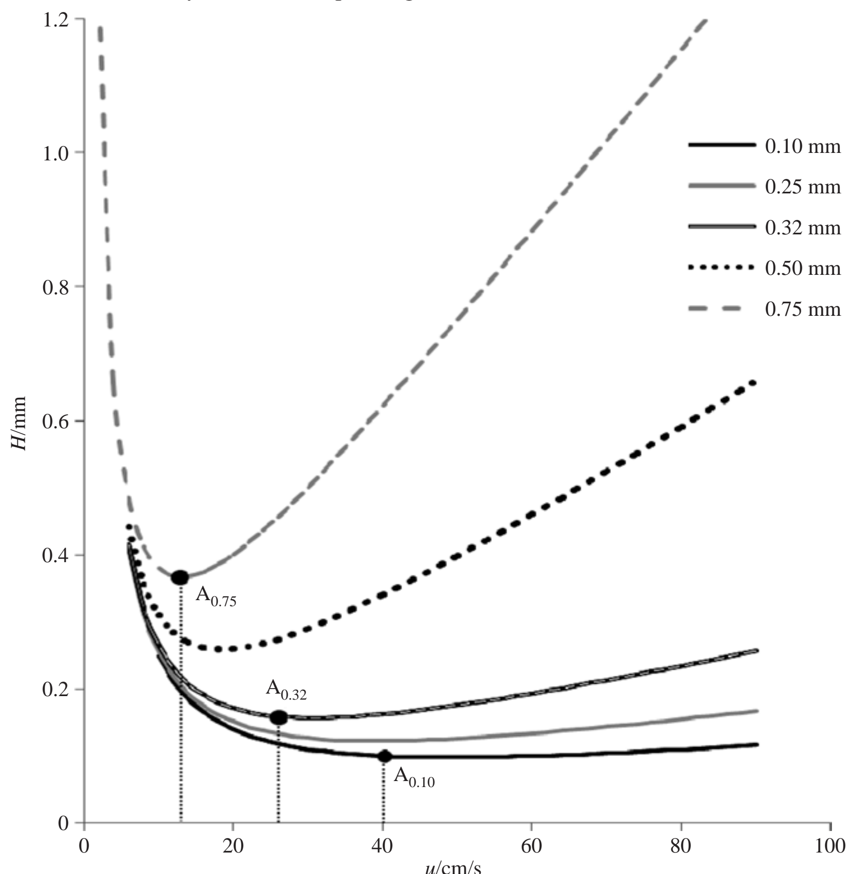

Table 6.1: GC parameters permitting fast GC/MS technology.

What parameter to change?	How to change the parameter for analysis time reduction
Column length	Use shorter columns
Temperature ramp slope	Apply steeper heating rate
Column i.d.	Consider narrow bore columns providing higher efficiency
Film thickness	Use thinner film coatings to improve GC separation
Carrier gas flow rate	Increase velocity (speed up the elution of the analytes)
Carrier gas type	Use hydrogen if possible

of the reduced sample capacity. Narrow i.d. and thin coating mean that a smaller amount of sample can be loaded on to the column compared to a conventional GC/MS. Therefore, high split ratios may be required to prevent column overload, which is addressed in the hardware issues. Notably, it is not an issue in terms of sensitivity, since narrower and higher peaks are generated in fast GC/MS, and the sensitivity is maintained.

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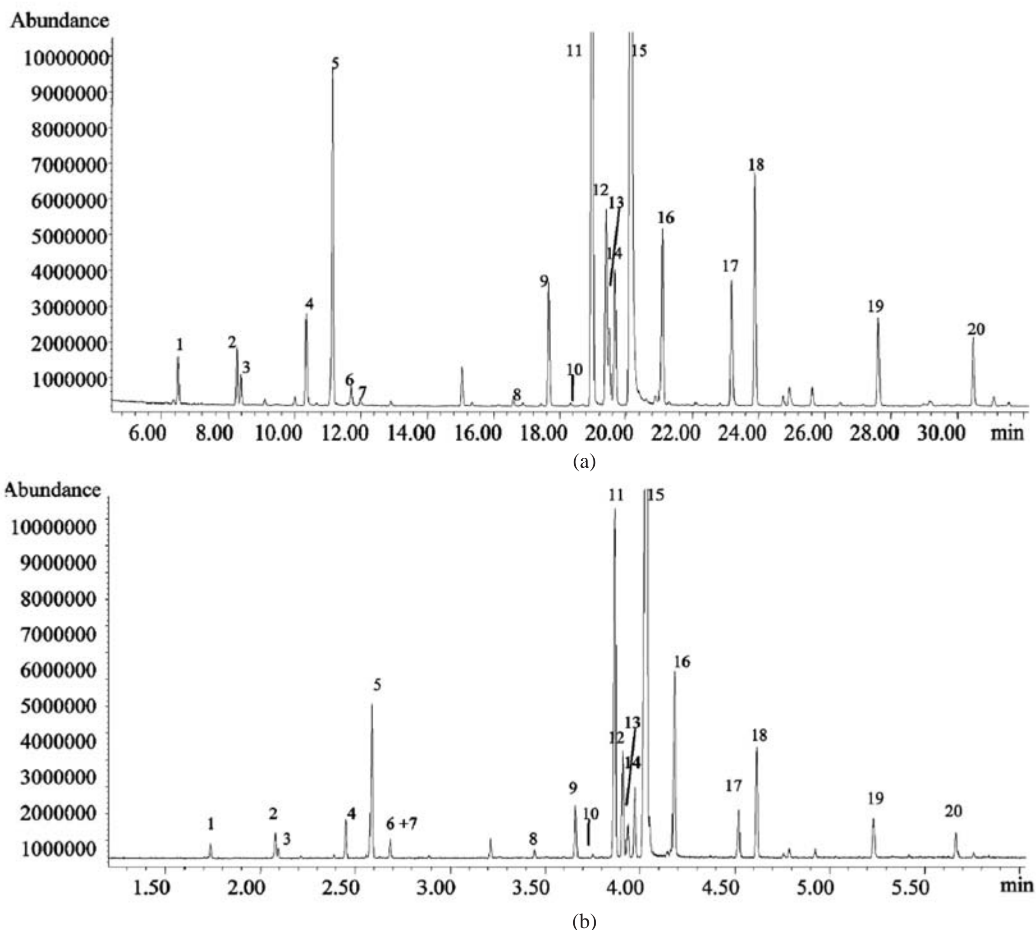
Figure 6.3: Comparison of (a) conventional and (b) fast GC/MS analyses of peppermint oil. Parameters: (a) column $L = 25$ m, i.d. $= 0.25$ mm, film thickness $= 0.25$ μm; split ratio = 1/100, He flow = 1 mL/min, ramp = 3°C/min; (b) column $L = 10$ m, i.d. $= 0.1$ mm, film thickness $= 0.10$ μm; split ratio = 1/200, He flow = 0.6 mL/min, ramp = 20°C/min. Trace GC ultra combined with a trace dual stage quadrupole mass spectrometer. (Source: Rubiolo, P., Liberto, E., Sgorbini, B., Russo, R., Veuthey, J.-L. and Bicchi, C. Fast-GC–conventional quadrupole mass spectrometry in essential oil analysis. *Journal of Separation Science*. 2008. 31: 1074–1084. Copyright Wiley-VCH Verlag GmbH & Co. KgaA. Reproduced with permission.)



Low-pressure GC/MS has been suggested to keep a high capacity of the column under fast GC/MS operation. Instead of short, narrow-bore columns, wide-bore columns possessing high sample capacity are used. In this method, the outlet of a separation column, typically 10 m long, 0.53 mm i.d. and with 0.25–1 mm film thickness, is connected to a vacuum source; therefore, the GC separation is performed at low pressure (LP-GC). Pressure affects the value of optimal linear velocity of the carrier gas. A transformation of the Golay equation in conjunction with the known relation between carrier gas flow and pressure in the column leads to the conclusion that lower pressure results in higher optimal velocity (Hail and Yost, 1989). A mass spectrometer is naturally operated at lower pressures, making it an ideal detector and providing LP-GC/MS conditions

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(Maštovská *et al*., 2001). Apart from faster run time, the LP-GC/MS set-up allows operation under relatively lower temperatures due to the reduced pressure. This feature helps thermolabile analytes to survive, which would be impossible at the normal pressure GC/MS.

6.1.2 What MS analyser contributes to a fast GC/MS approach?

Obviously, fast GC separation produces very narrow peaks, which have to be accurately detected. To preserve adequate peak shape and make them suitable for quantitative analysis, a very fast acquisition rate may be required. This statement was clearly illustrated in Figure 2.11 of Chapter 2 and the corresponding text.

A common classification of GC/MS approaches (Hajslova and Cajka, 2008) is presented in Table 6.2. As a general rule, 10 data points per upper half of the peak are sufficient for a proper peak reconstruction. Therefore, a minimal required acquisition rate can be calculated for different GC/MS approaches (see Table 6.2). The acquisition rate is a characteristic of the mass analyser (Table 6.3, Maštovská and Lehotay 2003).

A comparison of Tables 6.2 and 6.3 gives clear evidence of the usefulness of high-resolution time-of-flight (TOF) and sector analysers for fast GC/MS applications. The use of ion traps is restricted, while quadrupoles may provide quite reasonable performance. As an example, fast GC/MS analysis of essential oils allowed a six-fold reduction of run time (Rubiolo *et al*., 2008) from 36 to 6 min (Figure 6.3). If selected ion monitoring mode (see Chapter 2) is used, the acquisition rate significantly increases allowing very fast GC/MS analyses with quadrupole analysers. Comprehensive very fast and ultra-fast GC/MS applications, however, can be achieved only using high-speed TOF analysers.

Table 6.2: Classification of GC/MS approaches related to run times.

Type of GC/MS analysis	Typical separation time/min	FWHM*/ms	Required MS acquisition rate/spectra/s
Conventional	>10	>1000	< 10
Fast	1–10	200–1000	10–50
Very fast	0.1–1	30–200	50–350
Ultra fast	<0.1	5–30	>350

*FWHM: peak full width at half maximum.

Table 6.3: Characteristics of common mass analysers important for fast GC/MS data acquisition.

Mass analyser	Upper mass limit	Spectral acquisition rate, spectra/s (Hz)	Resolution
Quadrupole	80–1050 Da	15–33 (for 300 Da mass range)	~0.5 Da
Ion trap	650–1000 Da	~ 20 (for 300 Da mass range)	~1 Da
High-speed TOF	1000 Da	100–500	1400 FWHM
High-resolution TOF	1500 Da	200	50 000 FWHM
Sector	4000 Da	7 per decade*	Up to 80 000

*A decade is a factor of 10 in scan range (e.g. 100–1000 or 50–500 *m*/*z*).

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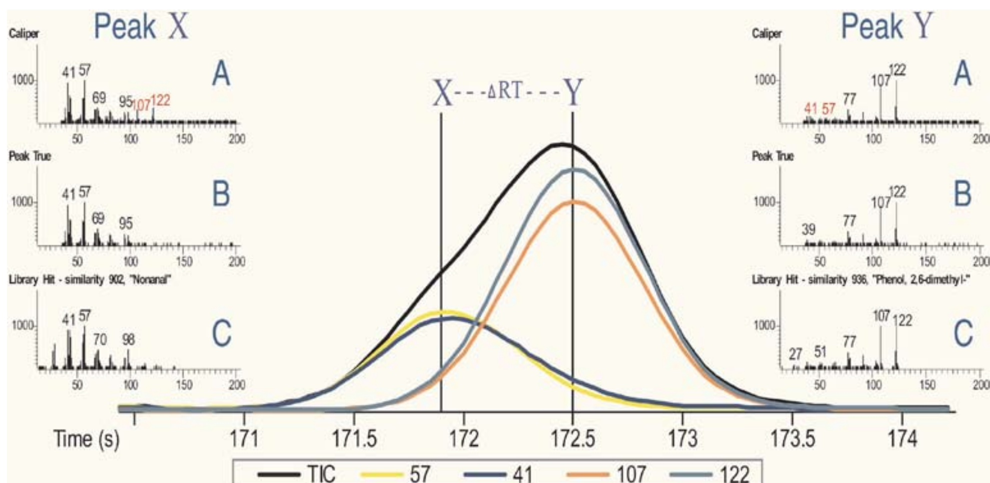
It is not only the acquisition rate that makes TOF analysers ideal for fast GC/MS applications. When high-temperature ramps and carrier gas velocities higher than optimal are used in order to shorten run times, GC separation conditions worsen. This means that analytes elute as overlapped peaks, corresponding mass spectra appear as 'mixed' and secure identification of the analytes becomes challenging. To avoid false identifications, such complex spectra must be refined. One of the refining procedures is a background subtraction (Chapter 2). This is also the easiest way to obtain cleaner spectra since the background peaks are usually consistent within a short time of the peak (or overlapped peaks) elution during a fast GC/MS experiment. A more complex situation would involve refining the spectrum of a given analyte from the peaks belonging to the coeluting substance. The most popular way to reach this goal nowadays is demonstrated in Figure 6.4.

Take into account a GC peak formed due to the coelution of two substances, X and Y. The total ion current (TIC) trace appears as a single, poorly shaped peak, and there is no direct evidence that this peak is in fact a superposition of two peaks. A mass spectrum recorded at any retention time along this peak (spectrum A in Figure 6.4) will be a mixture of mass spectra of substances X and Y. A software package creates mass chromatograms (Chapter 2) for each *m*/*z* value and then identifies all *m*/*z* values reaching their maximum at the same retention time (Figure 6.4). These *m*/*z* values (for example, *m*/*z* 57 and 41 in Figure 6.4, reaching their maxima at 171.9 s) and the intensities of the corresponding peaks constitute a reconstructed mass spectrum (spectrum B in Figure 6.4). Spectrum B corresponding to peak X is clearly refined from the peaks of *m*/*z* 107 and 122, belonging to substance Y. In a similar way, peaks of *m*/*z* 107 and 122 reach their maximum at 172.5 s, and are attributed to spectrum B of substance Y, refined from outsider *m*/*z* 57 and 41 peaks. Refined spectra B are used for the comparison to library hits (spectra C in Figure 6.4). If some of the fragment ions belong to several ingredients with close retention times, the software divides the intensities of their peaks according to the standard abundances of these ions in the library spectra of the identified compounds. The corresponding mass chromatograms may be used for quantitative analysis as well.

Usually this approach results in very high matches between a refined spectrum and a library hit (above 90% in the given example). However, to make this approach work properly in fast GC/MS, several criteria have to be fulfilled. First, a substance has to elute as a symmetrical peak

Figure 6.4: Peak deconvolution algorithm. (Courtesy of LECO Corporation.)



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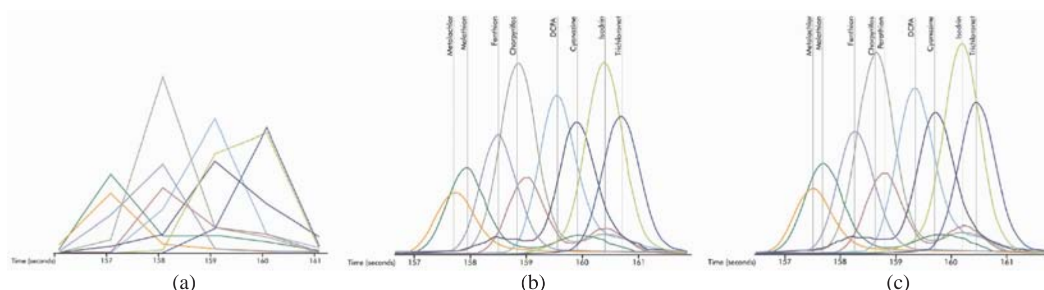
having one maximum, and this maximum should be the same for all the mass chromatograms of the analyte. This criterion can easily be affected by spectral skewing (Chapter 2). So, non-scanning instruments, primarily TOF, are preferable for deconvolution, since they produce the same mass spectrum along the whole elution of the analyte (note: the algorithm also works with scanning analysers in the case of relatively long run times). This issue was discussed in Chapter 2 (Figure 2.12). Second, peaks have to be as smooth as possible, in other words differentiable, which is necessary for automatic maximum finding. Smoother peak shape is provided by a higher number of spectra per peak; therefore faster acquisition rate is a benefit for deconvolution (Figure 6.5). Third, retention time difference (ΔRT in Figure 6.4) of two peaks has to be sufficient to detect two maxima. Clearly, faster acquisition rate shortens ΔRT, which makes deconvolution more effective in fast GC/MS applications. To illustrate this issue, the results of the analysis of pesticides performed at 1, 20 and 40 spectra/s are displayed in Figure 6.5. The 40 Hz acquisition rate is enough to distinguish the ΔRT difference in maxima of chlorpyrifos and parathion, while peaks of these analytes are attributed to the same maximum at 20 Hz. Additionally, the chlorpyrifos spectrum at 20 Hz is not refined enough for reliable identification by mass spectral library.

Summarising the above-mentioned, the high-speed TOF analyser is the most appropriate one for peak finding, deconvolution and fast GC/MS applications overall. Only TOF analysers are suitable for very fast GC/MS, especially if the sample is not very complex and analytes can be sufficiently deconvoluted. In this case very short columns (<5 m) and less than a minute run times can be used. This particular potential of TOF analysers and a very fast GC/MS mode enabled the implementation of two-dimensional GC/GC/MS (see below).

6.2 GC/MS WITH SUPERSONIC MOLECULAR BEAMS INTERFACE

Some innovations allow not only the speed of the analysis to be increased, but also better quality mass spectra to be obtained and the range of the compounds amenable to GC/MS analysis to be expanded. As has already been mentioned above, alongside the significant analytical advantages provided by GC/MS, this combination imposes certain constraints on the performance and capabilities of both techniques. For example, mass spectrometer vacuum requirements usually restrict the GC flow rate to a few (normally 1–2) mL/min, which limits the range of compounds amenable for standard GC/MS analysis in comparison with say, GC with FID. On the other hand, a GC run of compounds with different boiling points requires the ion source temperature to be optimised for the last to elute (least volatile) compound, which can deteriorate the quality of mass

Figure 6.5: Effect of acquisition speed for automated peak finding and deconvolution (pesticide analysis): (a) 1 Hz, no peaks found; (b) 20 Hz, eight analytes found and deconvoluted; (c) 40 Hz, all nine analytes resolved. (Courtesy of LECO Corporation.)



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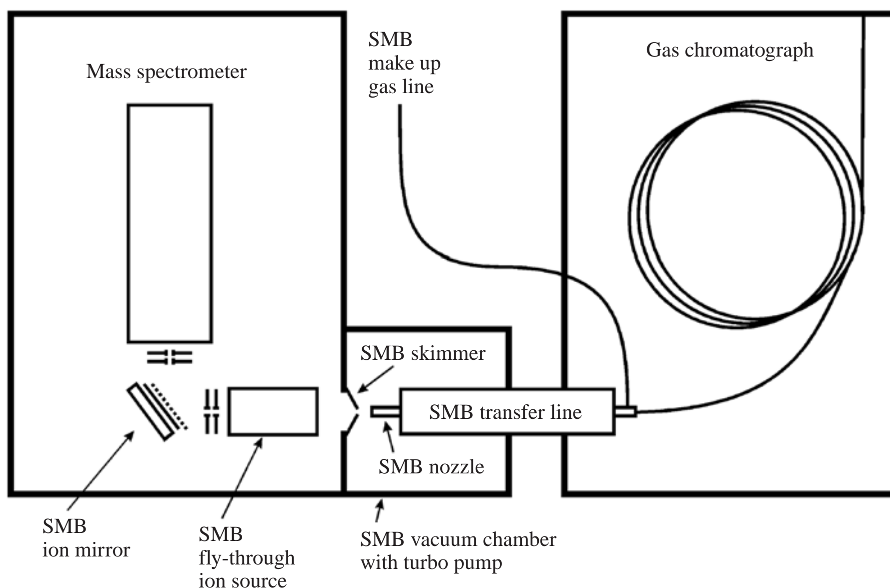
spectra of earlier eluted compounds. These and some other common GC/MS compatibility problems are illustrated and discussed below. They may be eliminated altogether in GC/MS with supersonic molecular beams interface (SMB GC/MS or supersonic GC/MS as a nickname, Figure 6.6) where new and unique features are emerging. The SMBs technique has been used for GC/MS coupling since the 1990s (Amirav, 1991; Dagan and Amirav, 1994). Various applications and features of the technique are reported elsewhere (Amirav *et al*., 2008; Fialkov and Amirav, 2008; Fialkov *et al*., 2003; 2006; 2007) while model '5975-SMB' (Aviv Analytical, Tel Aviv, Israel) is produced for its combination with the Agilent 5975 GC/MS and/or 7000 triple quadrupole.

As depicted in Figure 6.6, the SMB interface consists of a few parts: heated and temperature programmable transfer line with a small, shaped SMB nozzle (~0.1 mm in diameter) at its end, a vacuum chamber that accommodates the nozzle part of the transfer line and a skimmer in front of it, an SMB fly-through ion source and an ion mirror (Amirav, *et al*., 2008; Fialkov *et al*., 2006).

A GC column output is mixed with additional helium (He) make-up gas at about one atmosphere prior to the nozzle. Helium gas with seeded sample compounds flows through the nozzle at about 100 mL/min flow rate and expands into a vacuum, forming an SMB. The following features of SMBs are of primary importance and are practically used in the device: all species in the beam (sample molecules and He atoms) possess about the same velocity that is the final (supersonic) velocity of He atoms; the kinetic energy of the sample molecules is increased, correspondingly; the vibrational energy of the sample molecules is significantly decreased in accordance with the decrease of the internal energy via cold (slow) intra-beam collisions (that would correspond to the temperature of a few to a few 10s of Kelvin); sample molecules are propagated as a more narrow beam than He atoms (so-called jet separation phenomena). The inner portion of the beam, collimated by a skimmer, axially enters the cylindrical fly-through SMB electron ionisation (EI) ion source. The sample molecules fly along the ion source in its central

Figure 6.6: A schematic diagram of an SMB GC/MS.



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part where there are no electric fields, while 70 eV electrons, emitted by a long (~30 mm) filament, cross the beam in the radial direction and ionise the beam (and vacuum background) molecules. Ions of the beam molecules continue their flight along the ion source axis with the same velocity as the beam molecules, exit the ion source and are deflected by the SMB ion mirror towards a quadrupole mass analyser. Ions of vacuum background molecules that, mostly, do not fly along the ion source axis, hit the walls of the ion source and are neutralised.

It can be seen that there are several SMB interface features that enhance analytical capabilities and applicability of GC/MS:

- GC column flow rate can be practically 'unlimited' (up to 100 mL/min);
- sample molecules are vibrationally cooled prior to ionisation;
- the ion source has inherent 'inertness';
- the ion-source-related peak tailing issue is irrelevant;
- the ion source has an ultra-fast response time ($<$100 μs);
- most of the ions of background molecules do not enter the mass spectrometer, and thus the noise is reduced and there is no 'memory' effect.

Figure 6.7 (left panel) demonstrates the deterioration of the chromatographic signals of lower volatility compounds with the reduction of the ion source temperature (due to the dramatic increase of the residence time of molecules on the surfaces of the ion source with temperature reduction). It is obvious that, for the GC/MS analysis of a given mixture, the ion source temperature should not be less than 250°C.

However, the higher the ion source temperature, the lower the relative abundance of the molecular ion in the corresponding mass spectrum (Figure 6.7, right panel). This effect is due to the increased probability of fragmentation of any molecular ion (EI, 70 eV) with increased internal thermal energy of the corresponding molecule, as the latter parameter is directly proportional to the ion source temperature.

As pointed out above, conventional GC/MS suffers from a major contradiction between the chromatography quality and the quality of mass spectra, both of which are determined by the ion source temperature (Amirav *et al*., 2008). This effect is often the main reason for having a smaller relative abundance of the molecular ion in the experimental GC/MS mass spectra in comparison to the spectra in the National Institute of Standards and Technology (NIST) library, since many NIST mass spectra are obtained at lower ion source temperatures (or with direct inlet probes) to provide better quality. Note that the magnitude of this effect is compound dependent. For example, it is weak for small molecules with low hit capacity including, for example, octafluoronaphthalene (OFN). That is one of the reasons why OFN is used for the sensitivity specification of various GC/MS instruments.

The combination of GC/MS with SMB and its fly-through ion source is free from this conflict, since (i) sample molecules fly through the ionisation area without touching the walls of the ion source (therefore ion source peak tailing and related compound losses do not exist); (ii) sample molecules, cooled in the SMB, possess very low internal energy which corresponds to a few (or a few 10s of) degrees Kelvin and thereby undergo the least possible (for 70 eV EI) fragmentation.

The phenomena of 70 eV EI of cold molecules (cold EI) is demonstrated in Figure 6.8. Prominent molecular ions are detected in the mass spectra of such large *n*-alkanes as $C_{40}H_{82}$ (*m*/*z* 562) and even $C_{72}H_{146}$ (*m*/*z* 1011.2 (!)).

The TIC chromatograms shown in Figure 6.8 are also unusual. The left panel represents very fast chromatography analysis, while the right panel shows the chromatogram of compounds that are far heavier than the range of compounds amenable to standard GC/MS (Amirav *et al*., 2008;

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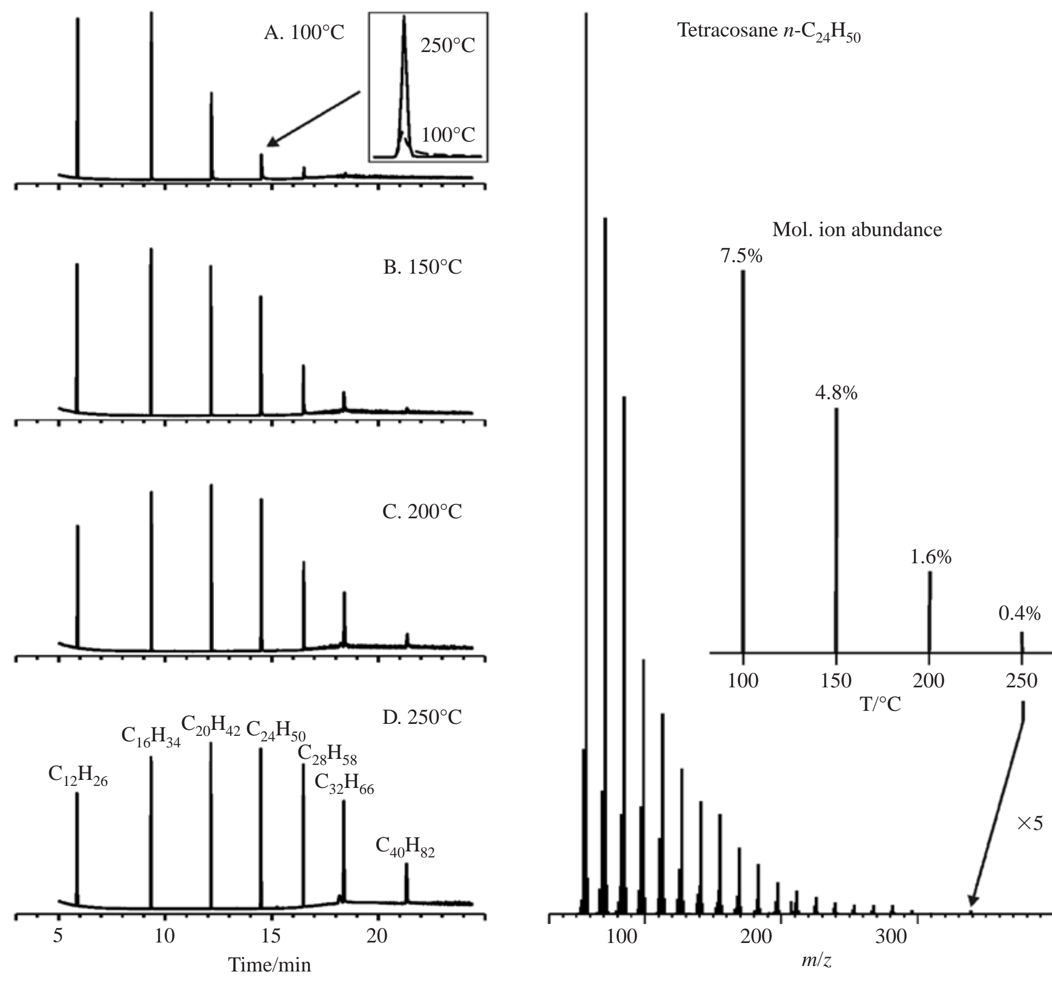
Figure 6.7: Ion source temperature effects on TIC chromatograms of alkane mixture (left) and tetracosane standard EI mass spectra (right). The chromatograms on the left show the effect of ion source temperature on the magnitude of intra-ion source peak tailing, which reduces the peak heights, while the mass spectrum and the insert on the right show the effect of the ion source temperature on the relative abundance of the molecular ion. A Varian 1200 GC/MS instrument was used with its standard ion source.



Fialkov and Amirav, 2008; Fialkov *et al*., 2003). Such a chromatogram of the Polywax 850 mixture of *n*-alkanes can be obtained with GC/FID (short column and high column flow rate), while conventional GC/MS would not work out anything useful above, say, C_{40} or so. Actually, useful mass spectrometric information for an *n*-alkanes mixture has already been lost at about C_{28} with standard GC/MS, since large alkanes provide very similar fragmentation patterns with very small or undistinguished molecular ions, fully vanishing for branched alkanes. SMB GC/MS, on the other hand, allows the analysis of a Polywax 850 mixture as above. The GC elution temperatures are decreased by about 20°C every time the GC column flow rate is doubled, or the column length is halved (Fialkov *et al*., 2003). The elution temperatures can be further reduced with thinner film thicknesses and slower temperature programming rates (see above). Thus, a 4 m

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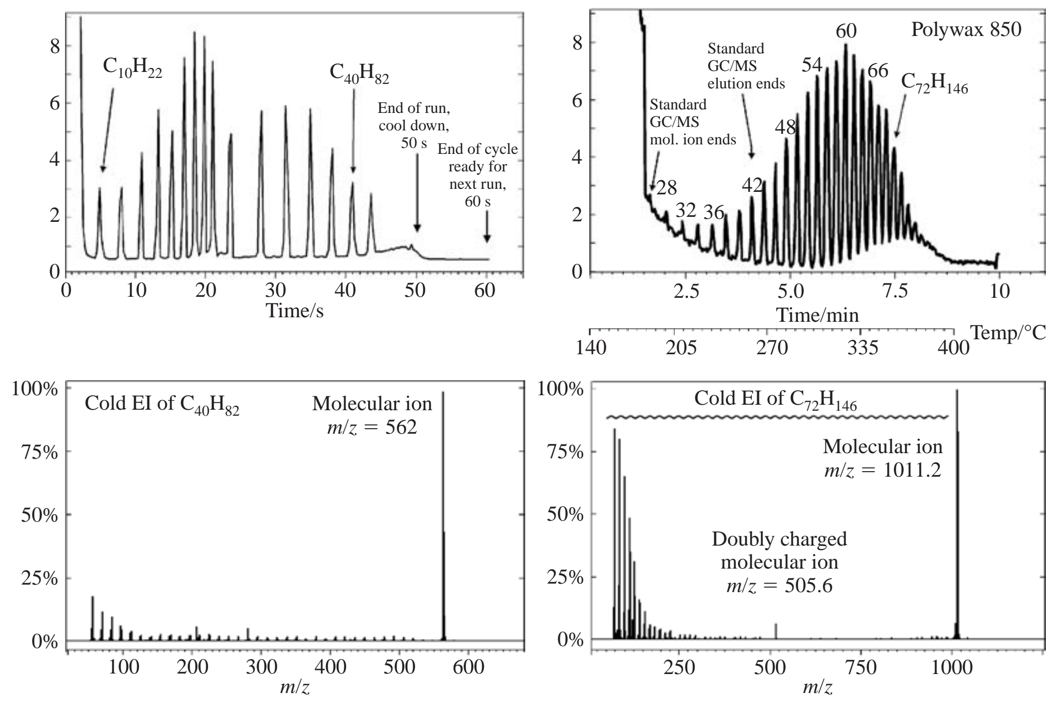
Figure 6.8: The analyses of aliphatic hydrocarbons with SMB GC/MS. Left panel shows ultra-fast analysis, while the right panel demonstrates the analysis of very heavy compounds. Full scan TIC chromatograms are shown in the upper traces with carbon numbers marking of a few compounds. The cold EI mass spectrum of $C_{40}H_{82}$ and $C_{72}H_{146}$ are shown in the bottom mass spectra. Polywax 850 sample (Restek, Bellefonte, PA, USA) was diluted at about 0.2% in xylene.



column with 32 mL/min flow rate was used for the Polywax 850 analysis with the SMB GC/MS. Evidently, the reduction of elution time allows very fast analysis, as shown in the left panel of Figure 6.8, where a 1.5 m column with 35 mL/min flow rate was used, together with a fast GC module (Fialkov *et al.,* submitted for publication) and column temperature program rate of 440°C/min, unlike in a standard GC.

With the 'high column flow rate and short column' approach, the range of compounds amenable to analysis with SMB GC/MS is significantly expanded, not only towards less volatile compounds, but also to thermally labile compounds, which may degrade in injector, column and/or ion source in standard GC/MS conditions. In a temperature-programmable injector, the elution temperatures of thermally labile compounds passing from the liner to the column are similarly reduced. Hence these thermally labile compounds survive and elute intact from the injector to the column, where they further elute at lower temperatures as described above and then fly through the ion source without any degradation. The effect of the column flow rate on the degradation of thermally labile explosives is shown in Figure 6.9. Both analyses were done with SMB GC/MS in the same conditions, while column flow rate was 16 mL/min (upper trace) versus 1 mL/min (lower trace).

The lower trace (1 mL/min) shows smaller triacetone triperoxide (TATP), nitroglycerine (NG) and 1,3,5-trinitroperhydro-1,3,5-triazine (RDX) chromatographic peaks, while the pentaerythritol tetranitrate (PETN) peak is completely lost. There is a chromatographic peak that could be

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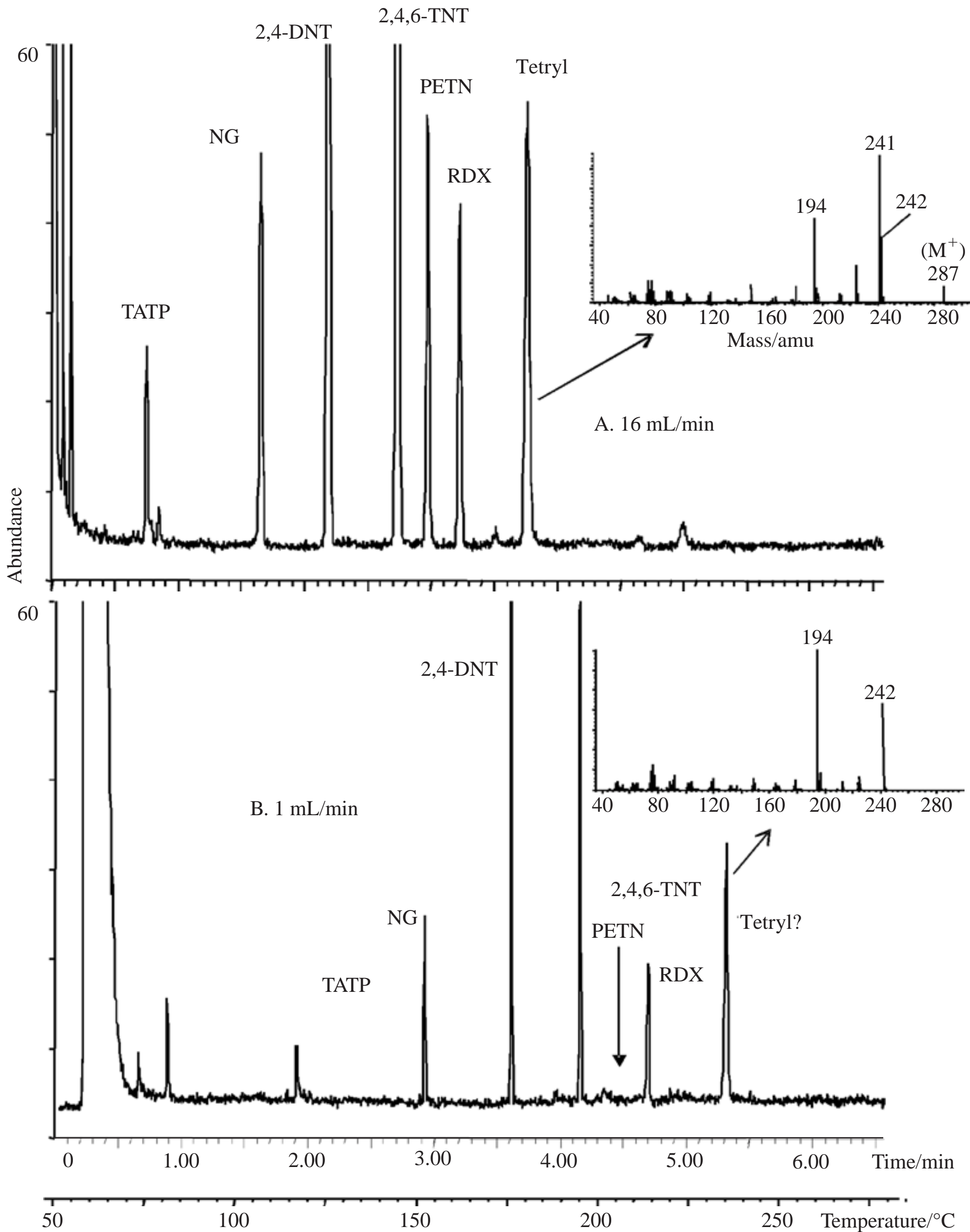
Figure 6.9: The analysis of explosives with the supersonic GC/MS using increased column flow rate for lowering the elution temperatures of the ingredients and thus their degree of degradation. The mass spectra of Tetryl are added in the inserts. A 6 m, 0.25 mm i.d. column was used with 0.5 μ DB5MS film and temperature programming rate of 35°C/min. The transfer line and nozzle temperatures were 200°C while the injector temperature was fixed at 180°C. The indicated column flow rates were 1 mL/min for lower trace B and 16 mL/min for upper trace A. (Source: Reprinted from *Journal of Chromatography A*, 991, Fialkov, A.B., Gordin, A. and Amirav, A., Extending the range of compounds amenable for gas chromatography–mass spectrometry analysis, 217–240, Copyright (2003), with permission from Elsevier.)



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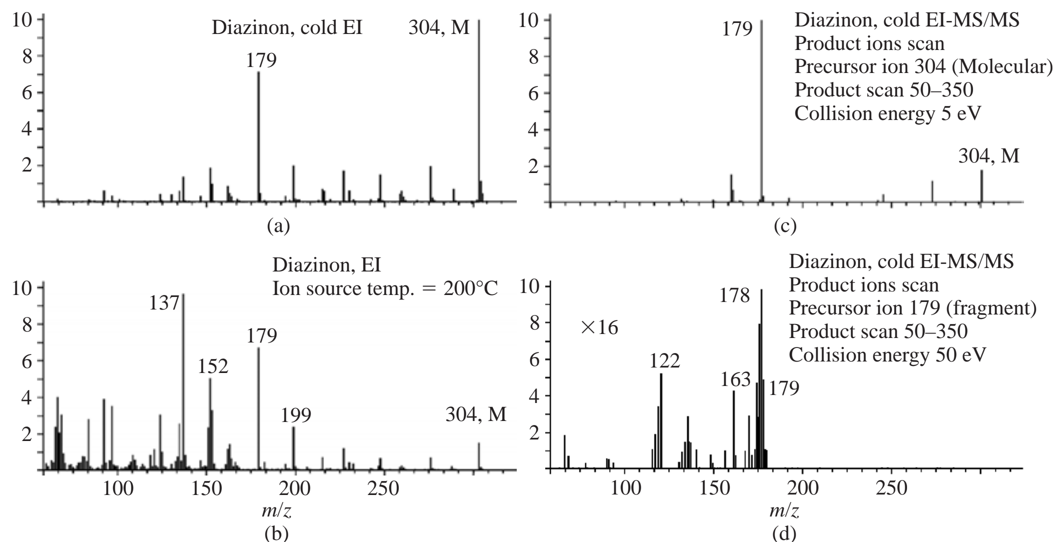
attributed to 2,4,6-trinitrophenylmethylnitramine (Tetryl); however, there is no molecular ion of Tetryl (*m*/*z* 287) in the corresponding mass spectrum. Therefore, this important ingredient may be erroneously identified as a Tetryl degradation product. The upper trace (16 mL/min) demonstrates the presence of PETN and Tetryl chromatographic peaks alongside those due to other explosives, while cold EI mass spectra (shown only for Tetryl) with enhanced molecular ion abundance confirm their identities. It is worth mentioning that without having a molecular ion in the mass spectrum it is hard to distinguish between Tetryl and its degradation product, namely *N*-methylpicramide (Fialkov *et al*., 2003) and to reliably identify any compound in general.

Many practical applications require target analyses of trace level compounds in complex mixtures. The leading technique for such applications is GC/MS/MS (Chapter 4). An SMB interface extends the range of analysable compounds and further improves the selectivity and sensitivity of GC/MS/MS (Fialkov *et al*., 2007). There are a few features that affect this, such as noise suppression and lower compound losses, but the most beneficial is the molecular ion enhancement (compare cold EI, Figure 6.10(a) and standard EI, Figure 6.10(b), mass spectra of pesticide diazinon ($M^{+\bullet}$ 304). There are several advantages for the use of the molecular ion as the precursor (parent) ion in MS/MS over the use of a high mass fragment as a precursor ion (if the molecular ion is not observed or it is too small). First of all, it is more reliable, because any fragment ion may be due to the presence of a homologue, structurally similar compound or any other sample ingredient with close retention time. Second, the larger are the masses used as precursor and product ions, the lesser is the matrix interference (Kochman *et al*., 2002). Moreover, the required collision-induced dissociation (CID) energy is usually smaller. Consequently, only one (or a few) product ions will be produced (see cold EI MS/MS, Figure 6.10(c), with dominant fragment of *m*/*z* 179 at CID 5 eV). If the molecular ion is weak and a high mass fragment is used

Figure 6.10: (a) Cold EI mass spectrum versus (b) standard EI mass spectrum at 200°C ion source temperature of diazinon. The contribution of molecular ion in the TIC is (a) 22.4% versus (b) 1.6%. Lower panel shows a comparison of MS/MS product scan spectra of diazinon obtained (c) with its molecular ion of *m*/*z* 304 with 5 eV CID energy and (d) with its major fragment ion (*m*/*z* 179) with 50 eV collision energy as precursors. (Source: Reprinted from *International Journal of Mass Spectrometry*, 251, Fialkov, A.B., Steiner, U., Jones, L. and Amirav, A., A new type of GC–MS with advanced capabilities, 47–58, Copyright (2006), with permission from Elsevier.)



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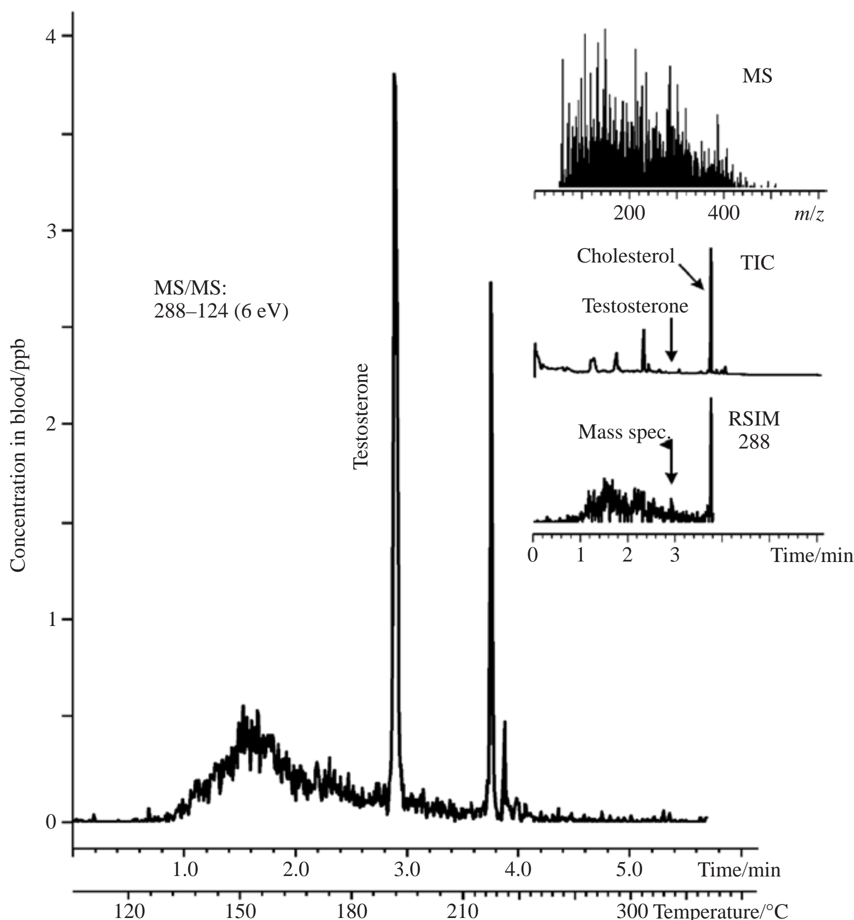
as the precursor ion (e.g. fragment of *m/z* 179 in case of standard EI of diazinon), then high CID energy is required to break apart the fragment because, as a rule, the fragment ion (usually even-electron) is more stable. As a result, multiple bond cleavages take place with the intensity redistributed between many fragments (Figure 6.10(d)). The resulting signal gain of cold EI MS/MS compared with standard EI MS/MS can be as much as a few hundred times higher.

The application of SMB GC/MS/MS for the analysis of testosterone in alligator blood shown in Figure 6.11 is a typical example of a trace level target compound analysis in a complex matrix. Note that due to the extended range of compounds amenable to the analyses with SMB

Figure 6.11: The analysis of testosterone in Florida alligator blood with the 1200-SMB; 4 m Varian VF5MS column with 0.25 mm i.d., 0.1 μm film thickness and 12 mL/min He flow rate was used. MS/MS was employed to analyse the molecular ion of underivatised testosterone (*m/z* 288) with 6 V collision energy and *m/z* 124 detected as the product ion. The right-hand side inserts were taken from other runs and are mass spectra at the testosterone elution time, TIC and RIC at *m/z* 288 for testosterone. Samples and detailed advice were given by John A. Bowden and Richard A. Yost from the University of Florida, Gainesville, Florida 32611, USA. (Source: Reprinted from *International Journal of Mass Spectrometry*, 260, Fialkov, A.B., Steiner, U., Lehotay, S.J. and Amirav, A., Sensitivity and noise in GC–MS: achieving low limits of detection for difficult analytes, 31–48, Copyright (2007), with permission from Elsevier.)



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GC/MS(MS) testosterone derivatisation is not required, contrary to the standard GC/MS analysis. The testosterone peak is not observed in the TIC chromatogram that is dominated by cholesterol. The mass spectrum at the testosterone elution time demonstrates a forest of peaks, nearly at every mass up to about *m*/*z* 400. A small peak protruding a little through the noise can be found at the testosterone elution time in reconstructed ion chromatogram (RIC) mode using testosterone molecular ion (*m*/*z* 288). Finally, MS/MS analysis with testosterone molecular ion (*m*/*z* 288) as a precursor and testosterone fragment ion (*m*/*z* 124) as a product with small CID voltage (6 eV) reveals the testosterone peak at about 4 ppb level in the sample with reasonable signal-to-noise ratio (Fialkov *et al*., 2007).

Finally, the more challenging an application or a request for the GC/MS analysis is, the stronger are (as above) the advantages and capabilities of SMB GC/MS, allowing higher sensitivity, better quality of mass spectra and broader range of compounds amenable to the GC/MS analysis – and that covers also the compounds usually considered to be not amenable for GC/MS, forcing GC/MS admirers to switch to LC/MS. Some features of SMB GC/MS are not mentioned here, and can be found elsewhere; these include cluster chemical ionisation (Fialkov and Amirav, 2003) and classic EI (Gordin *et al*., 2008) modes of SMB GC/MS; unique SMB GC/MS method of hydrocarbon mixtures (fuels) characterisation via a novel isomer abundance analysis (Fialkov and Amirav, 2008); application (method and software) of isotope abundance analysis for improved compound identification (Alon and Amirav, 2006); as well as optional instrumentation like the above-mentioned fast GC (Fialkov *et al*., submitted for publication), pulsed flow modulation GC/GC/MS (Poliak *et al*., 2008a; Poliak *et al*., 2008b) and open probe (Poliak *et al*., 2010) for having fast and easy surface sampling and direct sample introduction to SMB (fast-) GC/MS or to SMB MS.

6.3 COMPREHENSIVE TWO-DIMENSIONAL GC/GC/MS TECHNOLOGY

6.3.1 The theory of operation

The principle of GC/GC/MS is based on the separation of analytes in two sequential GC columns. Analytes are first separated in a primary column during a conventional GC run and characterised by the first retention time (t_R). During the run time the effluent from the primary column is 'heart-cut' into portions every several seconds. 'Heart-cutting' means focusing of the effluent portion by quick-freezing it into a condensed plug. The plug is then instantaneously heated and injected into a secondary column. The analytes in each heart-cut portion are then quickly separated in the secondary column, and characterised by the second retention time. The whole GC separation on a secondary column takes only a few seconds. During this time the next condensate plug forms. Then a new portion of condensed primary effluent is launched for the secondary separation. The MS detector is placed after the secondary column. The only mass analyser compatible with ultra-fast secondary GC/MS separation is a TOF analyser, hence all commercial instruments are GC/GC/TOF systems. The process is schematically represented in Figure 6.12.

The two columns are designed to provide complementary separation; therefore, different stationary phases are used in primary and secondary columns. The typical set-up consists of a non-polar primary column widely used for conventional GC/MS analysis. The polar secondary column provides an orthogonal separation. This 'non-polar/polar' set-up is the most common column combination for orthogonal separation; however, other examples are reported, including non-polar/chiral (Eljarrat *et al*., 2008), chiral/polar (Bordajandi *et al*., 2005a), chiral/non-polar (Bordajandi *et al*., 2005b) and so on.

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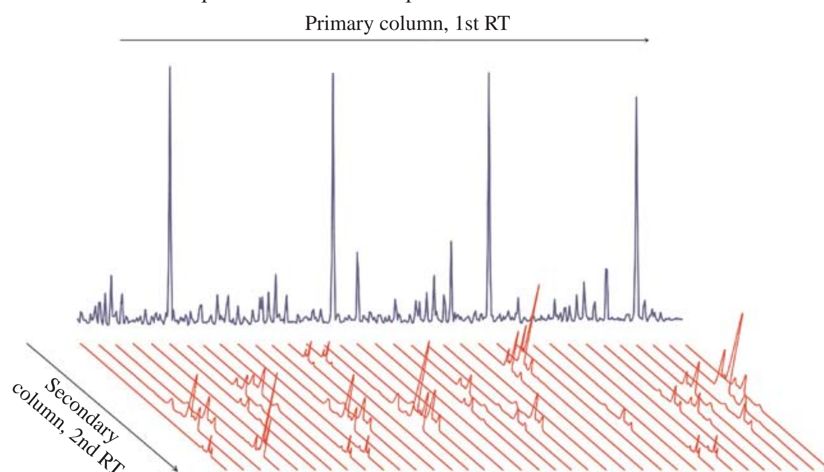
Figure 6.12: Scheme of a comprehensive GC/GC operation.



The first important condition for a GC/GC operation is a heart-cutter that allows injections of the primary eluate portions into a secondary column. This is achieved with a thermal modulator, an interface between the columns, placed in the very end of the primary column. Currently, there are two commercially produced GC/GC/TOF systems with different modulators, providing so-called four-stage and two-stage modulation using cold and hot gas jets. The gas in a cold jet is cooled by liquid nitrogen and needed for effective cryo-focusing of the effluent. The heated gas in a hot jet is used for launching the condensed plug into a secondary column. The four-stage modulation uses two hot and two cold gas jets; its principle is shown in Figure 6.13. In stage I, both cold jets are on, both hot jets are off, and all analytes freeze in the first focusing zone. In stage II, the cold jet 1 switches off and the hot jet 1 switches on, while all condensed analytes move to the second focusing zone where they condense again since the second cold jet is still on. At the same time some additional analytes may pass the first jets and condense in the second focusing zone (marked by * in Figure 6.13). In stage III cold jet 1 switches on again. This means that no more analytes can pass through the first jets and mix together with those trapped in the second focusing zone. This is a key feature in the analysis of distinct portions of the eluate. The last stage is designed for fast heating of the formed analyte plug followed by its separation in the secondary column. This is achieved by switching on the second hot jet. After that a modulator returns to the first step. During stages I, II and III, analytes are resolved in the secondary column and detected by TOF.

The principle of a two-stage modulation, so-called loop modulation, is very similar and described in detail elsewhere (Ledford, 2002). In brief, one cold and one hot gas jet are used, the cold one operates constantly, and the hot one pulses every few seconds. The end of the primary column is folded inside a modulator, so both jets can affect two zones of the column at the same time (Figure 6.14).

When the hot jet switches on, the plug of condensed analytes is released into the secondary column from the second focusing zone. At the same time a plug accumulated in the first focusing zone moves towards the second focusing zone and condenses there due to switching off the hot jet. The time between the hot jet pulses is designed to be the same as the time needed by the analyte to travel through the modulation column loop. The normal time for one modulation cycle is around 5 s, so ultra-fast separation in the secondary column is needed.

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Figure 6.13: Scheme of the four-stage modulation. Roman numerals represent the different modulation stages.

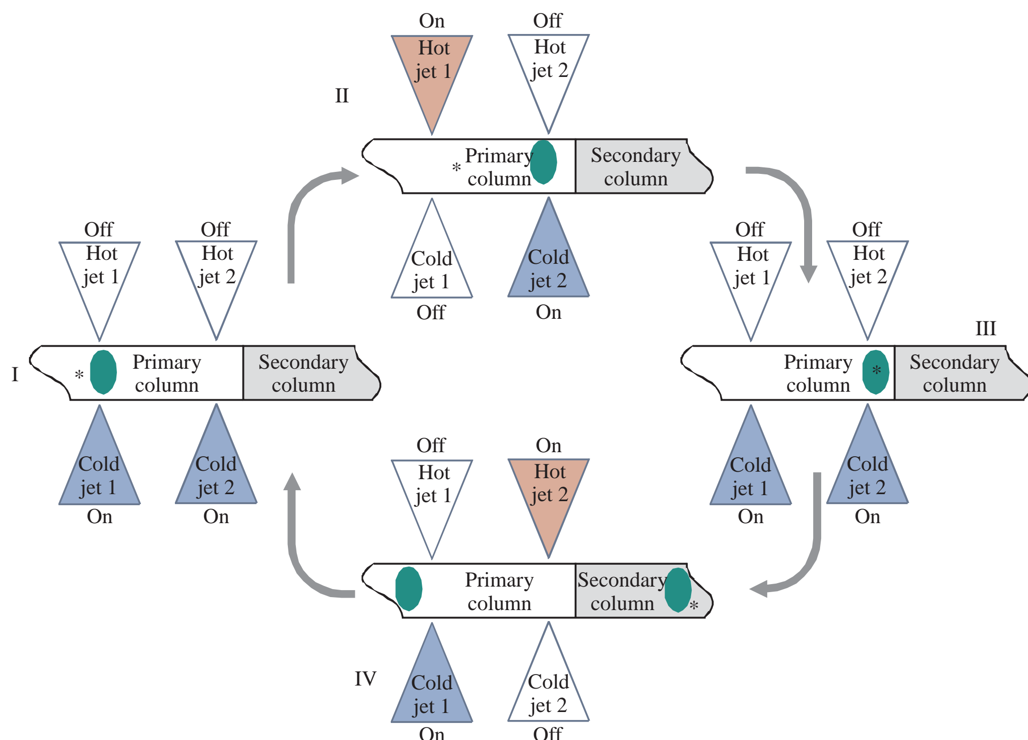
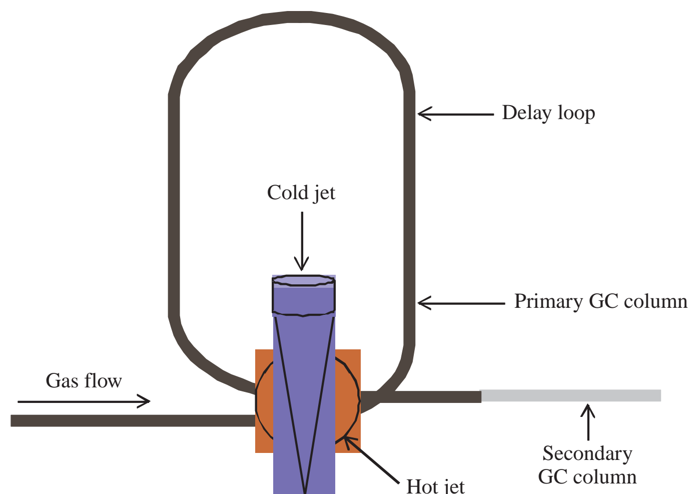


Figure 6.14: Loop modulation principle. The hot jet is perpendicular to the reader.



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All key ideas of fast GC/MS are then applicable for the secondary column in GC/GC/TOF. The typical secondary column is very short (≤1 m), narrow (i.d. ~0.1 mm) and has a thin film coating (~0.1 μm). The column is frequently placed in a secondary oven with a temperature offset ~20–30°C higher than in the primary oven. This feature accelerates the separation.

Graphical representation of the GC/GC/MS data is schematically shown in Figure 6.15. The modulation frequency is normally set to provide three to six heart-cuts during the elution of each peak in the first dimension. Since a conventional GC on a primary column provides typical elution times of 10–30 s, the modulation, i.e. sampling rate on to the secondary column, is performed at 0.1–0.5 Hz.

6.3.2 Advantages of the GC/GC/TOF approach

The advantages of GC/GC/MS over conventional GC/MS are significant. The first important feature of this approach is that it provides orthogonal separation of the substances based on their unrelated properties. Thus, substances which coelute from the primary column can often be resolved in the secondary column (Figure 6.15). This unique characteristic of GC/GC/MS allows easy peak deconvolution, refining of spectra and simplifies the identification of the analyte by mass spectra library search. As a special case of spectra refining, successful cutting of column bleed, that is background peaks, is inherent for any GC/GC/MS (see Figure 6.16).

The second important feature of GC/GC/MS is the possibility of more accurate quantification of the analytes compared with a conventional approach. This is common for fast GC/MS, and results in focusing of the analytes. Thus a broad peak in the first dimension is sliced into several sharp peaks in the second dimension, as displayed in Figure 6.15. The sum of the peak intensities obtained in the second dimension represents significantly better quantification in terms of accuracy and reproducibility.

The third important feature of GC/GC/MS is orthogonal separation in the second dimension. It allows simple classifications of the analytes in complex samples. An excellent example of simple classification is shown in Figure 6.16, where recorded mass spectra reveal the 'clouds' of peaks belonging to organic compounds of the same nature eluted in the particular areas of the two-dimensional plot. For instance, non-polar alkanes are eluted at $t_R < 1$ s in the second dimension, so they form a cloud at the bottom of the two-dimensional plot. Low boiling semi-polar naphthalenes appear as clouds higher than alkanes at $t_R \sim 1$ s (second dimension). Polar dibenzothiophenes elute at the top of the two-dimensional plot at $t_R \geqslant 3$ s (Figure 6.16). Such features of GC/GC/MS help to distinguish between the compounds with similar mass spectra.

Figure 6.15: Two- and three-dimensional views of GC/GC separation.

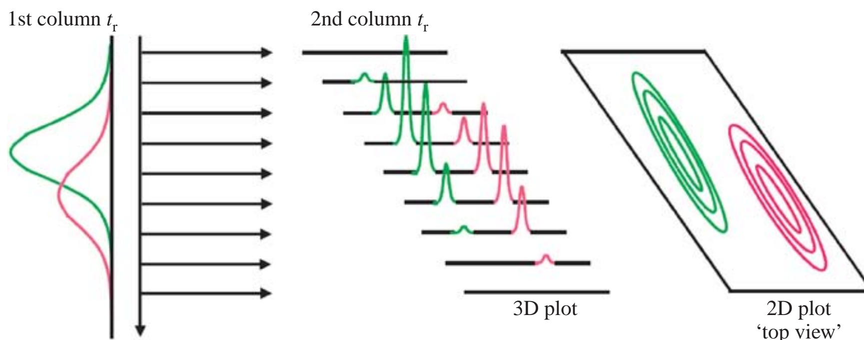

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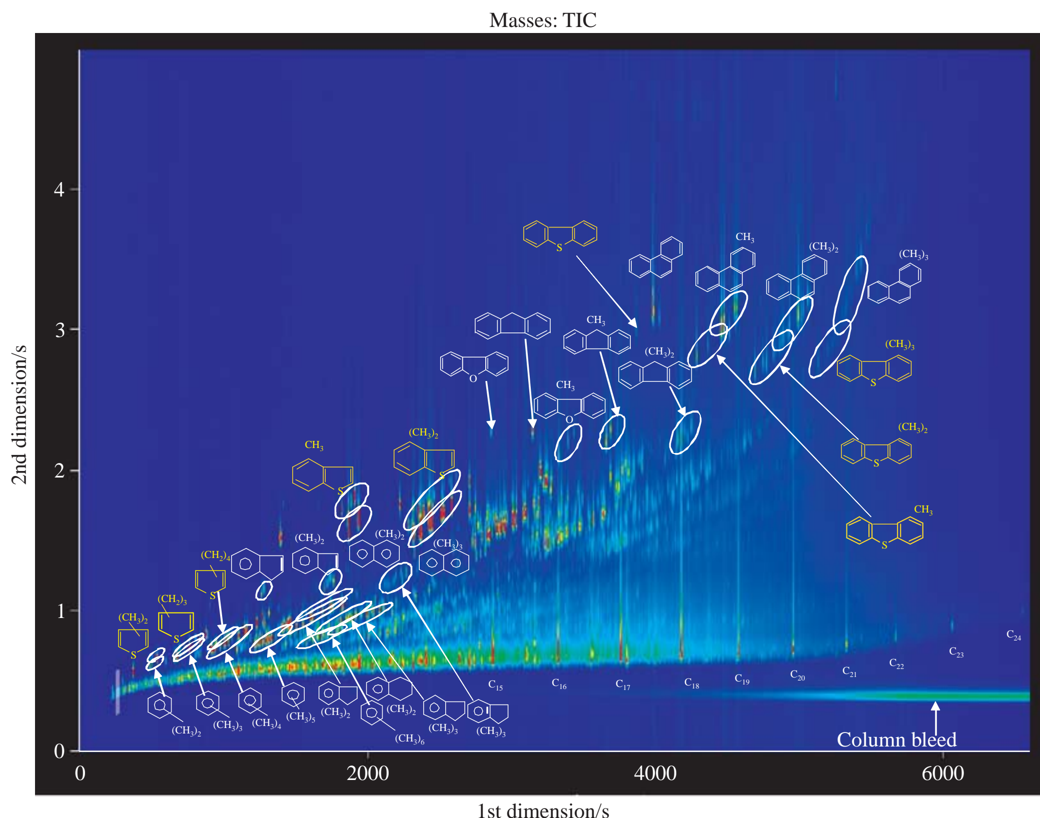
Figure 6.16: Analysis of raw diesel by GC/GC/MS (two-dimensional plot view). Non-polar primary and polar secondary columns are used. (Courtesy of LECO Corporation.)



Although these ingredients may be easily confused using only their mass spectra, they may be correctly identified according to their position in the chromatogram (e.g. fatty alcohols and related alkenes), as similar compounds (e.g. positional isomers) occupy a special area of the two-dimensional chromatogram. The appearance of an unknown compound with a mass spectrum similar to that of the identified ingredients in a different area of the two-dimensional picture means that an alternative structure should be assigned to this compound.

The advantages described allow informative analysis of extremely complex mixtures of organic compounds (oil fractions, various environmental contaminants, etc.), analyses of isomers, analyses of trace components and so on. Figures 6.16 and 2.17 (Chapter 2) demonstrate the power of this approach in analyses of a raw diesel sample and a sample of cigarette smoke respectively.

Sometimes the analytical task does not even require structural elucidation of all the ingredients. The following approach is called fingerprint analysis. It may be successfully used in many cases, dealing with environmental or forensic tasks.

Figure 6.17 represents a GC/GC/MS analysis of a light diesel in water samples before and after their treatment with sodium hypochlorite (Shaidullina and Lebedev, 2004). The task involved the question of what classes of hydrocarbons might be chlorinated during the preparation of drinking water. Although thorough processing of the results allowed identification of more than 2000 individual compounds, the original question may be answered simply visually. The answer is

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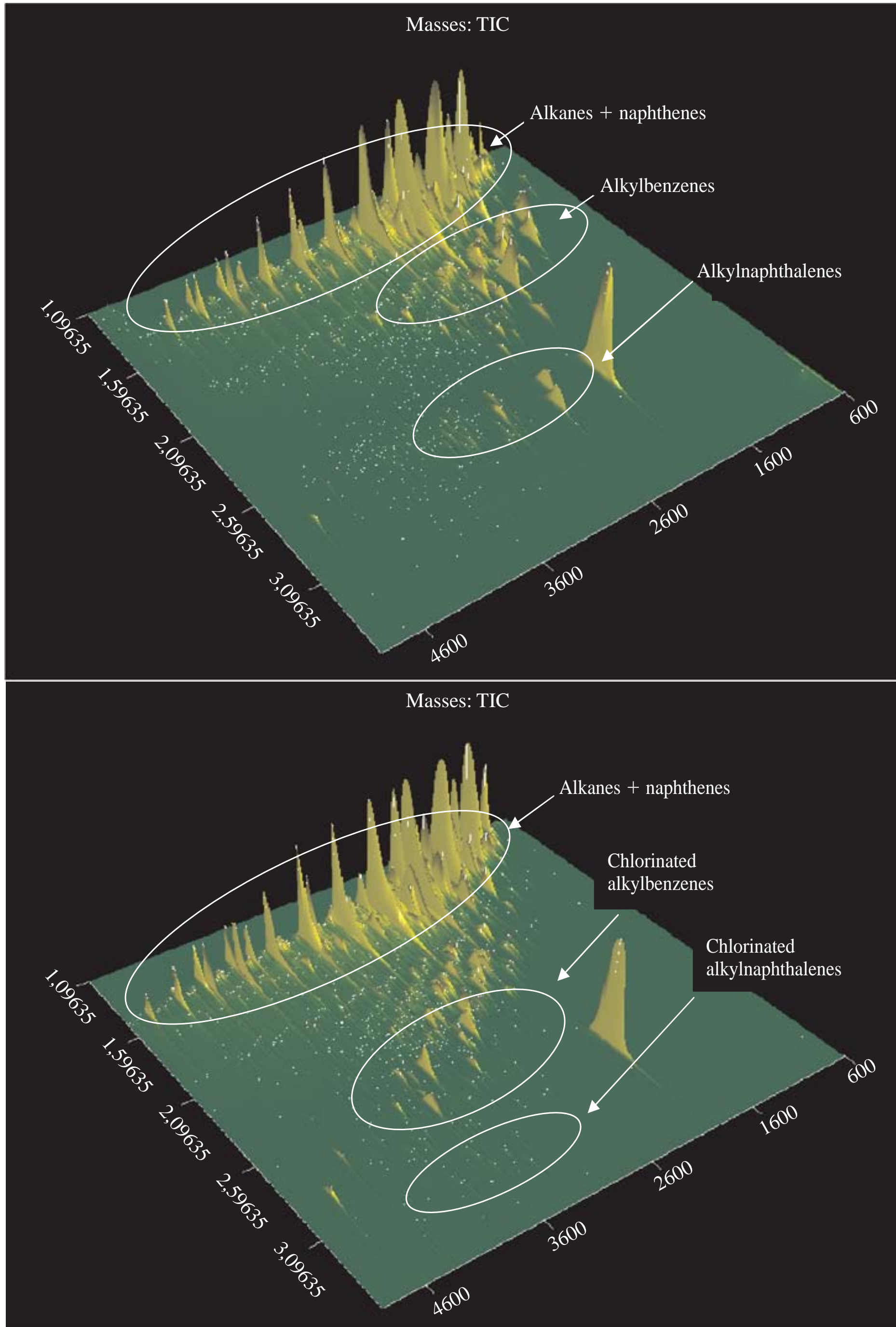
Figure 6.17: TIC chromatogram of the light diesel sample extracted from water before (top) and after (bottom) chlorination with sodium hypochlorite. (Source: Shaidullina, G.M. and Lebedev, A.T. (2004). A GC-GC-TOF study of transformation products of petroleum hydrocarbons under the conditions of aquatic chlorination. *Mass Spectrometry (Rus)*. 1, 1: 67–76. Reproduced with permission from *Mass Spectroketriya*.)



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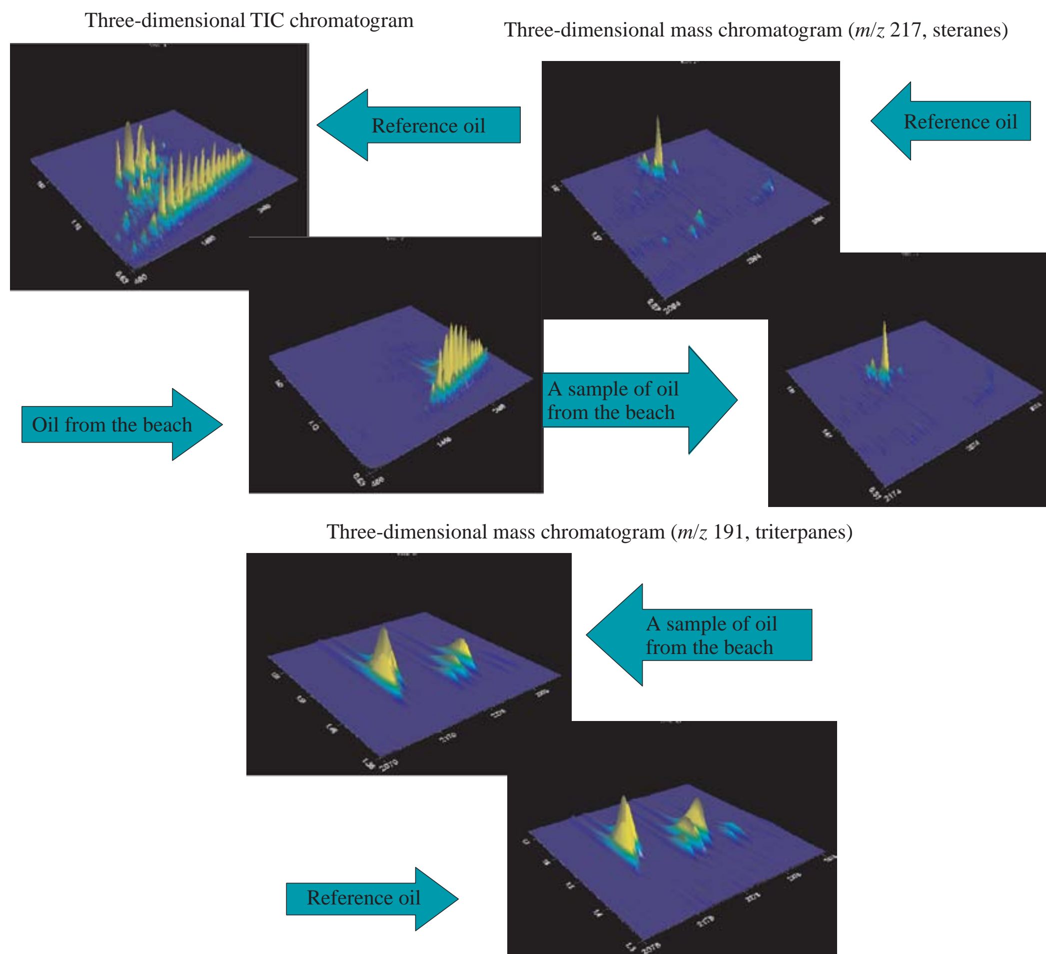
obvious even for non-professionals. The results (Figure 6.17) provide reliable information on the reaction activity of various classes of hydrocarbons. Thus the levels of inactive alkanes and naphthenes did not change after the aquatic chlorination. About 50% of the more reactive alkylbenzenes transformed to the corresponding chlorinated derivatives, while the most reactive alkylnaphthalenes completely disappeared with the formation of their many various chlorination products.

Another elegant example of the power of GC/GC/MS involves the results of the finding of the party at fault for an oil spill (Lebedev, 2010). An oil tanker met with an accident near the Sakhalin island coast. Several beaches of the island were polluted. The company was ready to pay the fee; however, according to the law, a scientific investigation was carried out. It was found that the GC results of the analyses of the samples from the polluted beaches and from the tanker were completely different. The question arose as to whether the beaches might have been polluted earlier by somebody else. Figure 6.18 represents the results of the GC/GC/MS analysis of two samples: from the tanker and from the beach. It can be seen that the TIC chromatograms of the

Figure 6.18: Three-dimensional chromatograms of the oil samples from the tanker and from the polluted beach (TIC, *m/z* 217 mass chromatogram and *m/z* 191 mass chromatogram).



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samples are completely different to one another. However, reconstruction of the mass chromatograms (see Chapter 2) using the ions characteristic for the oil biomarkers (*m/z* 191 for triterpanes and *m/z* 217 for steranes) allowed unequivocal proof to be obtained that the oil in both of the samples was identical. Similar pictures were obtained from the samples from other beaches. The result was clear for everybody.

The reason for the different picture in the case of the TIC chromatogram involves the fact that the samples were collected from the beaches about seven days after the accident. The processes of microbiological and photochemical degradation as well as evaporation and solution of various ingredients made the final composition very different to the original one. Nevertheless, fingerprint analysis on the basis of mass chromatograms appeared to be efficient and quite convincing.

6.4 CONCLUDING REMARKS

The innovations regarding the classic GC/MS method described in this chapter clearly demonstrate that the capabilities of this method are much wider than originally believed. Implementation of recently developed SMB and GC/GC/MS approaches for the environmental task will definitely allow fascinating results to be obtained in the not-too-distant future.

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