Comprehensive Separation Technologies Applied to the Petrochemical Industry

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This review will discuss the recent advancements and trends in comprehensive separations in the petroleum and chemical industry from the past 2-3 years. Specific emphasis will be placed on modulation for both LC×LC and GC×GC, as well as applications for both.

1. Introduction

1.1 Benefits of comprehensive analyses

In the early 1980's, J.C. Giddings first wrote about the potential advantages of using multidimensional chromatography, where two dimensional (2D) separations are governed by the one dimensional (1D) displacement processes, specifically selective and non-selective displacement processes [1]. In order to optimise the 2D separation for the greatest peak capacity, the 1D displacement processes should be selective and independent of each other. For both liquid and gas chromatography, the easiest way to ensure selective and independent 1D displacement processes is to utilise orthogonal stationary phases between the first and second dimensions. However, care must be taken with stationary phase selection, as Giddings also stated that the components resolved in the first dimension separation must remain separated through the second dimension separation [2].

As the two separations must be independent from one another, the eluent exiting the first dimension column must be transferred to the second dimension column. This is typically accomplished by either trapping a small amount of eluent until the end of the first dimension separation and then transferring that 'cut' to the second dimension column (e.g. heart-cutting), or through the use of a modulator to trap (nearly) all the eluent exiting the first dimension column and immediately transfer this to the second dimension column (e.g. comprehensive).

In order to achieve a comprehensive separation, the column stationary phases should be orthogonal to one another, and various column dimensions and stationary phases are available for both liquid chromatography (LC) and gas chromatography (GC). LC and GC columns have benefitted from smaller inner diameters (ID), smaller particles sizes and thinner films, respectively, stable stationary phase supports (e.g., fused silica capillary in GC and fully porous/solid core and porous shell particles in LC). All of these choices can help chromatographers when implementing comprehensive chromatography.

GC and LC instrumentation have also become more robust, reliable, and user friendly, as well as evolving in ease of implementation for comprehensive separations. In parallel, instrument control and data processing software platforms have been advancing in capabilities and user friendliness. Commercially available instruments are offered by the major supplies for both comprehensive LC (LC×LC) and comprehensive GC (GC×GC).

Even with the advancements made over the past two decades, comprehensive separations have not become commonplace in the petroleum and petrochemical industry; 1D separations still dominate the landscape for (routine) applications. This is in part due to the fact that comprehensive separations are still quite complicated. A new user of LC or GC can quickly learn the ropes and become proficient in 1D LC or GC separations. However, this is not the case with comprehensive separations; there is a large learning curve that novices to the technique will need to overcome. Not only is there an enormity of parameters that need to be optimised during method development, but also data interpretation requires more complex software. While routine applications are rather few, the number of applications described in the petroleum and petrochemical industry are rising.

1.2 Scope of this review

This review will discuss the recent advancements and trends in comprehensive separations in the petroleum and chemical industry from the past 2-3 years. Both LC×LC and GC×GC will be discussed.

LC separation modes as well as modulator approaches will be summarised. In terms of chemical applications, LC×LC has been applied extensively to polymer/copolymer analysis. Additional applications include surfactants, polymer additives and smaller molecules analysis from chemical processes.

Emphasis will be placed on how GC×GC has evolved and advanced with respect to petroleum and petrochemical analyses. Additionally, key points for consideration will be highlighted; for example, the selection of column sets based on the desired application, the type of modulator installed, and the detectors incorporated into the instrument setup will be discussed. The modulator is the heart of the GC×GC instrument, so special attention will be paid to the advancements made in modulator technologies in recent years, as well as the advantages and pitfalls of both flow and thermal modulators. Finally, the authors will discuss some emerging trends from the past several years, where an emphasis in source identification for environmental contamination and petroleomics are making headway.

2. Comprehensive LC

2.1 Background

For 2D-LC several separation schemes do exist, the major two include heart-cutting and comprehensive separations [3]. There are related modes to both, such as multiple heart-cutting and selective comprehensive/high-resolution sampling. These two have gained attention in recent years. Multiple heart-cutting allows targeted analysis across several areas of a one-dimensional separation. Peaks can be stored in loops or on cartridges for further analysis in 2D [4]. Selective comprehensive mode is particularly useful to detect impurities under a main peak, or to obtain additional peak capacity for just a part of the 1D chromatogram [5].

2.2 Comprehensive separation modes

In LC one can select from many separation modes. The most prominent is reversed-phase LC (RPLC). Other modes include hydrophilic interaction LC (HILIC), size-exclusion chromatography (SEC), ion-exchange chromatography (IEX) and LC at critical conditions (LCCC). A high degree of orthogonality can be achieved by executing very different or independent separations in both dimensions. For example the combination HILIC×RPLC can lead to very high coverage of the 2D separation space, as demonstrated for the separation of surfactants [6] or polyols [7]. For alkyl ethoxylates, HILIC separates by polarity (ethylene oxide distribution), while RPLC separates by non-polarity (alkyl chain length distribution). For polymer/co-polymer analysis LCCC×SEC also has a high degree of orthogonality as it separates the compounds by functionality type (end groups) in LCCC, while SEC separates based on molecular weight distributions [8].

2.3. Modulators

Ten-port or eight-port valves with two loops are very commonly used for modulation. Mobile phase compatibility is one key challenge when LC×LC is being considered, as strong eluents from the first dimension (^{1}D) can create sample breakthrough in the second dimension (^{2}D). Several advanced solutions exist to mitigate these issues as illustrated in Figure 1. One is active modulation (AM) via component trapping on solid-phase extraction (SPE) cartridges [9]. A third pump is used to co-feed weak eluent to promote trapping. This is an elegant way to achieve peak focusing during modulation. One drawback is the uncertainty of recovery during the trapping process as well as unknown longevity of the cartridges. Active solvent modulation (ASM) is based on a dedicated valve solution [10]. In ASM, strong eluent from ^{1}D is diluted with weak eluent in ^{2}D hereby strongly reducing mobile phase mismatch. ASM does not require a third pump, yet additional valve switches are required during modulation which could be more demanding on seals. At column dilution (ACD) can also mitigate strong solvent issues by co-feeding weak eluent from an additional pump [11]. Like with AM, ACD also requires three pumps for LCxLC operation. Additional modes include thermal modulation or modulation via vacuum.

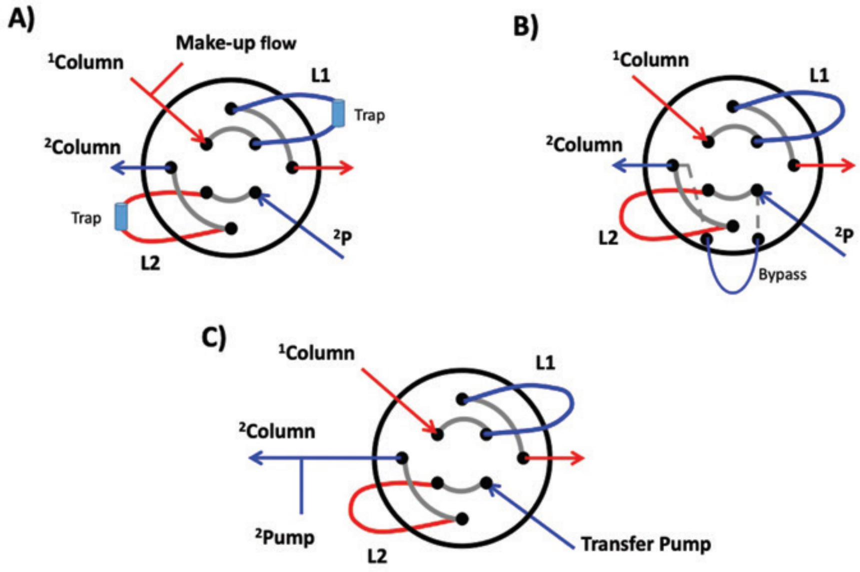

Figure 1: Overview of various modulators used for 2D-LC: Active modulation (A), Active solvent modulation (B) and At-column dilution (C). Image (B) is courtesy of D. Stoll & Agilent Technologies.

2.4 Applications and Trends

Industrial chemical processes can be complex as shown for a process intermediates sample analysis. Zhu et al. developed an ultra-high peak capacity LC×LC approach for separation of aromatic amines [12]. Sample complexity is high, as compounds have isomeric and oligomeric structures. The separation utilised six pentafluorophenyl (PFP) columns coupled in series for the first dimension, and a Zorbax PAH column in the second dimension. Even though both dimensions were operated in reversed-phase mode, good separation orthogonality was obtained. This dissimilarity of the two columns used was attributed to dipolar interactions with the PFP column and more of a shape selectivity/hydrophobicity type separation with the PAH column. Within 20 h of analysis time a peak capacity of greater than 11,000 was achieved to separate about 900 individual peaks (Figure 2).

A high sample complexity is seen with Bio-oils produced from the pyrolysis of biomass (e.g. Eucalyptus sawdust, spent coffee grounds). Key constituents in such samples include phenolics and ketones. These are of potential interest as feedstocks in the chemical industry. Lazzari et al. used an LC×LC separation scheme for quantitative analysis of up to 28 components in such matrices [13]. The aqueous phases which resulted from pyrolysis were studied in detail. Reversed-phase separations were used in both dimensions; an X-bridge amide column was used in the first dimension, and a Poroshell C18 column was used in the second dimension. Detection was carried out by UV absorbance and ESI-MS (ion trap). Calibration curves were made using various phenolic, aldehyde or hydroxyl ketone standards covering two orders of magnitude in concentration. Effective peak capacities of up to 1000 were achieved in about 1 h of analysis time. Recoveries ranged from 92% - 113%.

An interesting study using LC×LC coupled to inductively coupled mass spectrometry (ICP-MS/MS) was assessed for sulphur and vanadium species in petroleum residues [14]. The research was carried out with a focus to meet new requirements with regard to demetallation and dehydrosulfurization processes. Another aspect was to bring additional information regarding the species present in these matrices. It is shown that an off-line SEC×RPLC method can provide a higher peak capacity (2600 vs 1700) for the same analysis time of 150 min, than on-line RPLC×SEC. The dilution factor is similar with both approaches (close to 30) but also

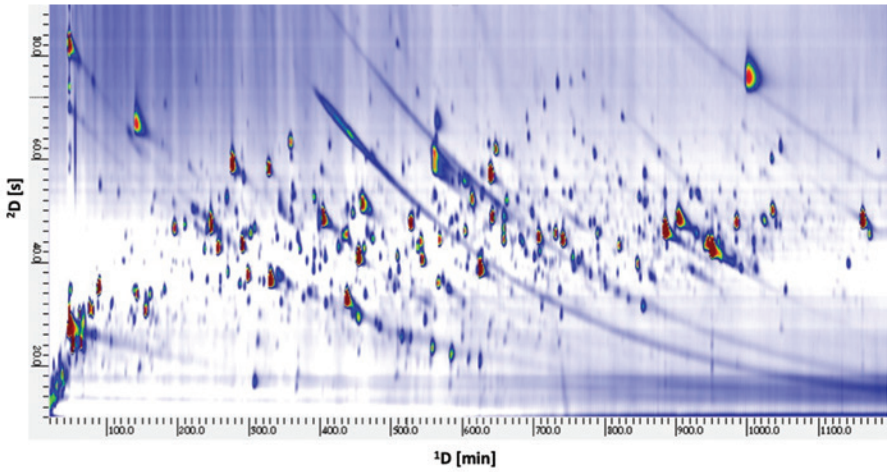

Figure 2: LCxLC plot showing the separation of aromatic amines from a chemical process. Both dimensions were operated in RP mode, with ^{1}D using a pentafluorophenyl stationary phase and ^{2}D using a high-density C18 bonded phase.

requires much less fractions to be analysed (12 vs 400). Asphaltenes which constitute the heaviest fraction of crude oils were analysed by the developed off-line SEC×RPLC method. The resulting 2D-contour plots show that co-elutions could be removed leading, for the first time, to new information on high molecular weight species containing sulphur and vanadium.

An LC×LC method with evaporative light-scattering detection (ELSD) was set up to study the composition of the complex mixture of oxidised polar and non-polar lipids [15]. The LC×LC-ELSD method employs size exclusion chromatography (SEC) in ^{1}D to separate the various lipid species according to size. In ^{2}D, normal-phase liquid chromatography (NPLC) was used to separate the fractions according to their degree of oxidation. The coupling of SEC with NPLC yields a good separation of the oxidised triacylglycerols (TAGs) from the large excess of non-oxidised TAGs. In addition, it allows the isolation of non-oxidised species that usually interfere with the detection of a variety of oxidised products (similar polarities). The method facilitates elucidating how lipid composition affects oxidation kinetics in emulsified foods and will aid in the development of more oxidation-stable vegetable oil products.

Copolymers made from polar and non-polar monomers can also constitute a considerable separation challenge. Yang, et al. recently reported the use of active solvent modulation (ASM) in the SEC×RPLC separation of vinyl acetate/acrylic acid copolymers and vinyl acetate/itaconic acid/acrylic acid terpolymers [16]. Sample breakthrough of the more polar components in the second dimension was avoided with ASM. As a result, heterogeneous copolymer composition could be monitored in random copolymer and terpolymer samples produced under various process conditions. This information provides insights to industrial polymer process development and optimisation.

In temperature gradient interaction chromatography (TGIC) the column temperature is varied to manipulate retention of polymer components without the use of a mobile phase gradient. The advantage of TGIC over solvent gradient LC is the improved compatibility with RI and light scattering detectors. Murima et al. highlighted a comprehensive branching analysis of polydisperse star-shaped polystyrenes using RP-TGIC×SEC separation scheme [17].

Pirok, et al. explored hyphenation of hydrodynamic chromatography (HDC) and SEC for the separation of hydrophobic polystyrene (PS) and poly(-methyl methacrylate) (PMMA) nanoparticles [18]. The goal was to determine particle size distribution (PSD) and molecular-weight distribution in one single analysis. Nanoparticles eluting from the ^{1}D HDC column were dissolved in tetrahydrofuran (THF) in an Agilent Jet Weaver mixer and then injected onto the ^{2}D SEC column. Stationary-phase-assisted modulation (SPAM) with C18 silica trap cartridges were used in the modulator loop. This was done to mitigate solvent incompatibility effects resulting from very different mobile phases used in the first and second dimensions.

A key trend in LC×LC is an enhanced focus on data analysis tools. Current research deals with retention modelling, peak tracking and advanced data analysis using Chemometrics [19, 20]. Mass spectrometry is being increasingly used for more universal peak detection and for compound identification. For LC×LC analysis of polymers universal detection is mostly done by evaporative light scattering detection (ELSD), which has limited linearity. Any improvements in this detection scheme will be beneficial for quantitative analysis. Further improvements are expected to occur in software - including data acquisition and data analysis. While 2D-LC systems are very robust already, further ease of use via enhanced system intelligence capabilities will enhance more unattended operation. Finally, automated method development tools are a pressing need for LC×LC as weeks or even months can be spent on developing new methods [21].

3. Comprehensive GC

3.1 Background

Multidimensional gas chromatography (MDGC) can take on many faces, and typically covers heart-cutting GC (GC-GC) and comprehensive GC (GC×GC). While this review focuses on comprehensive techniques, the authors would like to take a moment to mention GC-GC.

GC-GC is a multidimensional technique that transfers only a small fraction of the eluent from the ^{1}D column to the ^{2}D column. In this approach, the two separations are independent of one another, where the fractions from first dimension are generally selected based on targeted co-elutions requiring further separation. A Dean's Switch or valves can be used to collect and transfer the targeted fraction(s) to the second dimension separation. A perfect example is the development of the first automated paraffin, naphthene, aromatic (PNA) analyser in 1971, which quantitatively separated heavy naphtha into the PNA group types [22]. This MDGC application was later expanded upon to provide quantitative information on the paraffins, iso-paraffins, olefins, naphthenes, and aromatics, also known as PIONA, group types for lighter petroleum fractions [23]. The PIONA analyser, has been vetted by the American Society for Testing and Materials (ASTM) and is an industry standard for the evaluation of petroleum distillates with a boiling point less than 200˚C (ASTM-D5443) [24].

While GC-GC has made headway in terms of routine applications, GC×GC still struggles with implementation in routine environments. Even though GC×GC has advanced tremendously over the past two decades, it is still a complex technique compared to 1D separations, where column selection, modulator type, detector choice, and software platforms add to the confusion and complexity for users [25].

Table 1: Column set comparison between thermal and flow modulation in select petrochemical applications.

Application	Column Set (Thermal)	Column Set (Flow)	Reference
Light Cycle Oil	^{1}D: DB-5 (30 m x 0.32 mm x 0.25 μm) ^{2}D: BPX-50 (1 m x 0.1 mm x 0.1 μm)	^{1}D: DB-5 (10 m x 0.1 mm x 0.4 μm) ^{2}D: BPX-50 (10 m x 0.25 mm x 0.1μm)	[28]
Base Oils	^{1}D: Mega 17-MS (20 m x 0.18 mm x 0.18 μm) ^{2}D: Rxi-1MS (0.7 m x 0.15 mm x 0.15 μm)	^{1}D: Mega 17-MS (20 m x 0.18 mm x 0.18 μm) ^{2}D: Rxi-1 (9.1 m x 0.25 mm x 0.25 μm)	[29]
Heavy Petroleum Cuts	^{1}D: DB1-ht (10 m x 0.32 mm x 0.1 μm) ^{2}D: BPX-50 (0.5 m x 0.1 mm x 0.1 μm)	^{1}D: DB5-ht (10 m x 0.1 mm x 0.1 μm) ^{2}D: ZB35-HT Inferno (5 m x 0.25 mm x 0.1 μm)	[30]

Several of these points will be discussed, along with recent examples relevant for the petrochemical industry.

3.2 Column Sets: Reverse Phase Combination vs Normal Phase Combination

Terminology around GC×GC column sets has caused some confusion over the years, especially for users of both multidimensional LC and GC. A normal phase and a reverse phase GC×GC column set is not to be confused with normal phase and reversed phase LC. A normal phase column set in GC×GC utilises a nonpolar stationary phase in ^{1}D and a polar stationary phase in ^{2}D (nonpolar×polar), while a reverse phase column set will place the polar stationary phase in ^{1}D and the nonpolar stationary phase in ^{2}D (polar×nonpolar).

In terms of hydrocarbons separations, the choice between a normal phase column set and a reverse phase column set will depend on the desired information output. A normal phase column set will provide enhanced resolution and separation of the mono-, di-, and tri-aromatics compared to a reverse phase column set; however, for the same sample, a reverse phase column set will provide enhanced resolution and separation of the paraffins (n- and iso-) and naphthenes [26, 27]. Figure 3 illustrates this concept using a blended petroleum cut analysed both on a reverse phase column set and a normal phase column set. As can be seen, when a reverse phase column set is used, the paraffins elute above the aromatics in the 2D chromatogram, and when a normal phase column set is used, the aromatics elute above the paraffins in the 2D separation space. While further optimisation of these separation conditions is required, it can already be observed that the early eluting paraffins have better resolution using the reverse phase column set compared to the normal phase column set.

A plethora of GC stationary phases and column dimensions are commercially available. Once the choice has been made to use either a reverse phase or a normal phase column set, the correct column dimensions must be selected. The ^{1}D column is much longer than the ^{2}D column, but actual dimensions will depend on the type of modulator being used. Table 1 provides a few examples of column sets from petroleum/petrochemical applications where thermal and flow modulation were compared.

3.3 Modulators: Flow vs Thermal

The modulator is the device that differentiates GC-GC from GC×GC. In order for a separation to be fully comprehensive, the modulator must meet certain criteria: 1) all eluates from the ^{1}D column must be trapped while the separation continues, 2) the analytes must be refocused in either time or space, and 3) the modulator must rapidly inject the packets onto the ^{2}D column for further separation [31].

Selecting the correct modulation time is crucial. If the modulation time is too long, the analytes separated in the ^{1}D column will become re-mixed during the refocusing step, resulting in a sub-optimal second dimension separation. If the modulation time is too short, wraparound will be observed, which occurs when the modulation time is shorter than the retention time of the latest eluting compound in the ^{2}D separation.

In addition to the modulation time, sampling rate is another important parameter that must be considered. Each ^{1}D peak must be sampled three to four times in order to maintain the sensitivity of the resolution from the first dimension separation in the second dimension [32].

Two classes of modulators are available for GC×GC: thermal and flow modulators

3.3.1 Thermal Modulators

The first modulators for GC×GC were thermal based [33]. Thermal modulators utilise cooling and heating to effectively trap the eluent exiting the ^{1}D column and inject the contents onto the ^{2}D column. Different types of thermal modulators are available, specifically resistively heated trap, heated sweeper, and cryogenically focused [34]. Compared to flow modulators, thermal modulators can struggle to trap the more volatile compounds.

A cryogenic modulator utilising liquid nitrogen can trap analytes as low as C3. The liquid nitrogen pulse traps the analytes, and a hot jet pulse is then used to mobilise the analytes onto the ^{2}D column. In this setup, single stage and dual stage modulation is possible without the need for moving parts; however, not all laboratories are equipped to handle cryogenic liquids.

Cryogen-free thermal modulators are also commercially available, where chillers can cool dry nitrogen gas down to -90°C. Such systems are successful in trapping analytes as low as C8, and a hot jet pulse is used

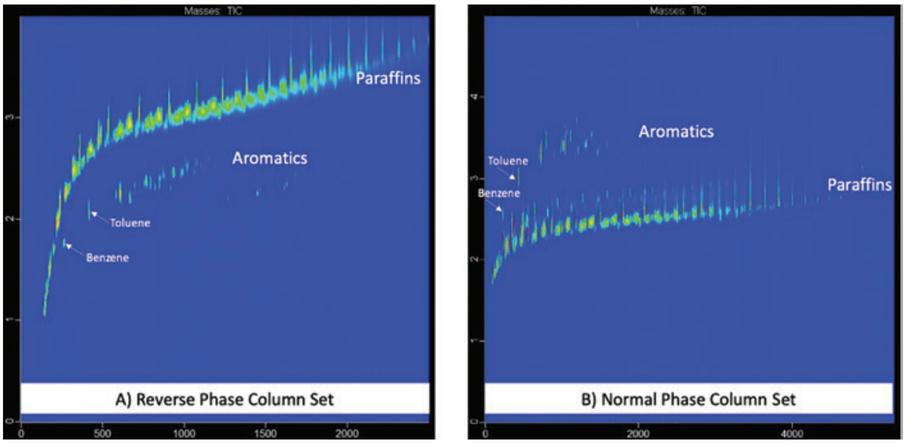

Figure 3: GCxGC-TOFMS analysis of a blended petroleum cut using A) a reverse phase column set, and B) a normal phase column set.

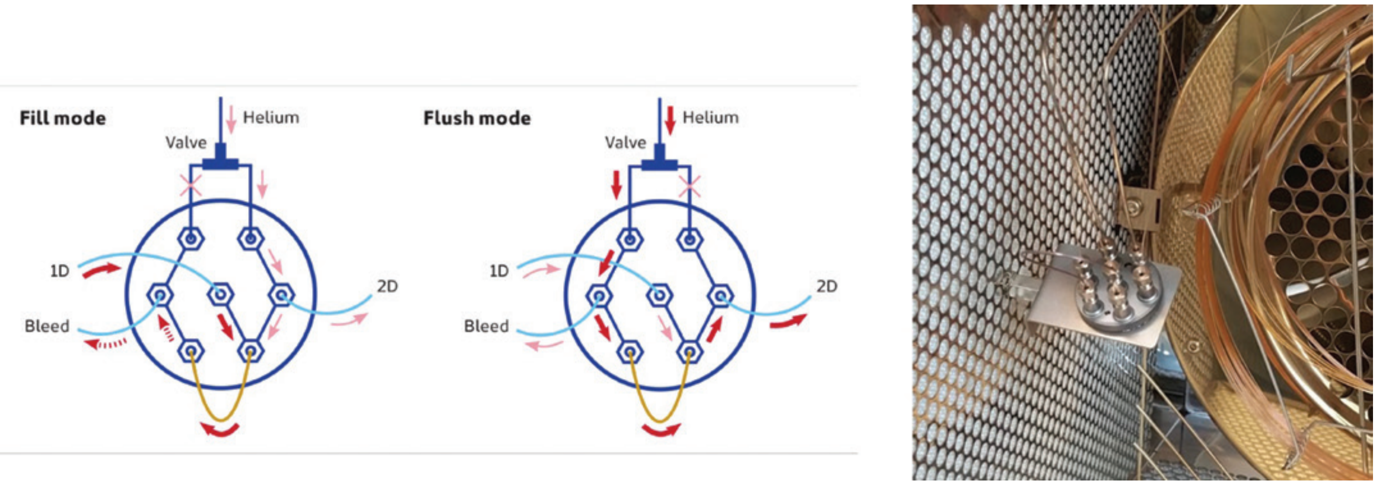

Figure 4: Schematic (Left) and photo (Right) of the RFF valve-based INSIGHT modulator for GCxGC. In fill mode, the primary column eluate enters the sample loop (with any overfill directed to a bleed line), while the modulation valve directs auxiliary carrier gas to the secondary column. The valve switches and the contents of the sample loop are flushed rapidly onto the secondary column as a narrow band. Image courtesy of SepSolve.

to release the trapped analytes onto the ^{2}D column. This modulator configuration also has no moving parts; however there is another option available which utilises specified modulator columns in combination with a thermoelectric cooler and micathermic heaters to trap analytes down to -50°C and release the analytes. Dual stage modulation is achieved on this solid state modulator by moving the modulator column back and forth, into and out of the cold zone. Four types of modulator columns are available depending on the boiling point range of the analytes: EV (C2 - C12), HV (C5 - C30), SV (C7 - C40), and DV (C9 - C40+) modulator columns.

Compared to flow modulators, thermal modulators are more easily coupled to MS detectors; this owes to the fact that thermal modulators do not require high flow rates for the second dimension separation.

3.3.2 Flow Modulators

Differential and diverting flow modulators are commercially available options for flow modulation, and they vastly differ in how they operate. Differential flow (or pulsed flow) modulators utilise switching valves to collect the eluent exiting the ^{1}D column in a loop. This loop is then flushed with the carrier gas to inject the contents onto the ^{2}D column. The first flow modulators operated using a forward fill/flush (FFF) approach, where the loop was filled and then flushed with the flow in the same direction [35]. Nowadays, the reverse fill-flush (RFF) modulator (Figure 4), which fills the loop in one direction and flushes the loop in the opposite direction [36], is preferred. In many aspects, the FFF and RFF modulators have similar performance in terms of detectability and when sample solutes have low or similar concentration; however, the RFF modulator outperforms the FFF modulator for samples with a wide dynamic concentration range [37]. Differential flow modulation relies on very fast ^{2}D flow rates to afford high peak capacity in the second dimension, where coupling to MS detection is more challenging and requires the ^{2}D column flow to be split, adding complexity to the instrumental setup.

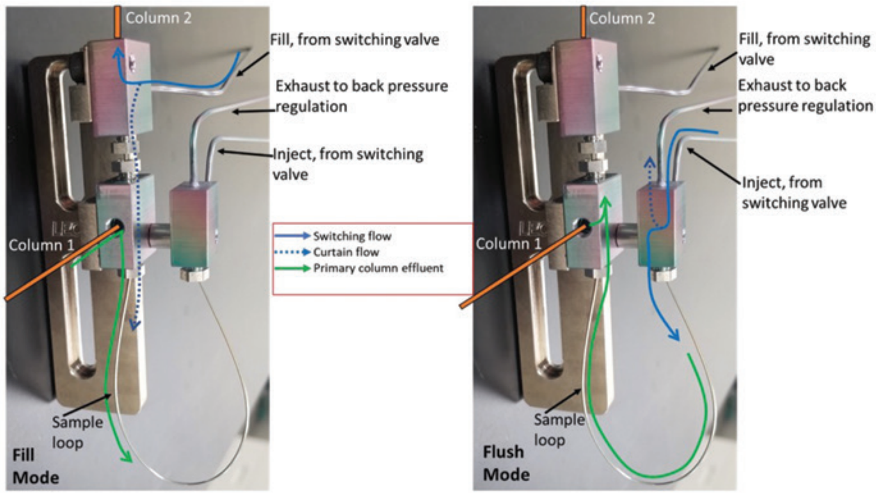

Figure 5: Prototype RFF modulator for GCxGC. Instead of an auxiliary pneumatic control module controlling the pressure and flow of gases, a back pressure regulator is used. In this design, the sample loop does not need to be changed when optimising or changing the modulation parameters. Image courtesy of LECO.

A new advancement in differential flow modulation is currently in development at LECO, where a back pressure regulator is being used for pressure control instead of an auxiliary pneumatic control module. This prototype RFF modulator (Figure 5) is expected to simplify method development, as the sample loop does not need to be changed when changing modulation conditions.

Diverting flow modulation utilises auxiliary gas flows to perform the modulation. In inject mode, the flow from the ^{1}D column is transferred to the ^{2}D column; however, in divert mode, the auxiliary gas flow opposes the ^{1}D column flow, diverting it to waste while supplementing the ^{2}D column flow [38]. Diverting flow modulation allows for ^{2}D column flow rates similar to those of thermal modulators, allowing for easy coupling to MS detectors. However, one drawback to the diverting flow modulator is the loss in overall sensitivity compared to other modulator types, which is a result of the ^{1}D column eluent being diverted to waste and thus, never reaching the second dimension.

Overall, flow modulators can handle a wider range in sample composition, especially for highly volatile samples, compared to thermal modulators. Flow modulators are capable of modulating compounds ranging from C1 - C40+.

3.4 Detectors

In principal, any GC detector can be coupled to a GC×GC separation; however, care must be taken in detector selection to ensure

Table 2: Recent Examples of Petroleomics Biomarker Evaluations.

Application	Techniques	Source	Potential Biomarkers	Reference
Petroleum oil & condensate	GC×GC-TOFMS GC-MS GC-IRMS*	Browse Basin, Australia	Methyladamantanes Methyldiamantanes Di-, tri-, tetra-methylbenzenes	[60]
Bitumen	GC×GC-TOFMS	Ondo State, Nigeria	1,2-benzenedicarboxylic acid, diisooctyl ester 1,2-dimethyl propyl benzene 1,2,4-benzenetricarboxylic acid(1,2-dimethyl)ester 1,3-benzenedicarboxylic acid, 5-(1,1-dimethyl ethyl) 1,2-benzenediol, 3,5-bis(1,1-dimethylethyl) 1,3-dimethylbutyl benzene 2,4-dimethyl benzo(H) quinolone	[61]
*Isotope ratio mass spectrometry (IRMS)				

reliable data is collected. The narrower the peak width in the ^{2}D separation, the higher the peak capacity. When considering two peaks with the same area, the peak with the narrower peak width will be taller, which will increase sensitivity; however, a narrower peak will mean that a faster data collection rate is required to ensure enough data points are collected for reliable quantification. The type of modulator and the ^{2}D separation conditions (column, flow, etc.) will affect the ^{2}D peak widths. Nonetheless, typical modulated peak widths range from 50 - 600 ms at the base, and the detector should sample a minimum of 6 - 10 data points per peak. Thus, a minimum data rate of 20 Hz is required, but 100 Hz is often preferred, to sufficiently sample peaks to obtain adequate peak shape.

The detector of choice for GC×GC petrochemical applications (e.g., PIONA quantification) is the flame ionisation detector (FID) [39]. The FID has excellent response to hydrocarbons and has a data collection rate greater than 100 Hz. This is not to say that other GC detectors have not been utilised. The electron capture detector (ECD) [40, 41], sulphur chemiluminescence detector (SCD) [42], nitrogen chemiluminescence detector (NCD) [43, 44], and nitrogen phosphorus detector (NPD) [45] are all playing a role in GC×GC petrochemical applications.

One of the most powerful detectors for GC×GC is the mass spectrometer. The time-of-flight mass spectrometer (TOF-MS) is one of the most widely used MS detectors in GC×GC applications; this is due to its fast acquisition rate, which is capable of sampling the narrowest (50 ms) of modulated peaks. Additional benefits include the compound library for identifications and the possibility to deconvolute co-eluting peaks in the ^{2}D chromatogram. Other MS detectors are also utilised in GC×GC applications, such as single quadrupole (qMS), high resolution (HR) TOF-MS, qTOF, and triple quadrupole (QqQ)MS, but to a lesser extent compared to TOF-MS [46].

When coupling MS detectors to GC×GC utilising differential flow modulation, one must consider the flow exiting the ^{2}D column, which can easily be greater than 20 mL/min, far exceeding the capabilities of the MS detector. Therefore, a splitter is typically used to direct only a small portion of the ^{2}D column flow to the MS detector and a larger portion to a second detector, such as an FID. While this does result in a loss of sensitivity, there is the added benefit of simultaneously obtaining MS data for identifications and FID data for quantification [29, 47].

3.5 Applications and Trends

With the advancements made in modulators designs, robustness, and in the data processing software, petrochemical applications have taken off in many different directions. Some of the more recent applications and trends will be highlighted here.

Improvements in modulation are still being investigated. In order to afford longer ^{2}D columns to increase the number of theoretical plates and thus peak capacity, stop-flow GC×GC was introduced in the early 2000's [48]. As the name suggests, the ^{1}D column flow is temporarily stopped during the modulation cycle while the ^{2}D separation occurs. While stop-flow GC×GC provides better resolution compared to conventional GC×GC, it is less attractive to some users and as such, wide-spread implementation has not occurred [49]. In 2020, an article was published introducing quasi-stop-flow modulation for GC×GC, which yielded excellent repeatability and chromatographic performance for the gasoline and light cycle oils evaluated [50]. The novelty in this approach was that neither an auxiliary pneumatic control module nor an elaborate microfluidic device was required, making this a simple, cost effective solution suitable for quality assurance laboratories.

There is an increasing trend toward the use of GC×GC for chromatographic fingerprinting; in the petroleum/petrochemical industry. The first application using GC×GC to identify the source of a marine oil spill was in 1999 [51]. Since then, GC×GC has proven invaluable in marine oil spill source identification using fingerprinting to compare samples and match the oil spill to a source. Recently, GC×GC-FID and GC×GC-HR TOF-MS were used to evaluate the complexity of the source oil from two iconic oil spills that occurred in the Gulf of Mexico, specifically the 1979-1980 Ixtoc I blowout and the 2010 Deepwater Horizon explosion; differences in the dibenzothiophene and alkylated dibenzothiophene regions of the GC×GC chromatograms enable differentiation between the Ixtoc I Oil and the Maconda Oil from Deepwater Horizon incident [52]. GC×GC fingerprinting is also being used to assess bioremediation, where recent examples include the evaluation of the photodegradation of polycyclic aromatic hydrocarbons (PAHs) in surface oil from marine oil spills and the biodegradation of PAHs and heterocyclics from refinery waste waters [53-55].

The complete characterisation of petroleum and its derivatives is known as petroleomics, and when first described, focus was placed on the analysis of petroleum using (ultra) high resolution mass spectrometry, such as with Fourier Transform Ion Cyclotron Resonance Mass Spectrometry (FT-ICR MS) [56]. In recent years, the significant impact GC×GC can have in the "omics" space has been realised with several articles being published in recent years [57-59]. While complete characterisation is often sought after, the identification of biomarkers is also an important aspect in 'omics' analyses; this is also the case in petroleomics. Table 2 highlights two recent examples of biomarker identification [60, 61].

4. Conclusions

The authors expect comprehensive separations to increase in the number of published applications for both comprehensive LC (LC×LC) and comprehensive GC (GC×GC). Further improvements are expected to occur in software - including data acquisition, data analysis, and method development - and hardware, such as modulator and detector technology.

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