Anal. Chem. **1999,** *71,* 1093−1099

Articles

Enhanced Chemical Analysis Using Parallel Column Gas Chromatography with Single-Detector Time-of-Flight Mass Spectrometry and Chemometric Analysis

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A parallel gas chromatographic instrument with time-of-flight mass spectrometric detection (GC/TOF-MS) is reported. An injected sample is first split between two GC columns that provide complementary separations. The effluent from the two columns is recombined prior to detection with a single TOF-MS. Switching from single to parallel columns increases the chemical selectivity of a GC/TOF-MS data set without increasing analysis time, by doubling the number of peaks, or features, in the chromatographic dimension. The resulting analyzer can be used to reduce analysis times for partially resolved peaks. Simulations compare the quantitative precision of parallel- and single-column instruments using the generalized rank annihilation method (GRAM). Results indicate that a parallel column GC/TOF-MS should substantially improve the chemical selectivity and quantitative precision of the analysis relative to a single-column instrument. For a column at half its peak capacity, for example, a single-column instrument met the target precision less than 75% of the time, while a parallel-column instrument achieved 95% success. Parallel-column analyses of methyl *tert*-butyl ether (MTBE) and benzene in gasoline samples were also performed to support the simulation studies. An objective chromatographic standardization technique corrected for retention time shifts before GRAM was applied. Although MTBE and benzene were poorly resolved in the 40-s runs, chemometric techniques successfully quantitated them.

Rapid separations are important for both industrial process monitoring and repetitive laboratory analyses. Analysis of chromatographic data sets in these areas traditionally requires complete resolution of chemical components. Thus, quantitation is performed by comparing a single number derived from an integrated peak area with a calibration curve. Other authors have emphasized the burden of complete chromatographic resolution.[1,2] These articles statistically and experimentally demonstrated that only a small fraction of the peak capacity in a column is actually available to resolve individual components into single peaks. The practical result of this is that complete chromatographic resolution of a complex mixture can be very time-consuming and in some cases essentially impossible.

One approach in dealing with incomplete chromatographic resolution is to perform multivariate analysis. Multivariate analysis of chromatographic data sets allows for the analysis of partially resolved components. Multivariate analysis of first-order data sets incorporates the selectivity found in the shape of a chromatographic profile to quantitate the analytes of interest. First-order techniques, like partial least squares (PLS), compare vectors of data that represent the chromatographic profile to perform quantitation.[3,4] A substantial reduction in analysis time can often be achieved when multivariate, first-order analysis is applied because analysis of low-resolution components can be performed. A potential drawback of first-order analysis of partially resolved signals is the requirement that either the calibration data sets contain every chemical component in the sample data set being analyzed or assumptions be made about the shape of the peaks. In contrast,

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10.1021/ac980814m CCC: $18.00
Published on Web 02/05/1999

second-order techniques allow for the analysis of partially resolved components, without these limitations. The ability to resolve and quantitate signals overlapped with signals not contained in the calibration standards data sets is known as the second-order advantage.[5] Chromatographic instruments with multichannel detectors, such as gas chromatography/time-of-flight mass spectrometry (GC/TOF-MS), are considered second-order analyzers.

Second-order chromatographic instruments can be improved by enhancing the chemical selectivity of the chromatographic separation. A parallel-column instrumental arrangement achieves this. The concept of parallel chromatographic separations has been previously presented. Most of the reported work used either a system that contains parallel columns with individual single channel detectors[6−9] or parallel columns with one single-channel detector.[10−13] In the dual-detector analyzer, a single injection leads to two chromatographic profiles per analyte. Thus, both the quantitative and qualitative results obtained in a given time period are improved. Although beneficial in some analyses, the dual single-channel detection approach lacks the second-order advantage and adds both complexity and expense by requiring two detectors. The parallel-column systems with one single-channel detector usually require that the entire chromatographic profile from one column precedes the other in time. This arrangement requires a relatively long analysis time.

The idea of parallel chromatographic columns performing simultaneous separations combined with multichannel detection was first proposed by Ramos et al., when second-order analysis methods for chemical data sets were just emerging.[14,15] Because a thorough understanding of second-order data analysis had not yet been developed, initial motivation centered on the case where an analyte is overlapped by different components in each of the parallel chromatographic separations. These pioneering studies combined multiple single-column GC/MS data sets to simulate a parallel-column analyzer.[14] In another study, liquid chromatography/multiwavelength absorbance data sets from a dual-detector parallel-column system were evaluated.[15] In the dual-detector system, data sets were joined prior to analysis as though from a single detector. These initial results were somewhat incomplete, because a true analyzer based on parallel columns and a single multichannel detector had not been experimentally demonstrated.

This report tests the hypothesis that analysis times can be dramatically reduced by combining two parallel columns with one multichannel detector and applying multivariate analysis to the resulting data. The columns will have polar and nonpolar stationary phases, to maximize the separation information. We build upon previous work by explaining the theoretical advantage of parallel columns in a determination of the net analyte signal (NAS) of each system. High-speed analysis of methyl *tert*-butyl ether (MTBE) and benzene in gasoline is studied experimentally with a parallel-column GC/TOF-MS analyzer to test the effectiveness of this system. The analysis of MTBE and other oxygenates in gasoline has become very important due to government regulations mandating their presence in automobile fuel in many urban areas. The addition of MTBE to gasoline increases octane values while reducing exhaust emissions. Several spectrometric[16,17] and gas chromatographic[18,19] techniques for the analysis of oxygenated compounds in gasoline blends have been reported. Most gas chromatographic analyses rely on relatively complex, multicolumn systems such as that described in ASTM method D4815.[18] These methods require column switching valves and multiple chromatographic flow control systems. The method reported here is mechanically simpler. Additionally, the parallel-column GC/TOF-MS analyzer optimizes the second-order analysis of partially overlapped chromatographic peaks, while preserving the capability of analyte identification and quantitation without assumptions about peak shape or the need for large sets of calibration standards.[20,21]

THEORY

First, we describe the mathematical characteristics of GC/MS data sets. Second, a brief introduction to the generalized rank annihilation method (GRAM) will be given. The theoretical advantages of parallel-column analyzers and second-order analysis are then discussed. In this section, lower case italic letters, *a*, will indicate scalars. Bold, lower case letters, **a**, denote vectors. Bold, upper case letters, **A**, denote matrices.

Second-Order Analysis. A GC/MS data set from a sample is represented as a matrix, **M**, each element of which, m_{ij}, represents the intensity measured at the *i*th retention value and the *j*th spectral value. A calibration standard for the analytes of interest results in a similar data matrix, **N**.

$$\mathbf{M} = \mathbf{X}\mathbf{Y}^{\mathrm{T}} = \sum_{1 \to p}^{k} \mathbf{x}_k \mathbf{y}^{\mathrm{T}}_k \qquad (1)$$

The superscript T denotes the transpose. As shown in this equation, **M** is bilinear in the sense that, if one set of variables (**X** or **Y**) is held constant, the resulting system is linear in the other. Thus, bilinear estimation problems exist when a single chemical component can be expressed as the outer product of two vectors, **x** and **y**. In this work, data sets from each chemical component can be described by the outer product of its chromatographic profile, **x**, and its spectral profile, **y**. The spectral profile could be, for example, a mass spectrum or a visible or near-infrared spectrum for a given compound. Data matrix **M** contains *p*

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chemical components and can be represented as the chromatographic profile of each of the components multiplied by the spectrum of each. In the ideal situation, no noise is present, and each chemical component has a spectrum and chromatographic profile that is unique and not a linear combination of the other components. In this case, the rank of the bilinear data matrix is exactly equal to the number of chemical components.

Quantitation of data sets collected on the parallel-column analyzer is performed using GRAM. GRAM predicts the concentrations, pure chromatographic profiles, and spectra of all components common to both the sample and standard. Previously, GRAM has been applied to the analysis of LC/absorbance,[22,23] LC/fluorescence,[24] GC/MS,[25] and comprehensive GC×GC[26] data sets. Two bilinear data sets are required to perform GRAM, one of which is the calibration standard. The chromatographic and spectral signals of the components of interest in these data sets must be linearly independent. Thus, there must be some degree of selectivity on the spectral axis, and some selectivity (resolution) on the chromatographic axis. This means that the single calibration standard can have somewhat overlapped components. The amount of selectivity necessary varies according to the quantitative precision required and noise in the data. Additionally, the concentrations of the chemical components must vary independently between the sample and standard. Currently there are several algorithms to perform GRAM.[27−30] In this work, the standard eigenvalue method described by Faber et al. is used.[27]

Parallel-GC Column Second-Order Analysis. The theoretical advantage of parallel-column chromatography is based on an examination of the sources of quantitative precision and accuracy for second-order analyses. Parallel columns generate two retention times per compound, which strengthens compound identification. However, recombining the effluent from two columns increases the number of overlapped peaks. It is not obvious that there would be a net improvement in most second-order analyses by using a parallel instead of a single-column configuration. The parallel-column advantage can be demonstrated by comparing certain figures of merit, such as selectivity, sensitivity, and net analyte signal.[5,31,32] The NAS for a given component k in a data set describes not only the magnitude of that component's signal but also that portion of its signal which is unique to it. For example, a component that is poorly resolved on the chromatographic axis will have a lower NAS than a component with an equal detector response but a higher resolution, i.e., higher selectivity. In general, a compound's quantitation will be more accurate and precise with a larger NAS.

The contribution of the chromatographic information to the NAS is given by

$$\mathbf{x}_k^* = (\mathbf{I} - \mathbf{X}_{-k}\mathbf{X}_{-k}^+)\mathbf{x}_k \tag{2}$$

where the vector $\mathbf{x}_k^*$ is a projection of the pure chromatographic profile of component k that is orthogonal to the chromatographic profiles of the other components.[33] In this equation, $\mathbf{I}$ is the identity matrix, $\mathbf{X}_{-k}$ is the matrix of pure chromatographic profiles of all of the components in the sample except the kth component, and the superscript + denotes the pseudoinverse. Thus, $\mathbf{x}_k^*$ is the portion of the signal of the kth component that is not contained in the space of the signals of other components in the samples. The spectral contribution to the NAS, $\mathbf{y}_k^*$, is calculated in the same fashion. A compound's overall NAS for a second-order analyzer, such as a GC/MS, is given by

$$\mathrm{NAS}_k = |\mathbf{x}_k^*| \cdot |\mathbf{y}_k^*| \tag{3}$$

where the lengths, or Euclidean norms, of the chromatographic and spectral contributions to the NAS are multiplied. When single- and parallel-column GC/MS analyzers are compared, the mass spectral information generated for each compound is the same, and so $\mathbf{y}_k^*$ remains constant. However, by increasing the number of unique features, or peaks, per analyte on the chromatographic axis, $\mathbf{x}_k^*$ should increase, resulting in a larger NAS_k. The relationship of NAS to quantitative precision will now be shown.

A compound's second order sensitivity is simply

$$\mathrm{sens}_k = \mathrm{NAS}_{k,\mathbf{M}}/c_{k,\mathbf{M}} \tag{4}$$

where $c_{k,\mathbf{M}}$ is the concentration of the kth component in sample $\mathbf{M}$. This equation is analogous to the calculation of sensitivity for single-measurement techniques. The variance of the kth compound's predicted concentration in $\mathbf{M}$, $\sigma^2_{\hat{c}_{k,\mathbf{M}}}$, using a second-order calibration technique like GRAM, is approximately given by[31]

$$\sigma^2_{\hat{c}_{k,\mathbf{M}}} \approx \frac{1}{\mathrm{sens}_k^2}\left[\left(\frac{c_{k,\mathbf{M}}}{c_{k,\mathbf{N}}}\right)^2\sigma_{\mathrm{N}}^2 + \sigma_{\mathrm{M}}^2\right] + \left(\frac{c_{k,\mathbf{M}}}{c_{k,\mathbf{N}}}\right)^2\sigma^2_{c_{k,\mathbf{N}}} \tag{5}$$

As can be seen, the error in predicted concentration is influenced not only by the noise in the sample and standard data sets ($\sigma_{\mathbf{M}}$ and $\sigma_{\mathbf{N}}$) but also by the uncertainty in the known concentration of the standard ($\sigma_{c_{k,\mathbf{N}}}$). It is also evident that as a compound's sensitivity is reduced, it becomes more difficult to precisely quantitate. Equation 5 closely predicts the concentration prediction error when noise in the data is uniformly distributed and uncorrelated. A modified form of this equation has been developed when additional noise terms become significant.[34] However, the trend seen in eq 5 still holds: the increased NAS of a component in a parallel- versus single-column system increases its second-order sensitivity, which in turn reduces the error in its quantitation. Through simulation, we will examine the hypothesis that

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parallel columns increase the portion of the chromatographic profile that is orthogonal to the profiles of the other chemical components, and thus the NAS. The increased NAS should then improve the quantitative precision of the analysis.

EXPERIMENTAL SECTION

In the parallel-column GC/MS arrangement, sample is split between two short columns of different stationary-phase polarity operating in parallel. Both column effluents are recombined at the TOF-MS detector. Two different parallel-column systems were used. Quantitation of MTBE in gasoline was performed with a 3-m, 100-μm-i.d. column with a 0.1-μm HP-1 (poly(dimethylsiloxane)) phase, and the same dimension HP-Wax (bonded poly(ethylene glycol)) column with a 0.2-μm phase (Hewlett-Packard, San Fernando, CA). These columns provide different elution orders, and thus complementary chemical selectivity. Flow entering and exiting the parallel columns was split using glass press-fit splitters (Hewlett-Packard). Two 30-cm lengths of 100-μm HP-1 served as connectors from the columns to both the injector and detector. Measurement of retention times indicated that independent flow rate variation between the columns was minimal. Parallel-column GC/MS analyses were performed with a HP 6890 gas chromatograph with an HP 7673 autosampler (Hewlett-Packard) and an experimental TOF-MS with electron impact ionization.[25] The column head pressure was 17 psi. All separations were performed at 27 °C. Sample aliquots of 0.5 μL were split 200:1 at the inlet. The TOF-MS integrated successive spectra and stored them at 12 spectra/s. The mass spectral information was condensed to one point per mass/charge unit over a range of 10−100 amu.

Five analytical standard solutions of synthetic gasoline containing MTBE and other oxygenate compounds and one solution containing only the oxygenate compounds served as samples and calibration standard, respectively (Supelco, Bellefonte, PA). To determine quantitation precision, 42 runs of the five samples and one standard (seven replicates of each) were injected onto the parallel column analyzer over a period of 2 days.

For analyses in which MTBE and benzene were quantitated simultaneously, a second system was used consisting of two 5-m, 250-μm capillary columns operating in parallel. The polar column had a 0.44-μm TCEP stationary-phase film (Supelco). The nonpolar column had a 0.25-μm AT-50 stationary-phase film (Alltech, Deerfield, IL). A 10-cm length of 350-μm deactivated silica served as a connector to the injector. A 30-cm length of 100-μm deactivated silica served as a connector to the detector. The column head pressure was 30 psi. Sample aliquots of 0.5 μL were injected with a split of 800:1. These separations were performed at 50 °C. Thirty spectra were recorded per second. The sample was prepared by adding volumetric amounts of MTBE, benzene, ethanol, and 1-pentanol (Aldrich Chemical, Milwaukee, WI) to a gasoline sample purchased from a local gasoline station. Before the sample was spiked, it contained no detectable amount of these compounds. The gasoline sample analyzed in this article contained 2% MTBE and 1% benzene. The standard contained only the four compounds used to spike the sample and was also prepared volumetrically. MTBE and benzene were each 20% of the standard.

The data were transferred to a Sun SPARC station, from which all data analysis was performed. Processing and simulations were done using MATLAB (The Mathworks Inc., Natick, MA). The algorithms used to perform singular value decomposition, the eigenvalue problem, and the eigenvalue similarity transform[35] were those included with MATLAB.

RESULTS AND DISCUSSION

Parallel- and single-column second-order analyzers were compared through simulation, to test whether increasing the chromatographic information would improve the analysis of overlapped compounds. The simulations incorporated typical selectivities and signal-to-noise values for GC/multichannel detection experiments. In the simulations, 1-s-wide Gaussian peaks were randomly distributed within a 1-min time window to represent GC peak profiles. Simulations of this type have previously been used by other authors to represent chromatographic separations for the purpose of studying the probability of peak overlap.[36] Acquisition rates of 20 spectra/s were used for the simulations. The simulated spectra and the noise present in the data sets were kept constant for all the simulations because moving from single to parallel columns does not affect these factors. The simulated spectra were single Gaussian peaks from a 25-channel spectrometer, with a resolution of 0.2 between the analyte's spectral peak and the other component peaks. The lack of similarity between shapes of simulated spectra and true mass spectra is not crucial because the net spectral contribution to the signal is similar and the systems being compared have the same spectra.[37] Random noise was added at a value that resulted in a signal-to-noise (S/N) ratio of 100 when two components had a chromatographic resolution of 0.3. The S/N ratio is the NAS (eq 3) divided by the noise. Thus, the overlap of interference signals affects the S/N ratio.

Figure 1 is an illustration of a worst case scenario from these simulations. This scenario illustrates how parallel columns improve second-order analysis even though the chromatogram is crowded with twice as many peaks as for a single-column analyzer. In this simulation, a single component is being analyzed in a sample of 20 components of equal concentration. Thus, overlapped components can be identified by peak heights greater than 1. Figure 1A is the chromatographic concentration profile of column A. In this separation, all but 7 of the 20 components are resolved on the chromatographic profile, yet the analyte of interest is completely overlapped with unknown interference 2. Figure 1B is the chromatographic profile of the same sample separated on column B. Different chromatographic selectivity was simulated by performing another random distribution of the retention times for the 20 components. In the second separation, the analyte of interest is significantly overlapped by a different unknown interference. In this separation, interference 1 elutes at nearly the same time as the analyte of interest. This example is a worst case scenario because there is no chance of quantitating the analyte of interest using either column A or B due to coelution of the analyte with unknown interferences. Second-order analysis techniques, like GRAM, require some degree of selectivity on both the chromatographic and spectral axes to deconvolve overlapped signals. Figure 1C is the parallel column separation of the same sample using columns A and B as the two parallel columns. The parallel column configuration results in two peaks for the analyte

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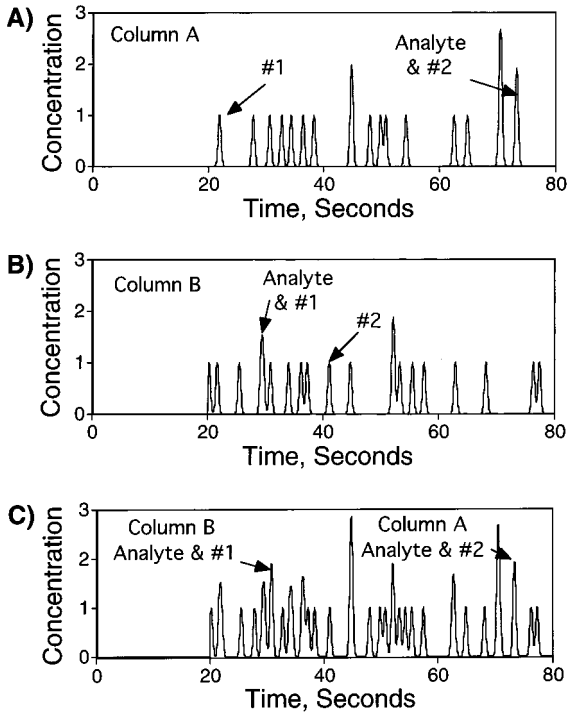

Figure 1. Advantage of parallel-column second-order analyzers. Overlap of randomly distributed components can be identified by peak heights exceeding 1. (A) On column A the analyte of interest is overlapped by unknown interference 2. (B) On column B the analyte of interest in the same sample is overlapped by unknown interference 1. (C) Although the analyte is not resolved on either column, parallel-column second-order analysis can be successful because no single interference, neither 1 nor 2, overlaps both of the analyte peaks.

of interest. The analyte peak resulting from the column A separation is still overlapped with interference 1, and the analyte peak from column B remains overlapped with interference 2. Although both analyte peaks from the parallel-column separation are overlapped by interferences, second-order quantitation can be performed because the parallel-column two-peak profile of the analyte of interest is different from the two-peak profile from each of the interferences. No single interfering compound completely overlaps both analyte peaks. This example is one very specific case in which a parallel-column second-order analyzer is obviously beneficial.

A large set of examples such as the one illustrated in Figure 1 were simulated and evaluated to compare the quantitative analysis power of single- and parallel-column analyzers. A precision requirement was set at 5% variance. If the variance in analyte concentration predicted by eq 5 for a GRAM analysis was above 5%, the analysis was considered unsuccessful. Given a set chromatographic run time of 80 s and the precision requirement, the sample complexity was varied by changing the number of components in the sample from 2 to 31. Ten repetitions of 1000 simulations with random peak distributions were performed for both the single- and parallel-column configurations for each of the 30 sample complexities. The average percent success values of the 10 repetitions are shown in Figure 2. The standard deviations of the percent success values are too small to be visible. Figure 2 can be seen as the confidence that a given peak will have less than a 5% variance in predicted concentration for parallel- and single-column analyses over a range of sample complexities, given a set chromatographic time and random peak distributions.

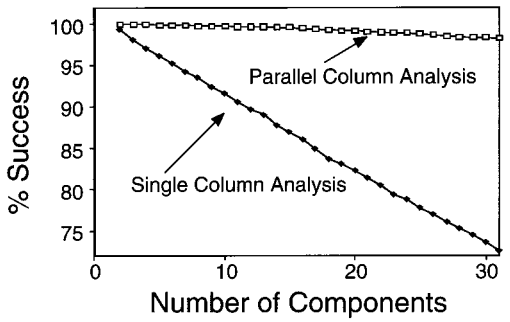

Figure 2. Results of simulations comparing parallel- and single-column multichannel detector analyzers for second-order analysis at multiple sample complexities. Percent success values were determined by setting a quantitative precision criterion explained in the text. Parallel-column analyzers demonstrate their advantage for complex samples.

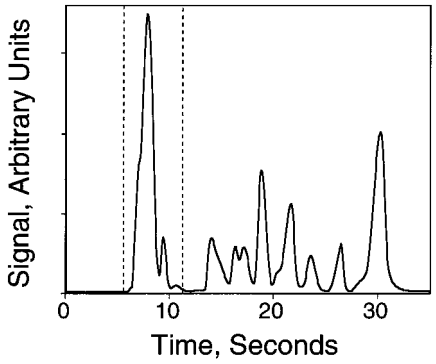

Figure 3. Total ion chromatogram of a gasoline sample analyzed with a parallel-column GC/TOF-MS. Dotted lines indicate the portion of the chromatographic data containing MTBE peaks used for analysis. Quantitation of MTBE in this gasoline sample and other samples was performed with calibration standards that did not contain gasoline.

The key result is that a parallel-column second-order analyzer is predicted to perform dramatically better than a single-column second-order analyzer. For example, while single-column analyzers meet the required precision less then 75% of the time with 30 interfering components in the chromatographic window, parallel-column analyzers remain successful over 95% of the time. It should be noted that as more components are added to the time window, well beyond 30, the results from parallel-column analyzers eventually decrease and meet the percent success of single-column analyzers. However, this occurs in such a low percent success region that no chromatographer would accept such a separation. Figure 2 shows results for a specific set of chromatographic conditions. Extensive simulations (not shown for brevity) support the notion that as sample complexity increases, parallel-column multichannel analyzers maintain their advantage over single-column multichannel analyzers when second-order analysis is performed.

The parallel column GC/TOF-MS analysis of MTBE in gasoline demonstrates an example of the rapid analysis of a small number of chemical components in a complex sample. This analysis for MTBE in synthetic gasoline was performed in less than 40 s. Figure 3 is the total ion chromatogram of these data. Synthetic gasoline samples containing 0.28, 3.47, 7.18, 10.78, and 14.32% MTBE were analyzed. The preparation and analysis of large sets of calibration standards can be very time-consuming. The second-

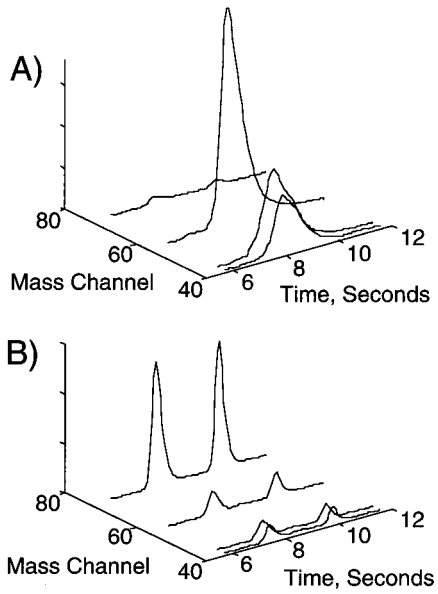

Figure 4. Subset of parallel-column GC/TOF-MS data used for second-order data analysis of MTBE in gasoline. (A) Gasoline sample and (B) standard data sets used for quantitative analysis of MTBE. The standard data set contains only MTBE. The chromatographic axis contains one MTBE peak from each of the two parallel columns.

order data analysis performed here requires only a single standard, dramatically shortening the calibration step. It should be noted that second-order analysis can be performed with multiple calibration standards if accuracy needs to be improved.[38,39]

The first step in analyzing the large matrix of data produced by a parallel-column GC/TOF-MS analysis was to use known information about the signal of the analyte of interest to choose a subset of data that is both reasonably selective and sensitive to the analyte. The mass spectral axis was reduced to m/z channels of 41, 43, 57, and 73, all channels for which MTBE had an appreciable signal. These channels were selected in order to reject a lot of noise and improve quantitative precision. It must be mentioned that second-order analysis imposes a lower limit on the number of required channels, since there need to be at least as many channels of data as there are components that show a response in those channels. Subsets of data chosen for the analysis of MTBE in gasoline are shown in Figure 4. A chromatographic time window containing both MTBE peaks was chosen for the subset. The dotted lines in Figure 3 illustrate this time window. The subset of data is still a matrix, thus preserving the second-order advantage. Figure 4A and B are data subsets from a gasoline sample and calibration standard, respectively. It can be seen that even in the subset of data the signal of MTBE remains overlapped with interfering components in gasoline. The two chromatographic profiles from MTBE are easily visible in Figure 4B. The profiles of MTBE are not as distinguishable in Figure 4A because none of the chromatographic or spectral channels are completely selective for MTBE. Because the analyte of interest does not have a purely selective channel, and future gasoline samples may contain unexpected interferences, second-order analysis is appropriate for the high-speed analysis of MTBE in gasoline samples. The GRAM-predicted signal for MTBE in the gasoline sample data

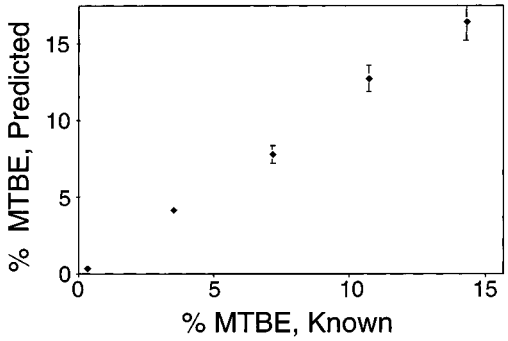

Figure 5. Quantitation results from the parallel column analysis of seven repetitions of five gasoline samples containing known amounts of MTBE. Second-order chromatographic standardization was applied prior to GRAM analysis. Error bars show the standard deviation from the analysis of 49 combinations of sample and standard data sets for each sample solution.

is essentially identical to that shown in Figure 4B, which is a good indicator for successful quantitation in the presence of interfering components.

The chromatographic axes of the sample and standard were aligned using second-order chromatographic standardization prior to GRAM. This standardization technique uses the precision of the spectral axis to objectively correct for retention time variations found in chromatographic data sets. This method aligns the sample and standard data sets by minimizing the residual variance, or error, found through factor analysis of the combined data sets. A standardization profile is created which shows the percent residual variance of different data set alignments. The minimum in this profile indicates the retention time correction to be made prior to quantitative analysis. A more detailed explanation of this technique is given elsewhere.[22,25] In this example, a retention time correction of 0.125 s was made to the data set in Figure 4A relative to Figure 4B. The average retention time correction necessary for all data sets was 0.12 s. After retention time standardization, quantitative and qualitative analysis was performed using GRAM on all data sets.

Quantitative results are shown in Figure 5. These results reflect the analysis of MTBE in five gasoline samples each run seven times using the parallel-column GC/MS analyzer coupled with GRAM and retention time standardization. The error bars are the standard deviation of the quantitative result for the analysis of 49 different combinations of sample and standard data sets. Quantitative results are very good, given that the analysis time is less than 40 s.

The advantage of second-order chromatographic standardization for the analysis of parallel column data sets is further demonstrated by the high-speed analysis of MTBE and benzene in a sample of gasoline. This example shows that second-order chromatographic standardization can be successfully applied to a relatively long time window of data from a parallel-column separation. The entire chromatographic profile was used in the multivariate analysis for this experiment because the retention times of the two MTBE and two benzene peaks were located throughout the chromatogram. Simultaneous quantitative analyses of MTBE and benzene in gasoline were performed with a parallel-column GC/TOF-MS separation of less than 35 s. Once again, the second-order advantage is demonstrated by performing the

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(39) Gui, M.; Rutan, S. C.; Agbodjan, A. *Anal. Chem.* **1995**, *67*, 3293−3299.

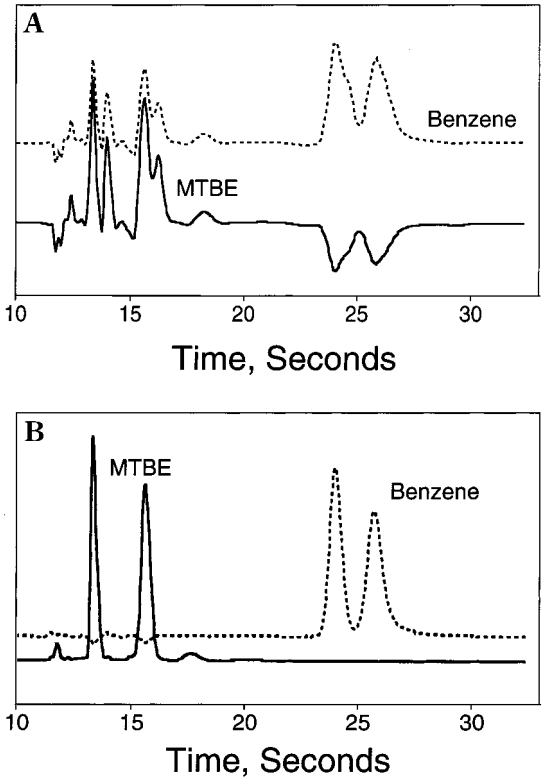

Figure 6. GRAM chromatographic profile predictions for MTBE (solid line) and benzene (dashed line), (A) without standardization using the 5-m parallel-column analyzer. Retention time variation between the sample and the standard data sets was detrimental to this deconvolution. (B) GRAM chromatographic profile predictions following second-order chromatographic standardization. A substantial qualitative improvement is seen when standardization is performed.

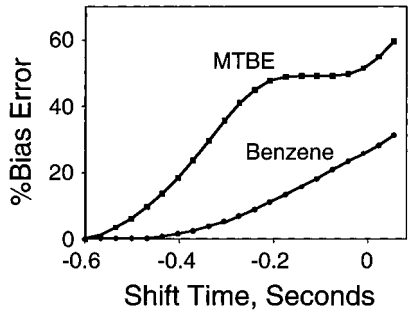

Figure 7. Improvement in quantitative accuracy resulting from second-order chromatographic standardization. Percent quantitative error of both MTBE and benzene is plotted against chromatographic shift. Zero shift is the data set alignment prior to standardization.

analysis of these two components in a complex sample using one standard that does not contain all the interfering components in the gasoline sample. The gasoline sample contained 2% MTBE and 1% benzene. Seven mass channels that were most sensitive to the components of interest were used in the analysis. Figure 6A contains the GRAM-predicted chromatographic profiles of MTBE and benzene produced using GRAM without the aid of second-order chromatographic standardization. The dashed trace, with positive peaks in the 25-s region and smaller signals in the earlier region of the chromatogram, is the predicted chromatographic profile of benzene. These profiles do not resemble the correct profiles, which should each contain one positive peak from the polar column separation and one from the nonpolar column separation. Second-order chromatographic standardization was used to minimize retention time variation between the sample and standard data sets before quantitation.[22,25] A considerably better GRAM prediction of the chromatographic profiles for these analytes is shown in Figure 6B. The two peaks from MTBE elute early in the chromatogram, followed by the benzene peaks. Figure 7 shows the influence of retention time variation on quantitation bias for one sample/standard combination. Bias in the quantitative analyses of MTBE and benzene relative to the results obtained after are shown. A shift time of zero indicates alignment before second-order chromatographic standardization was applied. The error in alignment of 0.6 s that was present before standardization resulted in a 26% increase in quantitative bias for benzene and a 52% increase in bias for MTBE.

CONCLUSION

Switching from single- to parallel-column chromatography crowds the chromatographic axis by doubling the number of peaks. However, we have shown that there is a theoretical advantage to parallel-column chromatography, when coupled with multichannel detection and multivariate analysis. The parallel-column arrangement is a suitable method of improving the high-speed GC/MS analysis of a broad range of complex mixtures, while not requiring extensive calibration models containing every possible chemical in the complex samples. Beyond increasing the chemical information obtained in a given time, parallel-column analyzers offer a means to simplify analytical method development and broaden the applicability of second-order chromatographic systems.

ACKNOWLEDGMENT

This work was supported by the Center for Process Analytical Chemistry (CPAC), a National Science Foundation, University/Industrial Cooperative Research Center at the University of Washington.

Received for review July 24, 1998. Accepted December 16, 1998.

AC980814M