PAPER

Check for updates

Strategies towards simpler configuration and higher peak capacity with comprehensive multidimensional gas chromatography†

Pannipa Janta,[a] Duangkamol Pinyo,[b] Yamonporn Yodta,[b] Porames Vasasiri,[b] Meinolf Weidenbach,[c] Matthias Pursch,[d] Xiuhan (Grace) Yang [iD] *[e] and Chadin Kulsing [iD] *[af]

Experimental and data analysis approaches in multidimensional gas chromatography (MDGC) comprising comprehensive multiple heart-cut (H/C) and comprehensive two dimensional GC (GC × GC) were developed with an example application illustrated for analysis of a technical glycol precursor sample. The GC × GC system employed a long ^{1}D (30 m) and a short ^{2}D (5 m) column with a flow modulator and a Deans switch (DS) as a splitter; meanwhile. The H/C system was applied solely as a DS located between long ^{1}D (30 m) and ^{2}D (60 m) columns without use of cryogenic trapping devices. The effects of injection time and ^{2}D column flow in GC × GC and the impacts of H/C window and number of injections (total analysis time) in H/C analysis were investigated. The analysis performance for each condition was evaluated according to peak capacity and number of separated compounds. The continuum between the two techniques was then established *via* the relationship between analysis time and analysis performance. The separation performances were improved with longer analysis time so that the suitable condition was selected within this compromise. Under the selected conditions, volatile compounds in the technical glycol precursor sample were identified according to the match between the experimental MS spectra and first dimensional retention indices (^1I) with that from the NIST2014 database and literature. An hour analysis with GC × GC resulted in a total peak capacity of 798, number of separated peaks of 61 and average MS match score of 887 ± 35; meanwhile, the corresponding numbers were improved to be 9198, 107 and 898 ± 24, respectively, with the 25 h comprehensive H/C analysis.

1 Introduction

Multidimensional gas chromatography (MDGC) is a high performance separation technique with enhanced peak capacity which has been reported for analysis of 'complex' samples such as petroleum, food, beverages, pharmaceutical and illicit drugs, and the environment.[1–4] Hyphenation with mass spectrometry

provides individual molecular-based information of volatile analytes enabling high confidence identification of several hundred compounds within a single analysis.[1–3,5,6] In general, MDGC employs two columns with different (ideally orthogonal) selectivities[7] which are connected sequentially *via* a device offering an effective heart-cut (H/C) or modulation process.[8,9] Compared with one dimensional (1D) GC, MDGC provides improved separation resolution and analyte peak capacity, reduced chemical background and improved detection limit. Due to the capability to analyse complex sample, sample clean-up steps such as liquid or solid phase extraction can also be reduced or eliminated avoiding the problem of sample loss during sample preparation which is important especially when sample amount is limited.[5]

Comprehensive H/C MDGC and comprehensive 2DGC (GC × GC) can be classified as a subclass of MDGC and are especially useful for untargeted analysis.[10] In these approaches, a sequential sampling strategy is applied which progressively shifts the H/C or modulation over the whole sample zone obtained from ^{1}D prior to ^{2}D separation.[3,10] The full comprehensive technique is conventionally performed using a single

[a]Department of Chemistry, Faculty of Science, Chulalongkorn University, Bangkok 10330, Thailand. E-mail: ckulsing@gmail.com; Tel: +66 802971178

[b]The Center for Advanced Analytical Technology, Dow Chemical Thailand Ltd, Map Ta Phut Industrial Estate, Rayong 21150, Thailand

[c]Polyurethanes Tech Center, Dow Deutschland Anlagen GmbH, 21677 Stade, Germany

[d]Analytical Science, Dow Deutschland Anlagen GmbH, 21677 Stade, Germany

[e]Dow Chemical China Investment Company, Shanghai 201203, China. E-mail: gxyang@dow.com; Tel: +86 2138513112

[f]Chromatographic Separation and Flavor Chemistry Research Unit and Center of Molecular Sensory Science, Department of Chemistry, Faculty of Science, Chulalongkorn University, Bangkok 10330, Thailand

injection and it is well known as GC × GC. Multiple injections and multiple H/C strategies are also applied in order to increase separation performance by use of a longer ^{2}D column which is called comprehensive H/C MDGC. With the expense of longer analysis time in the comprehensive H/C, the theoretical number of separated compounds (in a mixture of 681 model compounds with different functionalities) under the optimized conditions can be improved to be ~2 times greater than that obtained with GC × GC.[3] A compromise between time and separation performance should thus be made in each analysis. Whilst GC × GC approaches are well developed and applied, comprehensive H/C analysis has not been widely applied due to the complicated experimental setup, *e.g.* use of both a Deans switch (DS) and a cryogenic trapping device (or cryogenic modulator), of these approaches and the difficulty in data processing.[11–13] The cryogenic effect allows analyte pulse trapping with the subsequent release onto a ^{2}D column with a narrow band of the pulse enhancing ^{2}D separation. However, cryogenic approach involves additional devices, such as trapping channel and switching valve for automated on/off operation, cryogen consumption and system maintenance. In order to transfer a narrow H/C band without cryogenic device, H/C window should be significantly narrower than ^{2}D separation time.[14] To this end, simulation approach showing the compromise between separation time (H/C window) and analysis performance (number of separated peaks) has been proposed providing high peak capacity analysis of the petrochemical sample within a reasonable analysis time. However, experimental investigation of the concept as well as approach to generate a contour plot has not been reported. In addition, investigation on its advantages over the conventional GC × GC and further application of this technique are still a challenge.

In this study, cryogenic free approaches in compressive H/C techniques using a DS without a cryogenic device were developed and compared with the conventional GC × GC approach with flow modulation for analysis of a technical glycol precursor sample. The continuum between the two techniques was experimentally investigated in detail. Useful data presentation method was proposed. Effects of experimental conditions were then investigated. The selected comprehensive H/C and GC × GC results were evaluated, compared and discussed in terms of peak capacity and number of separated compounds. Relationship between the analysis time and separation performance was also established. The profile of volatiles in the technical glycol precursor sample was also reported.

2 Materials and chemicals

The authentic standard compounds were purchased from Merck (Darmstadt, Germany); Alfa Aesar, TCI and Sigma-Aldrich (St. Louis, MO).

2.1 Instrumental

An Agilent 7890A gas chromatograph hyphenated with an Agilent 5975C QMS (Agilent technologies Inc., US) was applied in this study. The split injection (with the ratio of 12 to 1) was

performed at 250 °C. Injection volume was set at 1 μL for injection of the alkane mixture (100 mg L^{-1} in hexane) and the sample.

2.1.1 GC × GC system. The GC × GC column set was a nonpolar DB-1MS (60 m × 0.25 mm inner diameter (I.D.) × 0.25 μm; J&W Scientific, US) as the first dimension (^{1}D) column with the same polar SUPELCOWAX 10 column (5 m × 0.25 mm I.D. × 0.1 μm; J&W Scientific, USA) as the ^{2}D column. The two columns were connected through a flow modulator (Agilent technologies Inc.). As shown in Fig. 1, the ^{2}D column end was further connected to the DS which behaved as a splitter *via* two restrictors to flame ionization detector (FID) and MS. The restrictor dimensions were 2.25 m × 0.18 I.D. and 0.75 m × 0.18 I.D. towards MS and FID, respectively. This is performed in order to reduce flow to MS. A modulation period (P_M) of 2, 4 or 6 s was applied. Helium was used as carrier gas with a flow rate of 0.8 mL min^{-1} applied as ^{1}D column flow. Different injection time of the flow modulator (0.15, 0.30, 0.60, 1.20 and 2.40 s) and ^{2}D column flow (7, 14 and 21 mL min^{-1}) were investigated to select the modulation and separation performance. An oven T program was set at 35 °C for 10 min, increased to 135 °C (4 °C min^{-1}), then to 250 °C (10 °C min^{-1}) and held at this temperature for 20 min with the total run time of 66.5 min. The ion source temperature, emission current and electron energy were set at 250 °C, 34.6 μA and 70 eV, respectively, with a mass range of 28–550 m/z.

2.1.2 Comprehensive H/C MDGC. The comprehensive H/C column set was ^{1}D nonpolar DB-1MS column (60 m × 0.25 mm I.D. × 0.25 μm; J&W Scientific, US) and ^{2}D polar DB-Wax column (60 m × 0.25 mm × 0.25 μm; J&W Scientific, US). The restrictor column (1.5 m × 0.1 mm; Agilent Technologies Inc.) was used to balance flow between first and second dimension. The three columns were connected through dean switch device (DS, Agilent Technologies Inc.) which the initial first dimension
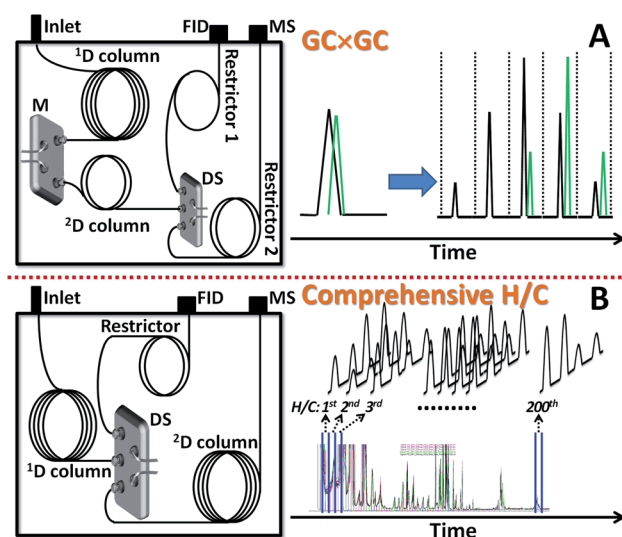

Fig. 1 Comprehensive MDGC systems used in this study: (A) GC × GC and (B) comprehensive H/C MDGC. M = modulator and DS = Deans switch.
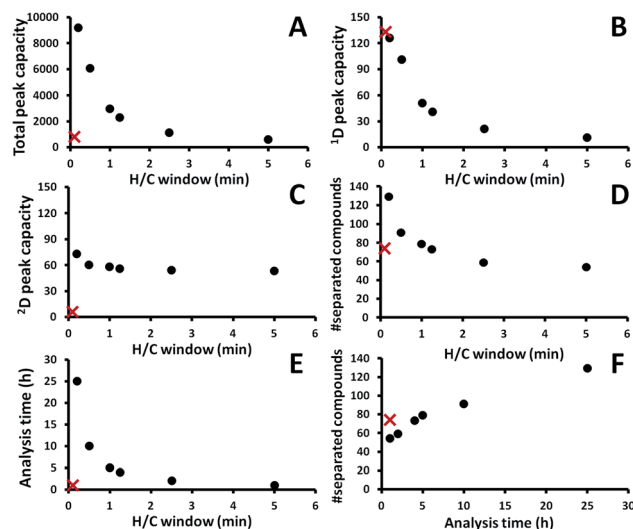
Fig. 2 Effects of H/C window ($t_{H/C}$) on separation performance in comprehensive H/C analyses (●): ^1n_c, ^2n_c, total n_c, number of identified compounds and analysis time (A–E, respectively), using the same ^{1}D and ^{2}D column flows of 2.3 and 4.7 mL min^{-1}, respectively. The number of identified compounds vs. analysis time plot is also shown in (F). The corresponding data for GC × GC analysis are shown by ×, and it can also be said that the H/C window in GC × GC is P_M.
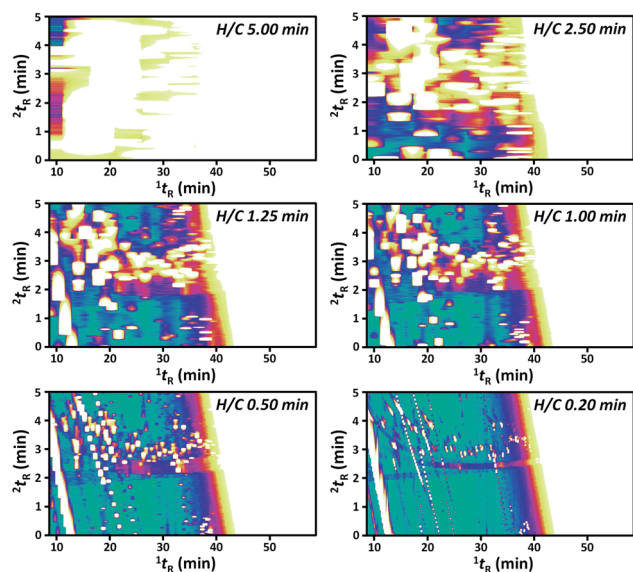

Fig. 3 Comprehensive H/C analysis results using different H/C windows.

Fig. 4 Comparison between the selected results in (A) comprehensive H/C and (B) GC × GC analyses used for compound identification in Table 1.

run). In this study, comprehensive multiple H/C was performed with different H/C windows ($t_{H/C}$, period to transfer an effluent from ^{1}D to ^{2}D column) of 5.00, 2.50, 1.25, 1.00, 0.50 and 0.20 min covering the range from 10 to 60 min of ^{1}D separation time. For each injection, several H/C were performed in a periodic strategy.[13] In this study, each H/C was performed within every 5 min (which is ^{2}D separation time, $^2t_{R,max}$). The number of injections for each comprehensive analysis was thus calculated as $^2t_{R,max}/t_{H/C}$. The number of runs for comprehensive H/C analyses with $t_{H/C}$ of 5.00, 2.50, 1.25, 1.00, 0.50 and 0.20 min were 1, 2, 4, 5, 10 and 25 runs, respectively. The corresponding H/C events for each comprehensive H/C analysis were summarized in Table S1 (ESI†).

2.2 Data analysis

General data acquisition and processing were performed by using Agilent Mass Hunter. Microsoft Excel 2007 and Fortner Transform 3.3 (Fortner, Inc., Savoy, IL) were used for data visualisation.

2.2.1 GC × GC. Peak identification and estimation of retention time (^1t_R and ^2t_R) and average peak widths at baseline ($^1w_{b,ave}$ and $^2w_{b,ave}$) of all the separated peaks excluding that of the solvent in ^{1}D and ^{2}D separation was performed by using GC image version 2.7r1 GC × GC. The estimation was performed by use of pixel based approach for identification of peak (blob) from a contour plot (http://www.gcimage.com/gcxgc/usersguide/statistics.pdf). The 2D contour plots in GC × GC

was connected from GC inlet to DS and restrictor column was connected from DS to the FID detector and the last second dimension was connected from DS to the MS followed the Fig. 1. Flow rates of helium were 2.3 and 4.7 mL min^{-1} in ^{1}D and ^{2}D separation, respectively. For each H/C analysis, GC oven temperature program and MS condition were the same as that applied in GC × GC. The total analysis time in comprehensive H/C analysis varies depending on the number of injections applied (an injection per run with the analysis time of 1 h per
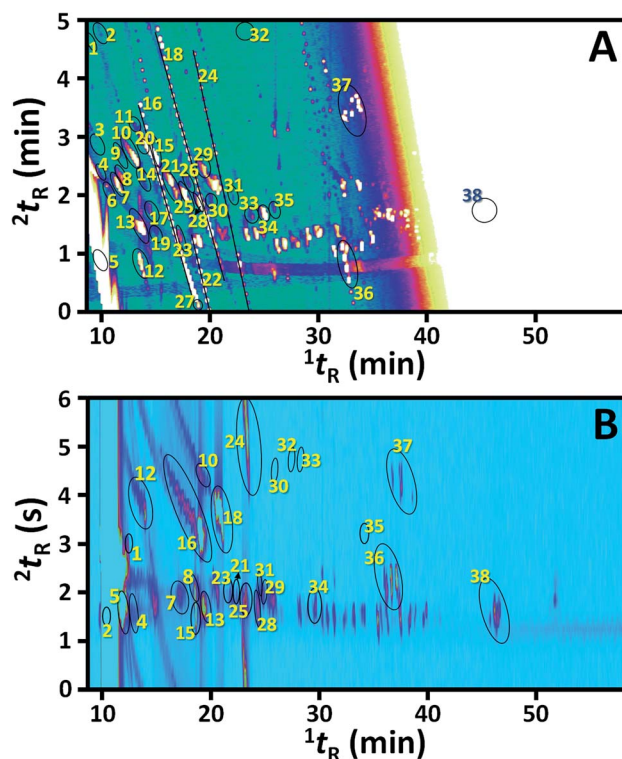
Table 1 Volatile compound profile in technical glycol precursor obtained using different methods[a]

No.	Compound	GC × GC		Comprehensive H/C		ΔI
		$I_{(expriment)}$	Match score	$I_{(expriment)}$	Match score	
1	Alcohol 1[b]	<600	940	<600	922	Not available
2	Alcohol 2[b]	<600	879	<600	941	Not available
3	Aldehyde 1[b]			<600	866	Not available
4	Aldehyde 2[b]	<600	831	<600	841	Not available
5	Ether 1[b]	<600	949	<600	934	Not available
6	Ester 1			604	830	±13
7	Aldehyde 3	618	937	621	933	±12
8	Ketone 1	659	844	616	853	±25
9	Cyclic ether 1[b]			629	748	±4
10	Ketone 2	657	926	637	773	±30
11	Alcohol 4[b]			<600	857	Not available
12	Alcohol 3[b]	<600	914	<600	908	Not available
13	Alkane 1[b]	670	933	667	922	±17
14	Ketone 3			667	819	±8
15	Ketone 4[b]	657	853	646	890	0
16	Alcohol 5[b]	661	937	663	933	±8
17	Ether 2[b]			680	832	±30
18	Alcohol 6[b]	710	935	688	921	±19
19	Oxygenate 1			692	828	±6
20	Ester 2			696	705	±1
21	Ketone 5	722	924	719	925	±3
22	Alcohol 7			754	814	±13
23	Alkane 2	732	721	729	884	±4
24	Alcohol 8[b]	742	964	732	899	±14
25	Aldehyde 4	741	931	741	930	±2
26	Aldehyde 5			744	861	±25
27	Alcohol 9			750	813	±6
28	Ester 3	761	896	763	912	±1
29	Ketone 6[b]	769	927	763	928	±5
30	Ether 3[b]	778	781	766	845	±12
31	Ester 4	809	915	807	760	±1
32	Alcohol 10	833	787	830	926	±10
33	Ester 5	836	882	833	868	±4
34	Ester 6	856	947	852	945	±1
35	Ester 7	873	707	869	906	±3
36	Glycol 1[b]	996	939	1006	951	±25
37	Glycol 2[b]	1046	877	1015	912	±2
38	Glycol 3[b]	1288	873	1284	877	Not available

[a] $\Delta I = \pm |I_{(experiment)} - I_{(literature)}|$. [b] Compound identification was confirmed by injection of authentic standard.

analysis were obtained by transformation of 1D modulated chromatogram data into a matrix. The matrix was further transformed into a 2D contour plot. All of these processes were performed by using GC image.

2.2.2 Comprehensive H/C. In generally, use of cryogenic trapping provides benefit in data analysis with simple calculation of ^2t_R of compounds within each H/C. For example with the 1.0 min H/C window applying along the period from 11.0 to 12.0 min in ^{1}D separation, all the H/C compounds can be cryogenically trapped and then released with the same starting time in ^{2}D separation.[12] However, the sampling process from ^{1}D column without use of cryogenic trap can lead to immediate elution onto ^{2}D column and thus variation of the start time in ^{2}D separation. In the case of 11.0–12.0 min heart cutting, compared with a compound with ^1t_R of 11.7 min, another compound with ^1t_R of 11.2 min will start eluting 0.5 min earlier

in ^{2}D separation. In this study without use of cryogenic trap, all the H/C compounds from 11.0–12.0 min will be set to have the same starting time in ^{2}D separation which is the in middle of the H/C period (11.5 min). This leads to the error of "half of the H/C window" in calculation of both ^1t_R and ^2t_R, e.g. ±0.5 min for the 1 min H/C window. Thus, narrower H/C window resulted in more accurate calculation of ^2t_R.

According to the approximation of starting time in ^{2}D separation above, ^1t_R and ^2t_R of a peak detected by MS in each multiple H/C analysis were approximated as

$$^1t_{R,approx} = t_{H/C_{mid}} = \frac{t_{H/C}}{2} = \frac{t_{H/C_{start}} + t_{H/C_{end}}}{2} \quad (1)$$

$$^2t_{R,approx} = t_{R,observed} - {}^1t_R \quad (2)$$

where $t_{H/C}$ is H/C window. $t_{H/C_{mid}}$ and $t_{H/C_{start}}$, $t_{H/C_{end}}$ are middle time, starting time and ending time of the H/C, respectively. $t_{observed}$ is the peak time observed with MS detector (after elution through 1D and 2D columns). In case of modulated (or split) peaks into different H/C fractions, calculation of ^1t_R and ^2t_R of a compound was performed by selecting the modulated peak with highest peak area for each compound.

In general, by considering a H/C event, when the applied H/C window ($t_{H/C}$) is significantly longer than average widths in ^{1}D separation ($^1w_{b,ave}$) of compounds, any compounds separated within the H/C interval will undergo under sampling process resulting in recombination (*e.g.* by cryogenic trapping process or being collected into the same loop) of the separated peaks into the same H/C fraction (^{1}D resolution loss) prior to ^{2}D separation. In other words, such process can convert the actual $^1w_{b,ave}$ into $t_{H/C}$, or $t_{H/C} = {^1w_{b,ave}}$ as previously reported in ref. [3]. In this study, there was no recombination effect since sample loop or cryogenic trapping approach was not applied. However, when considering only the raw 2DGC chromatograms observed with MS (see the system in Fig. 1A), the error discussed above occurs. This could also be considered with $t_{H/C} = {^1w_{b,ave}}$. In addition, when $t_{H/C}$ is narrower and closer to (or shorter than) $^1w_{b,ave}$ of compounds, under sampling effect can be reduced. In this case, peak splitting occurs and the apparent $^1w_{b,ave}$ will be scaled as the multiple of the H/C window. To this end, a general relationship applied for any H/C window can be proposed for approximation $^1w_{b,ave}$ as

$$^1w_{b,ave} = t_{H/C} \times \text{Roundup}\left(\frac{w_{b,ave,1DGC}}{t_{H/C}}\right) \quad (3)$$

where $w_{b,ave,1DGC}$ is average peak width at baseline of all the separated peaks excluded that of the solvent obtained from 1DGC analysis (*e.g.* with the DS off). "*Roundup*" is to result in the rounded number of a value in the parenthesis. The average width at baseline in chromatograms obtained in each H/C analysis (observed with MS detector after H/C) was herein assumed to be average widths in ^{1}D separation ($^2w_{b,ave}$).

The 2D contour plots in comprehensive H/C analysis covering 10–60 min in ^{1}D separation were obtained by combination of the elution profiles subtracted by $t_{H/C_{mid}}$ obtained from all the H/C fractions into a matrix. The matrix was then converted into a 2D contour plot by using Fortner Transform 3.3 (Fortner, Inc., Savoy, IL).

2.2.3 Peak capacity. Total peak capacity ($n_{c,total}$) is calculated here by filling in the whole available separation space between the first and the last eluting analytes of interest with the retention times of $t_{R,first}$ and $t_{R,last}$, respectively, and average peak widths at baseline of $w_{b,ave}$ according to

$$n_{c,total} = {^1n_c} \times {^2n_c} \quad (4)$$

$$^1n_c = 1 + \frac{^1t_{R,last} - {^1t_{R,first}}}{^1w_{b,ave}} \quad (5)$$

$$^2n_c = \frac{^2D \text{ separation time}}{^2w_{b,ave}} \quad (6)$$

where the superscripts 1 or 2 indicate that the parameters are in ^{1}D or ^{2}D separation, respectively. ^{2}D separation time is P_M in GC $\times$ GC (6 s) or $^2t_{R,max}$ in comprehensive H/C analysis (5 min).

2.2.4 Compound identification. Compounds in the technical glycol precursor sample were tentatively identified by comparison of their mass spectra and ^{1}D retention index (^1I) values with those documented in NIST14 library and literatures. For the ^1I determination, a mixture of alkanes was injected using the same experimental condition as that of sample analysis except the modulator was turned off. As analytes eluted from ^{1}D column in a linear T program, ^{1}D RI values were calculated by van den Dool and Kratz index using the relationship:[15]

$$^1I = 100n + 100\left(\frac{^1t_{R(i)} - {^1t_{R(n)}}}{^1t_{R(n+1)} - {^1t_{R(n)}}}\right) \quad (7)$$

where $^1t_{R(i)}$ is the retention time of analyte of interest on ^{1}D column. n and $n + 1$ are the numbers of carbons of alkane standards eluting in the positions bracketing the analyte i. Note that ^2I was not calculated in this study. However, the criterion that later eluting compounds (taking into account wraparound) in ^{2}D separation for each H/C fraction (or each modulation in GC $\times$ GC) should have higher ^2I literature values was applied. The compounds reported in this work were identified with MS match score of >650 and ^1I difference of ± 30 unit from the literature values. The number of separated compounds is obtained by counting all the separated peaks in each analysis. Note that MS identification was also performed in order to avoid repetitive counting caused by the modulated (split) peaks of the same compound during the sampling process in comprehensive H/C.

3 Results and discussion

A technical glycol precursor sample was separated by use of two different comprehensive MDGC systems (GC $\times$ GC and comprehensive H/C) prior to detection with FID and MS. The system configurations were shown in Fig. 1. The results were evaluated and compared according to total peak capacity, number of separated peaks and average MS match scores of the separated peaks in each analysis. Peak capacity[16] (n_c) can be calculated by filling in the whole available separation space between the first and the last eluting analytes with an average peak width assigned. However, selectivity has not been taken into account in n_c calculation. The aspect of selectivity was included in this study *via* calculation of the number of separated peaks in each separation. The experimental parameters related to these two comprehensive techniques were investigated and their results under the selected conditions were compared.

GC $\times$ GC employed long ^{1}D column (30 m) and short ^{2}D column (5 m) enabling fast ^{2}D separation of a technical glycol precursor sample (with compounds elution time mostly distributing within a window of 6 s). As a result, comprehensive GC $\times$ GC analysis was performed within a single run (a single injection). Flow modulation was applied in this approach which requires high ^{2}D flow for effective modulation process.[17,18] The

outlet flow was thus split to decrease flow to MS by using DS as a splitter[19] as shown in Fig. 1A. The flow was further reduced by use of a longer restrictor with the same I.D. to MS. Investigation of experimental conditions in GC × GC was provided in ESI.† A suitable condition employing constant ^{1}D and ^{2}D column flows of 0.8 and 14 mL min^{-1}, respectively, and the injection time of 0.60 s was selected for comparison with the comprehensive H/C analysis below.

3.1 Investigation of experimental conditions in the developed comprehensive H/C analysis

In order to improve ^{2}D separation, comprehensive H/C MDGC system consisting of a long ^{1}D column (30 m) and a long ^{2}D column (60 m) was applied. In general, H/C approaches can be coupled with a cryogenic trapping system allowing peak focusing/sharpening effect and application of independent temperature and flow in ^{1}D and ^{2}D separations.[11-13] The system in this study solely employed a DS without cryogenic trapping and splitting devices (Fig. 1B) with lower resolution and less flexibility in ^{2}D separations. However, it is easier to configure and maintain, and also effective (e.g. see the result in Fig. 2 with 0.20 min H/C). Unlike GC × GC with a single injection analysis, several more injections should be performed in order to preserve ^{1}D separation efficiency (by use of narrow H/C windows) and minimize wraparound effect.[3] Thus, this approach requires longer analysis time as well as more complicate method generation and data analysis (see the Experimental section above). For example, with a constant 0.2 min H/C window, a comprehensive H/C analysis covering from 10 to 60 min of ^{1}D separation time requires 250 times of H/C. In order to reduce the analysis time, cyclic multiple H/C strategy was performed in this study.[13] This approach applies constant H/C window ($t_{H/C}$) and ^{2}D separation time ($^2t_{R,max}$) throughout the whole comprehensive analysis and the number of injections can be the ratio of $^2t_{R,max}$ to $t_{H/C}$. In this study, a comprehensive analysis applied constant $^2t_{R,max}$ and $t_{H/C}$ of 5 and 0.2 min, respectively. This was found to be sufficient to elute most of the compounds (excluding those analyzed with 2.5 and 5.0 min H/C) in each H/C without wrapping around into the subsequent H/C. To this end, 25 injections (5 ÷ 0.2) were performed in order to complete the comprehensive analysis with 250 times of H/C. This means 10 H/C was performed in each injection.

3.1.1 Effects of H/C window and analysis time in comprehensive H/C analysis.
With constant ^{1}D and ^{2}D column flows of 2.3 and 4.7 mL min^{-1}, comprehensive H/C analyses of technical glycol precursor sample were performed using different $t_{H/C}$. The resulting separation performance and analysis time for all the conditions were shown in Fig. 2.

Note that the $n_{c,total}$ was calculated from $^1w_{b,ave}$ and $^2w_{b,ave}$, see the Data analysis section above. The performance in comprehensive H/C analysis (see (●) in Fig. 2A–D) was significantly improved with the narrower H/C window (shorter $t_{H/C}$) and thus with the increasing analysis time (Fig. 2E and F, respectively). The GC × GC analysis resulted in the total n_c of 798 (see × in Fig. 2A); whilst, the number was improved to be

9198 with the comprehensive H/C analysis using 0.20 min H/C window (Fig. 2A). This is also higher than that reported with the recent cryogen-free GC × GC technology[20] albeit with the requirement of much longer analysis time in our study. It should also be noted that the total n_c could be improved to be much higher than 9198 by decreasing ^1w_b, e.g. using the higher split ratio. In addition, the developed system also allows use of lower carrier gas flow on the ^{2}D column compared to that conventionally applied in GC × GC with flow modulation.[21] Our approach is thus more compatible with MS detector. The corresponding numbers of separated peaks were 61 and 107, respectively (Fig. 2F). The contour plots obtained from the comprehensive H/C analyses were shown in Fig. 3 revealing better results with the shorter $t_{H/C}$, see much greater resolution in the horizontal direction in Fig. 3 from 5.00 to 0.20 min H/C window. Shorter $t_{H/C}$ directly resulted in smaller $^1w_{b,ave}$, thus increasing ^1n_c, see also the trend in Fig. 2B. This also reduced sampling amount (which decreased $^2w_{b,ave}$) as well as reducing complexity (coelution) in each H/C pulse.[3] Thus, ^2n_c slightly increased (Fig. 2C) as also shown by the greater resolution in the vertical direction with the narrower H/C windows in Fig. 3. Furthermore, as discussed in the Data analysis section above, there is more error in ^{1}D time calculation with the longer $t_{H/C}$. This leads to the strong wraparound with the wider H/C windows (Fig. 3). To this end, use of longer analysis time (shorter $t_{H/C}$) improved total n_c with the larger number of separated compounds, reduced wraparound and reduced uncertainty in ^1t_R calculation (see the related discussion in Data analysis).

3.2 Comparison of analysis performances in comprehensive H/C and GC × GC

As already discussed above, the plots (●) in Fig. 2 showed the performance of comprehensive H/C analysis with different H/C windows. The corresponding performance of the selected GC × GC analysis is also shown by the data (×) in Fig. 2. With the analysis time of 1 h, GC × GC clearly showed greater performance than the comprehensive H/C as shown by the plot of the number of identified peaks in Fig. 2F. This is mainly due to 1 h operation in comprehensive H/C analysis unavoidably using the long $t_{H/C}$ of 5 min which critically suppressed ^{1}D performance (with ^1n_c of only 11); whilst, ^{1}D separation performance in GC × GC is largely preserved (^1n_c of 133). However, ^1n_c was improved significantly with longer analysis time in comprehensive H/C. With the expense of >4 h of analysis time, the H/C performance in all the aspects, except ^1n_c, became greater than that provided by GC × GC (Fig. 2). Note that in this study, the shortest $t_{H/C}$ was 0.2 min which was still longer than the applied P_M and resulted in lower ^1n_c in the H/C analysis (Fig. 2B). The ^1n_c could be further improved to be greater than that in GC × GC by use of $t_{H/C} < P_M$.

With the same temperature program, the results obtained using the investigated comprehensive techniques under the selected conditions were compared as shown in Fig. 4, which clearly showed much greater performance in ^{2}D separation with the comprehensive H/C analysis (Fig. 4A) with a larger number

of well separated peaks compared to that provided by conventional GC × GC (Fig. 4B). From the experimental results in Fig. 4, compound identifications were performed according to MS match library and ^1I comparison with the data provided in Table 1. Since it is a proprietary sample, only the compounds classes are listed in the table.

The numbers of focused compounds that were successfully identified were 27 and 38 compounds in GC × GC and comprehensive H/C, respectively. In addition, higher confidence in the analysis was obtained as illustrated by the improved average MS match scores from 887 ± 35 with GC × GC to 898 ± 24 with comprehensive H/C analysis for the set of compounds identified by both techniques, since greater separation performance was obtained in the later approach.

4 Conclusion

Cryogenic free strategies and the data analysis approach in comprehensive MDGC (GC × GC and comprehensive H/C) were developed with the example application for technical glycol precursor sample analysis. The GC × GC and comprehensive H/C experiments were investigated with the benefit of improved overall separation performance at longer analysis time, based mainly on the improved ^2D separation with a longer ^2D column in comprehensive H/C). Interestingly, the trend in Fig. 2F is matched with the theoretical trend simulated in the previous study.[3] The results clearly showed separation performance in the comprehensive analysis can be improved by use of longer ^2D column length and longer analysis time (mainly improving ^2n_c and ^1n_c, respectively). A compromise between time and separation performance should thus be made.

Under the selected conditions in this study, conventional GC × GC employing a flow modulator with suitable injection time and ^2D column flow completed the analysis in 1 h. The comprehensive H/C was applied with the cyclic strategies allowing 250 H/C times to be performed within 25 h by a DS. The system was sufficiently stable that the overall 2D contour plot combining all the H/C results could be generated. The operation with a narrower H/C window allows sampling of significantly sharp band of analytes from ^1D separation prior to ^2D separation. Thus, ^1t_R and ^1I calculation can be reliable, and use of cryogenic trapping can be avoided. Compared to GC × GC, such comprehensive H/C approach provided 12 times improved total peak capacity with 2 times of the number of separated compounds and more confidence with MS analysis (higher MS match score). To this end, ones could perform high performance comprehensive analysis by use of a single DS. With the expense of time, this technique is thus simple, useful and applicable for high resolution separation of any samples in the future.

Author contributions

Pannipa Janta: methodology, data curation, investigation, writing – original draft. Duangkamol Pinyo, Yamonporn Yodta and Porames Vasasiri: resources. Meinolf Weidenbach: supervision, project administration, funding acquisition. Xiuhan (Grace) Yang and Matthias Pursch: writing – review & editing, supervision, project administration, funding acquisition. Chadin Kulsing: conceptualization, software, formal analysis, writing – review & editing, visualization, supervision, project administration, funding acquisition.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Notes and references

1 Y. Nolvachai, C. Kulsing and P. J. Marriott, *TrAC, Trends Anal. Chem.*, 2017, **96**, 124–137.
2 S. E. Prebihalo, K. L. Berrier, C. E. Freye, H. D. Bahaghighat, N. R. Moore, D. K. Pinkerton and R. E. Synovec, *Anal. Chem.*, 2018, **90**, 505–532.
3 C. Kulsing, Y. Nolvachai, P. Rawson, D. J. Evans and P. J. Marriott, *Anal. Chem.*, 2016, **88**, 3529–3538.
4 C. Meinert and U. J. Meierhenrich, *Angew. Chem., Int. Ed.*, 2012, **51**, 10460–10470.
5 P. Q. Tranchida, P. Donato, F. Cacciola, M. Beccaria, P. Dugo and L. Mondello, *TrAC, Trends Anal. Chem.*, 2013, **52**, 186–205.
6 Y. Nolvachai, C. Kulsing and P. J. Marriott, *Anal. Chem.*, 2016, **88**, 2125–2131.
7 Y. Nolvachai, C. Kulsing and P. J. Marriott, *Anal. Chem.*, 2015, **87**, 538–544.
8 W. Khummueng, J. Harynuk and P. J. Marriott, *Anal. Chem.*, 2006, **78**, 4578–4587.
9 M. Adahchour, J. Beens, R. J. J. Vreuls and U. A. T. Brinkman, *TrAC, Trends Anal. Chem.*, 2006, **25**, 540–553.
10 C. Kulsing, Y. Nolvachai and P. J. Marriott, *TrAC, Trends Anal. Chem.*, 2020, **130**, 115995.
11 H. D. Waktola, C. Kulsing, Y. Nolvachai and P. J. Marriott, *J. Chromatogr. A*, 2018, **1549**, 77–84.
12 C. Kulsing, Y. Nolvachai, Y. F. Wong, M. I. Glouzman and P. J. Marriott, *J. Chromatogr. A*, 2018, **1546**, 97–105.
13 B. Mitrevski, R. L. Webster, P. Rawson, D. J. Evans, H.-K. Choi and P. J. Marriott, *J. Chromatogr. A*, 2012, **1224**, 89–96.
14 N. Thongdorn, T. Nhujak, P. Janta, A. Rueangthaweep, N. Hinchiranan and C. Kulsing, *Anal. Methods*, 2020, **12**, 5160–5167.

15 M. Jiang, C. Kulsing, Y. Nolvachai and P. J. Marriott, *Anal. Chem.*, 2015, **87**, 5753–5761.

16 Z. Liu, D. G. Patterson and M. L. Lee, *Anal. Chem.*, 1995, **67**, 3840–3845.

17 H. D. Bahaghighat, C. E. Freye and R. E. Synovec, *TrAC, Trends Anal. Chem.*, 2019, **113**, 379–391.

18 C. Duhamel, P. Cardinael, V. Peulon-Agasse, R. Firor, L. Pascaud, G. Semard-Jousset, P. Giusti and V. Livadaris, *J. Chromatogr. A*, 2015, **1387**, 95–103.

19 P. Boeker, J. Leppert, B. Mysliwietz and P. S. Lammers, *Anal. Chem.*, 2013, **85**, 9021–9030.

20 T. J. Trinklein, D. V. Gough, C. G. Warren, G. S. Ochoa and R. E. Synovec, *J. Chromatogr. A*, 2020, **1609**, 460488.

21 I. Aloisi, T. Schena, B. Giocastro, M. Zoccali, P. Q. Tranchida, E. B. Caramão and L. Mondello, *Anal. Chim. Acta*, 2020, **1105**, 231–236.