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Review

# Practical approaches to fast gas chromatography–mass spectrometry ☆

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**Abstract**

Fast gas chromatography–mass spectrometry (GC–MS) has the potential to be a powerful tool in routine analytical laboratories by increasing sample throughput and improving laboratory efficiency. However, this potential has rarely been met in practice because other laboratory operations and sample preparation typically limit sample throughput, not the GC–MS analysis. The intent of this article is to critically review current approaches to fast analysis using GC–MS and to discuss practical considerations in addressing their advantages and disadvantages to meet particular application needs. The practical ways to speed the analytical process in GC and MS individually and in combination are presented, and the trade-offs and compromises in terms of sensitivity and/or selectivity are discussed. Also, the five main current approaches to fast GC–MS are described, which involve the use of: (1) short, microbore capillary GC columns; (2) fast temperature programming; (3) low-pressure GC–MS; (4) supersonic molecular beam for MS at high GC carrier gas flow; and (5) pressure-tunable GC–GC. Aspects of the different fast GC–MS approaches can be combined in some cases, and different mass analyzers may be used depending on the analytical needs. Thus, the capabilities and costs of quadrupole, ion trap, time-of-flight, and magnetic sector instruments are discussed with emphasis placed on speed. Furthermore, applications of fast GC–MS that appear in the literature are compiled and reviewed. At this time, the future usefulness of fast GC–MS depends to some extent upon improvement of existing approaches and commercialization of interesting new techniques, but moreover, a greater emphasis is needed to streamline overall laboratory operations and sample preparation procedures if fast GC–MS is to become implemented in routine applications.
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*Keywords:* Reviews; Gas chromatography; Mass spectometry; Pressure-tunable selectivity; Fast gas chromatography–mass spectometry

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## 1. Introduction

Although many analytical chemists try to gain as much ‘‘free time’’ as possible by developing faster methods (often working ‘‘overtime’’ in the process), there is much truth in the old saying that ‘‘time is money.’’ Thus, just as the laws of thermodynamics dictate that there is no such thing as a ‘‘free lunch’’, there is also no such thing as ‘‘free time’’ (or is there?—the issue of ‘‘free time’’ in the laboratory will be discussed below). If the analytical chemist successfully implements faster analysis times, it is likely that either the number of samples for analysis will be increased or additional projects will be assigned. In theory, increasing the speed of analysis should increase sample throughput, reduce cost of analysis, and/or increase laboratory productivity. However, in some circumstances, the speed of analysis is not the limiting factor, thus faster methods may not recoup the initial development and

implementation costs. The good method development chemist understands the needs for the analysis, sets goals to truly meet these needs, envisions how their goals can be accomplished in theory, and then develops the approaches in practice. If analytical needs are not met, then all of the time spent in the development and evaluation of faster methods becomes ''wasted time'' (i.e. lost money). Ultimately, faster analytical methods must also be practical.

All decisions in an analytical process must address the purpose for the results. Speed and sample throughput can be primary considerations in some applications, such as process control, but these factors are never emphasized over the minimum quality of results to meet the purpose for the analysis. If the minimum criteria for detectability, reproducibility, and selectivity are not met, then analytical results are meaningless and there is no reason to conduct the analysis independent of how fast it is. Moreover, if ruggedness or reliability of the approach is poor, leading to extended instrument down time and/or many re-analyses, then the potential savings in time may be lost. Time of analysis is one of the practical constraints, along with available technology, costs, simplicity, space requirements, small sampling size, safety, and reliability, which limit the implementation of a desired methodology. These resource constraints must be prioritized and balanced to achieve the desired quality of results in the most efficient overall process possible.

Ideally, the desired attributes for the ultimate analytical method include: widely applicable, very sensitive (low detection limits), highly quantitative and qualitative (specific), fast, rugged, reliable, reproducible, inexpensive, easy to perform, portable, waste-free, and safe. In the myriad of applications involving the analysis of volatile and semi-volatile organic molecules, gas chromatography–mass spectrometry (GC–MS) possesses more of these desirable traits than any other current approach. In theory and practice, GC–MS has the ability to separate, detect, and identify a wide range of volatile and semi-volatile chemicals at (ultra)trace levels in complex samples. Faster GC–MS analysis has been a focus of research investigations since the initial combination of the two powerful analytical tools, but the advances made in the past decade in particular have led to exciting possibilities in achieving fast GC–MS analysis in a variety of routine applications. Other reviews on fast-GC [1–4] and fast GC–MS [5] have been published recently, including those that describe theoretical considerations in detail. The aim of this article was to critically review current approaches to fast analysis using GC–MS and to discuss practical considerations in addressing their advantages and disadvantages to meet particular application needs.

### *1.1. Practical scenarios and speed*

In an interesting editorial, Bertsch emphasized that the analytical step (GC–MS in this case) is only one component in an overall process to analyze samples [6]. He only addressed sample preparation and analysis in his letter, but other necessary steps in the overall process are to collect and transport the sample, process the data and review the results, and make the final reports. Other common required functions in modern routine laboratories involve receiving, storing, and tracking samples and materials, keeping up-to-date inventories, handling and disposing of hazardous waste, writing standard operating procedures, obtaining and testing methods, performing quality assurance/quality control (QA/QC) functions, ordering supplies, labeling solutions, archiving extracts and results, cleaning glassware and laboratory space, preparing standards, maintaining instruments, and several other mundane but indispensable tasks. Laboratory accreditation has become a critical need for many routine laboratories to conduct business or continue their functions, and the extensive requirements to obtain and maintain accreditation by the International Organization for Standardization or another certifying body often makes administration and support even more time-consuming and expensive (although systemization of these functions may improve laboratory efficiency in some respects). In this kind of laboratory environment, the maximum sample throughput does not necessarily depend on the analysis of samples per se, but on the laboratory support structure. All factors must be addressed to truly improve productivity and efficiency, not just time of the analytical separation and detection step.

*1.1.1. "Free time"*

Despite these caveats, it is still usually desirable to use faster methods of analysis. For a given number of samples, performing faster methods should give the laboratory personnel more time to conduct the expanding number of other laboratory functions. However, this also depends on when the time is saved during the procedures. For example, it is not uncommon for an analyst to run long sample sequences overnight using robotic autosamplers. If the instrumentation is reliable, robotic functions performed during non-business hours can be construed as "free time". For a fixed number of samples, it makes no difference to laboratory productivity if the analyses take 1 h or 16 h in an overnight sequence. Other automated procedures, such as the use of data processing by software programs, can also provide "free time" if they give acceptably accurate results that reduce data review and interpretation time by the analyst. Whether this savings in time is translated into savings in expenses depends on what type of time is saved and how the time is spent.

*1.1.2. Speed and sample throughput*

In practical terms, there is a distinction between speed of analysis and sample throughput. The speed is the time it takes to conduct the analysis of a single sample, which is often important in process control or urgent situations requiring rapid sample turnaround times, whereas sample throughput is the number of samples that can be analyzed in a given amount of time. Analytical methods that work in parallel, such as thin-layer chromatography, may give high sample throughput, but low speed. Conversely, methods performed sequentially, such as GC, can have high speed but not such great sample throughput. Depending on the application, speed may be emphasized over sample throughput, but usually sample throughput is the more important factor in a routine laboratory.

*1.1.3. Batch sample processing*

To illustrate these points, we have devised different possible scenarios in terms of time spent on the different parts of the analytical process, as shown in Figs. 1 and 2. In most types of analyses, analysts perform the procedural steps in batch processes. That is, the chemist will extract one sample after another or in parallel, then conduct cleanup of all the extracts, followed by solvent evaporation or addi-

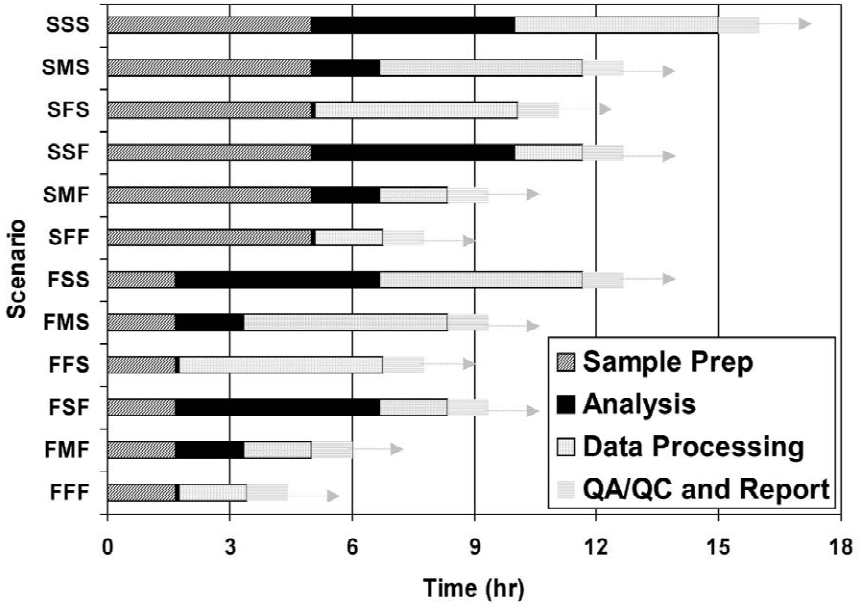


Fig. 1. Time needed to conduct the overall analysis of 10 samples in a batch processing approach. For sample preparation and data processing, F = 10 min and S = 30 min average time per sample, and for the analytical step, F = 1, M = 10, and S = 30 min per sample. The time to review and report the results is also shown in the figure, but its length is not defined.

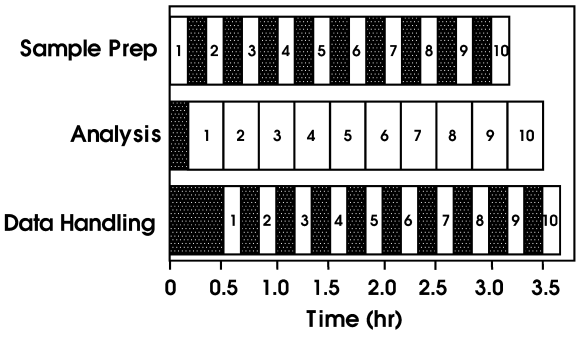


Fig. 2. Time needed to conduct the overall analysis of 10 samples in a sequential processing approach (10 min sample preparation time, 20 min analysis time, and 10 min data processing time). If complete sample preparation of each sample can be conducted quickly, then taking advantage of parallel operations can increase sample throughput vs. the batch processing approach as shown in Fig. 1.

tional steps, then set up an analytical sequence using an autosampler, and finally process the data and review the results. Fig. 1 shows the time spent in this type of scenario for a batch of 10 samples using different times for the sample preparation, chromatographic analysis, and data processing steps (the pre-analysis sample handling steps are not shown and the post-analysis steps leading to the reporting of results are indicated with an indefinite timeframe). In the figure, the first letter in the series on the *y*-scale refers to the sample preparation step, with ''F'' for ''fast'' average processing time of 10 min per sample (100 min for a batch of 10) and ''S'' for ''slow'' methods that take 30 min per sample (5 h for 10 samples). The second letter refers to the analytical step with F, M, and S (''fast'', ''medium'', and ''slow'') indicating 1, 10, and 30 min per sample, respectively. The last letter in the code represents the data processing and review step, which has the same designations and time frames as in the case of sample preparation. These assigned time frames are not unrealistic in typical applications involving GC–MS, or what is possible by using state-of-the-art fast GC–MS techniques. The time of analysis of a given sample in this batch process approach is 2 h in the FFF scenario and 10.5 h in the case of SSS, and sample throughput is 10 samples per 210 min (or average speed of 21 min/sample) in the fastest case and 10 samples per 15 h in the slowest scenario given (average of 90 min/sample).

As Fig. 1 shows, the gains in speed by using fast (10 min) and very fast (1 min) GC–MS are not substantial vs. the traditional 30-min analysis unless similar gains in speed are also achieved in the sample preparation and post-run processing steps. The literature contains some examples of very fast GC, and even ultra-fast GC analyses, but very few applications can achieve sample preparation times $<$10 min/sample. Niche applications for the analysis of volatiles or high-level components in simple matrices may be the only ones in this regard (e.g. gasoline). If faster sample preparation time is achieved in GC–MS analyses, it will involve large volume injection (LVI) to avoid solvent evaporation steps, and similar types of time-saving modifications (e.g. gains in selectivity of the analysis to avoid cleanup steps, or gain is sensitivity to enable injection of less concentrated extracts).

### *1.1.4. Sequential sample processing*

Rather than batch processing, Fig. 2 gives a different scenario in which 10 samples are analyzed sequentially (extraction of one sample, then its analysis, followed by data processing). In this situation, the other steps can be conducted during the unattended operation of the analytical step. For this approach to work, the sample preparation time for a single sample must be less than the chromatographic analysis time. In the scenario we have devised, the sample preparation time takes 10 min per sample, while the analytical step is 20 min per sample, and the data processing and review takes 10 min per sample. Thus, the speed of the analysis (turnaround time for a single sample) is 40 min, and the sample throughput is 10 samples per 220 min (or average speed of 22 min/sample). Both of these values are similar or better than the values for the FFF and FMF scenarios given in Fig. 1, despite that the same average times were used for the sample preparation and data reporting steps as in this case, and the time of analysis was two to 20 times longer per sample.

Note that analytical run times any less than 20 min/sample increases speed (albeit only for the first sample analyzed), but does not affect sample throughput. This is another example of how ''free time'' can exist in the laboratory. The length of time and timing of the different functions performed affects the time allotted for other functions, thus one

can take advantage of the entire amount of time given for that function to improve selectivity or sensitivity of the analysis.

*1.1.5. Solid-phase microextraction*

In any case, the development of faster sample preparation methods is critical, and solid-phase microextraction (SPME) and direct sample introduction (DSI) are two approaches aimed to address this need in GC–MS. In the case of SPME [7–9], a fiber or other coated surface [10–12] can be exposed to the sample (or its headspace) as the previous sample is undergoing chromatography. The extracted sample materials are thermally desorbed from the coating in the heated GC injection port. During the extraction step, longer exposure times typically lead to lower detection limits (with diminishing gains of return depending on the kinetics of the equilibration), and 30-min extraction times are typical in order to achieve the desired limits of detection (LOD) in the applications for which this type of approach is commonly used. This time frame is more typical of conventional GC–MS than fast GC–MS, but if sample throughput is increased, then it is 'fast'.

Beneficial features of SPME include unattended operation via robotics and the virtual elimination of maintenance of the liner and column. The disadvantages of SPME relate to strong matrix effects, complications in quantitation, lack of ruggedness and high cost of the fiber, variations from one fiber to another, and variability of LOD for different analytes depending on the equilibrium between the coating material and matrix. SPME has shown excellent applicability to measurements of volatiles in a variety of sample types, and in trace analysis of organics in clean matrices such as water, but it has limited utility in quantitative analysis of complex samples.

*1.1.6. Direct sample introduction*

Although the sequential type of analysis shown in Fig. 2 could be very amenable for performance by robotic instruments, that depends on the complexity of the tasks. Just as in batch operations shown in Fig. 1, a technician may be needed to conduct certain or all sample preparation steps, and since an injection sequence is not utilized in the Fig. 2 scenario, there is not an essential need for an autosampler. Manual operation is used with a form of LVI called direct sample introduction, or ''dirty sample injection'', (DSI) with a ChromatoProbe device [13–18], and recently an automated form of the approach has been introduced, which has been termed difficult matrix introduction (DMI) [19]. In DSI, an extract volume up to ≈20 μl is added to a disposable microvial which is placed in the GC inlet using a holder or probe device, and the injector temperature is held for a time near the boiling point of the extract solvent until it evaporates and is purged out the split vent. Then, the split vent is closed and the injection temperature is rapidly increased until the analytes are volatilized. During this time, the oven is held at a relatively low temperature to focus the analytes at the front of the column, and then an oven temperature program is used to separate the analytes. After the analysis, the injector and column oven are cooled back to initial conditions, and the spent microvial is removed and thrown away.

This approach has several advantages over SPME for quantitation of complex samples. In addition to the gains from LVI, DSI provides high recoveries in solvent-based extraction, thus decreases LOD (if matrix is not the limiting source of noise). The detection must be highly selective to reduce the need for sample cleanup, thus DSI is typically used with GC–MS(–MS) [15–19] and/or element selective detectors [14]. As in SPME, DSI also very importantly reduces instrumental maintenance because the non-volatile components that normally build up in the liner and front of the GC column are removed with the microvial after each injection. Another feature with DSI is the capability for intra-vial derivatization to extend the scope of analytes possible in GC analysis [20,21]. In appropriate applications, the derivatization reagent can be simply added to the microvial along with the extract, and sufficient time and temperature is given to complete the reaction just prior to injection. The derivatization reaction is faster in the gas phase than liquid phase, the carrier gas atmosphere has no oxygen or water to interfere in the reaction, and degradation of the derivatized analyte has less opportunity to occur because the analysis takes place immediately after the reaction.

In a similar vein, another aspect of the sequential analysis process as shown in Fig. 2 is that each extract is analyzed immediately upon completion of

the sample preparation process. This minimizes the effect of analyte degradation or other time-dependent processes on the results. When a batch of samples are analyzed in a sequence, the time spent by the first sample in the autosampler tray is different from the last sample analyzed, thus leading to inaccuracies if the analytes are unstable in the extract.

### *1.2. The analytical triangle and fast GC–MS*

Fig. 3 shows a representation of the relationship between speed, selectivity, and sensitivity in a method involving sample preparation, GC separation, and MS detection. Speed and selectivity are obvious parameters in each case, as is sensitivity of the MS detector, but we should point out that sensitivity in sample preparation relates to the concentration of equivalent sample in the final extract, whereas sensitivity in GC is measured in terms of the amount of sample that the GC system can handle (sample capacity) without frequent maintenance. The center triangle represents the overall combination of the different steps, which is achieved when the individual triangles are folded upon each other as indicated by the paired symbols at the corners of each triangle. Other factors are also able to be placed at the corners of the triangles in some instances, as listed below the figure, but they do not always form an inherent trade-off that limits the utility or performance of a method as in the case shown. We would like to note that even the triangular relationship itself is not necessarily correct because revolutionary concepts may be developed to greatly improve all aspects of the overall process (e.g. assembly lines and robotics in manufacturing, computerization and new mathematical algorithms in data processing). In the case of GC for example, the use of short, narrow multicapillary columns [22–26] in theory could increase the speed, selectivity, and sensitivity of analysis, but practical problems make this potential nearly impossible to achieve.

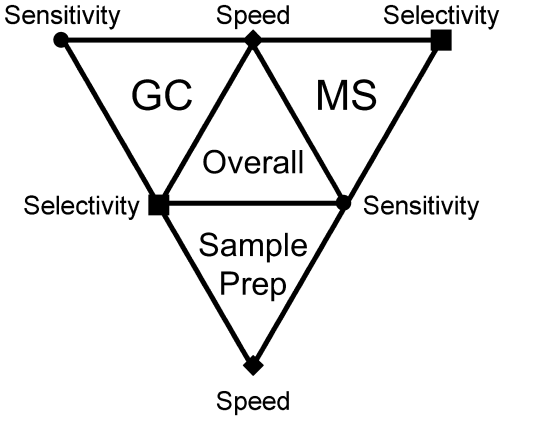


Fig. 3. The combination of analytical triangles in terms of speed, sensitivity, and selectivity for an overall GC–MS method (sample preparation, analytical separation, and detection). The corners of each aspect of the overall method are folded over according to the matching symbols to give the overall capabilities of the method. Other importance qualities of a method are also given below the figure.

Fig. 4 removes the sample preparation component from the illustration and focuses only on GC–MS for the optimization of speed. The critical feature of GC–MS that is not the case for fast GC using element selective detectors is that MS gives another adjustable degree of control in sensitivity and selectivity (element selective detectors can be very discriminating between analyte and matrix, but this is not the case from analyte to analyte). This overlapping control of sensitivity and selectivity allow one instrumental component (GC or MS) to compensate for worse performance in other components, as indicated by the compensation arrows in Fig. 4.

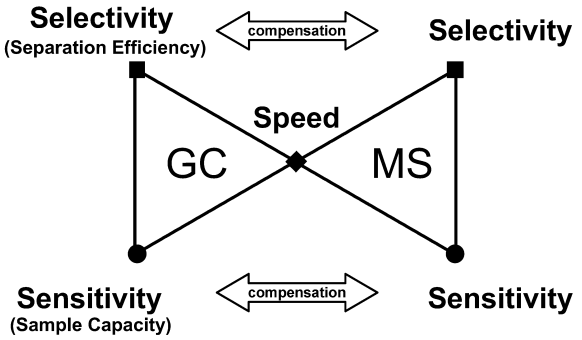


Fig. 4. The combination of GC and MS for optimization of speed. The sensitivity and selectivity of each approach can be used to compensate for losses in the other to provide a faster analysis of potentially the same quality.

## 2. Fast GC

In the case of GC, thorough discussions of the theory of fast GC have been presented in the literature previously [3,27–33], and instead of repeating a series of equations to show the relationships between all parameters, we shall only present the main implications of the theory in our discussion. Fig. 5 gives the simplified basic equation that determines retention time ($t_R$) of a compound and lists the main ways to speed the GC analysis. In the equation, $L$ is the column length (in cm), $\bar{u}$ is the average linear carrier gas velocity (cm/s), and $k$ is the unitless retention (or capacity) factor. The last analyte to elute from the column can serve as the indicator of speed of analysis for the purpose of this discussion, but in practice, additional time is usually needed to allow the less volatile matrix components to elute from the column plus oven cool-down and equilibration times. Unlike GC with selective detectors, chromatographic resolution ($R_s$) from other analytes is not necessarily the limiting factor in speed of analysis in GC–MS because co-eluting peaks can often be resolved spectrometrically. Thus, we make the assumption that $R_s$ is not the limiting factor in speed, but this may or may not be true depending on the specific application needs. In certain GC–MS applications, such as chiral separations or analysis of dioxin and/or PCB congeners [34], in which more than one closely eluting analyte can give the same mass spectrum, GC separation efficiency cannot be sacrificed for speed.

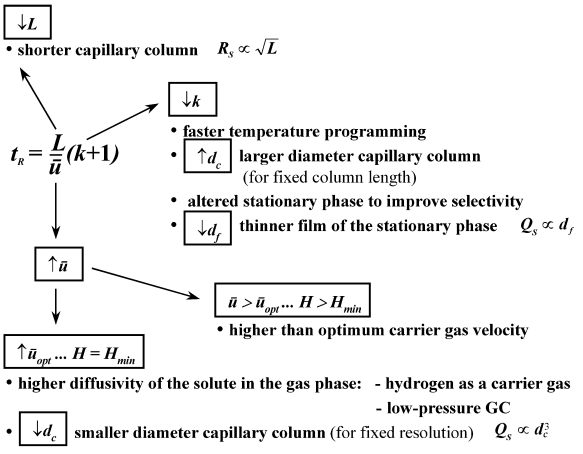


Fig. 5. The basic, simplified equation that controls retention time ($t_R$) in GC (i.e. speed of analysis) and the ways that speed can be increased.

### 2.1. Column length

As Fig. 5 shows, there are only so many practical ways to adjust the factors that decrease time of the GC analysis. One simple approach is to reduce $L$, which reduces the number of theoretical plates ($N$) in a directly proportional relationship but decreases $R_s$ less severely because $L$ is proportional to $\sqrt{R_s}$. Thus, nearly all fast GC and fast GC–MS methods utilize shorter columns (e.g. ≤10 m) in combination with other approaches.

### 2.2. Retention factor

As the equation in Fig. 5 dictates, another way to reduce $t_R$ is to reduce $k$, which can be adjusted by altering column temperature, selecting a different stationary phase (or combination thereof), using a wider column diameter ($d_c$), and/or reducing capillary film thickness ($d_f$). In conventional GC–MS, provided that column bleed is not an issue, the use of one type of column over another may improve the speed and quality of a separation to a small degree. For specialized applications, a sequential combination of different GC columns may provide improved or equivalent selectivity of the separation in a shorter amount of time. This concept is known as 2D-GC, GC×GC, comprehensive GC, modulated GC, or pressure tunable GC–GC (depending on the use and user). Among these approaches, the pressure-tunable concept is predominantly aimed at speed reduction, and Section 4.5 presents a brief overview of this fast GC–MS approach. A detailed discussion of comprehensive GC appears in another review article in this special issue [35].

Another way to decrease $k$ if all other parameters are the same involves increasing $d_c$ and/or decreasing $d_f$. This can have much greater effect on speeding the separation than altering the stationary phase in conventional GC. The reduction of $d_f$ also results in a directly proportional lower sample capacity ($Q_s$). Contrarily, a larger $Q_s$ (more sensitivity) results by increasing $d_c$, which also serves to

extend column lifetime (an important factor for practical analysis).

### 2.3. Column temperature

In the case of altering column temperature conditions to decrease $k$, the easiest way to achieve the required conditions for a more rapid elution would be to perform the analysis isothermally. This can greatly increase sample throughput because oven cool-down and equilibration times are eliminated, and split injection gives greater speed (no cryofocusing needed) and narrower band width than splitless injection. Split injection can be used in any fast GC–MS approach to potentially speed analysis in the same way. However, this injection technique acts to reduce the amount of sample introduced onto the column, thus sensitivity is sacrificed. In any event, isothermal GC is generally restricted to the analysis of compounds with a relatively narrow boiling point range. Rapid temperature programming is a more practical way to achieve faster GC separations in most applications, and this approach is discussed in more detail in Section 4.2

### 2.4. Flow rate

The last variable in the equation given in Fig. 5 is $\bar{u}$, which is inversely proportional to $t_R$, thus must be increased to cause a decrease in time of analysis. If the MS instrument can handle increased flow-rate, the most direct way to increase $\bar{u}$ is to use higher carrier gas flow. In this case, the separation efficiency is reduced by an amount according to the Golay–Giddings equation in which the theoretical plate height ($H$) will exceed the minimum $H$ ($H_{min}$), which occurs at the optimum $\bar{u}$ ($\bar{u}_{opt}$). According to theory, operating at $\bar{u}=2\bar{u}_{opt}$ causes only a 25% loss in separation efficiency and 12% loss in $R_s$ [36]. Use of high carrier gas flow-rate also serves to extend the analytical scope to thermally labile and non-volatile compounds because it decreases the analyte residence time in the hot inlet and reduces column elution temperature [37–39]. Lower elution temperature often translates into shorter cool-down times between injections thus increased sample throughput. Supersonic molecular beam (SMB)-MS is distinctly designed to operate at high gas flow rates, and this approach will be discussed in Section 4.4 for fast GC–MS. The use of high flow rates and lower elution temperatures had not been practical in GC–MS before, and GC–SMB-MS provides the means to explore new features, test theories, and determine the analytical implications in practice.

### 2.5. Optimal carrier gas velocity

Another conceptual way to speed GC analysis is to effectively increase the value of $\bar{u}_{opt}$ from the Golay–Giddings equation so that separation efficiency is not necessarily negatively impacted as $\bar{u}$ is increased. This can either be accomplished by: (1) using a shorter, narrower capillary column (decrease $L$ and $d_c$) to achieve the same (or better) separation efficiency in less time; or (2) increasing the diffusivity of the solute in the gas phase by using $H_2$ rather than He as a carrier gas and/or decreasing pressure in the column (low-pressure GC). $H_2$ has been employed as a carrier gas in GC–MS [34,40–46], but it is unusual and sometimes not possible due to chemical reactivity, instrumental design considerations, and/or surface effects. Impens et al. still applied He as a damping gas in an ion trap MS even though $H_2$ was the GC carrier gas [46], and unpublished experiments using $H_2$ have indicated changes in mass spectra and curious losses in the GC inlet of certain analytes (presumably due to reactions and/or surface effects). Furthermore, $H_2$ is a flammable hazard, thus it is not generally desirable for use in the laboratory unless necessary, especially since He can meet the carrier gas needs for most GC applications.

### 2.6. Capillary column terminology

Table 1 presents the capillary column terminology related to $d_c$ that we shall use in this article. In theory, capillary columns with any $d_c$ (or taper) may be used, but manufacturers have devised standard sizes that essentially limit the column dimensions that can be applied for general use in practice. Table 1 also gives the calculated maximum carrier gas flow-rate (for He) with respect to different $d_c$ at 100 p.s.i. (690 kPa) inlet pressure for a 10-m capillary column at 200 °C oven temperature under vacuum outlet conditions. The 100 p.s.i. inlet pressure was

Table 1
Classification of capillary column GC terminology with respect to column I.D. ($d_c$)

| Term | $d_c$ range (mm) | Standard commercial column width(s) (mm) | Max flow-rate[a] (ml/min) |
|---|---|---|---|
| Megabore | ≥0.5 | 0.53 | ≥660 |
| Wide bore | ≥0.3 to <0.5 | 0.32, 0.45 | ≥86 to <660 |
| Narrow bore | ≥0.2 to <0.3 | 0.20, 0.25, 0.28 | ≥17 to <86 |
| Microbore | ≥0.1 to <0.2 | 0.10, 0.15, 0.18 | ≥1 to <17 |
| Sub-microbore | <0.1 | Various | <1 |

[a] Flow rate calculated using He carrier gas at 100 p.s.i. (690 kPa), 200 °C oven, vacuum outlet conditions and 10-m column length.

chosen because it is the maximum pressure possible with common GC instruments, but options for some instruments allow as high as 150 p.s.i. Of course, the use of >660 ml/min flow-rate is not reasonable in practice, and extends into the turbulent flow domain at some point, but the reason for showing these values is to demonstrate how the use of very narrow capillaries effectively limits the flow-rate that can be applied in a GC–MS system. Another limitation is the pumping capability of the MS detector, and most commercial GC–MS instruments are designed to work optimally at 1–2 ml/min He flow-rate.

### 2.7. Microbore and low-pressure GC–MS

In the case of the microbore column approach to decrease $t_R$, even though separation efficiency may not be sacrificed for speed, $Q_s$ is reduced by a factor proportional to $d_c^3$ [47], which is much more severe than the directly proportional relationship between $Q_s$ and $d_f$ mentioned above. Other drawbacks of using microbore columns involve higher inlet pressures, faster and more precise injection, and faster detection needs to distinguish the narrower peaks that result. Low-pressure (LP)-GC–MS avoids these negative consequences, and actually may increase $Q_s$, with the only trade-off being reduced overall separation efficiency. The use of short, microbore columns in GC–MS and LP-GC–MS are discussed in Sections 4.1 and 4.3, respectively.

### 2.8. Speed enhancement factor

In practice, several of the factors listed in Fig. 5 can be applied simultaneously to increase speed of the GC separation while seeking to minimize the trade-offs. To account for these effects and enable easier comparison of different fast GC approaches, Dagan and Amirav [37] devised the speed enhancement factor (SEF) which normalizes separations to the standard use of a 30-m, 0.25-mm I.D. column with 0.25-μm $d_f$, and $\bar{u}$ of 34 cm/s using He carrier gas (1 ml/min He flow-rate in GC–MS). The equation derived from theory used to calculate the SEF is:

$$\mathrm{SEF} = \frac{3000}{L}\frac{\bar{u}}{34} = 88\frac{\bar{u}}{L}$$

It should be noted that the SEF does not necessarily reflect the exact reduction of the analysis time because the column temperature and its programming rate are not taken into account.

Dagan and Amirav also proposed that the SEF be used to provide definitions for the terms normal (conventional), fast, very fast, and ultra-fast GC [37]. Table 2 lists the proposed SEF values associated with the different terms and other factors as calculated by van Deursen et al. [48]. Fast GC analysis can usually be performed using modern conventional GC instruments, which enable sufficiently fast sample introduction, temperature and pressure programming, and spectral acquisition rates.

For very fast and ultra-fast GC techniques, specially designed or exceptional instrumentation are often needed, thus application of these techniques in practice is limited. For example, the practical band width of the injector or spectral collection frequency of the detector may limit the chromatographic peak width in ultra-fast GC–MS, not the chromatography itself. The calculated MS data collection rate to yield five points across Gaussian-shaped peaks of the stated full-width at half-maximum (FWHM) are also given in Table 2 (the reason for using five points will be discussed in Section 3.2). Only a TOF instrument

Table 2
Classification of GC analyses (in approximate terms) based on the speed enhancement factor (SEF), analysis time ranges, and peak widths (full width at half-maximum, FWHM)

| Type of GC analysis | SEF | Typical separation time | FWHM | Spectral collection frequency[a] |
|---|---|---|---|---|
| Conventional | 0.5–5 (typically 1) | >10 min | >1 s | <2.5 Hz |
| Fast | 5–30 (around 10) | 1–10 min | 200–1000 ms | 12.5–2.5 Hz |
| Very fast | 30–400 (around 100) | 0.1–1 min | 30–200 ms | 83–12.5 Hz |
| Ultra-fast | 400–4000 (around 1000) | <0.1 min | 5–30 ms[b] | 500–83 Hz |

[a] Frequency needed to give five points across full peak width (twice FWHM).
[b] Effective peak width determined by injection process, not chromatography.

has the capability to provide the 500-Hz data collection frequency in MS needed for a peak of 5 ms FWHM. However, it is questionable if this capability is needed because applications of ultra-fast GC–MS are impractical at this time.

## 3. MS detection in fast GC

The same trade-offs and compromises that must be made for faster GC separations also occur in MS, only somewhat different techniques and terminology are involved. Figs. 3 and 4 show the triangular relationship between speed, sensitivity, and selectivity in MS detection, and Table 3 lists practical ways to achieve the most prioritized feature (speed, sensitivity, or selectivity) using different types of commercial GC–MS instruments.

### 3.1. Capabilities of different mass analyzers

Table 4 gives typical specifications for commercial GC–MS instruments separated into different types of mass analyzers. The choice of a mass analyzer determines the mass range, mass resolution ($R_m$), sensitivity, spectral collection speed, and cost of the instrument. Fourier transform ion cyclotron resonance (FT-ICR) MS, ion trap-TOF, TOF–TOF MS and other highly specialized approaches are not considered here because the very high costs do not make them practical for routine GC applications (TOF, triple quadrupole, and magnetic sector instruments are already unaffordable for many laboratories). MS is the subject of many books and reviews [49–52], thus only a cursory discussion will be given below pertaining to fast GC–MS.

#### 3.1.1. Time of flight

Non-scanning mass analyzers, such as TOF, can provide very fast acquisition rates, high mass range, and/or high $R_m$, but their cost is substantially higher than the cost of low-resolution quadrupole or ion trap instruments. The high mass range feature of TOF is less necessary in combination with GC since volatility/thermolability effectively dictates the upper mass limit. Due to the nature of the ion separation process in TOF, the instrument can be designed to emphasize high speed or high $R_m$, which is why TOF specifications in Table 4 have been divided into two sections. TOF makes gains in the quality of the MS separation depending on the accurate measurement of time (a reference compound can be continuously introduced into the source to compensate for drift of the instrument parameters), thus TOF instruments rely heavily on electronics to process the MS information extremely quickly (e.g. 3.6 GHz in a high resolution instrument). To obtain reproducible and true spectra, a large number of transients need to be summed, which decreases the number of spectra/s that are produced.

#### 3.1.2. Quadrupole and ion trap

Whereas MS on a magnetic sector instrument offers high sensitivity, a relatively wide mass range, quite high scanning speed, and/or high $R_m$, the cost and space needs for the instrument limit its use to only specialized GC–MS applications, such as dioxin analysis. In routine practice, less expensive and less complicated scanning instruments (quadrupole or ion trap analyzer) are used. Any routine laboratory should already possess at least one GC–MS of this type, and if fast GC–MS is to become widely used routinely in diverse applications, the large majority

Table 3
Practical approaches in MS to achieve speed, sensitivity, or selectivity, and the compromise(s) that must be made to achieve the specified priority (Q = quadrupole)

| Priority | How is it achieved? | MS technique | What is sacrificed? |
|---|---|---|---|
| Speed = more points per GC peak | Reducing the sampling, i.e. decreasing the number of raw spectra (microscans) to be averaged in full scan mode or decreasing the time spent per ion in SIM mode (dwell time, isolation time) | Q, ITD, sector | Reproducibility of spectra and/or ion ratios |
| | Reducing the scan range in full scan mode or the number of monitored ions in SIM | Q, ITD, sector | Selectivity (ability to identify/confirm)<br>Analytical scope |
| | Increasing spectrum storage rate, i.e. decreasing the number of transients to be summed | TOF | Sensitivity<br>Selectivity (resolution) |
| | Decreasing the resolution | Sector | Selectivity (resolution) |
| Sensitivity = increased signal, i.e. potentially decreased LOD if not limited by noise | Using SIM | Q, sector | Analytical scope (targeted analysis only) |
| | Decreasing spectrum storage rate, i.e. increasing the number of transients to be summed | TOF | Speed |
| | Increased ion storage time | ITD | Speed |
| | Decreasing the resolution | Sector | Selectivity (resolution) |
| | Using softer ionization | CI | Analytical scope<br>Selectivity (ability to identify/confirm) |
| Selectivity = decreased chemical noise, i.e. potentially decreased LOD depending on the extent of sample interferences | Increasing the resolution | Sector | Speed<br>Sensitivity |
| | Using high-resolution TOF | TOF | Speed |
| | Using $MS^n$ | ITD, combination of analyzers (e.g. Q–Q, Q–TOF) | Analytical scope (targeted analysis only)<br>Sensitivity<br>Speed |
| | Enhancing molecular ion | SMB-MS (Q, TOF)<br>CI | Analytical scope<br>Selectivity (ability to identify/confirm) |

of fast GC–MS applications would have to use one of these type of instruments.

The ion trap MS detector (ITD) gives the additional benefit of improving selectivity through $MS^n$ (usually, $n = 2$ for small molecule applications) with little or no additional capital expense vs. quadrupole MS instruments, whereas even the 'low cost' triple quadrupole MS–MS instruments are twice the cost of single quadrupole or ITD instruments. ITD stores ions in time to improve sensitivity vs. quadrupole instruments in full scan mode, but this can lead to problematic space charge effects, and unlike quadrupole instruments, little or no gain in speed or sensitivity is achieved by narrowing the mass range.

Quadrupole MS is the most popular mass analyzer for a variety of reasons, mainly due to its ruggedness and reliability, and best library compatibility since quadrupole MS was most commonly used to gener-

Table 4
Comparison of different mass analyzers used in GC–MS

| Mass analyzer | Upper mass limit (amu) | Spectral acquisition rate | Resolution, $R_m$ | Estimated cost ($US) |
|---|---|---|---|---|
| Quadrupole | 800–1050 | 4500–10 000 amu/s (15–33 spectra/s for 300 amu mass range) | 0.5 amu peak width ($R_m = 2m$, 10% valley) | 50–100 k |
| Ion trap | 650–1000 | Up to 5600 amu/s (19 spectra/s for 300 amu mass range) | 1 amu peak width ($R_m = m$, 10% valley) | 50–100 k |
| High speed TOF | 1000 | 100–500 spectra/s | 1400 FWHM at $m/z$ 502 | 130–170 k |
| High resolution TOF | 1500 | 10 spectra/s | 7000 FWHM at $m/z$ 614 | 150–200 k |
| Sector | 4000 | 0.15 s/decade[a] (7 spectra/s per decade) | Up to 80 000 (10% valley) | >200 k |

All values are the highest in current GC–MS market. In terms of other factors, pumping capacities were similar in instrument specification sheets (210–260 l/s), as were LOD, but the latter strongly depended on specific instrumental conditions (compound, MS mode, speed, mass range, $R_m$). Data processing time was not taken into account for scanning instruments.

[a] A decade is a factor of 10 difference in scan range (e.g. 10–100 or 50–500 $m/z$).

ate the library spectra. Quadrupole GC–MS can be operated in two modes: (i) full scan (of a selected mass range, e.g. 50–500 $m/z$); and (ii) selected ion monitoring (SIM). In the SIM mode, sensitivity is enhanced by monitoring only a few selected $m/z$ ratios, thus proportionally increasing the acquisition time of the ions of interest, but spectral information is sacrificed. These issues will be discussed further in the following section.

### 3.2. Sacrifices and compromises in MS detection

#### 3.2.1. Points across a peak

In any chromatographic application, the detector's data collection rate must be fast enough to give enough points across a peak, and MS is no exception (except that skewing of spectra becomes an issue for quadrupole and sector instruments). Independent of spectral quality, though, there are many discrepancies in the literature, even in theoretical studies [53–56], concerning how many points are actually needed to define a chromatographic peak. Some recent sources indicate 15–20 points [48] are required for quantitative purposes, or 10–20 [34], whereas others state that 8–10 [57], 5–6 [58], or as little as 3–4 points work well enough [59] to meet quantitative needs. Using Gaussian peak shapes, Baumann showed that 7–8 points recovered 99.99% of the peak, but 3–4 points only degraded the peak recovery by ±1.44% [56]. In a detailed theoretical review, Dyson showed how as many as 350 points may be needed to achieve 0.1% accuracy of a peak measurement [53]. This number of points to define a peak is unrealistic in practice with MS instruments.

Part of the confusion can be blamed on GC–MS manufacturers who use this issue to help market their high-speed instruments or justify the capabilities of slower instruments to meet application needs. The truth of the matter depends on the application. In the case of GC–MS, the definitive practical answer to this fundamental question is: 'Collect as many points across the peak as possible to meet quantitative and qualitative needs of the application'.

For example, a common quadrupole MS instrument is capable of a data collection rate of ≈50 Hz with a 1 amu scan range (interestingly, SIM on the same instrument can only achieve 33 Hz at the minimum dwell time setting of 10 ms). Of course, the selectivity of this type of detection is no better than what a single ion can provide, but that is the sacrifice for the speed in this system. Conversely, a single point within a GC peak is sufficient for confirmation or identification of an analyte provided that the quality of the spectrum is satisfactory. No quantitative information is needed in that case and more time can be spent to improve selectivity.

Fig. 6 gives the experimental evidence in the case of a quadrupole MS instrument on the reproducibility of peak area and peak height with respect to spectral sampling rate [58]. This plot indicates that five to six

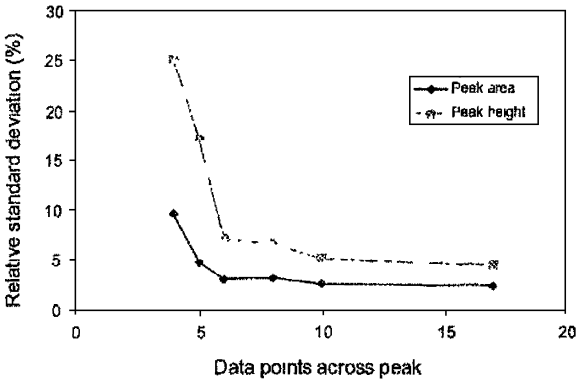


Fig. 6. The measured relationship between data points across a peak vs. RSD of peak area and height in a GC–MS analysis using a quadrupole system [58]. Reprinted with permission from the publisher.

points across a peak essentially achieves the minimum relative standard deviation (RSD) of peak area or height in the given analysis. Even in this quadrupole system, in which the spectral skewing effects are known to occur, the evidence indicates that claims of needing more than approximately eight points across a peak *for quantitation purposes* are overstated. Furthermore, the greatest source of error in quantitative analysis does not usually involve integration of the peak, but more error commonly arises from sample preparation procedures.

Another source of confusion about this issue comes from whether the baseline points at the beginning and end of the peak should be counted or not in the assessment of ''points across a peak''. Use of FWHM or full peak widths is another potential discrepancy. When a ''peak'' consists of a triangle with two baseline points and an apex, our view is that the apex point is the single point that defines the peak, but others would count that as three points [60]. In our opinion, only points that occur above the baseline should be counted as ''points across the peak''. This definition was not stated in the paper from which Fig. 6 was taken, thus the true number may only be three to four points across a peak using our definition, which agrees with the experimental and theoretical assessment of others [56,59], and the experiences of many GC–MS operators in practice (it is almost universal in conventional GC–MS using full scan or MS–MS mode that adequate quantitation is obtained with data collection frequency of 2–4 Hz for ≈2-s peak widths).

### 3.2.2. Data processing

Another facet of this discussion involves data processing. Current software programs often provide automatic mathematical manipulation of the data to yield chromatographic peaks to fit pre-defined peak shapes. A variety of different mathematical models are often applied, and some software programs automatically choose the type of peak shape model to use for integration depending on the best-fit relationship. Otherwise, the software allows the analyst to choose another type of peak shape in manual functions (as well as smoothing and tailing factors). Thus, fewer points may still meet application needs, but this should be evaluated empirically in each application.

Another factor in the data collection rate pertains to chromatographic resolution and peak deconvolution. In detection applications in which the analytes give no distinct differences in response (e.g. element selective detectors or MS analysis of congeners/isomers), only $t_R$ can be used to distinguish the analytes. In this case, data acquisition rates that give more than five to six points across a peak may be needed to aid chromatographic resolution [61]. Otherwise, in normal MS applications, the orthogonal degree of selectivity provided by MS overcomes the need for such a high degree of chromatographic resolution. In the literature, much of the discussion about fast GC–MS originates from the chromatographer's point of view, and a chromatographer tends to prefer baseline resolution between peaks. Although more selectivity in the separation can be beneficial in some respects, in other respects the time spent to resolve co-eluting compounds by GC is wasted if the compounds can be adequately resolved by the MS detector.

### 3.2.3. Deconvolution

Mass spectral deconvolution software is an effective and efficient tool to resolve co-eluting peaks in GC–MS and thus very important to fast GC–MS. Deconvolution programs are so powerful because they automatically perform nearly perfect background subtraction of distinct MS spectra to identify individual components within a mixture that has

been minimally separated by chromatography. This makes compound identification in GC–MS much better, faster, and easier than can be accomplished by a human operator. Human operation simply cannot conduct adequate background subtraction in a complex chromatogram, and a highly trained person could spend hours trying to do what a deconvolution program can do in seconds. MS deconvolution features have been included in GC–MS software programs for at least a decade (particularly for targeted analyte searching), but now that computers provide so much power for lower cost, deconvolution programs are able to search extensive MS libraries reasonably quickly to identify non-targeted compounds in the chromatogram.

The automated mass spectral deconvolution and identification system (AMDIS) from NIST [62], which is available for free on the Internet [63], can distinguish between compounds with different mass spectra separated in time by half a scan apart. Other commercial mass spectral deconvolution programs for chromatography are also available [34,64]. Using practical settings in the programs, some sacrifice in sensitivity is made by using deconvolution in full scan mode [65] (settings to maximize sensitivity tend to make too many false peaks from noise), but review of the deconvoluted results along with analyst experience and judgment can minimize these losses while still saving a great amount of data processing and review time.

### 3.2.4. Speed or selectivity gains with deconvolution

In chromatography, a good, practical measure of selectivity in a separation is peak capacity, which is the number of peaks that could be accommodated in a separation [66]. In simplistic terms, this is essentially a function of $t_R$ divided by peak width. As stated previously, MS can provide an additional degree of selectivity to compensate for losses in GC separation power (which can be used to achieve an equivalent gain in speed for a given degree of selectivity). For example, a spectral collection rate of 5 Hz for a peak width of 1 s provides the ability to resolve 10 times more compounds by their distinct mass spectra if the deconvolution program can distinguish peaks separated by half of a scan width. Similarly, a 10-fold faster separation could be conducted to achieve the same effective peak capacity as GC with non-selective detection (element selective detectors typically have a higher degree of selectivity toward chemical noise). Actual peak width is immaterial in this calculation, and the effective peak capacity in GC–MS is a factor of 2 greater than the number of spectra acquired across the GC peak. Thus 10 points per peak yields a 20-fold higher effective selectivity in GC–MS than GC without MS.

Fig. 7 gives an example of this feature and the power of deconvolution in fast GC–MS. The figure shows the comparison of different data acquisition rates (5 and 40 spectra/s) in the analysis of a mixture

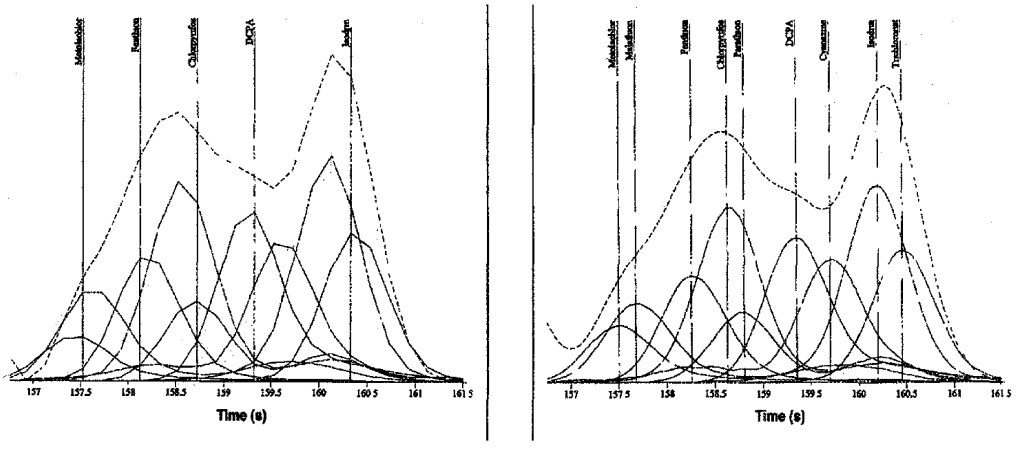


Fig. 7. Comparison between the MS deconvolution and identification of 10 co-eluting pesticides in LP-GC–TOF–MS at (A) 5 and (B) and 40 spectra/s acquisition rate [34]. Reprinted with permission from the publisher.

of pesticides in fast LP-GC–TOF-MS using deconvolution and automatic compound identification via MS library searching [34]. At the higher acquisition rate, the software program was able to locate nine of the 10 co-eluted compounds in the 4-s GC elution window whereas only five of the 10 pesticides were identified at the five spectra/s rate. Note that only the smallest peak was not identified at the fast rate due to sensitivity limitations, and only every other analyte was identified in the latter case due to identification limitations in the software. Also note that 10 points were still achieved across the 2-s-wide peaks (with $t_R \approx 2.6$ min) at the 5-Hz spectral acquisition rate, and the deconvolution program worked well to retrieve all of the components in either case, but the identification of the peaks was easier for this particular software program at the higher rate. The unidentified and/or low level peaks that have been resolved by the program can be reviewed and judged manually to make additional compound identifications (all automatic software programs should undergo human review to verify accuracy in the peak assignments and results in any event).

### *3.2.5. Mass spectral quality*

Of course, more points are better than fewer points across a peak if all other factors are equal, but the other factors are rarely equal in MS. When the scan rate in quadrupole (Q), ion trap MS detection (ITD), or sector (or sampling rate in TOF instruments) is increased, the quality of the spectra is invariably decreased. Nearly all MS instruments require spectra averaging (or summation in the case of TOF) because collection of single data events does not necessarily give reproducible spectra, especially at lower concentrations. Even if analyte concentration is adequate at the apex of a peak, the low concentrations at the start and end of a peak are especially problematic, and peak shape and integrated results at the chosen quantitation masses may be poor. Thus, except for simple applications with few targeted analytes, quality of the spectra cannot be sacrificed for speed.

### *3.2.6. Scan range*

Another way to generate more points across a GC peak with scanning MS instruments is to reduce the scan range in full scan mode or number of ions in SIM mode. This does not necessarily affect selectivity for targeted compounds, but it effectively reduces the analytical scope of how many compounds can be included in the analysis. SIM is essentially limited to targeted compounds only, which is fine for multi-analyte applications [67], but only full-scan MS can provide enough information for searching of a virtually unlimited number of unknown compounds in a chromatogram.

In the case of TOF, the mass range does not play a role in the spectral acquisition rate, and the way to increase or decrease the collection frequency is to

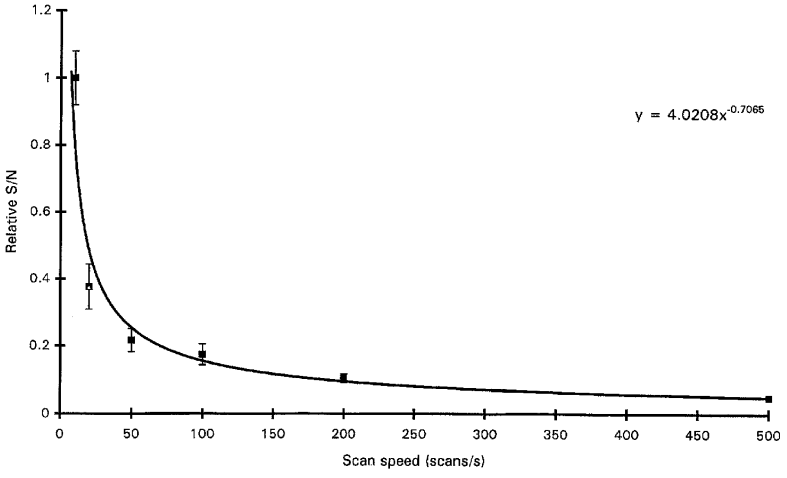


Fig. 8. Relationship between $S/N$ and spectral acquisition rate in TOF [68]. Reprinted with permission from the publisher.

alter the number of transients that are summed to give a single mass spectrum (data point). In terms of ultimate potential instrument performance, sensitivity is sacrificed for gains in speed in TOF. Fig. 8 shows the effect of ''scan speed'' (i.e. spectral acquisition rate) on average $S/N$ for organophosphorus pesticides in GC–TOF-MS analysis [68]. This figure demonstrates the fivefold loss of sensitivity as data acquisition frequency was increased from 10 to 50 Hz, but less significant change in sensitivity occurred from 50 to 500 Hz. In the case of selectivity on a TOF instrument, $R_m$ is unaffected by data collection rate in theory, but in practice, spectral quality is adversely affected when fewer transients are summed. This leads to less accurate assignment of the mass of the detected ion, which leads to more possible molecules that could give the same mass, thus reduced selectivity in the analysis.

*3.2.7. Data file size*

An additional drawback of higher spectral collection rates relates to the size of the data file produced and time to conduct data processing of so many points in a chromatogram (particularly because each point gives a unique MS spectrum). Although this issue is becoming less of a concern as computers are able to store and process larger files more quickly (and at lower prices), it is still a factor to consider for common applications.

*3.2.8. Detectability*

The literature contains numerous examples of the analysis of standards in solvent (as given in Table 5), in which instrument white noise limits LOD for the analytes, but in real-world applications involving diverse matrices, chemical noise from the matrix more often than not becomes the limiting source of noise. Thus, increasing sensitivity does not necessarily lead to decreased LOD in practice, nor does decreased sensitivity always lead to increased LOD. The bottom line in detectability is $S/N$, not sensitivity.

For example, Table 3 indicates how the use of MS–MS or high resolution MS decreases sensitivity, but lower LOD are obtained using these techniques almost universally in real-world applications [69]. Fig. 9 gives an excellent demonstration of this point in the case of increasing mass resolution in a sector instrument [70]. Notice that the response is reduced by a factor of 10 in the higher resolution chromatogram, but tremendous gains in $S/N$ are made due to significantly decreased chemical noise (increased selectivity).

*3.2.9. Speed limits for increased selectivity*

The maximum spectral collection rate in MS–MS with an ITD is ≈4 Hz, which means a peak for adequate quantitation must be wider than ≈1 s. For a typical sector MS instrument as used in Fig. 9, the data collection frequency for a scan range of 400 amu is ≈3 Hz to achieve $R_m$ of 2000 (or 10 Hz for $R_m$ of 300). To achieve $R_m$ on the order of 40 000 in a magnetic sector instrument, the data collection rate is too slow (0.03 Hz for 50–500 $m/z$ scan range) for even conventional GC–MS [71]. In the case of TOF, theory indicates that both high speed and high resolution can occur simultaneously for a wide mass range, but data processing is the limiting factor in practice.

*3.2.10. Matrix-limited noise*

As stated previously, the most common problem in GC–MS in real-world applications comes from matrix co-elutions. The use of fast GC, in which separation efficiency is reduced, acts to compound this problem due to the chance of more co-elutions from matrix components. Greater cleanup in sample preparation may be effective to reduce background interferences, but then again, such prep-scale types of cleanup are not very selective and problematic individual interfering peaks may still thwart the analysis depending on many uncontrollable factors. As expressed in the Introduction, cleanup also adds to the overall time of analysis. Furthermore, GC–MS by nature is applicable to a wide range of compounds, and the desired polarity and volatility range of analytes is likely to overlap with a large number of matrix components of similar polarity and volatility. Ideally, the reason for using GC–MS in the first place is to avoid cleanup steps and take advantage of the ''universal selectivity'' of the approach. Unfortunately, additional cleanup is still needed for GC–MS analysis in some methods than GC analysis with element selective detectors [72,73] because MS detects all eluted compounds, not just those with

Table 5
Applications of fast GC–MS in the literature

| Analytes/matrix | GC column dimensions | Fast GC technique | MS conditions | GC–MS time[a] | GC injection | Ref. |
|---|---|---|---|---|---|---|
| 144 SVOCs (pesticides, nitroaromatics, phenols, PAHs)/solvent | 5 m×0.53 mm×0.5 μm, CP-Sil 8 CB + 3 m×0.18 mm restrictor | Short megabore column LP-GC–MS Fast T program (60 °C/min) | TOF, 120–520 amu, 40 spectra/s | 4.5 min | 1 μl splitless | [34] |
| 86 SVOCs (OC pesticides, PAHs, PCBs – Araclor 1248)/ gasoline and engine oil (1:3) | 20 m×0.25 mm×0.25 μm, DB-5ms | Shorter column Fast T program (32 °C/min) | Quadrupole, full scan 120–500 amu, 2 spectra/s | 5 min (8×) | Thermal desorption, splitless | [64] |
| 72 pesticides/solvent | 10 m×0.53 mm×0.25 μm, CP-Sil 8 CB + 0.6 m×0.1 mm restrictor | Short megabore column LP-GC–MS | ITD (MS–MS mode) | 32 min (2×) | 5 μl PTV | [111] |
| 20 pesticides/carrot sample | 10 m×0.53 mm×1 μm, RTX-5Sil+ 3 m×0.15 mm restrictor | short megabore column LP-GC–MS Fast T program (60 °C/min) | quadrupole (SIM) | 6 min (3×) | 1–5 μl splitless | [101] |
| 20 OC pesticides/solvent | 7 m×0.18 mm×0.18 μm, DB-200+ 7 m×0.18 mm×0.18 μm, DB-5 | Pressure-tunable columns Short microbore columns Fast T program (50 °C/min) $H_2$ carrier gas | TOF, 25 spectra/s | 2.5 min | 1 μl split (5:1) | [44] |
| 17 triazine pesticides/water 10 OP pesticides/water | 5 m×0.1 mm×0.1 μm, CP-Sil 8 CB | Short microbore column Fast T program (50 °C/min) | TOF, 35–300 amu, 10 spectra/s | 4–5 min | 1 μl split (5:1) | [68] |
| 17 pesticides/water | 10 m×0.1 mm×0.1 μm, HP-1 | Short microbore column Fast T program | Quadrupole (SIM) | 8.5 min (2×) | 40 μl PTV | [112] |
| 13 pesticides/coriander | 6 m×0.2 mm×0.33 μm, DB-5ms | Short column High flow-rate (10 ml/min) | SMB-EI-quadrupole, Full scan, 3.2 spectra/s | 8 min | 1 μl PTV splitless | [39] |
| 12 OC pesticides/mole liver | 5 m×0.1 mm×0.1 μm, DB-5 | Short microbore column Fast T program (100 °C/min– resistive heating | Quadrupole (SIM) | 4 min | 1 μl splitless | [58] |
| 9 acidic pesticides (as methyl esters) surface water | 20 m×0.18 mm×0.18 μm, DB-5ms | Shorter microbore column Fast T program (60 °C/min) | TOF, 50–300 amu, 30 spectra/s | 3.8 min (8×) | 1 μl split (10:1) | [113] |
| 7 pesticides/apple | 5 m×0.1 mm×0.1 μm, DB-5 | Short microbore column Fast T program (100 °C/min– resistive heating) | Quadrupole (SIM) | 3 min | 0.5 μl splitless | [58] |
| 16 PAHs (EPA 610)/ sediment and tea | 5 m×0.1 mm×0.1 μm, CP-Sil 8CB | Short microbore column Fast T program (50 °C/min) | TOF, 35–300 amu, 10 spectra/s | 6 min | 1 μl split (5:1) | [68] |
| 16 PAHs (EPA 610)/solvent | 5 m×0.05 mm×0.17 μm, DB-1 | Short microbore column Fast T program | Magnetic sector, Full scan 50–500 amu, 9.55 spectra/s, $R_m$=300 | 13 min | 0.3 μl splitless | [70] |
| 8 PAHs (including large ones) /solvent | 6 m×0.32 mm×0.33 μm, HT-5 | Short column High flow-rate (12 ml/min) | SMB-HSI-quadrupole, Full scan | 8 min | Splitless | [38] |
| 6 PAHs/drinking water | 10 m×0.25 mm×0.25 μm DB-5 | Short column High flow-rate (5 ml/min) $H_2$ carrier gas | SMB-HSI-TOF, 50–400 amu, 10 spectra/s | 3 min | 1 μl splitless | [40] |
| 116 PCBs (congener-specific) sediment | 40 m×0.1 mm×0.1 μm, DB-XLB | Microbore column $H_2$ carrier gas | TOF, 120–520 amu, 20 spectra/s | 10.5 min | 0.25 μl splitless | [34] |
| PCBs (Araclor 1248)/solvent | 7 m×0.05 mm×0.05 μm, DB-1 | Short microbore column Thin film of stationary phase | ITD, 50–650 amu, 2.7 spectra/s | 4 min (10×) | 1 μl split (500:1) | [114] |

| | | | | | | |
|---|---|---|---|---|---|---|
| 12 acidic drugs/surface water | 10 m×0.1 mm×0.1 μm, DB-17 HT | Short microbore column<br>Fast T program (55 °C/min) | TOF, 50–380 amu,<br>40 spectra/s | 5.4 min<br>(10×) | 0.5 μl splitless | [113] |
| 6 drugs (amitriptyline, caffeine, chlorpromazine, imipramine, lidocaine, phenylbutazone)/urine | 4 m×0.25 mm | Short column<br>high flow-rate (6 ml/min) | SMB-HSI-quadrupole,<br>Full scan | 3 min | 0.1 μl splitless | [102] |
| 3 drugs (methaqualone, phenylbutazone and heroin)/solvent | 0.5 m×0.53 mm | Short megabore column<br>High, programmed flow-rate (300–2000 cm/s) | SMB-HSI-quadrupole,<br>Full scan 40–400 amu,<br>5 spectra/s | 20 s | 0.1 μl splitless | [102] |
| Cocaine and heroin metabolite (6-MAM) han | 6 m×0.25 mm×0.25 μm, DB-1 | Short column<br>High flow-rate (10 ml/min)<br>Fast T program (40 °C/min) | SMB-HSI-quadrupole,<br>Full scan 50–400 amu<br>(or SIM), 2.5 spectra/s | 10 min | 10 μl DSI | [16] |
| Ropivacaine and bupivacaine/ human plasma | 10 m×0.1 mm×0.4 μm, HP-1 | Short microbore column<br>Fast T program (100 °C/min) | Quadrupole (SIM) | 3 min<br>(4×) | 50 μl PTV | [115] |
| 4 thermally labile underivatized steroids solvent | 3 m×0.53 mm | Short megabore column<br>High flow-rate (60 ml/min)<br>Fast T program (50 °C/min) | SMB-EI-quadrupole,<br>Full scan | 1.2 min | Splitless (fast SPI injection) | [37] |
| 3 free underivatized phytosterols tobacco | 10 m×0.25 mm×0.25 μm, DB-5 | Short column | Triple quadrupole<br>MS–MS | 31 min | 1 μl splitless | [116] |
| 114 VOCs/environmental samples (water) | 20 m×0.18 mm×1 μm, DB-VRX | Shorter microbore column | Quadrupole, full scan<br>35–260 amu, 3 spectra/s | 8 min<br>(4×) | Purge-and-trap,<br>split (60:1) | [117] |
| 10 VOCs/model mixture | 0.3 m×0.05 mm×0.17 μm, OV-1 | Short microbore column<br>Isothermal analysis | TOF, 40–200 amu,<br>500 spectra/s | 500 ms | 1 μl head-space, split (220:1) | [48] |
| 10 VOCs/model mixture | 2.7 m×0.05 mm×0.05 μm, DB-1 | Short microbore column<br>Isothermal analysis | TOF, 35–200 amu,<br>35 spectra/s | 12 s | 0.1 μl split (1000:1) | [60] |
| 7 VOCs (priority air pollutants)/ model mixture | 3 m×0.05 mm×0.2 μm, DB-5 | Short microbore column<br>Fast T program (80 °C/min) | Magnetic sector,<br>25–500 amu, 2 spectra/s | 1 min | 0.5 μl splitless SIV | [118] |
| 25 gasoline-range hydrocarbon compounds/model mixture | 10 m×0.18 mm×0.18 μm, DB-Vax+<br>10 m×0.18 mm×0.18 μm, DB-5 | Pressure-tunable columns<br>Short microbore columns<br>$H_2$ carrier gas | TOF, 200 spectra/s | 1.8 min | 5 μl head-space, split (20:1) | [43] |
| 30 alkylates/reference standard mixture | 5 m×0.05 mm×0.17 μm, DB-1 | Short microbore column<br>Fast T program (40 °C/min) | Magnetic sector, full scan<br>60–200 amu,<br>12.2 spectra/s, $R_m$ = 300 | 1.5 min<br>(10×) | 0.5 μl split (1200:1) | [70] |
| 30 flavor volatiles/tomato<br>34 flavor volatiles/strawberry | 30 m×0.25 mm×0.25 μm, HP-5 | Fast T program (60 °C/min) | TOF, 40–300 amu,<br>40 spectra/s | 4 min | SPME (6 min) | [119] |
| 50 components/lime oil<br>25 components/lemon oil | 7 m×0.18 mm×0.18 μm, DB-200+<br>7 m×0.18 mm×0.18 μm, DB-5 | Pressure-tunable columns<br>Short microbore columns<br>Fast T program (50 °C/min)<br>$H_2$ carrier gas | TOF, 35–350 amu,<br>25 spectra/s | 2.5 min<br>(10×) | 0.1 μl split (150:1) | [45] |
| 48 components/lime oil | 10 m×0.1 mm×0.1 μm, RTX-5MS | Short microbore column | Quadrupole, full scan<br>50–350 amu, 5 spectra/s | 15 min | 1 μl split (100:1) | [120] |

VOC, volatile organic compound; SVOC, semi-volatile organic compound; PTV, programmable temperature vaporization; SIV, sample injector valve; SPI, septum equipped temperature programmable injector; HSI, hyperthermal surface ionization; OC, organochlorine; OP, organophosphorus.

[a] Factor given in parentheses is the increased speed factor vs. the conventional GC–MS method.

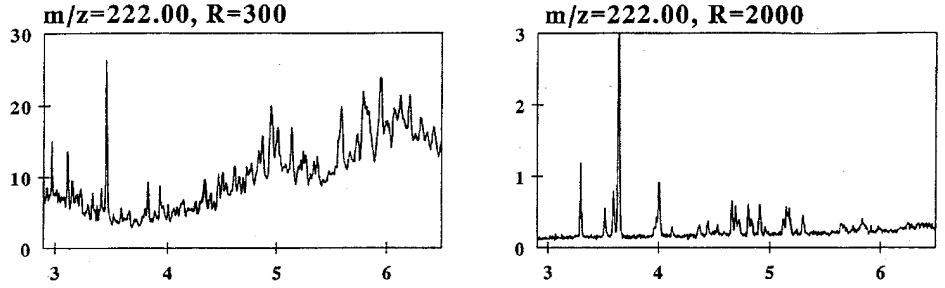


Fig. 9. Relationship between mass resolution vs. sensitivity (and LOD) in magnetic sector MS [70]. Although a 10-fold lower signal occurs as $R_m$ is increased from 300 to 2000 ($m/z$ 220.00), the $S/N$ increases greatly Reprinted with permission from the publisher.

halogens, nitrogen, phosphorus, sulfur, or other heteroatoms.

As discussed before, the use of MS deconvolution is one way to reduce this problem, but full scan mode must be used in this case, which reduces sensitivity in quadrupole and sector instruments, as does the use of deconvolution itself. For quadrupole and sector instruments, use of SIM is a common way to increase sensitivity for a limited number of targeted analytes, but worse background matrix problems could occur depending on the specifics of the analytes and interfering compounds. Using softer ionization techniques, such as chemical ionization (CI), meta-stable atom bombardment (MAB), or field ionization (FI), may decrease detection limits in two ways: more intense ions are generated and chemical noise is decreased (fewer fragments overall and fewer interferences occur at higher $m/z$). However, CI does not commonly provide enough information to confirm the identity of the analytes. SMB-MS is an approach that provides an enhanced molecular ion while maintaining structural information from fragmentation using electron ionization (EI). The unique traits of GC–SMB-MS are discussed in Section 4.4.

### *3.2.11. Tandem MS*

Like SIM, MS–MS is generally used for targeted analytes, but unlike SIM, MS–MS provides superior ability to identify the analytes. Not only does MS–MS provide the extra degree of selectivity from the mass spectrum obtained from an isolated precursor ion, but the conditions used to produce the product ions instill an added measure of selectivity because interfering precursor ions may not break apart at those conditions, and if they do, they often lead to distinctly different product ions. For this reason, $MS^n$ in ITD has an exceptional ability to avoid spectral interferences, but it is more susceptible to indirect matrix effects and self-CI than quadrupole systems.

### *3.2.12. Identification and confirmation by GC–MS*

A very important aspect in the application of any GC–MS method involves its desired ability to provide almost unequivocal confirmation of compound identity. This issue is especially important in fast GC–MS because the approach stretches the boundaries in confirmation developed for conventional GC–MS. This subject is too intricate for a satisfactory discussion in this article, but it is central to the practicality of fast GC–MS. Traditionally, the common criteria needed for confirmation in GC–MS include: (1) the relative abundance ratios of the ions in the mass spectrum must match those of the reference standard; (2) the chromatographic peak must have the same $t_R$ as a reference standard of the compound; (3) the $S/N$ ratio of each $m/z$ used for confirmation must be $>3$; and (4) a blank must not have severe interferences or indicate carry-over. However, no single set of confirmation criteria can suit the needs of all applications, thus qualitative decision-making must suit the purpose of the analysis [74].

A variety of confirmation criteria have been devised for certain types of applications [75–77], and although these criteria make sense intuitively, little evidence has been collected to show statistically or empirically how much more confidence in the qualitative result that some criteria provide over others. A quantitative measure of confidence in the qualitative result should be devised for MS, and legal cases now depend more on objective forms of

measurement than the subjective expert witness used in the past [74]. The qualitative factors can be assessed during method development in fast GC–MS through empirical verification of the consistency of mass spectra, limits of confirmation, and avoidance of interferences. This can be done in a similar fashion and at the same time as quantitative aspects of the method are validated. The ultimate qualitative test in GC–MS is to determine rates of false positives and negatives through blind analyses of many different samples prepared by an independent party. Otherwise, statistical analysis of the MS data to eliminate the universe of other possible compounds that could provide similar results would also provide convincing evidence for analyte identification.

## 4. Specific approaches to fast GC–MS

As mentioned in Section 2, there are five current approaches to fast GC–MS, all of which typically utilize short capillary columns: (1) microbore GC–MS; (2) fast temperature programming GC–MS; (3) LP-GC–MS; (4) GC–SMB-MS at high carrier gas flow-rate; and (5) pressure tunable GC–GC–MS. Each of these approaches will be discussed in the following sections.

### *4.1. Microbore GC–MS*

The only advantage of the microbore method vs. the other four approaches is that separation efficiency need not be compromised for speed of analysis. This inherently means that the peak widths will be narrower in microbore GC than in the approaches that sacrifice GC separation efficiency. The narrower peaks mean that instrument performance tolerances are more rigid, which generally leads to greater cost and complexity and less ruggedness and reliability. Thus, microbore methods necessitate that the instruments must be able to accommodate higher inlet pressures, narrower injection band widths, lower dead volumes, faster MS spectral acquisition rates, and greater data processing power. Although current quadrupole, ITD, and sector GC–MS instruments are all capable of being applied to microbore GC–MS [78], TOF is generally considered to be the detector of choice for microbore applications due to the higher possible spectral acquisition rate to still achieve full scan information. We should note just as other mass analyzers can be used in microbore GC–MS, TOF can also be used in fast GC applications that give normal peak widths. In that case, the increased $R_m$ becomes more valuable than the increased speed of spectral acquisition.

In terms of sensitivity, proponents of microbore methods maintain the greater $S/N$ ratio achieved by having sharper analyte peaks still give low LOD even though less sample is introduced into the column. However, this effect usually does not overcome the reduced amount injected and overall LOD is higher [2]. Furthermore, the effect of sharper peaks may improve detectability for injection of clean samples and standards, but the argument does not hold true for applications in which chemical noise is more prevalent. This is frequently the case in real-world analysis. The need for high spectral acquisition rates limits the degree of selectivity that can be achieved in MS detection, thus chemical noise from the matrix is still likely to be the limiting factor. MS deconvolution makes this approach more applicable, but its use leads to a further reduction in sensitivity [65].

Independent of detection, the repeated injections of complex extracts deterioriate performance of microbore columns quickly (the use of DSI may help improve ruggedness in this case). Whether or not the potential gains in selectivity provided by microbore GC are more than the gains that MS can provide in a less selective fast GC method remains an issue of debate. The loss in $Q_s$ by using microbore columns is a real and undebateable factor, however, and this also means that fewer extracts can be injected into a microbore GC column before maintenance will be needed. This alone is enough for analysts not to consider using microbore methods in many routine applications. In fact, few applications of this type of approach were found in the literature except for mixed standard solutions in solvent (as shown in Table 5).

### *4.2. Fast temperature programming GC–MS*

Increasing the temperature programming rate is a simple way to increase the speed of the GC separation without the need for special instrumentation (unless very fast rates are used as mentioned below).

Like the use of a short column, fast temperature programming GC–MS is often combined with other techniques to reduce analysis time. The studies of Blumberg and Klee [79] and Amirav [80] implicate that faster temperature programming rates lead to higher compound elution temperature, decreased separation efficiency, greater thermal breakdown of susceptible analytes, and potentially longer oven cool-down times. However, it should be noted that the initial oven temperature affects the cool-down time more than the final temperature because it usually takes longer for an oven to cool from 100 to 50 °C than 300 to 100 °C.

In practice, fast temperature programming can be accomplished: (1) with conventional GC ovens [81,82]; (2) by resistive heating [58,82–88]; or (3) using a recently introduced microwave oven [89]. The latter option has not been evaluated yet in fast GC applications and thus will not be discussed further here.

Modern oven-based GC instruments provide maximum temperature programming rates of 1–2 °C/s, which seems to be the practical limit of the temperature programming capability of conventional GC systems. Although the design of conventional air bath ovens has improved since the introduction of the first temperature-programmable GC in 1959, the thermal mass of the oven limits the heat-up and cool-down rates, thus, the full theoretical potential for fast GC analysis cannot be met using a conventional oven. The manufacture of significantly smaller GC ovens causes practical difficulties related to installing and housing a capillary column. To provide maximal sample throughput, not only must the temperature programming rate be fast, but so must the cool-down and equilibration time, and bulky ovens are just not as well suited for high speed as other, more efficient temperature control options, such as resistive heating.

In resistive heating, electrical current is employed to heat a conductive material (a metal) that encases the analytical column, and temperature is determined by resistance measurements. Thus, the thermal mass of the heater is minimized and the heat-up and cool-down rates can be very fast. Commercial systems have recently become available in which a fused silica capillary column is inserted into a resistively heated metal tube or enclosed in thermal wrapping tape, achieving temperature programming rates up to 20 °C/s [87,88]. A practical drawback of the approach is the difficulty in accessing the column to perform routine maintenance. However, even if the same temperature programming rate is applied in an oven-based GC, the resistive heating technique still provides two prominent advantages: (i) very rapid cool-down rate which results in higher sample throughput [82]; and (ii) very good $t_R$ repeatability [82,83]. A conventional GC instrument (with stated maximum oven ramp rate of 2 °C/s) can only achieve a comparable $t_R$ repeatability as in fast resistive heating at rates not exceeding ≈1 °C/s [90]). Nearly all applications presented in Table 5 apply fast temperature programming rates to increase speed of analysis.

### 4.3. Low-pressure GC–MS

In the 1960s, Giddings [91] demonstrated that applying a vacuum at the column outlet would result in greatly reduced analysis times in GC. Special devices are needed to create low-pressure conditions throughout the GC column when non-MS detection is used [92], but since MS already requires a vacuum for optimal analysis, it conveniently provides the low pressure for GC without the need for an additional external vacuum system. In fact, all GC–MS methods discussed in this article, except SMB-MS, utilize vacuum outlet conditions, thus the term ‘‘vacuum outlet GC–MS’’ [93,94] is not very descriptive, which is why ‘‘low-pressure GC–MS’’ is a preferable expression of this concept in high-speed applications.

In the 1980s, a series of theoretical studies discussing advantages of low pressures for improving the speed of analysis was published [95–98]. According to theory, the gain in speed becomes more pronounced for short, wide columns [3,48,98,99] because they can be operated at very low pressures along the entire column length. Unfortunately, the vacuum conditions extend all the way to the injector unless precautions are made. In exploratory studies, special injection methods were tested and compared [94,100]. The simplest way to solve this injection problem is to employ a short, narrow restriction capillary connected to the front of the wider ana-

lytical column [93,94]. In this manner, the analytical column is kept under low-pressure conditions, but the inlet remains at usual GC inlet pressures, thus the same injection methods can be used as in conventional GC. An additional benefit is that the restriction column also serves as a retention gap (or guard column) in the analysis of relatively dirty samples [101].

In contrast to fast microbore GC, the use of megabore columns in LP-GC provides increased $Q_s$ by a factor of $d_c^3$, which even exceeds the capacity of conventional GC–MS. Speed of analysis and increased $Q_s$ are the two main advantages of LP-GC–MS, but other advantageous features [93,101] include: (i) no alterations to current instruments are needed; (ii) peak widths are only slightly less than in traditional GC methods, thus MS spectral acquisition rate does not have to be much faster than that commonly used in GC–MS; (iii) peak heights are somewhat increased which can lead to higher $S/N$ ratios and lower detection limits (if not limited by matrix interferences); (iv) reduced thermal degradation of thermally labile compounds; and (iv) improved peak shape of relatively polar analytes (reduced tailing).

Disadvantages of the LP-GC–MS approach involve the reduced overall separation efficiency and the design of traditional GC–MS detectors to work optimally at 1–2 ml/min effluent flow rates. This latter point is demonstrated in Fig. 10 which shows how the sensitivity of the quadrupole MS was affected by flow-rate of the carrier gas. Fortunately, this is not a severe problem because diminishing returns in speed are achieved when dramatic losses in sensitivity begin to occur (e.g. a threefold increase in speed was achieved at optimal sensitivity in LP-GC–MS, but a 20% further gain in speed led to a 10-fold loss in sensitivity [101]).

### 4.4. Supersonic molecular beam GC–MS

GC–MS with common commercial instruments has a practical 1–2 ml/min flow limitation due to MS instrument designs. Higher flow rates can often be accommodated according to manufacturer specifications, but this may lead to losses in sensitivity as shown in Fig. 10 (some newer model instruments have differential pumping as an optional feature, which should allow the introduction of higher flow rates with reduced sensitivity loss). GC–SMB-MS is

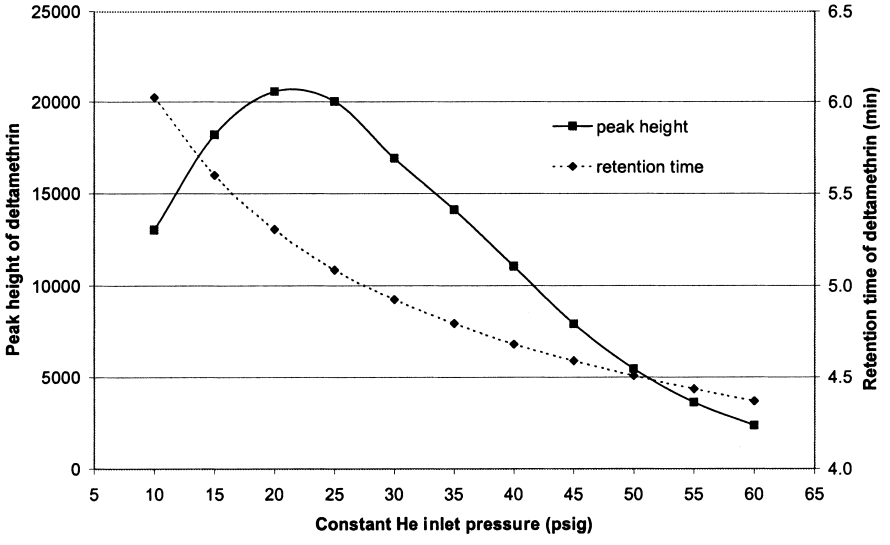


Fig. 10. Influence of the column inlet pressure (10–60 psig) on the response (peak height) and $t_R$ of 10 ng injected deltamethrin (a pesticide) in LP-GC–MS in a quadrupole instrument (SIM mode) using an analytical column of 10 m×0.53 mm I.D., 1 μm film thickness coupled with a 3 m×0.15 mm I.D. restriction capillary at the inlet end [101]. An optimum sensitivity occurred for $t_R$ of ≈5.3 min at 20 psig (2.6 ml/min at 90 °C), and further gains in speed deteriorated sensitivity. Reprinted with permission from the publisher (Elsevier).

a very promising technique and instrument to vastly extend the acceptable flow-rate range because SMB-MS *requires* high gas flow-rate at the SMB interface (e.g. 130 ml/min He) [38,102,103]. However, only a single prototype GC–SMB-MS instrument exists at this time, and the approach is not yet commercially available.

In GC–SMB-MS, a nozzle of 100 μm is placed between the GC outlet (1 atm) and the MS (vacuum). As organic molecules pass through the small opening, they form a supersonic molecular beam (SMB) and are supercooled in the process. The low thermal energy creates unique mass spectral properties that have many advantages over conventional GC–MS, which include: (1) the selectivity of the MS detection in EI is increased because an enhanced molecular ion occurs for most molecules at the low temperatures of SMB, thus losses of selectivity in the GC separation can be made up by increased selectivity in the MS detection; (2) the use of very high gas flow rates increases speed and also enables GC analysis of both thermally labile and low-volatility chemicals, thereby extending the scope of the GC–SMB-MS approach to many analytes currently done by liquid chromatography (LC); (3) the SMB-MS approach allows more versatility in selection of injection techniques and column dimensions for fast GC–MS; (4) reduced column bleed and matrix interference results due to lower elution temperatures and enhanced molecular ions; (5) better peak shapes occur because tailing effects in the MS ion source are eliminated; and (6) no self-induced chemical ionization takes place, thus the isotopomer pattern can be deduced accurately to give chemical formulas associated with spectral peaks (assuming that $S/N$ ratios are sufficient). All of these features and others are extensively described in a series of publications about GC–SMB-MS [37–39,80,102,103].

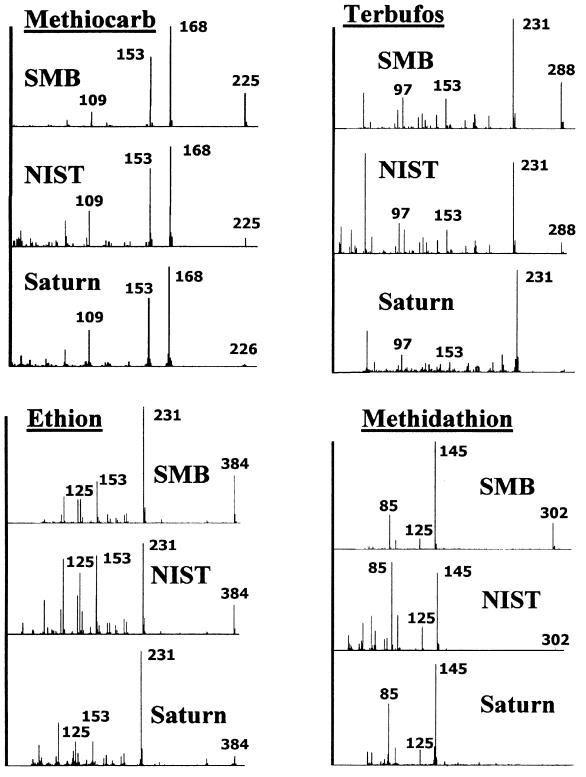


Fig. 11. The effect of an enhanced molecular ion in the mass spectrum of pesticides in SMB-MS compared to the NIST'98 library spectrum and ITD instrument (Saturn) [39]. Reprinted with permission from the publisher (Elsevier).

Fig. 11 gives an example of the enhanced molecular ion of mass spectra observed in GC–SMB-MS vs. those found in the NIST'98 spectral library and measured by a commercial ITD instrument [39]. The typical EI fragmentation pattern also still occurs, but the ion intensities shift toward the higher masses. MS library searching is still possible in SMB-MS with existing software, and a greater chance of identifying chemicals occurs due to the presence of a prominent molecular ion. As in the case of at least one other modern GC–MS instrument, the electron energies in EI can be tuned to further increase the abundance of the molecular ion if desired in SMB-MS.

### 4.5. Pressure-tunable GC–GC–MS

For complex mixtures, fast GC–MS analyses performed with short columns may become rather difficult because of the reduced selectivity. A possible solution to this problem is the use of two columns with different stationary-phase chemistries combined in series (GC–GC). Pressure-tunable (also known as stop-flow) GC–GC is a unique technique in which column pressures are adjusted at the column junction [4,41–45,104–110]. An increase in the junction point pressure leads to a lower pressure drop in the first column (thus reduced $u$ and slower rate of compound elution), and a greater head

pressure on the second column (thus increased $u$). In this circumstance, the injected compounds will have increased residence time in the first column and decreased residence time in the second column. This increases the influence of the stationary-phase chemistry of the first column and decreases the influence of the second column. Accordingly, a reduction in the junction point pressure has the opposite effect. Therefore, pressure-tunable GC–GC can alter retention patterns, which can be used to improve the quality of the separation with respect to the utilization of time.

If the column junction pressure is changed during the course of an analysis, selectivity programming is achieved [106,108]. In one effective approach, the pressure is set initially to give a good separation of the most volatile components, and after their elution, the pressure is changed to facilitate the separation of the next eluting group of components. This process can be repeated as many times as necessary to achieve a high-speed separation of a known set of analytes. Using electronic pressure control (and computer-driven pressure pulses if needed), the junction-point pressure can be set very accurately and reproducibly [41].

A limitation of pressure tuning and programming is that a change in the junction point pressure used to increase the separation of a particular component pair usually results in reduced separation of one or more other component pairs. Also, there is no guarantee that the second column will not undo the separation provided by the first column. Thus, the selection of column types and dimensions as well as the junction point pressure for a specified set of target compounds always necessitates compromises.

Pressure-tunable GC–GC represents an interesting approach for fast GC–MS analysis, but as in GC–SMB-MS, the lack of commercial availability is currently a severe limitation in the applicability of this approach. Also, the added complexity of so many adjustable parameters to optimize in complicated separations may significantly add to time and effort needed for method development.

## 5. Applications of fast GC–MS

Table 5 gives several examples of fast GC–MS applications as found in the literature. Although the applications have been sorted by analytes in column 1 of the table, the intent of the papers can basically be divided into three groups. In the first group, the authors try to demonstrate the potential of state-of-the-art instrumentation and future possibilities rather than to actually use fast GC–MS in a real-life application. In this type of paper, analytes are simply added to neat solvent for introduction into the GC–MS, and important parameters for real-world analyses, such as sensitivity and ruggedness of the approach, are not discussed. Representative examples include very fast and ultra-fast analyses (e.g. 12 s [60] and 500 ms [48] separations of 10 compounds), which essentially have the sole purpose of demonstrating the speed that these systems can achieve, despite the impractical nature of the approaches (Bertsch editorialized about such attempts at world records in high-speed GC [6]).

The second kind of paper demonstrates features of fast GC–MS to show its feasibility for possible applications, but does not necessarily conduct the application in real samples. Examples include demonstration of the potential for MS deconvolution and library matching software to automatically locate and identify co-eluted peaks in fast GC–MS separations [34,43,45,48,58,68,70,113,114]. In another case, Veriotti and Sacks used various component mixtures to describe how to reduce time of their separation using a pressure-tunable column ensemble [43–45]. Amirav and co-workers explored a combination of carrier gas high flow rates with SMB-MS to speed up the separation and also to extend the range of compounds amenable for GC–MS analysis. Using this approach, they managed to lower elution temperatures significantly (along with analyte residence times), thus enabling the analysis of low volatile compounds (such as PAHs with more than six aromatic rings [38]) and thermally labile analytes (such as carbamates [37,39] and underivatized steroids [37]).

The third group of authors focused mainly on reducing the analysis time of existing (conventional) GC–MS methods, however, the speed was not the only objective. Their papers usually describe analysis of real-world samples and include a comparison of the developed fast GC–MS method with the conventional one, mainly in terms of LODs, reproducibility,

selectivity and, of course, time. In Table 5, the factors in parentheses under the column showing GC–MS time give the time savings achieved using the fast GC–MS method. There are several examples of these type of applications, such as analysis of pesticides in food [58,101] and water [68,112,113] samples, PAHs in sediment [68], drugs in biological samples [16,102,115], VOCs in environmental samples [117] and/or congener specific analysis of PCBs in sediment [34]. As mentioned in the Introduction, fast GC–MS methods should meet the needs for a given application, and ideally, they should also provide other advantages, such as decreased LODs and/or reduced degradation of thermally labile compounds [101,116].

## 6. Conclusions

The transition of state-of-the-art approaches from the research and development stage into practice is an interesting process in analytical chemistry. Only when a new approach has been clearly demonstrated to be superior in practical applications by independent parties does it gain acceptance in routine laboratories. To the chagrin of researchers, the novelty of the analytical approach has no bearing the real world applications. The only thing that matters is the bottom line of how the new approach performs in comparison to competing approaches for specific analytical needs. A novel, state-of-the-art approach may have 10 important advantages over other existing approaches, but if it has one essential disadvantage, such as lack of ruggedness, unreasonably high cost, poor sensitivity, etc., it will not be used in routine applications. The analyst in the field recognizes these limitations quickly when applying a new technique, and this type of information is disseminated readily among routine laboratories despite the best efforts of proponents of the new approaches.

However, when a new approach meets a critical need, such as electrospray ionization in LC–MS, it rapidly becomes the method of choice and laboratories are willing to pay potentially exhorbitant costs. Whether the current approaches to fast GC–MS meet the bottom line needs of routine laboratories depends on the application, but few methods using fast GC–MS have been implemented thus far in practice. Interestingly, the problem does not reside as much with the fast GC–MS techniques themselves as with sample preparation methods and overall operations of a laboratory. The use of current state-of-the-art fast GC–MS approaches is often like driving a racing car in city traffic—the potential for very high speed exists, but this potential can rarely be applied.

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