Analytica Chimica Acta 913 (2016) 160–170

Contents lists available at ScienceDirect

Analytica Chimica Acta

journal homepage: www.elsevier.com/locate/aca

Extension of the two-dimensional mass channel cluster plot method to fast separations utilizing low thermal mass gas chromatography with time-of-flight mass spectrometry

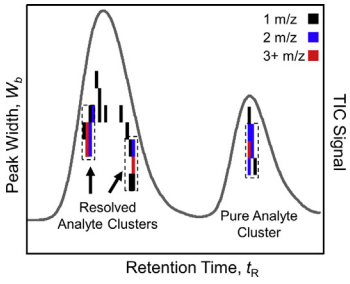
Brian D. Fitz, Robert E. Synovec*

Department of Chemistry, Box 351700, University of Washington, Seattle, WA 98195, USA

HIGHLIGHTS

- Low thermal mass gas chromatography, LTM-GC, was coupled to TOFMS.
- Novel approach for the analysis of fast LTM-GC-TOFMS data is presented.
- A traditional peak capacity of 340 was achieved in a 2 min temperature programmed separation.
- The mass cluster method achieved an effective peak capacity of 10,000 in 2 min.
- The mass cluster method is useful in conjunction with current chemometric tools.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 14 August 2015
Received in revised form
28 January 2016
Accepted 29 January 2016
Available online 30 January 2016

Keywords:
Gas chromatography
Low thermal mass (LTM)
Peak capacity
TOFMS
Chemometric data analysis

ABSTRACT

Implementation of a data reduction and visualization method for use with high-speed gas chromatography and time-of-flight mass spectrometry (GC-TOFMS) is reported. The method, called the "2D *m*/*z* cluster method" facilitates analyte detection, deconvolution, and identification, by accurately measuring peak widths and retention times using a fast TOFMS sampling frequency (500 Hz). Characteristics and requirements for high speed GC are taken into consideration: fast separations with narrow peak widths and high peak capacity, rapid data collection rate, and effective peak deconvolution. Transitioning from standard GC (10–60+ minute separations) to fast GC (1–10 min separations) required consideration of how to properly analyze the data. This report validates use of the 2D *m*/*z* cluster method with newly developed GC technology that produces ultra-fast separations (~1 min) with narrow analyte peak widths. Low thermal mass gas chromatography (LTM-GC) operated at a heating rate of 250 °C/min coupled to a LECO Pegasus III TOFMS analyzed a 115 component test mixture in 120 s with peak widths-at-base, w_b (4σ), of 350 ms (average) to produce a separation with a high peak capacity, n_c ~ 340 (at unit resolution $R_s = 1$). The 2D *m*/*z* cluster method is shown to separate overlapped analytes to a limiting R_s ~ 0.03, so the effective peak capacity was increased nearly 30-fold to n_c ~10,000 in the 120 s separation. The method, when coupled with LTM-GC-TOFMS, is demonstrated to provide unambiguous peak rank (i.e. the number of analytes per overlapped peak in the total ion current (TIC)), by visualizing locations of pure and

* Corresponding author. Department of Chemistry, Box 351700, University of Washington, Seattle, WA 98195-1700, USA.
E-mail address: synovec@chem.washington.edu (R.E. Synovec).

http://dx.doi.org/10.1016/j.aca.2016.01.045

chromatographically overlapped *m/z*. Hence, peak deconvolution and identification using MCR-ALS (multivariate curve resolution – alternating least squares) is demonstrated.

1. Introduction

Gas chromatography mass spectrometry (GC–MS) is a powerful and widely used analytical technique for the separation, identification, and quantification of volatile and semi-volatile compounds in complex mixtures. GC is capable of resolving hundreds, if not thousands of compounds in a single analysis. Many researchers have dedicated significant effort into reducing analysis time while maintaining the separation efficiency. These efforts are due largely to major technological advances in microbore capillary column implementation [1,2], column heating technology [3–22], flow control [23], injection methods [24–34], and detectors [35]. One of the most promising avenues of advancing the fast GC field is based on resistive heating technology. Two main categories of resistive heating have been developed over the years: Direct resistive heating, which resistively heats a metal separation column directly; and indirect resistive heating, which heats a metal column (or tube) in close proximity to a fused silica separation column. One example of the latter category, low thermal mass gas chromatography (LTM-GC), uses a coiled toroid consisting of a resistive heating element, thermocouple, and fused silica capillary column wrapped in foil to minimize heat loss [7]. LTM-GC is capable of heating at rates up to 1800 °C/min (30 °C/s), and in principle can perform a traditional temperature programmed GC separation (~50 °C–300 °C) in ~8 s. A traditional oven bath GC operating at the maximum heating rate capable, 30–50 °C/min, would take several minutes to accomplish the same temperature program.

However, reducing the run time of a GC separation via use of a fast temperature program may inadvertently compromise chromatographic resolution between analytes, manifested as a loss in separation peak capacity, n_c. Resolution, R_s, is a metric of separation and efficiency between adjacent analytes, defined as the difference in retention time, t_R, between analytes, divided by the average peak width at base (4σ), w_b, of the analytes. If resolution is compromised, this may compromise the ability to obtain information from the data from the overlapped analyte peaks. Mass spectral matching, which is ubiquitously used for analyte identification [36], can be significantly compromised by chromatographic overlap. Spectral matching relies on pure target and library spectra and uses an algorithm to match the ratios of spectral fragment intensities of target versus library spectra [37,38]. In order to obtain pure spectra from chromatographically overlapped peaks, mathematical deconvolution is often required. GC-TOFMS also provides a bilinear data structure which is amenable to multivariate data analysis techniques to elucidate pure spectra from overlapped analytes [39–41].

Recently, a study involving LTM-GC with flame ionization detection (FID) for fast, high peak capacity separations involving different sample injection methodologies was reported [42]. The peak capacity, n_c, is a metric of the number of peaks that can be adequately resolved in a given time, defined as the separation window, t_{sep}, divided by the average peak width at base, w_b. An n_c of nearly 300 (at unit chromatographic resolution, $R_s = 1$) was achieved in a 60 s separation [42], using a rapid column heating rate, 250 °C/min. The w_b produced were extremely narrow, reaching ~30 ms on a 5 m × 100 μm inner diameter (i.d.) column for the least retained analyte. Overall, LTM-GC facilitates fast separations, providing similar chemical information in a fraction of the time compared to traditional time-scale GC. The n_c is generally reported at unit resolution, $R_s = 1$. However, if the benefits of peak deconvolution are also considered, the effective n_c is further normalized by dividing n_c initially calculated at unit resolution, by the new R_s limit. For example, common peak finding algorithms that simply count peak maxima, can do so at a R_s limit of 0.5 [43], thus the n_c for such a peak counting algorithm would be doubled relative to n_c at unit resolution. This concept is applied in the study reported herein.

Previously a novel data reduction and visualization method for GC-TOFMS data using two-dimensional mass channel (*m/z*) cluster plots was reported, referred to herein as the "2D *m/z* cluster method" [44]. To summarize, the vector signal at each *m/z* associated with a chromatographic peak is converted into a single data point consisting of a retention time, t_R, and peak width, *W*, with the coordinate (t_R, *W*). All of the points per *m/z* are plotted (*W* versus t_R) to produce a 2D *m/z* cluster plot. Each pure analyte peak produces a cluster of points (one point per *m/z*), since points at a given coordinate accumulate, providing chemical selectivity in both dimensions, *W* and t_R. Peak signals per *m/z* of overlapped analytes produce points in the cluster plot with inflated *W*, at intermediate t_R relative to the corresponding t_R of peak signals of pure analyte *m/z*, with the linear combination of the multiple peak signal vectors for the interfered *m/z* producing wider peaks. Thus, both dimensions of a cluster plot provide chemical information as well as a novel way to visualize GC-TOFMS data. Additionally, *m/z* clusters for each analyte are significantly narrower than the corresponding chromatographic peak, significantly increasing the resolution, with an R_s limit ~0.03. The method can also be used to determine the number of analytes in overlapped peaks (i.e. the rank), as well as provide a significant increase in the overall effective peak capacity.

Herein new algorithmic parameters, methods, and instrumentation with the 2D *m/z* cluster method are implemented. The primary focus is the use of LTM-GC system coupled to a time-of-flight mass spectrometer (TOFMS). A relatively fast heating rate was applied (250 °C/min) and a short column used (10 m × 100 μm i.d.), compared to previous work (33 °C/min heating rate, 30 m × 250 μm i.d. column) [44], to produce a much faster separation with significantly narrower peaks. A rapid spectral collection rate of 500 Hz is implemented (5-fold faster than previously applied) with additional key preprocessing in order to optimally apply the 2D *m/z* cluster method. The peak width-at-base, w_b, is used as the peak purity metric since it is more selective for interfered *m/z* compared to w_{hh} previously applied. Due to its various benefits for deconvolution, multivariate curve resolution alternating least squares (MCR-ALS) was evaluated. MCR-ALS has been used extensively for deconvolution, calibration, and quantification [45–49]. A key parameter in using MCR-ALS is knowing the rank of the data input for deconvolution. The 2D *m/z* cluster method provides a novel approach to objectively obtain the rank of the matrix for MCR-ALS, thus improving the deconvolution. Based on previous implementation of the 2D *m/z* cluster method combined with algorithmic improvements to the method and use of the LTM technology, a 30-fold increase in effective peak capacity is hypothesized (i.e. effective n_c of 10,000 in 120 s).