Molecular Fingerprints and Speciation of Crude Oils and Heavy Fractions Revealed by Molecular and Elemental Mass Spectrometry: Keystone between Petroleomics, Metallopetroleomics, and Petrointeractomics

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Sara Gutiérrez Sama[1,2,4], Mathilde Farenc[1,4], Caroline Barrère-Mangote[1,4], Ryszard Lobinski[2,4], Carlos Afonso[3,4], Brice Bouyssière[2,4] and Pierre Giusti [, 1,4]*

[1] TOTAL Refining and Chemicals, Total Research and Technologies Gonfreville, BP 27, 76700 Harfleur, France

[2] CNRS/ Univ Pau & Pays Adour, Institut des Sciences Analytiques et de Physico-Chimie pour L'Environnement et les Materiaux, UMR5254, Lcabie, 64000, Pau, France

[3]CNRS/Université de Rouen, UMR 6014 COBRA, 1 rue Tesnière 76821 Mont Saint Aignan Cedex, France

[4] TOTAL RC – CNRS – Univ. Pau - Univ. Rouen, Joint Laboratory: C2MC - Complex Matrices Molecular Characterization

ABSTRACT

Petroleum and its fractions are some of the most complex mixtures found in analytical chemistry. Mass spectrometry currently plays an increasing role in the characterization of these matrices. Since the last review on this topic in 2011, several new approaches have been introduced, and these approaches increasingly use sample fractionation by extraction and/or liquid chromatographic techniques. This review considers molecular mass spectrometry and inorganic mass spectrometry. The combination of both techniques paves the way to "petrointeractomic" approaches.

INTRODUCTION

Petroleum is one of the most complex mixtures on earth. It has been described by Boduszynski as a "continuum distribution of molecular weight, structure and functionality from the low boiling point to the non-distillable residue".[1] For many years, petroleum has been used as a benchmark for evaluating the performance of the most sophisticated analytical instruments. Recent advances in modern analytical methods currently provide detailed information on the molecular composition of petroleum. The use of analytical techniques, such as comprehensive gas-phase chromatography or ultra-high-resolution mass spectrometry, is at the origin of the development of untargeted methods for the characterization of petroleum, sometimes referred to as "petroleomics" in analogy to the "omics" approaches in biology, such as genomics and proteomics.[2] Interestingly, this approach can easily reflect the biological origin of petroleum, which was first demonstrated in the identification of petro-porphyrins more than 80 years ago.[3]

In this review, we will discuss various petroleomic approaches to the analysis of petroleum on the molecular and elemental levels. We will also show how the new methods can be used to obtain information on molecular aggregation to obtain insight into "petrointeractomics".

MASS SPECTROMETRY

Molecular Ion Mass Spectrometry. Mass spectrometers use different the behaviors of ions in magnetic or electric fields to determine their mass-to-charge ratios. Because each molecule is composed of different isotopes, the use of the monoisotopic mass instead of the average molar mass is preferred, as it corresponds to a specific isotopic composition.[4,5] Each element and each isotope have a non-integer mass (except the ^{12}C isotope), which allows a mass defect (the difference between the nominal mass and the monoisotopic mass) to be calculated.[6] Thus, the mass defect of an ion determined by mass spectrometry can be used as a unique identifier of its molecular formula, and the accurate measurement of the mass of an ion can be used to determine its molecular formula. Although a molecular formula alone cannot be used to determine the exact structure, when combined with bonding rules, it provides invaluable molecular-level information for complex mixtures.

An exhaustive review[7] on the analysis of petroleum by mass spectrometry was published in 2011 by Rodgers and McKenna. Below, we will present only the developments in the analysis of petroleum using mass spectrometry made in the last three years. The extreme complexity of petroleum mixtures requires the use of ultra-high-resolution mass spectrometry, which is able to separate the 3.4 mDa difference between the nominal masses of C_3 and SH_4 units. For instance, this mass difference is observed between the *m/z* 328 nominal masses of a $C_{23}H_{30}S$ thiophenic compound and $C_{25}H_{28}$ (a hydrocarbon aromatic molecule). Currently, such a high resolving power is only routinely available with Fourier transform instruments, which either use a strong magnetic field (Fourier transform ion cyclotron resonance, FTICR) or an electric field (Orbitrap). In addition to high resolution, these instruments offer highly accurate mass measurements. In particular, FT-ICR instruments using strong magnetic fields provided by superconducting magnets are known to routinely offer sub-ppm mass accuracy in the typical mass range used in petroleomics (*m/z* 100-1000).[8] With such a high mass accuracy, unique

molecular formula can be assigned to each detected ion using common chemical limitations based on the type of molecules expected in a petroleum sample and the type (chemical functionality) of species detectable under specific ionization conditions.[9,10] Data reduction techniques are employed to visualize such a complexity and are presented and discussed in this review.

The other important part of mass spectrometry is ionization. Many ionization methods exist, and they use different approaches to charge molecules in the condensed or gas phase.[11,12] A detailed discussion of the ionization methods is beyond the scope of this review. Due to the large molecular diversity in the components of petroleum, an exhaustive characterization of petroleum involves the use of several different ionization sources. Advances in ionization techniques have provided new molecular-level information about petroleum products (Table 1).

The main ionization methods currently used for the analysis of heavy fractions are electrospray[13] (ESI) and atmospheric pressure photoionization[14] (APPI), as discussed by McKenna and co-workers.[15] The importance of the choice of ionization technique was shown by Gaspar et al.[10] The main advantage of ESI is the coarse selectivity between basic and acidic compounds.[16] As a very soft ionization method, ESI allows intact species to be obtained, which is particularly important for the mass spectrum to be a good representation of the actual molecular composition of the sample. The samples are usually dissolved in a mixture of toluene and methanol with formic or acetic acid added for positive ionization and ammonium hydroxide or tetramethylammonium hydroxide (TMAH) added for negative ionization. The presence of these additives improves the formation of protonated ($[M+H]^+$) and deprotonated ($[M-H]^-$) molecules, respectively, during ionization. ESI is also very selective and primarily leads to the ionization of nitrogen-containing species. It is therefore a useful tool for the speciation of nitrogen-containing compounds, e.g., as shown by Chen et al.[17] in the case of

hydrotreated and untreated shale oil. In practice, the most basic molecules, e.g., those containing a pyridine moiety (i.e., basic nitrogen molecules) are ionized in positive ESI mode, whereas the most acidic molecules, such as alkyl-carbazole molecules, are ionized in negative ionization mode. ESI has been used to characterize different fractions of vacuum gas oil, and the observed differences in composition were identified at the molecular level and correlated to the boiling point.[18]

ESI provides easy access to the basic or acidic compounds present in the petroleum mixtures[19] but can also access other compounds through the use of additives, such as lithium ions to observe S_xO_y compounds[20] or silver ions to observe sulfur-containing compounds.[21] The ability of negative ESI to target acidic species was used together with partial least squares regression to predict the total acid number (TAN) of crude oil samples.[22] Thus, ESI is a powerful tool for observing targeted families of compounds, especially polar compounds.

To obtain information about less polar compounds, in particular, non-basic or non-acidic compounds such as polycyclic aromatic sulfur heterocycles (PASHs), other sources need to be used. These sources include APPI and atmospheric pressure chemical ionization (APCI).[23] Both sources lead to the ionization of molecules in the gas phase through a reaction cascade involving charge exchange and/or proton transfer processes. This cascade is initiated by a corona discharge in APCI and by a vacuum-ultraviolet lamp in APPI. To optimize the ionization yield of APPI, a dopant, typically toluene, is used.[14] Toluene is particularly suitable for the analysis of petroleum products because it is commonly used as a solvent to dissolve the sample. APPI is particularly efficient for the ionization of aromatic compounds as well as cycloalkanes, and thus facilitates the ionization of all fractions of saturates, aromatics, resins, and asphaltenes (SARA) separation.[24] APCI has also been used to characterize PASHs, such as thiophenic compounds.[25] In numerous studies, a combination of at least two sources, i.e., ESI and APPI, was used to characterize the same sample.[26] This approach provides detailed

and comprehensive characterization. Two recent papers showed the importance of choosing the right source for the targeted species by comparing the ionization of the same sample by various sources. Lababidi and Schrader[27] analyzed a crude oil sample using liquid chromatography-UV (LC-UV) and liquid chromatography-mass spectrometry (LC-MS) methods with four ionization sources: ESI, APPI, APCI and atmospheric pressure laser ionization. A very different response was obtained in each. More compounds were ionized by APPI than by the other ionization sources, and ESI was the most selective source. Similarly, Farenc et al.[28] compared the direct introduction of heavy petroleum fractions using ESI, APCI, APPI and atmospheric solid analysis probe (ASAP). The ASAP source was shown to provide a similar ionization profile as APPI, as it is capable of speciating sulfur-containing species. Other ionization sources such as direct analysis in real time (DART)[29] and direct APCI (DAPCI)[30] can be used for the characterization of petroleum samples.

Ion Mobility Spectrometry. Ion mobility spectrometry coupled to mass spectrometry (IMS-MS) has recently been used for the characterization of petroleum samples. Ion mobility spectrometry is a post-ionization gas-phase separation technique that is based on differences in the size, shape, and charge of ions. The ion collision cross section (CCS), an intrinsic property of molecules such as molecular mass, can be determined from the experimentally measured ion drift time from IMS. The first application of IMS-MS was realized by Becker et al.[31] in the study of asphaltene aggregation. Crude oils have also been analyzed by this method, which proved to be efficient for the fingerprinting of petroleum crude oils.[32] IMS-MS is a powerful tool for the fingerprinting and characterization of complex mixtures, as it organizes compounds with the same number of carbons according to their double bond equivalent (DBE).[33,34] IMS-MS has proven to be an efficient method for rapidly characterizing petroleum samples without the requirement of sample pretreatment[35] or preparation.[36] By comparing a feed and a process product, Maire et al.[37] highlighted the presence of PASHs by using IMS-MS. The same

approach was utilized to characterize naphthenic acid extracted from oil sand and to identify the isomeric species.[38] A review on this subject was recently published.[39] The ability to identify isomers was used by Lalli et al.[40] to structurally characterize naphthenic acid extracted from a bitumen sample by solid phase extraction. Finally, the IMS peak width corrected to ion diffusion was shown to be particularly interesting to estimate? the isomeric content of petroleum samples.[41] The first experiments with IMS coupled to MS were performed with a traveling wave ion mobility spectrometer (TWIMS) developed by Giles et al.[42] TWIMS allows for the continuous separation of ions and can be coupled to a time of flight analyzer. Currently, few other techniques exist that can be coupled to an FT-ICR spectrometer, including high-field asymmetric waveform ion mobility spectrometry (FAIMS)[43,44] and trapped ion mobility spectrometry (TIMS).[45,46] FAIMS can be used as a CCS range filter and is easily adaptable to every mass spectrometer, as it can be added to any ionization source. On the other hand, TIMS gives access to the highest CCS resolution but must be designed to operate inside the mass spectrometer.

An easy way to represent bi-dimensional IMS-MS data is through the 2D iso-abundance plot of *m/z* as a function of drift time. As proposed by Maire et al.,[37] this 2D graph highlights the XXX?? content of the petroleum sample. As shown in Figure 1, a sample was compared before and after hydrotreatment using the 2D iso-abundance plot to highlight the species removed by the hydrotreatment method.

The ion mobility provides access to the structural differences within the same class of compounds, as shown in a plot of drift time *vs*. m/z created by Lalli et al.[40] (Figure).

In the same way, Farenc et al.[41] demonstrated how the ion mobility peak width corrected with the ion diffusion factor could be used to obtain valuable information about the isomeric content of petroleum fractions. In particular, the authors showed that petroleum samples with similar contents in the DBE *vs* C# compositional space could be significantly different in terms

of their isomeric contents. The CCS determination can also be used to obtain information about the 3D structure of a molecule.

Elemental Mass Spectrometry. Inductively coupled plasma (ICP) facilitates the formation of positively charged ions of all the isotopes present in a sample after their atomization in a plasma at more than 7000 K. The combination of this ion source with a mass analyzer (ICP-MS) was first introduced in the 1980s.[58] Now commercially available, ICP-MS instruments have proven to be useful in a large range of environmental, geochemical and biochemical studies. Due to its excellent sensitivity and multi-element capabilities, ICP-MS is the most sensitive instrument employed in the analysis of trace elements in petroleum and organic matrices. However, petroleum products are too viscous to be analyzed directly, so sample preparation methods are needed. The most important methods, discussed in detail in several reviews,[59,60] are listed below.

Dilution in an organic solvent, such as toluene, xylene or tetrahydrofuran (THF), is a fast and simple way to prepare petroleum samples for ICP-MS analysis. Other sample preparation methods include mineralization, mainly by microwave acid digestion with HNO_3 or H_2O_2, and emulsification. These methods possess an advantage of introducing the sample in an aqueous form, which avoids the formation of polyatomic interferences and the quenching of the plasma that may occur during the injection of organic matrices into an ICP-MS instrument.

However, the above three pretreatment techniques do not provide access to the low detection limits needed for the quantitative determination of trace elements in crude oil and oil products. This low limit can be achieved by the combination of counter-current chromatography with ICP-MS to preconcentrate the trace metals, including rare earth elements, present in oil samples.[61]

In addition, several developments have been proposed for petroleum analysis in terms of the injection of samples by desolvation systems, such as ultrasonic nebulizers (USN),[52] direct

injection nebulizers (DIN),[62] direct injection high efficiency nebulizers,[63] micro-nebulizers, or electrothermal vaporization (ETV)[55] to reduce the amount of organic solvent that enters the plasma.[56] The use of small quantities of petroleum samples by micro flow injection analysis (μFIA)-ICP-MS was developed by Giusti et al.[57] by heating the nebulization chamber. This method decreases the matrix effects and thus enhances the ultimate limits of detection.

REPRESENTATION OF MS DATA

The high molecular complexity of petroleum leads to the generation of very complex mass spectra. Different graphic approaches have been used over the years to address this complexity. There are two types of graphical representation approaches: (i) one that takes advantage of molecular formula assignment, such as in van Krevelen diagrams, and (ii) one that uses the exact mass (mass defect) in Kendrick plots.

Kendrick Mass Analysis. The Kendrick diagram is based on a mass scale of M(CH_2) = 14.0000 μ? Da proposed by E. Kendrick [50] in 1963. This diagram can be used even if the molecular formula of the compound is unknown. The experimental IUPAC mass, corresponding to M(C) = 12.0000 μ, is easily converted into the Kendrick mass. The calculation of the Kendrick mass is given by the following formula:

$$Kendrick\text{'s mass} = \text{experimental } IUPAC \text{ mass} \times (14.00000/14.01565)$$

As demonstrated by Marshall,[8] data can be represented using the Kendrick mass defect as a function of the nominal Kendrick mass, as shown in Figure . The Kendrick mass defect is given by the difference between the nominal Kendrick mass and the Kendrick mass. The main advantage of this plot is that it clearly highlights compounds with the same repeat unit, usually CH_2, which corresponds to compounds with the same heteroatom content and DBE. Thus, the technique allows facile comparison of complex samples to identify compositional differences prior to elemental composition assignment.

Van Krevelen Diagram. Another method of representing data was developed by D.W van Krevelen[49] and is called the van Krevelen diagram. The elemental composition $C_cH_hN_nO_nS_s$ is needed for this representation, which typically plots the H/C atomic ratio as a function of the O/C or N/C atomic ratio. The first use of this diagram in petroleomics was reported by Kim et al.[48] in 2003 (Figure), but it has also been used for many types of natural organic samples.[64] This diagram can be used to easily compare two samples, but its main drawback is the lack of information about the molecular mass. **(I know what you mean, but this is a bit confusing..)**

Compositional Space (DBE/C#). In van Krevelen plots, the H/C ratio is directly related to the degree of unsaturation, or DBE. The DBE value can be readily calculated from the $C_cH_hO_oN_nS_n$ molecular formula of a compound via the equation DBE = c-h/2+n/2+1. The DBE value is a very good indicator of molecular structure; for instance, a DBE value of 4 for a petroleum hydrocarbon compound will is characteristic of 1 aromatic ring or 4 aliphatic rings.[65] DBE *vs* number of carbons for specific classes of compounds was shown to be a good indicator of the molecular structure, as it provides a graphical representation of the sample from which direct chemical information can be obtained.[66] Currently, the plot of DBE iso-abundance as a function of carbon number, is the most common method to represent data. This plot helps visualize the continuous petroleum compositional distribution obtained from high-resolution mass spectrometric data with regards to a given heteroatom class.[51]

Kendrick plots provide information about the aromaticity and mass of compounds. The relative abundance of the different compounds is often shown using a color code (Figure 5).

This representation is the most colorful and allows one to quickly compare different samples. However, this representation can only be applied to a single class, and the representation of all the classes in a sample requires multiple plots. A Kendrick plot provides an easy comparison between samples, such as the composition of vanadyl porphyrins under different reaction times[67] or the characterization of asphaltene before and after hydroprocessing.[68]

Hexagonal Class. While the previous representation methods present data for a single class, Zhurov et al.[47] proposed a method for simultaneously presenting all the classes of a sample. A graph of the relative abundance (in a colorimetric scale) with respect to a compound class is given in 3D vector space. Each axis of this vector represents the number of heteroatoms, S, N or O, in the class. The remaining corners of the hexagon, which has the CH class in the center, correspond to the classes containing a mixture of the two nearest heteroatoms. Classes with three heteroatoms are combined in a different hexagon with the NOS class at the center. Finally, another graph is used for metal porphyrins, with N_4 in the center and the metals at the corners, and vanadium and nickel are opposite of each other. This method can be used for petroleum sample fingerprinting, as it facilitates easy sample comparison. This representation can also display different data sets in the same graph by simply splitting the sample color-blot into different parts. The representation provides access to useful information but may take a long time to develop.

SAMPLE FRACTIONATION AND HYPHENATED TECHNIQUES

The very high complexity of petroleum samples cannot be resolved by mass spectrometry alone. The first reason is that it is impossible to separate isomeric species, as they have the same mass and molecular formula ~~by definition~~. The other reason is ionization discrimination,[28] together with matrix effects,[69] which hinder complete characterization. In fact, many molecular families in the petroleum mixture cannot be detected because of low ionization efficiencies, and only the most abundant species / those that are easily ionized are detected.[70] For this reason, the use of separation/fractionation techniques prior to MS analysis is required to obtain a complete view of the molecular composition of petroleum. The combination of mass spectrometry with separation techniques has always been an important tool in the analysis of complex samples, and in particular, in the characterization of petroleum-related samples.[7,71] Sample simplification can either be carried out off-line prior to sample

analysis as a preparative step or on-line, by hyphenated separation techniques with mass spectrometry. In general, most separation techniques can be coupled to mass spectrometry. The limiting factor is essentially the acquisition speed of the mass spectrometer, as most ultra-high-resolution mass spectra are obtained within several seconds of acquisition with Fourier transform mass spectrometry instruments. In the future, with the advent of very high-field FT-ICR[72,73] and the use of new acquisition or signal processing,[74,75] the ability to obtain ultra-high-resolution spectra with on-line chromatographic techniques will become easier. In the following section, several general approaches for sample separation/fractionation are discussed together with more specific methods.

Asphaltene Precipitation. Asphaltene precipitation is one of the most common fractionation methods for crude oil, and it creates two fractions, called "asphaltenes" and "maltenes". Asphaltenes represent the most polar fraction of a petroleum matrix; this fraction precipitates in the presence of alkanes but is soluble in hot toluene. The asphaltene fractions obtained from *n*-pentane, *n*-hexane and *n*-heptane are named C5, C6 and C7, respectively. The deasphalted oil (maltenes) fraction is soluble in alkanes. Several standard methods, such as ASTM D6560, provide a precise protocol for the precipitation of asphaltenes, which can contain up to 95% of the metal compounds present in crude oil.[76] Precipitation of the asphaltenes (deasphalting) can also be accomplished by the clay-gel absorption chromatographic method[77], which reduces the metal content by concentrating the metal-containing compounds in this fraction. Because asphaltene molecules contain many aromatic and heteroatomic functional groups, they are known to self-aggregate, which makes characterization of this fraction difficult.

Normal-phase and Reverse-phase Liquid Chromatography. Liquid chromatography (LC) is an interesting tool for the analysis of petroleum matrices and can be easily coupled with MS. This technique is used to separate the different molecules present in petroleum samples according to their physical and/or chemical properties, such as molecular size or polarity, and

can be carried out either in a column (HPLC) or on a surface (thin layer chromatography, TLC). Normal-phase (NP) and reverse-phase (RP) high-performance liquid chromatography (HPLC) techniques are used for lighter fractions. NP columns are more frequently used than RP columns because of the solubility of the samples of interest in organic solvents. Coupled to gel permeation chromatography (GPC) with ICP-MS detection, NP-HPLC was found to provide additional information about the speciation of nickel and vanadium-containing compounds in petroleum products.[78] However, RP-HPLC is carried out for the separation of porphyrins,[71] which are then detected on-line by ICP atomic emission spectroscopy (ICP-AES)[79] or graphite furnace atomic absorption.[80]

TLC is another type of LC that is particularly useful for petroleum analysis. TLC plates are low cost and single-use, which are some of the main advantages of this technique in the analysis of heavy petroleum products. With TLC, the analysis can be performed without prior deasphalting steps, while chromatography columns can be deteriorated by the irreversible adsorption of heavy and/or polar hydrocarbons on the stationary phase and by on-column asphaltene precipitation. Automation of the plate preparation and elution processes increases the chromatographic resolution, the reproducibility of the migrations, and the accuracy of the analyses. An automated TLC/HPTLC procedure can be performed using dedicated instrumentation.[81] Additional information beyond that of the traditional UV-vis and fluorescence activity measured by densitometry is usually necessary for identification of the compounds. This information can be obtained from infrared (IR) spectroscopy, nuclear magnetic resonance spectroscopy or MS[82,83] after the removal of the stationary phase and extraction of the analyte or by direct analysis of the analyte on the stationary phase (*in situ*). Femtosecond-laser ablation-ICP-MS has been used to analyze the vanadium and nickel components of asphaltenes[84] on TLC plates. TLC-laser desorption ionization FT-ICR MS[85]

and DART-MS[29] have been employed in the analysis of crude oil, paraffins and porphyrin standard compounds.

SARA separation is the most widely used sequential extraction method for separating a crude oil sample into different fractions based on solubility and polarity through the use different organic solvent mixtures. This method facilitates the separation of four fractions from petroleum products: saturates, aromatics, resins and asphaltenes, as illustrated in Figure 6.

The classical method of performing a hydrocarbon group-type separation consists of (i) asphaltene precipitation and (ii) an open column chromatographic separation using clay and silica gel as the adsorbent. Standard method ASTM D2007, revised in 2011, is considered a reference for SARA determination. In addition, for evident reasons of facility accessibility and automation, many methods that utilize HPLC for the analysis of hydrocarbon groups have been proposed for the characterization of petroleum samples. Suatoni et al.[86-88] developed a technique for the fast and accurate group type determination in oil samples using a silica column. Silica gel columns coated with silver nitrate[89] or an amino bonding agent can be used to separate saturates from olefins.[90] This technique has facilitated the analysis of hydrocarbon group types in a large number of petroleum products, such as heavy crude oils and gas oil fractions, and established correlations between their properties and chemical compositions using ultraviolet (UV) or refractive index detectors.[5,91-93] There are very few examples of SARA with MS coupling; however, we consider SARA to be worth mentioning in this review since it is commonly used as a rapid preparative technique for obtaining well-separated fractions that can be studied by other analytical techniques, including mass spectrometry.[94,95]

To avoid the preparative deasphalting step prior to hydrocarbon group type analysis, complete SARA fractionation can be carried out by TLC. The advantages of TLC are its low cost, simple instrumentation requirement and high sample throughput. Cebolla and Membrado published several studies on the analysis of hydrocarbon group types in petroleum samples.[96-

[98] The coupling of TLC with laser ablation (LA) ICP-sector field-MS was developed by Vorapalawut et al.[99] to characterize Ni, V, Fe and S and the SARA fractions in crude oils of different origins.

More recently, an automated version of the system (HPLC-2) was developed by Robbins.[100] This system has been applied to the quantitative measurement of the mass and aromaticity of refinery heavy distillates using two detectors: a diode array detector and an evaporative mass detector. The advantage of this method is the ability to separate a number of the hydrocarbon group types, including saturates, mono-, di-, tri-, tetra-, and penta-aromatics, polar compounds, and sulfides. **(New paper will be out before submission of this one… since it is from 1998, you may want to cite the HPLC-3 manuscript).**

Gel Permeation Chromatography. Pre-fractionation of heavy petroleum products, such as pitches and asphaltenes, can be accomplished by size exclusion chromatography (SEC) to decrease the wide polydispersity of the products prior to MS analysis. Off-line or on-line coupling of SEC with mass spectrometry can be used.[101] This separation technique, also known as GPC in organic applications, is very popular for petroleum analysis due to the importance of the size distribution of the aggregates on the optimization of the catalyst pore size for the hydrotreatment.[60,71,78,102,103] This technique also provides the characteristic size distribution profiles of the samples.[78,104] Prep-scale GPC columns allow narrow molecular weight fractions to be obtained at higher solvent flow rates and sample injection volumes than those employed in conventional GPC columns. Thus, more material can be collected for further MS analysis of the fractions, and the identification of individual molecular species can be performed to improve the characterization in terms of the molecular size and structure.[105,106] SEC is used for the analysis of heavy fractions via element-specific detection, such as ICP-AES[107-109] or ICP-MS.[78,102,103,110] The analysis of SARA fractions, separated on a silica gel chromatographic column, has been performed off-line via GPC ICP-MS by Vargas et al. for the quantification

of V, Ni and S compounds in petroleum products (vacuum residues). The low molecular weight fractions were found to have the lowest content of highly polar compounds.[94,95,111]

Interfacial Material (IM) Isolation. In the case of emulsion studies, the molecular composition of the water/oil interface of a crude oil, known as the interfacial material (IM), is of particular interest because it defines the emulsion stability. Because IM represents a very small part of a crude oil sample, a specific extraction step must be conducted prior to molecular characterization. Wu developed a method based on the use of heavy water (D_2O) to create a water/oil emulsion for the isolation of the IM from crude oil.[112] Later, the "wet silica method" was developed by Jarvis et al.[113] This method allows for the simple and fast isolation of the IM for subsequent molecular analysis by using hydrated silica as the stationary phase. Clingenpeel et al.[114] reported that the optimum water content was of 66 g water/ 100g silica. The IM isolated by both methods could be further analyzed by various analytical techniques, such as FT-ICR MS[113] or GPC ICP-MS.[115]

Ultrafiltration. Ultrafiltration (UF) is another method for decreasing the size polydispersity of heavy petroleum fractions and crude oils. This technique allows for the recovery of large quantities of the separated fractions for further characterization of their structures and chemical compositions. This method separates asphaltenes using porous membranes with a 1-1000 kDa molecular weight cut-off, leading to a higher size selectivity than that obtained by fractionation based on solvent solubility.[116] Thus, pure crude oil samples can be obtained with negligible asphaltene loss and the removal of water from emulsions.[7] UF also allows for the separation of small asphaltene aggregates from larger ones. These small aggregates exhibit a lower aromaticity, higher aliphatic composition and lower metal concentration, preferentially enriched in vanadium over nickel, with respect to the larger asphaltene aggregates.[117]

When molecular exhaustivity is the target, the sample must be fractionated before characterization. Two different strategies can be used: (i) pretreatment of the sample or (ii) hyphenated techniques. The main reported methodologies are summarized in Table 2.

ON THE WAY TO PETROINTERACTOMICS

Boduszynski proposed the "continuum distribution of molecular weight" in crude oil samples. This distribution, originally proposed after the analysis of crude oil by field ionization and field desorption mass spectrometries,[1] has been fully demonstrated in all the different crude oil fractions by the use of FT-ICR MS techniques.[7,15,118-121] These distributions can be seen in all the representations of the MS data presented previously in this paper. However, all these techniques suffer from a loss of crucial information: the interactions of all these molecular families with each other. In GC analysis, the interactions are lost in the injector or on the stationary phase, as is also the case in normal-phase LC, and in the ionization source in MS.

Aggregates have been suggested to trap other kind of molecules (metals porphyrins, aliphatic compounds, etc.) within aggregates based on experimental results[122,123] and molecular modeling[124] studies.

Thus, interactions between molecules must be considered if the properties of crude oil from the well to the refinery are to be understood. Because the overall properties of the crude can be affected by aggregates or "hidden" molecules that are trapped or chelated, the design of an experimental setup for studying these molecular interactions is of primary importance.

This "petrointeractomic" information is likely to be obtained in the coming years by using a combination of separation techniques that could preserve the supramolecular information, or aggregation state, and MS techniques.

CONCLUSION

This review has provided an overview of the different MS strategies used to characterize petroleum samples. Due to the complexity of this type of sample, three main complementary

strategies have been employed. The first is the use of high- to ultra-high-resolution techniques. In this case, direct introduction can provide significant results and allow for the use of a variety of ionization sources with different specificities. Moreover, the large quantity of data produced by high-resolution instruments lead to the necessity of pretreatment before their use. The main methodologies and their specificities and applications were summarized in Table 1. However, due to the limitation of each individual type of atmospheric ionization mode in MS, the sample must be fractionated before analysis to obtain the largest amount of molecular information. Supramolecular knowledge, the third level of information, requires separation according to size or shape and is, from our point of view, the essential link to understanding some of the unexplained properties and behaviors of crude oil.

AUTHOR INFORMATION

Corresponding Author

* *Telephone: +33-235-551-432. Fax: +33-235-551-284. E-mail: pierre.giusti@total.com

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Tables

Table 1. Comparison of the main high-resolution MS techniques applied to the direct detection of petroleum samples

Elemental/ Molecular	Specificity		Method	Applications
Molecular	All petroleum samples and fractions Many ionization sources available [10,27] Need for data treatment method	Ionization sources	ESI	***Highest selectivity for basic and acidic compounds[16]*** Suitable for speciation of nitrogen[17], S_xO_y species with lithium cationization[20], sulfur with silver cationization,[21] acids[22]
			APCI	***Facilitates ionization of polar to nonpolar compounds.*** Suitable for sulfur compounds such as PASHs,[23] including thiophenic compounds[25]
			APPI	***Highest ionization efficiency***[15] Requires a dopant, such as toluene[14] Facilitates ionization of all SARA fractions[24]
			ASAP	***Similar to APPI, no sample preparation[28]***
			DART	***No sample preparation, possibility to analyze surfaces, TLC plates, etc.***[29]
		Data treatment	Hexagonal class	***Provides an overview of the heteroatomic class composition of a sample***[47]
			van Krevelen	***Provides a fingerprint of the sample as a diagram representing all of its components according to their H/C and O/C ratios[48,49]***
			Kendrick	***Provides a fingerprint of the heteroatomic classes as a diagram representing the Kendrick mass defect vs nominal mass*** [8,50]
			Compositional space	***Provides a fingerprint of the heteroatomic class as a diagram representing DBE vs number of carbons***[51]
Elemental	All petroleum samples and fractions Different sample preparation methods available			Mineralization or emulsification of samples through the use of new-generation nebulizers[52-57], which limits destabilization of the plasma

Table 2. Comparison of the main pretreatment strategies used for simplification of petroleum samples

Method	Principle	Applications
Hydrocarbon group type simplification (SARA type and other types)	***Separation of the sample into several fractions by solubility in different solvents*** The first step is often asphaltene precipitation, which is followed by adsorption chromatography and elution with a solvent of a different polarity. *Preparative scale before analysis or on-line detection* TLC-style SARA is suitable for characterization of heavy compounds	Characterization of the petroleum sample fractions by suitable techniques
IM isolation by the wet silica method	Extraction of the IM from a sample diluted with heptol by hydrated silica. The IM is recovered by elution with methanol.[113,114]	All water/oil interface or emulsion properties
Preparatory scale GPC	Separation of a large amount of sample by preparatory scale GPC columns	Aggregation studies of heavy compounds Decreasing the polydispersity of samples before MS analysis[105,106]
Ultrafiltration	Separation of a sample using porous membranes[116]	Aggregation studies of heavy compounds Speciation of asphaltene by size[116]

Figures

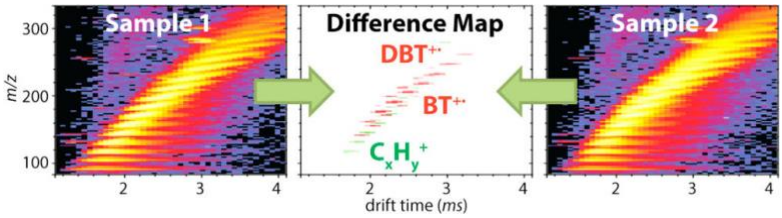

Figure 1. Comparison of diesel fuel before and after hydrotreatment, as analyzed by IMS-MS

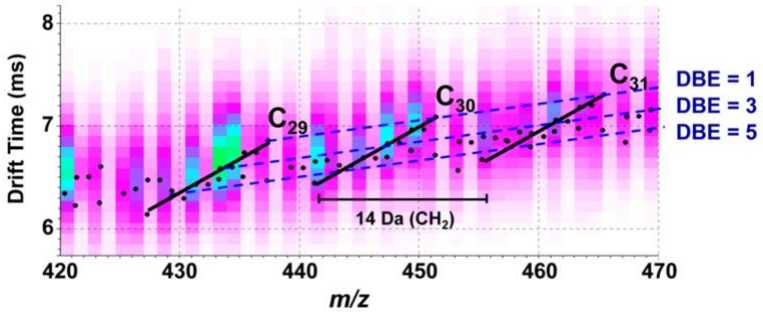

Figure 2. Scale-expanded segment of drift time *vs m/z* from a naphthenic acid fraction. Copyright 2015 American Chemical Society

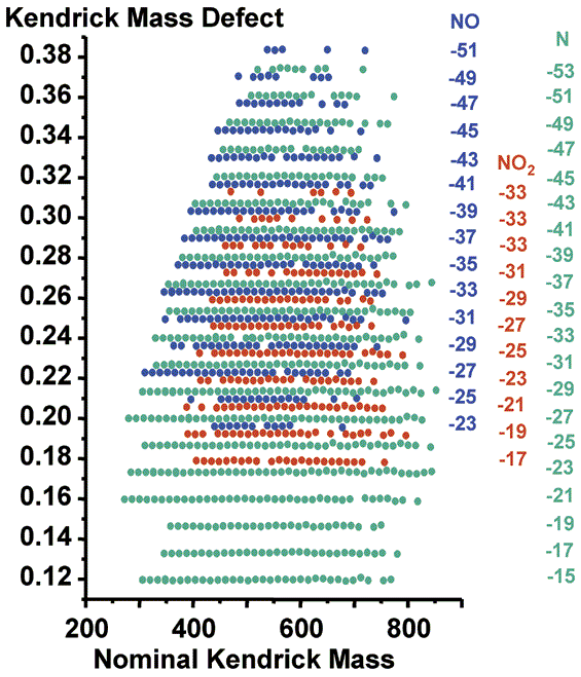

Figure 3. Kendrick mass defect *vs* nominal Kendrick mass (full mass range) for even-mass ^{12}C ions. Copyright 2001 American Chemical Society

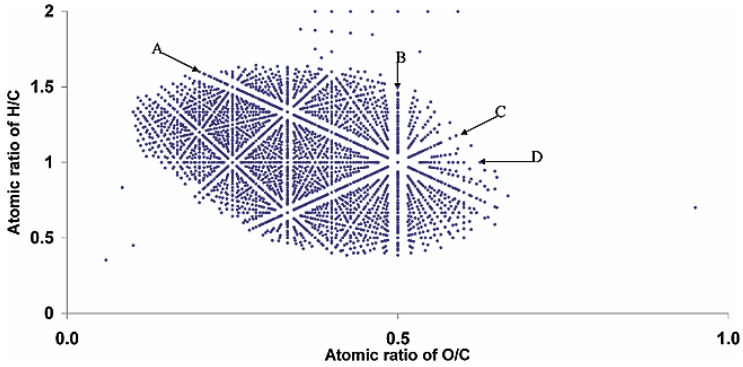

Figure 4. The van Krevelen plot for elemental data calculated from the ultra-high-resolution mass spectrum of dissolved organic matter in the McDonalds Branch basin. Copyright 2003 American Chemical Society

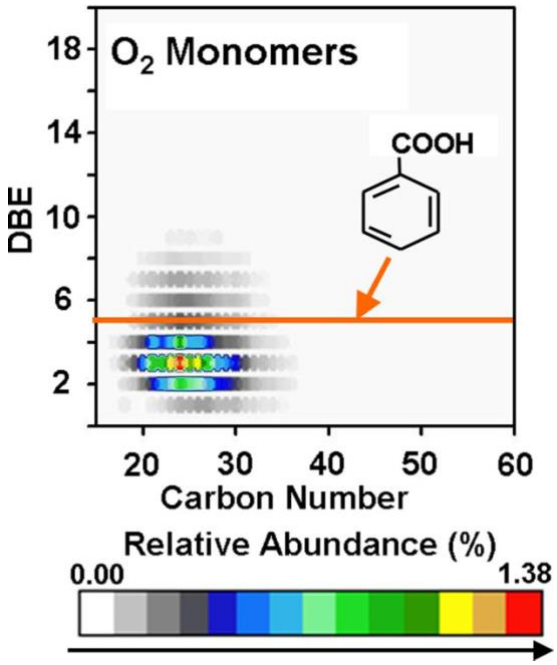

Figure 5. Plots of DBE *vs.* carbon number for a distillation fraction from Athabasca bitumen. The O_2-containing molecules (carboxylic acids) are not aromatic because their DBE values are below 5.[2]

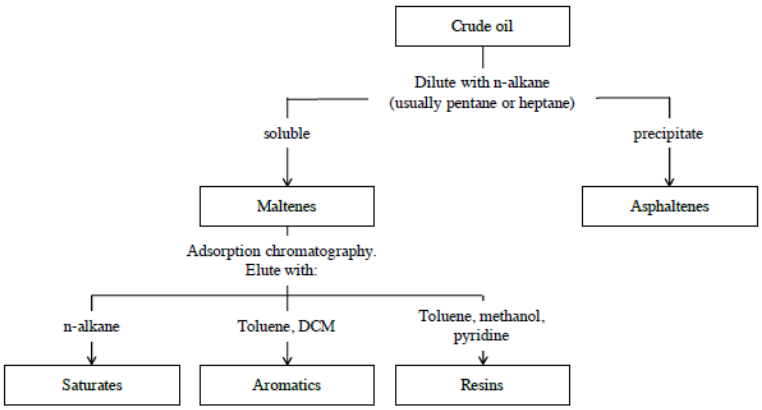

Figure 6. SARA separation scheme of crude oil (Later, D. W.; Lee, M. L.; Barlte, K. D.; Kong, R. C.; Vassilaros, D. L. Anal. Chem. 1981, 5 3, 1612-1620.[10]