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Rapid and Ultra-Sensitive GC/MS Analyses with a Microchannel Plate Array Detector

Part I: Possibilities of Simultaneous Ion Detection in Narrow-Bore GC/MS

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Summary

Identification and detection limits for scanning and non-scanning mass spectrometers are discussed. It is theoretically deduced and experimentally confirmed that these limits are on the low pico- and femtogram levels, respectively, when using conventional secondary electron multiplier-amplifier systems. The sensitivity can be increased at least tenfold by pulse-counting techniques, instead of current amplification, provided the chemical noise is sufficiently low. The potential advantages of a detection system for simultaneous ion detection in a significant mass range, for obtaining complete mass spectra in fast GC/MS analyses, are demonstrated. A double focusing mass spectrometer was constructed, using the well-proven Mattauch-Herzog principles. By application of an "electronic photoplate", substance identification in the low femtogram range on a millisecond time scale, so far only accessible for single ion monitoring techniques, is feasible.

1 Introduction

Narrow-bore open tubular columns are used to advantage for high-speed gas chromatographic separations of minute quantities of complex samples [1]. Both analysis times and minimum detectable amounts decrease (at least) proportionally to the reduction in column dimensions. Among the various hyphenated techniques for the separation and identification of sample components, GC/MS is still unsurpassed. Some types of modern mass spectrometers are capable of scanning more than twenty spectra per second from subnanogram amounts of analytes. The successful application of 50 μm i.d. columns in GC/MS has been demonstrated [2]. For even faster GC separations, *e.g.* with 10 μm i.d. columns, present state-of-the-art scanning MS systems, including electronics and data systems, are no longer applicable. These systems fail in terms of required scan speed and sensitivity.

A solution to this problem is a mass spectrometer with simultaneous detection of ions in a significant mass range [3,4]. Fortunately, well-proven double focusing ion optics such as the Mattauch-Herzog geometry with a linear focal plane, have been known for a long time. These types of mass spectrometers were used in the past with photoplates as detectors [5]. Along with the exciting progress in microelectronics, devices have become available which make an "electronic photoplate" possible [6,7]. A GC/MS system has been constructed using a mass spectrometer with a microchannel plate (MCP) array detector, and a special multicollector system for partial simultaneous recording (PSR).

In forthcoming papers the merits of this instrument for high speed GC/MS analyses will be described. In this paper, the limitations of the conventional detection system of this instrument, and of single detector mass spectrometers in general, are discussed. Furthermore, results of fast GC/MS analyses, using narrow-bore capillaries coupled to this mass spectrometer, are shown. Preliminary results obtained with the MCP/PSR detection system are too premature to report on. However, detection limits in the low femtogram range, for complete mass spectra permitting substance identification, are anticipated.

2 Theoretical

2.1 Limitations of Ion Detection at Extremely Fast Scanning Rates (Qualitative GC/MS Analyses)

2.1.1 Scanning Speeds and Data Aquisition

Modern mass spectrometers dedicated for GC/MS/DS analyses (DS = data system) are able to scan a mass decade (dec) between 0.02 s (linear scan for quadrupole analyzers) and 0.05 s (exponential scan for magnetic sector field instruments) at low resolving power. That means, for example, that the measuring time per mass peak, at a scan rate of 0.02 s/dec (mass range 50-500 dalton) for linear scanning with unit resolution at mass 500, or for exponential scanning with 0.05 s/dec (*e.g.* for non-iron magnets) at 500 resolution (constant over the mass range), is approximately 45 μs. The required sampling frequency for a reasonable peak centroid determination and mass assessment, therefore, is of the order of 200 kHz. Even if MS/DS technology were to allow faster scanning rates and higher sampling frequencies (or shorter integration times), it can easily be seen that there are physical, and analytically relevant, limitations. Physical limitations are imposed by ion transit times between ion source and detector, ranging between 5 and 50 μs, depending on

ion mass. Analytical limitations are governed by the small GC peak widths, *e.g.* a few milliseconds when using short 10 μm i.d. columns.

2.1.2 Sensitivity and Limits of Detetion

Sensitivity figures for electron ionization (EI) in the order of 0.2 pA for a sample flow of 1 pg/s, at low resolving power (500 to 1000) for an ion with an abundance of 5-10% of the total ionization, can be obtained with high performance GC/MS/DS systems. Mass peaks in the scanning mode can be recognized with 10-20 ions reaching the MS detector during the measuring time per peak. Consequently, the minimum amount of substance required on column for GC/MS/DS analyses, using normal 0.25 mm i.d. columns with GC peak widths of 1-5 s, is between 2-10 pg for a mass spectrum (mass range up to 500 dalton) which can be used for substance identification, for instance by library search methods. Obviously, background levels have to be correspondingly low.

Detection limits, for given operational conditions, theoretically depend on sample flow only. For scan speeds inversely proportional to GC peak widths, the absolute amount of substance on-column required is also theoretically independent of the type of column. In practice, due to constant background ions (chemical noise), narrow-bore GC columns for rapid analyses offer advantages regarding low detection limits. The low end is mainly determined by the maximum scan speed available with MS/DS technology, while column saturation effects narrow the dynamic range of rapid GC/MS/DS analyses in the scanning MS operation mode.

2.2 Considerations Concerning Single or Multiple Ion Detection (Quantitative Analyses)

Standard secondary electron multiplier (SEM) and amplifier systems can measure ion currents as low as a few times 10^{-17} A at a bandwidth of 10 Hz. This means that the lowest possible signal is in good accordance with the limits of detection resulting from the overall basic sensitivity of mass spectrometers, as the following calculation shows: A sample flow of 0.25 fg/s results in an ion current of 5×10^{-17} A under the conditions mentioned above. In other words, a total amount of 2-10 fg on column is the detection limit in the single or multiple ion detection mode.

An ion-counting system, consisting of a SEM, pulse amplifier and counter, can detect currents down to the 10^{-19} A range, when 100 ms counting time is applied. Therefore, use of such a detection system for very low ion current measurements should result in detection limits of 100-500 ag (attogram) on column.

2.3 Possibilities of Array Detectors for Simultaneous Ion Detection

The limitations of scanning systems with respect to extremely low detection limits are obvious, as discussed earlier. Summarizing, the discrepancy of measuring time per mass in the microsecond range, as compared to the total scan time in the millisecond range, is the limiting factor.

To overcome this "waste" of continuously present signals, a simultaneous detection system has to be used. It is easy to comprehend that, with such a device, complete spectra can be recorded with single ion detection sensitivity. The perspective of this approach for rapid trace analysis is striking. We have developed an analytical task in this demanding direction, which is principally based upon experience with photoplates as means for simultaneous detection [5], making use of today's state-of-the-art technologv

3 Experimental

The analytical system incorporates a Carlo Erba SFC 3000 chromatograph (Milan, Italy) coupled to an AMD Intectra mass spectrometer/data system (Beckeln, FRG). The mass spectrometer is of the Mattauch-Herzog geometry, which is the ideal type of analyzer for simultaneous ion detection, since double focusing conditions are achieved on a straight focal plane. Therefore, simultaneous detection of ions at low or high resolving power in a mass range of more than two mass decades is admitted. Nier-Johnson geometries, usually used with commercial instruments, do not have this feature, or, if modified, only in a limited mass range [8].

Figure 1 shows the schematic of the total GC/MS/DS system. The mass spectrometer is equipped with a MCP/PSR ion detection system for simultaneous ion current recording over 60% of a mass decade. The detection system consists of a two-stage Galileo Chevron CEMA 3115 microchannel plate array detector (Sturbridge, Massachusetts), a special thousand-channel multicollector system, pulse amplifiers and pulse counting devices.

The GC column used throughout (except for Figure 6) was a 24 m × 0.22 mm i.d. fused silica capillary, coated with 0.2 μm of OV-1. The column, operated isothermally at 40°C, was directly inserted into the ion source. Split injections (1:130) were carried out at 250°C, with 1 μl injections. Helium carrier gas was used at an inlet pressure of 1.8 bar (abs.). The samples were alkyl iodides, dissolved in cyclohexane.

The experiments condensed in Figure 6 were carried out using a 3 m × 40 μm i.d. column, with an inlet pressure of 20 bar (abs.) and a split ratio of $1:10^5$. The samples were trapped on-column at −20°C and subsequently reinjected by rapid heating [9]. The oven temperature was maintained at 140°C during these experiments.

The ion I^+ at *m/z* 126.9 was monitored, to avoid as much as possible chemical noise present. (Hydrocarbons with a positive mass defect yield fragment ions at *m/z* 127.1.)

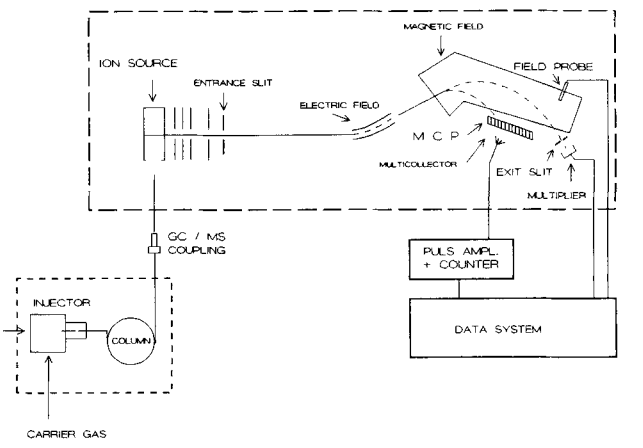


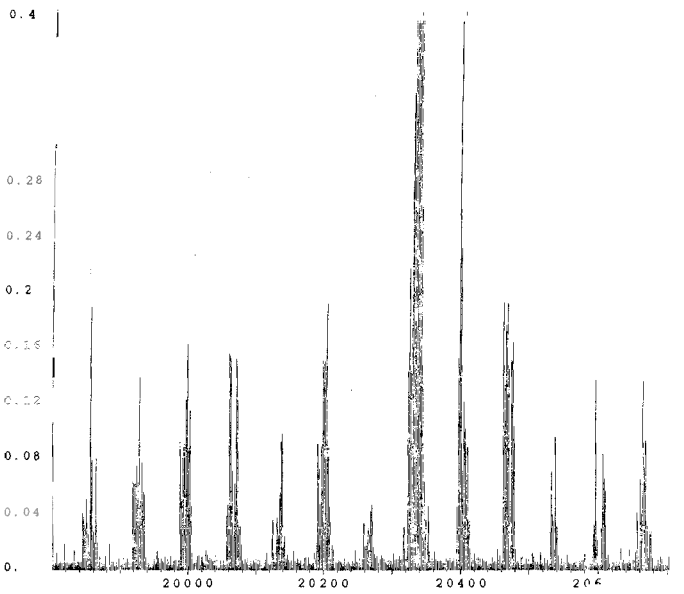
Figure 1

Schematic of the GC/MS/DS system.

The mass spectrometer was operated in the EI mode under the following conditions: electron energy: 90 eV, electron current: 0.70 mA, accelerating voltage: 6 kV, resolution: 1000, electron multiplier: 2 kV (3×10^6 gain). The time scales in Figures 2, 3, 5, and 6 are in datapoint units.

4 Results and Discussion

Whenever a high sample throughput per time unit is required, or when extremely high separation efficiencies are needed in a reasonable time, narrow-bore GC columns must be used. The disadvantage of narrow-bore columns is, however, their low sample capacity, resulting in a small working range when using conventional detectors. Apart from the need for more sensitive detectors, it is of essential importance to establish an analytical procedure for substance identification at the lowest level possible. As mentioned before and illustrated below, scanning mass spectrometers can not be applied for sub-picogram amounts of material.



Raw mass spectrum, showing detection limits for individual ion mass currents. (Scan speed 1 dec/s, amplifier filter 3 kHz, sampling frequency 20 kHz.)

Figure 2 shows, for demonstration purposes, the limit of ion detection for MS/DS systems in the scanning mode. A raw data analysis of this spectrum demonstrates that experimental and theoretical data are in good accordance. Based on a measured multiplier gain and a calculated scan time per peak, a 40 mV peak (corresponding to 1.2×10^{-15} A) should contain 7 ions within the statistical errors.

Since the amplifier filter setting and the sampling frequency were chosen such that a single ion pulse may be sampled one or two times, it can be seen that 5-10 ions are required for the detection of a mass peak.

This means that for a mass resolution of 500, the minimum ion current for obtaining complete mass spectra with a useful dynamic intensity range (*e.g.* for library search purposes) has to be between 10^{-14} A and 2×10^{-13} A. The resulting limits of detection for qualitative GC/MS analyses with narrow bore capillaries have already been mentioned before.

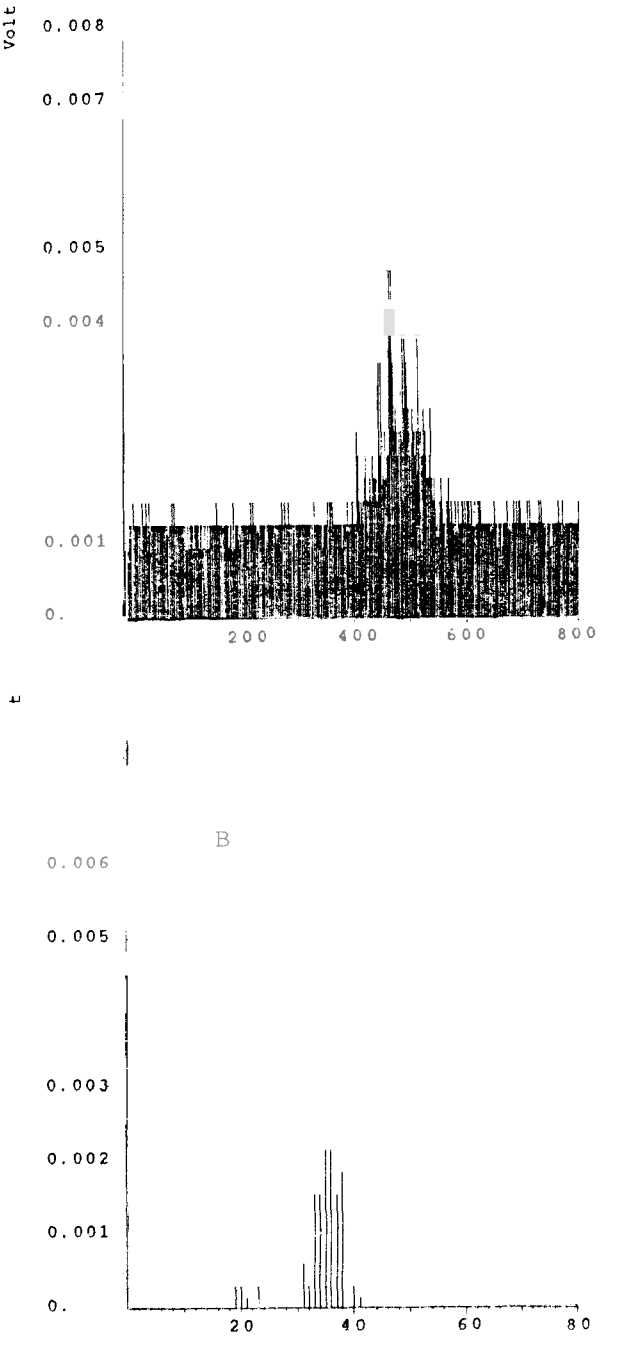


Figure 3

Single ion monitoring traces at detection limits, using a conventional amplifier with 10 Hz filter and 100 Hz sampling frequency (A), and an ion counting system with 300 ms integration time (B) (voltage sweep over m/z 126.9).

Figure 3 demonstrates the limits of ion detection for single ion monitoring techniques. Figure 3A shows the unsmoothed original raw data at the detection limit, using a conventional amplifier system. A signal to noise ratio of 5:1 for an ion current of 2×10^{-17} A for a measuring time of 1.2 s for the ion signal has been obtained. Figure 3B demonstrates the advantages of an ion counting system. It can clearly be seen that the zero line is absolutely constant and no thermal or other noise is visible. In this case an ion current of 3×10^{-18} A has been measured, indicating a limit of ion detection of about 4×10^{-19} A. (A single ion corresponds to 0.3 mV.)

After the basic investigations on ion detection limits, a calibration curve for methyl iodide was measured at mass 126.9, in the range from 90 pg down to 9 fg, using the conventional amplifier and SEM system. In **Figure 4** the linearity of the calibration curve is shown.

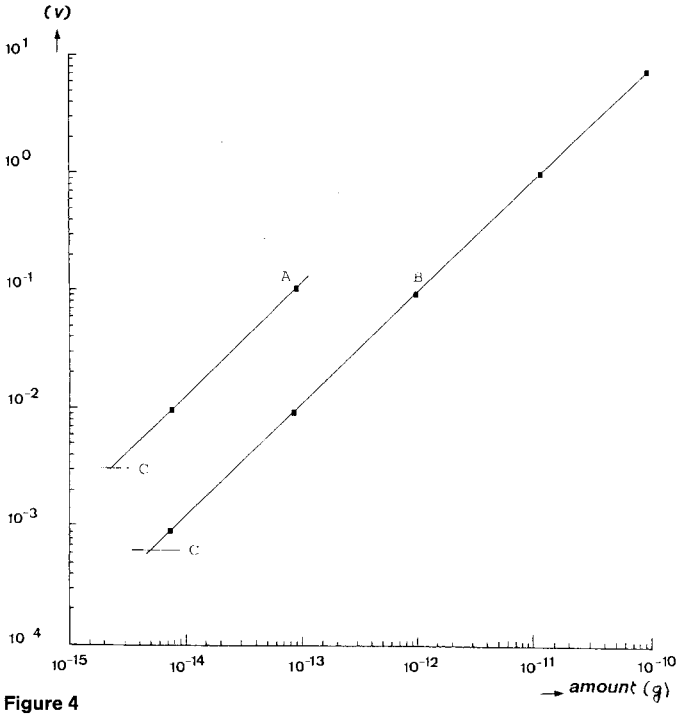


Figure 4

Calibration curves of the ion current of I^+ (m/z 126.9) *vs.* the amount injected on-column, using CH_3I dissolved in cyclohexane and the conventional SEM-amplifier system. A: SEM at 2.5 kV (gain 3×10^7), B: SEM at 2 kV (gain 3×10^6), C: noise levels.

Using the ion counting detection system, one would be able to measure an ion current signal of methyl iodide at mass 126.9 of 5×10^{-19} A, corresponding to a limit of detection of 500 ag (attogram). The chemical noise at this level is, however, difficult to eliminate.

Figure 5 shows mass chromatograms of I^+ at m/z 126.9 at detection limits. The *S/N* ratio with pulse counting is only slightly higher than with amplifying. This is caused by chemical noise. As can be seen in trace B, the detector noise is absolutely zero when no ions reach the detector. In the absence of chemical noise, the detection limit by counting would be 900 ag in this instance.

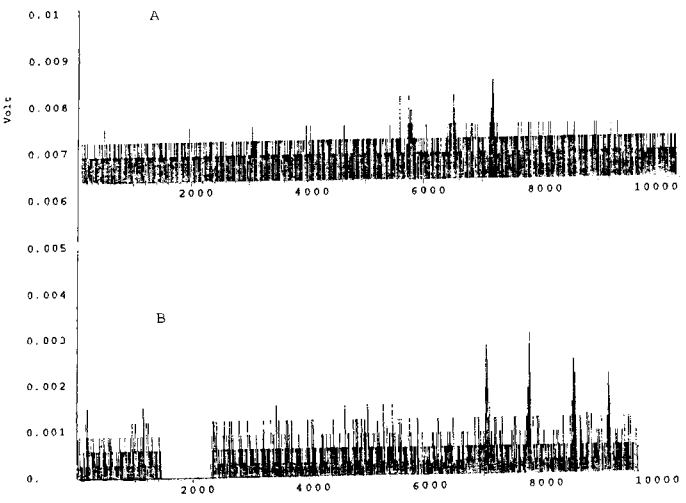


Figure 5

Single ion traces of m/z 126.9 for three (A) and four (B) injections of 9 fg of CH_3I on column, showing chemical noise and detection system noise. A: conventional amplifier with 10 Hz filter and 100 Hz sampling frequency, B: ion counting system with 166 ms integration time; detection system noise between data points 1600-2400.

It should be emphasized that the ion current of I^+ at m/z 126.9 is only 25-30% of the total ion current of CH_3I. Moreover, throughout the experiments reported, the spectral resolution was 1000.

Figure 6 shows the mass chromatogram for m/z 126.9, obtained by the separation of five alkyl iodides on a narrow-bore column.

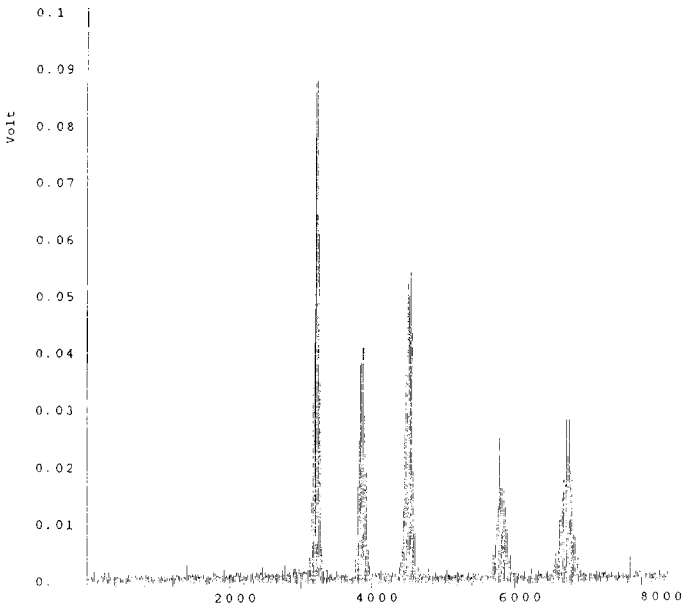


Figure 6

Single ion trace (m/z 126.9) of a chromatographic separation of a mixture of alkyl iodides on a 3 m × 40 μm i.d. column. (Amplifier filter 100 Hz, sampling frequency 2 kHz, 1 pg/compound on-column.)

Since the time scale is in datapoint units, the total analysis time of 7000 points at 2 kHz is 3.5 s. Peak widths vary between 50 and 100 ms. The compounds were, in order of elution: ethyl, 2-propyl, 1-propyl, 2-butyl, and 1-butyl iodides. The single ion currents represent 10, 5, 5, 2, and 2%, respectively, of the total ion currents of the compounds.

Further reduction in column dimensions can result in the separation of ten compounds in one second, yielding chromatographic peak widths of a few milliseconds [8]. Research towards the application of these kind of columns in GC/MS, with the novel array detector – pulse counting system, is in progress.

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