

Laboratory Mass Spectrometry of Intact Atmospherically-Relevant Particles

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Abstract

The physical and chemical properties of atmospheric aerosols profoundly impact the climate and human health. With diameters from sub-nanometer to tens of microns, a multitude of different experimental techniques suited to specific size ranges must be employed to characterize them. While mass spectrometry can be performed *on* particles of any size by destroying them and characterizing their molecular and atomic compositions, the masses *of* atmospheric nanoparticles with sizes below 10 nm can be measured with enough precision to observe discrete changes of their chemical composition while they remain intact. This enables direct study of their structure and reactivity in well-controlled laboratory experiments, complementing ambient field measurements. Here, we review the application of mass spectrometry and unique experiments based on mass spectrometers to measure the composition, stability, structure, and formation mechanisms of aerosol particles. We discuss the instrumentation employed in these experiments, including ion mobility separation, ion trap reactivity, and laser spectroscopy, that are often combined with mass spectrometry, and highlight illustrative examples of these techniques to prototypical atmospheric nanoparticles. We also highlight emerging mass spectrometry techniques that could extend these studies to larger nanoparticles and enable new insights into current unsolved problems involving atmospheric nanoparticles.

Keywords:

atmospheric particles, aerosols, clusters, mass spectrometry, climate

1. Introduction

Atmospheric aerosols greatly impact human health and the earth's climate.(1; 2) These particles cause severe respiratory illnesses and influence the energy flux (radiative forcing) of the atmosphere.(3; 4) In the latter case, the thermal effects brought on by aerosols on global climate contribute to some of the largest uncertainties in anthropogenic radiative forcing (as shown in Figure 1a), and impact the accuracy of existing climate models.(5; 6) Aerosols scatter incoming solar radiation (direct effect) or seed clouds that increase earth's albedo (indirect effect), and have a net cooling effect on global temperature. While

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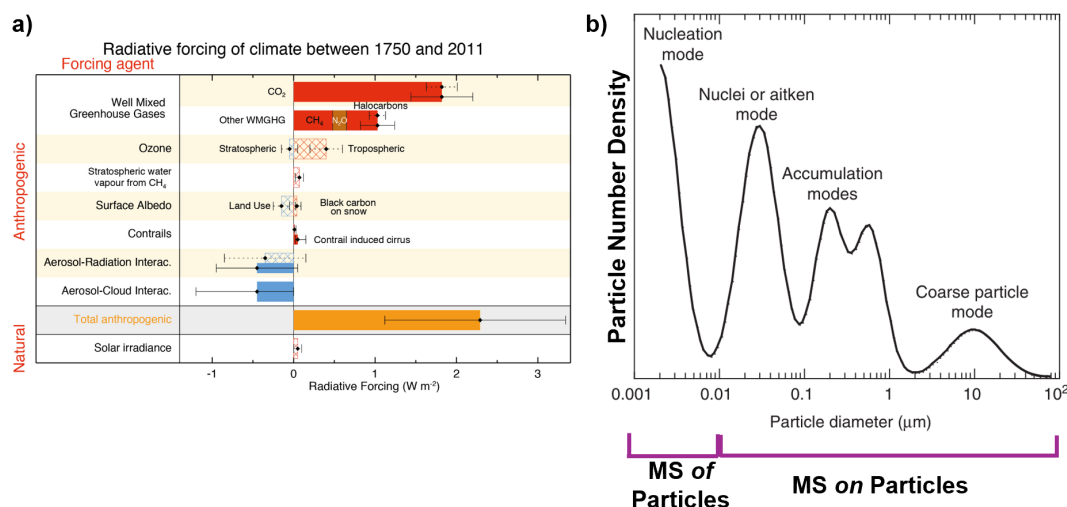


Figure 1: (a) Natural and anthropogenic factors that affect global radiative forcing. Aerosols likely have a net cooling effect on global temperature and contribute the largest uncertainties in current climate models. (b) Multi-modal size distribution of atmospheric particles. Laboratory-based MS studies probe particles belonging to the nucleation and Aitken modes (MS of particles) while field studies perform MS on particles of any size. Adapted with permission from reference (5) and (17).

significant progress has been made to understand these effects, identifying the various sources and sinks of particles remains a major challenge in developing reliable models of present-day, pre-industrial and pristine environments.

Aerosols vary widely in size, number concentration, chemical composition and, in spatial and temporal distribution.(7; 8; 9) Typically ranging in diameter from 0.001 μm - 100 μm , aerosols are classified as shown Figure 1b. Nucleation mode particles include those freshly made from the clustering and uptake of trace vapors in the atmosphere (new particle formation, NPF). The small, thermodynamically stable clusters formed via NPF contribute to 10-90% of particles in the atmosphere.(10; 11; 12; 13; 14) Aitken mode particles are formed by the accretion of vapors on nucleation mode particles.(15; 16) Accumulation mode particles are composed of those that were either formed by the growth of smaller particles via coagulation and condensation processes while coarse particles are made by mechanical processes such as wind and erosion or are directly emitted (primary particles such as dust, soot, and sea spray) into the atmosphere.(8)

Atmospheric particles are chemically complex and require powerful analytical techniques to be applied for their characterization. Field studies of atmospheric aerosols offer information on particle abundances,(18) chemical composition, variation in particle size,(19) and regional conditions that promote particle growth.(20; 21) Laboratory efforts to investigate aerosols can be broadly categorized as techniques that analyze aerosols obtained by direct sampling from the atmosphere or by their production in simulation chambers,(22; 23) sea spray chambers,(24) or other validated sources of atmospherically-relevant particles.(25) These efforts have identified sulfates, nitrates, organics,(26; 27) ammonia,(28) sea salt, metal oxides,(29) and iodine-containing

compounds(30) as some of the key chemical species in atmospheric particles, largely by the application of mass spectrometry (MS) methods. Efforts are ongoing to link particle composition and state to their roles in atmospheric processes such as cloud formation.(31)

The majority of MS studies have been performed *on* particles, which is to say that the goal of the studies is to measure the mass of the molecules composing the particle. More rarely is the mass *of* the particle measured, as for most particles, this information is largely redundant with increasing particle sizes. The multitude of chemical species making up particles larger than 10 nm makes it impossible to directly infer composition from particle mass. However, with the advent of high resolution, high precision mass analyzers, for the smallest of particles, it is now possible to determine exact chemical composition from particles composed of up to several tens of molecules, or even larger for particles formed in well-controlled laboratory settings.(32; 33; 34) Filtering of particles by mass can be performed non-destructively, yielding a compositionally pure “sample” of particles for further study. Such unambiguous identification of particle composition leads to detailed study of their chemical transformation from an exactly known starting point, rather than inferring these changes from measurements of a disperse ensembles of particles.

MS is routinely used to selectively detect the amount of a given substance/analyte and determine the chemical composition of that analyte. The production and detection of fragments—groups of atoms or smaller portions of the analyte—provide insight into the structure of the analyte via MS. Owing to the availability of different ionization and analysis schemes, MS can be applied to the qualitative and quantitative examination of both ensembles of particles and individual clusters. In this review, we use the acronym MS to refer to both the technique and the instrument. In MS, the measurable quantity is the mass-to-charge ratio (m/z) of an collection of ions, and when the charge is unity the m/z corresponds to the ion’s mass. Thus, the analyte not only has to be an innate ion or ionized in order to be detectable by MS, the m/z that an ion is detected as decreases as the charge of the ion increases. For example, the largest analytes detected by MS include biomolecules and long-chain polymers that typically have masses between several hundred kDa and a few MDa, with the former often, being multiply charged, detected at lower m/z values.(35; 36; 37; 38; 39; 40) A hypothetical spherical cluster of mass ≈ 300 Da (≈ 1 nm in diameter) that grows into a climatically relevant size (≈ 10 nm) will obtain a mass of ≈ 3 MDa. If singly charged, the m/z of this particle will be close the detection limit of common MS analyzers, thereby requiring the development of new instrumentation capable of detecting such a particle. In the next sections, we will provide an overview of ionization and mass analysis techniques routinely applied to atmospheric nanoparticles, discuss extensions of these techniques to gain information beyond simply mass and relative abundance, and highlight new insights gained with these techniques, primarily in the context of NPF. We will then sketch paths towards more detailed studies of small particles as well as extensions of mass analyzers to larger particles.

2. Common Instrumentation Themes

A basic idea of MS instrumentation is important to understand the scope of MS experiments. All MSs have three main components: an ion source (typically at atmospheric pressure), a mass analyzer, and a detector (latter two components are at high vacuum). Ions are transported from one component to another using ion guides, which constrain ions using radio-frequency (RF) fields while allowing background gas to be pumped away.⁽⁴¹⁾ Mass analyzers are broadly classified into low- and high-resolution analyzers (LR-MS and HR-MS, respectively) based on the smallest difference in m/z between two peaks that can be reliably distinguished. LR-MS, such as quadrupole mass analyzers (QMA/QMS), is ideal for quick identification of m/z and abundances of different chemical components in a mixture but offer a resolution of 1000-3000. HR-MS is ideal for distinguishing the various chemical species that make up complex mixtures such as atmospheric particles, including isomers and isotopologues. HR-MS that can separate ions with mass differences of 0.001 Da and resolving powers of 50,000-100,000 or higher are preferred in the analysis of atmospheric particles and require the use of sophisticated and expensive instrumentation. Time-of-flight (TOF), Orbitrap and Fourier transform ion cyclotron resonance (FT-ICR) are commonly applied high resolution techniques.^(42; 43)

Both commercial and custom-built MS benefit from the use of ion traps, designed to capture and store ions using electromagnetic fields. Ions can be trapped by a RF electric fields (Paul traps) or by a combination of electric and magnetic fields (Penning trap). FT-ICR MS, for example, uses a Penning trap while TOF analyzers are often coupled with Paul traps.⁽⁴⁴⁾ Trapped ions are cooled by multiple collisions with buffer gases such as helium to reduce their internal energy and limit any fragmentation. Carefully controlled collisions between ions and buffer gas (Collision Induced Dissociation (CID)) can lead to fragmentation, where analysis of the fragment masses offers insight into the structure of the ions.⁽⁴⁵⁾ Mass selection, where an ion of a specific m/z is isolated, prior to, and after, ion trapping enables the study of cluster/size specific effects in laboratory MS experiments. For example, isolated and trapped ions can be exposed to different reactive vapors and any resulting changes in m/z can be detected, providing a way to study the kinetics and thermodynamics of gas phase reactions. Coupling MS with other analytical techniques such as chromatography, ion mobility spectrometry (IMS) and spectroscopy offers enhanced characterization, including information on the size, chemical behaviour and structure of the analyte.^(41; 46; 47)

A discussion on the various instruments used in field studies of atmospheric particle is outside of the scope of this review but will be briefly discussed here. The Aerosol MS (AMS), the Aerosol TOF MS (ATOFMS), and the Atmospheric Pressure Interface TOF MS (APiTOF) are often used to examine ambient particles.^(48; 49; 50; 51; 52; 53) The AMS can measure the mass of an ensemble of particles having a particular aerodynamic diameter, while the ATOFMS measures the mass of single particles. Both instruments apply MS *on* particles and provide insight into the chemical constitution of the sampled particles, but are not

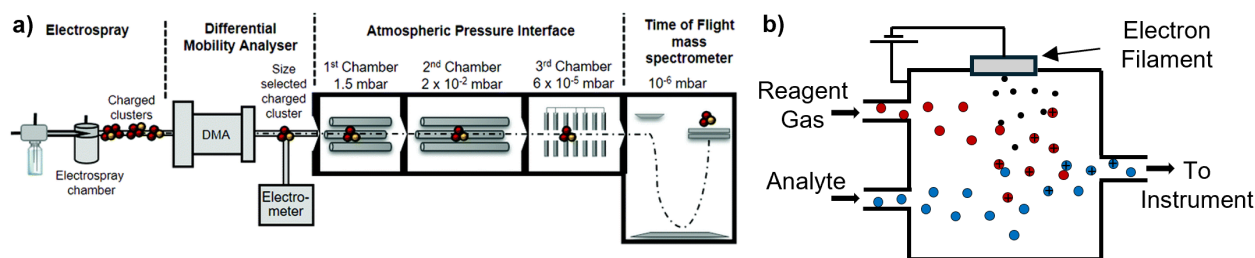


Figure 2: (a) Schematic of APiTOF with a ESI source and a differential mobility analyzer. (b) Schematic of the CI source. Red circles are the reagent gas molecules, blue circles are analyte molecules and black circles are electrons that ionize the reagent gas. The APiTOF was adapted with permission from reference (55).

sensitive to particles with diameters of several tens of nanometers. The APiTOF, shown in Figure 2a, is used to probe the mass and composition of nucleation mode particles and is sensitive to ambient ions and clusters.(53) An ionization source and a mobility analyzer are often included in the sampling region of the APiTOF the sampled particles are directed into the MS using ion guides and are ultimately detected by a TOF analyzer.

2.1. Particle Ionization Techniques/Sources

Since only ions can be analyzed, ionization is an important component of MS. Electron ionization (EI) and photoionization (PI) are two commonly used ionization techniques. In EI, high energy (70 eV) electrons from an electron beam collide with the vaporized sample, resulting in the formation of a radical cation. The energy imparted in these collisions is enough to induce bond cleavage and the formation of fragment ions. Analysis of the fragments offers some details on the bonding motifs in the ion, but the mass spectrum often does not contain the intact molecular ion. The extensive fragmentation and the lack of the molecular ion pose a challenge to the precise measurement of the molecular weight and identity of the compounds present in the analyte. Thus, EI is a harsh technique and not preferred for the analysis of intact atmospheric particles.(54) Softer ionization techniques, such as chemical ionization (CI) and electrospray ionization (ESI), produce molecular ions without inducing fragmentation. ESI has been used to generate atmospheric particles in a laboratory environment, while the chemical constituents of aerosols have been ionized by CI or PI after being sampled and vaporized. PI, CI and ESI are discussed below.

2.1.1. Photoionization

PI occurs when an atom or molecule absorbs a photon, usually from a laser, and ejects an electron to form a cation. In order to induce ionization, the energy of the photon has to exceed the ionization energy (IE) of the chemical species.(56) PI efficiency (PIE), the ratio of number of ions formed to the number of photons absorbed by the molecule, typically increases as photon energy approaches the IE of the molecule. However, PIE is reduced considerably if the dissociation energy of the molecule is lower than its

IE and the absorption of a photon results in dissociation and not ionization of the molecule. Hence, PI can only be used to ionize those samples that have lower IE than dissociation energy.(57) PI has been applied to ionize vaporized molecules from ambient particles as well as particles made in a controlled laboratory environment.(58; 59; 60; 61; 62; 49) Laser desorption ionization (LDI), a type of PI, has been used to ionize atmospheric particles that have been collected on a filter and re-vaporized for prior to ionization. Generally, ionization of most chemical species needs photons with 10 eV or higher energy, requiring access to synchrotron facilities or high power lasers in the laboratory. The use of latter can result in extensive fragmentation and prevent proper mass analysis. A custom-built PI-TOFMS uses frequency-tripled light from a Nd:YAG laser to irradiate a mixture of Xe:Ar in the PI-chamber of the instrument.(63) Ionization of this inert gas mixture produces tripled light at 118 nm than can ionize the analyte. While this set up has been used to ionize species that have large ionization potentials such as iodine oxides I_xO_y , PI of atmospherically relevant species is a challenging task in the laboratory and is harder to achieve in field studies.(64).

2.1.2. Chemical Ionization

CI ionizes an analyte through ion-molecule reactions between an ionized reagent gas and the analyte molecule, akin to an acid-base reaction. In the ionization chamber the partial pressure of the reagent gas is maintained higher than that of the analyte, ensuring frequent collisions. The reagent gas is first ionized by collisions with electron or alpha particles, creating charged species that then ionize the analyte. CI leverages differences in proton affinities, with the analyte typically having higher affinity in cation mode. Unlike in proton-transfer reaction MS (PTR-MS), which uses hydronium ions for ionization, CI offers customization of reagent ions based on the proton affinity of the analyte.(65) For example, nitrate CI-MS is used for acidic analytes, while water-CI-MS suits basic analytes.(66; 67; 68; 69; 70) Various CI-MS methods, such as those using ethanol, acetate, or iodide, have enabled the detection of both cationic and anionic species in the atmosphere, including amines, acids, and unsaturated organics.(71; 72)

2.1.3. Electrospray Ionization

In ESI, a solution containing the analyte(s) flows through a capillary held at several kilovolts. At the capillary tip, a conical droplet (Taylor cone) forms and, aided by coaxial gas flow, emits a fine mist of droplets. There is considerable debate regarding the formation of gas-phase ions via the ESI process, but the general consensus is that a highly charged droplet forms initially, which then undergoes multiple cycles of solvent evaporation and fission to produce ions.(73) ESI results in little to no fragmentation, and offers fine control over spray and solution conditions to produce clusters with sufficient concentration for MS detection. While ESI is a versatile method for producing both cationic and anionic species, the formation of particles by ESI is mechanistically different from that occurring in the atmospheric. Therefore, the relative abundances

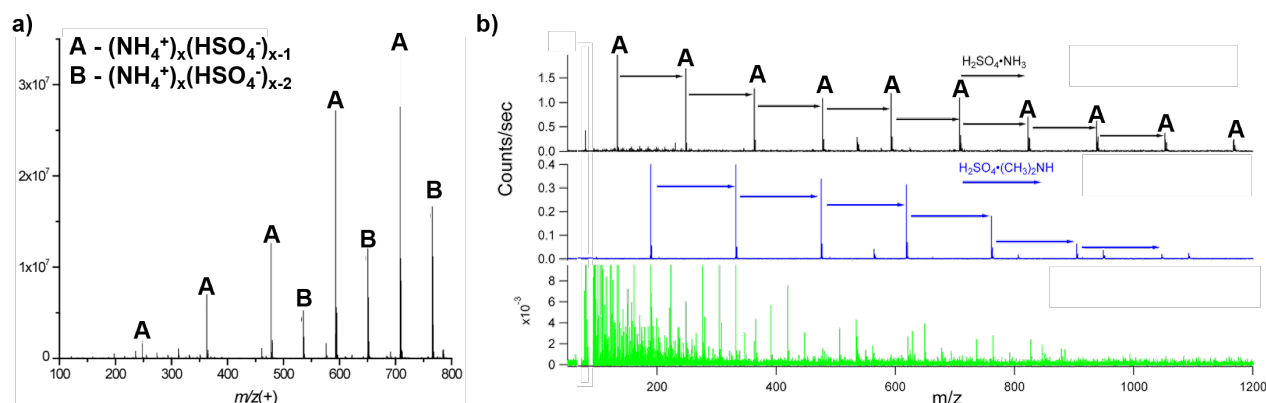


Figure 3: (a) Cationic ammonium bisulfate clusters generated by ESI. (b) CI-MS obtained from CLOUD showing cationic ammonium bisulfate (black), dimethylaminium bisulfate (blue) and ammonium-dimethylaminium bisulfate clusters (green). Peaks marked A are $(\text{NH}_4^+)_x(\text{HSO}_4^-)_{x-1}$ clusters and peaks marked B are $(\text{NH}_4^+)_x(\text{HSO}_4^-)_{x-2}$ clusters. These images are adapted with permission from references (74) and (23).

seen in an ESI-MS should not be extrapolated to infer concentrations of similar species during atmospheric particle formation events. Figure 3 shows cationic ammonium bisulfate clusters produced by ESI.(74; 33) The composition of the ions, $(\text{NH}_4^+)_x(\text{HSO}_4^-)_{x-1}$, is identical to the ammonium bisulfate clusters detected by the atmospheric simulation chamber, Cosmics Leaving Outdoor Droplets (CLOUD), using CI-APiTOF. This demonstrates that ESI is effective in producing ions that are atmospherically relevant in a laboratory setting.(23)

The success of ESI in generating atmospherically relevant particles has led to the development of customized sources, such as the electrostatic precipitation ESI (EP-ESI) source.(75) EP-ESI involves a two-step process: aerosols are first ionized by corona discharge in an ionization chamber, then deposited onto a metal filament by electrophoretic motion. The filament acts as the emitter, and the deposited aerosols dissolve into the Taylor cone of the electrospray, eventually forming ions. In a proof-of-concept study, EP-ESI detected nanogram quantities of collected materials, making it valuable for chemical analysis of $\text{PM}_{2.5}$ and smaller particles in lab studies. The synthesis of particles/molecular clusters via ESI is sensitive to the environment in the ionization chamber. A custom-designed nano-ESI emitter, housed in a air-tight capsule with controlled temperature and pressure, has been used to produce ammonium and aminium bisulfate clusters.(33) The clusters, produced by electrospraying the respective salt solutions or through exchange reactions in the gas phase between nascent ions and amine vapors, were compositionally identical to those detected by CLOUD. This setup separates the ESI emitter from changes in the laboratory environment, and has been used to synthesize many atmospherically relevant clusters.(76; 33; 77; 78; 79)

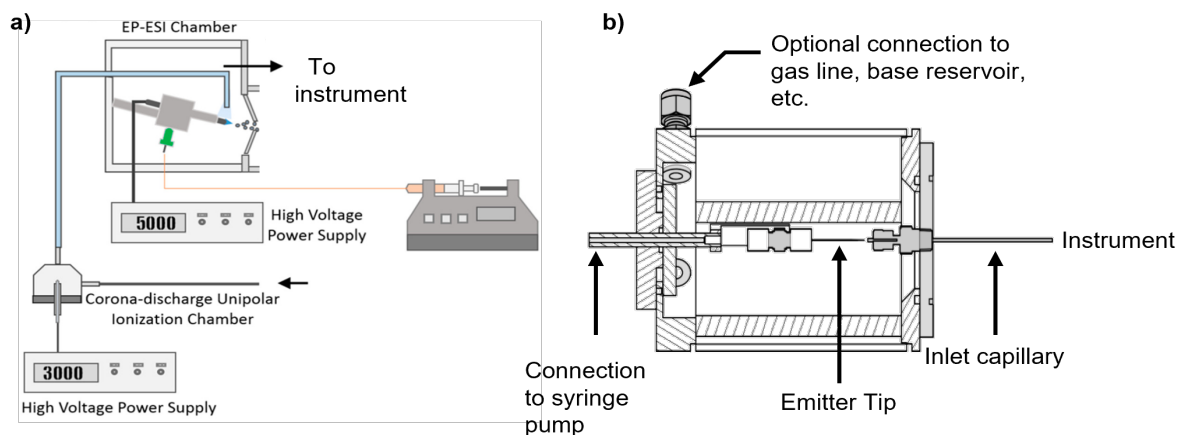


Figure 4: Custom-built ESI sources: (a) EP-ESI for directly sampled ambient aerosols and (b) Nano-ESI chamber designed for careful control of the ESI-environment. Adapted with permission from references (75) and (33).

3. Changes to Particle Compositions Due to Sampling

High-resolution and high-sensitivity MS techniques have enabled the investigation of the chemical composition of both ambient aerosols and clusters. The ionized sample is guided into the MS and undergoes collisions with the background gas in the presence of electric fields. These collisions are far more energetic than any collision that ions are likely to experience in the atmosphere. The collisionally-excited ions can undergo fragmentation, resulting in the detection of only the fragments and not the particles that were initially sampled. The Atmospheric Cluster Dynamics Code (ACDC) is used to model the kinetics of cluster growth, and often, discrepancies in the distribution of clusters predicted by ACDC and those sampled in a mass spectrometer are due to fragmentation.(80; 81) Computational efforts to model the extent of fragmentation a cluster can undergo inside a MS like the APiTOF have shown that clusters undergo fragmentation while moving between the various differentially pumped chambers of the instrument, with highest fragmentation occurring between the first and second chambers. The study also established that the high pressures (7 mTorr - 1 Torr) maintained in these chambers also contributed to greater fragmentation. The degree of fragmentation was found to be dependent on the type of clusters, with sulfuric acid-bisulfate clusters losing sulfuric acid molecules and dimethylamine-sulfuric acid clusters exhibiting fragmentation patterns that were highly dependent on the size of the cluster. Typically, larger clusters undergoing fragmentation to a greater extent and via multiple pathways.(55; 82; 83) Extensive fragmentation can skew the interpretation of the results, introducing significant uncertainties in terms of whether the measured/observed results are truly representative of the sampled species. This is an important detail to consider when applying MS to the study of ambient aerosols.

4. Mass Spectrometry of Ambient Particles

While it is beyond the scope of this review, we provide a brief overview of non-laboratory MS measurements applied to atmospheric particles. In field measurements, most mass spectrometry studies focus on particles larger than ~ 100 nm, characterizing the chemical complexity, number concentration, spatial and temporal variation and distinguished between natural and anthropogenic sources of atmospheric particles.(84; 85; 86; 20; 87; 88; 89; 90) Typically, particles over a given geographical area are studied at a specific time, with the overall motivation for the study deciding the duration and frequency of the experiment. Both the AMS and the ATOFMS have been key to the analysis of ambient aerosols.(91; 85; 92; 93)

For nucleation mode particles under 100 nm, there has been relatively less study. Field-portable instruments are critical to gain direct insight into the composition of particles in the natural environment, and these same instruments are also useful for sampling from well-controlled atmospheric simulation experiments such as CLOUD.(84) The APiTOF with various CI sources is widely used to determine the composition of neutral sub-3 nm particles, and without CI, it can detect naturally charged species in the atmosphere.(94; 95) These measurements have provided invaluable data for ongoing debates about the relative roles of neutral and charged NPF, suggesting that neutral species outnumber charged ones by around an order of magnitude, but that charged particles are associated with faster growth rates.(23) From field studies that used the APiTOF, we have a better understanding of the role of a wide array of highly oxygenated organic molecules (HOMs) in NPF,(13) mechanism of volatile organic compounds formation,(92) the observation that nitrogen oxide-containing species such as organo-nitrates drive nighttime particle formation, or to being to pick apart the complicated role of diverse biogenic vapors in particle growth and aging.(84; 96; 18; 97) Here, the ability to unambiguously determine the chemical composition of new particles is critical to understanding what chemical properties are associated with growing particles. In all of these measurements, it is important to consider the effects of fragmentation in the atmospheric pressure interface as described above as well as the different transport efficiencies of particles of widely varying masses, both of which can bias interpretation of the mass spectra.

5. Mass Spectrometry and Structure Determination

The motivation to characterize the structure of clusters is two-fold. First, theoretical approaches compute the growth rate of molecular clusters, one monomer at a time.(80) ACDC, for example, requires accurate thermodynamic parameters that are typically obtained from high-accuracy quantum chemical calculations. Multiple methods that search the potential energy surface (PES) to identify the minimum energy structure (MES) have been developed.(98; 99; 100) An initial set of configurations, determined through low accuracy, low-cost quantum chemical methods, are filtered and refined with more accurate methods to hopefully locate the global MES.(101; 102) A variety of methods have been developed to identify the MES, resulting in a pool

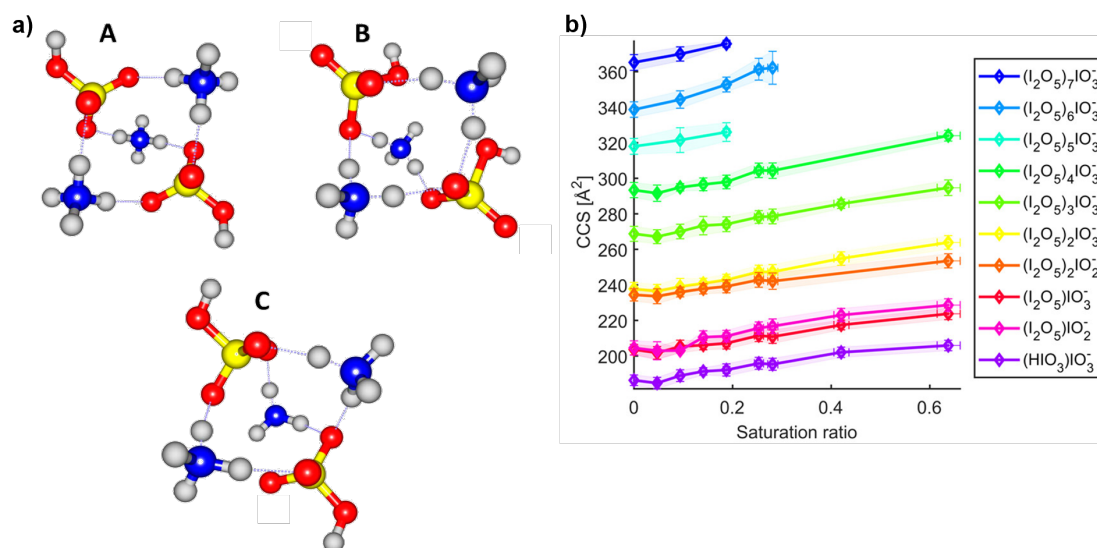


Figure 5: (a) Three different equilibrium geometry structures for the $(\text{NH}_4)_3^+(\text{HSO}_4^-)_2$ cluster, predicted by different levels of theory. (b) Change in CCS of $(\text{I}_2\text{O}_5)_x(\text{IO}_a^-)$ where $x=1-7$ and $a=2-3$ as a function of saturation water vapor ratio. Adapted with permission from (103) and (34).

of candidate structures. For example, consider the three differed MES predicted for the $(\text{NH}_4)_3^+(\text{HSO}_4^-)_2$ cluster by a set of three calculations shown in Figure 5a.(103) The true MES structure was found to be a slightly modified version of structure A through spectroscopy experiments. Comparing experimental observables with quantum chemical predictions aids in confirming the best-match structures, advances the development of better screening criteria and improves the efficiency and accuracy of theoretical structure search methods. Second, the unique structural markers of small clusters such as $(\text{NH}_4)_3^+(\text{HSO}_4^-)_2$ can be used to map the structural motifs in larger, more complex particles. Only a handful of techniques, such as electron scattering of trapped ions and single particle X-ray scattering, can directly probe the structure of gas phase species.(104; 105) Often requiring access to user-facilities such as a synchrotron, the adaptation of such techniques to probe the structure of atmospheric aerosols is challenging. Hence, laboratory-based MS have been combined with structure-sensitive techniques to indirectly probe the structures of mass-selected atmospherically relevant clusters.

5.1. Probing structure through ion mobility measurements

In IMS, ions are separated based on their collision cross sections (CCS) with buffer gases while under the influence of an electric field.(106) Smaller ions are more mobile and travel faster than larger, slower ions. While mobility is the parameter traditionally measured as a function of time or a differential electric field, the measured mobilities are often converted into a calculated CCS value. CCS varies with size and shape of the ion and is directly related to that particular ion's mobility equivalent diameter. The differential mobility

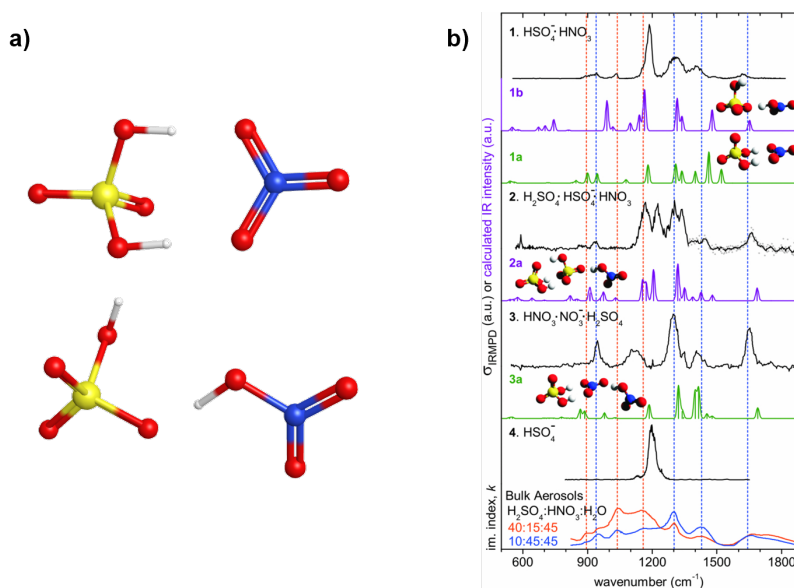


Figure 6: (a) Two possible structures for the $\text{HSO}_4^-(\text{HNO}_3)_1$ cluster. The proton can be located on either H_2SO_4 or HNO_3 as shown. (b) Experimental IRMPD spectra of three mixed clusters and HSO_4^- . Adapted with permission from (103).

analyzer (DMA) has been coupled with MS to characterize aerosols and clusters.(107; 34) In this method, ions are passed between two parallel plate electrodes that have voltages such that the electric field is stronger and longer-lived in one direction compared to the other. The trajectory of the ions is always perpendicular to the gas flow, and the alternating electric fields ensure that mobility varies in different directions, allowing for separation. Varying the potential difference between the plates also aids in ion separation. The ions transmitted through the DMA are directed into an MS, where they are detected.

The stability of cationic dimethylamine-sulfuric acid clusters were studied using a DMA attached to a QSTAR XL MS.(107) Cationic clusters, particularly $[\text{H}^+((\text{CH}_3)_2\text{NH})_x(\text{H}_2\text{SO}_4)_{x-1}]$, exhibited significant dissociation during transfer between analyzers, with hydration via a humidified buffer gas reducing dissociation by stabilizing interactions within the clusters. Conversely, negatively charged clusters $[(\text{HSO}_4^-)(\text{CH}_3)_2\text{NH})_x(\text{H}_2\text{SO}_4)_y]$ dissociated through the loss of dimethylamine and sulfuric acid pairs, with no difference observed under dry or humidified conditions. All clusters, irrespective of the charge on them, showed water uptake, leading to slight increases in measured CCS. Similarly, iodine pentoxide-iodic acid clusters $((\text{I}_2\text{O}_5)_x(\text{HIO}_3)_y(\text{IO}_a))$ where $x=0-7$, $y=0-1$ and $a=2-3$ were examined, demonstrating greater stability and less dissociation compared to dimethylamine-sulfuric acid clusters.(34) Hydration facilitated the conversion of I_2O_5 to HIO_3 , with moderate CCS increases indicating limited water sorption. These findings suggest that, under atmospheric conditions, small ionic clusters are only mildly hydrated and do not behave as nanodroplets, underscoring the importance of considering hydration effects when modeling cluster properties.

5.2. Spectroscopy

Two spectroscopic techniques are often employed to examine the structure of atmospheric clusters: vibrational and electronic spectroscopy. Both techniques leverage the ability of MS to mass-select clusters and track changes in structure and properties as a function of composition and hydration. Vibrational spectroscopy provides a way to track the structural changes brought on by size and hydration. Electronic spectra often contain no structural information, but offer insights into the strength of bonding interactions between cluster components. In this section, we briefly review these techniques and discuss a few insights obtained through spectroscopy experiments performed in a MS. For more details on the spectroscopy of atmospherically relevant particles, refer to the following references.(108; 109; 110; 111)

5.2.1. Vibrational Spectroscopy

Direct absorption spectroscopy of gas-phase molecular ions in a MS is impossible due to low ion densities and high spectral congestion from other absorbing species or complex ions. Action spectroscopy, where changes brought on by the absorption of one or more photons are measured instead of measuring absorption of life. Thus, action spectroscopy provides indirect information on the structure and energy levels of the analyte. In a MS, a change in m/z is detected owing to the dissociation of the analyte or a weakly bound adduct brought on by light absorption. Infrared photodissociation (IRPD), infrared multiphoton dissociation (IRMPD), and cryogenic ion vibrational predissociation spectroscopy (CIVP) have become the preferred methods to obtain IR spectra of gaseous ions. The IR spectrum is obtained by plotting photodissociation cross-section versus photon energy or wavelengths. CIVP and IRMPD are usually performed in custom-built instruments with cryogenically-cooled ion traps to obtain a linear vibrational spectrum. Both techniques are valuable for mapping the various bonding arrangements in the analyte, but insights into structure are obtained by comparing experimental spectra with those predicted by quantum chemical calculations. Typically, shifts in vibrational modes or differences in degenerate resonances are determined in order to elucidate the structure. Vibrational spectroscopy has been used to understand binding, hydration, and acid-base chemistry in atmospherically relevant clusters.(111)

Anions composed of sulfuric acid and nitric acid have been detected in the atmosphere.(112) While the composition of the smallest clusters was $\text{HSO}_4^-(\text{HNO}_3)_x$ ($x = 1,2$), field studies could not identify the charge-carrying species. The location of charge in atmospheric clusters influences their chemical reactivity and stability, making it important to determine the location of the proton in these clusters. IRMPD spectra of $\text{H}_2\text{SO}_4/\text{HNO}_3$ clusters (Figure 6a) reveal that the HSO_4^- peak (around 1190 cm^{-1}) appears only in $\text{HSO}_4^-(\text{HNO}_3)$ and $\text{HSO}_4^-(\text{H}_2\text{SO}_4)(\text{HNO}_3)$, while nitrate was the charge carrier in $(\text{HNO}_3)(\text{NO}_3^-)(\text{H}_2\text{SO}_4)$.(113) Thus, sulfuric acid is unlikely to be the charge carrier despite its higher gas-phase basicity. CIVP has been applied to determine the MES of a wide range of atmospheric particles and also in elucidating atmospheric reaction mechanisms. The formation of photoactive nitrosyl halides (XNO_2) from N_2O_5 on

sea-spray aerosol surfaces, studied by CIVP, was found to include halide insertion into N_2O_5 leading to XNO_2 or HNO_2 .(114)

5.2.2. Electronic Spectroscopy

Negative ion photoelectron spectroscopy (NIPES) provides a way to directly acquire details on the strength of binding between different cluster components. Typically, gaseous ions or molecules are irradiated with monochromatic light (from a laser) with sufficient energy to eject an electron from the molecule/ion. The kinetic energy (KE) of this electron, the photoelectron, is measured, and the electron binding energy (BE) is calculated based on the photoelectric effect $BE = h\nu - KE$.(109) A histogram of the BEs emitted by the photoelectrons is plotted as a NIPES spectrum, from which the relative energies of the ground and excited states of both the anion and the corresponding neutral species can be determined. Photoelectron spectra can be compared with calculations to obtain structural information, but is typically combined with ab initio molecular dynamics calculations to determine the key binding interactions between cluster components.

As an example, consider the NIPES spectra of HSO_4^- along with $\text{HSO}_4^-(\text{Sol})_n$ shown in Figure7, where $n=1,2$ and Sol refers to succinic acid (SUA), water or sulfuric acid.(115) These spectra, obtained by irradiating the clusters at 157 nm, show that HSO_4^- has four bands of which X is the lowest energy feature. On comparing the HSO_4^- spectrum with spectra 5 and 7 in the figure, it is clear that binding with water shifts X to higher BE and the intensity pattern is somewhat retained. Bonding with SUA or H_2SO_4 , however, substantially shifts the four bands and there are no similarities between three spectra and that of HSO_4^- . Thus, the two acids have a larger stabilization effect on HSO_4^- than water and also affect the structure of the HSO_4^- . Adding a second solvent molecule leads to further stabilization of HSO_4^- , with both SUA and H_2SO_4 forming multiple hydrogen bonds with HSO_4^- . The formation of $(\text{SUA})(\text{HSO}_4^-)$ was also found to be more thermodynamically favorable in comparison to $\text{HSO}_4^-(\text{H}_2\text{O})$ cluster. In this manner, NIPES has been applied to probe the hydrogen bonding topology and the charge carrying species in many clusters that are key to the initial stages of atmospheric nucleation.(116; 117; 118; 119)

6. Mass Spectrometry and Photochemistry

The rates of photochemical reactions of atmospheric particles vary by orders of magnitude based on the nature of the chemical species involved. Absorption of light results in the formation of transient excited state species which may dissociate, isomerize, transfer energy to other molecules or engage in chemical reactions. Aerosol precursors generate reactive species (such as (OH^\bullet) , IO, and XNO_2) that participate in reactions that influence the atmosphere's chemistry. Irradiating an ensemble of particles can produce several photofragmentation products, where identifying the initial species undergoing the photochemical reaction becomes impossible. Mass selection of a single cluster prior to photo-excitation, however, can provide effective isolation and precise analysis of the elementary steps of atmospherically relevant reactions. For

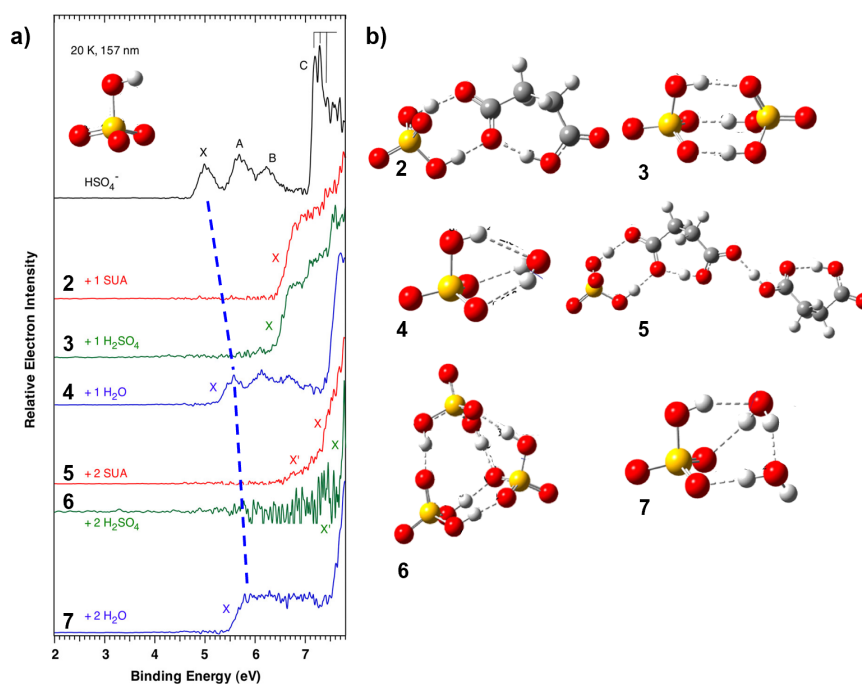


Figure 7: (a) NIPES spectra of HSO_4^- along with $\text{HSO}_4^-(\text{Sol})_n$, where $n=1,2$ and Sol refers to succinic acid (SUA), water or sulfuric acid is shown. Peaks X, A, B and C on HSO_4^- spectrum refer to characteristic electron binding energies (BE) of the ion. The blue dashed line have been added to track the shift in BE induced by water. (b) Lowest energy structures computed for each of these clusters is shown.

example, the photochemical reactions of sea salt-glyoxylic acid and I_xO_y clusters have recently been studied through UV spectroscopy. (120; 121; 64) ESI-generated cations, $[Na_nCl_{n-2}(C_2HO_3)]^+$ where $n = 5-11$, were guided into an FT-ICR mass spectrometer coupled to a Nd:YAG laser system. The UV photodissociation spectra of these clusters displayed two absorption bands between 225-400 nm, with loss of $Na_xCl_{x-1}(C_2HO_3)$ or Na_xCl_{x-1} being the most prominent fragmentation pathways. The carbon dioxide radical ($CO_2^{\bullet-}$) was also detected as a photolysis product, forming from the cleavage of a C-C bond in glyoxylate. The $CO_2^{\bullet-}$ photofragment was only detected in the 300-400 nm UV range and was likely stabilized by the salt, making it a transient species in the troposphere. The photochemical lifetime of the clusters was found to be approximately 10 hours, implying that glyoxylic acid/glyoxylate played a role in the photochemical aging of SSA. Hydration of sodium glyoxylate clusters resulted in increased photodissociation but did not result in the formation of the *gem*-diol form of aqueous glyoxylic acid, confirming that glyoxylate will remain photo-active in the actinic wavelength range.

The photochemical reactions of various I_xO_y have been probed in several studies recently. In one study, the authors combined pulsed photolysis, photodepletion and photoionization TOFMS (PI-TOFMS). (64) IO, produced in situ by the reaction between triplet oxygen and iodine, underwent further reactions to form larger I_xO_y . The photodepletion of these I_xO_y species was carried out at 355 and 532 nm and products were detected by PI-TOFMS. IO and I_2O_4 showed significant depletion at 355 nm, with sufficiently large photolysis cross sections suggesting that these species are not likely to participate in particle growth. The photolytic lifetimes of different I_xO_y species suggest that photolysis of more photolabile species such as I_3O_7 and I_5O_{12} is likely to slow down particle formation while less photolabile species are likely to contribute more to particle growth in the atmosphere. Another study probed the UV photodissociation of $(I_2O_5)_{0-3}(IO_3^-)$ clusters and found that loss of O atom, I_2O_4 and I_2O_5 were the major photofragmentation pathways in the actinic region. (122) Loss of I_2O_5 was found to be much faster than the loss of O, with estimated rates indicating that photolysis of these clusters is likely to compete with particle formation under ambient conditions. The O-loss fragment likely left behind a triplet cluster that could then undergo further complex reactions with other particle constituents such as organics and amines.

7. Energetics and Reaction Dynamics with Mass Spectrometry

In order to be climatically relevant, an atmospheric cluster initially composed of a few molecules needs to form adducts by uptaking other vapors. Each step of the particle formation process has to be efficient and offer enough stability to the cluster to ensure growth to the next size out-competes coagulation, absorption by larger particles, or evaporation. Thus, understanding the intricate details of energetics and kinetics at each step is paramount. Additionally, simulation of the aforementioned processes also requires exact rates and thermodynamic parameters such as binding free energy (ΔG). Here, we describe laboratory MS

experiments that have probed the kinetics and thermodynamics of cluster formation and reactions. We also highlight the need for experimental validation of predicted rates and thermochemical parameters.

7.1. Ion Trap Kinetics and Thermodynamics

Probing the kinetics, energetics and mechanisms of atmospherically relevant reactions via MS requires the use of ion traps. The duration (“trapping time”) for which the ions are stored in the ion traps can be controlled affects how long ions are exposed to the changing RF fields in the ion trap and ultimately, impacts the observed ion signal. Obtaining mass spectra as a function of trapping time provides a way to track the kinetics of a reaction and Arrhenius analysis (plot of rate constant vs $1/T$) of the recorded data provides insight into the temperature dependence of the rate constant and any activation barriers. Introduction of reactive vapors into the ion trap can lead to new product peaks that, when studied across different ion trap temperatures, provide an insight into the energetics of the reaction. van’t Hoff analysis (plot of equilibrium constant $\ln K$ vs $1/T$) of mass spectra recorded under steady state conditions establishes the temperature dependence of the equilibrium constant and to extract the enthalpy change (ΔH) and entropy change (ΔS) of the reaction.

The kinetics of base exchange in small ammonium bisulfate, ammonium nitrate and ammonium methanesulfonate clusters were examined in a FT-ICR-MS. These studies focused on measuring the rates of the substitution of amines such as methylamine, dimethylamine and trimethylamine for ammonia and found that the observed substitutions were all pseudo first order reactions.(123; 124; 125) Figure 8b shows a typical reaction profile and statistical fit for the reaction of the $[(\text{NH}_4^+)_8(\text{HSO}_4^-)_7]^+$ cluster with dimethylamine. While dimethylamine readily replaced ammonia, the reverse was not observed, indicating that substitution is driven by proton affinity and amine exchange is highly favorable.(123) The measured rates were also independent of cluster size, and near unity uptake coefficients indicated that the conversion from ammonium to aminium salt clusters is likely rapid in ambient conditions. Similar results were obtained for the ammonium nitrate clusters, while ammonium methanesulfonate clusters showed slower exchange. Regardless of the acid in the cluster, amines will displace ammonia. Furthermore, the exchange of a surface ammonia was more rapid than the exchange of an ammonia at the core of the cluster. The kinetics of nucleation of sulfuric acid, water and ammonia has been in quadrupole ion trap MS.(126; 127; 128; 129; 130) The observed rates, for $\text{H}^+(\text{H}_2\text{SO}_4)_s(\text{H}_2\text{O})_w$, $(\text{HSO}_4^-)(\text{H}_2\text{SO}_4)_s(\text{H}_2\text{O})_w$, and $\text{NH}_4^+(\text{NH}_3)_n(\text{H}_2\text{SO}_4)_s$ cluster systems, were in the low-pressure limit, and highly dependent on the reacting species and not on the pressure at which the reactions were monitored.

Incorporation of water into sulfuric acid-bisulfate anionic clusters was more favorable compared to incorporation of sulfuric acid into protonated water clusters. This laboratory study supports field studies that showed anionic nucleation of sulfuric acid-water system as more favorable than cationic or neutral nucleation. In fact, neutral nucleation was found to be slower than ion-induced nucleation under tropospheric

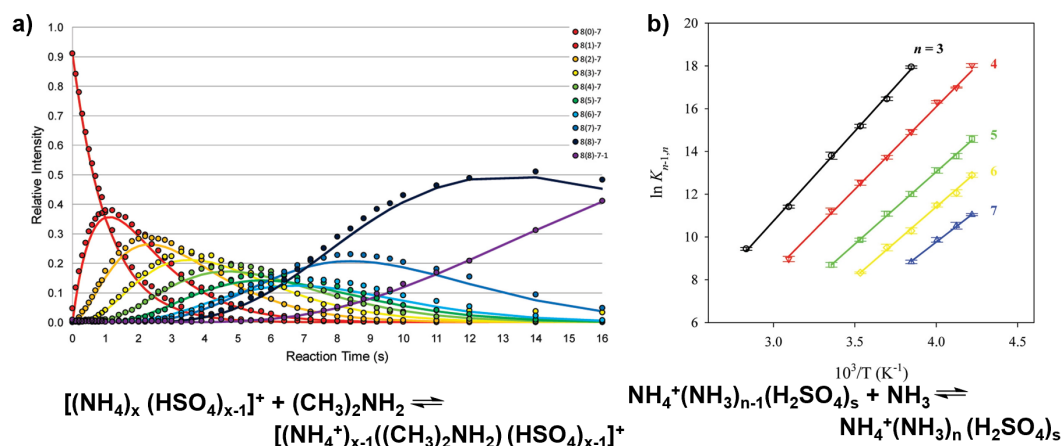


Figure 8: (a) Reaction profile for the uptake of dimethylamine by $(\text{NH}_4^+)_8(\text{HSO}_4^-)_7]^+$ cluster. The bracketed number in the legends showed the number of ammonia(s) replaced by dimethylamine in the cluster. The lines are statistical fits to pseudo first order kinetics observed for this reaction. (b) A van't Hoff plot depicting the measured equilibrium constants for the addition of NH_3 to the $(\text{NH}_4^+)(\text{NH}_3)_n(\text{H}_2\text{SO}_4)_2$ clusters in an ion trap. Adapted from references (130) and (123).

conditions.(131) Extensive hydrogen bonding and proton transfer between ammonia and sulfuric acid results in fully ionized cluster components $(\text{NH}_4^+(\text{NH}_3)_n(\text{H}_2\text{SO}_4)_s)$. The corresponding structures were 50 kcal mol⁻¹ more stable than clusters composed entirely of neutral ammonia and sulfuric acid, with clusters where $n \geq s$ were found to be particularly stable. Thus, sulfuric acid is stabilized to a greater extent by ammonia and water, making sulfuric acid-ammonia nucleation more spontaneous in the free troposphere.

7.2. Fragmentation/Dissociation Experiments

The deliberate, controlled dissociation of mass-selected ions offers insights into cluster structure. In order to induce fragmentation, a cluster's internal energy must be raised above its dissociation threshold. This process, called ion activation, can be achieved in a myriad of ways including collision induced dissociation (CID),(45; 79) surface induced dissociation (SID),(132; 133; 134) IRMPD, (135; 113; 108; 78; 79) and ultra-violet photodissociation. Since the m/z of both the initial cluster and the resulting fragments are analyzed, techniques that use multiple stages of mass detection are referred to as MS/MS or MSⁿ, where n refers to the number of mass analysis steps employed. According to the principle of microscopic reversibility, cluster fragmentation can be considered as the reverse of cluster growth pathways.(136; 137; 138) Analyzing the composition and abundances of fragments produced at different energies gives clues to the cluster formation mechanism and the ordering of the binding strengths of different cluster constituents. In this section, we will highlight studies that have used CID and SID to obtain insights into stability of molecular clusters and the energetics of cluster growth.

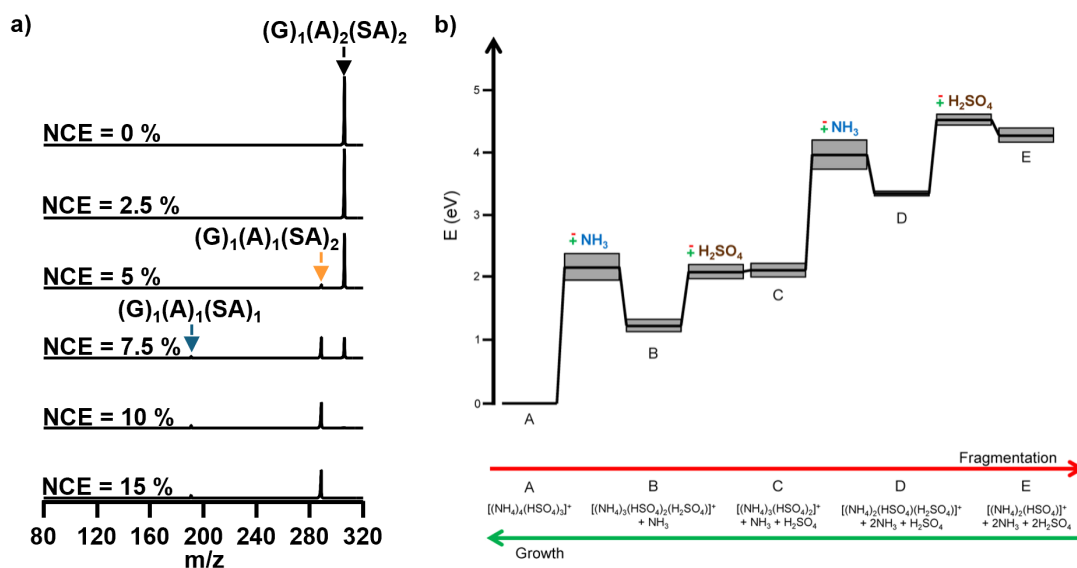


Figure 9: a) CID mass spectra of $(G)_1(A)_2(SA)_2$ cluster, where G, A and SA refer to glycine, ammonia and sulfuric acid. NCE refers to normalized collisional energy, an internal scale for collisional energy in the Thermo LTQ XL. (b) Potential energy surface for the two step, sequential loss of ammonia and sulfuric acid from the $[(NH_4^+)_4(HSO_4^-)_3]^+$ cluster. Adapted from (79) and (139).

7.2.1. Collision-induced dissociation

In a CID experiment, mass-selected clusters collide with molecules of a neutral, non-reactive gas, such as helium, in the ion trap or collision cell of a MS.(45) Multiple collisions between the ion and the neutral gas molecules result in an increase in the internal energy of the ion, ultimately leading to the fragmentation of the cluster. Fragmentation leads to the formation of at least two species: an ion, lower in mass than the precursor ion, and at least one neutral molecule that corresponds to the difference in mass between the fragment ion and the precursor ion. The degree of fragmentation depends on the internal energy of the activated ion, with greater internal energies corresponding to greater fragmentation.

Our group recently used CID to probe the stability of atmospherically relevant glycine ammonium bisulfate clusters.(79) The experiments were carried out in a QIT-MS (Thermo LTQ XL). Both bare ammonium bisulfate and glycine ammonium bisulfate clusters exhibited preferential loss of ammonia or an ammonia-sulfuric acid pair. The absence of any glycine-loss fragments from the mixed clusters showed that glycine was bound more strongly to sulfuric acid than ammonia. Quantum chemical calculations, however, revealed comparable binding free energies (ΔG_b) for glycine, ammonia, and sulfuric acid and that the energy required to remove an ammonia-sulfuric acid pair from a mixed cluster is ≈ 10 kcal/mol greater than the energy required to remove glycine. This suggests that removing glycine from the cluster is substantially easier, a result that was not experimentally observed. Applying the calculated ΔG_b to cluster growth models could

lead to substantial errors in the computed growth rates (as rate depends exponentially on ΔG_b). Thus, this work reiterates the need for experimental validation of computed ΔG_b .

7.2.2. Surface-induced dissociation

In an SID experiment, mass-selected precursor ions are accelerated to a specified KE before colliding with a surface. Upon impact, the kinetic energy of the ions is converted into internal energy, leading to fragmentation. Collisions with the carefully constructed surface, usually self-assembled monolayers of large organic molecules such as 1-dodecanethiol, induce extensive fragmentation of the ion. The energy transfer between the ion and the surface is much more efficient than the transfer of energy through multiple collisions in CID. SID and CID are conceptually similar experiments but SID offers better control over collision energies. As a result, activation energies can be determined more accurately using SID.(140; 134)

SID experiments of $[(\text{NH}_4^+)_6(\text{HSO}_4^-)_5]^+$ and $[(\text{NH}_4^+)_5(\text{HSO}_4^-)_4]^+$ clusters established that the incorporation of ammonia into small, prototypical ammonium bisulfate clusters is a barrier-controlled process.(139) Upon SID, both clusters demonstrated the same two major fragmentation pathways: a) the two-step sequential loss of ammonia and sulfuric acid, and b) the one-step loss of ammonium bisulfate. The experimentally measured energies required to induce the loss of ammonia and ammonium bisulfate from the clusters always exceeded the theoretical predictions, suggesting the existence of a reverse activation barrier for the addition of these monomers. Loss of sulfuric acid was kinetically controlled, suggesting that growth by sulfuric acid is not barrier controlled. Accommodating an ammonia molecule requires a considerable rearrangement of the electrostatic interactions within the sulfuric acid-rich cluster, and a similar phenomenon was observed for cluster growth by the addition of an ammonium bisulfate molecule. The presence, and height, of the activation barrier to the addition of ammonia to a sulfuric acid cluster can impact cluster distribution in the atmosphere, making it an important detail to account for cluster growth models.

8. Future Needs

Thus far, we have discussed some insights into atmospheric aerosol particles obtained from laboratory-based MS. Here, we take the opportunity to highlight a few areas where technological development is required to extend the benefits of applying MS-based methods to study the physical and chemical properties of atmospheric particles.

8.1. Energy-Resolved CID

CID experiments performed in modern MS are significantly influenced by instrument specific parameters such as an internally-defined scale of collisional energies that are not consistent between instruments. In an ideal CID experiment, a well-thermalized ion packet is subjected to carefully controlled single collisions. In practice, the internal energy of the ion packet is influenced by the ion source and the ion transfer

optics between the source and the collision cell/ion trap.(141; 142) The distribution of KE in the parent ions is not known prior to activation, increasing the uncertainty in the energy transferred during the CID process. In most instruments, ions are excited/activated by the application of an excitation voltage unique to the precursor ion being examined. Non-ideal trapping conditions and space-charge effects can hinder true resonance and lead to inefficient fragmentation. Guided-ion beam (GIB) MS are an alternate way to obtain quantitative binding energies of atmospheric particles. In a typical GIB-MS experiment, the KE of the ions are set to a desired value before colliding with a neutral background gas.(143) Monitoring the reactant and product ion intensities yields the reaction cross section as a function of KE, which can be modeled to determine binding free energies. GIB-MS has been used to obtain quantitative thermochemical parameters for many different systems including alkali metal-nuclei acid complexes and could be extended to atmospheric particles as well.(144; 145; 146)

8.2. Charge Detection Mass Spectrometry

Climatically relevant particles are much larger than 10 nm in diameter, a size range that is beyond the upper mass limit of most MS. Large particles such as viruses, anti-bodies, and nanoparticles have been characterized by charge detection mass spectrometry (CDMS).(32; 147; 148) CDMS is a single particle technique where an ion passing through a conducting cylinder induces a proportional charge on the cylinder (image charge) that is amplified and recorded. In ion trap CDMS, the cylinder is embedded in an ion trap and the ion oscillates back and forth through cylinder. Fourier transform of the recorded image charge yields the ion's oscillation frequency from which the m/z of the particle can be determined.(148) CDMS has been used to measure the mass of heterogeneous samples and could be extended to examine larger atmospheric particles as well.(149) When coupled with a structure-sensitive technique like vibrational spectroscopy, CDMS could trace the chemical changes brought about by the aging of atmospheric particles and also provide a way to examine aerosol phase and mixing states. Such an instrument is currently under development in our lab. Additionally, combining SID and CDMS could offer unique structural insights into larger, more complex particles that are held together by non-covalent interactions.(150; 151)

8.3. Variable Temperature Mass Spectrometry

Although ubiquitous in the atmosphere, water's role in NPF and the effect of humidity on NPF rates are yet unclear. The extent of hydration of clusters is largely dependent on cluster type and size. Probing the hydration of clusters via MS is challenging because sampling techniques typically transfer enough energy to the cluster, any evaporate any bound water.(84; 85; 88) Spectroscopy and DMA-MS have offered some insights into water-containing new particles but do not provide quantitative thermodynamic parameters of water binding, which is vital to comprehend water's role in particle growth.(107; 116; 152; 34; 76; 77) Our group recently probed the thermochemistry of hydration of lanthanide complexes by VTMS, where the

lanthanide complexes were hydrated step-by-step in a variable temperature ion trap in the presence of a water-seeded buffer gas.⁽¹⁵³⁾ By monitoring the partial pressure of water and ion intensities of both dry and any hydrated complexes, we were able to carry out van't Hoff analyses to derive the free energies required to bind water to these complexes. Ours is a modified, low temperature additive version of the VT method employed by Froyd and Lovejoy.⁽¹³⁰⁾ Adapting this approach to determine the thermodynamics of vapor uptake of atmospherically-relevant molecular clusters can provide a quick way to validate computational predictions as well as complement structural information obtained from IR-MS.

9. Conclusions

We have shown the breath of information that is made available through measuring the mass of intact particles. Laboratory-based MS studies have provided molecular level insights into particle formation and growth rates. Additionally, combining structure sensitive methods with MS has provided further details into the intermolecular interactions that govern particle formation and growth. We have highlighted different ionization methods, most commonly used MS instrumentation, as well as MS-based spectroscopy, kinetics and thermodynamics experiments. We have also discussed efforts to extend MS based insights out of the current size limitations and highlighted key areas where more research and development is required. We hope that the studies discussed here establish the ability of MS to unravel details of complex analytes like atmospheric aerosols.

Declaration of competing interest

The authors are not aware of any affiliations, memberships, funding source that might be perceived as influencing the objectivity of this review.

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