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# Solid Analysis by Mass Spectrometry

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**General Uses**

- Qualitative and quantitative elemental and molecular analysis of inorganic and organic materials
- Bulk material analysis
- Measurement of trace impurities in materials
- Elemental and molecular profiling/mapping in materials

**Examples of Applications**

- Verification of alloy and ceramic compositions
- Determination of molecular weight and structural/compositional information of synthetic polymers
- Trace impurity analysis of epoxies, plastics, and metal alloys
- Material profiling of natural and synthetic materials

**Samples**

- *Form*: Solid
- *Preparation*: Varies with ionization/introduction method, ranging from no sample preparation to some requiring digestion prior to analysis

**Limitations**

- Multiple ionization methods require dissolution of solid samples prior to analysis
- Often complicated data analysis of unknown materials or impurities
- Analytes of interest must be ionizable

**Estimated Analysis Time**

- Sample preparation varies between ionization/introduction methods from no sample preparation to dissolution of materials which can be extensive
- Analysis requires up to 1 hour
- Data reduction time varies depending on the type of analysis, i.e., bulk, trace impurities, isotope ratio, or profiling analysis

**Capabilities of Related Techniques**

- *Glow discharge mass spectrometry*: Exhibits little to no ion interferences, but not as fast, precise, or sensitive as inductively coupled plasma mass spectrometry for solutions and easily dissolvable materials
- *Secondary ion mass spectrometry*: Capable of profiling elemental, isotopic, or molecular composition at high depth resolution (~50 nm), with quantitation possible through appropriate standards
- *Laser ionization mass spectrometry*: Little sample preparation with fast analysis, but not typically quantitative

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# Introduction

Since development, mass spectrometry (MS) has become a research tool that permeates throughout scientific fields. With roots in physical and chemical sciences, MS has opened the door to multiple avenues of research such as quantitative gas analysis, characterization of new elements, and fast identification of trace elements or contaminants. MS was even used in the Manhattan Project for the separation of uranium isotopes. With advancements in and expansion of the technique, a range of MS methods have been successfully employed for the analysis of solids, including metals, ceramics, plastics, polymers, semiconductors, and biological materials.

Novel ionization techniques are constantly being developed, with ambient ionization greatly advancing the capabilities of solid analysis MS. Ambient ionization techniques ionize analyte material outside of the MS mostly through thermal desorption, laser desorption, or impact by charged droplets or ions. This chapter endeavors to familiarize the reader with a selection of different ionization designs and instrument components to provide knowledge for sorting the various analytical strategies in the large field of solid analysis by MS.

# General Principles of Mass Spectrometry

Mass spectrometry has been widely used for material analysis, providing information ranging from elemental composition to molecular identification, with options for surface analysis and depth profiling of solid materials. The name "mass spectrometry" however is a misnomer, with MS techniques determining the mass-to-charge (*m/z*) ratio instead of mass. Generally, the principle consists of ionizing neutral analytes (elements or molecules) to generate charged gas species which travel differently based on the instrumental environment, including magnetic and electric fields. By discerning the way in which these charged species move through different environments, the *m/z* of the species can be determined. Data analysis however can be complicated and is very specific to the type of MS technique and the information desired. For example, many mass spectrometers can operate in both positive ion and negative ion mode, i.e., observing positively or negatively charged species, while many analytes can only ionize in one mode. Various ionization mechanisms are discussed further in Gas Analysis by Mass Spectrometry (Division 3:C).

Ionization sources, which act as the introduction method to the MS, can also result in different types of adducts, including different salts and ammonia. For instance, an analyte (A) can often be ionized to result in $[A+H]^+$, where H is hydrogen. However, that same analyte in many systems is detected as $[A+Na]^+$, where Na is sodium salt. These species have the same charge but different mass. Ionization sources can also be "hard", resulting in species fragmentation, or "soft" which results in little fragmentation. Understanding and discerning differences in the various techniques within this expansive field of MS can inform experimental design and lead to improved analysis.

Depending on the sample type (i.e., solid, liquid, or gas), the introduction of the analyte can vary. Driven in large part by material characterization and a new wave of interest for the analysis of solid samples, ambient ionization methodology has expanded and diversified, with many ionization sources requiring little to no sample preparation and/or little sample consumption. Table 1 shows a selection of solid analysis MS techniques, with the ones discussed here in more detail highlighted.

However, for all mass spectrometers, the mass analyzer separates ions based on the *m/z* values. This process is typically electrically driven, while many traditional analyzers utilized magnetic fields for the separation. The various mass analyzer options include, but are not limited to, quadrupole, triple quadrupole, magnetic sectors, time-of-flight, ion trap, and orbitrap. Here two of the main analyzers, triple quadrupole and time-of-flight, will be discussed, while many are examined in other chapters. As with ionization sources, there are multiple mass analyzer systems which can be employed based on experimental design.

Combinations of different ionization sources and mass spectrometer techniques allows analysts to customize the material analysis to suit their sample and the desired information to be drawn from the analysis. Understanding the fundamental principles, instrumentation, and operational requirements related to solid sample analysis by mass spectrometry will aid in identifying appropriate characterization techniques for various materials.

# Instrumentation

## Triple Quadrupole Mass Spectrometer (TQMS)

As the name suggests, a quadrupole analyzer is composed of four metal parallel electrical rods around a central axis. Through applying direct current and oscillating radio frequency potentials across the quadrupole rods (two rods of each potential), an oscillating electric field can be created within the quadrupole. Ionized species traveling through this electric field follow oscillating paths around the central axis; however, the oscillation path varies species to species based on the weight and charge of the species. Therefore, some species are destabilized traveling through the quadrupole (non-resonant ions), with only ions of a certain *m/z* following a stable path and are able to pass fully through the system (resonant ions) for a certain applied frequency. By changing and tuning the potentials applied to the rods, the oscillating electric field is changed and, therefore, the range of *m/z* able to move through the quadrupole is adjusted, effectively filtering those ions.

While there are single quadrupole mass analyzers (Gas Analysis by Mass Spectrometry, Division 3:C), many mass spectrometry systems capable of solid analysis utilize a TQMS composed of three sets of quadrupole cells in succession. In these systems, while full *m/z* scans (i.e., scanning a range of *m/z*) can be collected, the additional quadrupole cells provide distinct advantages. By adjusting the potentials applied, the first quadrupole cell can act as a focuser, only allowing a select *m/z* species to be passed to the next quadrupole. This quadrupole, termed the collision cell, contains neutral or reactive gas molecules which "smash" into the analyte species, forming fragments. These fragments are then passed to the final quadrupole, which scans a *m/z* range to analyze the fragments.

## Systems **& Equipment**

While the design of the triple quadrupole is complex, it is also elegant, and the details are worth understanding. The overall design layout can be seen in Figure 1. A TQMS consists of an ionizer (discussed in later sections), three quadrupoles (one of which is a collision cell), and an ion detector.

**Quadrupole.** Each quadrupole chamber consists of four rods, two opposite rods with applied potential of (U+Vcos(ωt)) and two opposite rods with –(U+Vcos(ωt)), where U is DC voltage, Vcox(ωt) is radio-frequency alternating AC voltage, and ω is angular frequency. The different applied voltages determine the oscillating trajectory of ions traveling through the center of the system, allowing only certain *m/z* ions to remain on the correct path. All other ions are ejected from the flight path required to pass fully through the quadrupole, encounter one of the rods, and are discharged. Essentially, the quadrupole acts as a mass filter. Varying the potentials and angular frequency allow not just a change in the range of *m/z* that can pass through the filter, but also allows for isolation of single *m/z* ions for fragmentation in the collision cell quadrupole.

**Collision cell.** The advantage of utilizing three quadrupoles, as opposed to a single quadrupole, is the ability to fragment a particular ionized species. By selecting a *m/z* species in the first quadrupole chamber and introducing the species to a collision-inducing quadrupole chamber, a targeted MS/MS spectrum can be generated, facilitating species identification. In collision induced dissociation, excited ions from the first quadrupole energetically collide with an inert gas pumped into the collision cell, typically helium or argon. Collisions result in an increase in internal energy which induces the ionized species (precursor ions) to dissociate into fragments. By adjusting the collision energy (1-100 eV), the degree of fragmentation can be increased or decreased. The collision quadrupole is also only subjected to radio-frequency potentials, allowing all fragmented product ions to pass through the cell to the final quadrupole, which acts in the same manner as the initial quadrupole.

# Time-of-Flight Mass Spectrometer (TOF-MS)

As the name implies, a time-of-flight MS measures the *m/z* of an analyte by recording the ion species flight time over a specific distance. Imagine a group of ions with varying masses moving in the same direction with constant kinetic energy. With acceleration from an external electric field toward an ion detector, these ions will have different velocities based inversely on the square root of their *m/z*, resulting in lighter ions traveling faster and reaching the detector earlier than heavier ions. This description is somewhat simplified. It assumes that all the ions have a similar initial kinetic energy and start at the same position, with both affected by the nature of the ionization source. However, a significant advantage of TOF-MS compared to other MS systems is its ability to perform parallel ion detection. Unlike the TQMS and many mass spectrometers which function as “mass filters” scanning a narrow range of masses of interest, TOF-MS systems do not require scanning as the ions arrive at the detector at different times. This allows TOF-MS to not only detect all ions present in an analyte, but TOF-MS also has an essentially unlimited mass range compared to other MS systems, which has been appealing for the analysis of biological macromolecules.

## Systems & Equipment

Basic TOF-MS systems consist of four parts: an ionizer (discussed in following sections), an acceleration chamber, a field free drift region, and an ion detector.

**Acceleration Chamber.** Following sample ionization, the resulting ions are exposed to a strong electrical field within the acceleration chamber. This chamber is typically composed of a stack of plates with center holes, except for the back plate. Ions enter the stack from the side and a high voltage pulse is applied to the back plate, causing the ions to accelerate through the stack of plates and into the field-free drift region. The potential energy of the ion is related to both the strength of the voltage pulse and the ion's charge. When accelerated into the drift region, this energy is converted into kinetic energy (i.e., velocity), and ions of different charge and mass will travel at different speeds.

**Field Free Drift Region.** Ions entering the drift region have a kinetic energy ($K$) that is proportional to the species charge ($z$). With the energy applied ($U$) within the acceleration chamber, the amount of kinetic energy ($K$) and the velocity ($v$) of an ion with mass $m$ are as followed:

$$K = Uz \qquad \text{(Eq. 1)}$$

$$v = \sqrt{\frac{2Uz}{m}} \qquad \text{(Eq. 2)}$$

To determine the time ($t$) it takes for an ion to travel the length of the drift region ($L$) and reach the detector, the following equation is used:

$$t = L/\sqrt{\frac{2Uz}{m}} \times \sqrt{\frac{m}{z}} \qquad \text{(Eq. 3)}$$

Therefore, the time an ion takes to reach the detector is related to the square root of the species $m/z$. TOF-MS utilizes a pulsed energy technique, meaning that ions are accelerated as a group into the drift region where their various velocities cause them to reach the detector at different times.

**Linear versus Reflectron Flight Tube.** TOF-MS systems are often combined with other MS technologies. For instance, quadrupole TOF systems (Q-TOF) are very common dual MS systems, with the mass filter and collision cell increasing the utility of the TOF-MS. Many TOF-MS systems utilize a "reflected" flight path (aka reflectron) rather than the linear flight path explained previously (Figure 2). Reflectron instruments incorporate an electrostatic ion mirror at the end of the linear flight tube which utilizes potential gradients to reverse the direction of the ions. Off-axis by design, the ions are reflected toward the detector rather the ionization source. This configuration provides better $m/z$ resolution by correcting for broad initial kinetic energy distributions.

## Mass Spectrometer Practical Considerations

**Specimen Preparation.** As Table 1 illustrates, there are numerous ionization/sample introduction methods to mass spectrometry systems. A few select examples are discussed in further depth in following sections.

**Ion detector.** As with the types of ionization/sample introduction methods, there are various types of ion detectors with most relying on the amplification of the detected signal. The most common detectors in modern MS are electron multipliers. These ion detectors amplify an ion signal through a cascade of electron emissions beginning with an ion species striking a dynode and emitting several electrons. Those electrons are drawn by an electric field to a second dynode, hitting it and producing several more electrons each. Similar behavior causes those electrons to hit a third dynode, and so on. These electrons are collected by a metal anode which generates an electrical signal and is illustrated by the spectra observed. Electron multipliers show exceptionally high signal gain.

**Calibration and Accuracy.** To obtain quality *m/z* spectra, the mass spectrometer must be tuned and calibrated prior to usage. While this varies between instrument vendors, it typically consists of a mixture of ionizable, highly purified molecules of known *m/z* or known atomic composition. Using a calibration standard allows for instrument variations to be accounted for over time and the mass accuracy is determined using analyte peaks. One method for evaluating instrument mass accuracy measurement is by calculating the root mean square (*RMS*) error as followed:

$$RMS = \sqrt{\frac{\sum(E_{ppm})^2}{n}} \qquad \text{(Eq. 4)}$$

where $E_{ppm}$ is the ppm error and $n$ the number of masses considered in the calibration. Typically, the error should be below 5 ppm RMS. Adjusting instrument parameters and mass calibration ensures good sensitivity and accurate mass analysis. Frequency of instrument tuning and mass calibration will depend on the desired use, as well as the ionization method. Some ionization sources are interchangeable on a single instrument, which, when switched would require re-tuning.

Relating the separation of two *m/z* values to the width of their peaks is measured as mass resolution and the mass-resolving power is defined as full width at half the maximum height. High-resolution MS instruments can provide ion *m/z* measurements to several decimal places (i.e., exact mass measurements instead of nominal masses). This allows high-resolution MS to differentiate between molecular formulas which have the same nominal mass. For example, methylisocyanate ($C_2H_3NS$), isobutylamine ($C_4H_{11}N$), and 1-methylguanidine ($C_2H_7N_3$) all have nominal masses of 73. A high-resolution MS would be able to distinguish between these compounds because their exact masses are 72.9986, 73.0891, and 73.0640 Da respectively.

**Data Analysis and Reliability.** While MS spectra appear complicated, analytical chemists rarely try to assign species to every single peak in a spectrum. Instead, characteristic peaks and molecular ions are identified. This reveals the *m/z* of the molecule present. When

tandem mass spectrometry is employed, precursor ions are selected and fragmented, creating product ions which provide further molecular information.

Interpretation of MS data relies on multiple factors, one of which is charge. As previously stated, MS techniques measure *m/z* not mass. Determining the mass of a singly charged analyte ions ($A^+$) is simple; however, often molecules can form multiply charged ions, complicating the determination of the molecule's mass. Many of the ambient ionization techniques discussed here or in Table 1 are soft ionization techniques, meaning that in addition to little or no fragmentation, multiply charged ions are far less likely. However, with these sources, adduct effects can still influence the assignment of the molecular ion, and there are differences in the relative abundance of these ions compared to that of the molecular ion. Often isotope effects can facilitate the identification of atoms present in a molecule. For instance, molecules containing chlorine (Cl) illustrate two molecular ion peaks, one at 1/3 the height of the other and separated by 2 atomic mass units. This is due to both 37-Cl and 35-Cl isotopes within the population of molecules, with 37-Cl being 25% the natural abundance of chlorine compared to 75% 35-Cl.

Important considerations in reliability and tuning is the peak shape and the need for calibration. Mass spectrometry reliability relies heavily on the upkeep of the instrument. Timely maintenance, tuning, and mass calibration are crucial to acquiring accurate MS spectra.

# Ionization Sources

As discussed previously, ion sources create atomic and molecular ions, typically through desorption by a laser or high heat. With the flurry of recent developments in ambient ionization, there are numerous ionization techniques with select methods shown in Table 1. With the large number of ionization techniques, this chapter has selected two atomic and two molecular ionization sources to discuss in detail below, inductively coupled plasma and thermal ionization MS providing atomic information and direct analysis in real time and matrix assisted laser desorption ionization MS analyzing molecular compositions.

## Inductively Coupled Plasma (ICP)

Inductively coupled plasma mass spectrometry (Figure 3) is a common atomic analysis technique used to determine the metal and non-metal composition of a variety of solids and liquids. Over the years and with improved technology, ICP-MS now offers low detection limits with high throughput. Some manufacturers claim to have detection limits in the part per quadrillion (ppq) range but of course, it depends on a variety of factors including sample matrix, sample load, introduction system, age of instrument, contamination/cleanliness, etc. Although solids can be analyzed via this technique, they must either first be dissolved into liquid form or, with optional add-on instrumentation, can be analyzed directly. Once in liquid form the samples can be analyzed for determination of metals and non-metals both semi-quantitatively and quantitatively, with the ability to scan most of the periodic table of elements.

### Systems & Equipment

A typical ICP-MS instrument includes a peristaltic pump, nebulizer, spray chamber, torch/injector, RF coil, ion source (plasma), cones, and collision/reaction cells, Figure 3.

**Peristaltic Pump.** There are several pump sizes and rates (rpm) in which different manufacturers use to get the sample liquid from the sample vial to the instrument. Most commonly the peristaltic pump uses two pieces of pump tubing, one for the sample intake and the other for waste.

**Nebulizer.** The function of the nebulizer is to convert liquid sample to aerosol. There are a wide variety of different types and materials for nebulizers, most common are pneumatic nebulizers usually made of glass or, for highly corrosive sample liquids, various types of polymers. The nebulizer uses a gas, typically argon, to force the liquid sample through a small orifice creating a fine sample aerosol. Both sample matrix and oxide ratios can cause low signal intensities and create spectral interferences, including those caused by polyatomic species. Depending on the sample matrix and oxide ratio an operator can change the nebulizer flow to maximize signal intensity and/or minimize interferences. Nebulization plays a vital role with instrument optimization and if not optimized correctly could cause erroneous results.

**Spray Chamber.** Within the spray chamber, the aerosol collides with chamber walls which sends the larger sample droplets to waste and allows only the smallest droplets to be introduced to the plasma. The spray chamber also stabilizes the nebulization stream allowing for a more constant flow pattern by removing residual pulse flow from the peristaltic pump. Spray chambers can be made of glass, quartz and a variety of different polymers, as well as be in cyclonic, barrel and conical configurations. The correct spray chamber can help improve precision between measurements and decrease system contamination. For example, barrel spray chambers have increased surface area the sample encounters and, therefore, requires more rinses to the system to prevent carryover or memory effects, resulting in increased analysis time.

Spray chambers can be coupled with a cooling device, such as a Pelletier cooler or chiller, to provide thermal stability and control over the amount of sample reaching the plasma, in addition to decreasing oxide species. Generally, proper instrument optimization suppresses oxide species to levels less than 3%, although with newer technology some manufactures have been able to achieve less than 1.5%.

**Torch/Injector.** The injector is part of the introduction system that guides the fine aerosol from the spray chamber through the torch and directly into the plasma. The injector is available in different sizes depending on analysis. Quartz and alumina are most common, although there are other materials available depending on the type of sample material. The torch is responsible for containing and sustaining the plasma and is usually made of quartz. The torch is composed of three concentric channels which allow for argon to flow freely to the torch, with one end of the torch centered within an RF coil, and both working together to create and sustain the plasma.

**RF Coil.** This coil carries the energy from the RF generator to the coil to producing the plasma power, typically 750 – 1500 W.

**Ion Source.** The plasma generated by the above components is the source used to create atomic ions. An ICP uses high purity gas, usually argon, which flows inside the concentric channels of the torch, while a radio frequency (RF) load coil creates an oscillating electric and magnetic field. A spark from the ignitor is applied to the argon gas flowing through the torch. This spark ionizes argon atoms by removing an electron from the outer orbital of an argon atom and creates positively charged argon ions and electrons; both begin to interact with the electric and magnetic field. This begins to create a chain reaction of collisions resulting in additional argon ions and electrons created. Through this process heat is generated and these reactions will be sustained until the flow of argon gas is paused. The RF coil sits above the torch and a bullet shaped plasma (6,000 – 10,000 K) lays at the tip of the torch, acting as an excellent ion source. Ion species typically formed by the plasma are singly charged species since the ICP is very effective at removing a single electron from the outer orbital, although doubly charged species (i.e., ions with a +2 charge) also form. Ions with lower ionization potentials form ions more efficiently than ions with high ionization potentials, such as Cl, I, F, etc., which have ionization potentials near or higher than the ionization potential of argon.

There are different zones within the plasma which contribute to the ionization process. The zone just outside the torch is known as the Pre-heating Zone (PHZ), where desolvation, evaporation, and dissociation of the sample takes place. For a very short time in the PHZ, the aerosol becomes small solid particles which quickly turn to the gas phase prior to entering Initial Radiation Zone (IRZ). Here the gas particles are atomized and flow through the Normal Analytical Zone (NAZ). This is where the sample is ionized. Temperatures in the NAZ are approximately 5,000 – 8,000 K. Once the sample has been ionized the ions are extracted through an interface using multiple cones. These cones are known as sampler cone, skimmer cone and, on some instruments, a hyper skimmer cone, with the purpose of gradually stepping the vacuum from atmospheric pressure to ~$10^{-6}$ torr. Once through the cones the ions enter the collision cell and quadrupole mass filter.

**Collision/Reaction Cells.** Like other analytical instrumentation, ICP-MS is a great tool for trace metal analysis. However, this method does suffer from interferences. Collision/Reaction cells are used to remove polyatomic ions with the same mass of the analyte of interest. For example, argon (40)-chloride (35) has a mass of 75 Da, coincidental with arsenic (As), thus becoming an interference if arsenic is the analyte of interest. Collision cells use a non-reactive gas (such as helium) to fill a small chamber, and as the ion of interest and polyatomic ion (interferent) pass through the cell, collisions with helium atoms results in a decrease in the ion kinetic energy. The larger polyatomic ion $ArCl^+$ collides with more helium atoms than the smaller As ion, thus losing more energy than the $As^+$. An energy barrier is established at the exit of the cell, so that ions with less energy (i.e., $ArCl^+$) cannot exit the cell, while ions with more energy (i.e., $As^+$) can exit the cell and pass to the analytical quadrupole and detector. This is known as Kinetic Energy Discrimination or KED.

Reaction cells differ from collision cells in several ways. First, a reactive gas is used to remove interferences via chemical reactions instead of non-reactive collisions. Because chemical reactions are used, the laws of kinetics and thermodynamics are followed, meaning that interferences can be removed very efficiently. Reactions with large rate constants occur very quickly, allowing a higher degree of interference reduction than in collision cells. Any reactive gas can be used in reaction cell technology, with some of the most common being hydrogen, oxygen, ammonia, and methane. The choice of gas depends on the analyte and interference. The reactions are controlled with a low-mass bandpass so that new interferences are not formed. Because they follow the laws of kinetics and thermodynamics, chemical reactions are very reproducible. To further ensure repeatability, all ions in the cell are at thermodynamic equilibrium due to the voltages on the cell: ions are not accelerated through the cell, nor is there an energy barrier at the cell exit.

**Optional Laser-Ablation** is used for the direct surface analysis of solid samples or can provide surface profiling capabilities. Ablation occurs in multiple stages, with the first being irradiation with the laser which causes electronic excitation of the material followed by ejection of electrons from the sample surface. Second, energy is transferred through the sample target causing melting, vaporization, ionization, and the formation of a plasma plume. Neutral ablated material (in aerosol or particle form) is transported by an argon stream into the ICP, decomposed, atomized, and ionized prior to MS analysis. Lasers are typically frequency-quintupled Nd:YAG (neodymium doped yttrium aluminum garnet crystal, 213 nm) focused to produce variable spot sizes from <5 μm to 300 μm.

**Mass Spectrometer.** There are typically three types of mass spectrometers coupled with ICP sources: a quadrupole mass filter, a triple quadrupole, or a magnetic sector. Single quadrupoles and magnetic sectors are discussed in depth in Gas Analysis by Mass Spectrometry (Division 3:C). Briefly, the first MS, a single quadrupole, is similar to the triple quadrupole with the obvious exception that only one quadrupole mass filter is used. By varying the applied potential across the metal rods, the quadrupole can affect the trajectory of ions through the quadrupole and only allow ions of small *m/z* ranges to pass through to the ion detector. In a similar way, magnetic sectors alter the trajectory of ions through a flight tube. However, these systems accomplish this with an applied electric and/or magnetic field.

**Additional Instrumentation.** ICP-MS can also be coupled with other instrumentation to aid in the analysis process, depending on the analytical goals. Solid sampling is typically accomplished with spark or laser-ablation systems, while gas and liquid chromatography systems are used for sample introduction when required to separate different forms of the same element prior to measurement. Sample prep varies widely and is highly dependent on the sample type and analytical goals.

## Practical Considerations

Examples of various ICP-MS analyses can be found in Example 1 and 2 at the end of this chapter, as well in select literature references.

**Specimen Preparation.** ICP-MS can analyze liquids and solids. While gases can theoretically be analyzed, calibration is difficult. For liquids, all that is required is the liquid solution be less than or equal to 0.3% total dissolved solids (TDS) entering the plasma, although techniques and accessories are available to accommodate higher levels of dissolved solids. It is important to acidify sample solutions to preserve the dissolved metals. Then it is ready to be aspirated into the system.

Solids must be digested (liquified) to be analyzed via ICP-MS, unless coupled to an additional instrument like laser-ablation. Typically, a known amount of solid sample is weighed, and strong acid is added to the sample vessel. Depending on the sample composition, various acids are used, such as nitric acid, hydrochloric acid, and hydrofluoric acid. Sometimes heat is added via hot plate, digestion block, or microwave to accelerate the dissolution of the sample. After the sample is dissolved it is cooled and diluted via an acidic solution (~2%) to a known volume. The sample is ready for instrumental analysis to determine solid composition.

**Calibration and Accuracy.** ICP-MS instruments are typically capable of semi-quantitative and quantitative analysis and have large linear dynamic ranges by using pulse and analog detection modes. Pulse mode cannot process large signal, thus when large signal is present the operator or system switches to analog mode for detection. While an operator has full control over which mode is used, it is often operated in a dual mode so that the software determines when to switch between modes. To use this function the instrument must be calibrated for both modes.

**Data Analysis and Reliability.** Quantitative data analysis is carried out using a set of known solutions to construct a calibration curve. The calibration standards are prepared using certified multielement stock standards and diluted using acidified blank solution. The calibration curve is usually checked with quality checks prepared in the same fashion. Quality checks are of known values to target a specific concentration within the calibration curve. However, the quality checks are typically prepared with a different certified multielement stock standard than the calibration standards were prepared from. Calibration standards, quality checks and samples are analyzed on the instrument using the same instrument setting and parameters. The percent recovery of the quality checks provides a quantitative analysis to measure the reliability of the instrument/calibration and, thereby, the data provided in sample analysis.

## Direct Analysis in Real Time (DART)

Since ambient mass spectrometry was first introduced with desorption electrospray ionization (DESI) and direct analysis in real time (DART), the molecular analysis of a large variety of samples was simplified. By creating ions outside of the instrument at atmospheric pressure, i.e., in the open laboratory environment, ambient mass spectrometry is a soft ionization technique which requires little to no sample preparation or pre-separation. Since the landmark introduction(s) of DESI and DART another ~50 different atmospheric pressure desorption/ionization techniques have been developed, all with similar underlying methodology. These methods form ions by “wiping off” sample analyte molecules using energetically charged particles, species, or laser beams. Of these methods,

DART has become one of the most established, with a vast range of applications ranging from pesticide monitoring to detection of explosives and warfare agents to forensic and environmental analysis, to name just a few.

## Systems & Equipment

DART mass spectrometry is based on the atmospheric pressure interactions of electronically or vibronically excited-state species from gases such as helium, argon, or nitrogen with the sample and atmospheric molecules. This interaction can ionize species directly from solid surfaces, liquids and gases. A typical DART instrument includes an enclosed ionization source, a reaction zone (extending from the source exit to the sample), and the interface (extending from the sample to the entrance of the mass spectrometer), Figure 4.

**Ion Source.** Formation of the ions that will interact with the atmospheric gases and sample material occurs within three compartments in the ionization source. A cutaway view in Figure 4 shows the general principle of the DART ionization source. Within the first, helium (typically) gas (~3.5 L $min^{-1}$, 50-550 °C) flows through the chamber where a corona discharge (~2 mA), between a needle electrode and a perforated, grounded disk electrode, produces ions, electrons, and excited-state (metastable) atoms and molecules. Passing through perforated electrode grids results in cations, anions and electrons being extracted from the gas stream. The perforated electrodes are set to positive or negative potentials depending on the ionization mode needed for sample analysis. Excited neutral gas molecules, including metastable species, remain to exit the ionization source into the reaction zone. The perforated exit grid electrode has three main roles, it prevents ion-ion and ion-electron recombination, promotes ion drift toward the mass spectrometer interface by exerting a repelling force to push the excited neutral gas molecules, and it is a source of electrons for some ionization mechanisms.

**Reaction Zone and Interface.** Ions formed in the DART source are released into the reaction zone and immediately interact with and ionize the surrounding gas (laboratory air) and sample. While the excited ionizing species released by the ion source are typically helium species, ionized air created through ionization with this helium species are the primary source for analyte ionization. Following the excitation in the ion source (Eq. 5), the energy stored in helium (He) is greater than what is possible for other noble gas atoms (He*>Ne*>Ar*), with an excited electronic state energy of 19.8 eV, above that needed to ionize most molecules.

$$He + energy \rightarrow He^* \quad \text{(Eq. 5)}$$

Several sample (M) ionization mechanisms can occur depending on the mode of analysis; however, the dominant positive-ion formation mechanism is through ionized water ($H_2O$) clusters as followed:

$$He^* + H_2O \rightarrow H_2O^{+\cdot} + He + e^- \quad \text{(Eq. 6)}$$
$$H_2O^{+\cdot} + H_2O \rightarrow H_3O^+ + OH^\cdot \quad \text{(Eq. 7)}$$
$$H_3O^+ + nH_2O \rightarrow [(H_2O)_n + H]^+ \quad \text{(Eq. 8)}$$

$$[(H_2O)_n + H]^+ + M \rightarrow [M + H]^+ + nH_2O \quad \text{(Eq. 9)}$$

Negative-ion formation has multiple ionization methods as well, including deprotonation by dissociation, direct electron capture, and anion attachment. In addition, surface Penning ionization, where electrons are produced by the reaction of excited atoms with the surface of the exit electrode ($N_{surface}$) or neutral gas species ($N_{gas}$), is also a possible ionization route. This negative-ion formation mechanism is as followed:

$$He^* + N_{gas} \rightarrow {N_{gas}}^{+\cdot} + He + e^- \quad \text{or} \quad He^* + N_{surface} \rightarrow {N_{surface}}^{+\cdot} + He + e^- \quad \text{(Eq. 10)}$$

$$O_2 + e^- \rightarrow {O_2}^{-\cdot} \quad \text{(Eq.11)}$$

$${O_2}^{-\cdot} + M \rightarrow M^{-\cdot} + O_2 \quad \text{(Eq. 12)}$$

Between the reaction zone and interface, the helium flow may be insufficient to maintain proper mass spectrometer vacuum conditions; therefore, a pump interface can be inserted to provide additional suction of the gas containing ions toward the inlet of the mass spectrometer.

## Practical Considerations

Examples of various DART MS analyses can be found in Example 3 and select literature references at the end of this chapter.

**Specimen Preparation.** The main advantage of a DART introduction method is the requirement for little to no sample preparation. A solid, liquid, or gas, even living organisms, can be subjected to DART-MS in an open atmosphere without pretreatment. However, DART can be coupled with various separation techniques with typically no additional DART instrument manipulation. This can include gas chromatography-DART (GC-DART), liquid chromatography-DART (LC-DART), and thin-layer chromatography (TLC). Spot analysis of TLC plates has even been used to track nanogram levels of pharmaceuticals. GC- and LC-DART coupling only requires that the GC or LC gas or liquid to be eluted in the reaction zone of the DART source.

**Calibration and Accuracy.** A typical DART-MS system is qualitative but capable of semi-quantitative analysis. As a possible analyte introduction method to a variety of mass spectrometry types, including TOF, TQMS, ion trap, and orbitrap, the sensitivity, resolution, and mass accuracy are more dependent on these instruments than the DART ion source. However, calibration of the interface distance and angle can have dramatic effects on sensitivity. For example, with the DART source at a distance further than optimal from the MS inlet, i.e., a large reaction zone and interface section, the signal intensity can decrease significantly due to poor transfer of gas and ionized analyte from the interface to the MS inlet. With the DART source too close to the inlet, the signal to noise can decrease due to overload of excited or ionized material in the MS.

**Data Analysis and Reliability.** Analysis of DART-MS data is identical to that discussed in the various mass spectrometry detectors. In data analysis, the reliability of the utilized detector, in addition to the reliability of the DART ionization source must be considered

for analysis. These systems, as with any mass spectrometry method, rely heavily on the analyte material and, while the energy stored in the excited gas stream is above that required to ionize most molecules, there can be difficulty in how efficiently the species are ionized.

# Thermal Ionization (TI)

Comparatively, thermal ionization sources operate based on a simple theory to atomically analyze materials. Ionization is achieved through deposition of material, either liquid or solid, on a conducting metal filament which is heated to a very high temperature. Ions are then formed by electron transfers between the analyte species and the filament. Thermal ionization MS (TIMS) systems are especially useful in isotopic analysis applications such as geological fields and nuclear applications, in addition to bulk elemental analysis.

## Systems & Equipment

Typically, TIMS is composed of the filament(s), accelerator, sector, and detector. Unlike many of the ionization techniques described here, TIMS systems typically utilize magnetic sector mass spectrometers. While sectors are discussed extensively in the Gas Analysis by Mass Spectrometry (Division 3:C), sectors will be touched on briefly here.

**Filament Ionization Chamber.** The ionization source of TIMS systems uses temperature to thermally ionize solid or dried liquid samples for introduction into a mass spectrometer. Following sample deposition onto a conducting metal filament, typically tungsten, platinum, or rhenium, electric current heats the metal and sample to high temperatures. With temperatures often exceeding 1000 °C, element ions are formed through electron transfer with the filament. Positive species are formed from electron transfer from the atom to the filaments, while negative species are formed from electron transfer from the filament to the atom. Ionization efficiency depends heavily on an atom or molecule's ionization potential and electron affinity. Typically, metals can be analyzed in positive ion mode while non-metals and transition metals can be observed in negative ion mode.

TIMS systems can utilize single, double, and triple filament methodologies to ionize sample atoms. Their use depends largely on sample characteristics and experiment methodology. Single filament sources evaporate and ionize sample utilizing the same filament surface. In double filament systems, the filament holding the sample is used for evaporation while the second filament ionizes the evaporated sample. Double filament sources allow more flexibility of sample evaporation rates and ionization temperatures than single filament sources where these settings are tied to each other. This is often used with samples that evaporate at lower temperatures than they are ionized. Triple filament systems are often used where direct comparison of two different samples under identical source conditions are required.

**Accelerator and Sector.** Similar to TOF-MS systems, TIMS accelerates ions toward the mass spectrometer by exposing species to an electrical potential gradient (up to 10 kV) which are focused into a beam through slits and electrostatically charged plates. Typically, TIMS systems separate ions by their $m/z$ by passing through an electromagnetic sector analyzer. Briefly, sector mass spectrometers use electric and/or magnetic fields to alter the

trajectory of ions based on how they move through the applied field which is dependent on the size and charge of the ion. As described in the TOF-MS theory, ions of different masses have different velocities, $v$. When applied to an electric field ($E$) and a magnetic field ($B$), the force ($F$) applied to a particle with charge $q$ is as follows:

$$F = q(E + v \times B) \qquad \text{(Eq. 13)}$$

With velocity after acceleration dependent on mass, lighter ions will be deflected by the applied fields more than heavier ions. Resulting in separate beams of ions based on the ions *m/z* which are directed to ion detectors and converted into voltage.

### Practical Considerations

Examples of various TIMS analyses can be found in select literature references at the end of this chapter.

**Specimen Preparation.** TIMS sample preparation varies sample to sample. Often liquid samples are deposited onto the conducting metal filament and allowed to dry fully, creating a thin film. Many solid samples require complete dissolution prior to analysis, similar to that described for ICP-MS sample preparation.

**Applications.** The predominant application of TIMS has long been elemental analysis, including isotope ratio analysis in areas ranging from geochemistry to nuclear forensics and cosmochemistry to urine analysis. Select examples of recent TIMS isotope analysis are provided in the "Select References" section at the end of this chapter.

**Calibration and Accuracy.** Like other mass spectrometers, TIMS systems require calibration and tuning with standard elemental reference materials (National Institute of Standards and Technology) or by internal calibration techniques. Instrumental biases like mass fractionation (isotope ratio changes during evaporation) must be corrected for in measured isotope ratios. TIMS provides excellent sensitivity, precision and accuracy for precise isotope ratio measurements; however, progress in ICP-MS is increasingly replacing these systems due to less restriction on an elements ionization potential.

**Data Analysis and Reliability.** Analysis of TIMS data can be complicated compared to many other MS systems. Isotope count-rates typically must be adjusted by subtracting background and isobar signal contributions, species that have the same mass number but have different exact masses.

TIMS reliability is dependent on mass calibration and tuning, with isotope identification requiring especially accurate *m/z* measurements.

## Matrix Assisted Laser Desorption Ionization (MALDI)

Desorption ionization sources tend to be considered soft ionization techniques, meaning molecular ion formation occurs without breaking chemical bonds within the species. MALDI-MS has become a powerful tool for the analysis of large, non-volatile and thermally labile compounds often difficult for other ionization sources. This includes

proteins, large inorganic compounds, synthetic polymers, and various other materials. MALDI ionization occurs via two steps, Figure 5. First, sample material is dissolved in solvent containing small organic matrix molecules. The mixture is dried resulting in a thin film of analyte-doped matrix crystals. The second step relies on the matrix molecules having a strong absorption in the laser wavelength. Through short pulses of irradiation, the laser rapidly heats the matrix crystals and ablates portions of the film. Ablation results in material being expelled in the gas phase concurrent with ionization, and the ions accelerated into the mass spectrometer. While the majority of sample preparation in MALDI involves dissolving a sample in solution, this is mainly due to the extensive use of MALDI in biological studies. However, MALDI imaging has used ionic matrix solutions to open the door for MALDI in the analysis of solid samples.

## Systems & Equipment

Typically, MALDI ionization systems are mainly composed of the matrix, acceleration grid, focusing lens, laser, and mass spectrometer.

**Matrix.** Choosing a matrix is the most important step in MALDI analysis, with different matrix molecules being ideal for different analytes. There are a few criteria for picking a suitable matrix compound, including possessing a strong laser absorbance, being stable under vacuum, and often acidic to act as a proton donor. Matrix molecules tend to be small organic molecules such as sinapinic acid (used for proteins) and 2,5-dihydroxybenzoic acid (used for polar synthetic polymers). Picking a matrix compound is often based on trial and error or experience with similar analyte materials. This is a result of the still poorly understood ionization mechanism, with multiple mechanisms likely at play. The prevailing mechanisms are discussed in more detail below.

**Acceleration Grid and Focusing Lens.** The role of these components is to extract and focus ions from the source and efficiently pass them through the mass spectrometer. The acceleration grid uses voltage variations to accelerate ions toward the mass spectrometer. More information for this component can be found in the previous TOF-MS section. The focusing lens typically uses electric potentials spread along parallel plates to create an electric field that bends the ion beam toward a focal point to optimally be transferred to the mass spectrometer. The focusing lens also separates the acceleration region from the field free drift region in the mass spectrometer, typically TOF-MS.

**Laser and Ionization.** Typical lasers utilized in MALDI systems are nitrogen gas lasers (337.7 nm) or frequency-tripled (355 nm) and quadrupled (266 nm) Nd:YAG lasers. These lasers irradiate a sample-matrix film which causes matrix molecules to absorb the laser energy. This energy transforms into thermal energy and causes sublimation of the matrix, driving analytes into the gas phase. Within the hot plume produced, the analyte species are ionized, but the exact mechanisms for ionization are debated. One hypothesis is multiphoton absorption, where the matrix ($M_{at}$) absorbs one photon (*, excited state), then another (charged radical) and then interacts with the analyte ($A$) species, illustrated as followed:

$$M_{at}M_{at} \xrightarrow{2h\nu} M_{at}^{*}M_{at}^{*} \rightarrow M_{at} + M_{at}^{+\cdot} + e^{-} \qquad \text{(Eq. 14)}$$

$$M_{at}^{*}M_{at}^{*} + A \rightarrow M_{at}M_{at} + A^{+\cdot} + e^{-} \quad \text{(Eq. 15)}$$

with laser energy represented with *hv*. This results in a deprotonated matrix and protonated analyte.

The prevailing mechanism however is believed to be the transfer of protons between the matrix molecules and the analyte molecules, creating singly charged ($[M+H]^+$ or $[M-H]^-$) ions. This mechanism presumes that an excited state matrix molecule is more acidic or basic than the analyte and therefore it can give up or accept a proton from the analyte as followed:

$$M_{at} + hv \rightarrow M_{at}^{*} \quad \text{(Eq. 16)}$$

$$M_{at}^{*} + A \rightarrow (M_{at} - H)^{-} + [A + H]^{+} \quad \text{(Eq. 17)}$$

While the exact mechanisms are not fully understood, analyte ions signals tend to depend not just on the matrix compounds but also the laser intensity.

**Mass Spectrometer.** Due to the analysis of large molecules, MALDI systems are typically coupled with a TOF-MS system described in more detail in a previous section.

**Imaging system.** The utility of MALDI ionization sources increased significantly with the development of imaging mass spectrometry (IMS). The technique typically involves a calibrated sample stage which can move while the mass spectrum is recorded, resulting in spatial distribution analysis of molecular species. Images are constructed by correlating ion intensity to relative position that the data was acquired from and are similar to the heatmaps observed in Example 3 for DART-MS analysis.

## Practical Considerations

Examples of various MALDI MS analyses can be found in Example 4 and select literature references at the end of this chapter.

**Specimen Preparation.** More so than many of the ionization sources, MALDI sample preparation can be extensive, with three potential methods discussed here. The first, dried droplet, is the easiest and most utilized method. Solid samples are dissolved in solvent and mixed with the matrix solution. Sample solutions should be acidic to prevent neutralization of the matrix. The mixture is dispensed on a metal plate and dried at ambient temperature. The second method, thin layer, involves dissolving the matrix molecules in acetone and dispensing the solution on the metal target. Acetone is chosen based on how quickly it spreads and dries. Sample solution is then deposited on top of the target and allowed to dry. This method provides more homogenous matrix crystals and can yield high resolution spectra and low detection limits. The final method is identical to the previous method; however, the sandwich method applies a final layer of matrix on top of the sample layer.

Preparation of multiple matrix-analytes spots on the metal plate allow for faster analysis of multiple different samples or matrix-analyte mixtures. Advances in MALDI techniques has also made solid analysis, with sample integrity maintained, more straightforward. This is typically achieved by attaching a solid sample to the MALDI metal plate followed by deposition of ionic matrix solution on top which is allowed to dry prior to analysis.

**Calibration and Accuracy.** Homogeneous dispersion of the analyte and matrix improves signal intensity, consistency, and mass resolution. Therefore, MALDI analysis often requires optimization of both the matrix constituents and the laser intensity depending on the sample type. MALDI systems tend to be as accurate and precise as the MS system to which they are coupled, typically TOF-MS. However, advances in MALDI matrices has greatly expanded the range of samples which can be ionized with this methodology.

**Data Analysis and Reliability.** MALDI spectra are typically very simple to analyze due to the majority of displayed ions being singly charged. Coupled with a TOF analyzer, MALDI systems are capable of fast and precise analysis of molecules ranging from 100 Da to 100 kDa. Data analysis process and reliability are discussed more above in the mass spectrometer section.

## Related Ionization Source Techniques

This chapter is designed to familiarize the reader with select ionization and mass spectrometry technique. The vast range of ionization methods prohibits a full coverage of every technique. Two other common ionization methods, glow discharge and secondary ion, are discussed briefly here and in greater detail in other chapters within this handbook.

**Glow Discharge Mass Spectrometry** (GDMS) ionizes compounds from solid surfaces via a gas discharge between a cathode and anode in a low-pressure gas (0.1-10 Torr). The sample is introduced as the cathode in these systems followed by the application of an electric current across the electrodes. This causes the breakdown of the gas, typically argon, and acceleration of ions towards the electrodes. The bombardment of argon ions on the sample surface results in kinetic energy transfer and surface atom ejection. Atoms are ionized via multiple ionization mechanisms.

The main application for GDMS is in bulk metal analysis. As opposed to inductively coupled plasma mass spectrometry, GDMS can analyze solid samples with very little material (i.e., non-destructive), while it is limited to positive ion analysis and the need for solid standards. Additional advantages of GDMS compared to ICP-MS include:

- Decreased possibility of the loss of volatile elements and false positives related to contamination during sample preparation.
- High resolution MS can provide superior sensitivity and better resolution.
- Greater ability to measure insoluble or difficult to digest materials (*e.g.* silicon carbide, aluminum oxide, graphite, etc.)

**Secondary Ion Mass Spectrometry** (SIMS) is a technique that uses an internally generated beam of ions, either positive or negative, to generate ions from a sample surface which are then accelerated and analyzed by a mass spectrometer. These ion beams bombard a sample ejecting charged particles (secondary ions) from the surface. Generally, beams of positive ions (e.g. $Cs^+$, $O_2^+$, $Ar^+$) generate negative ions from the surface, while negative ion beams (e.g. $O^-$) produce positive ions from the surface. Since SIMS is performed under vacuum, samples are required to be solid materials that are stable in a vacuum system.

Most SIMS systems are used for elemental and isotopic analysis due to high sensitivity and depth profiling. SIMS analysis also consumes very little sample making this technology useful in samples of limited size, for example quantification of ion implants or contaminants in conductors and semiconductors, with small niches in analysis of meteorites and nuclear materials. Disadvantages of this technique include requiring suitable standards to obtain quantitative information and the sensitivity is dependent on the matrix and ion beam selected.

# Applications and Interpretation

The large number of ionization methods can make choosing a technique for specific samples daunting, with consideration in terms of sample type, desired information (i.e., molecular vs elemental vs isotopic, etc.), ionization advantages and limitations, cost, and availability required. A few literature examples references of semiconductors, microelectronics, photovoltaics, battery technology, and proteomics are included in this chapter, while some glass, aluminum metal, and polymer analysis examples are covered in depth below. However, analysis requirements vary between sample materials and requires an experienced analyst to choose efficient ionization techniques for analysis. Specifics on the characterization of various materials are covered more in depth throughout this handbook.

## Example 1: Glass Filters.

ICP-MS can be used to determine the concentration of residue content on a glass filter, in this example lead and calcium. Note: ICP-MS can measure most of the periodic table of elements apart from light elements such as H, He, C, N, O, F, Ne, and many of the actinides.

**Sample Preparation.** Three 46 mm glass filters were collected from different locations within the sampling area. Samples for digestion were weighed to approximately 0.1 grams and nitric acid (10 mL), hydrochloric acid (3 mL) and hydrofluoric acid (2 mL) were transferred to a Teflon microwave digestion vessel. This mixture was heated in a microwave digester at 180 $^oC$ for 60 minutes. When completely dissolved, the samples were normalized to 50 mL with acidified water and weighed.

**Data Reduction.** To obtain reliable quantitative measurements for this sample, the following were required:

- Analysis of an instrument performance check to ensure the instrument was optimized. Each manufacturer has target specifications the instrument must meet

to be optimized. When the instrument has met or exceeded manufacturers criterion the instrument was ready for analysis.

- Calibration blank and calibration standards were analyzed for each analyte. Calibration curves were plotted by known analyte concentration vs. signal intensity. A correlation coefficient close to one was ideal for a more accurate analysis.
- Quality control checks were analyzed following calibration to verify the calibration curves were valid and accurate measurements were applied.
- Internal standards were used to monitor matrix interference and instrument drift. The ranges used were 80% to 125% recovery range. If the values were outside this range, the quantitative measurements were suspect.

**Data Analysis.** Samples were analyzed, and signal intensities compared against the calibration curve to yield a concentration. As each sample was analyzed, data was generated with concentration information along with intensities and internal standard recoveries as shown in Table 2.

When raw data values were generated and found to be within the working calibration range, calculations were assessed using the initial weight (sample weight), final weight (50 mL) and dilution factor(s). This yielded a final concentration in parts per million (ppm) and, from this, weight percent in the original material was calculated.

## Example 2: Aluminum Wire and Sheet Verification.

ICP-MS can be used to verify the composition of aluminum wire and aluminum sheet. The following elements were analyzed: magnesium (Mg), vanadium (V), copper (Cu), Zinc (Zn), titanium (Ti), gallium (Ga), and iron (Fe).

**Sample Preparation.** Five different types of aluminum wire and sheet were provided for analysis. Triplicate replicates of sample were weighed to 0.1 grams and acids (10 mL of nitric acid and 5 mL of hydrochloric acid) were added into Teflon microwave digestion vessels for digestion. The contents were heated for 10 minutes at 95 $^{o}$C. The temperature was increased to 120 $^{o}$C for an additional 20 minutes but samples required an additional 10 mL of nitric acid and 5 mL of hydrochloric acids to dissolve completely. Samples were normalized to 100 mL and subsequent dilutions were prepared to obtain signal in the working range of the instrument.

**Data Reduction.** See example 1 Data Reduction.

**Data Analysis.** See example 1 Data Analysis and Table 3.

## Example 3: Nonpolar poly(dimethyl siloxane) (PDMS) polymers.

Direct analysis in real time mass spectrometry can be used to determine the extent of spreading of mold release formulations, consisting of PDMS and solvent.

**Sample Preparation.** While the materials received were a liquid, trimethylsilyl (TMS) terminated PDMS, in order to observe variations in spreading behavior in a mold release the sample required deposition and drying on a surface prior to analysis. Standards of TMS-PDMS, ranging in viscosity from 5 cSt to 50 cSt, were diluted to 20 mg/mL in hexane to facilitate spreading, similar to how these polymers would be used as a mold release. Approximately 2 microliters are spotted on two locations on a clean glass slide spaced evenly from the edge of the slide, as well as from each other.

**Data Reduction.** To obtain reliable, quality spectrum in this sample, the following were required:

- The MS was tuned and mass calibrated to ensure good sensitivity, peak shape, and accurate *m/z* values. This can vary instrument to instrument and between ionization modes but consists of a mixture of highly purified and ionizable molecules of known *m/*z to adjust and optimize instrument parameters. The mass calibration should span that of the instrument mass range.
- A background spectrum of the glass slide was collected prior to the spotting and drying of the TMS-PDMS solution, ensuring no contaminants were present on the slide or within the instrument.
- The DART spray was adjusted according to the position of the spots on the glass slide to ensure the linear rail moved the samples within the optimal reaction zone positions. This was completed by randomly spotting standard solutions on a glass slide and observing the signal to location correlations, adjusting to identify ideal width placement on the slide.

**Data Acquisition.** Following air drying, the glass slide was mounted in the linear rail of a DART ion trap MS system. Data was acquired by setting the gas (He) temperature of the DART ion source to 500 °C with a MS scan range of *m/z* 50-2000. The linear rail then moved the glass slide across the reaction zone of the DART gas at a raster speed of 0.2 mm/min. The *m/z* signals versus retention time (related to the y-axis location on the glass slide) were then plotted via heatmap, Figure 6. With this method not only was the TMS-PDMS thin film polymer profile observable, but the spatial analysis revealed that with changes in the heat treatment temperature during drying, the degree of TMS-PDMS spreading on the slide increased for the lower average molecular weight 5 cSt polymer, Figure 7.

## Example 4: Parachute nylon polymer material.

Matrix assisted laser desorption ionization mass spectrometry can be used to directly measure the molecular mass of high-mass polymeric materials such as nylon. While gel permeation chromatography can give a rough mass distribution, MALDI is able to perform the analysis directly from the solid material.

**Sample Preparation.** Materials were received as microcalorimetry devices with a nylon 6,6 coating, chemical structure shown in Figure 8. MALDI matrix 2-(4'-hydroxybenzeneazo)benzoic acid (HABA) was deposited on the surface and allowed to dry under ambient conditions. Figure 9 shows scanning electron microscopy of the matrix

crystals following drying. Poly(methymethacrylate) calibration standard was prepared by mixing with the same matrix compound and dispensed on a non-coated microcalorimetry device. This standard was allowed to dry under ambient conditions prior to analysis.

**Data Reduction.** The following were required for accurate and reliable spectra in these materials:

- The TOF-MS was tuned and mass calibrated with a mixture of highly purified and ionizable molecules. This ensures accurate *m/z* values and good sensitivity.
- A background spectrum of the matrix compound on an uncoated microcalorimetry device was collected prior to the analysis of nylon 6,6 coated devices to ensure matrix effects were accounted for and understood.
- The plate location was adjusted to ensure efficient irradiation of the sample spots on the device.
- Laser intensity was adjusted according to signal intensity and the amount of energy required for matrix excitation and ablation.

**Data Acquisition.**
Prior to the analysis of the nylon 6,6 coating, a poly(methylmethacrylate) calibration standard was analyzed directly from the same type of device and same matrix complex, Figure 10. The polymer envelope distribution was preserved even after deposition on the microcalorimetry device, demonstrating the viability of these devices as a sample platform.

Following air drying of the matrix molecules, the nylon 6,6 coated devices were mounted in the MALDI chamber and data was acquired with a MS range of *m/z* 100-13,500, Figure 11. With this method, nylon 6,6 parachute material exhibited reference nylon 6,6 mass spectrum, with the inset figure numbers indicating cyclic polymer chain length. Analysis also revealed polymer chains with various end groups (data not shown) which is information that gel permeation chromatography is unable to provide. In addition, with the new imaging capabilities of MALDI systems, surface distribution of these polymer films would now be possible.

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# Tables

**Table 1: Summary of select ionization techniques with those highlighted directly discussed here.**

| Ionization Technique Name | Acronym | Sample State | Typical MS types | Type of ionization | Typical Analytes | Typical uses (Bulk (B) or Profiling (P)) | Spatial Resolution |
|---|---|---|---|---|---|---|---|
| Laser-ablation inductively coupled plasma | LA-ICP-MS | solid | quadrupole | hard | elemental ions | B, P | 100-10 µm |
| Inductively coupled plasma | ICP | solid, liquid | quadrupole | hard | elemental ions | B | - |
| Direct analysis in real time | DART | solid, liquid, gas | triple quadrupole, time-of-flight, ion trap | soft | small molecules, polymers | B, P | NA |
| Glow discharge | GDMS | solid, liquid | sector, quadrupole, time-of-flight | hard | elemental ions | B | - |
| Secondary ion | SIMS | solid | time-of-flight | hard | elemental ions, small molecules, polymers | P | ~100 nm |
| Laser ablation electrospray ionization | LAESI | solid, liquid | triple quadrupole, time-of-flight, orbitrap | soft | small molecules, proteins | B, P | 350-15 µm |
| Electrospray laser desorption ionization | ELDI | solid, liquid | quadrupole, ion trap, orbitrap | soft | small molecules, polymers, proteins | B, P | ~5 µm |
| Laser ionization | LIMS | solid | triple quadrupole, time-of-flight, orbitrap | hard | elemental ions | B, P | ~10 µm |
| Matrix-assisted laser desorption ionization | MALDI | solid | triple quadrupole, time-of-flight | soft | small molecules, polymers, proteins | B, P | ~10 µm |
| Desorption electrospray ionization | DESI | solid, liquid | triple quadrupole, ion trap, orbitrap | soft | small molecules | B, P | 50-20 µm |
| Thermal ionization | TIMS | solid, liquid | sector | hard | elemental ions, isotope | B | - |

**Table 2: Glass filter ICP-MS analysis. Note: Samples were not run in triplicate due to lack of sample, thus Standard deviations are zero.**

| Sample ID | Weight Percent (wt. %) | |
|---|---|---|
| | calcium | lead |
| Filter blank | 4.38 | 0.30 |
| Filter 1 | 6.50 | 1.12 |
| Filter 2 | 6.45 | 1.13 |
| Filter 3 | 6.04 | 1.15 |

**Table 3: Aluminum wire and sheet ICP-MS analysis.**

| Sample | Concentrations (ppm) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | magnesium | vanadium | copper | zinc | titanium | gallium | iron | carbon | sulfur |
| wire | 0.92 ± 0.18 | 0.16 ± 0.02 | 0.34 ± 0.05 | 2.03 ± 0.32 | 11.95 ± 4.38 | 0.24 ± 0.03 | ND | 85.87 ± 12.13 | 5.95 ± 5.07 |
| sheet | 0.58 ± 0.16 | 1.23 ± 1.89 | 1.08 ± 0.25 | 0.78 ± 0.47 | 0.22 ± 0.092 | 0.08 ± 0.03 | 19.71 ± 4.41 | 107.37 ± 13.27 | 3.80 ± 0.68 |

# Figures

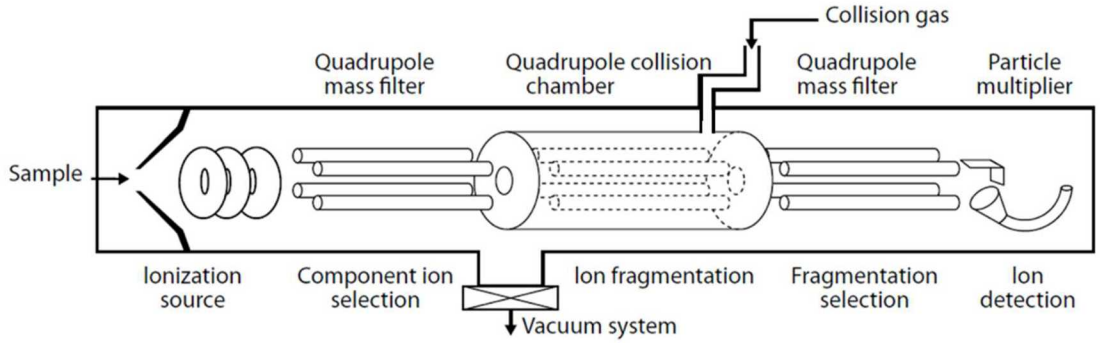


**Figure 1: Triple quadrupole mass spectrometer (TQMS) schematic.**

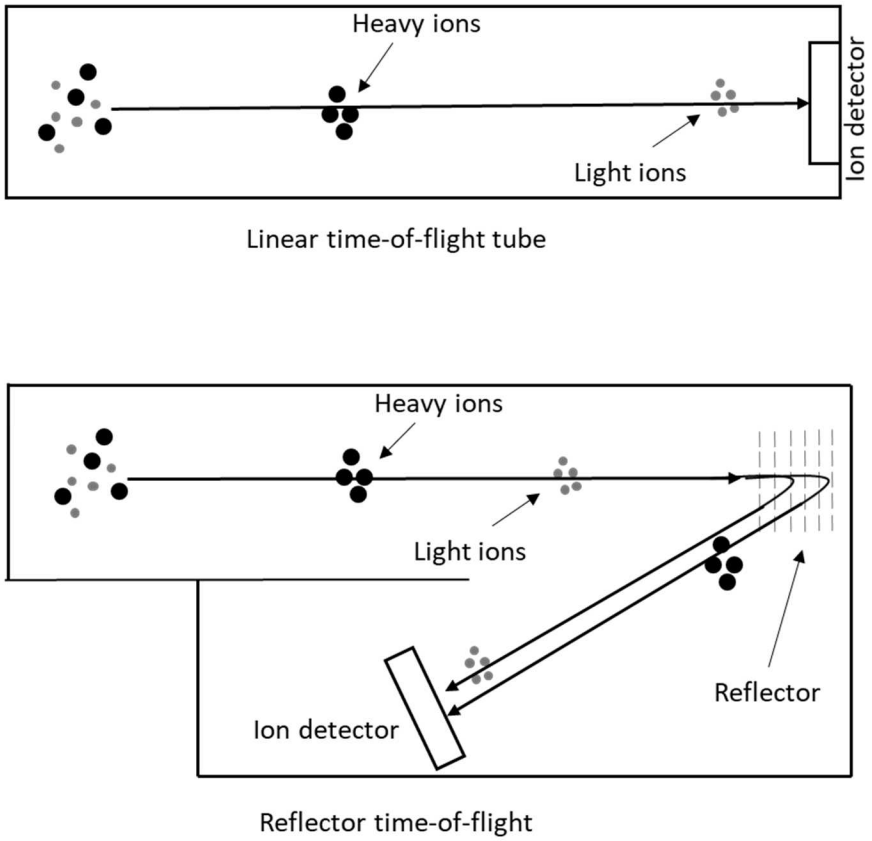


**Figure 2: Time-of-flight mass spectrometer (TOF MS) linear (top) and reflectron (bottom) flight paths.**

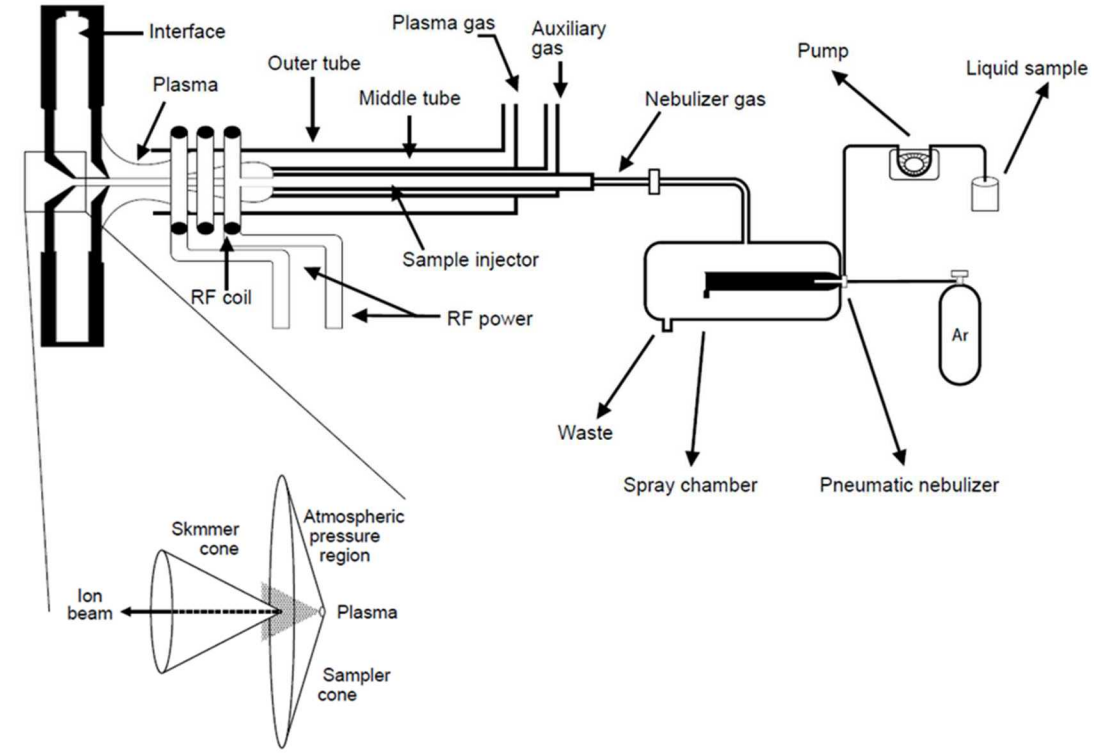


**Figure 3: Inductively coupled plasma (ICP) ionization source schematic. Note that the components are not scaled in relation to each other.**

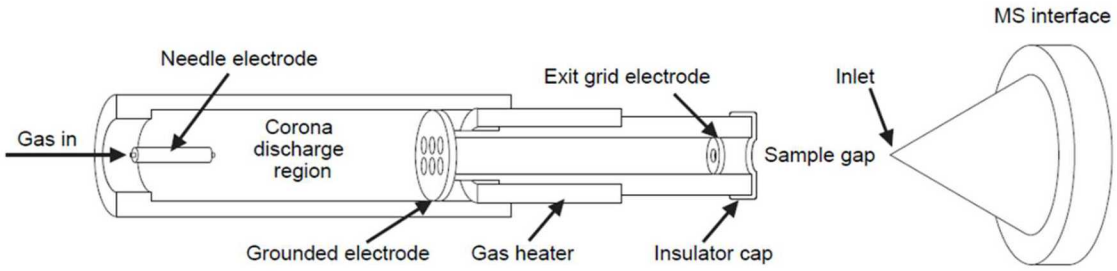


**Figure 4: Direct analysis in real time (DART) ionization source schematic.**

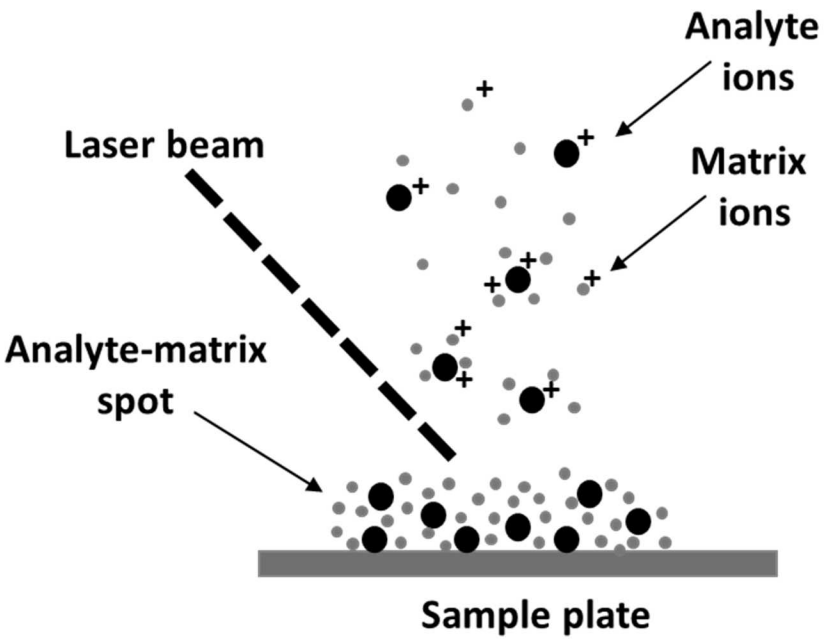


**Figure 5: Matrix-assisted laser desorption ionization (MALDI) schematic.**

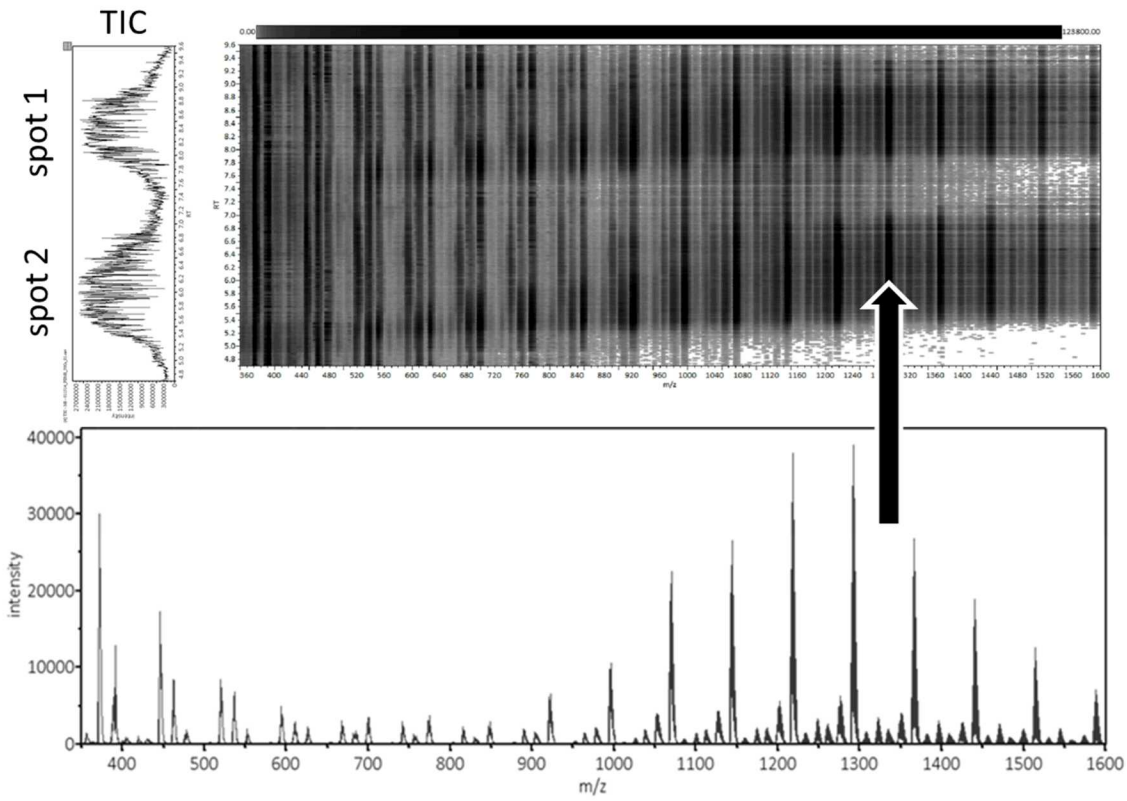


**Figure 6: Total ion chromatogram (TIC), heatmap, and sample spectra of TMS-PDMS (50cS) mold release formula on a glass slide.**

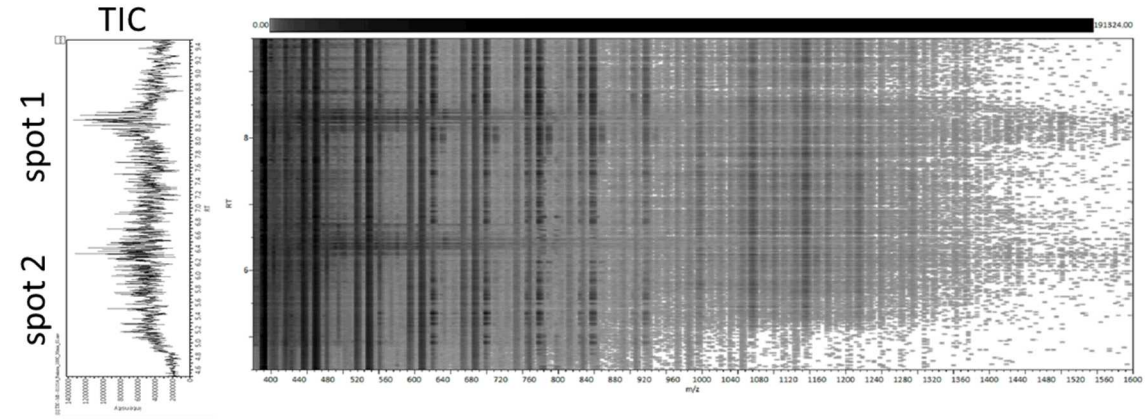


**Figure 7: Total ion chromatogram and heatmap of heat treated TMS-PDMS mold release formula on a glass slide.**

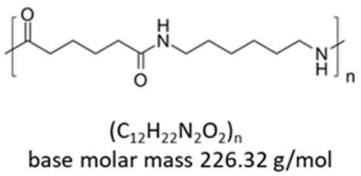


**Figure 8: Nylon 6,6.**

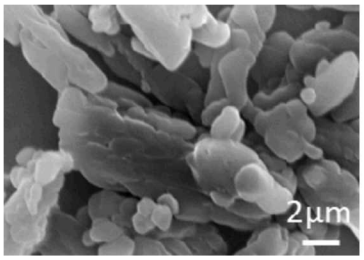


**Figure 9: Matrix crystals form on microcalorimetry device.**

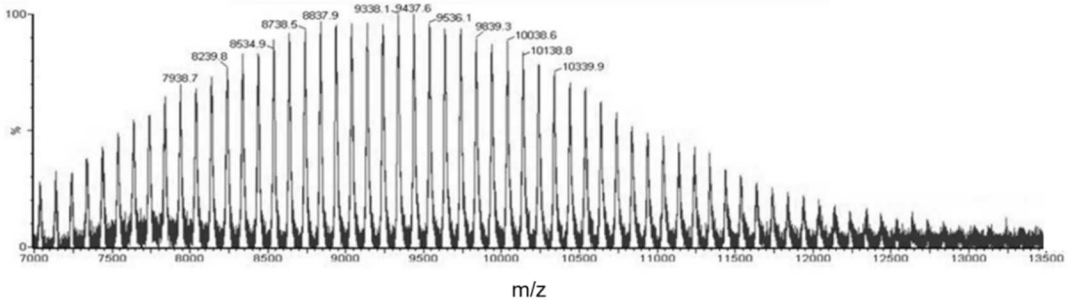


**Figure 60: MALDI MS spectrum of PMMA calibration standard on uncoated microcalorimetry device.**

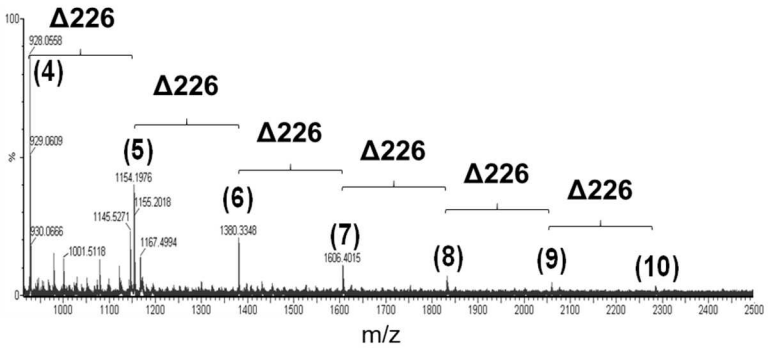


**Figure 71: MALDI MS spectrum of nylon 6,6 coated microcalorimetry device.**