Among the different techniques for mass analysis, ultra-high-resolution Fourier transform ion cyclotron resonance (FTICR) is the method of choice for highly complex samples, as it offers unrivaled mass accuracy and resolving power, combined with a high degree of flexibility in hybrid instruments as well as for ion activation techniques. FTICR instruments are readily embraced by the biological and biomedical research communities and applied over a wide range of applications for the analysis of biomolecules such as carbohydrates, lipids, nucleic acids, and proteins. In the field of natural organic matter (NOM) analysis, petroleum-related studies currently dominate FTICR-MS applications. Recently, however, there is a growing interest in developing high-performance MS methods for the characterization of NOM samples from natural aquatic and terrestrial environments. Here, we present an overview of FTICR-MS techniques for complex, non-petroleum NOM samples, including data analysis and novel tandem mass spectrometry (MS/MS) methods for structural classifications. © 2020 The Authors. Mass Spectrometry Reviews published by John Wiley & Sons Ltd.

Keywords: Fourier transform ion cyclotron resonance (FTICR); natural organic matter (NOM); data analysis; fragmentation; electron-based ion dissociation (ExD)

I. INTRODUCTION

Over 100 years ago, Francis W. Aston proved the existence of stable isotopes (Aston, 1919). In recognition of this contribution, he was awarded the Nobel Prize in Chemistry in 1922 “for his discovery, by means of his mass spectrograph, of isotopes, in a large number of non-radioactive elements, and for his enunciation of the whole number rule” (Squires, 1998). Rapid progress in the later 20th century contributed significantly to further developments of mass spectrometry (MS) (Glish & Vachet, 2003), making mass spectrometry one of the most powerful analytical methodologies today for identifying the elemental compositions of known and unknown compounds (Aebersold, 2003; McLafferty et al., 1999; Rodgers & McKenna, 2011).

Nowadays, high-resolution mass spectrometry (HRMS) instruments such as Fourier transform ion cyclotron resonance mass spectrometry (FTICR-MS) (Amster, 1996; Marshall, Hendrickson, & Jackson, 1998) are used extensively in the field of pharmaceutical, biological, biomedical and environmental analyses. The widespread use of FTICR-MS is mostly due to its superior mass accuracy and ultra-high mass resolving power. For example, an analyte at a concentration of one part-per-billion (ppb) can be routinely detected and distinguished within a complex chemical mixture (Moyer et al., 2003), while the fine structure of isotope peaks in the mass spectra can also be measured with a mass error of less than 200 ppb (Nikolaev et al., 2012). During the 45 years since the inception of FTICR-MS (Comisarow & Marshall, 1974), a large number of FTICR review articles have been written, contributing to all aspects from application to instrumentation (Holliman, Rempel, & Gross, 1994; Meng et al., 2005; Nikolaev, Kostyukevich, & Vladimirov, 2016; Park and Lebrailla, 2005; Qi & O’Connor, 2014; Sinz 2006). At the same time, most of the FTICR literature on natural organic matter (NOM) is dedicated to petroleum-related analyses (Cho et al., 2015; Headley, Peru, & Barrow, 2015; Liu et al., 2017), with significantly fewer studies on organic aerosols, plants (Park et al., 2013), food (Ibáñez et al., 2015), and beverages (Cooper & Marshall, 2001). The present article provides an overview of recent progress in NOM analyses by FTICR-MS, with particular emphasis on non-petroleum research. The article describes applications as well as method and technical developments, namely: (i) lignin analysis; (ii) beverage analysis; (iii) LC-MS of NOM; (iv) electron-based ion fragmentation (ExD) methods, including two-dimensional (2D) FTICR-MS; (v) aerosols; (vi) dissolved organic matter (DOM); and (vii) timber analysis. In these applications, FTICR-MS is able to readily assess the complexity of ultra-complex NOM by assigning thousands of compounds with elemental formulae and has also shown its potential to explore their chemical structures.

II. LIGNIN

Lignin is the second most abundant natural polymer after cellulose and a potential source of energy materials (Fig. 1). It is also a
promising source for value aromatic chemicals (Zakzeski et al., 2010). Lignin degradation products are usually phenols with 6–10 carbon atoms, which can be transferred to petroleum-like alkanes via hydrodeoxygenation (Zhang et al., 2013). Moreover, the lignin-originated phenols often have two or more hydroxyl groups, which can serve as reaction sites for synthesis of high value-added polymers such as polyurethane, polycaprolactone and epoxy resin (Tapin et al., 2006). From an earth science point of view, lignin is also a useful biomarker of land-derived organic matters due to its high resistance to degradation (Bugg et al., 2011). Therefore, lignin in sediments has frequently been utilized in geochemical studies of soil, atmosphere, lakes, and marine environments to trace the source of organic matter (Dittmar & Lara, 2001; Simoneit et al., 2004; Khatami et al., 2019), to understand anthropogenic activities and reconstruct the paleoenvironment (Jex et al., 2014). Nevertheless, comprehensive structural characterization of the lignin cleavage products remains a major challenge. The product mixtures often contain thousands of components (including constitutional isomers and isobars) with variable relative abundances (Kiyota, Mazzafera, & Sawaya, 2012). Characterization of individual components at the molecular level, to locate the desired high value-added components, is therefore extremely complicated. Due to the complexity of the structural motifs and variable relative abundances, analytical methods such as ultraviolet (UV)/infrared and nuclear magnetic resonance mostly provide only crude estimates of average structures and important information on lower abundant building blocks is often missed (Brinkmann, Blaschke, & Polle, 2002; El Mansouri, Vilaseca, & Salvadó, 2012).

Fortunately, FTICR-MS exhibits very high mass accuracy in the sub-ppm range, while consuming only very small amounts of the sample. For example, full-scan analyses of lignin samples generated thousands of mass-to-charge ratio (m/z) features per sample. The individual compounds’ accurate masses and elemental formulae, however, were readily determined (Qi & Volmer, 2019a). As lignins exhibit a similarly complex set of components as crude oil (the “petroleome”), Morreel et al. coined the term “lignome” to describe the full suite of lignin-associated phenolics. The required profiling and identification methods (Morreel et al., 2010a,b) are similarly extensive as those used for crude oil, necessitating chromatographic separations, HRMS (Jarrell et al., 2014; Owen et al., 2012) and subsequent tandem MS (MS/MS) experiments to obtain detailed information on individual structures. Morreel et al. (2010b) elucidated the gas-phase fragmentation behavior of several standard compounds linked to the lignome using collision-induced dissociation (CID), which can be used for detailed characterization of lignin oligomers. Owen et al. (2012) demonstrated a strategy for the identification of lignin degradation products in the negative ion electrospray ionization (ESI) mode, giving elemental compositions from accurate mass measurements by FTICR-MS, followed by detailed CID experiments for structural information. These and several other structural protocols only work for a few selected compounds, however, but are not well-suited for obtaining detailed information on thousands or tens of thousands of individual components in heterogeneous lignin mixtures. For example, Figure 2 shows the peak density of a full-scan mass spectrum of lignin degradation products. A region of 0.3 m/z units was further expanded in the figure, exhibiting a total of 19 assigned features (Qi, Hempelmann, & Volmer, 2016a). Even though each peak represented a chemically distinct compound, most of their structures remained unknown in the analyses. Moreover, different ionization techniques, such as ESI, atmospheric pressure photoionization (APPI), atmospheric pressure chemical ionization (APCI), laser desorption/ionization (LDI), and matrix-assisted laser desorption/ ionization (MALDI), exhibited different selectivities for the various types of organic compounds (Hertzog et al., 2017; Kew et al., 2018;
Qi & Volmer, 2019b). For example, Figure 3 shows a van Krevelen diagram to visualize the data obtained from FTICR-MS analyses (Kim, Kramer, & Hatcher, 2003), by arranging the molar ratio of hydrogen-to-carbon (H/C ratio) as ordinate and the molar oxygen-to-carbon ratio (O/C ratio) as abscissa. The diagram shows variations of observed NOM ion species due to the use of different ionization techniques. A similar phenomenon can also be observed with respect to different NOM extraction methods (Mopper et al., 2007).

Considering the enormous complexity of the lignin degradation products, scientists adapted data analysis methods that are widely applied in petroleomics research. Lignin was merely used as an example to demonstrate how the complexity of full-scan mass spectra can be reduced and the data qualified, and how hidden information at the molecular level can be revealed. Similar strategies can be applied equally well to other complex NOM samples. The following section explains the graphical and statistical procedures with the goal of obtaining the maximum number of mass spectral features.

Kendrick mass defect (KMD) plots are the most straightforward approaches, providing useful overviews of very complex mass data sets (Hughey et al., 2001). A KMD plot is widely applied for crude oil samples to identify different compound classes (Hughey et al., 2001). In the original application, the m/z scale was converted from 14.01565 to 14.00000 u using the repeating CH2 unit (Equation 1):

$$\text{Kendrick m/z} = \text{IUPAC m/z} \times \left(\frac{14}{14.01565}\right)$$  

(1)

Hence, compounds with the same number of heteroatoms and DBE, but different number of CH2 units, will have identical KMDs according to Equation 2:

$$\text{Kendrick mass defect} = \text{nominal Kendrick m/z} \times \frac{m/z\text{-exact Kendrick m/z}}{\text{IUPAC m/z}}$$  

(2)

Importantly, KMD is not limited to the CH2 group; any functional group of interest can be used as base for KMD. Dier et al. (2016) applied KMD plots to interrogate full-scan mass spectral data of lignin degradation products acquired by ESI (Fig. 4): the differences of mass defect along a vertical line provide information on the oxygen content of the products; that is, higher KMD values show higher oxygen content. Most degradation products were observed in the m/z range of 200–500, indicating formation of monomeric to trimeric lignin units, and the measured KMD values and elemental formulae showed that the majority of degradation products exhibited low oxygen content.

The concept of KMD plots was then further expanded to “two-dimensional (2D) mass defect matrix plots,” to process the bulk of the features in the data sets (Qi, Hempelmann, & Volmer, 2016a). Utilizing homologous structural units as complementary m/z scaling
factors offered systematic line-ups of the different lignin linkages using structure-specific metrics. This procedure can directly deduce the candidates’ m/z values and chemical structures from the genealogical links between products and their formation mechanisms. For example, Figure 5 illustrates a small region that was further expanded from the 2D plot. In this magnified view, three series of data points are highlighted (red, green and brown). The measured m/z value for the first (red) point was 163.0389. This precursor ion was revealed by CID to be the [M – H]− species of coumaric acid. The two following, related red data points on the vertical y-axis indicated that two methoxy (OCH3) groups can be attached to the compound. Similarly, on the x-axis, the green and brown data points were both aligned with the coumaryl alcohol series horizontally, which indicated that they shared the same core structure. Subsequent CID experiments confirmed that the structures of these compounds were linked via hydroxyphenyl additions to the coumaric acid core. In addition to the horizontal and vertical axes, the slopes of the slanted lines also exhibited diagnostic potential: reactions that involved loss or gain of a specific elemental formula of structural-related compounds were identified from these trend lines, as theoretically each reaction pathway has its own trend line with characteristic slope and intercept. Figure 6 illustrates that methoxylation was favored over hydroxylation for the selected decomposition products, as abundances were several orders of magnitude higher than those of hydroxylation products.

**FIGURE 4.** (a) KMD plots of a degraded lignin sample for all measured m/z features; (b) data restricted to monomeric/dimeric/trimeric content. The color scale represents relative intensity. Reprinted from Dier et al. (2016), with permission from the American Chemical Society. KMD, Kendrick mass defect. [Color figure can be viewed at wileyonlinelibrary.com]

**FIGURE 5.** 2D mass defect matrix plot for a decomposed lignin sample. Blue points represent features in the KMD plot and correspond to degradation products from the sample. The squared area is enlarged (inset) and proposed core structures of the three compound species (red, green, brown) are highlighted in the expanded plot. Reprinted from Qi, Hempelmann, & Volmer (2016a), with permission from Springer Publishing. 2D, two dimensional; KMD, Kendrick mass defect. [Color figure can be viewed at wileyonlinelibrary.com]

**FIGURE 6.** Top: Visualization of hydroxylation (blue) and methoxylation (red) reaction trend lines for two biphenyl compounds in the 2D matrix plot. The circular points represent acrylic acid-substituted biphenyls; triangular points correspond to biphenyl-2-carboxylic acid. Reprinted from Qi, Hempelmann, & Volmer (2016a), with permission from Springer Publishing. 2D, two dimensional; KMD, Kendrick mass defect. [Color figure can be viewed at wileyonlinelibrary.com]
In addition to the above analyses, which generated the molecular-ion species using different atmospheric pressure ionization techniques, Crawford et al. (2017) utilized ambient ionization techniques to directly provide an analytical assessment of solid lignin powder. In that work, desorption electrospray ionization (DESI) and direct analysis in real time (DART) were systematically compared for direct surface sampling of solid lignin samples, in comparison to the conventional liquid-based infusion methods as described above. The KMD filtering also provided concrete visualization of monomeric, dimeric and trimeric lignin species and allowed core lignin compounds to be quickly and visually compared (Fig. 7).

Van Krevelen diagrams are also widely applied graphical tools for analysis of complex mixtures (Kim, Kramer, & Hatcher, 2003). Qi, Hempelmann, & Volmer (2016b) used a van Krevelen plot to visualize the transformation of lignin compounds during UV oxidation. As seen in Figure 8, the abscissa, representing the O/C ratio, demonstrated significant differences between the photo-degraded sample and the control: the number of species extended much further in the photo-irradiated sample, confirming the formation of oxygenated species. The ordinate (H/C ratio) on the other hand exhibited similar ranges for the two samples, showing comparable double bond equivalents (DBE), suggesting that the degree of unsaturation and the core structural elements were likely not altered during the oxidation process. It is
also interesting to observe that a large number of additional new compounds accumulated in the encircled region, which are aromatic compounds of low oxygen content at low \( m/z \) values. These new compounds corresponded to the large number of low intensity signals in the spectrum, which were the fragments of the UV irradiation. The structural hypotheses deduced from information in the Van Krevelen diagram was subsequently confirmed by MS/MS.

### III. HETEROATOMIC CLASS HISTOGRAMS, DBE VERSUS C NUMBER PLOTS—SCOTCH WHISKY

Scotch whisky is a complex mixture of thousands of NOM-like compounds, the exact identities of which are largely unknown. FTICR-MS is therefore an important tool for exploring the complexity of these spirit drinks and the chemistry of their maturation processes (Garcia et al., 2013).

Kew et al. (2018) compared ESI, APPI, APCI, and LDI mass spectrometry for the analysis of Scotch whisky and illustrated the different distributions of heteroatomic classes by the investigated ionization modes. As shown in Figure 9, the maximum number of oxygen atoms for the four ionization modes extended to 19. LDI provided information starting at \( O_1 \) and delivered generally the largest number of elemental formulae. APPI exhibited very few formulae below \( O_4 \), indicating that it preferably ionized oxygen-rich aromatic compounds (e.g., lignin-derived compounds). It is interesting that the oxygen distribution patterns were somewhat similar for ESI, LDI, and APPI, while APCI was unusual in that it exhibited a local maximum for \( O_4 \) compounds. LDI showed higher abundance for compounds below \( O_4 \). Additionally, DBE versus carbon number plots from that work also illustrated that there was an overlap between the ionization techniques, but complementary data were still obtained by each technique.

In addition, Kew et al. (2017) analyzed a comprehensive set of 85 authentic Scotch whiskies and discovered that the resulting spectra can provide unique chemical fingerprints for each sample. The authors utilized a violin plot to compare the heteroatomic class distribution chemistry of malt and blend whisky (Fig. 10).

It was evident that malt whiskies (with unimodal distribution centered around \( O_{10} \)) exhibited a higher count at each heteroatomic class than blended whiskies (centered at \( O_5 \)). The blends generally exhibited narrower unimodal distribution, whereas malts showed a larger distribution. Interestingly, the \( O_5 \) class was very different between malts and blends. A principal component analysis (PCA) model (Fig. 11a) was constructed from the 85 samples. The blend whiskies were more closely clustered as compared to the malts. This observation was consistent with the heteroatomic class distribution analysis discussed above, which showed greater diversity in the malt sample types. An orthogonal projection to latent structures discriminant analysis (OPLS-DA) model was then constructed, which showed that the malt versus blend model successfully distinguished these two whisky types (Fig. 11b). Upon further analysis, the blended sample was found to represent a premium blended whisky with a high malt content. The three closely positioned single malt outliers (Fig. 11b, top left, circled) represent the same samples grouped as the bottom right outliers in the PCA plot (Fig. 11a). Such distribution plots suggest that the classification of whisky may be possible with statistical analysis of the mass spectral data.

### IV. LC-MS of NOM

Liquid chromatography (LC) is a well-established technique in many bioanalytical fields that reduce the complexity of the sample. Utilization of LC can also aid FTICR-MS analyses for discrimination of various isobaric and isomeric compounds as well as other difficult-to-distinguish molecules from complex samples. Reversed-phase (RP) liquid chromatography in positive ESI mode has dominated untargeted LC-MS applications. However, many NOM samples, in particular DOM, are water-soluble and highly-polar, which are then not well-retained by commercial RP phases (Jarrell et al., 2014). Regular RP separations therefore requires modifications for analyzing environmental samples.

Sandron et al. (2018) used very long monolithic columns (110 cm length \( \times \) 3 mm diameter) to achieve high chromatographic peak capacity for RP-LC-MS characterization of DOM from marine and freshwater sources. The long columns provided the collection of 15 fractions from each DOM sample. Subsequent 2D separation using a second RP column showed that different compounds with the same \( m/z \) values were separated across fractions, highlighting the immensely complex nature of the DOM samples.
Ladd et al. (2019) evaluated hydrophilic interaction liquid chromatography (HILIC) coupled with ESI-MS for characterization of DOM from Arctic soil water extracts. The results showed that the HILIC was more effective for retaining and separating small and highly-polar compounds compared to RPLC (Fig. 12).

Dier et al. (2017) developed phosphonium-based stationary phases for improved separation of highly complex lignin degradation mixtures, as demonstrated by successful separation of the abundant isobaric components of lignin products as well as by sorting chemical classes into distinct retention time regions. The additional separation dimension of unique selectivity allowed for more precise compositional analysis of the complex samples. Most recently, Kim et al. (2019) coupled the novel quadrupolar detection (QPD) FTICR-MS with LC for NOM analysis. QPD retained the resolution, but half the sample acquisition time, thus making FTICR detection times compatible with online LC-MS. Finally, studies by Kujawinski et al. (Kujawinski et al., 2009; Kido Soule et al., 2010) and Boiteau et al. (2019) showed improvements of LC-HRMS approaches to characterize environmental samples and their kinetic properties.

V. ELECTRON-BASED ION FRAGMENTATION OF NOM

Tandem mass spectrometry (MS/MS) has developed rapidly in the last 40 years, making it one of the most important analytical techniques for structural elucidation of organic compounds. Various fragmentation techniques have been developed for MS/MS, most of which can be classified into one of the following two categories: (1) threshold ion activation techniques (such as CID), which excite vibrational modes of the molecules for intramolecular dissociation (Sleno & Volmer, 2004); and (2) electron-based ion fragmentation techniques (ExD), which generate radical ions to initiate the subsequent dissociation process (Zubarev, Kelleher, & McLafferty, 1998). CID is the most widely applied MS/MS method today, as it offers high fragmentation efficiency and compatibility with the time frame of liquid chromatography (Srebalus Barnes & Lim, 2007; Medzihradszky & Chalkley, 2015). However, a major drawback is that CID frequently removes labile modifications and triggers rearrangements, which can lead to wrong structural interpretations (Wuhrer, Deelder, & van der Burgt, 2011). ExD offers complementary information to CID (Zubarev, 2003; Cooper, Håkansson, & Marshall, 2005; Qi & Volmer, 2017). Electron-capture dissociation (ECD) was initially only implemented on FTICR instruments, but is now starting to expand to orbitraps, ion trap and time-of-flight (TOF) instruments (Robb et al., 2014; Baba et al., 2015; Fort et al., 2018). ECD suffers from low electron-capture efficiency and extended spectral accumulation times to acquire a useful mass spectrum. Nevertheless, ExD methods provide valuable structural information in comparison with CID (Qi et al., 2014; Qi & Volmer, 2016). This section introduces several novel ExD applications for different types of organic compounds.

The first example describes the analysis of polyketides, which are complex organic compounds produced by plant, bacteria and fungi. Many of them are medically important, as they exhibit high biological activities; e.g., lovastatin, epothilones and erythromycin A (Weissman, 2009). Detailed structural characterization of these compounds is important to understand and manipulate their biosyntheses. CID-based MS/MS techniques are frequently used for this purpose, however,
very few diagnostic ions are obtained due to predominant water losses (Crowe et al., 2002). To circumvent these undesired CID reactions, Wills, Tosin, & O’Connor (2012) utilized an electron-based ion fragmentation technique, namely electron-induced dissociation (EID), to study two polyketide isomers, lasalocid A and iso-lasalocid A using FTICR-MS. In the experiments, the tetrahydropyran ring of lasalocid A was cleaved to form extensive fragmentation levels, whereas cleavage of the terminal tetrahydrofuran ring of iso-lasalocid A was not observed. This allowed the two isomers to be distinguished for the first time (Fig. 13).

The next example illustrates the structural analysis of porphyrins, which are a group of hetero-macrocyclic compounds, composed of four modified pyrrole subunits. These macrocycles contain highly conjugated π-electron systems and exhibit intense absorption bands in the visible light region. For this reason, they have been widely utilized in medical photodynamic therapy (O’Connor, Gallagher, & Byrne, 2009). Kaczorowska & Cooper (2011) demonstrated that the MS/MS behavior of octaethylporphyrin and its Fe(iii) complex differed significantly between CID and EID. EID produced abundant characteristic fragments through α- and β-cleavages, as

FIGURE 13. Illustration of CID (or “CAD,” for collisionally activated dissociation) and EID fragments of lasalocid A (a and c) and iso-lasalocid A (b and d) using the lithiated precursor ion (m/z 597.39) for fragmentation. Reprinted from Wills, Tosin, & O’Connor (2012), with permission from ACS Publications. CID, collision-induced dissociation; EID, electron-induced dissociation.

FIGURE 14. FTICR mass spectrum of cholesterol. (i) Theoretical isotopic distribution of the M⁺⁺ ion of cholesterol. (ii) Mass-scale expansion of the ions generated from cholesterol and their elemental formulae. (iii) Isotopic fine structure of the peak at m/z 386.35, with permission from Springer (van Agthoven et al., 2015). FTICR, Fourier transform ion cyclotron resonance.
MS analysis, even though they are readily visible in the full spectrum are impossible to be isolated for subsequent MS/MS analysis, even though they are readily visible in the full spectrum are impossible to be isolated for subsequent MS/MS analysis, allowing the concept of “two-dimensional Fourier transform ion cyclotron resonance mass spectrometry”. 2D FTICR-MS allows data-independent fragmentation of all ions without precursor isolation, and the correlation of fragments to their precursors can be achieved by modulating the ion cyclotron radii of the precursor ions (Pfaendler et al., 1988; Ross et al., 1993). Proof-of-concept studies have shown that although requiring larger amounts of sample, 2D FTICR-MS was compatible with CID and ExD ion activation techniques and offered different sequence coverages in the proteomics field (Floris et al., 2018a,b). More recently, van Agthoven et al. (2015) utilized this approach to study the fragmentation mechanisms of cholesterol. By using APPI for ionization, both radical ions and protonated molecules, along with oxidation products and fragment ions were produced. It is important to point out that the masses of the protonated molecule and $^{13}$C isotope of the radical molecular ions differed by only 4 mDa (Fig. 14), which are impossible to be isolated in quadrupole-based MS/MS systems, in order to obtain individual fragmentation spectra. This problem was solved via 2D FTICR-MS because various ions were fragmented with and without precursor isolation, and fragmentation patterns resulting from different dissociation pathways were easily differentiated directly from the 2D mass spectrum (van Agthoven et al., 2015).

Although 2D FTICR-MS shows great promise, it is still in a developmental stage, requiring advanced instrumentation and software as well as significant operator expertise on the ExD part. Also, ExD usually requires the analyte to be multiply-charged and suffers from fragmentation efficiency problems. These drawbacks currently limit the structural characterization to individual compounds or a restricted number of analytes. The full characterization of hundreds or thousands of components in highly complex mixture samples is still out of reach.

VI. RECENT DEVELOPMENTS

This section focuses on selected recent applications of FTICR-MS to the analysis of NOM, with significant impact on climate, oceans, and natural resources research.

VII. Aerosols

Aerosols are solid or liquid particles suspended in a gas, with diameters ranging from approximately $10^{-9}$ m (= molecular clusters) to $10^{-4}$ m (=rapid sedimentation) (Pöschl, 2005). They play an important role in the atmosphere's chemistry/physics and can directly impact global climate, regional air pollution, biological organisms and human health. For example, clouds are the most typical aerosols in the atmosphere, which consist primarily of condensed water. By scattering and absorbing solar and terrestrial radiation and acting as cloud condensation, aerosols can influence visibility, the energy balance of the earth,
the hydrological cycle, atmospheric circulation and the abundance of greenhouse gases (Lohmann & Feichter, 2005).

Mass spectrometry is the most common tool for studying aerosols in the laboratory (Fárník & Lengyel, 2018). NOM samples from natural or anthropogenic sources can be formed in molecular beams and these are mostly studied by HRMS. Various HRMS and data analysis methods have been developed to provide detailed insight into the atmospheric chemistry. Reinhardt et al. (2007) compared the performance of TOF-MS and FTICR-MS for laboratory-generated secondary organic aerosol (SOA) samples using ESI and MALDI. Figure 15a illustrates that the MALDI and ESI spectra agree well and that laser fragmentation was not a major problem for the aerosol samples. Figure 15b shows an expanded small segment of the mass spectra measured by TOF-MS and FTICR-MS. In this example, the resolving power of the TOF mass spectrometer was around 5,000 to 10,000, compared with 400,000 of the FTICR instrument. Estimating the elemental compositions of the peaks with TOF-MS would have resulted in highly ambiguous assignments: for the shown example, the peak actually consisted of three components with different elemental formulae, which the FTICR instrument resolved easily.

This comparison clearly demonstrated that high resolving power is a prerequisite for reliable information on complex aerosol samples. Orbitrap and FTICR-MS are therefore the methods of choice in this field (Zuth et al., 2018; An et al., 2019; Wu et al., 2019).

In addition, heteroatoms such as sulfur, nitrogen, phosphorus and other elements from geochemical cycling can be introduced into NOM samples due to various weathering processes. The heteroatoms strongly increase the physicochemical diversity of the sample. Therefore, even higher resolving powers, mass accuracy and dynamic range are required for identification of heteroatom-containing compounds (Vetere & Schrader, 2017). For example, the difference between C3 and SH4 is approximately 3.4 mDa (a common mass doublet in sulfur-containing species); for a nominal mass of 600, a mass resolving power of at least 350,000 is required for correct elemental composition assignments. This number becomes proportionately higher for higher masses or for unequal relative abundances (Cho et al., 2014). Other mass doublets in NOM compounds also require very high mass resolving power, for example, $^{13}$CH versus $^{12}$C (4.5 mDa), mentioned above, or $^{12}$C$_4$ versus SH$_3^{13}$C (1.1 mDa) (Purcell et al., 2006; Koch et al., 2007).
Obviously, low and medium mass resolving mass analyzers cannot resolve these doublets and produce broadened and asymmetrical peaks, with poor mass accuracy and ambiguities in peak assignments. Glacier-derived NOM is a significant source of ancient but highly bioavailable carbon to the downstream ecosystems. Stubbins et al. (2012) examined the radiocarbon age and chemical composition of dissolved NOM in snow, surface water, ice and glacier outflow samples from Alaska, to determine their original sources. FTICR-MS was utilized to reveal the unique molecular fingerprints from these samples and to document the presence of combustion products in the anthropogenic aerosols (Fig. 16). The data suggested that aerosols derived from fossil fuel burning might be an important source of pre-aged NOM in glacier surfaces.

According to global models, the anthropogenic components of atmospheric nitrogen deposition to the ocean accounts for up to one third of the ocean’s external nitrogen supply, and 10% of anthropogenic CO2 uptake. Altitier et al. (2016) used FTICR-MS to study the molecular composition of rainwater and aerosol nitrogen collected from Bermuda and found that the organic nitrogen in marine aerosol originates primarily from biological production in the surface ocean, in contrast to the 80% level, which was previously estimated from anthropogenic activity on land. Recently, Bao et al. (2017) utilized a similar method to study the molecular composition of water-soluble black carbon from the China coastal seas and found that it was significantly positively correlated with water-soluble organic carbon in marine aerosols. This finding proved that atmospheric aerosol deposition significantly contributes to the oceanic carbon pool.

VIII. DISSOLVED ORGANIC MATTER

The accelerated global warming changes the extent and age profile of sea ice across the Arctic region (Cohen et al., 2014). Vancoppenolle et al. (2013) reported that continuous loss of the multi-year sea ice (MYI) leads to a domination of the Arctic ice pack by the first-year sea ice (FYI), a process that significantly alters the ecology and biogeochemistry of the Arctic Ocean. DOM in FYI consists of abundant microbial assemblages, whose biological impact is largely unknown. Underwood et al. (2019) isolated fresh sea-ice DOM from the algal-rich bottom.
layer of FYI, consisting of three fractions: (1) sea-ice-derived DOM filtered through glass fiber filters; (2) a high molecular weight (HMW) DOM fraction retained on a 100 kDa filter; and (3) a low molecular weight (LMW) fraction retained between 10 and 100 kDa filters. The three fractions were then incubated over 9 days and changes of compounds after the treatment were characterized by FTICR-MS (Fig. 17), showing that utilization of DOM was influenced by molecular size: the HMW and LMW fractions greatly promoted the growth of particular taxa, meanwhile, uptake of sulfur- and nitrogen-rich low molecular weight DOMs shifted bacterial community composition. These results prompted an early warning that, as the climate continues to warm, DOM released from FYI will dominate and may cause wide-ranging consequences across the Arctic Ocean region over the coming decades.

IX. TIMBER

Trade of illegally logged timber is thriving rapidly in the 21st century. According to an estimate by the International Criminal Police Organizations, at least 15% of the global timber trade violates either national law or international treaties. In particular in some tropical countries, illegal timber may account for >70% of the nations’ production, amounting to $10 to 100 billion a year (Irwin, 2019). A single piece of plywood can contain dozens of different tropical timbers, and sadly, the global paper trail that accompanies timber is notoriously easy to manipulate.

To fight illegal trade and spot signatures of illicit timber, various HRMS-based methods have been developed to track the species, country of origin and even the region of the timber. For example, Espinoza et al. (2014) utilized direct analysis in real time (DART) ionization coupled to HRMS, to analyze agarwood samples obtained from five countries. In these analyses, 85% of the samples were correctly assigned to either cultivated or wild harvested agarwood for their respective geographic provenance. McClure, Chavarria, & Espinoza (2015) used the same technique to allow species determination of protected Dalbergia trees from Africa, Madagascar, and Asia. Most recently, Zhang et al. (2019) combined DART- and FTICR-MS to extract chemical information from xylarium wood specimens and accurately discriminate *Pterocarpus santalinus* from *Pterocarpus tinctiorius*.

The trade of illegally logged timber is a rising trend in recent years and wood anatomists are more than ever required to fight this thriving crime. Using advanced MS technologies, it is now possible to accurately reveal characteristic chemical fingerprints of the wood products, which can aid the fight against illegal logging to protect endangered timber species.

X. CONCLUSIONS

Today, FTICR-MS plays a vital role in environmental research, mainly due to its unrivaled resolving power and mass accuracy. FTICR-MS information revealed from NOM samples helps scientists to explore relations between long-range transport, biogeochemical cycling, climate change, rare-earth element, and human activities. However, most studies still simply utilize information provided by full-scan experiments, as shown in this overview. Progress is slower in comparison to the biological and biomedical fields (e.g., metabolomics and proteomics). There is therefore significant room for improvements in environmental analysis, for example, by implementing enhanced data analysis strategies and different ion fragmentation techniques, some of which have been illustrated in this article.

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