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New operational modes for multidimensional and comprehensive gas chromatography by using cryogenic modulation

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Abstract

Historically, hardware and method-related concerns have limited the use of multidimensional gas chromatography in the routine laboratory. This paper presents a new approach that offers the potential to significantly alter the manner in which multidimensional gas chromatography is conducted, based on the use of a modulated cryogenic trap which can be moved longitudinally along the column. Two columns are directly coupled, and no switching valves are used. It is demonstrated that a heartcut section can be cryofocused and zone-compressed, and then rapidly remobilized at the prevailing column oven temperature without any supplementary heating. A short second dimension column is used, giving fast second dimension analysis. This allows a large number of heartcuts to be programmed for any one analysis. The 'ultimate' manifestation of multidimensional gas chromatography is the comprehensive GC technique (GC×GC). This is now simply effected by performing very rapid heartcuts at intervals on the order of 1/5th of the peak width of primary dimension peaks, and requires that the second dimension be able to complete the analysis of each collected zone on a similar timeframe. This paper uses a semi-volatile aromatic mixture to demonstrate these selected operational modes, that can be achieved with the longitudinal modulation method. The flexibility that arises from this approach is shown by the ability to swap between selected whole-peak enhancement and comprehensive modes during the one analytical run. The increased sensitivity that follows from peak compression is a further advantage, which would be beneficial for trace analysis.

Keywords: Gas chromatography; Cryogenic trapping; Coupled columns; Hydrocarbons, aromatic

1. Introduction

Single-column gas chromatography analysis has become the standard approach for measurement of volatile and semi-volatile constituents in numerous applications. However this does not necessarily provide the best analytical result in terms of unique identification of components of the sample. In many analyses there is considerable opportunity for peak overlaps, both on a statistical basis of random separation of peaks [1–3] and also on the basis of observed separations achieved for real samples. The single dimension provides a specific mechanism for separation, and can be a combination of boiling point, polarity and/or specific solute–phase interactions depending upon the chemical construction of the stationary phase.

In order to expand the analytical separation space,

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chromatographers have developed a range of multidimensional solutions based on more than one separation dimension. These may be collectively termed multidimensional gas chromatography (MDGC), and a sample can now be subjected to multiple separation mechanisms. Whilst these approaches have been known for many years, and have been shown in research studies to provide much better separation for selected target peak overlaps, they are rarely used in the routine chromatography environment, presumably because of the perceived complexity in setting up the MDGC experiment. Cortes [4] has presented a comprehensive discussion of conventional MDGC technology. A selection of these traditional methods is presented in Fig. 1 as an outline of the range of approaches used. In Fig. 1a the heartcut valve is switched to pass the selected zone to column 2 for further separation. By placing a

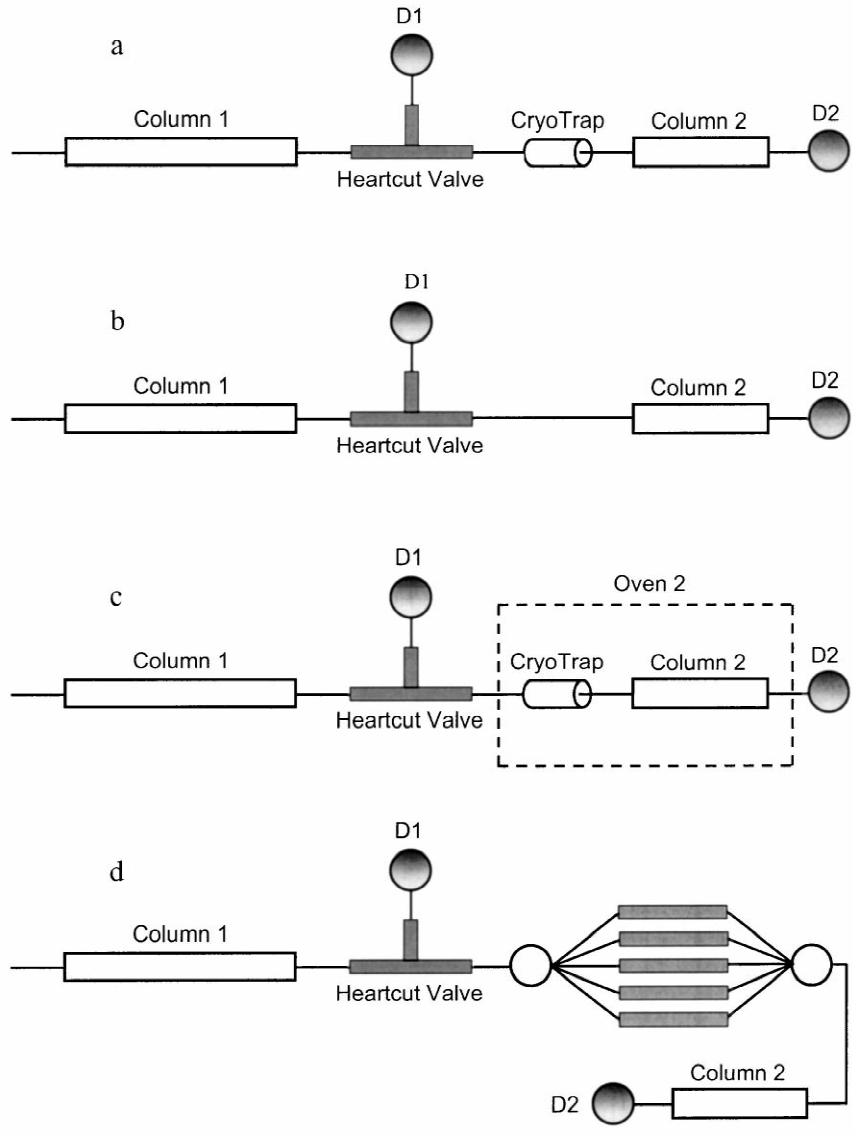

Fig. 1. (a–d) Illustration of different possible multidimensional gas chromatography designs incorporating heartcut valves, multiple detectors, multiple columns, dual ovens and cryogenic traps (see text).

cryogenic trap at the start of column 2, the heartcut zone can be compressed so that the introduced band is of minimum dispersion and resolution of components on column 2 is not biased by peak broadening on column 1. Trapped components may be analyzed on column 2 by cooling down the oven, turning off the cryo-fluid then temperature programming the oven to elute the heartcut peaks. Alternatively the cryotrap may comprise some mechanism that allows it to be rapidly heated up (usually electrically) to flush components out to column 2. If column 2 selectivity is poorer than that of column 1 for the collected band of solutes, then the multidimensional approach will give an inferior result. By omitting the cryotrap, Fig. 1b shows that the heartcut zone is not compressed, but merely travels along column 2. If peaks swap positions on the two columns, then this process may lead to inferior separation than that given on just the first column. The dual oven system of Fig. 1c allows independent heating of the two columns. This can further enhance separation by optimization of retention factors, although for a particular zone of peaks, their boiling point similarity will make this approach of limited scope. The cryotrap can be used in a manner as outlined above for Fig. 1a. The much more complex arrangement of Fig. 1d, based on that promoted by Wilkins [5], describes a multi-trap unit that could isolate (continuous) segments of the first GC column elution. By providing a heartcut valve it would be possible to reject some regions from being passed to column 2.

Orthogonality is maximized by having two columns of different retention mechanisms. Clearly any GC column has a boiling point contribution to its retention property, but it will be subtle differences in the two columns' retention mechanisms (such as polarity or shape selectivity) that determine the ability to resolve components. Whilst also a coupled column method, the pressure tuning method — also called multichromatography [6] — subjects the whole sample to the sequential columns but it does not isolate selected peak zones for enhanced separation, and so the specific advantages of MDGC are not available.

MDGC would appear to have value in improving peak separation, but is of limited utility due to factors such as being more complicated than single column analysis (due to calibration, the need to balance flows, the need to carefully select heartcut zones, the need to couple columns) and also the perceived problems of arranging columns properly in the switching valve(s). Also, the MDGC method can only effectively be applied to a small number of regions of the chromatogram. In this sense it is only a targeted analysis applicable to specific problem zones of a chromatogram. Each analysis will require careful interpretation and event time selection. The two key components of MDGC are the heartcut mechanism, and the cryotrap and subsequent remobilization method. Pressure balanced systems (the Deans switch) [7] use pressure variation to sweep effluent either to D1 or to column 2. Other systems have a closure in the D1 line that causes column 1 effluent to divert to column 2. A separate carrier flow to column 2 must be provided. A further recently described device (termed moving-column stream switching) involves pushing column 2 into a position such that column 1 effluent now preferentially passes to column 2 instead of to D1 [8].

Comprehensive GC (GC×GC) expands the MDGC method into a generally usable format that does not rely on targeting specific zones of a first dimension analysis. Bushey and Jorgensen [9] defined the conceptual framework for continuous coupled column comprehensive chromatography where rapid analysis on a second column provides repeating analysis for the first column effluent. In this way, the column 1 effluent is completely subjected to two-dimensional study, and it now only becomes a question of technical implementation of the experiment. The schematic diagram representing this is shown in Fig. 2. The modulator can be any mechanism that delivers the performance required according to Jorgensen's requirements of a comprehensive system. In GC, Phillips and coworkers [10–13] developed the rotating thermal modulator or sweeper system, located at a thick film 'accumulator' column which can zone compress and pulse peaks to the second column. This has been shown to be useful through applications directed to the petroleum analysis area [12,14–16].

A second approach introduced by the present authors uses a cryogenic trap that moves longitudinally along the column [17,18]. There is no need to have the extra column between the two coupled

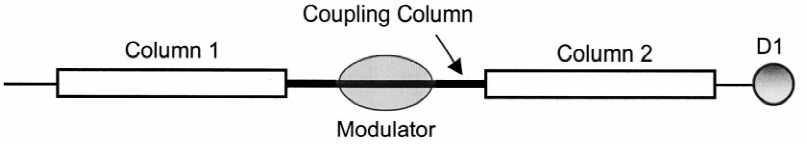

Fig. 2. Typical experimental design of a comprehensive chromatography system incorporating a first dimension column, modulator device with coupling column, second dimension column and detector.

columns, and so only a simple direct joining of the two dimensions can be used. Whilst this device has been described in a selected range of applications, from an injection aid, to studying phase bleed [19], enhancing detection sensitivity [20], and also for comprehensive gas chromatography [21–23], the present paper demonstrates the flexibility of the cryogenic system to provide a range of different modes of operation during capillary gas chromatography.

2. Experimental

2.1. Instrumental parameters

A HP6890 gas chromatograph (Hewlett-Packard, Wilmington, DE, USA) was used throughout this study fitted with a split/splitless injector, flame ionization detection (FID) system and a 6890 series automatic liquid sampler. The injector was operated in the split mode (40 ml/min; 40:1 split ratio) at 280°C, and the FID system was operated at 325°C at an acquisition rate of 100 Hz with a 50 ml/min N_2 makeup gas. For the semi-volatile analysis, an oven temperature program of 40°C (1 min hold), 1°C/min to 250°C was used. Helium (99.996% pure) was used as the carrier gas, and the constant flow mode EPC option was chosen, although constant flow control is affected by coupling two columns of different internal diameters.

2.2. Multidimensional/comprehensive chromatography parameters

A longitudinally modulated cryogenic system (LMCS) as previously reported [18] was used to achieve the multidimensional and comprehensive chromatography modes. A modulation frequency of 0.16 Hz (1 complete modulation every 6 s) was used in the comprehensive procedure, with a rest time of 1 s in the remobilize position for the cryogenic trap. This timing procedure can be simply defined by the nomenclature '[6,1]'. The first dimension was a 30 m×0.25 mm I.D., 1.0 μm d_f BPX5 phase column (SGE International, Ringwood, Australia) and was operated at an initial head pressure of 13.0 p.s.i. (40°C); the second dimension consisted of BPX50 phase column of dimensions 80 cm×0.10 mm I.D., 0.10 μm d_f (SGE International) which resulted in an equilibrium pressure at the junction of the two columns of 6.4 p.s.i. (40°C) (1 p.s.i.=6894.76 Pa). This gave first and second dimension column average linear carrier gas velocities of 15 and 84 cm/s, respectively. Liquid CO_2 is provided to the cryogenic trap, where it expands and cools the trap. A pneumatic device moves the trap back and forth along the column which is located through the center of the trap. Further operational details may be found elsewhere [17,18,21].

2.3. Standards

A semi-volatile aromatic mix (part no., SVM-124-1) from Ultra Scientific (North Kingstown, RI, USA) was used throughout this study and was diluted as necessary in pesticide grade methylene chloride. *n*-C_{14}, *n*-C_{16} and *n*-C_{18} alkanes were added to this mixture for some analyses.

3. Results and discussion

3.1. Semi-volatile analysis using conventional capillary gas chromatography

Fig. 3 is a typical GC trace of a semi-volatile aromatic sample, with added alkanes. Table 1 lists the components of the mixture. It is acknowledged that the retention time of this analysis is long. With

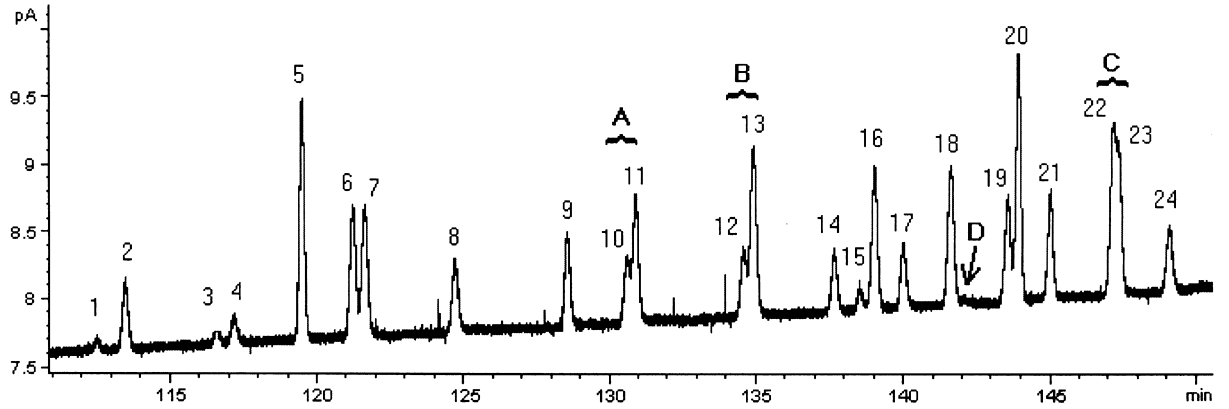

Fig. 3. Chromatogram of several semi-volatile aromatic compounds with co-injected *n*-alkanes, ranging in polarity and boiling point. Refer to Table 1 for peak identification. Refer to the text for discussion relating to the poorly resolved peak pairs A, B and C, and the almost indistinguishable peak D.

the current interest in fast GC methods, one may question why such a long retention is used in the present study (and as are often used in GC×GC work). Simply, the GC×GC method relies on multiple second dimension analyses for each first dimension peak. If we intend to use a second dimension separation time of up to 4–5 s on the second column, then first dimension peaks must be about 20–30 s in base width. Optimization of the second column to achieve total elution times of <2 s may be more acceptable, allowing the first column to be operated with faster elution conditions.

Table 1
Identification[a] of semi-volatile compounds

1. Hexachlorocyclopentadiene	2. Tetrachlorobenzene
3. 2,4,5-Trichlorophenol	4. 2,4,6-Trichlorophenol
5. Tetradecane[b]	6. 1-Chloronaphthalene
7. 2-Chloronaphthalene	8. 2-Nitroaniline
9. Dimethylphthalate	10. 2,4-Dinitrotoluene
11. Acenaphthylene	12. 3-Nitroaniline
13. Acenaphthene	14. Pentachlorobenzene
15. 4-Nitrophenol	16. Dibenzofuran
17. 1-Naphthylamine	18. Tetrachlorophenol
19. 2-Naphthylamine	20. Hexadecane[b]
21. Diethylphthalate	22. Fluorene
23. 4-Chlorophenyl phenyl ether	24. 4-Nitroaniline

[a] Compounds are listed in order of elution under the conditions used. Some identifications are tentative, since authentic individual components were not available in all cases. Some active compounds in the mixture are not eluted on this set of columns.

[b] Alkanes were added to the sample to provide comparative results for these non-polar analytes.

Under the analysis conditions used several co-eluting compounds are observed. Two peaks labeled A and B in Fig. 1 have resolutions (R_s) of 0.95 and 1.16, respectively, and one pair labeled C with a R_s of 0.41. A minor component marked D on the GC trace is also observed partially overlapping another peak, and the spiked hexadecane now overlaps 2-naphthylamine. Signal-to-noise ratios are rather poor in this example, due to the low on-column concentration and wide base widths of the order of 25–30 s. The largest peaks (C_{14} and C_{16} *n*-alkanes) have a signal-to-noise ratio of 21:1, and peak heights range from 0.1 to 1.8 pA with solute D almost indistinguishable at 0.03 pA.

3.2. Longitudinal modulation GC result — comprehensive gas chromatography

Longitudinal modulation permits regular pulsing of collected segments of peaks into the second dimension column. This zone compression leads to enhanced peak height response. Co-eluting bands at the end of the first column can potentially be separated on the second column, according to considerations and criteria expressed in the Introduction. Fig. 4 is the time–response result for modulated peaks of the semi-volatile mixture. The individual peaks can be easily recognized by comparison with Fig. 3. A pure peak has a sequence of pulsed responses which occur at precisely defined positions after each modulation event. Where components

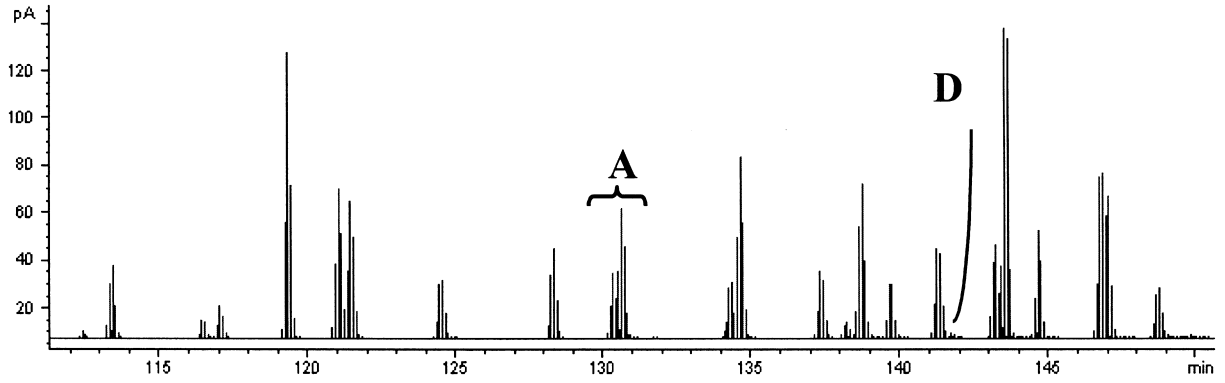

Fig. 4. Comprehensive chromatogram of the same semi-volatiles sample shown in Fig. 3 using the LMCS with a [6,1] timing modulation. This represents the detector time–response data that is generated with the LMCS in the comprehensive mode before transformation into the two-dimensional data array. Sections labeled A and D are the same regions so denoted on Fig. 3.

overlap, we are specifically looking for the pulsed response to show two (or more) peaks for each modulation such as the overlapping pair labeled A. These co-eluting analytes have a pre-modulation first dimension resolution of 0.95 (Fig. 3), and after they have been zone compressed and modulated (Fig. 4)

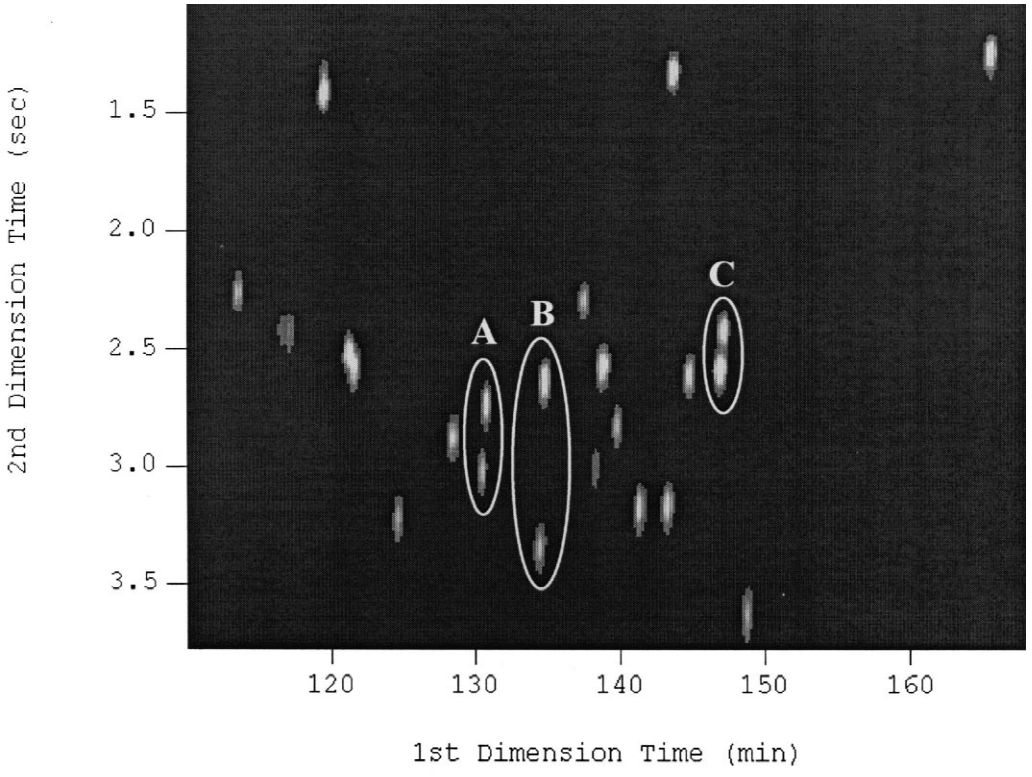

Fig. 5. Comprehensive gas chromatography contour plot of the semi-volatile components. Peak pairs A, B and C are now essentially completely resolved in the comprehensive mode. Note: the first dimension time scale in this representation has been extended to also include the n-C_{18} normal alkane (top right).

their second dimension resolution is now 1.6 (see below).

Additionally, Fig. 4 demonstrates the significantly enhanced peak responses with larger peak heights of the order of 80 pA. C_{16} peak response for the maximum pulse is 140 pA compared with 1.8 pA in Fig. 3. A series of pulses can also be seen for the peak marked D in Fig. 3, demonstrating the sensitivity improvement that is gained when a zone compression technique is used.

These time–response data can be transformed into the three-dimensional result shown in Fig. 5. Each peak is now a contour peak shape, with definable width in both first and second time dimensions. On the polar second column alkanes elute rapidly, and have ^2t_R (retention times in the second dimension, measured after the movement of the trap) values of <1.5 s. All other solutes show greater retention, with nitroanilines as a class most strongly retained with ^2t_R of approximately 3.5 s for 4-nitroaniline. This result suggests we need not have a [6,1] modulation frequency, and [4,1] would have been adequate since we know that nothing elutes later than 4 s on the second dimension column. Peaks marked A and B were the overlapping pairs of peaks marked A and B in Fig. 3. These are now completely resolved and the

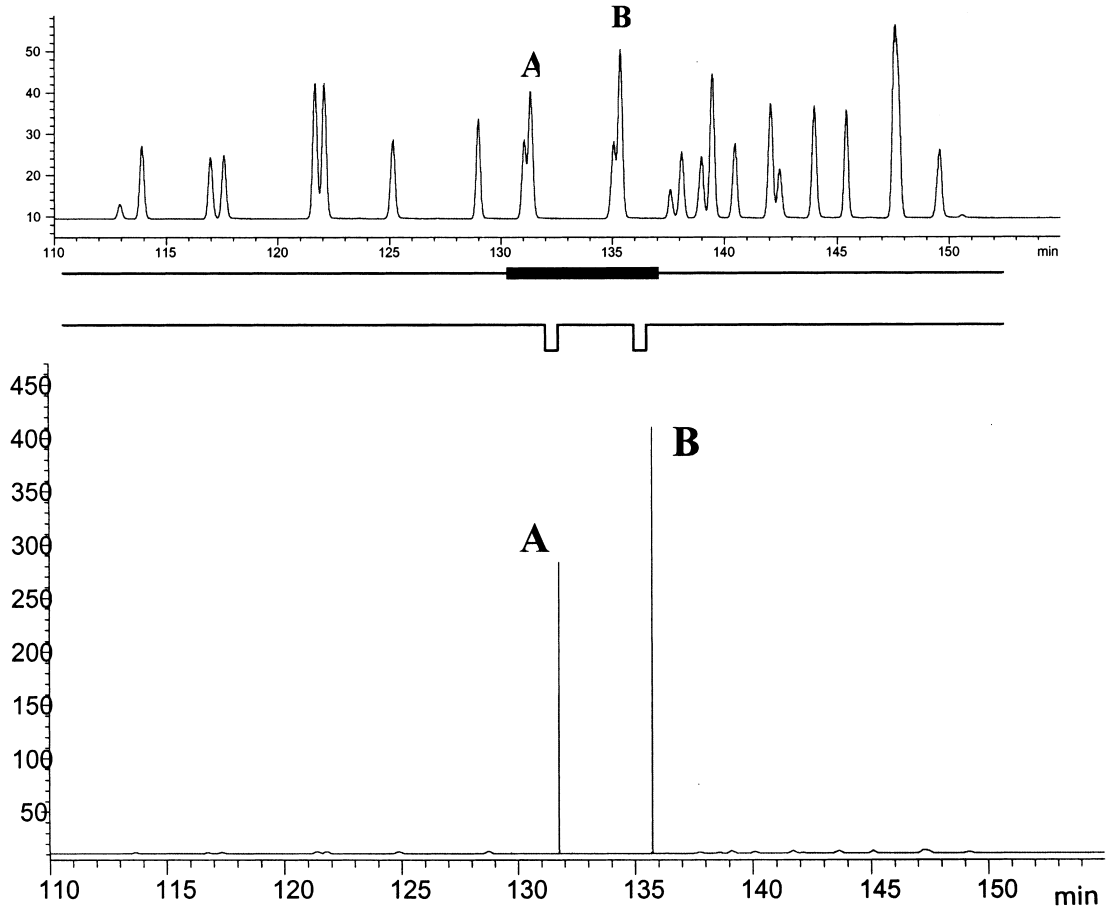

Fig. 6. Upper chromatogram: normal GC trace of semi-volatile components (without any alkanes present). Central lines: upper line shows the time that the cryofluid is supplied to the trap (given as a heavy line); lower line indicates when the trap is moved to permit collected solute to be pulsed to the second column. Lower chromatogram: result of the selected cryotrapping of peak pairs A and B by time programming the LMCS to cryogenically focus and elute peaks at pre-determined elution times from the first dimension column. Careful inspection shows the presence of the normal GC non-enhanced peaks along the baseline of this chromatogram.

poorly separated peaks C in Fig. 3 can now be observed as separated contour peaks in Fig. 5. Whilst expressions defining the extent of resolution of neighbouring peaks in the GC×GC experiment do not appear to be widely used (and will formally require peak dispersions in each dimension), an approximate value of R_s~1.3 may be appropriate here for these two latter solutes.

3.3. Selected peak enhancement — an analogue to conventional multidimensional analysis

We have previously shown [19] that we can separately trap individual compounds and pulse them to a detector using a single column set-up. In that study, separation on the short length of column between trap and detector was not considered. Here the aim is to show that using a second column of different phase permits multiple component trapping with their subsequent complete separation on the short second column.

Repeating the above sample injection with CO_2 supplied to the trap for the period from about 129 to 135 min allows peaks marked A and B in Fig. 3 to be selectively trapped and each pair pulsed to the second column. All other solutes pass unhindered through the modulation trap when no CO_2 is supplied, and so each of these solutes eluted from the first column will not be enhanced. Fig. 6 shows how this experiment in conducted. The upper — normal GC — trace shows an injection of a more concentrated sample of semivolatiles (no added alkanes). The 'CO_2 on' time is shown by the heavy line, from about 130 to 137 min, and modulation events are marked as pulses. The LMCS result is compared on the lower trace. The concentration of the latter sample was reduced, since the non-modulated peaks (only just visible on the lower trace) have smaller heights than their respective heights in the upper trace.

The modulated pairs, marked A and B, appear as single responses, however each consists of two resolved peaks. By selecting and expanding the time axis for the peaks marked B, we see the result in Fig. 7. Acenaphthene and 3-nitroaniline now have swapped retention orders compared with their first dimension elution. Peak maximum retentions differ by 0.012 min = 0.72 s, which is consistent with their two

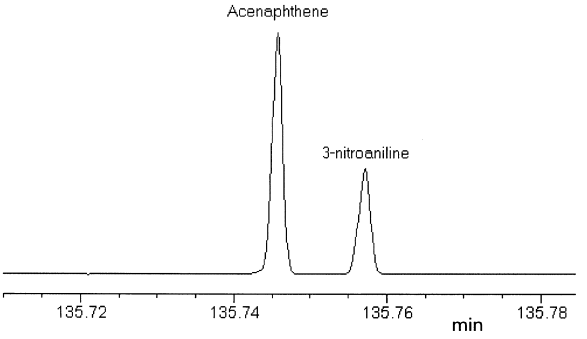

Fig. 7. Expanded region of peaks marked B from Fig. 6 indicating the resolution achieved between these two peaks on the second dimension column. The narrow focused band produced by the cryotrap, the rapid remobilization, and the phase selectivity allows their separation on the short (80 cm) column.

respective peaks in Fig. 5, and thus improving the resolution from 1.16 in the normal GC mode to 3.75 for the trapped peaks pulsed to column 2. Since all of each peak is fully collected into one modulation event, the heights of these peaks are even more greatly enhanced and on the basis of peak widths (200 ms vs. 30 s), a sensitivity increase of 150-fold is obtained. This result has implications for improved performance of MDGC by using the cryogenic modulator. Conventional MDGC may be carried out in a number of ways, and conventionally involved a heartcut operation to pass a poorly resolved section from one column to a second column by means of an appropriate switching procedure [24]. The second column normally has a cryogenic trap positioned at the start to refocus the chromatographic bands. This is not an absolute requirement, but does have advantages [25]. To analyze the selected heartcut(s) on the second column, the oven is usually cooled (if temperature programming is used), the cryogen switched off, and then the oven heated up again. The result in Fig. 7 demonstrates that a heartcut event with cryotrapping can now be followed by rapid 're-injection' on the second column at the prevailing oven temperature, and every heartcut set of peaks can be treated similarly. Indeed, with the experimental set-up illustrated here, if only a few selected solutes are of interest, a separate heartcut valve is not required. It is only necessary to temporally separate the undesired components from the target components in different modulation events. This has con-

siderable ramifications for many MDGC applications.

3.4. Multi-modal chromatography by using LMCS

Section 3.3 presented a limited demonstration of the capability of LMCS to be used in different modes, and provide different types of data. In that example, in the single run both regular GC and whole-of-peak zone compressed enhanced chromatographic peaks, with subsequent separation were achieved. Clearly, if a region of a chromatogram consisted of such complexity that the collection and enhancement process described above was not able to separate all peaks, then it is possible to introduce the rapid modulation GC×GC mode for that section of the chromatogram which requires this improved separation process. We have recently proposed that the cryogenic modulation system may be flexible enough to switch between such modes during an analysis [18]. Fig. 8 is an example where in this one chromatogram three modes of operation are conducted — normal, selective whole peak enhancement, and comprehensive modes. Hence, we can

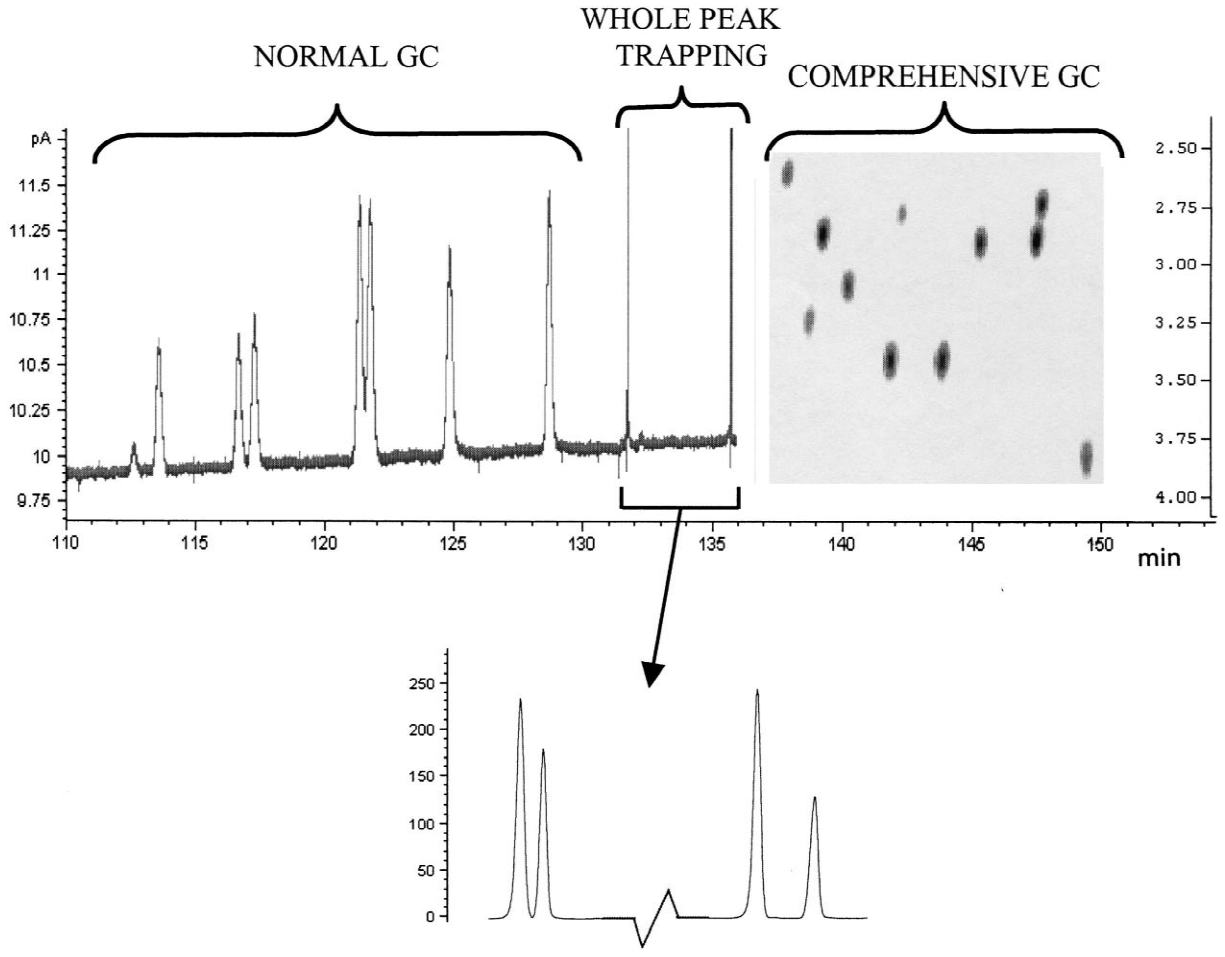

Fig. 8. Demonstration of multi-mode chromatography which incorporates normal GC, selective whole-of-peak enhancement and comprehensive GC×GC modes in the one gas chromatographic analysis. The latter two modes are achieved by use of the LMCS device. Cryofluid is not provided to the trap during the normal GC section. An expanded section of the pairs of peaks obtained in whole-of-peak trapping is provided. Note their peak heights compared with those of the normal GC peaks. The right hand scale is the second dimension retention times of the GC×GC portion of the analysis.

refer to this as multi-modal chromatography. Once the peak group B on Fig. 6 are eluted, the modulator can then be operated at [6,1] timing frequency to give the comprehensive result. Data produced in this final part of the chromatogram would be transformed into the three-dimensional presentation format, and whilst this is done manually here, there is no reason why a fully automated sequence cannot be developed. Thus if there is no particular need to operate the cryogenic system in the comprehensive mode throughout the analysis, but if the selective mode and its better sensitivity is more suited, then that mode may be implemented as required.

4. Conclusions

This paper has applied the LMCS in a number of new modes. In particular, it illustrates that by choosing when to introduce the cryogenic coolant and operating the modulation device in a variety of ways, different presentations of chromatographic data are possible. The potential of the LMCS to provide comprehensive GC expands the separation space for the semi-volatile solute sample chosen for this present study, and permits both improved separation of previously poorly resolved components and significantly also gives superior detection sensitivity. Since one component, apparently only just observable in the normal GC mode, can subsequently give much larger peak heights and would allow it to be quantified, then clearly the LMCS has considerable relevance in providing greater analytical performance in many applications, especially where extracted solutes may be near to detection limits. Further ways of using the LMCS to generate new capabilities in gas chromatography are immediately recognized, and such ways make some commercial heart-cutting procedures redundant. Further demonstration of these will be reported in subsequent communications.

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