REVIEW

Methods for characterization of organic compounds in atmospheric aerosol particles

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Abstract Atmospheric aerosol particles of primary or secondary, biogenic or anthropogenic origin are highly complex samples of changing composition in time and space. To assess their effects on climate or human health, the size-dependent chemical composition of these ubiquitous atmospheric constituents must be known. The development of novel analytical methods has enabled more detailed characterization of the organic composition of aerosols. This review gives an overview of the methods used in the chemical characterization of atmospheric aerosol particles, with a focus on mass-spectrometry techniques for organic compounds, either alone or in combination with chromatographic separation. Off-line, on-site, and on-line methods are covered, and the advantages and limitations of the different methods are discussed. The main emphasis is on methods used for detailed characterization of the composition of the organic compounds in aerosol particles. We address and summarize the current state of analytical methods used in aerosol research and discuss the importance of developing novel sampling strategies and analytical instrumentation.

Abbreviations
2D-TAG Two-dimensional thermal-desorption aerosol gas chromatography–mass spectrometry

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ACE	Aerosol chip electrophoresis
AMS	Aerodyne aerosol mass spectrometer
APCI	Atmospheric-pressure chemical ionization
APPI	Atmospheric-pressure photoionization
ATOFMS	Aerosol time-of-flight mass spectrometer
BBOA	Biomass-burning organic aerosol
CI	Chemical ionization
C-ToF	Compact time-of-flight
CVI	Counterflow virtual impactor
DESI	Desorption electrospray ionization
DMA	Differential mobility analyzer
DSAE	Dynamic sonication-assisted extraction
DVB	Divinylbenzene
EI	Electron ionization
ESI	Electrospray ionization
FTICR	Fourier-transform ion cyclotron resonance
GC	Gas chromatography
GC×GC	Comprehensive two-dimensional gas chromatography
HPAEC	High-resolution anion-exchange chromatography
HPLC	High-performance liquid chromatography
HR	High resolution
IC	Ion chromatography
IR	Isotope ratio
IT	Ion trap
LC	Liquid chromatography
LDI	Laser desorption/ionization
MAE	Microwave-assisted extraction
MARGA	Monitor for aerosols and gases in air
MS	Mass spectrometry
NAMS	Nanoaerosol mass spectrometer
nano-DMA	Nanometer-aerosol differential mobility analyzer
NR-PM	Non-refractory particulate matter with diameters
OA	Organic aerosol

OC	Organic carbon
PAHs	Polycyclic aromatic hydrocarbons
PDMS	Polydimethylsiloxane
PILS	Particle-into-liquid sampler
PLE	Pressurized liquid extraction
PM_{10}	Particulate matter with diameters <10 mm
$PM_{2.5}$	Particulate matter with diameters <2.5 mm
PUF	Polyurethane foam
REMPI	Resonance-enhanced multiphoton ionization
PMF	Positive matrix factorization
RSMS	Rapid single-particle mass spectrometer
SAE	Sonication-assisted extraction
SFE	Supercritical fluid extraction
SOA	Secondary organic aerosol
TAG	Thermal-desorption aerosol gas chromatography–mass spectrometry
TD	Thermal desorption
TEOM	Tapered-element oscillating microbalance
TOF	Time-of-flight
UCM	Unresolved complex mixture
UHPLC	Ultra-high-performance liquid chromatography
UHR-MS	Ultra-high-resolution mass spectrometry
VOC	Volatile organic compound
XAD	Polystyrene-divinylbenzene resin (trade name)

Introduction

A major challenge in atmospheric chemistry studies is to elucidate the sources, structure, transformation and formation processes, and fate of the clearly ubiquitous yet poorly understood organic atmospheric compounds. This requires detailed characterization of the size-dependent chemical composition of the aerosols, which is not a simple task because of the complexity of the molecular composition of organic aerosols. In recent years, particular attention has been given to nanoparticles (diameter <100 nm). Nanoparticles are important precursors for the formation of larger particles that are known to strongly affect global climate, and they may also affect atmospheric chemistry in general because their reactivity is typically high. In addition, nanoparticles have been revealed to have possible adverse health effects for humans [1, 2]. Although much effort has been focused on characterization of the organic compounds in atmospheric particles, recent research suggests that a substantial fraction of organic compounds have not been or have very rarely been determined, particularly among the nanoparticles. The development of novel analytical methods, for both sampling and analysis, has enabled more detailed characterization of the chemical composition of aerosols. However, there are still several challenges in the characterization of aerosol particles, including high chemical diversity in combination with high chemical reactivity and consequent rapid changes of the composition during sampling and analysis. In addition, particularly for ultrafine particles (<100 nm), it is challenging to collect a sufficient mass of the particles for analysis.

Several methods have been used for sampling and analysis of aerosol particles, from on-line to on-site and off-line analyses. Currently, mass spectrometry (MS) is the most commonly used technique for chemical analysis of atmospheric aerosol particles, either alone or in combination with chromatographic techniques. MS-based techniques provide the high sensitivity and selectivity required for aerosol analysis. For collection of the atmospheric particulate matter (PM), the traditional method relies on collection of PM on filters or other substrates, with subsequent chemical analysis of the collected material in the laboratory. Some techniques enable real-time (on-line) analysis of the chemical composition of the aerosols. On-site analysis combines sampling on-line with analysis, but does not enable real-time analysis because longer (from a few minutes to a few hours) sampling time is required. All three methods are needed in the characterization of atmospheric aerosols. Off-line MS techniques enable detailed molecular-level analysis of aerosol samples, which is essential to gain fundamental knowledge regarding aerosol chemistry, mechanisms of particle formation, growth, and atmospheric aging. On-site techniques offer several benefits of the off-line methods with the additional benefit of on-line sampling, thus avoiding problems related to sample handling. On-line techniques, however, enable even detection of individual particles, often with simultaneous measurement of particle size distributions and aerodynamic characteristics, and are ideally suited for field studies that require high temporal resolution. Use of these measurements yields insights into aerosol sources and behavior not available from any of the methods alone.

Analytical methods for the analysis of atmospheric particulate matter

Off-line analysis

Off-line analysis relies on separate sampling and analysis. Several methods can be used for sampling, the most common ones being sampling on filters. After sampling, extraction is typically required before the analysis. Several methods have been used both for extraction and for analysis. The workflow and methods used in off-line analyses are summarized in Fig. 1.

Sampling and storage

Several sampling methods have been used in the collection of aerosol particles. The sampling time should be as short as possible, to reduce artefacts and to ensure the representativeness of the samples in terms of their nature and their physical
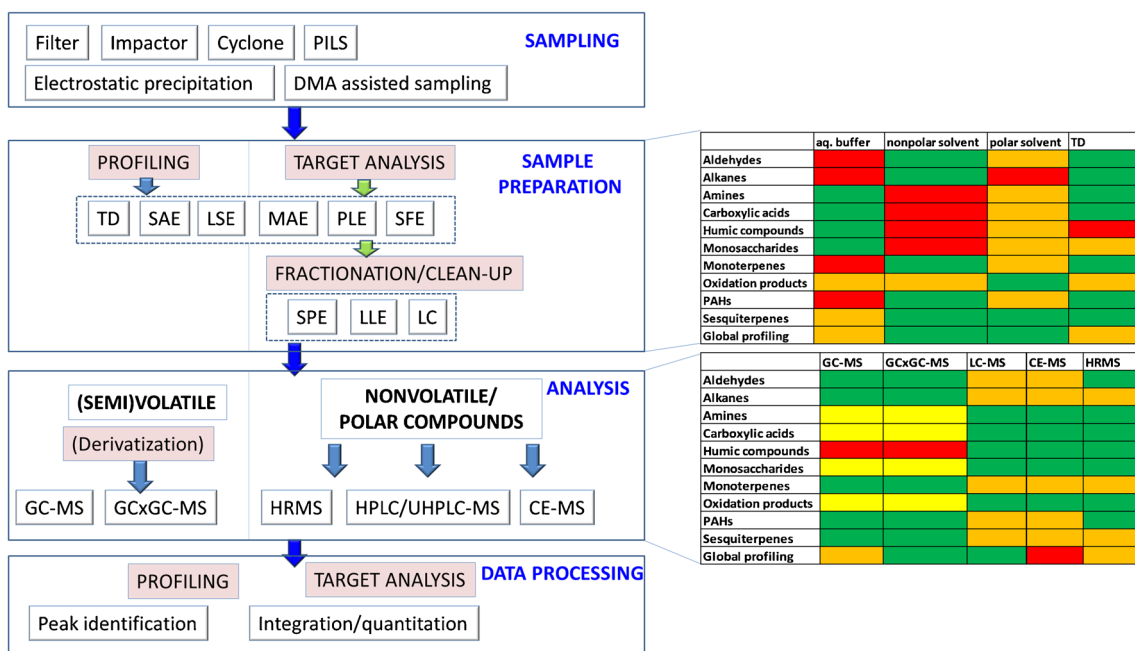
Fig. 1 Summary of methods available for off-line sampling and analysis of atmospheric aerosols

and chemical characteristics. Sampling times vary with ambient loadings, sampling rates, substrate blanks, and the sensitivity of the analytical method, typically ranging from several hours to a day or even longer.

For sampling of aerosols, a variety of films and foils have been used with impactors to collect size-resolved samples. Grease or mineral oil are quite common adhesives on impactor stages, but polyurethane foam (PUF) has also been widely used because it provides decreased bouncing of particles and the possibility of collection with high flow rates [3, 4]. Filters, however, are the most commonly used collection substrates. Quartz as a filter material is far superior to others because of its thermal stability, high particle-collection efficiency, and low cost. Before use, it is usually baked at 550–700 °C for at least 6 h. The biggest disadvantage of quartz, and the reason filters should be cleaned before sampling, is adsorption of organic gases, which leads to a positive artefact [5]. Positive artefacts caused by adsorption of organic carbon (OC) on quartz filters may account for 39 %, or even more [6]. Inhomogeneity of filter batches is also a disadvantage, because even filters from the same manufacturer may differ in capacity [7]. To address this problem, zero samples and correction for positive artefact are of great importance if quartz is used. Correction can be done using the back-up filter technique or a parallel filter where particles are first removed with a Teflon filter. It should be noted, however, that if quartz is used as sampling and back-up filter the sampling time should be more than a few hours, because underestimation of positive artefact may occur. To ensure trapping of volatilized compounds, a quartz back-up filter can be impregnated with carbon [8] or polystyrene-divinylbenzene resin (XAD) [9]. To minimize positive

artefacts, denuders coated with an adsorbing substance, for example activated carbon or XAD, are frequently used, but they cannot, in general, be used with high-volume samplers [2, 10–12]. However, corrections with back-up filters and blanks are still highly recommended. Because of the high flow rates used with quartz filters, negative artefacts are also possible. For instance, nitrate volatilization has led to a negative artefact of ca. 50 % [2, 13], and loss of alkanes [14] and polycyclic aromatic hydrocarbons [15] caused by volatilization has been observed. Evaporative loss during sampling can be measured with, e.g., a tapered-element oscillating microbalance (TEOM), and should be taken into account [16]. In addition, reduced pressure during sample collection, e.g. with impactors, can affect the adsorption of some particles (e.g. semi-volatile organic compounds) and thus result in losses of compounds [17]. Teflon has been used as sampling media quite often because of negligible positive artefact [18]. However, negative artefact resulting from evaporation of semivolatiles exists as it does for quartz filters [19, 20]. Teflon membrane cannot be easily pre-cleaned, and so may contribute some organic impurities. Comparison of quartz and Teflon filtering media was done in several studies, but no straightforward conclusions could be drawn [21]. Regenerated cellulose, polycarbonate, and nylon are also used as filter materials, but mostly for inorganic analysis [22, 23]. In addition to positive and negative artefacts, samples can be altered by chemical reactions during sampling or by reactions with filter media [24]. Oxidation of, e.g., terpenes and even PAHs, caused by oxidative gases (ozone, nitrogen oxides, and hydroxyl radicals), is a well-known phenomenon during long-duration sampling on filters, but can be avoided by removing, e.g.,

ozone with denuders coated with KI, MnO_2, or Na_2SO_3 [25], or activated carbon [26]. In addition, water vapor can both adsorb to or desorb from filter materials before, during, and after sampling. Cellulose fibers are particularly moisture sensitive, whereas quartz filters and Teflon membranes have a low moisture uptake. Because temperature has a significant effect on the gas-particle distribution, variation of temperature may cause additional artefacts during sampling.

Off-line sampling is typically done using size separation (PM_{10}, $PM_{2.5}$), and this is also the technique used and accepted by environmental-protection authorities [15, 27]. If large volumes of sample are required, however, size separation is difficult to perform. Thus high-volume sampling is typically done without size separation, using simple quartz-fiber filters at relatively high flow rates (tens of cubic meters per hour). Even though high-volume impactors and virtual impactors can provide conventional cut off even at almost cubic-meter-per-hour flow rates [28–31] and cyclones can operate at several cubic meters per second, they were not widely adopted. Size-separated aerosol particles, typically with sizes of PM_{10} or $PM_{2.5}$, are collected either on filters or impactor plates by the cyclone and impactor. Impactors are more popular because particles of different aerodynamic sizes can be collected simultaneously whereas cyclones separate just one size at a time. Impactors, for example the NanoMOUDI, can also collect small particles (down to 10 nm) with a relatively high sampling rate (up to 10 Lpm) [32]. Another sampling technique for collecting small particles (0.8 nm–1.1 μm) is electrostatic precipitation [17, 33–35]. This system operates at high sampling rates (>30 Lpm) with reduced pressure drop. The main advantage of this sampling method compared with other samplers relates to the significant exclusion of particles that are outside a chosen mobility range, thereby avoiding contamination by larger particles, especially if a differential

mobility analyzer (DMA) is used before the precipitator. The disadvantage is that, because of the reduced pressure of the impactor stages, loss of semi-volatile organic compounds in the nanoscale fraction has been observed [35]. This sampling system has also been connected with thermal-desorption chemical-ionization mass spectrometry. In addition to electrostatic precipitation, nanometer-size particles can be sampled on filters using a differential mobility analyzer for size separation. DMA classifies charged particles by their mobility in an electric field and, depending on geometry, can provide a very sharp cut-off size distribution. Sample rates of a few liters per minute were used, which required collection times of up to several days [36, 37]. The most common size-segregating methods for collecting aerosol particles are presented in Table 1.

Newer sampling techniques have also been tested for aerosols. Solid-phase microextraction (SPME) has been combined with needle-trap technique to determine gaseous (free) and particle-bound compounds, e.g. PAHs in barbecue and cigarette smoke. In this approach both aerosols and the gas phase were collected, air was sampled actively with a needle-trap (divinylbenzene (DVB)–carboxen), and SPME (polydimethylsiloxane (PDMS), PDMS–DVB, and carboxen–PDMS) was used to passively sample gases. After sampling, samples were analyzed by GC. This combination enables the determination of compounds in both phases, which is important for more accurately relating chemical concentrations to potential environmental effects. However, it should be noted that because SPME is not a quantitative extraction technique careful calibration, which may be difficult to perform on-site, is needed for reliable quantitation.

In the optimum case, the samples are analyzed immediately. In many cases, however, samples have to be transferred and

Table 1 Comparison of size-segregating methods for collecting aerosol particles

	Typical sampling rate (Lpm)	Advantages	Disadvantages
Cyclone	16	Cheap and simple; high flow rates possible	Size cut difficult to characterize and calibrate
Impactor	Up to 1100, typically 80	Very sharp cut-off diameter, minimal contamination by larger particles; several different cut sizes can be collected simultaneously; high flow rates possible	Assembly challenging; O-rings and grease used to collect largest particles may contaminate samples; without grease, particle bounce may be a problem; may bias partitioning of some submicron semivolatile organic compounds because of pressure drops
Virtual impactor	Up to 500	Commercially available with cut sizes at $PM_{2.5}$ and PM_{10}; custom made down to 135 nm[a]; no grease or surfaces that contaminate sample	Not generally available at different cut sizes
Electrostatic precipitation and DMA-assisted sampling	Up to 10	Suitable also for small particles, minimal contamination by larger particles	Long sampling times lead to alteration of samples

[a] Micromachined cascade virtual impactor with a flow-rate distributor for wide-range airborne-particle classification

stored before analysis. Materials used for sample handling, including transport and storage, should be free from organic compounds and plastic components to prevent contamination of samples. Typically, pre-annealed aluminium foil for media is used in transporting the filters in preannealed glass jars, using Teflon sealing tape and lid liners to minimize potential contamination of samples.

Analysis

The first step of analysis is extraction of the analytes. In most cases liquid extraction, often assisted with high temperature and pressure, ultrasounds, or microwaves, is used. Thermal desorption or nanospray desorption are also possible for several applications. Commercially available systems with the ability to heat and pressurize liquids include pressurized liquid extraction (PLE) [38], microwave-assisted extraction (MAE), and supercritical fluid extraction (SFE) [39, 40]. Sonication-assisted extraction (SAE) and, especially, dynamic sonication-assisted extraction (DSAE) have also given promising results [41]. Recently, the Quick Easy Cheap Effective Rugged and Safe (QuEChERS) approach has been used for the extraction of specific compounds in aerosol particles [42]. The solvents used vary from nonpolar solvents to aqueous mixtures, depending on the target analytes. The enhanced extraction techniques are typically much faster and often more selective than traditional liquid extraction and Soxhlet extraction, and consume smaller amounts of organic solvents and reagents. It should be noted, however, that most solvent extraction methods require concentration before the analysis, a step that can cause loss of analytes through coevaporation. Moreover, temperature during the extraction should be controlled. Easily degradable or volatile compounds might require cooling during SAE, which can be done by adding ice cubes or ice packs into an ultrasonic bath [43]. Thermal desorption (TD) is a more straightforward extraction method. A recent study revealed that solvent extraction contributed the greatest uncertainty to the quantification of organic aerosol species, particularly for high-molecular-weight unsaturated acids and alcohols [44]. Compared with solvent extraction TD-GC–MS has higher sensitivity, decreased analysis time, reduced risks of analyte loss and sample contamination, and requires less sample mass [45, 46]. However, degradation of labile or reactive species is a serious concern during TD experiments because of the high temperature required for the desorption. In addition, TD tends to underestimate the levels of PAHs with five or more rings [47]. Another limitation of TD in combination with GC is that only volatile analytes can be determined. Over 50 % of aerosol mass can be highly oxidized, meaning that GC is not a suitable technique for their separation before detection. To overcome this limitation, simultaneous derivatization, e.g. by silylation, during the TD step can be used [48]. For example, anhydrous sugars, alcohols and phenols, fatty acids, and resin acids have been analyzed from particulate matter from a filter dampened with *N*-methyl-*N*-trimethylsilyl-trifluoroacetamide (MSTFA) before TD-GC. Limits of quantification as low as 17 pg have been obtained using this technique for levoglucosan [49]. Other simultaneous derivatization methods can also be used, including coating of the resins or filters with *O*-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine (PFBHA) or 2,3,4,5,6-pentafluorophenyl hydrazine (PFPH) [50, 51].

After solvent extraction, aerosol samples can be analyzed as such, although a concentration step is typically needed using, e.g., simple solvent evaporation. However, because of the heterogeneity of aerosol constituents, clean-up or fractionation is advantageous, especially for applications where only specific compound groups or even individual compounds are analyzed. In non-targeted screening, however, clean-up and fractionation steps can lead to losses of compounds of interest. Solid-phase extraction is the most popular technique which, with a variety of stationary phase, offers enhanced selectivity for sample preparation. Hydrophilic–lipophilic balance (HLB), C18, and ion-exchange materials are most frequently used to concentrate compounds selectively or to remove salts [52, 53]. In some cases use of a combination of materials is advantageous, as has been revealed in the determination of humic-like substances (HULIS) in atmospheric aerosols [54]. In the first step, a C18 solid-phase extraction was performed to separate HULIS from inorganic and hydrophilic organic sample constituents in aqueous sample solutions. The second isolation step was conducted on a strong anion exchanger to separate HULIS from remaining carbonaceous compounds.

After conventional extraction and preconcentration or clean-up, most analyses are done with either gas or liquid chromatography (GC and LC) combined with a suitable detector, most often a mass spectrometer (MS). Capillary electrophoresis (CE) is used less frequently. The use of high-resolution mass spectrometry (HRMS), often combined with tandem mass spectrometry (MS^n), for structural identification is also a rapidly growing area of research in aerosol chemistry. The HRMS instruments include time-of-flight MS (TOFMS), hybrid quadrupole-time-of-flight (QTOFMS), and Orbitrap. Lately, ultra-high-resolution mass spectrometry (UHR-MS) has been used to analyze higher-molecular-weight aerosol compounds. A combination of high-performance liquid chromatography and Fourier-transform ion-cyclotron-resonance mass spectrometry (HPLC–FTICR-MS) can be helpful in providing exact elemental compositions and thereby enabling the experimenter to come closer to a molecular identification [55]. However, high instrumentation cost is a limiting factor for the wide use of UHR-MS. MS systems have a fast enough scanning rate for LC and GC analysis. Recently, ion mobility has been introduced into the commercial QTOFMS systems [56]. Ion-mobility separation as an integral part of the detection system offers an additional separation dimension, which

greatly increases detectable and identifiable components in complex biological samples and enables the separation of isobaric molecules without increasing the analysis time. Triple-quadrupole MS instruments (QqQMS) are, however, a good option for sensitive quantitative targeted analysis using multiple reaction monitoring, and can also be used for class-specific detection through precursor-ion and neutral-loss scanning.

GC-based analysis

GC–MS is the traditional method for analysis of aerosols and has been used for quantitative analysis of different organic compounds including PAHs, alkanes, ketones, aldehydes, carboxylic acids, monoterpenes, and sugars [57–60]. Derivatization is typically required before analysis of polar compounds, for example alcohols, carboxylic acids, and amines. Typical derivatization methods include silylation, formation of carbamates with isobutyl chloroformate or O-benzylhydroxylamine, conversion of carboxylic acids to their dibutyl esters and butoxy acetals by derivatization with 1BF3 in n-butanol, and derivatization with PFBHA. Some of the derivatization methods can even be incorporated in the sampling step or done during the thermal extraction. The conventional methods are, however, performed after solvent extraction (and evaporation of solvent). Modern instruments enable derivatization to be performed automatically in the autosampler unit, thus minimizing manual steps and improving the reliability of the procedure.

Solvent-based extraction is still the most common sample-preparation method for GC analysis, but thermal-desorption methods have been gaining popularity. TD-GC–MS methods have been used, e.g., for determination of PAH and alkanes [61], of semi-volatile organic components [62], and of more polar compounds including alcohols, ketones, aldehydes, and organic acids [63, 64]. If necessary, derivatization can be done by methylation [65–67] or by silylation [68]. The latest commercial thermal desorbers enable quantitative recollection of split flow (both tube and trap desorption split flow) for repeat analysis and have built-in internal-standard-addition capabilities. Thus the main challenges of TD-GC methods, i.e. one-shot analysis and quantitation with internal standards, are avoided.

In most applications, a single-quadrupole system with electron ionization (EI) has been used. The GC–EI-MS spectrum is highly useful in the identification of organic compounds because of the large commercial spectral libraries for EI-MS spectra. However, if the compound spectrum is not found in the spectral libraries identification is a challenge because, as a result of the heavy fragmentation, the molecular ion is often not detected. Soft ionization using chemical ionization (CI) enables detection of molecular ions and, therefore, for identification purposes a combination of GC–EI-MS and GC–CI-

MS data, particularly with HRMS systems, is a powerful tool, combining the information of the fragmentation and the molecular ion.

GC has also been combined with compound-specific isotope-ratio mass spectrometry (IRMS) [69–73]. GC–IRMS is a promising tool to improve our understanding of the sources and the atmospheric fate of organic trace compounds. Determination of the isotopic composition of chemical species in aerosols can give more detailed understanding of emission sources and of sources involving chemical and physical processes in the atmosphere. Figure 2 shows the schematic presentation of GC–IRMS. After GC separation, prompt high-temperature conversion into CO_2, H_2, N_2, or CO is required for stable isotopic measurements of C, H, N, and O, respectively.

Although GC–MS has been revealed to be a reliable technique for targeted analysis, it has limitations in terms of separation efficiency and sensitivity. Even with the high resolution of GC, there are still coelution of peaks, interfering matrix constituents, and a large band of material that elutes as part of an unresolved complex mixture (UCM), complicating identification and quantification of individual compounds. Even spectral deconvolution software has been revealed to fail when co-eluting peaks have common mass fragments or when a constant background is present. Comprehensive two-dimensional (2D) gas chromatography (GC × GC) offers enhanced separation efficiency in comparison with the traditional GC–MS approach, and in the last decade it has been gaining popularity in air and aerosol analysis [74–80]. In particular, GC × GC in combination with a fast-acquisition mass spectrometer, e.g. a time-of-flight mass spectrometer (TOFMS), provides extremely high analytical resolution with mass-spectral information. An example of the resolving power
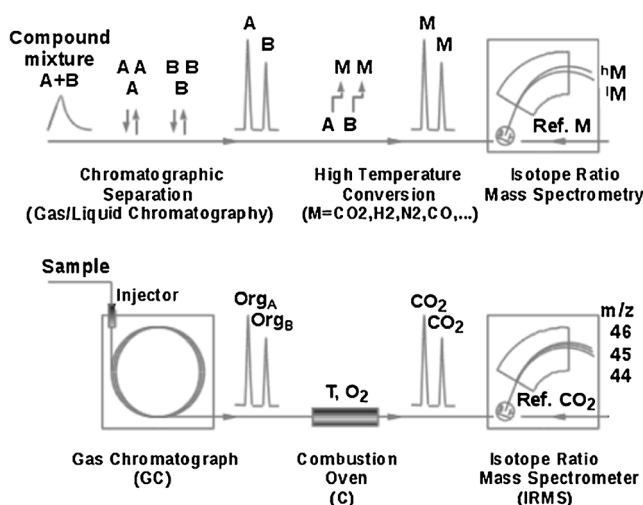

Fig. 2 Illustration of analytical steps in compound-specific measurement of stable isotope composition (*upper panel*) and an example of δ^{13}C analysis in atmospheric samples containing organic compounds (*lower panel*) (reproduced, with permission, from Ref. [69])

of the GC × GC–TOFMS is the analysis of partially oxidized organic compounds associated with to PM$_{2.5}$ aerosols [81]. The non-selective direct thermal desorption combined with GC × GC–TOFMS yielded an extremely complex chromatogram with over 10,000 organic compounds. The method resolved a volatility range equivalent to C7 to C30, and polarity range from alkanes to mono-substituted acids. Another example of the enhanced separation efficiency of 2D TD-GC × GC–TOFMS compared with more conventional GC–TOFMS analysis revealed that GC × GC–TOFMS had a tenfold increase in the number of peaks detected and produced highly structured chromatograms ideal for rapid screening purposes [82]. More importantly, the comprehensive 2D-GC

approach reduced the limitations of TOFMS deconvolution observed in 1D; this led to improved library matches and more confident analyte identification.

The concentrating-modulation feature of GC × GC–TOFMS not only improves the spectral quality but also improves the signal intensity relative to normal GC–MS analysis. This has been revealed to enable detection and identification of several compounds that have not been identified previously in aerosol particles [83]. An example of the improvement of sensitivity and quality of spectral identification is shown in Fig. 3 where, in GC–MS analysis, the small peak of alloaromadendrene is overlapped by the peaks of alkanes or alkenes (not shown) and dodecanal. The GC–MS spectral

Fig. 3 Comparison of GC–MS and GC × GC–TOFMS in the characterization of rural aerosols. Spectral quality improvement of alloaromadendrene: extracted ion chromatogram and mass spectrum obtained by (**a**) GC–MS and (**b**) GC × GC–TOFMS and from (**c**) NIST library spectrum (reproduced, with permission, from Ref. [84])
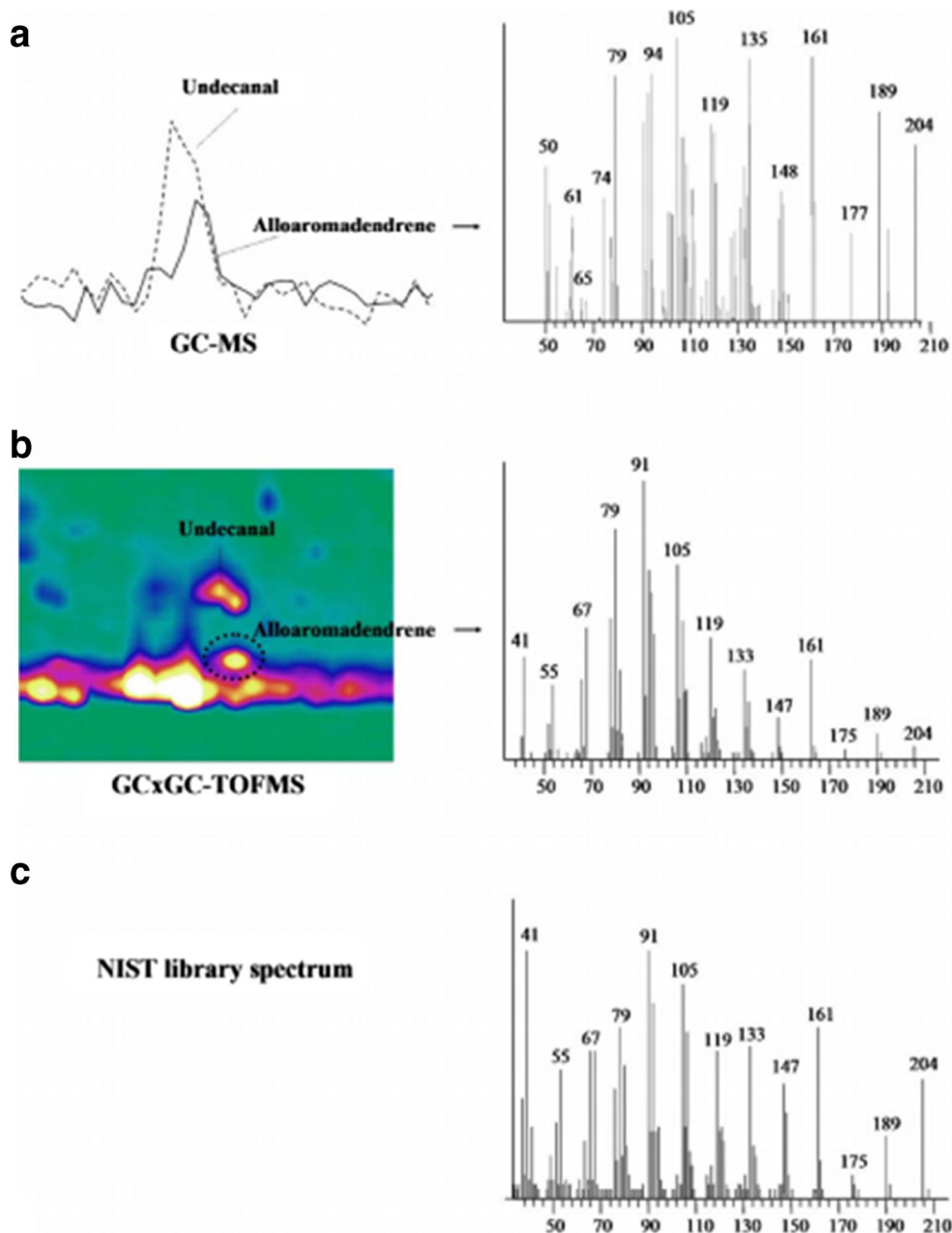
match is low because of the many interfering fragments. In the GC × GC–TOFMS analysis, the concentrating modulation (Fig. 3a) and the additional separation column in the second dimension improves the separation and the compound is clearly separated from less polar components and, more importantly, from more polar dodecanal. As a result the spectral match improved substantially, and the intensity pattern was closer to the library spectrum.

High sensitivity is particularly important in the analysis of nanoparticles, where the mass of the sample is very small. A recent study revealed that GC × GC–TOFMS was superior to GC–TOFMS and GC–qMS in terms of sensitivity for the analysis of alkanes and PAHs in nanoparticles (Table 2) [85]. Here, the wood-burning aerosol had a particularly high amount of matrix components and the UCM prevented the detection of several target compounds even after spectral deconvolution.

LC-based analysis

Liquid-chromatography (LC) methods, particularly in combination with MS, have also been gaining popularity for aerosol analysis, particularly because of the increasing interest in high-molecular-weight compounds that are difficult to analyze with GC-based techniques. LC, usually combined with mass spectrometry, has been used particularly in the analysis of water-soluble organic species, including humic and fulvic acids [84, 86–88], amines [89], organosulfate products of secondary organic aerosol (SOA) chamber studies and ambient aerosols [90, 91], humic substances [92, 93], carboxylic acids and high-molecular-weight dimers [94, 95], oxidation products of α-pinene [96], monosaccharides [97, 98], nitroaromatics [64], and biogenic hydrocarbons [99]. LC

separation methods include reversed-phase liquid chromatography (RPLC), size-exclusion chromatography, and hydrophilic-interaction chromatography (HILIC), which is used for very polar compounds that have poor retention in RPLC. Recently, many ion-chromatography methods have been replaced by HILIC because HILIC eluents are compatible with MS, whereas it is much more challenging to combine IC with MS.

Different MS systems, mainly with electrospray ionization (ESI), have been used, including QqQMS [90, 100], ITPMS [90, 95, 96, 101], and hybrid triple quadrupole-linear ion trap (QqQ-LITMS) [64] in the tandem mass experiments, whereas TOFMS [95, 102], quadrupole-TOFMS [94, 99], and direct infusion with FTICRMS [103] have been used as additional tools for accurate mass measurements and identification of compounds detected in aerosols. In some cases, however, ESI is useless and atmospheric-pressure chemical ionization (APCI) or atmospheric-pressure photoionization (APPI) must be used. For example, when analyzing oxy-PAHs from aerosol extract, it was noticed that APCI with post-column liquid mixing was superior to other ionization sources because it produced both positive and negative ions, whereas APPI produced only negative ions and ESI was not useful at all [102]. Several adduct ions may form during normal-pressure ionization, which decreases sensitivity. To determine correct molecular-weight assignments and increase sensitivity for less polar species, a series of low-concentration mobile-phase additives (LiBr, NaCl) can be used, where exclusively [M + Cat]$^+$ adducts form. In the study of Hamilton et al. lithium bromide produced better fragmentation patterns, with more structural information than in the other cases and with no reduction in sensitivity for the analysis of polar compounds and oligomers in SOA samples by ESI-LC–MS–MS [101]. In

Table 2 Comparison of three GC-based methods for the analysis of alkanes and PAHs in wood-combustion nanoparticles (modified from Ref. [59])

Compound	Method								
	GC × GC–TOFMS			GC–TOFMS			GC–QMS		
	RSD (%)[a]	LOD (μg L^{-1})	LOQ (μg L^{-1})	RSD (%)[a]	LOD (μg L^{-1})	LOQ (μg L^{-1})	RSD (%)[a]	LOD (μg L^{-1})	LOQ (μg L^{-1})
Dodecane	4.03	0.2	0.6	2.97	2.7	8.2	1.6	17	52
Hexadecane	4.88	1.4	4.3	5.03	14.7	44.6	6.6	32	99
Eicosane	5	1.4	4.3	5.64	13.2	40	7.2	14	42
Tetracosane	4.28	3.7	11.3	4.91	14	42.5	7.1	32	99
Octacosane	2.29	7.9	23.9	4.01	21.2	64.4	8.9	49	150
Acenaphthene	1.57	1.1	3.2	4.5	4.8	14.7	4.9	24	72
Phenanthrene	5.42	0.6	1.8	5.96	3.3	9.9	6.1	14	42
Pyrene	4.74	0.5	1.5	6.18	4.7	14.3	5.6	9	26
Chrysene	8.5	1.3	3.9	6.88	6.2	18.9	6.2	23	68
Benzo[a]pyrene	7.78	3	9.2	5.54	13.6	41.1	7.7	17	51

[a] Determined at 500 μg L^{-1} level (n=10)

aerosol analyses with LC–MS, mass-scanning methods have included MS full-scan acquisition with accurate mass, acquiring precursor and fragment exact-mass data simultaneously with MS^e scan, precursor-ion scan, and multiple reaction monitoring. The most popular fragmentation method in MS–MS experiments is collision-induced dissociation, but higher energy collision dissociation has also been used [100]. One of the main limitations of the LC–MS-based methods is the same as for direct-infusion MS, i.e., matrix effects. However, the matrix effects have a substantially smaller effect in LC–MS than in the direct-infusion approach because the chromatographic separation reduces sample complexity, thereby alleviating matrix interferences in the ionization process. Systematic matrix effects caused by gradient elution can be minimized by using a proper set of internal standards, preferably labelled standards for each target analyte, or class-specific standards for non-targeted screening approaches.

Comprehensive two-dimensional liquid chromatography (LC × LC) provides enhanced separation power by combining two LC modes with different separation mechanisms [103, 104]. An example of LC × LC–TOFMS in aerosol analysis is the quantitative determination of organic acids in aerosol particles [105]. The first dimension separation was based on ion-exclusion mode, and the second dimension on RP separation. This 2D combination enabled the separation of the two isomers of pinonic acid and pinic acid. An additional benefit of the enhanced separation in the LC × LC system is the reduced effect of matrix suppression on the quantitative results [106]. Commercial LC × LC instruments are available.

Previously, LC–QqQMS instruments have been used in aerosol analysis because of their high sensitivity in the SRM mode. However, triple quadrupoles offer only unit mass resolution and thus are poorly suited for the identification of unknown compounds. The sensitivity of the most recent HRMS instruments, for example TOFMS, QTOFMS, and Orbitrap, is currently close to that of the QqQMS instruments, while also offering the possibility of the identification of previously unknown compounds [107]. Modern LC–HRMS instruments, with fast duty cycles, enable acquisition of high and low-collision-energy data simultaneously, to provide both data on precursor ions and fragmentation data for all detectable molecular ions. Thus, it can be expected that these instruments will gain popularity for aerosol analysis.

CE-based analysis

Most of the biogenic aerosol or secondary organic aerosol contains highly oxidized and polar organic compounds. Thus capillary electrophoresis can be easily used to analyze, e.g., organic acids, which in some cases comprise over half of aerosol mass. Coupling CE with MS combines excellent separation capabilities on the basis of differences in electrophoretic mobility with the power of MS for analyte

identification and structure elucidation, thus providing an alternative to LC–MS for the analysis of polar compounds in atmospheric aerosol. Use of CE-MS with suppressed electro-osmotic flow (EOF) and acidic background electrolyte (BGE) at different pH values made possible differentiation between weak organic acids (e.g. carboxylic acids) and strong organic acids (e.g. sulfonic acids) [108]. However, high-resolution MS was needed to confirm the identification of acids. Low-molecular-weight and highly polar dicarboxylic acids are challenging for LC analysis, but are ideal analytes for CE. Indeed, C_2–C_{10} dicarboxylic acids were determined from $PM_{2.5}$ aerosol samples collected at an urban site in Helsinki with indirect UV detection. Analysis took only 5 min, but because of low concentrations samples had to be preconcentrated by SPE [109]. CE-MS analysis proved an attractive alternative to the more established HPLC–MS methods, and was found suitable to determine low concentrations of nitrophenols in aerosol particles [110]. For in-situ applications, microchip electrophoresis was coupled on-line with a growth-tube particle collector for semi-continuous measurement of aerosol ion composition. This so-called aerosol chip electrophoresis (ACE) could provide a useful complement to existing aerosol-monitoring technology, especially when less expensive and rapid analyses are desired [111]. Despite its advantages, CE is rarely used in atmospheric analytical chemistry. However, CE does have potential; especially for in-situ applications, because of the possibility for miniaturization and on-line coupling [112]. The main limitation of CE is that preconcentration is required before the analysis because of the very low injection volumes used in CE. In addition, CE-MS interface is more complex, and thus less robust, than, e.g., LC–MS interface.

MS with direct infusion or direct desorption

Mass-spectrometry systems have also been used for the off-line analysis of aerosols without prior separation, either using direct infusion of the extracted filters, or by direct desorption from the filters.

The direct-infusion HRMS systems have been recently reviewed [113]. Typically, the MS systems used for direct-infusion methods use either an Orbitrap or FT-ICRMS system with ESI interface. The resolution of an FT-ICRMS system can be up to 600,000, whereas the maximum resolution of Orbitrap is ca. 100,000. Direct infusion has been used both for a variety of chamber experiments [114] and in the analysis of ambient aerosol samples [57, 112, 115–117]. In most cases, ESI has been used for the ionization. Figure 4 illustrates the advantages of high resolving power for the analysis of organic compounds in aerosols [117]. With HRMS (Orbitrap) four individual peaks around m/z 251 were resolved in the spectrum of SOA produced from an ozone-initiated oxidation of isoprene. If the same mass spectrum was recorded with a

Fig. 4 Positive-ion-mode ESI-MS stick spectrum of isoprene/O_3 SOA (panel (**a**)). Panel (**b**) zooms in on peaks near m/z 251 recorded at the Orbitrap resolving power R=100,000. Panel (**c**) shows how the same mass range would look if recorded at a typical resolving power of a reflection-TOF instrument, R=5000 (reproduced, with permission, from Ref. [117])
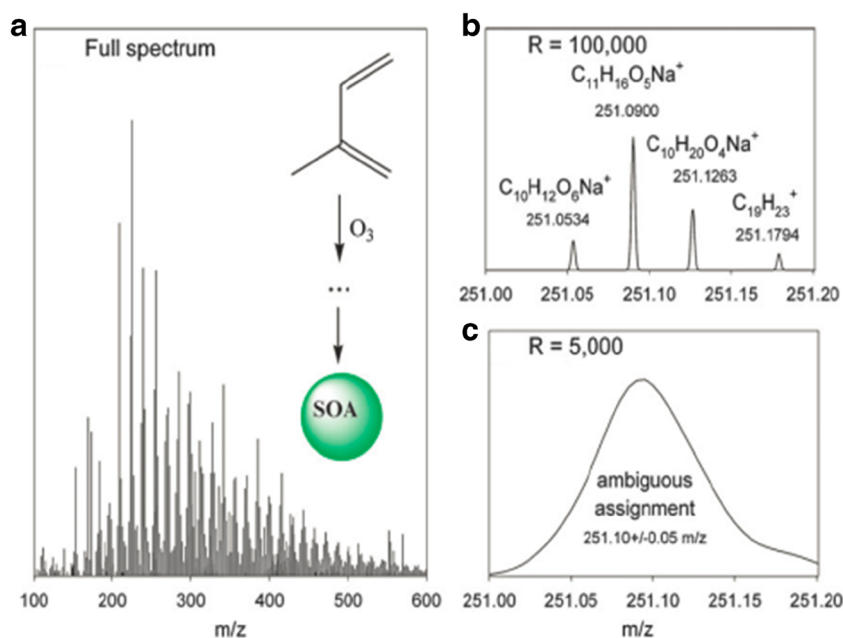
resolution of 5000 (Fig. 4c) all these peaks would be merged, making identification or quantitation impossible. Another recent example based on a nanoESI-UHRMS (Orbitrap) system revealed the potential of direct-infusion HRMS, which enabled identification of up to 850 elemental formulae from $PM_{2.5}$ filter samples [118].

Direct-MS systems have also been used for direct analysis of aerosols collected into filters using desorption electrospray-ionization mass spectrometry (DESI-MS) [119–121]. In these techniques, sample extraction and ionization happens almost simultaneously, making them ideal candidates for semi-online applications with low sample requirements and short solvent–analyte interaction time [122]. This method has been used for the determination of organic acids (dicarboxylic acids, long-chain fatty acids) from biomass-burning aerosols, using ion-trap MS as the detector. No extraction was needed before analysis. Nanospray desorption electrospray ionization (nano-DESI) in combination with high-resolution mass spectrometry (HR-MS) has been used to analyze a diverse mixture of oxygenated hydrocarbons, organosulfates, organonitrates, and organics with reduced nitrogen in sub-micron aerosols collected in Los Angeles and Shanghai [123]. It was noticed that the choice of solvent affects selectivity and must be optimized for each compound group.

Even with recent advances in MS instrumentation, the online MS approach without any preseparation has several limitations, including a limited in-spectrum dynamic range and ion suppression. Also, it is not possible to differentiate the different isomers with MS alone and the reliable determination of compounds present at low concentrations is difficult. Quantitative analysis is also challenging because it is not possible to include isotope-labeled standards for each compound, and

accurate quantification can potentially be hindered by interferences arising from isotopes, isobars, and isomers of the compounds of interest. Another limitation is isobaric overlap of the M + 2 isotope with the monoisotopic peak of the compound with one double bond fewer.

On-site measurements

On-site measurements for aerosol analysis have mainly been based on two different approaches, namely TD-GC and particle-into-liquid-sampler-LC systems (PILS-LC). The GC-based systems have been used for relatively broad characterization of semivolatile compounds in aerosols, whereas the PILS-LC systems are used mainly for targeted analysis of specific water-soluble compounds, for example carboxylic acids and ionic species.

The GC-based approach has been used for the analysis of semivolatile organic compounds in aerosol particles. The approach is based on a combination of collection by particle impaction with analysis by thermal desorption and GC–MS (thermal-desorption aerosol gas chromatograph, TAG) [124]. In the TAG system, ambient atmospheric particles, typically $PM_{2.5}$ or PM_1, are collected by means of humidification and inertial impaction. The sample is then thermally desorbed, and analyzed by GC–MS. The sample collection is done concurrently with the analysis of the prior sample, with sampling time typically approximately 60 min [125–127]. A sophisticated version of the TAG includes GC × GC instead of single GC (Fig. 5) [129, 130].

Comparison of in-situ and off-line analyses with TAG, using the GC × GC approach, revealed that fewer compounds were visible in in-situ measurements [131]. The main reasons
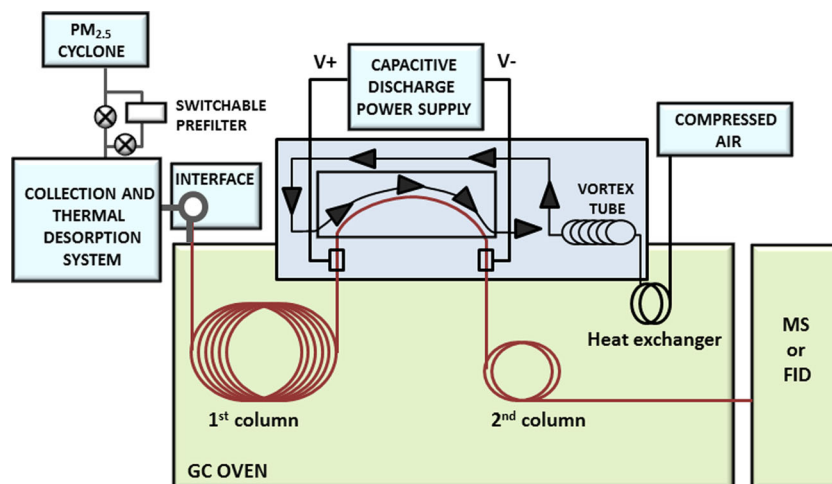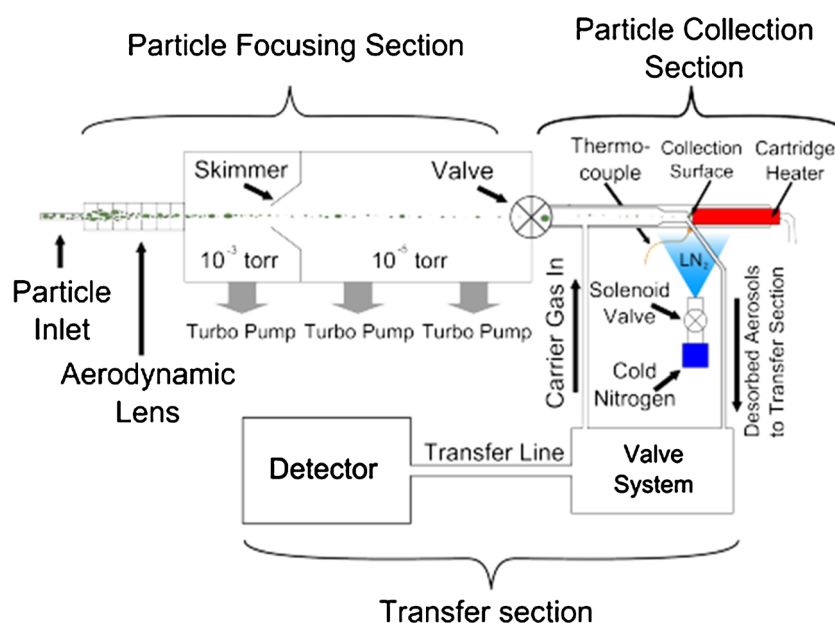
Fig. 5 TAG-GC × GC–MS system (modified after Ref. [128])

for this were that the off-line cartridge samples were more concentrated than the on-line samples for the field measurements and that the sensitivity of TOFMS was different from that of the FID used in this first version of the TAG-GC × GC system. In addition, sampling artefacts for off-line measurements probably caused some of the observed differences.

A recent study presented a novel type of sampling system connected on-line with GC–MS (Fig. 6) [133]. The collection is achieved by a high-vacuum environment on a collection surface (max. −165 °C). After sampling, the analytes are thermally desorbed in a flow of carrier gas and transferred into the GC–MS for analysis. The system has been used for the collection and analysis of particles in the size range 70–500 nm. The results have been in good agreement with offline measurements.

For water-soluble compounds, in-situ systems based on LC are available. The most common method is based on ion chromatography (IC). Several commercial systems are available for the analysis of both anions and cations, including the PILS-IC and the gas particle with IC (GP-IC; DIO, TFS). PILS has been recently reviewed by Timonen et al. (2010), including both the principle of the PILS and its applications in aerosol analysis.

Typically, detection in the PILS-IC system is based on electrochemical detection, and the main area of application is inorganic-ion analysis [134]. However, PILS has a high potential for wider applications because liquid sample flow can be coupled on-line with several instruments. A recent study presented an online PILS-IC–MS method for the analysis of levoglucosan [135]. The LC method was based on high-resolution anion-exchange chromatography (HPAEC),

Fig. 6 Schematic of ACM instrument with three main sections consisting of aerodynamic lens and the vacuum system, the particle-collection section, and the transfer section (reproduced, with permission, from Ref. [132]

and the mass spectrometry was based on quadrupole (Fig. 7). The analysis cycle was 8 min. The method had generally good agreement with off-line analysis of filter samples by the same analytical system. However, correlation with on-line measurement with HR-ToF-AMS was not very good. In comparison with the off-line method, PILS-HPAEC–MS somewhat underestimated levoglucosan concentrations. The smaller results from the PILS-HPAEC–MS method may be caused by sample loss inside the PILS, possible evaporation or degradation of analytes in the PILS, or higher analytical uncertainty for the lower concentrations in the HPAEC–MS. Compared with the on-line measurements, it was concluded that both methods detected similar evolution of the concentrations, but the HPAEC–MS had more variation in the concentrations. The different results were explained by the fact that the on-line AMS system measured the $C_2H_4O^{+2}$ fragment, which obviously was not related to levoglucosan or other anhydrosugar molecules alone. In another application, PILS was coupled on-line with HPLC–MS via a solid-phase extraction (SPE) step. Strong anion-exchange material was used in SPE, which enabled preconcentration of organic acids before the analysis. Although the PILS-SPE-HPLC–MS combination is promising, a long sampling time was needed to obtain a sufficient amount of compounds for the analysis [128].

The same sampling principle as in PILS is adopted in monitor for aerosols and gases in air (MARGA). Here, in addition to aerosols, atmospheric gases are sampled with a rotating wet denuder and analyzed by ion chromatography. The instrument was recently used for analysis of ammonia and nitric and nitrous acids in gas and aerosol samples collected in the boreal forest [131]. In theory MARGA can be used for on-site on-line measurement of less abundant organic species as well, but to date no applications have been published.

On-line analysis

On-line systems for the chemical characterization of submicron aerosol particles in real time are typically based on mass spectrometry, and different instruments have been developed, including commercial instruments. Generally, on-line MS can be divided into bulk-aerosol mass spectrometry and single-particle mass spectrometry. Bulk-aerosol MS means that the average chemical composition of thousands of particles in the submicron size range is analyzed. Single-particle MS uses pulsed-laser ionization techniques for the evaporation and ionization of particles in the size range from ~100 nm to ~3 μm [132].

Currently, aerosol mass spectrometry (AMS) is the best known MS system used for aerosol analysis, and it has been used for the investigation of both organic and inorganic particles in both the field and the laboratory [137]. The most common AMS systems are presented in Fig. 8. The AMS operates by using an aerodynamic lens to sample submicron particles into vacuum where they are aerodynamically sized, thermally vaporized on a heated surface, and chemically analyzed via mass spectrometry.

Ionization in AMS systems is typically achieved by EI, CI, or LDI [136, 139]. EI is the most commonly used method, and EI spectral libraries have been built to assist compound identification. EI is a harsh ionization technique which produces abundant fragment ions from a single compound, and thus the obtained spectra consist of thousands of fragments that make the data interpretation very challenging. CI and LDI are softer ionization techniques and produce fewer fragments, which makes molar mass studies more feasible. An example of LDI with AMS is nano-AMS (NAMS) [140–143]. In NAMS, individual particles are charged with a unipolar charger before entering the instrument, and size-selectively captured in the

Fig. 7 Schematic presentation of PILS-HPAEC-MS system. Arrows represent the flow of the aerosol sample and liquids within the system. *SUP* = suppressor, *CC* = conductive cell, *STD* = standard solution (reproduced, with permission, from Ref. [136])
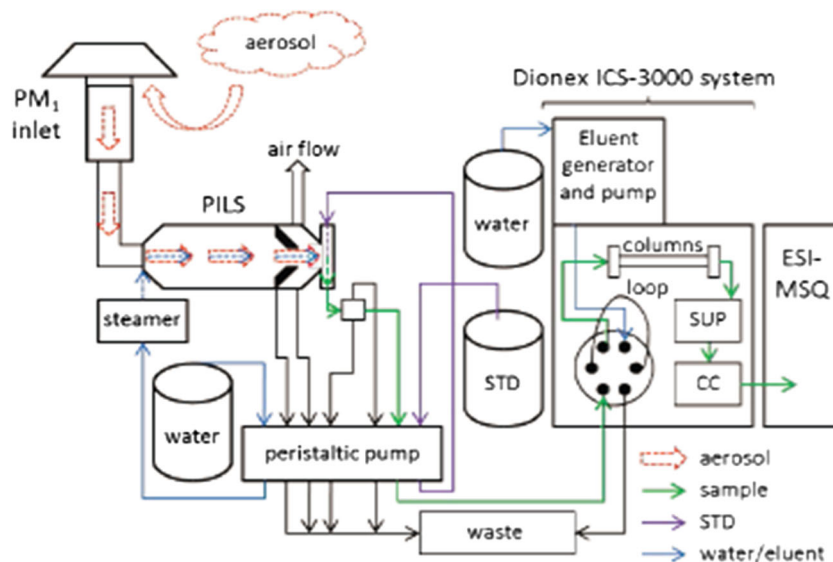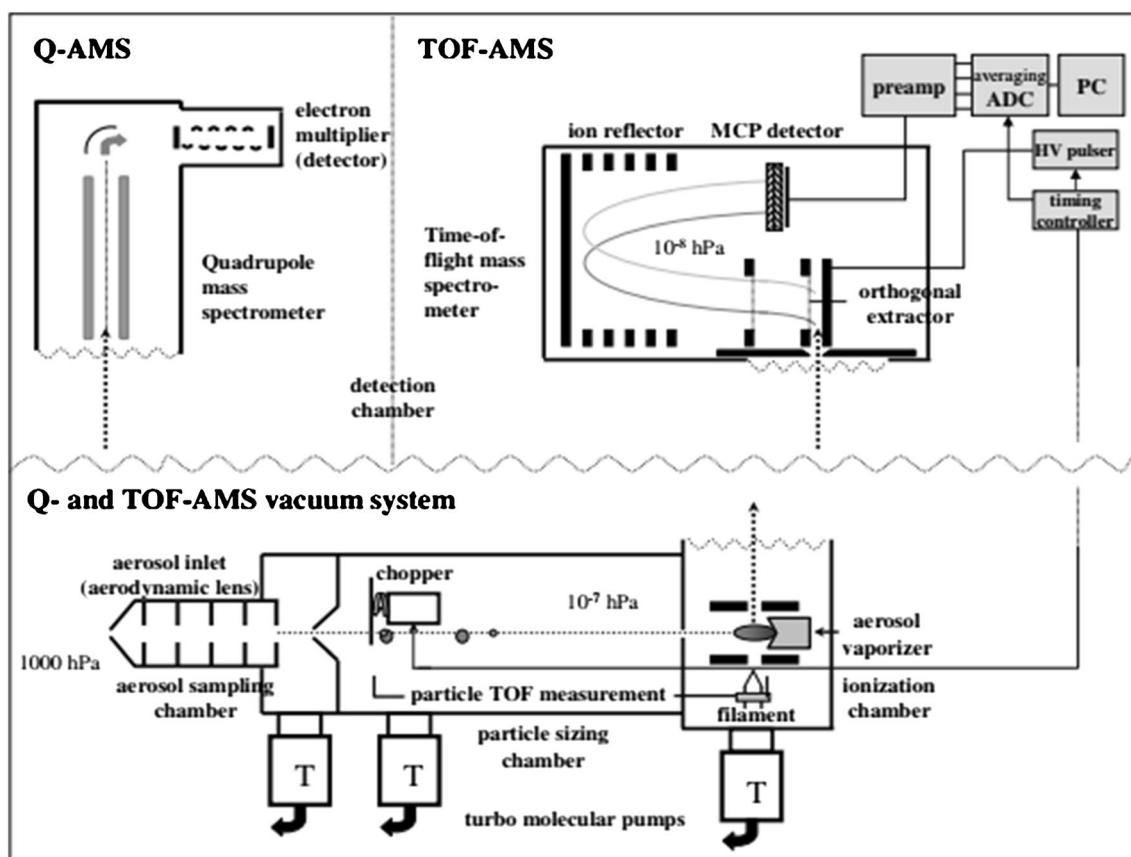
Fig. 8 Schematic diagram of AMS systems (reproduced, with permission, from Ref. [138])

trap and subsequently ionized by laser ionization (Nd:YAG laser at 532 nm). The advantage of this configuration is the ability to size and analyze particles in the 10–30 nm range. It should be noted that in LDI observed intensities are highly affected by matrix effects, type of laser, flux energy, and wavelength. Thus the ion signal intensities in NAMS mass spectra are strongly affected by plasma energetics. Whereas EI normally produces a standard type of spectrum, LDI does not, and this makes the interpretation of the spectra more challenging. Typically, averaging the spectra is used; this is a reasonable trade-off between precision of the analysis and high-enough time-resolution. Other single-particle measurement systems based on LDI are the rapid single-particle mass spectrometer (RSMS) [144, 145], ultrafine aerosol TOFMS (UF-ATOFMS) [146], and AMS with valve collection system [147]. For selected classes of compounds, for example PAHs, resonance-enhanced multiphoton ionization (REMPI) with intense UV laser pulses can be used [148]. Recently, quantitative features of single-particle analysis have been improved by using pseudo-internal standards for correction of matrix effects [149, 150].

Although most aerosol mass spectrometers use either a linear quadrupole or TOF-MS, ion-trap mass spectrometers have been successfully used for single-particle analysis [151].

The ion trap offers a multitude of desirable properties: versatility, compact size, high duty cycle, high sensitivity, full spectrum collection for single particles, large accessible mass range, and tandem-mass-spectrometry capabilities for further speciation. The high-resolution version of TOFMS (HRToF-AMS) is capable of mass resolution ranging from 3000 (in V-mode) to 4500–5000 (in W-mode), with m/z range from 1 to 1200 [152]. The detection limit of the AMS varies from 0.003 μg m^{-3} (C-TOF-AMS) to <0.04 μg m^{-3} (HR-ToF-AMS, W-mode) [153].

The mass spectra obtained by AMS can be used to quantify organic mass. However, the spectra are very complex and this makes the identification of most individual organic molecules very challenging. MS–MS techniques would be a useful approach in the identification of the compounds, but this approach has not yet been widely used in aerosol analysis. Soft ionization should be used in MS–MS studies to preserve the structural information of the molecular ion before entering the detector. An example of the MS–MS approach is presented in Fig. 9, using APCI-IT-MS [155]. The figure shows MS^2 fragmentation of m/z 185, measured at the boreal field site, with the online MS^2 spectrum on m/z 185 of α-pinene, limonene, and Δ3-carene ozonolysis products in the laboratory. Comparison of the MS–MS spectra from the laboratory

Fig. 9 Online MS^2 experiments from field samples (Hyytiälä, Finland) and from laboratory chamber studies using ozonolysis (reproduced, with permission, from Ref. [154])
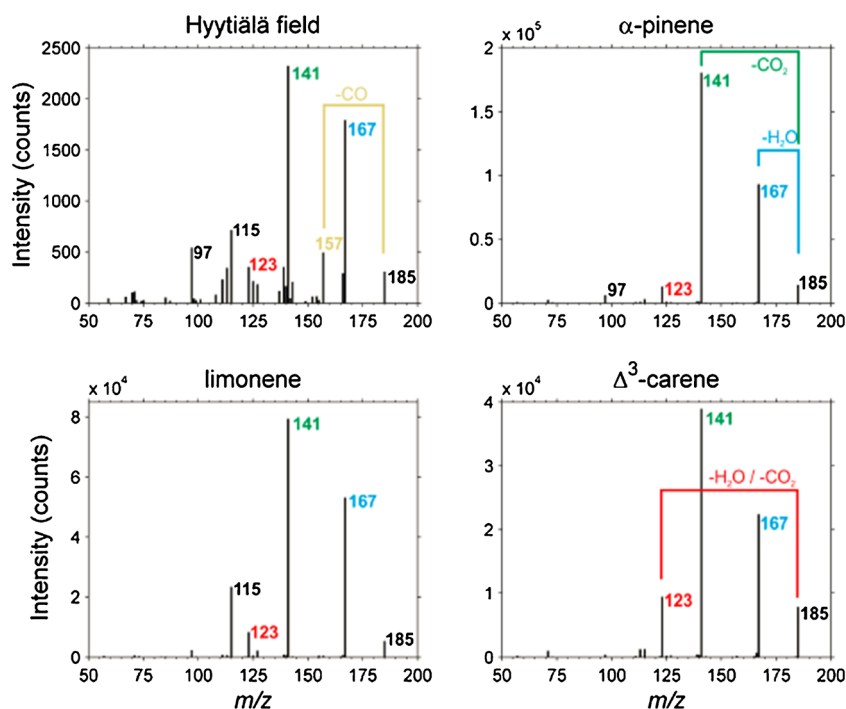
experiments with the actual samples aids in the identification of the compounds.

Method validation, data handling, and identification procedures

Most of the qualitative studies of atmospheric aerosols have not included strict method validation and extensive quality-assurance procedures, but quantitative methods and methods used by authorities for air quality control require sufficient validation of the method. Certified reference materials (CRMs) are available for atmospheric aerosol particles, but they are not always suitable for validation because of the limited number of quantified compounds. Combined aerosol sample made from previously analyzed samples provides a good alternative to CRMs. Several CRMs are available through NIST, e.g. 1648a (urban particulate matter), 1649b (urban dust), and 2787 (fine particulate matter <10 μm). These materials are well characterized only for analysis of PAHs, PCBs, and metals. Other values are not certified. Some compounds or compound groups, e.g. sugar polyols, ergosterol, and amino acids, have been characterized in these CRMs by separate studies, but are not certified [156, 157]. To ensure accuracy of the measurements, internal standards or the standard-addition method are frequently used. Because most of the studies are dealing with a limited number of compounds, labelled standards are recommended, particularly for direct infusion and for LC–MS analysis, where matrix effects have a major effect on the quantitative analysis [158]. Matrix effects are also present in AMS measurements, and recently

methods enabling quantitative analysis by using pseudo-internal standards have been developed [155, 156]. However, for newly characterized compounds, e.g. organosulfates, for which authentic or labelled standards are not yet available, surrogate standards can be used for correction of errors arising from sample preparation and analysis [138]. For nontargeted analysis, group-specific internal standards can be used; however, the quantitation is then not fully accurate because this type of standard cannot fully compensate for the analytical variation.

Data handling and identification of compounds is a crucial part of aerosol analysis when non-targeted analysis is performed. These non-targeted methods produce a large amount of data, and therefore several computer-aided methods have been developed both for data preprocessing and for data analysis and identification. Particularly for direct-infusion MS and on-line AMS measurements, sophisticated tools are needed for data processing, including different multivariate methods that allow for the improved separation of the organic ambient-aerosol component into distinct chemical classes [154, 159, 160].

Single-particle analysis presents a particular challenge in terms of data interpretation because data sets typically consist of tens to hundreds of thousands of individual particle spectra. To facilitate data analysis, automated procedures are typically used for the classification of the mass spectra. Several different types of algorithm have been used to group similar particle-composition types, including artificial neural networks and factor analysis [161]. The artificial neural network groups particles on the basis of similarities among their

spectra. The fast adaptive resonance algorithm ART-2a has found use in the classification of individual nanoparticle spectra obtained by RSMS [162], UF-ATOFMS [163], and NAMS [164]. Clustering of single-particle mass spectra with the K-means algorithm enables the use of a user-defined number of clusters (K) on the basis of their spectral similarity [156]. Factor analysis, for example positive matrix factorization (PMF) and multivariate curve resolution, has been used particularly with AMS methods. Factor analysis deconvolves a time series of simultaneous measurements into a set of factors, representing groupings of chemical compounds that correlate in time, and their time-dependent concentrations. These factors can then be related to emission sources, chemical composition, and/or atmospheric processes. Multivariate factor analysis thus offers a quantitative and simplified description of the thousands of individual organic species [165]. However, this also means that the factor-analysis methods lose the diversity of particle compositions present in a given profile.

Direct-infusion MS also requires specific software for data processing and identification. A similar approach can be used for identification in LC–HRMS and CE-HRMS analyses, together with retention and migration-time data. In the interpretation of the mass spectra, the first step is to ensure that the signal of interest really corresponds to a monoisotopic ion and not to a natural isotopologue ion or an adduct ion. Elemental compositions can be deduced from accurate mass measurements and used for further database queries. To aid the identification, several chemical databases containing huge numbers of chemical structures are available to assist structural elucidation after fragmentation of the metabolite (e.g., ChemSpider) [166]. Also, several in-silico software packages for predicting in-silico spectra for compounds are available [167]. Compound identifications are mainly made through mass-based searches, i.e., searching the m/z value of a molecular ion of interest against the database(s), at a given tolerance range. The compounds having molecular masses within a specified tolerance range are regarded as putative identifications. For verification of the identification, authentic standard compounds should be analyzed together with the actual compounds using MS–MS. The main problem with this approach is that even putative identification cannot be made with sufficient accuracy, because of the existence of isomers and the limited accuracy of mass spectrometers [168]. In the worst case, one molecular ion can have more than 100 putative identifications, making the manual verification very tedious and time-consuming and thus poorly suited for the identification of large numbers of compounds. Several in-silico methods have been developed for identification, particularly for the interpretation of tandem mass spectra [169–171]. A possible structure or substructure of an unknown molecular ion can be obtained by comparing the spectrum with hypothetical spectra predicted through in-silico fragmentation approaches. Prediction can be made by, e.g., using a rule-based predictor, which relies on fragmentation pathways collected from the literature. Commercial tools are available for rule-based prediction, e.g. ACD Fragmenter (ACD/Labs) [172] and Mass Frontier (Thermo Scientific). Other in-silico fragmentation tools are also available, including Fragment Identificator (FiD) [173] and MetFrag [24]. These rely on a different principle, namely generating a list of possible fragments through combinatorial disconnection of chemical bonds in the compound. The isotopic abundance pattern can serve as a powerful additional constraint for removing wrong elemental-composition candidates. The actual ratios of the stable isotopes differ slightly for each element within a narrow range. Therefore each monoisotopic molecular ion is always accompanied by additional isotope ions, and the abundance of the isotope ions is dependent on the actual elemental composition. Hence this can be used as a powerful filter in calculating unique elemental compositions from mass-spectral data. It has been revealed that high mass accuracy (1 ppm) and high resolving power alone are not sufficient for obtaining a small number of molecular-formula candidates for the elucidation of molecular structure in MS determination. However, using an orthogonal isotopic-abundance-pattern filter, it is possible to reduce substantially the number of molecular-formula candidates. Identification requires the use of accurate mass measurements for the determination of elemental composition, combined with MS^n experiments to obtain information on the molecular fragments. It should also be noted that one compound may produce multiple peaks because of the presence of isotopes, adducts, and neutral-loss fragments. Therefore, ion annotation is crucial to recognize a group of ions likely to originate from the same compound. Unfortunately, construction of universal spectral databases for API-MS is challenging because of the poor reproducibility and high inter-instrument variability of fragmentation patterns.

Hyphenated methods combining chromatography with mass spectrometry require different tools for data processing. In targeted methods, no specific data processing is typically needed, but for nontargeted profiling methods tools for identification of unknown compounds are often needed. For example, several automated methods have also been developed for the processing of multidimensional MS data produced, e.g., by GC × GC, particularly for the identification of compounds and chemical groups [84, 174, 175]. Automated procedures have been developed both for classification of chemically related compounds into groups and for automated identification of individual species. The implementation of such classification and identification procedures simplifies the interpretation of data, making rapid peak classification, searching, and identification easier.

In GC–MS-based applications, conventional GC–MS methods are typically used in target-compound analysis whereas GC × GC–TOFMS systems are used in non-

targeted profiling. In non-targeted profiling, the main challenge is identification of the compounds. Typically, by using the available spectral libraries, usually together with retention-index data, putative identification can be obtained for a large number of compounds. However, a large fraction of the detected compounds remains unidentified. Thus, different procedures have been developed to assist the identification. One approach relies on group-type identification of the compounds detected by GC × GC–TOFMS. The procedure is based on primary and secondary retention times and MS fragmentation patterns developed by Welthagen et al. [174]. The idea of using fragmentation patterns in mass-spectral data to identify and to classify compounds is a well-established technique developed for GC–MS. In GC × GC–MS analyses, classifiers help to identify unknown peaks and aid in statistical analysis because of improved spectral quality resulting from better separation and the possibility of including first and second-dimension retention-time restrictions on compound-class assignments. Three types of classifier were used: domain-knowledge classifiers (based on fragmentation-pattern and retention-time rules), a substructure-type classifier (multivariate classifier based on mathematical transformations), and a category-type classifier (multivariate classifier partly based on domain-knowledge transformations) [175]. The identified compound groups can be plotted as bubble-plots. In addition to classifying peaks for further statistical analysis, use of a bubble plot can help a GC × GC user quickly evaluate group-type separations achieved by a particular column combination. The bubble plot can be used for rapid visual recognition of pattern changes in monitoring studies. This was convincingly revealed in a three-year monitoring program, in the characterization of urban-air particulate matter ($PM_{2.5}$) from Augsburg (Germany) [175]. The data consisted of approximately 15,000 peaks, out of which approximately 700 compounds were identified.

An automated procedure for the identification of individual compounds in atmospheric samples was developed by Kallio et al., and was used for the data analysis of rural aerosol samples [81]. In this procedure, retention indexes, quality variables (minimum required similarity, signal-to-noise value, allowed retention-index difference between experimental and library values), modulation variables, library files, and retention times of reference compounds were used to construct a program for data analysis. The automated procedure was compared with manual identification and it was concluded that the automated procedure worked well if the concentrations were sufficient (above ca. 10 ng m^{-3}), but for very low concentrations (low ng m^{-3}) manual search was more accurate.

Comparison of the techniques

Comparison of the methods used in the analysis of the chemical composition of aerosols is not straightforward, particularly if the off-line and on-line methods are compared (Table 3). Each method has its own advantages and disadvantages. Although the on-line methods can give information about the aerosol composition with high time resolution, the sensitivity and selectivity of the instruments does not enable detailed characterization of the composition. The mass resolution of the AMS systems is currently limited to ca. 5000, which is far less than the mass resolution obtained with laboratory-based instruments which can have a resolution of 600,000. In addition, both on-line AMS and direct-infusion MS cannot differentiate the different isomers. Accurate quantification can be potentially hindered by matrix effects and interferences arising from isotopes, isobars, and isomers of the compounds of interest. Addition of chromatographic separation before the MS step improves the separation and minimizes several of the above-mentioned challenges. Both GC and LC, and even GC × GC, can be used on-site, combined with relatively short on-line sampling (from minutes to a few hours). The combination of on-line sampling avoids several problems of off-line sampling, sample preparation, and analysis, and typically enables the use of shorter sampling times. However, it is typically not possible to use high-end HRMS systems with on-site systems. HRMS, and particularly the ultra-high-resolution MS systems, for example Orbitrap combined with chromatography, enable detection and identification of hundreds or even thousands of compounds in a single run. In addition, in contrast with on-line and on-site analysis, off-line sampling typically enables several (different) analyses to be performed from a single sample. However, off-line methods typically require longer sampling times which, with the transport, storage, and sample preparation required, may cause significant changes in the composition of the samples, particularly for the reactive species. The novel, very sensitive instruments would enable the use of shorter sampling times, particularly if the larger part of an individual (filter) sample would be used for the analysis. However, because off-line sampling is difficult to automate, this would require more manual effort during the sampling.

Comparison of the individual methods, e.g. for off-line analysis, is not easy either. The most efficient separation can be achieved by combining chromatography with HRMS, and among such methods a combination of GC × GC–HRMS enables extremely high separation efficiency. Commercial GC × GC–HRTOFMS systems are currently not available, but are expected to be on the market very soon. GC–HRMS and LC–HRMS systems are already available and they are both well suited for detailed chemical characterization of aerosols. GC is still the method of choice for many of the applications in aerosol characterization, because most of the compounds present in aerosol particles are sufficiently volatile to be analyzed by GC-based techniques. In addition, identification of unknown compounds is easier with GC–MS because of extensive commercial spectral libraries for EI-MS and the

Table 3 Comparison of the main features of methods for analysis of atmospheric aerosols

	LC–TOFMS, QTOFMS, Orbitrap	LC–QqQMS	GC–qMS, QqQMS	GC–TOFMS, GC × GC–TOFMS	CE–MS	DI-MS	AMS, TOFMS
Mode	Off-line	Off-line	Off-line and/or on-site	Off-line and/or on-site	Off-line and/or on-site	Off-line	On-line
Approach	Profiling, semiquantitative	Targeted, quantitative	Targeted, quantitative	Profiling and targeted quantitative	Non-targeted and targeted	Non-targeted and targeted	Profiling and semiquantitative
Sample amount[a]	fg–ng	fg–ng	pg–ng	fg–ng	ng	ng	pg–ng
Analysis time	5–40 min	5–40 min	5–40 min	5–40 min	5–40 min	5–20 min	Seconds–minutes
Reproducibility	Moderate	Good	Good	Good	Moderate	Moderate	Low–moderate
Instrument cost	Moderate–high	Moderate–high	Moderate–high	Moderate–high	Low–moderate	Moderate–high	Moderate
Comments	Suitable for a wide range of compounds; identification of unknowns requires tandem MS	Suitable for a wide range of compounds	Only suitable for small compounds (MW < 700); polar compounds require derivatization; huge spectral libraries available; retention indexes can be used for verification of identification; can be used as on-site instrument	Only suitable for small compounds (MW < 700); polar compounds require derivatization; huge spectral libraries available; clean spectra as a result of very high separation efficiency; retention indexes can be used for verification of identification; can be used as on-site instrument	Suitable for a wide range of compounds; coated capillaries for improving migration-time repeatability	Suitable for a wide range of compounds; identification of unknowns is challenging; matrix effects make quantitation and sensitivity challenging; not possible to separate isomeric compounds	Enables real-time monitoring and single-particle measurements and analysis of nanoparticles; highly affected by matrix effects, laser type, flux energy, and wavelength; isomeric compounds cannot be separated
Data processing	Moderate	Easy	Easy	Moderate	Easy–moderate	Challenging	Challenging
Applications	Humic acids, carboxylic acids, oxidation products, polar compounds, large molecules	Humic acids, carboxylic acids, amines, polar compounds, large molecules	Alkenes, PAHs, aldehydes, mono and sesquiterpenes, monosaccharides, amines, volatile compounds	Alkenes, PAHs, aldehydes, mono and sesquiterpenes, monosaccharides, amines, volatile compounds	Humic acids, carboxylic acids, amines, polar compounds	Humic acids, carboxylic acids, amines, oxidation products, polar compounds, large molecules	Alkanes, PAHs, monoterpenes, ozonolysis products, compound groups

[a] Sample amount is defined as amount of specific compound injected into the instrument

availability of retention indexes that aid in the identification. Particularly, combining GC–EI-(HR)MS and GC–HRMS with soft ionization is a good tool for identification of unknown compounds by combining the fragmentation data with information on the molecular ion. Matrix effects are usually not a serious problem in GC–MS, unlike in LC–MS. However, polar compounds require derivatization before their GC analysis, adding another step to the sample preparation. A recent study compared GC–MS and IC for the determination of alkylamines in aerosol particles [176]. The study revealed that the GC–MS approach is superior to the IC approach for the quantification of primary and secondary alkylamines because of its lower detection limits and higher accuracy. The lower accuracy of IC was caused by evaporation losses of amines during the sample concentration. LC, and particularly UHPLC in combination with HRMS, is, however, a method of choice for those compounds that are difficult or impossible to analyze with GC, including compounds with high molecular weight or thermally labile compounds. The novel HRMS instruments can provide both data on precursor ions and fragmentation data for all detectable molecular ions in a single run, and sensitivity and linear range are also sufficient for the quantitative analysis of trace compounds.

Currently only one commercial system is available for on-line MS-based analysis of aerosol particles in real-time, namely AMS. In particular, the new AMS with TOFMS gives reasonable mass resolution (up to 5000) and thus enables monitoring of the chemical composition of aerosols with good accuracy. However, with EI the interpretation of mass-spectral data is challenging, and it may be difficult to find unique fragments for specific compounds. Soft ionization produces fewer fragments, and thus the interpretation is more straightforward. On-site instruments, for example PILS-IC, MARGA, TAG, and TAG using GC × GC–TOFMS, do not provide actual real-time monitoring, but they do enable monitoring of the chemical composition over a reasonable time span, typically less than 60 min. By combining an additional separation before the (MS-based) detection, more compounds can be detected and identified in comparison with AMS. In many cases the results are more reliable, as was revealed for levoglucosan, for which the molecular fragment used for detection with AMS was not sufficiently specific and the method gave different results from the on-site analysis with PILS-HPAEC–MS [134].

Conclusions

No single instrument is sufficient for providing detailed data on aerosols, and thus the best option, when possible, is to combine on-line or on-site measurements with off-line measurements. Off-line measurements with state-of-the-art instruments are essential, particularly for the identification of novel compounds. However, they are not suited for the analysis of labile and reactive compounds, for which on-site instruments provide sufficient separation efficiency and sensitivity. On-line systems, for example AMS, are the best option for fast real-time monitoring of target compounds. A combination of data on these types of method and further development of more robust methods both for sampling and analysis, particularly for nanoparticles, will enable more detailed and reliable elucidation of the sources, structure, transformation and formation processes, and identification of poorly understood organic atmospheric compounds.

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