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Evaluation of quadrupole-time-of-flight mass spectrometry in comprehensive two-dimensional gas chromatography

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ABSTRACT

Quadrupole time-of-flight mass spectrometry (Q-TOFMS) has been evaluated with respect to its applicability in comprehensive two-dimensional gas chromatography (GC × GC). At a maximum acquisition frequency, while approximately 50 full accurate mass spectra on disk were acquired per s (50 Hz) in scan mode, the sampling rate in target mode (MS/MS) was strongly dependent on the number of target ions selected. The number of selected precursor ions per time window proportionally decreased the acquisition rate for each ion; one precursor ion ≅31.35 Hz; two ions ≅16.68 Hz; and for 8 precursor ions, a sampling rate of just 4.18 Hz was found. When Q-TOFMS was used in simultaneous mode, where in addition to the acquisition of target ion MS/MS signals, it also collects the full mass spectrum, sampling rates were even lower. It is demonstrated that Q-TOFMS generates sufficient data points over each peak in GC × GC operation in scan mode using TOFMS acquisition only, or is able to collect sufficient data points for relatively wide chromatographic peaks (≥600 ms) in the target mode (MS/MS), however only if one or two precursor ions are selected per time window. Mass accuracy was found to perform within specification (<5 ppm), even for the fastest acquisition operation (50 Hz). Spectral deconvolution is demonstrated to work better in GC × GC than in 1D GC mode. Data visualisation in target GC × GC mode presents difficulties when there are overlapping target windows comprising different numbers of precursor ions.

1. Introduction

Comprehensive two-dimensional gas chromatography (GC × GC) has proven advantages over classical one-dimensional GC (1D GC) in many areas, especially for more complex samples [1]. However, additional hardware requirements (modulator; columns), consumables (cryogenic fluids), data processing complexity, the requirement for fast detection acquisition, and skilled operators limit its wider applicability. While a noticeable trend in simplifying the hardware by employing cheaper [2], miniaturised [3] or consumables-free modulators [4], and ease of data processing has been observed in the last decade, the requirement for fast detection cannot be relaxed.

Flame ionisation detection (FID) is considered an ideal detector for GC × GC due to speed and almost universal response. The need for identification met limited success with the quadrupole mass spectrometer (qMS) due to relatively slow scan speed and was first reported with GC × GC in 1999 [5]. The acquisition speed of time-of-flight MS (TOFMS) is more compatible with GC × GC operation, where peak widths are routinely in the order of 100–400 ms, and although considerably more expensive it has become the general MS detector of choice since its introduction in early 2000 [6,7].

Ochiai et al. in 2007 [8] applied high-resolution TOFMS (acc-TOFMS) to GC × GC, increasing selectivity for group type separation of selected chemical classes by using MS with a 0.05 Da wide mass window. Following this initial work, several other papers have appeared recently applying high-resolution TOFMS in GC × GC [9–14]. A maximum sampling rate of 25 Hz was achieved for acc-TOFMS in full mass spectrum acquisition. A general conclusion is that accurate mass detection overcomes interferences in complex sample analysis and it aids non-target structural identification by accurate mass measurement.

In contrast to accurate mass MS, several authors used unit mass resolution tandem mass spectrometry (MS/MS) in GC × GC in order to discriminate against the matrix. Poliak et al. [15] used pulsed flow modulation with a supersonic molecular beam to analyse diazinon

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and permethrin in coriander. Interestingly, the authors stated that the combination of GC × GC and MS/MS does not necessarily significantly improve the overall analysis, even though a different kind of "selectivity" is reported. No 2D/3D plot was presented.

Hashimoto et al. [10,12] applied neutral loss scan (NLS) GC × GC-MS/MS to detect halogenated compounds in several environmental samples reporting "an effective approach for global detection of organohalogens". 2D NLS plots (19 *m/z* for fluorine, 35 *m/z* and 37 *m/z* for chlorine, 79 *m/z* and 81 *m/z* for bromine) were presented at 20 Hz acquisition rate. For a comparative GC × GC-acc-TOFMS method, both insufficient dynamic range for environmental pollutants present at widely varying concentrations, and the amount of data generated were the main drawbacks. Similarly, Fushimi et al. [16] found thermal desorption (TD) GC × GC-MS/MS both more sensitive than TD-GC-HRMS and that it was able to reduce matrix interference. These authors also stated that the retention time on the ^{2}D column cannot be determined uniquely and so it cannot be compared with ^2t_R in another MS/MS group. They concluded that because the number of points differed among groups, the software program GC Image (v2.0) could not discriminate the start of each group. Tranchida et al. [17] found that GC × GC with tandem MS was beneficial in offering increased information content, especially in simultaneous full mass scan and MRM data acquisition.

To the best of our knowledge, an extended systematic evaluation of tandem acc-MS in GC × GC has not been reported. So whilst both GC × GC and MS/MS have developed as independent systems and for particular applications, it is of interest to examine the potential for hyphenation of coupled columns with tandem acc-MS.

Here we present basic data for an exploration of the benefits and limitations of the Q-TOFMS in GC × GC mode, with presentation of data visualisation as 2D plots or on a 3D surface. Different modes of data acquisition were tested, and different acquired data densities with multiple precursor ions visualised using manual data processing or with commercially available data visualisation software. Data reported here are specific to the Agilent Q-TOFMS system, and whilst general observations may be pertinent to other manufacturers, detailed operational performance and achievable acquisition rates may vary.

2. Experimental

2.1. Chemicals and samples

An alkane mixture consisting of *n*-C13 and *n*-C14 at 2.37 ppm, and *n*-C15 and *n*-C16 at 23.7 ppm in *iso*-octane (Agilent Technologies Certified Reference Material, p/n 5188–5372) was used to test the sampling frequency for a different number of target ions in MS/MS and different time segments. Four other components (C10–C12 straight chain fatty acid methyl esters, and dicyclohexylamine; Supelco, Bellefonte, PA, USA) were spiked in the alkane mixture at a concentration of 4 ppm for the study of overlapping retention time windows. Tributyl phosphate (TBP) and triphenyl phosphate (TPP) at 1 ppm in acetone (both from Sigma-Aldrich, St. Louis, USA) were used for the data density experiment using different MS and MS/MS ranges. A shale oil sample from our previous study [18] was diluted 20 times in dichloromethane and was used for GC × GC-acc-Q-TOFMS experiments. All reference chemicals and standards were of analytical grade or better.

2.2. Instrumental

An Agilent 7200 accurate mass Q-TOFMS GC/MS instrument connected to a 7890A gas chromatograph (Agilent Technologies, Santa Clara, CA, USA) was used in the study. A 30 m long HP-5ms column (low polarity; 0.25 mm ID, 0.25 μm film thickness; Agilent Technologies) was used as a first dimension (^{1}D) column, and a 1.2 m long BPX50 column (moderately polar 50% phenyl; 0.1 mm ID, 0.1 μm film thickness; SGE, Ringwood, Australia) was used as a second dimension (^{2}D) column. The columns were connected with a deactivated pressfit (Restek, Bellefonte, USA) through a longitudinally modulated cryogenic system (LMCS, Chromatography Concepts Ltd, Doncaster, Australia) used as a modulator. Modulation was performed at 0 °C and the modulation period was 4 s (unless otherwise stated). The end of the ^{2}D column was connected to a Deans switch (DS) device and then to the Q-TOFMS via a 0.8 m length of (0.1 μm ID) deactivated fused silica (dfs). The other DS outlet was sealed. The DS device was employed to perform backflushing and for column change without venting the Q-TOFMS.

All GC conditions were the same for all samples used in the study, except the oven temperature program which was adjusted for the type of samples. Alkanes were run at 160 °C starting temperature and increased to 180 °C at 4 °C/min, while for TBP and TPP the oven program started at 180 °C, and increased to 280 °C at 8 °C/min. The oven temperature program for shale oil analysis started at 80 °C and increased to 280 °C at 4 °C/min. The following conditions were the same for all samples: injector temperature 250 °C; split ratio 20:1; constant carrier flow velocity 1 mL/min (helium). For comparison purposes, 1D GC-Q-TOFMS experiments were performed under the same conditions described above, except the modulator was not activated.

The Q-TOFMS was operated in two main modes: MS (full mass scan) and targeted MS (product ion scan or MS/MS); or with both modes operating 'simultaneously'. The ion source temperature was 230 °C, emission current 35 μA, electron energy 70 eV, collision energy 25 eV (when performed) and acquisition time 20 ms were the same for all Q-TOFMS experiments. A mass range of 40–140 *m/z* for MS/MS (acquired mass range of TOFMS when in MRM mode) and 38–238 *m/z* for MS (acquired mass range of TOFMS when in full mass acquisition) was applied in all alkane mixture experiments. The MS/MS and MS ranges were changed from 40 to 100 *m/z* to 40 to 340 *m/z* in the TBP and TPP study. A mass range of 50–500 *m/z* was selected for both MS and MS/MS modes in experiments involving shale oil analysis. 1 μL injections were made throughout.

2.3. Data acquisition and processing

MassHunter ver. B.06.00 (Agilent Technologies) was used for data acquisition and processing, and a NIST algorithm (National Institute of Standards and Technology) was used for spectrum searching through the NIST 11 MS library. Data visualisation was performed in parallel by using two approaches. The manual approach involved MassHunter data export in *csv* file format, data conversion in 2D matrix using in-house software (2D GC converter) and finally data visualisation by using Transform software (ver. 3.3, Fortner Research LLC, USA). Alternatively, commercially available GC Image software initially ver. 2.3 then upgraded to ver. 2.4 (GC Image LLC, Lincoln, NE, USA), which can directly import MassHunter files, was used. Assessment of data acquisition rates were generally determined by calculating the number of data points in a given time period.

3. Results and discussion

The Q-TOFMS instrument operates in two modes: MS (scan) and targeted MS (MS/MS). Because TOFMS continuously acquires full mass spectra at user-selected mass ranges, specific modes available to tandem quadrupole MS instruments (product ion scan, precursor ion scan, SRM/MRM) can be mimicked by using extracted ion presentations for the TOFMS channel. Thus, dedicated neutral loss experiments are not possible when using the Q-TOFMS. When used