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Algorithms for the Qualitative Assessment of Gas Chromatograms

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Abstract

An important aspect of automating instruments is automating the detection of system malfunctions that render the generated data unanalyzable. This paper describes a set of algorithms that have been developed to detect and measure features associated with symptoms of analysis failure in gas chromatograms. Each algorithm is individually tested and validated qualitatively by comparing the algorithm output with the opinions of experienced chromatographers. When these algorithms are input into an expert system, the output can be used to detect and diagnose the underlying malfunction that causes the symptoms.

Introduction

The increasing demand for sample analyses has increased the need for instrument automation. Currently chromatography instruments can be automated with autosamplers, which allow for the unattended analysis of large batches of samples. However, chromatography data continue to be evaluated by experienced technicians to determine if the data are suitable for analysis. If a batch of samples is run unattended, the data from each sample are not evaluated when they are generated. A failure in either the sample preparation or the equipment operation can render the analysis (and potentially the analyses of the remaining samples in the batch) useless. In addition, continued operation of an instrument after a fault has occurred can result in instrument damage.

An important aspect of automating instruments is the rapid and accurate detection and diagnosis of sample preparation failures or instrument malfunctions (1). A system has been developed to detect and diagnose gas chromatography (GC) analysis failure automatically. This analysis assessment system consists of algorithms that can be used to detect symptoms of an analysis fault and an expert system that uses the symptoms to diagnose the fault (2). Specific problems related to both instrument malfunction and sample preparation can be identified. Automatic detection and identification of malfunctions can be used to terminate batch processing, notify operators of the malfunction, or signal the instrument to correct the problem. For instance, the detection of an inappropriately concentrated sample can be used to run a procedure that cleans the instrument automatically before analysis of the next sample in the batch.

In this article, a set of algorithms is described that has been developed to detect and measure features associated with symptoms of analysis failure in gas chromatograms. Algorithms were developed to identify features that are commonly used to troubleshoot chromatography data. Chromatogram features were chosen from instrument troubleshooting guides and prior work in this field (3–5). A list of algorithms developed in this project appears in Table I. Information flow through the assessment system is depicted in Figure 1. As shown in Figure 1, a chromatogram is processed into a symptom file that contains the output of the symptom detection algorithms. The symptom file is passed to an expert system that diagnoses any fault which produces the symptoms (other groups have developed feature extraction systems for a neural network fault-diagnostic system [T. Lu and J. Lerner. Spectroscopy and hybrid neural network analysis. *IEEE Proceedings*, in press.]).

Symptom detection algorithms result in either a binary value or a fuzzy value (Table I). Binary values are produced for symptoms that are either present or absent, such as clipped peaks. Fuzzy values are produced for symptoms that are present in varying degrees, such as leading peaks. Thresholds are used to determine the precise output value for each symptom. Thresholds for algorithms with binary outputs are determined by the occurrence of a single event; thresholds for algorithms with fuzzy outputs are determined through a statistical study of acceptable and faulty data. All output values are mapped on a 0–1 scale; 0 indicates the complete absence of a symptom, and 1 indicates the maximum expected degree of severity.

It is not feasible to search for all symptoms in all types of samples. For example, it is not reasonable to apply algorithms that are used to measure peak features to the chromatogram of a blank sample in which no peaks are expected. For this reason, chromatograms are classified by sample type for processing by

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the analysis assessment system. For each sample type, a different set of features is extracted. Three sample types are distinguished in this work: blanks, standards, and unknowns. The chromatograms of blank samples are expected to contain no peaks. Chromatograms of standard samples are expected to be well-characterized, with a predetermined number of peaks of known size. Calibration samples, which are used to define method calibration curves, are considered standard samples. Unknown samples produce chromatograms with very few expected features. Unknown samples are expected to have one or more retention time marker compounds added before analysis. Table I indicates the algorithms applied to each sample type.

Experimental

Data were generated on Varian 3600 and Varian 3400 GC instruments (Walnut Creek, CA). To generate data that contained identifiable symptoms, faults were induced in the instrument or sample before analysis. The induced faults tested were an overconcentrated sample, a leaking septum, column bleed, column degradation, a contaminated injector, loss of makeup gas pressure, and a leaking syringe.

Blank samples consisted of hexane. A standard sample of five pesticides (0.1 pg/µL lindane, 0.2 pg/µL heptachlor, 0.1 pg/µL aldrin, 0.2 pg/µL dieldrin, and 1.2 pg/µL methoxychlor) was created. Concentrations were increased by a factor of 100 to generate overconcentrated samples. One hundred thirty chromatograms of this standard sample were obtained by using a DB-17 column with nitrogen makeup gas at a flow rate of 30 mL/min. The column temperature was increased from 80°C to 240°C at 10°C/min. The injector temperature was increased from 80°C to 250°C at 180°C/min, and the detector was held at 300°C. To generate the column bleed and column degradation faults, the DB-17 column was preceded by a 2-m carbowax megabore column, which provided a more readily degraded stationary phase.

Additional standard chromatograms were generated from commercial Aroclor samples (Supelco, Bellefonte, PA) prepared at concentrations ranging from 50 ppb to 800 ppb. Over 400 Aroclor chromatograms were collected. The Varian 3600 instrument that was used was equipped with a split–splitless injector, a DB-5 column (30 m × 0.25-mm i.d., 0.25-µm film thickness) (J&W Scientific, Folsom, CA), and an electron-capture detector. The nominal helium carrier gas flow rate was 1.8 mL/min. The injector and detector temperatures were 280°C and 350°C, respectively. The column oven was held at 80°C for 1 min following injection and then increased at 15°C/min to 350°C, followed by a 3-min hold.

After the chromatograms were acquired, they were translated into the Analytical Instrument Association (AIA) data interchange file format (6) for analysis by the assessment system. The feature extraction algorithms were developed using the Matlab (Mathworks, Nantik, MA) numerical computation system.

Procedures

Several processing steps were performed on the data before the application of the feature extraction algorithms:

Filtering

The chromatogram was filtered with an 11-tap finite impulse response filter to reduce noise in the signal so that the output

Table I. Symptom Detection Algorithms and their Attributes

			Application			
Symptom	Value	Threshold	Blank	Standard	Calibration	Unknown
Retention time shift	Fuzzy	Statistical		X	X	X
Spike precision*	Fuzzy	Statistical		X	X	X
Sensitivity change	Fuzzy	Statistical		X	X	
Peak tailing	Fuzzy	Statistical		X		X
Unresolved peaks	Fuzzy	Statistical		X		
Band broadening	Fuzzy	Statistical		X	X	X
Clipped peaks	Binary	One peak		X		X
Negative dip after peak*	Binary	One neg. dip		X	X	
Irregular baseline drift	Fuzzy	Statistical	X	X		
Rising baseline	Fuzzy	Statistical	X	X	X	X
Elevated baseline	Fuzzy	Statistical	X	X	X	X
High noise	Fuzzy	Statistical	X	X	X	X
Irregular spikes	Binary	One spike	X	X	X	X
Ghost peaks	Binary	One peak	X	X		
Extra peaks	Binary	One peak	X	X		
No peaks	Binary	One peak	X	X	X	X
Replicate precision	Fuzzy	Statistical		X	X	
Peak leading	Fuzzy	Statistical		X		X
Surrogate precision*	Fuzzy	Statistical		X	X	
High background*	Fuzzy	Statistical	X	X	X	X
Rounded peaks*	Fuzzy	Statistical		X	X	X

* Algorithms are under development.

sequence of the filter was a least-squares fit to the data (7–9). The sampling interval and noise level of the test chromatogram were such that an 11-tap filter provided adequate filtering.

Peak Tables

Peak tables were created from the filtered chromatograms. A very simple peak-identification criterion was used to preserve features in the chromatogram that are important in qualitative assessment. An N-point chromatogram that was filtered to reduce noise was denoted as the amplitude sequence $x(n)$, where $n = 0$ to $N - 1$, and its associated time sequence was denoted as $t(n)$. The initial peak-detection criterion was used to define a peak as any sample in $x(n)$ that has an amplitude greater than samples on both sides of it: $x(n - 1) < x(n)$, and $x(n) > x(n + 1)$. Similarly, a valley was defined to be any sample in $x(n)$ that has an amplitude less than samples on both sides of it: $x(n - 1) > x(n)$ and $x(n) < x(n + 1)$ (The case of equal amplitude is considered in the following discussion of clipped peaks.). When this simple criterion is used, it is not unusual to detect up to 4000 peaks in a chromatogram.

The i^{th} retention peak in $x(n)$ was parameterized by its amplitude and time, $p_r(i)$ and $t_r(i)$; the amplitude and retention time of its leading valley, $v_a(i)$ and $t_a(i)$; and the amplitude and retention time of its tailing valley, $v_b(i)$ and $t_b(i)$. The retention times of the peak and valleys were obtained by using the derivative of the chromatogram (2).

Peak width was calculated after peak detection. The width of a single peak was determined as follows. First, the highest valley $v(i) = \max[v_a(i), v_b(i)]$ on either side of the i^{th} peak $p_r(i)$ was found. Next, the time locations of both the leading and tailing sides of the peak, $t_a(i)$ and $t_b(i)$, respectively, were found so that the amplitude at both locations was the fraction W_f of the difference between the peak and the highest valley:

$$x[t_\alpha(i)] = x[t_\beta(i)] = W_f \times [p_r(i) - v(i)] \qquad \text{Eq 1}$$

The peak width was then estimated to be $w_r(i) = t_\beta(i) - t_\alpha(i)$. In most cases, the fractional peak width was set to $W_f = 0.5$ so that peak widths were estimated at 50% peak height.

The relative height of the i^{th} peak was defined as the distance between the peak amplitude $p_r(i)$ and a point that is the intersection of a line connecting the leading and tailing valleys and the line $t = t_r(i)$. The area of the i^{th} peak is the product of the width of the peak at 50% and its relative height.

Peaks in the peak table that were generated as described above were matched to peaks in the peak table that were generated by the instrument data analysis software (available in the AIA data file). The peak tables that were generated by the instrument data analysis software (the Varian GC Star software) were not used in this qualitative assessment because the peak-detection and peak-filtering parameters exclude chromatogram features that are critical for qualitative assessment. However, by matching the peaks in the peak table above to peaks that are detected by the instrument software, the peaks (and peak parameters) that are important to the chemist can be identified. For example, the peak-detection thresholds in the instrument software describe the expected intensity of the experimental data. A second "system peak table" was created that lists the peak heights and widths, calculated as described above, for the peaks matching the retention times of the peaks that were listed in the AIA data file.

Retention Time Markers

Retention time markers (RTMs) are peaks that result from compounds that are added to the sample before injection. Typically there are two or three RTMs in a chromatogram. The detection of several symptoms was based on the analysis of RTM peaks. Identification of RTMs in a chromatogram consisted of a series of steps in which peaks that were potential RTMs were first identified, then peaks that were clearly not RTMs were eliminated, and finally adjacent peaks were clustered to form the RTMs.

Initially, peaks that were found within 15 s of the expected retention time of the RTM were selected as candidate RTMs. If no peak was found, the absence was noted. If one or more peaks were found in the 15-s window, the peak closest to the expected retention time was selected. Due to potential splitting of the RTM peak (resulting from an instrument malfunction), peaks that were adjacent to the candidate RTM were inspected for inclusion into the final RTM parameter estimates. For an adjacent peak to be included in the RTM, two conditions were required: the amplitude of the peak must have been within a factor of the amplitudes of the calibration RTMs, and the width

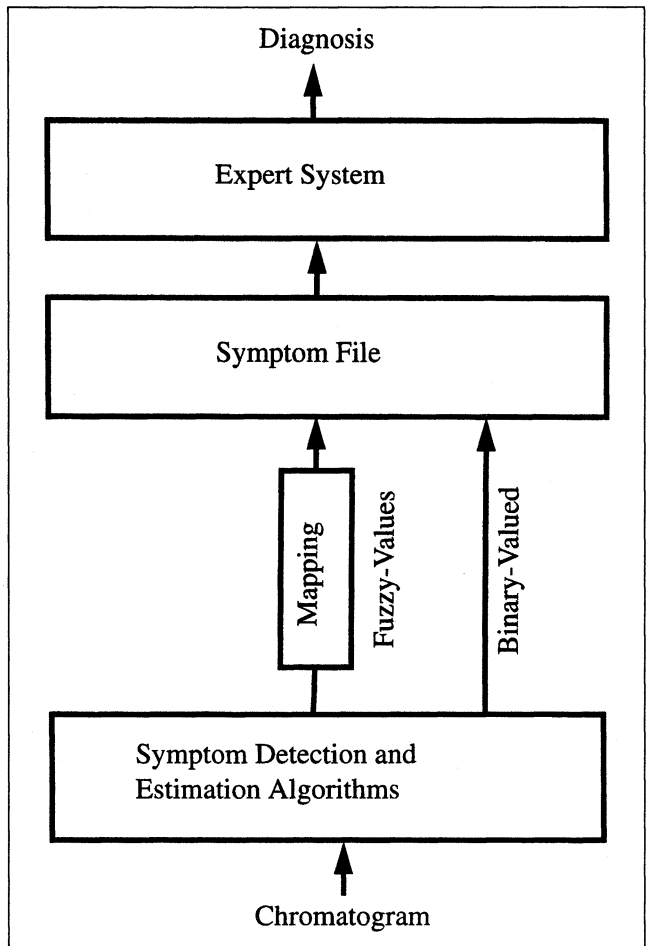

Figure 1. Information flow through the analysis assessment system.

of the peak must have been within a factor of the widths of the calibration RTMs. If multiple peaks were included in an RTM, the retention time and amplitude were the average of all the peaks that were included. The peak width and area were estimated by using the algorithms previously described. A reference file that contains the nominal time locations, amplitudes, widths, and areas of the RTMs was created by using standard samples prior to processing the unknowns.

Baseline Estimation

The baseline of a smoothed chromatogram was estimated by averaging splines constructed from sets of local minima. Averaging splines constructed in this manner reduced the tendency of localized oscillations to occur, as is often found in splines that are constructed from a single set of minima. In the smoothed chromatogram $x(n)$, the first point of the chromatogram was $x(0)$ and the last point was $x(N-1)$. A set of local minima was formed by partitioning $x(n)$ into M contiguous, nonoverlapping segments and selecting the minimum value of $x(n)$ within the segment. The number of points in each segment was given as $M_b = \lfloor N/M \rfloor$, and the last segment contained the remainder of the points.

The segment of $x(n)$ in the m^{th} segment was denoted as $x_m(n)$. The set of local minima was

$$\{\hat{x}_0\} = \{x(0), \min[x_1(n)], \min[x_2(n)],\ldots,\min[x_M(n)], x(N-1)\} \quad \text{Eq 2}$$

A spline was then constructed from this set of local minima:

$$\hat{b}_0(n) = \text{spline}(\{\hat{x}_0\}) \quad \text{Eq 3}$$

Next, the set of segments was shifted by M_s points, and a new set of local minima was formed. The i^{th} set of local minima, formed from the i^{th} shift, was denoted as $\{\hat{x}_i\}$. The spline formed from this set of local minima was

$$\hat{b}_i(n) = \text{spline}(\{\hat{x}_i\}) \quad \text{Eq 4}$$

Splines continued to be formed in this manner for P shifts until the first segment of the $(P-1)^{th}$ shift overlapped the second segment from the 0^{th} shift. The baseline estimate was found by averaging all P splines:

$$\hat{b}(n) = \frac{1}{P}\sum_{i=0}^{P-1}\hat{b}_i(n) \quad \text{Eq 5}$$

The value for the number of samples in a segment was set to $M_b = R(0.03 \times N)$, and the number of samples in a shift was set to $M_s = R(M_b/7)$, where R is the rounding operator. For the chromatograms used in this study, these values were found to yield good results. The splines used to construct the baseline estimate were produced by the Matlab function "spline()".

Creating Fuzzy Values

To interface with the expert system, the output of a symptom-detection algorithm was required to be either a binary value or a fuzzy value in the range 0–1. For binary symptoms, the value of 0 indicated that the symptom was not present, and the value of 1 indicated that the symptom was maximally present. For symptoms that produce nonbinary values, fuzzy values were used to indicate the varying intensity of the symptom (The type of output that was provided by each algorithm is listed in Table I.). Mapping was required in order to convert the output of the algorithm to a fuzzy value in the appropriate range. The output of a symptom detection algorithm was denoted as X, maximum and minimum thresholds were denoted as T_{max} and T_{min}, and the output of the mapping was denoted as V. A linear mapping of X to V that meets the range requirement on the fuzzy value is given by the following equation:

$$V = \begin{cases} 0 & X < T_{min} \\ \dfrac{X - T_{min}}{T_{max} - T_{min}} & T_{min} \le X \le T_{max} \\ 1 & X > T_{max} \end{cases} \quad \text{Eq 6}$$

The maximum and minimum thresholds were based on the mean (m_x) and standard deviation (σ_x) of the calibration data and on a reference value (X_{ref}). The reference value represents the nominal value of the output; for example, $X_{ref} = 1$ for peak leading or tailing, and $X_{ref} = 0$ for retention time shift or sensitivity change. If $m_x \ge X_{ref}$, the maximum and minimum thresholds are given by the following equations:

$$T_{min} = m_x \quad \text{Eq 7}$$

$$T_{max} = m_x + 2\sigma_x \quad \text{Eq 8}$$

If $m_x < X_{ref}$, which often occurs in the leading peaks symptom, the thresholds and symptom value must be reflected around X_{ref} in order for the mapping to apply. In this case,

$$T_{min} = (X_{ref} - m_x) + X_{ref} \quad \text{Eq 9}$$

$$T_{max} = [X_{ref} - (m_x - 2\sigma_x)] + X_{ref} \quad \text{Eq 10}$$

$$(X_{ref} - X) + X_{ref} \rightarrow X \quad \text{Eq 11}$$

The number of significant figures in the fuzzy output value was rounded to the nearest 0.01.

Symptom Algorithms

Raw output from symptom-detection algorithms was denoted as X_{zz}, where zz is a designator for the symptom. The mapped output from the algorithms was denoted as V_{zz}.

Clipped Peaks

A clipped peak occurs when the amplitude of the peak exceeds the maximum amplitude allowed by the detector. Since filtering can introduce artifacts into the chromatogram that make detection of clipped peaks difficult, this algorithm was applied to the chromatogram before it was filtered. Clipped peaks were detected by normalizing the unfiltered chromatogram and searching for regions in which the amplitude equaled 1. If more than five sequential points in the normalized chromatogram had an amplitude of 1, a clipped peak was detected, and the binary symptom value $V_{cp} = 1$. If clipped peaks were detected, the chromatogram was deemed unsuitable for analysis.

In this event, symptom processing halted, and a set of preselected values was written into the symptom file (2).

Irregular Spikes

Irregular spikes were detected by comparing the widths and relative heights of peaks in the system peak table with the average widths and average relative heights of the calibration RTMs, $\langle W_r \rangle$ and $\langle H_r \rangle$ (brackets $\langle X_r \rangle$ denote an average operation). For computational efficiency (to rapidly screen up to 4000 peaks in the peak table), the peak widths that were used in this algorithm were base-to-base and were denoted as $w_r^*(i)$. By definition, spikes are very narrow peaks, thus $w_r^*(i) \approx wt_r(i)$. Relative peak heights were computed by using the peak height estimation algorithm previously described. The criterion for the detection of irregular spikes was as follows: If $w_r^*(i) \leq 0.125 \times \langle W_r \rangle$ and $h_r(i) \geq 0.2 \times \langle H_r \rangle$ for any peak i, then the binary symptom value is 1 ($V_{is} = 1$); otherwise, $V_{is} = 0$ (10).

No Peaks

Peaks from all samples except blanks were expected in the system peak table that was generated from chromatograms. If there were no entries in the system peak table for standard, calibration, or unknown chromatograms, the symptom value $V_{np} = 1$; otherwise, $V_{np} = 0$. If this symptom was detected, processing terminated, and a set of preselected values was written into the symptom file (2).

Ghost Peaks

Ghost peaks are peaks that appear when there should not be any peaks (e.g., peaks in the chromatogram of a blank sample). The ghost peak algorithm was used to scan the peak table to find any peaks that were detected in a blank sample. If peaks were detected, the binary value for this symptom was set to 1 ($V_{gp} = 1$).

Extra Peaks

Extra peaks occur when peaks that result from components of a previous sample appear in the chromatogram. They are distinguishable from normal peaks in that their widths tend to be much larger or much smaller than the widths of neighboring peaks. The algorithm used to detect ghost peaks was a least-median-squares procedure (11). A least-median-squares procedure is a modification of a least-squares procedure that reduces the disruptiveness of outliners in the data.

When temperature programming is used in GC, the peak widths in chromatograms tend to increase quadratically with retention time. Thus, the model that was used for the extra peak algorithm is a quadratic. To fit the observed changes in peak width, the quadratic should be concave upwards, centered at the origin, and greater than 0 at the origin. With a quadratic of the form $w(t) = at^2 + bt + c$, the preceding conditions result in the restrictions $a > 0$, $b = 0$, and $c > 0$. Two peaks were randomly selected from the system peak table and the base-to-base widths of the peaks were used to solve for the parameters (a,c) of the quadratic. If the criteria $a > 0$ and $c > 0$ were not met, two more peaks were randomly selected. Once acceptable parameters were found, the median of the squared difference between the quadratic and the peak widths was computed. This process was repeated 100 times, and the parameter set that minimized the difference (a^*,c^*) was retained. The standard deviation σ_{ep} between the quadratic $w_o(t_i) = a^* t_i^2 + c^*$ and the model peak widths for every peak, $w_r^*(t_i)$, was computed next. If the computed peak width was more than 4 standard deviations different than the actual peak width, $w^*_r(t_i) > w_o(t_i) + 4\sigma_{ep}$ or $w^*_r(t_i) < w_o(t_i) - 4\sigma_{ep}$ for any peak i, then the binary symptom value for extra peaks was set to 1 ($V_{ep} = 1$).

High Noise

The first 20 s of a chromatogram are generally devoid of peaks and can therefore be used to monitor detector noise. Noise in a chromatogram consists of two components: baseline drift and a random component superimposed on the baseline. A segment $x_f(n) = \{x(n) | 0 \leq n \leq n_f\}$ was extracted from the start of the chromatogram. The value n_f was selected so that $t(n_f) = \min[t_r(1)/2, T_f]$, where $t_r(1)$ is the location of the first detected peak, and $T_f = 10$ s. A linear regression was performed on $x_f(n)$, and the 95% confidence interval of the slope $b \pm \theta_b$ and error standard deviation s were computed. A noise estimate for the segment was computed as $N_0 = 3s$. These three values were compared to corresponding average values in the calibration data. If $N_0 > X\langle N_0 \rangle$ or $b - \theta_b > X\langle b - \theta_b \rangle$ or $b + \theta_b > X\langle b + \theta_b \rangle$, where $X = 3$ for average values greater than 0 or $X = 0.3$ for average values less than 0, then V_{hn} was set to 1. The threshold, X, was 3.0 when the average value was positive and 0.3 when the average value was negative to ensure that the product of the threshold and the average value was larger than the average value.

Rising Baseline

A rising baseline is detected if the amplitude of the tail of the baseline is substantially larger than the amplitude of the front of the baseline. In this algorithm, the average values of the front and tail sections of the chromatogram were used as baseline estimates. As in the high noise algorithm, a segment from the front end of the chromatogram was extracted: $x_f(n) = \{x(n) | 0 \leq n \leq n_f\}$, where n_f was previously selected. A segment from the tail end of the chromatogram was selected in a similar manner: $x_t(n) = \{x(n) | N - 1 - n_f \leq n \leq N - 1\}$, where N is the number of samples in the chromatogram. The average of the front section was denoted as $F = \langle x_f(n) \rangle$, and the average of the tail section was denoted as $T = \langle x_t(n) \rangle$. If $F > 0$ and $T > 3F$, or if $F \leq 0$ and $T > 0.3F$, then

$$X_{rb} = |T - F| \qquad \text{Eq 12}$$

Otherwise, $X_{rb} = 0$. The output value for the rising baseline symptom, V_{rb}, was found by mapping X_{rb} into a fuzzy value with $X_{ref} = 0$.

Irregular Baseline

A line was fit to the averaged spline baseline estimate, $b(n)$. The error standard deviation s of the linear regression was computed. If $s > T_{ib}$, where T_{ib} is a threshold, then $V_{ib} = 1$; otherwise, $V_{ib} = 0$. Threshold T_{ib} was three times the average error standard deviation of the same calculation performed on the calibration chromatograms.

Elevated Baseline

Elevated baseline is an indication of the amount of offset left on the autoscale system of the chromatographic instrument. The linear regression on the segment $x_f(n)$ was computed, and the upper confidence level of the intercept parameter, $X_{eb} = b + \theta_b$, was compared to the threshold T_{eb}. The threshold is the average upper confidence level of the calibration chromatograms $T_{eb} = (b + \theta_b)$. If $X_{eb} > 10T_{eb}$ for $T_{eb} > 0$ or if $X_{eb} > 0.1\ T_{eb}$ for $T_{eb} \leq 0$, then $V_{eb} = 1$; otherwise, $V_{eb} = 0$.

Peak Leading and Tailing

Several research groups have published algorithms for fitting and determining the parameters of exponentially modified Gaussian peaks and overlapping peaks (12). In this work, simpler algorithms were used because it is common for chromatograms from unknown samples to contain an undetermined number of overlapping peaks. Simpler algorithms were also used because a significant percentage of the peaks in a chromatogram did not exhibit Gaussian profiles. Estimating parameters of these peaks by using a Gaussian model would not have been appropriate. In this work, simpler algorithms worked well for providing the information needed.

Peak asymmetry (skew) was estimated by using Equation 1 and setting W_f to 10%. The leading time is defined as $A_i = t_r(i) - t_\alpha(i)$, the tailing time is $B_i = t_\beta(i) - t_r(i)$, and the asymmetry is $S_i = B_i/A_i$. Peaks with $S_i < 1$ are leading peaks, and peaks with $S_i > 1$ are tailing peaks. The value of tailing peaks was computed by averaging the skew values of all leading peaks, $X_{lp} = \langle S_i \rangle\ \forall\ S_i < 1$, and the tailing value is computed by averaging the skew of all tailing peaks, $X_{tp} = \langle S_i \rangle\ \forall\ S_i > 1$. Output values V_{lp} and V_{tp} for leading and tailing were determined by applying the fuzzy value mapping to X_{lp} and X_{tp} with $X_{ref} = 1$.

Retention Time Marker Shift

An RTM shift occurs when the retention times of the marker peaks differ from retention times in the calibration chromatograms. The average deviation of the locations of the RTMs $\hat{T}_r(i)$ in the chromatogram being evaluated from the expected retention time $T_r(i)$ was calculated with the following equation:

$$X_{rt} = \langle |T_r(i) - \hat{T}_r(i)| \rangle \qquad \text{Eq 13}$$

If the i^{th} retention time marker was not found, $T_r(i)$ was set to the largest allowable retention time shift of 15 s. The value for retention time shift V_{rt} was found by mapping X_{rt} into a fuzzy value by using $X_{ref} = 0$.

Band Broadening

Band broadening occurs when the full widths at half the height of peaks toward the tail end of a chromatogram are significantly greater than the full widths at half the height of peaks at the front end of the chromatogram. The value for band broadening was computed as

$$X_{bb} = |\hat{W}_r(N) - \hat{W}_r(1)| \qquad \text{Eq 14}$$

where $\hat{W}_r(N)$ is the width of the last RTM, and $\hat{W}_r(1)$ is the width of the first RTM. The lower threshold is the mean of the band-broadening values that are found from analysis of the calibration chromatograms. The upper threshold is the mean plus twice the standard deviation of the band-broadening values that are found in the calibration files. The output value V_{bb} was found by mapping X_{bb} into a fuzzy value with $X_{ref} = 0$.

Replicate Precision

Replicate precision and reproducibility is a measure of how closely a chromatogram matches a reference chromatogram. A

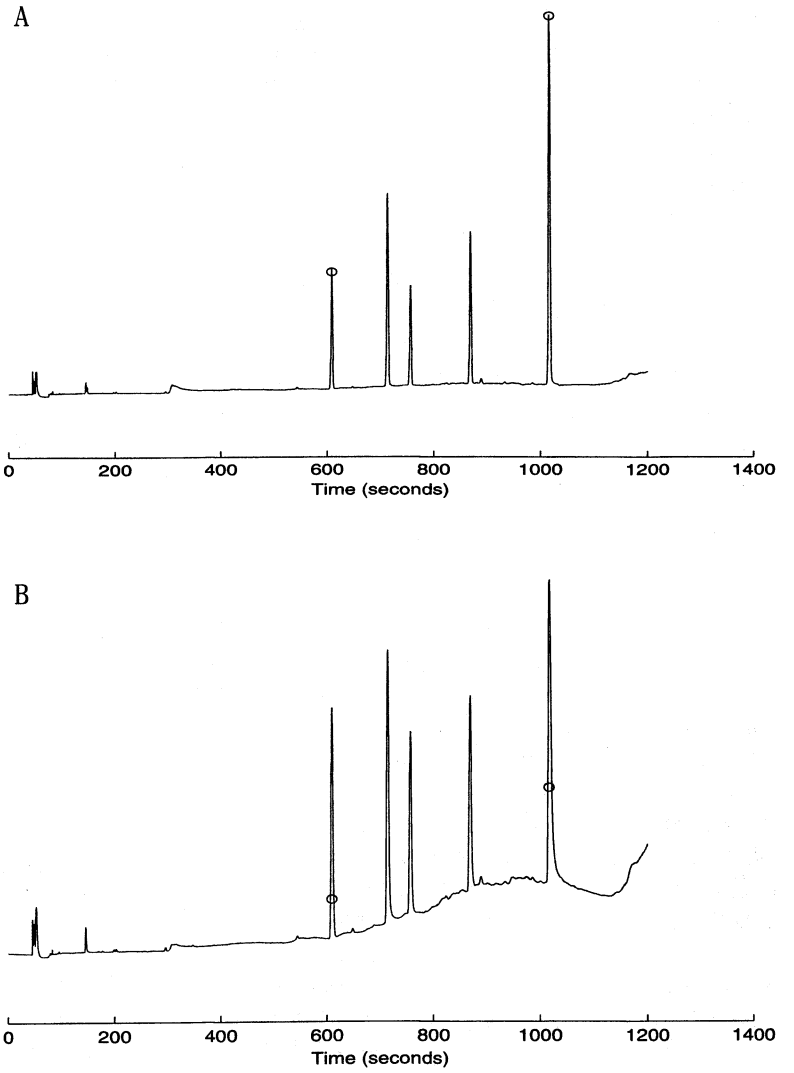

Figure 2. (A) A nominal chromatogram of the pesticide mixture. (B) A chromatogram of the pesticide mixture produced by an instrument with low makeup gas flow. The circles on the plots are the expected positions of the RTMs.

reference chromatogram was denoted as $x_r(n)$. The fractional change in total chromatogram area from $x_r(n)$ to $x(n)$ was computed in the following equation:

$$X_{rp} = \frac{\left| \sum_n x(n) - \sum_n x_r(n) \right|}{\sum_n x_r(n)} \quad \text{Eq 15}$$

The output value V_{rp} was found by mapping X_{rp} into a fuzzy value with $X_{ref} = 0$.

Sensitivity Change

The total sensitivity change was found by averaging the sensitivity change over all retention time peaks. The sensitivity change for the i^{th} retention time marker was

$$S(i) = \frac{\left| \hat{A}_r(i) - A_r(i) \right|}{A_r(i)} \quad \text{Eq 16}$$

The average sensitivity change was $X_{sc} = \langle S(i) \rangle$. If the i^{th} retention time marker was not found, the area was set to $\hat{A}_r(i) = 4\langle A_r(i) \rangle$, which maximized the output value of this symptom. The output value for sensitivity change, V_{sc}, was found by mapping X_{sc} into a fuzzy value with $X_{ref} = 0$.

Table II. Symptom Files for the Chromatograms in Figure 2B

Sample information	
Sample name	N/A
Sample i.d.	0
Sample type	Calibration
File information	
File source	GCProcCalibration v2.1
Retention time file name	MU_FL_D.RTM
Induced cause	
Induced cause	Makeup gas loss
Severity	1000.0
Symptoms	
Clipped peaks	0.000
No peaks	0.000
Rising baseline	1.000
Irregular baseline	1.00
Elevated baseline	0.000
Tailing peaks	0.000
Leading peaks	0.180
Unresolved peaks	0.000
Ghost peaks	–2.000
Extra peaks	1.000
Negative dip after peak	–2.000
Irregular spikes	0.000
Sensitivity change	1.000
Retention time shift	0.520
Band broadening	1.000
Spike precision	–2.000
Surrogate precision	–2.000
Replicate precision	1.000
High noise	1.000
High background	–2.000

The value –2.000 indicates that the algorithm for this symptom was not executed and no value is available.

Unresolved Peaks

The efficiency of a chromatographic system is expressed in terms of its resolution. The resolution, R_s, is defined by the separation of two peaks. Assuming the peaks are Gaussian, the resolution for the i^{th} peak can be expressed as

$$R_s(i) = 1.18 \frac{t_r(i+1) - t_r(i)}{w_r(i+1) - w_r(i)} \quad \text{Eq 17}$$

where $t_r(i)$ and $t_r(i + 1)$ are the retention times of two adjacent peaks, and $w_r(i)$ and $w_r(i + 1)$ are the corresponding widths at half the height of the peaks (13). Resolution was computed for all peak pairs in the chromatogram from a standard sample. The minimum resolution value between two peak pairs was considered to be the measure of unresolved peaks

$$X_{up} = \min[R_s(i)] \quad \forall i \quad \text{Eq 18}$$

The output value V_{up} was found by mapping X_{up} into a fuzzy value with $T_{min} = 0.5R_{min}$ and $T_{max} = R_{min}$, where R_{min} is the minimum resolution between peak pairs in the calibration data.

Results and Discussion

The algorithms were developed iteratively, in consultation with experienced chromatographers. Each algorithm was individually tested and validated qualitatively by comparing the algorithm output with the opinions of the experienced chromatographers. Agreement between the experienced scientists and the detection of the symptom with use of the algorithm was considered validation. Figure 2 illustrates a standard chromatogram of the five pesticides and a chromatogram of the same sample that was generated with a low makeup gas flow. Table II contains the output of the symptom detection algorithms applied to the bottom chromatogram in Figure 2 (a value of –2 in Table II indicates that the chromatogram was not processed with the corresponding algorithm).

The symptom detection algorithms were developed as part of an automated analysis assessment system described in Figure 1. The symptom detection algorithms were further refined and validated as they were integrated with the expert system. Chromatograms that were generated from instruments with induced faults were processed by the analysis assessment system. Successful tests of the analysis assessment system occurred when the system diagnosed the fault that was induced in the instrument when the chromatogram was generated. When there was a discrepancy between the system diagnosis and the known instrument fault, the diagnosis of the expert system was evaluated by chromatography experts, and the symptom detection algorithms or the expert system knowledge was modified. Algorithm modifications included revising

algorithms or adjusting threshold limits, and expert system modifications included revising the knowledge table and the knowledge processing.

A detailed discussion of the expert system that was used in the fault diagnosis system appears elsewhere (5). After extensive refinement of the expert system knowledge base, the induced fault in 95% of the faulty data presented to the analysis assessment system was correctly identified by using the system.

The analysis assessment system is currently being installed in an automated environmental testing laboratory (14). The expert system is being refined and tested on a broader range of instrument faults (15). Ongoing work includes development of algorithms for rounded peaks as well as spike and surrogate precision. An alternative RTM algorithm is being developed to trend changes in the marker retention time in each file run through the system. Relative trending will be pursued as a compliment to the existing algorithm that is used to monitor absolute deviation in retention time from the calibration files.

Conclusion

Algorithms have been written for use in recognizing features in chromatograms that correspond to symptoms of instrument faults. These symptoms are used by experienced chromatographers to diagnose the cause of an analysis failure. The feature extraction algorithms are required to provide input for an expert system-based automated analysis assessment system that uses the detected symptoms to diagnose the underlying fault. This expert system captures the heuristic troubleshooting knowledge from the experts in the form of "if x and y, then z" rules that express the relationship between symptoms and faults. These algorithms are used to provide the input antecedents in the rules and are processed through the knowledge base by the inference engine.

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