CHAPTER 4

Mass Spectrometry

4.1 Introduction and History

The earliest forms of mass spectrometry go back to the observation of canal rays by Goldstein in 1886 and again by Wien in 1899. Thompson's later discovery of the electron also used one of the simplest mass spectrometers to bend the path of the cathode rays (electrons) and determine their charge to mass ratio. Later, in 1928, the first isotopic measurements were made by Aston. These basic experiments and instruments were presented to most readers in first-year general chemistry. More modern aspects of mass spectrometry are attributed to Arthur Jeffrey Dempster and F.W. Aston in 1918 and 1919. Since this time there has been a flurry of activity [not only concerning minor advances in components of mass spectrometers such as different types of instrument interfaces (direct injection, GC, and HPLC) to different ionization sources (electron and chemical ionization) but also new types of ion separators. For example, double focusing magnetic sector mass filters were developed by Mattauch and Herzog in 1934 (and recently revised into a new type of mass filter), time of flight MS by Stephens in 1946, ion cyclotron resonance MS by Hipple and Thomas in 1949, quadrupole MS by Steinwedel in 1953, and ion trap MS by Paul and Dehmelt in the 1960s. Mass spectrometry was coupled with ICP as a means of sample introduction in 1980. Although not specific to ICP, even as recent as 1985, Hillenkamp and Michael Karas developed the MALDI technique (a laser-based sample introduction device) that radically advanced the analysis of protein structures and more types of mass analyzers will certainly be developed. Ion mobility spectrometers capabilities have recently advanced and are the basis of luggage scanning at air ports. This chapter will deal only with basic mass spectrometer instruments used in the analysis of atomic cations.

4.2 Components of a Mass Spectrometer

4.2.1 Overview:

The sample introduction systems (automatic sampler to torch) are almost identical on optical and mass spectrometry ICP units (Section 3.3.2). While the ICP-AES is interfaced with an optical grating system, the plasma in an ICP-MS instrument must enter into a vacuum so that atomic cations can be separated by a mass filter. The common components of a modern ICP-MS are shown in Figure 4.1 (the sampling interface is not shown). The torch and the plasma were discussed in Section 3.3.3 (Animations 3.1 and 3.2). For MS systems, the detector is axially aligned with the plasma to follow the flow trajectory of the argon. After the analytes are ionized in the plasma at atmospheric pressures, they must enter into a low pressure system before they can be accelerated and separated by mass to charge (m/z) ratios. This pressure difference is accomplished with a series of cones between the plasma and the mass analyzer. The first cone, the sample cone, is a protruding cone, usually made of Ni, that has a small hole (1.0 mm in diameter) at its tip to allow the cations and Ar to pass. The next chamber interface contains another cone (the skimmer cone) with an even smaller diameter hole (equal to or less than 0.1 mm in diameter) that allows less sample to enter into the low vacuum chamber (~10^{-5} torr which is about 10^{-8} atm). The smaller hole in the skimmer cone helps maintain a lower vacuum in the mass filter chamber. As the cations enter this second chamber, they are exposed to accelerating lens (negatively charged plates) that place a fairly uniform amount of kinetic energy on the cations. Then the neutral particles and photons are filtered out by a second type of lens (Section 4.2.4). The specific design of the lens varies among different manufactures despite the fact that they accomplish the same goals. Most higher-end systems have a reaction cell placed just before the mass filter. This cell removes polyatomic interferences (that have the same mass as the analyte of interest) by gas phase chemical reactions (Section 4.2.5). Then, the cations enter into the mass filter that

separates the different atoms with respect to their mass to charge ratio (m/z) before they eventually enter into a detector. Mass analyzers that have higher than unit resolution, such as a double-focusing mass filter, bypass the reaction cell since polyatomic interferences have different masses at three or four significant figures. Given the large amount of data and the extremely short scan times of the MS, computer operation and computer enhanced data collection are required. The most variation between various ICP-MS manufactures is the presence or absence of a reaction cell and the type of mass filter.

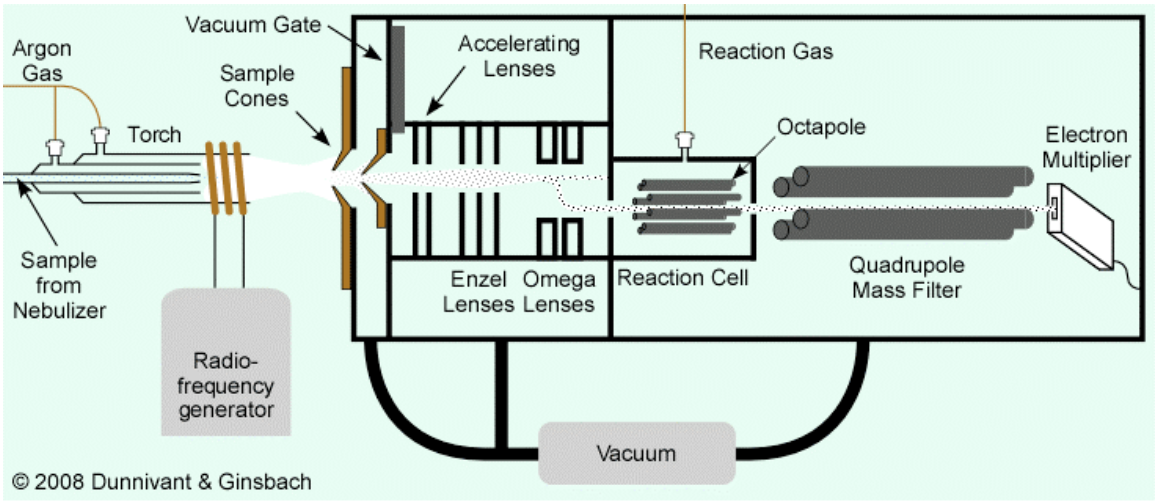


Figure 4-1. A Common ICP-MS with a Quadrupole Mass Filter.

4.2.2 Sample Introduction

The most common sample introduction system for an ICP-MS is made up of a nebulizer and spray chamber like an ICP-AES system (Section 3.3.2). While the majority of applications use this setup, there are some specialized applications that allow solid samples to be analyzed. Solid samples can be placed directly into the ICP with a graphite rod that contains a small quantity of sample (Section 3.3.2). Other sample introduction procedures cause solid samples to sublimate before they enter the plasma. One common form of sample introduction not presented here is the glow discharge system that is used heavily by the semiconductor and metallurgy industries.

Another solid introduction technique is laser ablation which is becoming more common especially for geological and materials science applications. In laser ablation, the automatic sampler and peristaltic pump for liquid samples are replaced with the working components of the laser ablation system. This consists of a small chamber to hold the solid sample on a movable stage, a laser to ablate (heat and vaporize the solid), a viewing window or CCD camera to align the laser to a specific spot on the sample, and an argon gas stream to purge the ablation chamber and rapidly transport the vaporized sample to the inlet of the plasma. The laser is focused on a 10- to 25-μm section of the sample and a pulse of energy from the laser vaporizes the sample. The sample is transported to the plasma as a short pulse of vapor that is atomized and ionized in the plasma, and the generated cations are analyzed by the MS unit. Given the relatively small sampling area of the laser, numerous analyses can be conducted for a given sample and an average of analyte concentrations are determined. Common laser types include Nd-YAG, ruby, CO_2, and N_2. The only requirement of the laser is that it has sufficient power to ablate and vaporize refractory (high bond energy) sample matrixes. Obviously one of the quantitative limitations of the laser ablation technique is obtaining reference standards. While solid reference standards can be relatively easily made and obtained, it is almost impossible to match the matrix of all samples. Detection limits for this technique are in the range of 0.1 to 10 ppm which is much higher (poorer) than aqueous sample detection limits in an ICP-MS. As a result of the difficulties encountered with instrument calibration, qualitative analysis is commonly performed.

4.2.3 Mass Analyzer Interface:

Sample cations enter into the mass filter from the plasma through a series of nickel or platinum cones that contain a small hole (from 1.0 mm to less than 0.1 mm) in the center. These cones are necessary to achieve the pressure drop that is required for the mass analyzer. The low pressure of the system, 10^{-5} torr,

minimizes the collision of the chemically reactive analyte cations with ambient gases. Thus, maintaining a confined beam of ions. A photograph of a cone is shown in Figure 4-2. Cones are one of the most maintenance intensive components of an ICP-MS since they require frequent cleaning, but the cleaning process is easy and relatively fast. After cleaning, cones must be conditioned prior to use by exposing the clean cones to a mid- to high-range reference standard via the plasma for 20 to 30 minutes. This conditioning process will avoid analyte loss on the cone and memory effects (the persistent present of an analyte in a blank run typically occurring after a high concentration standard or sample has been analyzed).

Figure 4-2. Photograph of a Sampler (the larger one) and a Skimmer Cone for ICP-MS.

The low pressure in the spectrometer chamber is maintained with two vacuum pumps. First, an external rotary vacuum pump is used to remove gas molecules down to a pressure of 10^{-1} to 10^{-4} torr; a rotary vacuum pump is a positive-displacement pump that consists of vanes mounted to a spinning rotor. After a sufficient vacuum has been reached, a turbo molecular pump takes the vacuum down to 10^{-5} to 10^{-6} torr. A molecular pump operates by using high speed (90 000 rpms) rotating blades to literally knock gaseous molecules out of the chamber. The low vacuum pressures are needed to minimize secondary collisions between analyte cations and ambient atmospheric molecules that would deflect the cations path away from the mass filter and detector and interfere with the desired trajectory in the mass filter.

4.2.4 Lenses

After entering into the evacuated region, a number of lenses are used to manipulate the path of the ions flowing from the plasma. First and foremost are the accelerator lenses. An accelerator lens consists of two to three plates with a relatively large hole in them (typically larger than the hole in the cones). Each plate has an increasingly negative charge placed across them that result in the attraction of the cations towards the plate increasing their kinetic energy. The hole in the center allows most of the cations to pass directly through the plate. The imposed kinetic energy is needed to pass the cations through the subsequent reaction cell, mass filter, and on to the detector with sufficient energy to dislodge electrons on the surface of the detector (an electron multiplier device).

The next type of lens used in the MS is a focusing lens that centers the cations into a small beam. This lens is used to focus ions into the center of the reaction cell (if present) and the mass filter. One such electrical lens is the Einzel lens that is analogous to a focusing lens in an optical spectrophotometer. An Einzel lens contains six parallel plates, three on each side of a rectangular box, that are exposed to various electric potentials (Figure 4-3). These potentials create an electrical field that bends the cations near the outside of the plates toward the focal point. The lens stretches the length of a given beam of ions since ions on the outside (near the plates) have to travel a longer distance to reach the focal point.

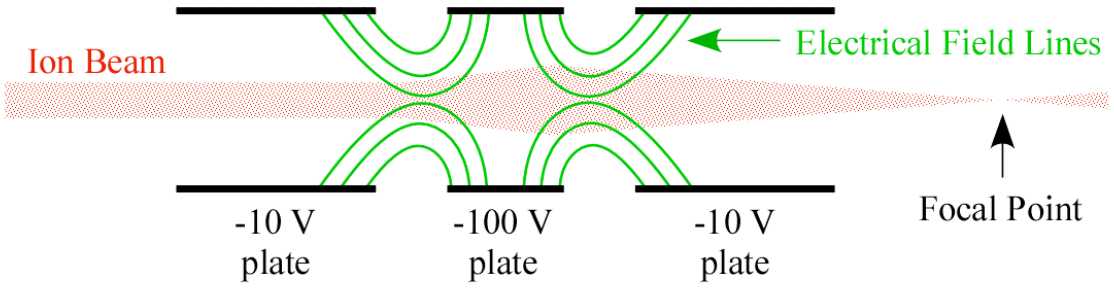


Figure 4-3. Diagram of an Einzel Lens used to focus a beam of ionic particles.

The final class of lenses removes neutral (elemental) atoms and photons that enter through the cones. Both photons and neutrals would be detected by the universal detector (an electron multiplier) and would give false signals and increase the instrumental noise if they are not filtered. Besides causing increased noise, neutrals passing through the mass filter can become adsorbed onto metal components that can interfere with their proper function. There are two major types of lenses that remove neutral particles and photons; a Bessel box and Omega lens. A Bessel box, also referred to as a photon stop, is comprised of two photon stops, an Einzel lens, and a set of three lenses that comprise the Bessel box (Figure 4-4). The first photon stop (located before the Einzel lense) prevents particles from flowing directly down the evacuated chamber. The Einzel lens focuses the particles into the Bessel box and around the second photon stop. The positive voltage (+4 V) on the outside of the Bessel box and the negative voltage on the second photon stop (-9 V) direct the cations back to the exit slit. Neutral particles and photons are unaffected by the electrical field and are removed.

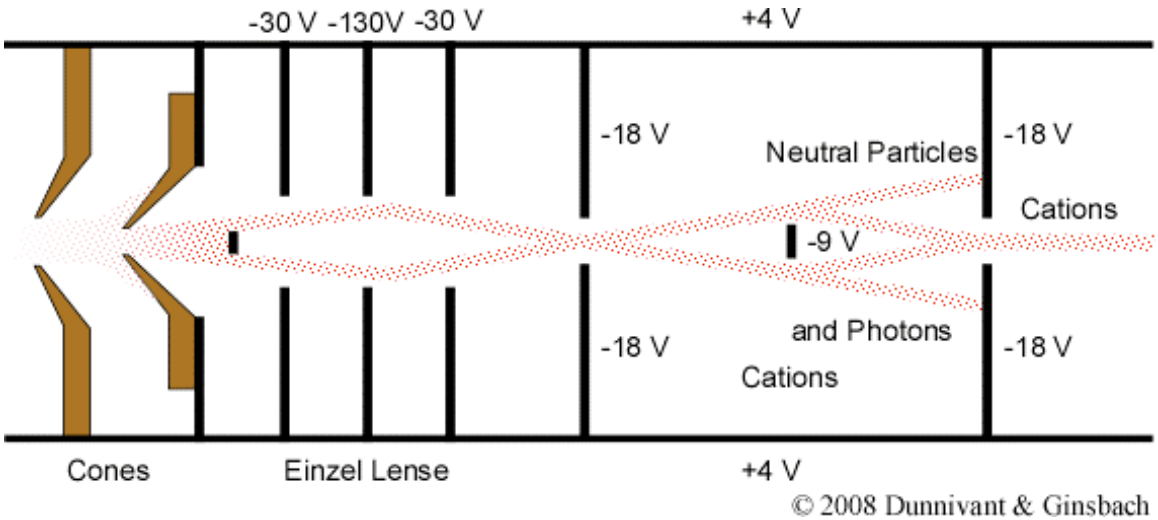


Figure 4-4. A Bessel Box photon stop.

Another type of lense, an Omega lens, filters out the photons and neutral particles. A cross-section of an Omega lens consists of four electrodes, two near

the top and two near the bottom of the ion beam is presented in Figure 4-5. The lens works by carefully balancing the charges of the electrodes to deflect the beam of cations, but not the neutral species or the photons from the plasma. This deflection is accomplished by placing a positive charge on the first top electrode and a negative charge on the first bottom electrode that acts to deflect the beam of cations downward in the front of the lens (refer to Figure 4-4). Next the beam needs to be stabilized with respect to the horizontal direction to guide the beam into the reaction cell or mass filter, so an opposite set of electrodes is present, one with a negative charge on the top and one with a positive charge on the bottom. The net result is the deflection of the cations towards the mass analyzer in the absence of particles and photons that continue straight and collide with the end plate. Both systems are subject to contamination and need to be maintained (usually every six months or so depending on use).

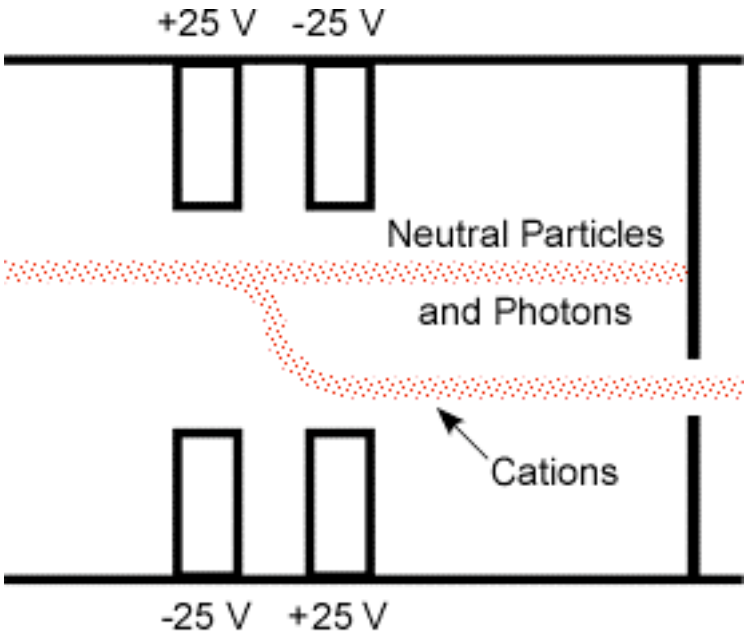


Figure 4-5. An Omega Lens.

4.2.5 Mass Interferences and Reaction Cells:

ICP-MS instruments separate and detect analytes based on the atoms mass to charge ratio. Since the plasma in an ICP system is adjusted to maximize singularly charged species, sample identity is directly related to atomic mass. While atomic emission spectrometry, ICP-AES, can be relatively free from spectral interferences (with monochromator systems that produce nm resolutions to three-decimal places), certain elements have problematic interferences in ICP-MS analysis due to the limited unit resolution (one amu) of most mass filters (especially the most common quadrupole mass filters). All ICP systems are subject to the nebulizer interferences given in the previous chapter. Spectral interferences are divided into three categories: isobaric, polyatomic, and doubly-charged species. Isobaric interferences occur in mass analyzers that only have unit resolution. For example, $^{40}Ar^{+}$ will interfere with $^{40}Ca^{+}$ and $^{114}Sn^{+}$ will interfere with $^{114}Cd^{+}$. High-resolution instruments will resolve more significant figures of the cation's mass and will easily distinguish between these elements. Polyatomic interferences result when molecular species form in the plasma that have the same mass as the analyte of interest. Their formation can be dependant on the presence of trace amounts of O_2 and N_2 in the Ar or sample, certain salts in the sample, and the energy of the plasma. For example, $^{40}Ca^{16}O^{+}$ can overlay with $^{56}Fe^{+}$, $^{40}Ar^{23}Na^{+}$ with $^{63}Cu^{+}$, and $^{80}Ar_2^{+}$ and $^{80}Ca_2^{+}$ with $^{80}Se^{+}$. The final type of interference occurs with doubly charged species. Since mass analyzers separate atoms based on their mass to charge ratio, $^{136}Ba^{2+}$ interferes with the quantification of $^{68}Zn^{+}$ since their mass to charge ratios are identical. The presence of any of these types of interferences will result in overestimation of the analyte concentration. Fortunately there are several ways of overcoming these interferences.

The easiest, but most expensive, way to overcome all three spectral interferences is to use a high-resolution mass analyzer, but, at a minimum, this can double to quadruple the cost of an analysis. Most inexpensive alternatives include the use of interference equations to estimate the concentration of the interfering element or polyatomic species, the use of a cool plasma technique to

minimize the formation of polyatomic interferences, and the use of collision and/or reaction cells prior to the entry to the mass filter. These three techniques will be discussed in detail below.

Interference Equations: Most elements are present on the Earth in their known solar abundance (the isotopic composition of each element that was created during the formation of our solar system). Important exceptions are elements in the uranium and thorium decay series, most notably lead. For these elements, the isotopic ratios are dependent upon the source of the sample. For example, lead isotope ratios found in the environment can be attributed to at least three possible sources: geologic lead, leaded gasoline, and mined lead shot from bullets.

Interference equations are mathematical relationships based on the known abundances of each element that are used to calculate the total concentration of all of the isotopes of a particular ion. Isobaric correction is relatively easy when two or more isotopes of each element (the analyte and the interfering isotope) are present in the solar abundance. There are two ways to correct for this type of interference: (1) the analyte of interest can be monitored at a different mass unit (different isotope), or (2) the interfering element can be quantified as a different isotope (mass unit) and the result can be subtracted from the analyte concentration. Polyatomic interferences can be corrected for in the same manner but to a less effective degree. This type of correction is illustrated in the following example taken from the ICP-MS primer from Agilent Technologies Company, a manufacturer of ICP-MS systems.

Example 4.1 Arsenic is an important and common pollutant in groundwater and an industrial and agricultural pollutant. The analyte of interest is ^{75}As but $^{40}Ar^{35}Cl$ has an identical mass on a low-resolution mass filter system, and since most water samples contain chloride, this interfering ion will be present in varying concentrations. These can be

corrected for by doing the following instrumental and mathematical analysis. Note that all analysis suggested below require external standard calibration or for the instrument to be operated in semi-quantitative mode (a way of estimating analyte concentrations based on the calibration of a different element or isotope).

1. Acquire data at masses 75, 77, 82, and 83.
2. Assume the signal at mass 83 is form ^{83}Kr and use this to estimate the signal from ^{82}Kr (based on solar abundances).
3. Subtract the estimated contribution from ^{82}Kr from the signal at 82. The residual value should be the counts per second for ^{82}Se.
4. Use the estimated ^{82}Se data to predict the size of the signal from ^{77}Se on mass 77 (again, based on solar abundances).
5. Subtract the estimated ^{77}Se contribution from the counts per second signal at mass 77. The residual value should be from $^{40}Ar^{37}Cl$.
6. Use the calculated $^{40}Ar^{37}Cl$ data to estimate the contribution on mass 75 from $^{40}Ar^{35}Cl$.
7. Subtract the estimated contribution from $^{40}Ar^{35}Cl$ on mass 75. The residual is ^{75}As.

This process may seem complicated but is necessary to obtain accurate concentration data for As in the absence of a high-resolution mass filter. It should also be noted that this type of analysis has limitations. (1) If another interference appears at any of the alternative mass units used, the process will not work. (2) If the intensity of interference is large, then a large error in the analyte concentration will result.

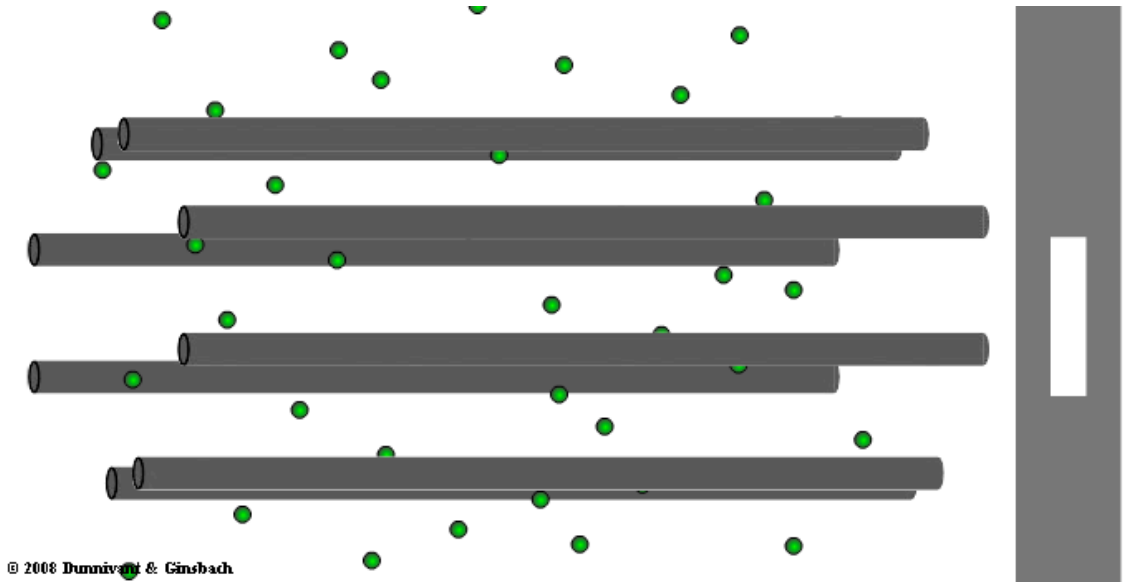
Cool Plasma Technique: The ionization of Ar-based polyatomic species in the normal “hot” plasma can be overcome by operating the radiofrequency at a

lower wattage (from 600 to 900 W) and therefore lowering the temperature of the plasma. This technique, a function on all modern ICP-MS systems, allows for the removal of polyatomic interferences in the analysis of K, Ca, and Fe. One downside is the tendency to form more matrix induced oxide cations.

Collision/Reactor Cells: The limitations of the two techniques described above, and the price of high-resolution mass spectrometry, led to the development of collision and reaction cells in the late 1990s and early 21th century to remove these interferences. Numerous Ph.D. dissertations, as well as research and development programs in industry, are active in this area and there are books specifically devoted to this topic. Two basic types of approaches have been used, (1) a collision cell that uses He to select for an optimum kinetic energy by slowing interfering ions relative to the analyte and only allowing the passage of the higher energy analyte and (2) reaction cells that promote reactions between a reagent gas and the interferences in order to remove them from detection.

The actual collision/reaction cell is a quadru-, hexa- or octa-pole that is considerable smaller than the subsequent quadrupole (mass filter) and is enclosed in a chamber that can contain higher pressures then the surrounding vacuum chamber. No mass separation occurs in the multi-pole since only a DC current is applied to the poles. Instead, the main purpose of the multi-pole is to keep the beam focused/contained to provide a space for the necessary collisions or chemical reactions to occur. While the number of poles in the reaction cell varies with different instruments, the larger number of poles allows for a more effective cell since the cross-sectional area of the ion beam is larger for an octa-pole over a hexa- or quadu-pole. The majority of collision/reaction cells can be operated in either mode by altering the gas utilized by the system. The price of the instruments increases slightly with the addition of these cells, however removing interferences with a collision cell is still less expensive than the alternative; a high-resolution mass filter.

Collision Cells: In a collision cell a non-reactive gas, usually He, is used to remove polyatomic ions that have the same mass to charge ratio as the analyte of interest. These multi-pole collisions cells are relatively small as compared to the mass filtering quadrupole and confine the ion beam from the plasma. Helium gas is added to the cell while the analyte of interest (an atomic species) and the interferent (a polyatomic species) move through the chamber. Polyatomic species are larger then atomic species and therefore collide with the He gas more often. The net result of these collisions is a greater reduction in the kinetic energy (measured in eVs) of the polyatomic species in relationship to the atomic species. As the polyatomic and analyte ions exit the collision cell, they are screened by a discriminator voltage. A discriminator voltage is the counterpart to an accelerating lens and contains a slit with a positive voltage; this process is commonly referred to as kinetic energy discrimination. When a positive voltage is applied to this gate, only cations possessing sufficient kinetic energy will pass through the slit. Smaller cations retaining more of their energy, after being subjected to the collisions with He, will pass through the slit while larger polyatomic cations that have been slowed by the He collisions will be repelled by the voltage. The polyatomic species that do not pass into the mass analyzer collide with the walls of the chamber, are neutralized and removed by the vacuum system. Common interferences that are removed in this manner are sample matrix-based interferences such as $^{35}Cl^{16}O^{+}$ from interfering with $^{51}V^{+}$, $^{40}Ar^{12}C^{+}$ from interfering with $^{52}Cr^{+}$, $^{23}Na^{40}Ar^{+}$ from interfering with $^{63}Cu^{+}$, $^{40}Ar^{35}Cl^{+}$ from interfering with $^{75}As^{+}$, and plasma-based interferences such as $^{40}Ar^{16}O^{+}$ and $^{40}Ar^{38}Ar^{+}$. Interfering polyatomic species can be reduced down to ppt levels through kinetic energy discrimination. An animation of a collision cell is shown in Animation 4.1.



Animation 4.1. A Collision Cell.

Reaction Cells: The physical structure and design of a collision cell, depending on the manufacturer, is similar or identical to that of a reaction cell. However, instead of utilizing an inert gas such as helium, more reactive gases are introduced into the cell. H_2 is the most common reactive gas but CH_4, O_2, and NH_3 are also used. Table 4.1 shows a variety of reaction gases and their intended use.

Table 4.1 Reagent Gases used in Collision and Reaction Cell ICP-MS Systems. (Source: Koppenaal, et al., 2004, *J. Anal. At. Spectrom.*, 19, 561-570)

Collision Gas	**Purpose**
He, Ar, Ne, Xe	Used as a collision gas to decrease the kinetic energy of the polyatomic interference
H_2, NH_3, Xe, CH_4, N_2	Used in charge exchange reactions
O_2, N_2O, NO, CO_2	Used to oxidize the interference or analyte

H_2, CO	Used to reduce the interference
CH_4, C_2H_6, C_2H_4, CH_3F, SF_6, CH_3OH	Used in adduction reactions to remove interferences

The purpose of the reactive gas is to break up or create chemical species, through a set of chemical reactions, and change their polyatomic masses to one that does not coincide with the mass of the analyte of interest. These cells have significantly extended the elemental range of ICP-MS to include some very important elements; the most important being $^{39}K^+$, $^{40}Ca^+$, and $^{56}Fe^+$ which had previously been difficult to measure due to the interferences of $^{38}Ar^1H^+$, $^{40}Ar^+$, and $^{40}Ar^{16}O^+$, respectively. The removal of interferences can be divided into three general categories: charge exchange, atom transfer, and adduct formation (i.e. condensation reactions).

A generic reaction for a charge transfer reaction would be

$$A^+ + B^+ + R \rightarrow A^+ + B + R^+$$

where A^+ is the analyte, B^+ is the isobaric interferent, and R is the reagent gas. An example of a charge exchange reaction is removal of the cationic Ar dimer in the analysis of selenium.

$$^{80}Se^+ + {}^{80}Ar_2{}^+ + H_2 \rightarrow {}^{80}Se^+ + {}^{40}Ar^{40}Ar + H_2{}^+$$

The neutral Ar dimer is now removed by the photon stop and vacuum and $^{80}Se^+$ is easily transported through the mass filter. Another specific case would be the interference of $^{40}Ar^+$ with the measurement of $^{40}Ca^+$. The reaction is

$$^{40}Ca^+ + {}^{40}Ar^+ + H_2 \rightarrow {}^{40}Ca^+ + {}^{40}Ar + H_2{}^+$$

In this reaction, the interfering cationic species is neutralized and removed by the vacuum and does not enter the MS. It should be noted that in charge exchange reactions, the ionization potential of the reagent gas must lie between the ionization potentials of the interfering ion and the analytes in order to promote charge transfer from the interfering ion instead of the analyte. Such a requirement is not necessary for atom transfer and adduction formation/condensation reactions. Two such reactions follow.

Atom Addition Reaction

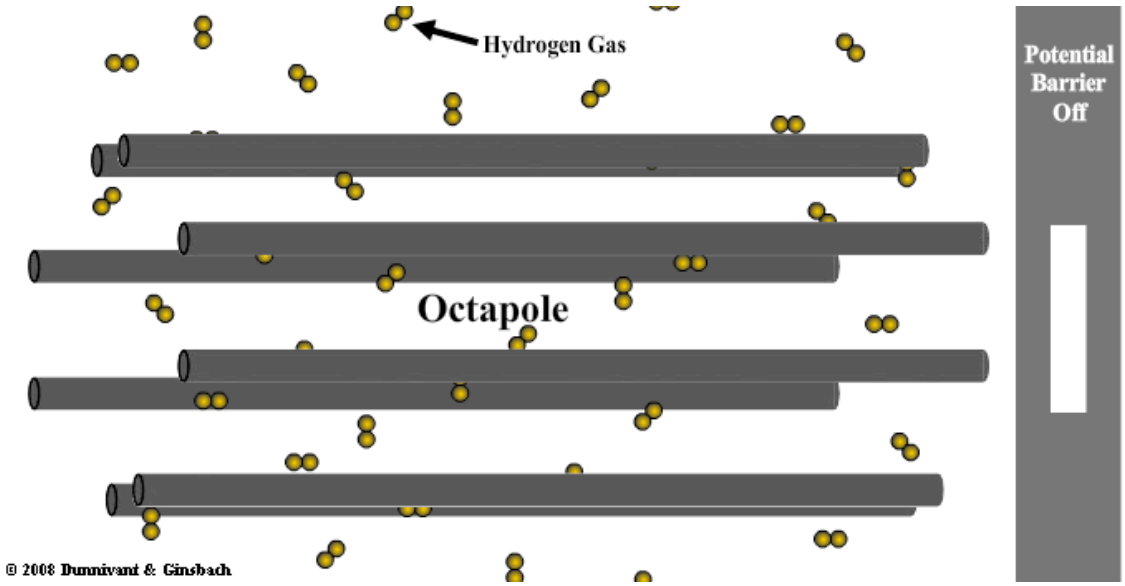
$$A^+ + B^+ + R \rightarrow AR^+ + B$$

$$Fe^+ + ArO^+ + N_2O \rightarrow FeO^+ + ArO^+ + N_2$$

In this case the interference of ArO^+ with the measurement of Fe is removed by oxidizing the Fe to its oxide that has a different mass from the argon oxide and quantifying Fe as FeO^+.. Another example is given below for the removal of ^{90}Zr interference in the detection of ^{90}Sr.

$$^{90}Sr^+ + {}^{90}Zr^+ + 1/2O_2 \rightarrow {}^{90}Sr^+ + {}^{90}ZrO^+$$

These chemical reactions in the cell create cations that can potentially interfere with other analytes, hence it is not uncommon for these problematic analytes to be measured singularly (no multi-elemental analysis). As a result, the reaction cell mode is frequently utilized for singular applications or for argon interferences (ex. $^{40}Ar^+$ and $^{40}Ar\,^{16}O^+$) with hydrogen since the products of the reaction do not interfere with other analytes of interest. If possible, operating the collision/reaction cell in the collision mode is preferable since the interferences are removed from the system. After the spectral interferences have been removed by either process, the ion beam is separated by mass to charge ratio with the mass filter. An animation of a typical reaction occurring in a reaction cell with H_2 is shown in Animation 4.2.



Animation 4.2. Reaction Cell.

4.2.6 Mass Filters (Mass Analyzers)

Mass analyzers separate the cations based on ion velocity, mass, or mass to charge ratio. A number of mass filters/analyzers are available. These can be used individually or coupled in a series of mass analyzers to improve mass resolution and provide more conclusive analyte identification. This text will only discuss the most commonly available ones for ICP systems.

The measure of "power" of a mass analyzer is resolution, the ratio of the average mass (m) of the two adjacent ion peaks being separated to the mass difference (Δm) of the adjacent peaks, represented by

$$R_s = m/\Delta m$$

Resolution (R_S) is achieved when the midpoint between two adjacent peaks is within 10 percent of the baseline just before and after the peaks of interest (the valley between the two peaks). Resolution requirements can range from high-resolution instruments that may require discrimination of a few ten thousands

(1/10 000) of a gram molecular weight (0.0002) to low-resolution instruments that only require unit resolution (28 versus 29 atomic mass units; amu). Resolution values for commonly available instruments can range from 250 to 500 000.

Before introducing the various types of mass analyzers, remember our current location of the mass analyzer in the overall ICP-MS system. The sample has been introduced to the nebulizer, atomized and ionized by the plasma, accelerated and manipulated by various lenses, sent through a collision/reaction cell, and finally enters the mass analyzer. Now the packet of cations need to be separated based on their momentum, kinetic energy, or mass-to-charge ratio (m/z). Often the terms mass filter and mass analyzer are used interchangeable, as is done in this Etextbook. But, first a controversy in the literature needed to be addressed with respect to how a mass filter actually separates ions.

Some resources state that all mass analyzers separate ions with respect to their mass to charge ratio while others are more specific and contend that only quadrupoles separate ions by mass to charge ratios. The disagreement in textbooks lies in what components of the MS are being discussed. If one is discussing the affect of the accelerator plates **and** the mass filter, then all mass filters separate based on mass to charge ratios. This occurs because the charge of an ion will be a factor that determines the velocity a particle of a given mass has after interacting with the accelerator plate in the electronic, magnetic sector, and time of flight mass analyzers. But after the ion has been accelerated, a magnetic section mass filter actually separates different ions based momentums and kinetic energies while the time of flight instrument separates different ions based on ion velocities (arrival times at the detector after traveling a fixed length). In the other case, no matter what the momentum or velocity of an ion, the quadrupole mass analyzer separates different ions based solely on mass to charge ratios (or the ability of the ion to establish a stable path in an oscillating electrical field). These differences may seem semantic but some users insist on

this clarification. For the discussions below, in most cases, mass to charge will be used for all mass analyzers.

4.2.6.1 *Magnetic sector mass filter:* It has been known for some time that the trajectory of point charge, in our case a positively charged ion, can be altered by an electrical or magnetic field. Thus, the first MS systems employed permanent magnets or electromagnets to bend the packets of ions in a semi-circular path and separated ions based on their momentum and kinetic energy. Common angles of deflection are 60, 90, and 180 degrees. The change in trajectory of the ions is caused by the external force of the magnetic field. The magnitude of the centripetal force, which is directly related to the ions velocity, resists the magnetic field's force. Since each mass to charge ratio has a distinct kinetic energy, a given magnetic field strength will separate individual mass to charge ratios through space. A slit is placed in front of the detector to aid in the selection of a single mass to charge ratio at a time.

A relatively simple mathematical description will allow for a better understanding of the magnetic field and the ions centripetal force. First, it is necessary to compute the kinetic energy (KE) of an ion with mass *m* possessing a charge *z* as it moves through the accelerator plates. This relationship can be described by

$$KE = \tfrac{1}{2}\, mv^2 = zeV$$

where e is the charge of an electron (1.60×10^{-19} C), v is the ion velocity, and V is the voltage between the two accelerator plates (shown in the Animation 1.5 below). Fortunately for the ionizations occurring in the plasma, most ions have a charge of +1. As a result, an ions' kinetic energy will be inversely proportional to its mass. The two forces that determine the ions path, the magnetic force (F_M) and the centripetal force (F_C), are described by

$$F_M = Bzev$$

and

$$F_C = (mv^2)/r$$

where B is the magnetic field strength and r is the radius of curvature of the magnetic path. In order for an ion of particular mass and charge to make it to the detector, the forces F_M and F_C must be equal. This obtains

$$BzeV = (mv^2)/r$$

which upon rearrangement yields

$$v = (Bzer)/m .$$

Substituting this last equation into our first KE equation yields

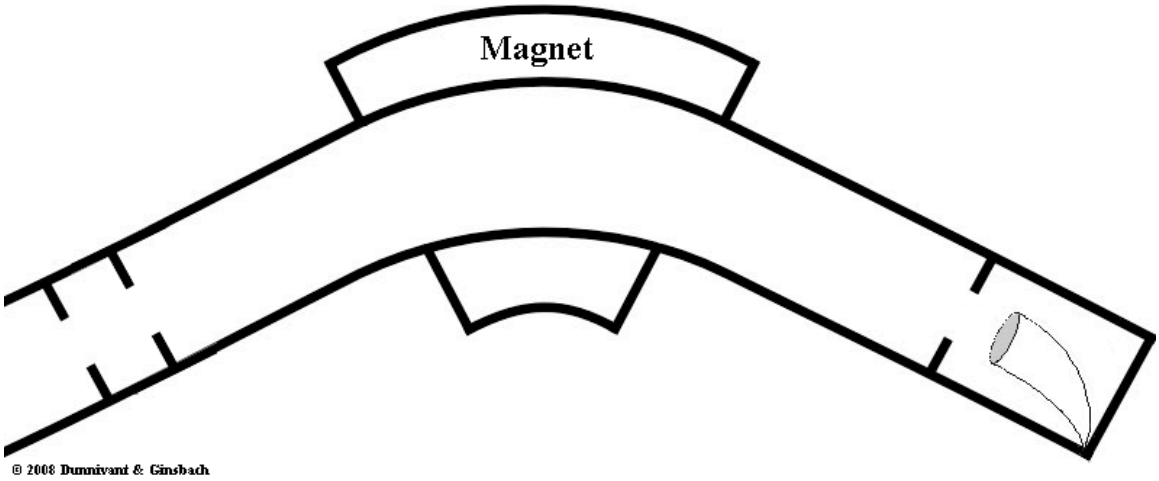
$$m/z = (B^2r^2e)/2V$$

Since e (the charge of an electron) is constant and r (the radius of curvature) is not altered during the run, altering the magnetic field (B) or the voltage between the accelerator plates (V) will vary the mass to charge ratio that can pass through the slit and reach the detector. By holding one constant and varying the other throughout the range of m/z values, the various mass to charge ratios can be separated. One option is to vary the magnetic field strength while keeping the voltage on the accelerator plates constant.

In general, it is difficult to quickly vary the magnetic field strength, and while this is problematic in chromatography it is of little consequence with ICP instruments. Generally, several complete mass to charge scans are desired for

accurate analyte identification and this can be completed ICP analysis by simply sampling longer. This entire problem can be overcome in modern magnetic sector instruments by rapidly sweeping the voltage between the accelerator plates, in order to impart different momentums on the ions, as opposed to sweeping the field strength. This second mass scanning technique holds the magnetic field constant while changing the centripetal force placed on the ions by varying the voltage on the accelerator plates. Due to the operational advantages of this technique, most electromagnets hold the magnetic field strength (B) and vary the voltage (V) on the accelerator plates.

The magnetic sector mass filter is illustrated in Animation 4.3 below. As noted above, although B and r are normally held constant, this modern design is difficult to animate, so we will illustrate a magnetic sector MS where B, the magnetic field, is varied to select for different ions. After ions pass the cones at the ICP MS interface, they are uniformly accelerated by the constant voltage between the two accelerator plates/slits on the left side of the figure. As the different ions travel through the electromagnet, the magnetic field is varied to select for different m/z ratios. Ions with the same momentum or kinetic energy (and therefore mass) pass through the exit slit together and are measured by the detector, followed by the next ion, and so on.



Animation 4.3. Illustration of a Magnetic Sector MS.

While magnetic sector mass filters were once the only tool used to create a mass spectrum, they are becoming less common today. This is due to the size of the instrument and its weight. As a result, many magnetic sector instruments have been replaced by quadrupole systems that are much smaller, lighter, and able to perform extremely fast scans. Magnetic sector instruments are still used in cases where extremely high-resolution is required such as with double-focusing instruments (discussed later in this section).

4.2.6.2 *Quadrupole mass filter:* Quadrupole mass filters have become the most common type of mass filters today due to their relatively small size, light weight, low cost, and rapid scan times (less than 100 ms). This type of mass filter is most commonly used in conjunction with ICP systems because they are able to operate at a relatively high pressure (5×10^{-5} torr) as compared to lower pressures required in other mass filters. The quadrupole has also gained widespread use in tandem MS applications (a series of MS analyzers).

Despite the fact that quadrupoles produce the majority of mass spectra today as mentioned earlier, they are not true mass spectrometers. Actual mass spectrometers produce a distribution of ions either through time (time of flight mass spectrometer) or space (magnetic sector mass spectrometer). The quadrupole's mass resolving properties are instead a result of the ion's stability within the oscillating electrical field.

A quadrupole system consists of four rods that are arranged at an equal distance from each other in a parallel manner. Paul and Steinwegen theorized in 1953 that hyperbolic cross-sections were necessary. In practice, it has been found that circular cross sections are both effective and easier to manufacture. Each rod is less than a cm in diameter and usually less then 15 cm long. Ions are accelerated by a negative voltage plate before they enter the quadrupole and

travel down the center of the rods (in the z direction). However, the ions' trajectory in the z direction is not altered by the quadrupole's electric field.

The various ions are separated by applying a time independent dc potential as well as a time dependent ac potential. The four rods are divided up into pairs where the diagonal rods have an identical potential. The positive dc potential is applied to the rods in the X-Z plane and the negative potential is applied to the rods in the Y-Z plane. The subsequent ac potential is applied to both pairs of rods but the potential on one pair is the opposite sign of the other or commonly referred to as being 180˚ out of phase (Figure 4-6).

Mathematically the potential that ions are subjected to are described by the following equations:

$$\Phi_{X\text{-}Z} = +(U + V\cos\omega t)$$

and

$$\Phi_{Y\text{-}Z} = -(U + V\cos\omega t)$$

where Φ is the potential applied to the X-Z and Y-Z rods respectively, ω is the angular frequency (in rad/s) and is equal to 2πv where v is the radio frequency of the field, U is the dc potential and V is the zero-to-peak amplitude of the radio frequency voltage (ac potential). The positive and negative signs in the two equations reflect the change in polarity of the opposing rods (electrodes). The values of U range from 500 to 2000 volts and V ranges from 0 to 3000 volts.

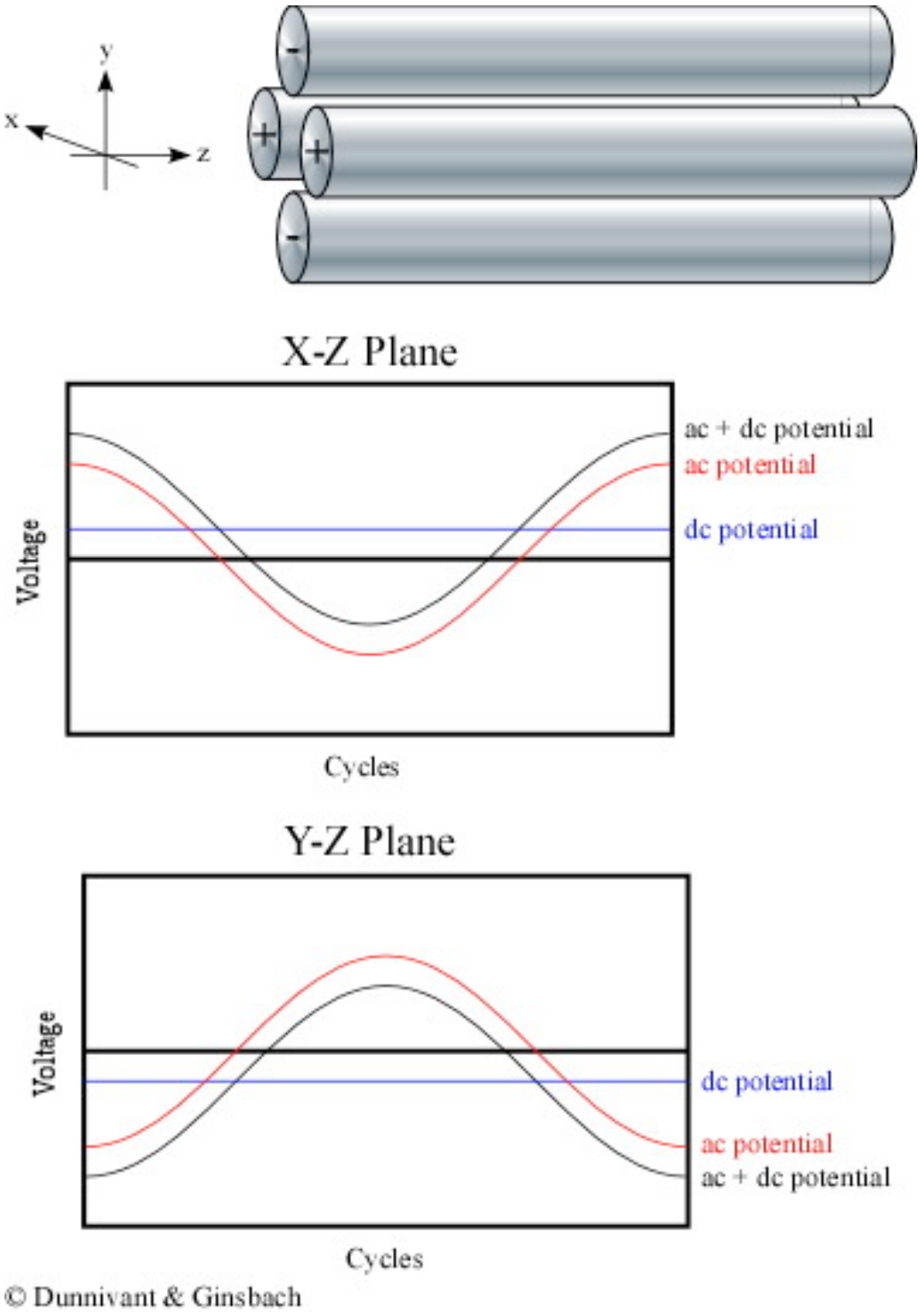


Figure 4-6. AC and DC Potentials in the Quadrupole MS.

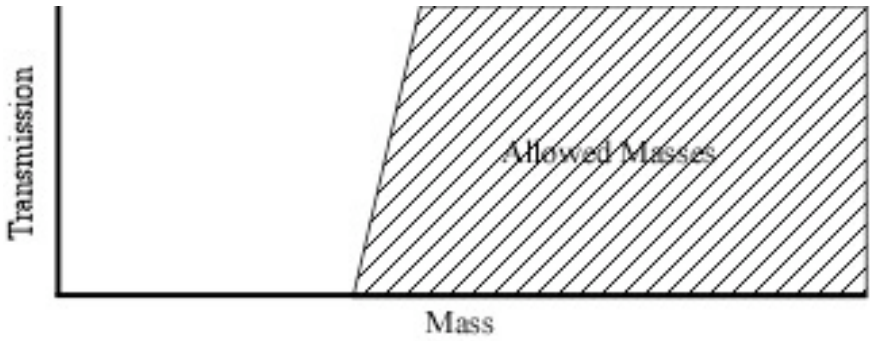
To understand the function of each pair, consider the rods in the X-Z plane in isolation. For now, imagine that only an ac potential is applied to the rods. Half the time when the potential was positive, ions (cations) would be repelled by the rod's charge and would consequently move towards the center of the rods. Likewise, when the potential was negative, ions would accelerate towards the rods in response to an attractive force. If during the negative ac potential, an ion comes into contact with the rod, it is neutralized and is removed by the vacuum. The factors that influence whether or not a particle strikes the rod during the negative cycle include the magnitude of the potential (its amplitude), the duration of time the ions are accelerated towards the rod (the frequency of the ac potential), the mass of the particular ion, the charge of the ion, and its position within the quadrupole.

Now imagine that a positive dc potential (at a fraction of the magnitude of the ac potential) is applied to the rod in the X-Z plane. This positive dc potential alone would focus all of the ions towards the center of the rod. When the ac and dc potentials are applied at the same time to the pair of rods in the X-Z plane, ions of different masses respond differently to the resulting potential. *Heavy ions are largely unaffected by the alternating current and as a result respond to the average potential of the rods. This results in heavy ions being focused towards the center of the rods. Light ions, on the other hand, will respond more readily to the alternating ac current. Ions that are sufficiently light will have an unstable trajectory in the X-Z plane and will not reach the detector. Only ions heaver than a selected mass will not be filtered by the X-Z electrodes. As a result, the X-Z plane electrodes only filter light ions and form a high pass mass filter* (Figure 4-7).

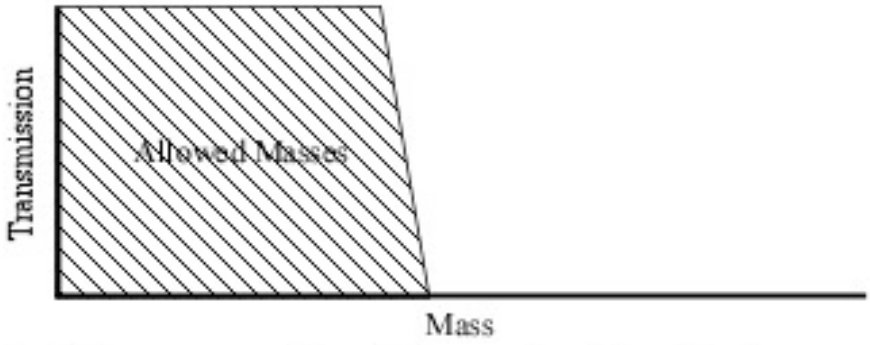
The rods in the Y-Z plane have a negative dc voltage and the ac potential is the same magnitude but the oppose sign as the potential applied to the X-Z plane. Heavy ions are still mostly affected by the dc potential, but since it is negative, they strike the electrode and are unable to reach the detector. The

lighter ions respond to the ac potential and are focused towards the center of the quadrupole. The ac potential can be thought of as correcting the trajectories of the lighter ions, preventing them from striking the electrodes in the Y-Z plane. These electrical parameters result in the construction of a low mass pass filter.

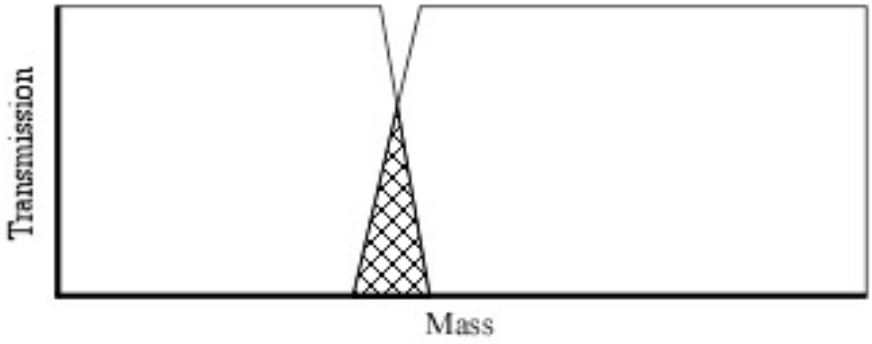
When both the electrodes are combined into the same system, they are able to selectively allow a single mass to charge ratio to have a stable trajectory through the quadrupole. *Altering the magnitude of the ac and dc potential changes the mass to charge ratio that has a stable trajectory resulting in the construction of mass spectra.* These ions possess a stable trajectory at different magnitudes and reach the detector at different times. The graph of the combined effect, shown in Figure 4-7c, is actually a simplification of the actual stability diagram.



a) The high pass mass filter in the X-Z plane allows heavy ions to be transmited through the quadrupole and reach the detector



b) The low pass mass filter in the Y-Z plane allows light ions to be transmited through the quadrupole and reach the detector



c) The combined effect of the dc and oscilating ac potential results in an area stability for a specific mass to charge ratio.

Figure 4-7. A “Conceptual” Stability Diagram

One way to generate an actual stability diagram is to perform a series of experiments where a single mass ion is introduced into the quadrupole. The dc

and ac voltages are allowed to vary and the stability of the ion is mapped. After performing a great number of experiments the resulting plot would look like Figure 4-8. The shaded area under the curve represents values of ac and dc voltages where the ion has a stable trajectory through the potential and would reach the detector. The white space outside the stability diagram indicates ac and dc voltages where the ion would not reach the detector.

While any ac and dc voltages that fall inside the stability diagram could be utilized, in practice, quadrupoles keep the ratio of the dc to ac potential constant, while the scan is performed by changing the magnitude of the ac and dc potential. The result of this is illustrated as the mass scan line intersecting the stability diagram in Figure 4-8. The graphs below the stability diagram correspond to specific points along the scan and help to illustrate the ions' trajectories in the X-Z and Y-Z plane (Figure 4-8). While the mass to charge ratio of the ion remains constant in each pair of horizontal figures, the magnitude of the applied voltages are changing while their ratio stays constant. As a result, examining points along the mass scan line in Figure 4-8 is equivalent to shifting the position of the high and low pass mass filters with respect to the x axis illustrated in Figure 4-7. Even though the mass is not changing for the stability diagram discussed here, the mass that has a stable trajectory is altered.

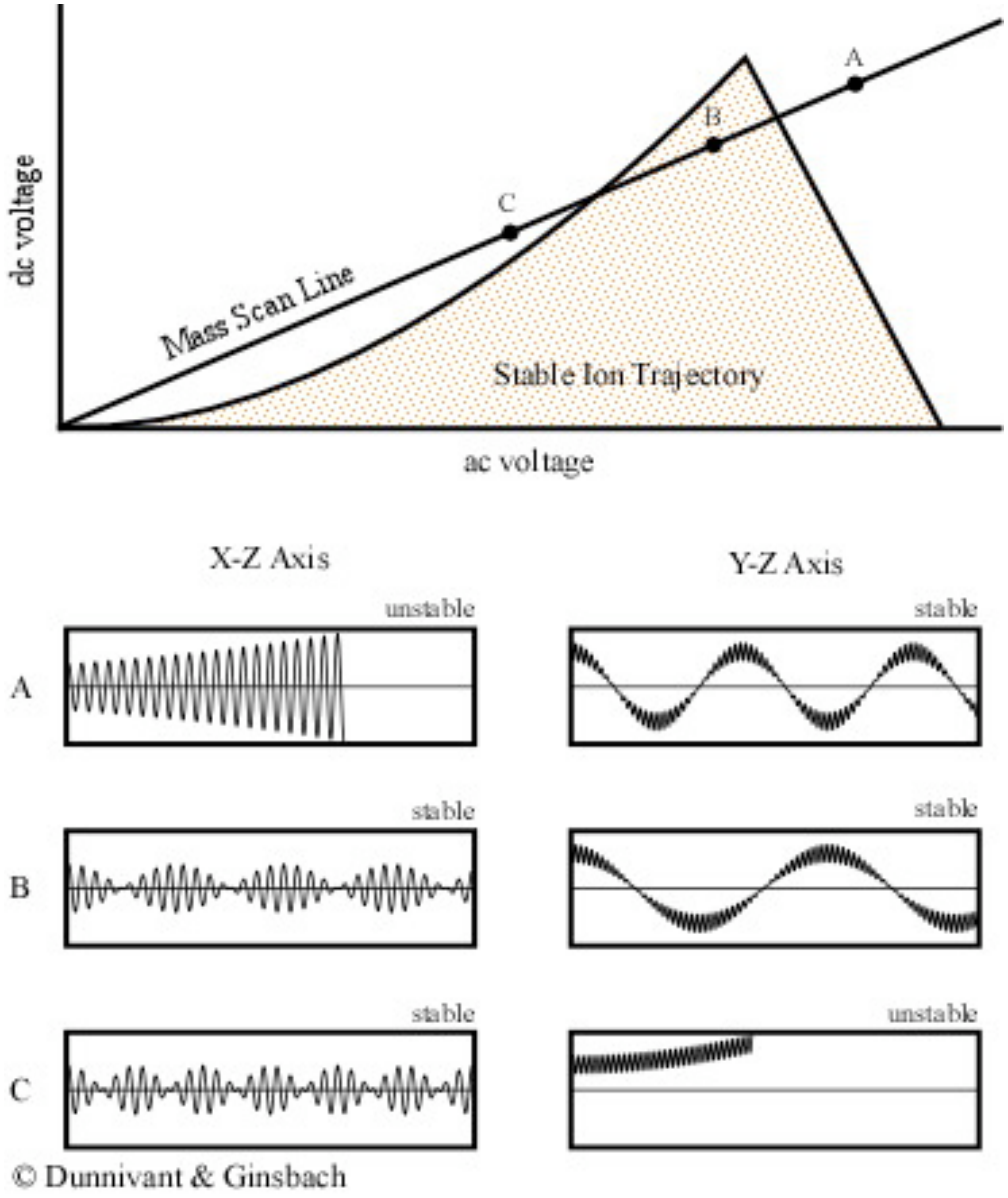


Figure 4-8. Stability Diagram for a Single Ion Mass. Used with permission from the Journal of Chemical Education, Vol. 75, No. 8, 1998, p. 1051; copyright © 1998, Division of Chemical Education, Inc.

In the above figure, the graph corresponding to point A indicates that the ion is too light to pass through the X-Z plane because of the high magnitude of the ac and dc potentials. As a result, its oscillation is unstable, and it eventually impacts the electrode. The motion of the Y axis is stable because the combination of the ac potential as well as the negative dc potential causes

destructive interference. This is the graphical representation of the ac potential correcting the trajectory of the light ions in the Y-Z plane. At point B the magnitude of voltages has been altered so the trajectories of the ion in both the X-Z and Y-Z plane are stable and the ion successfully reaches the detector. At point C, the ion has been eliminated by the low mass pass filter. In this case, the ac potential is too low to allow the ion to pass through the detector and it strikes the rod. This is caused by the ions increased response to the negative dc potential in the Y-Z plane. The trajectory in the X-Z axis is stable since the dc potential focusing the ion towards the center of the poles overwhelms the ac potential.

Until this point, the stability diagram shown above is only applicable to a single mass. If a similar experiment were to be performed using a different mass, the positions of the ac and dc potential on the x and y axes would be altered but the overall shape of the curve would remain the same. Fortunately, there is a less time consuming way to generate the general stability diagram for a quadrupole mass filter. This derivation requires a complex understanding of differential equations and is beyond the scope of an introductory text, but the solution can be explained graphically (Figure 4-9). The parameters in the axes are explained below the figure.

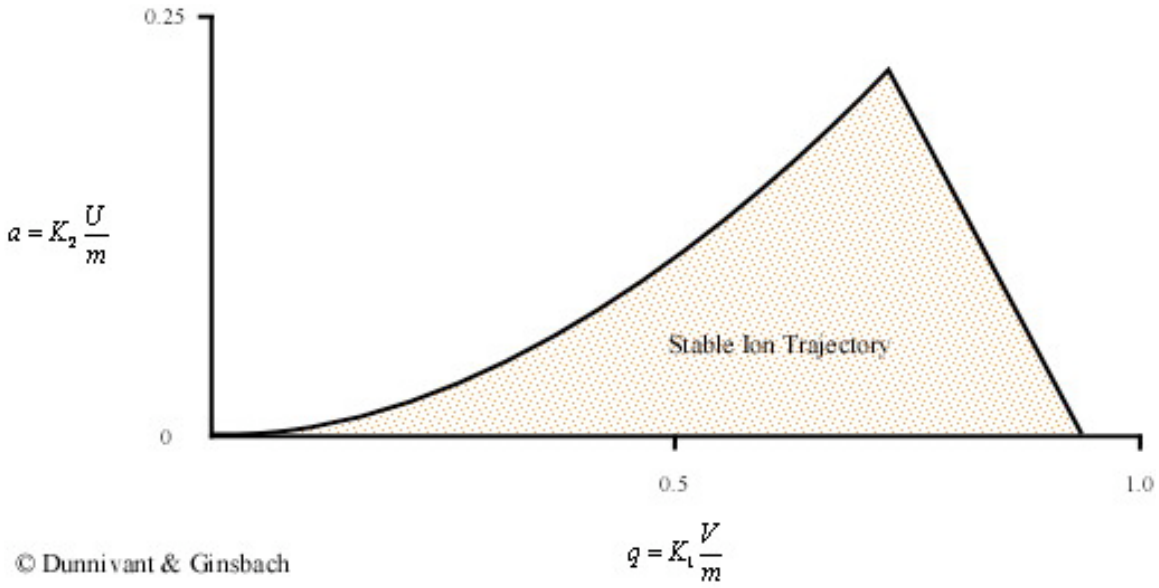


Figure 4-9. The General Stability Diagram

While this derivation is particularly complex, the physical interpretation of the result helps explain how a quadrupole is able to perform a scan. The final solution is dependent on six variables, but the simplified two-variable problem is shown in Figure 4-9. Utilizing the reduced parameters, a and q, the problem becomes a more manageable two-dimensional problem. While the complete derivation allows researchers to perform scans in multiple ways, this discussion will focus only on the basic mode that makes up the majority of mass spectrometers. For the majority of commercially available mass spectrometers, *the magnitude of the ac potential (V) and the dc potential (U) are the only parameters that are altered during run time*. The rest of the parameters that describe K_1 and K_2 are held constant. The values for K_1 and K_2 in the general stability diagram can be attributed to the following equations:

$$K_1 = \frac{2e}{r^2\omega^2}$$

$$K_2 = \frac{4e}{r^2\omega^2}$$

The parameters that make up K_1 and K_2 are exactly what we predicted when listing the variables earlier that would affect the point charge. Both K terms

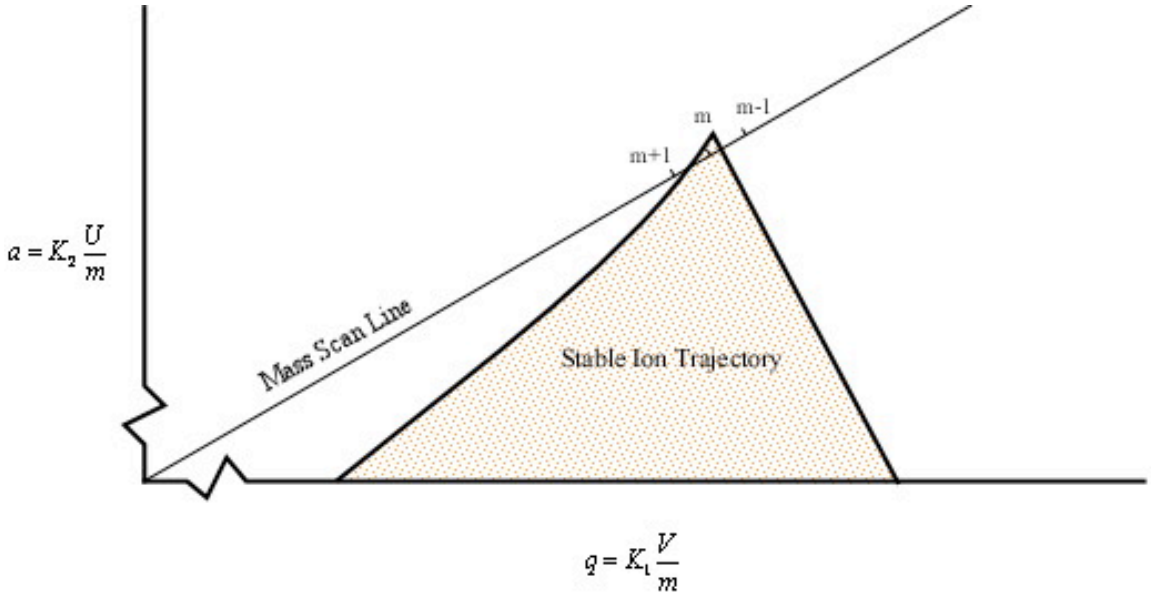
depend upon the charge of the ion *e*, its position within the quadrupole *r*, and the frequency of the ac oscillation *ω*. These parameters can be altered, but for the majority of applications remain constant. The charge of the ion (e) can be assumed to be equivalent to positive one, +1, for almost all cases. The distance from the center of the quadrupole (r) is carefully controlled by the manufacturing process and an electronic lens that focuses the ions into the center of the quadrupole and is also a constant. Also the angular frequency (ω) of the applied ac waveform can be assumed to be a constant for the purposes of most spectrometers and for this discussion.

The first important note for the general stability diagram is the relationship between potential and mass. The general stability diagram (Figure 4-8) is illustrated where there is an inverse relationship between the two. Figures 4-9 and 4-10 shows the lighter ions (m-1) are higher on the mass scan line and the heavy ions (m+1) are lower on the line. This is why in Figure 4-8 at point A, the molecule was too light for the selected frequencies, and it was too heavy at point C.

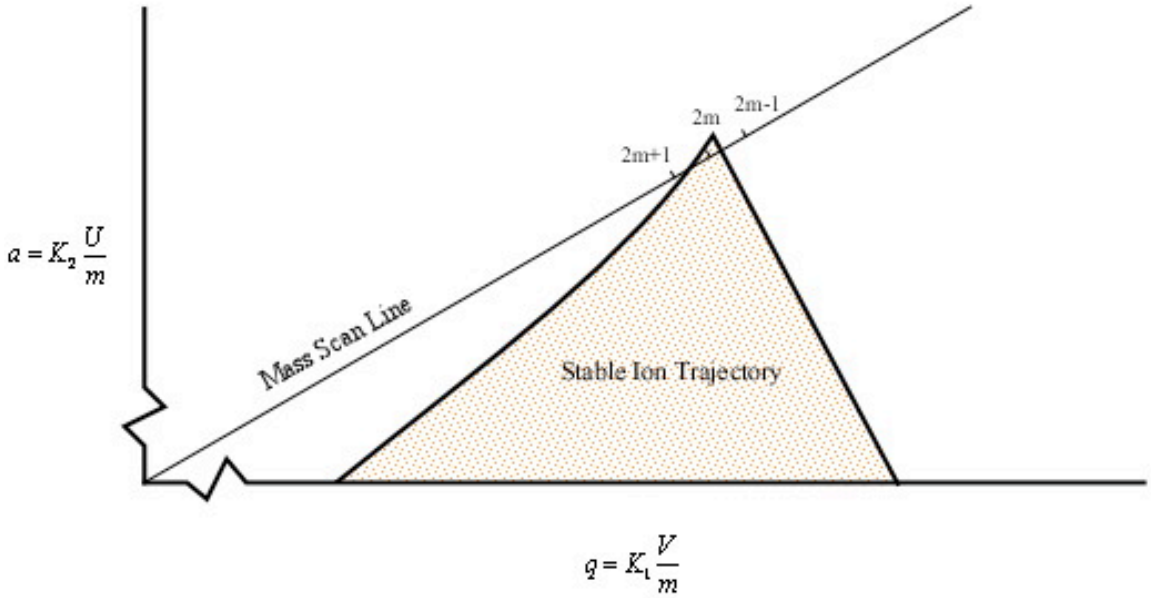
From the general stability diagram, it is also possible to explain how an instrument's resolution can be altered. The resolution is improved when the mass scan line intersects the smallest area at the top of the stability diagram (Figure 4-10). The resolution can be improved when the slope of the mass line is increased and the slope is directly related to the ratio of U and V. The resolution will subsequently increase until the line no longer intersects the stability diagram. While it would be best for the line to intersect at the apex of the stability diagram, this is impractical due to fluctuations in the ac (V) and dc (U) voltages. As a result, the line intersects a little below this point allowing the quadrupole to obtain unit resolution (plus or minus one amu).

Once the resolution has been determined, the ratio of the ac to dc potential is left unchanged throughout the scan process. To perform a scan, the

magnitude of the ac and dc voltages is altered while their ratio remains constant. This places a different mass inside the stability diagram. For example, if the ac and dc voltages are doubled, the mass to charge ratio of the selected ion would also be doubled as illustrated in the second part of Figure 4-10. By scanning throughout a voltage range, the quadrupole is able to create the majority of mass spectra produced in today's chemical laboratories.



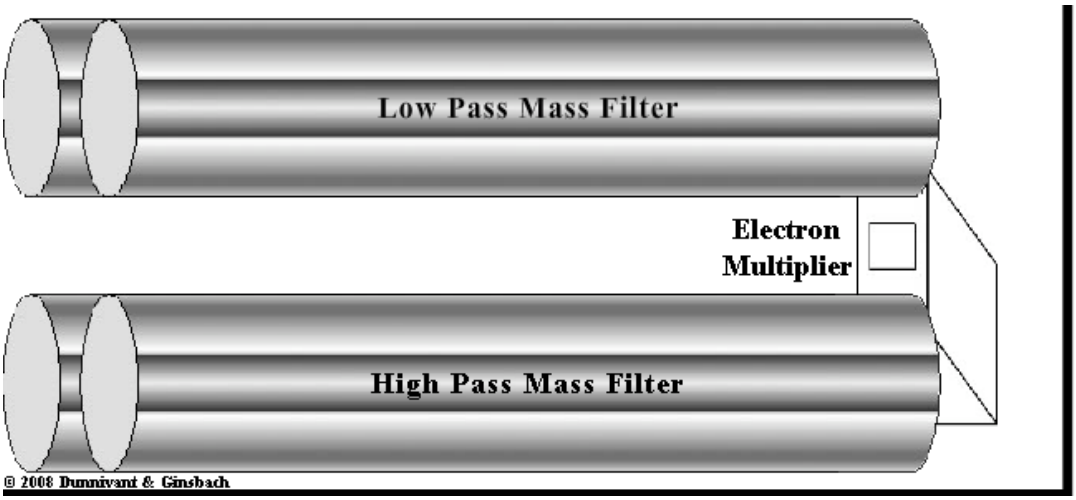
a) This stability diagram illustrates a single value for both U and V where only particles of mass m are allowed to reach the detector.



b) This stability diagram illustrates a single value for both U and V that is double the value of figure a). As a result, the particles corrisponding to a mass of 2m are able to reach the detector.

Figure 4.10 Quadrupole Mass Scan. Used with permission from the Journal of Chemical Education, Vol. 63, No. 7, 1998, p. 621; copyright © 1986, Division of Chemical Education, Inc.

View Animation 4-4 for an illustration of how the trajectory of ions of different masses are changed during a mass scan.



Animation 4.4 Illustration of Cations in a Quadrupole Mass Filter.

4.2.6.3 *Quadrupole ion trap mass filter:* While the operation of the ion trap was characterized shortly after the linear quadrupole in 1960 by Paul and Steinwedel, its application in the chemical laboratory was severely limited. This was due to difficulties associated with manufacturing a circular electrode and performance problems. These performance problems were overcome when a group at Finnigan MAT lead by Stafford discovered two breakthroughs that lead to the production of a commercially available ion trap mass filter. The first ion trap developed used a mode of operation where a single mass could be stored in the trap when previously all of the ions had to be stored. Their next important discovery was the ability for 1 mtorr of helium gas to improve the instruments resolution. The helium molecules' collisions with the ions reduced their kinetic energy and subsequently focused them towards the center of the trap.

After these initial hurdles were cleared, many new techniques were developed for a diverse set of applications especially in biochemistry. This is a result of its comparative advantage over the quadrupole when analyzing high molecular mass compounds (up to 70,000 m/z) to unit resolution in commonly

encountered instruments. The ion trap is also an extremely sensitive instrument that allows a molecular weight to be determined with a small number of molecules. The ion trap is also the only mass filter that can contain ions that need to be analyzed for any significant duration of time. This allows the instrument to be particularly useful in monitoring the kinetics of a given reaction. The most powerful application of the ion trap is its ability to be used in tandem mass spectrometry.

The ion trap is made up of a single ring electrode that is placed in the X-Y plane between two end cap electrodes (Figure 4-11). Both an ac and dc voltage can be applied to the ring electrode while only an ac voltage can be applied to the end cap electrodes. The two end cap electrodes and the ring electrode ideally have a hyperbolic shape to establish an ideal field however in practice, non-ideal fields can operate effectively. While the ion trap is applying force to the charged ions in three directions, the problem can be simplified into a two-dimensional problem. Since the ring is symmetrical, the force in any direction is always the same. As a result of this symmetry, movement of the molecules can be expressed in terms of r and z where $r = \sqrt{x^2 + y^2}$ where x and y are coordinates. For commercially available instruments, r_0 (the distance from the center of the trap to the ring electrode is either 1.00 or 0.707 cm.

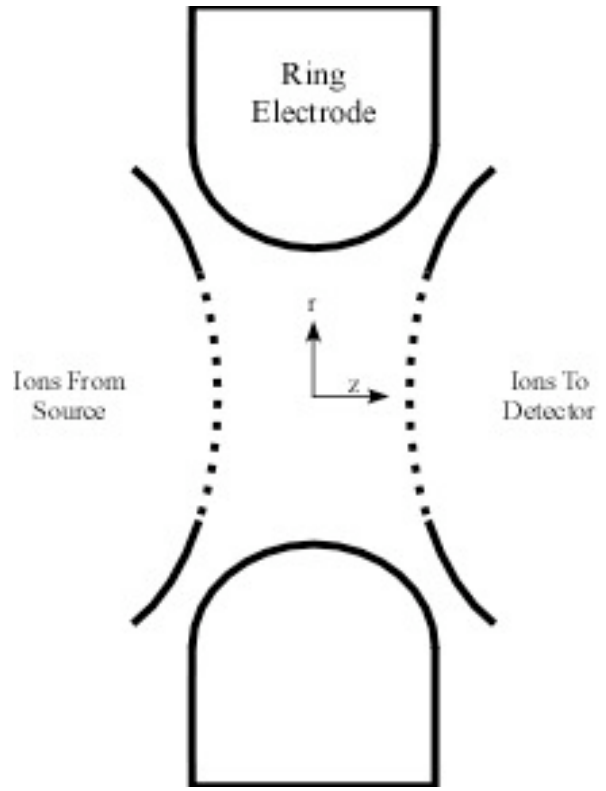


Figure 4-11. A Cross Section of the Ion Trap

After the sample molecules have been ionized by the ionzation source, they enter into the ion trap through an electric gate located on a single end cap electrode. This gate functions in the same fashion as the one that is utilized in time of flight (TOF) mass spectrometry (Section 4.2.6.4). The gate's purpose is to prevent a large number of molecules from entering into the trap. If too many sample molecules enter into the trap, the interaction with other molecules becomes significant resulting in space-charge effects, a distortion of the electrical field that minimizes the ion trap's performance. Once the ions enter the trap, their collisions with the helium gas focus the ions towards the center of the trap. An ac frequency is also applied to the ring electrode to assist in focusing the ions towards the center of the trap.

In the ion trap, the ring electrode oscillates with a very high frequency (typically 1.1 MHz) while both the end cap electrodes are kept at a ground potential (U equals 0 Volts). This frequency causes the ions to oscillate in both

the r and z direction (Figure 4-12). The oscillation in the r direction is an expected response to the force generated by the ring electrode. The oscillation in the z direction, on the other hand, may seem counter intuitive. This is a response to both the grounded end cap electrodes and the shape of the ring electrode. When the ac potential increases, the trajectory of the ion becomes unstable in the z direction. The theoretical basis for this motion will be discussed later. While it would be convenient to describe the ion trap's function as a point charge responding to an electrical field, the complexity of the generated field makes this impractical.

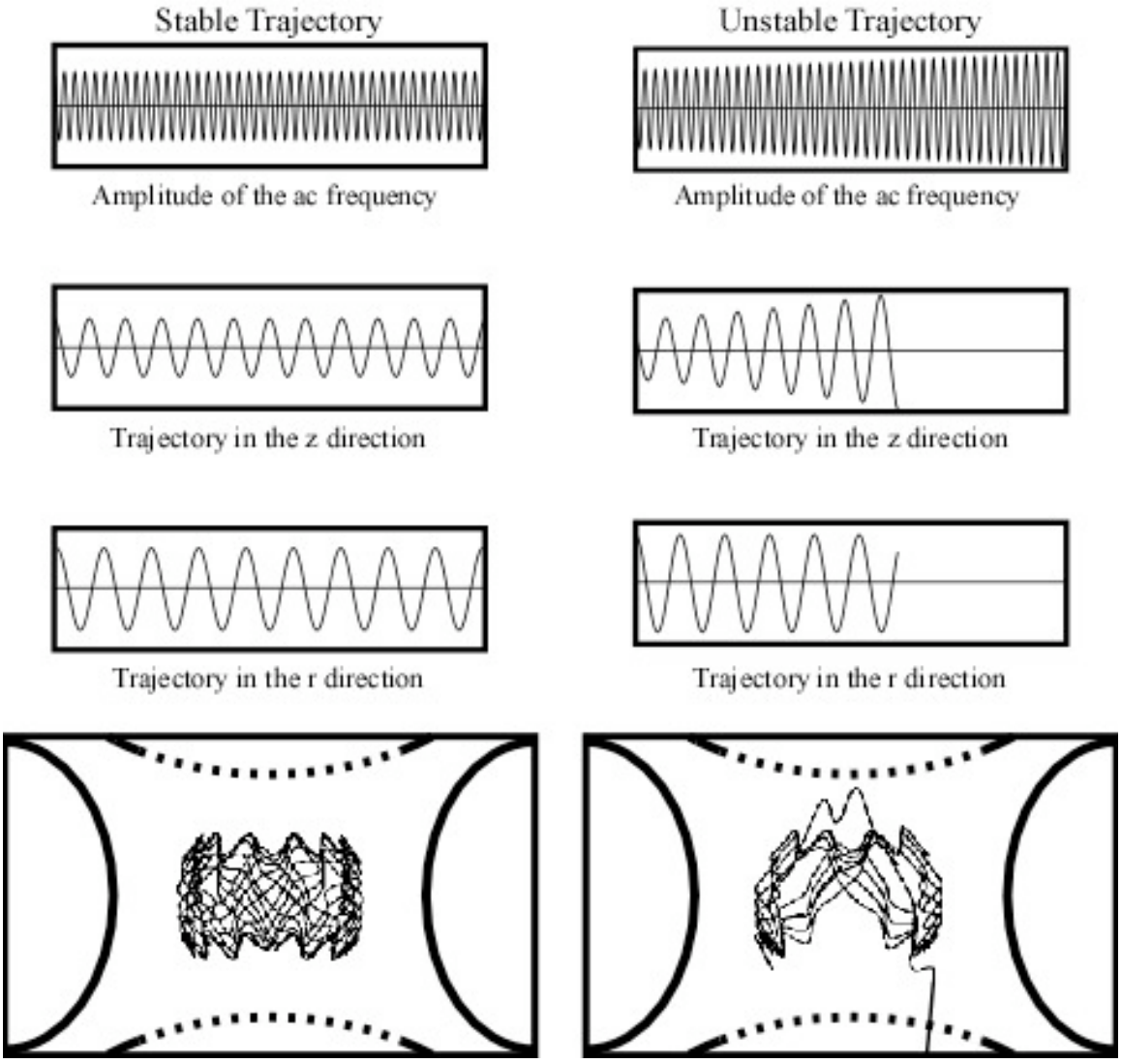


Figure 4-12 The Trajectories of a Single Mass Within the Electrical Field. Figure 6 from Wong and Cooks, 1997. Reprinted with permission of Bioanalytical Systems, Inc., West Lafayette, IN.

The simplest way to understand how the ion trap creates mass spectra is to study how ions respond to the electrical field. It is necessary to begin by constructing a stability diagram for a single ion. Imagine a single mass to charge ratio being introduced into the ion trap. Then, the ac and dc voltages of the ring electrode are altered and the ions stability in both the z and r directions are determined simultaneously. If this experiment was performed multiple times, the stability diagram for that single mass would look similar to Figure 4-14.

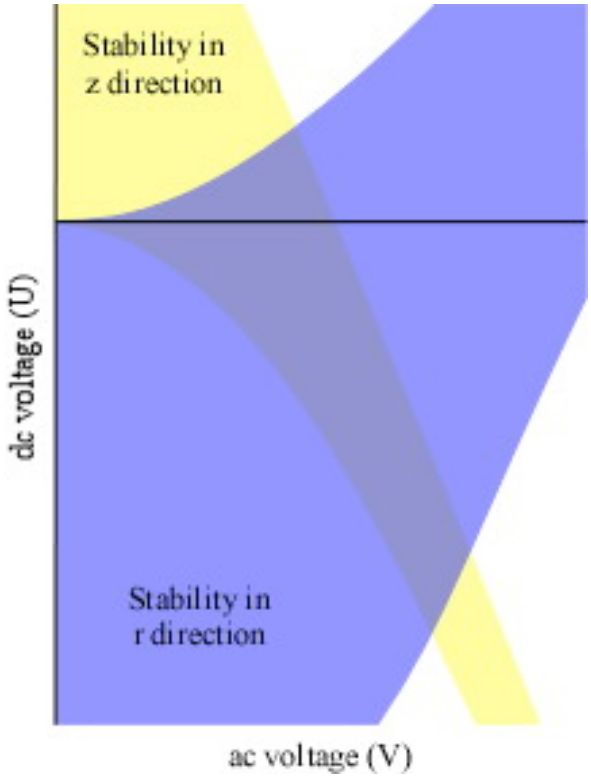


Figure 4-13 A Single Mass Stability Diagram for an Ion Trap. Adapted from Figure 5 from Wong and Cooks, 1997. Reprinted with permission of Bioanalytical Systems, Inc., West Lafayette, IN.

The yellow area indicates the values of the ac and dc voltages where the given mass has a stable trajectory in the z direction but the ion's trajectory in the r direction is unstable. As a result, the ion strikes the ring electrode, is neutralized, and removed by the vacuum. The blue area shows the voltages where the ion has a stable trajectory in the r direction, but not in the z direction. At these voltages, the ion exits the trap through the slits in the end cap electrode towards a detector. The detector is on if the analyst is attempting to generate a mass spectrum, and can be left off if the goal is to isolate a particular mass to charge ratio of interest. The gray-purple area is where the stability in both the r and z directions overlap. For these voltages, the ion has a stable trajectory and remains inside the trap.

Similar to the quadrupole mass filter, differential equations are able to expand the single mass stability diagram to a general stability diagram. The derivation of this result requires an in depth understanding of differential equations, so only the graphical result will be presented here (Figure 4-14). The solution is simplified from a six-variable problem, similar to the quadrupole discussion earlier, to a simpler two-variable problem.

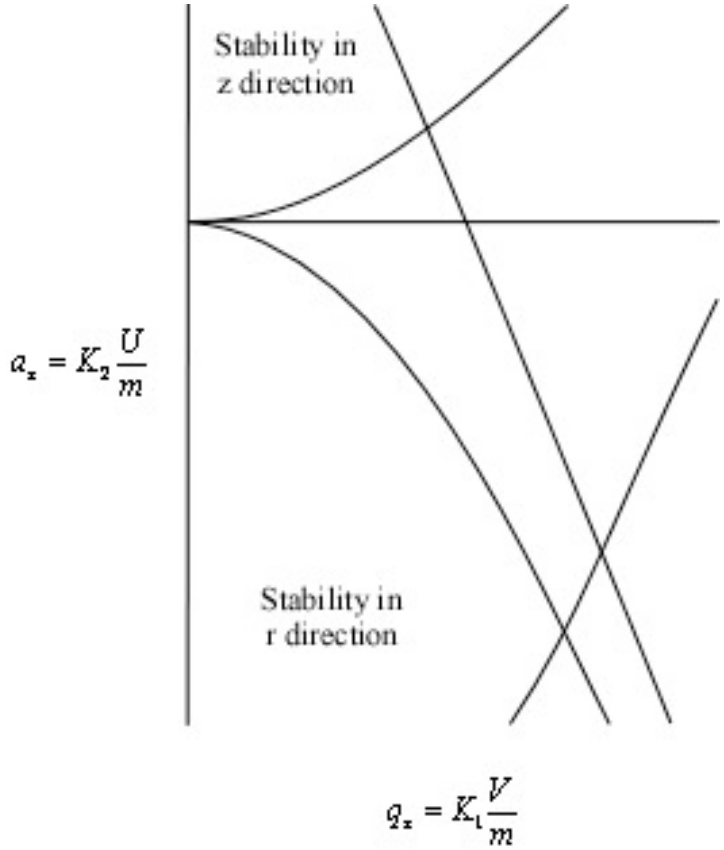


Figure 4-14 A General Stability Diagram. Adapted from Figure 5 from Wong and Cooks, 1997. Reprinted with permission of Bioanalytical Systems, Inc., West Lafayette, IN.

From the general stability diagram it becomes visible how scans can be performed by just altering the ac voltage on the ring electrode. But before we discuss the ion trap's operation it is necessary to understand the parameters that affect ions stability within the field. The terms K_1 and K_2 are characterized by the following equations:

$$K_1 = \frac{4e}{r_0^2 \omega^2}$$

$$K_2 = \frac{-8e}{r_0^2 \omega^2}$$

As expected, these parameters are very similar to the ones that resulted from the general stability diagram for the quadrupole mass filter. These parameters, like in the quadrupole, are also kept constant during a scan. The charge of the particle (*e*), the distance from the center of the trap to the ring electrode (r_0), and the radial frequency of the ac voltage (ω) are all kept constant during the run. While it would be possible to alter both the ac and dc voltages, in practice it is only necessary to alter the ac voltage (V) of the ring electrode. The dc voltage (U) on the other hand, is kept at zero. If the dc voltage is kept at a ground potential, increasing the ac voltage will eventually result in an unstable trajectory in the z direction. When ac voltage creates a q_z value that is greater than 0.908, the particle will be ejected from the trap towards a detector through the end cap electrode. As illustrated below, the q_z value is dependent on the mass to charge ratio of the particle, each different mass has a unique ac voltage that causes them to exit the trap.

For example, let's place four different ion masses into the ion trap where each has a single positive charge. The general stability diagram in Figure 4-15 is identical to Figure 4-14 except that it is focused around a dc voltage (U) of zero and the scale is enlarged; thus, a_x is equal to zero through a scan. A mass scan is performed by starting the ring electrode out at a low ac voltage. Each distinct mass has a unique q_z value, which is visually illustrated by placing these particles on the stability diagram (line). As the ac frequency begins to increase, the q_z values for these masses also increases. Once the q_z value becomes greater than 0.908, the ions still have a stable trajectory in the r direction but now have an unstable trajectory in the z direction. As a result, they are ejected out of the trap through the end cap electrode towards the detector.

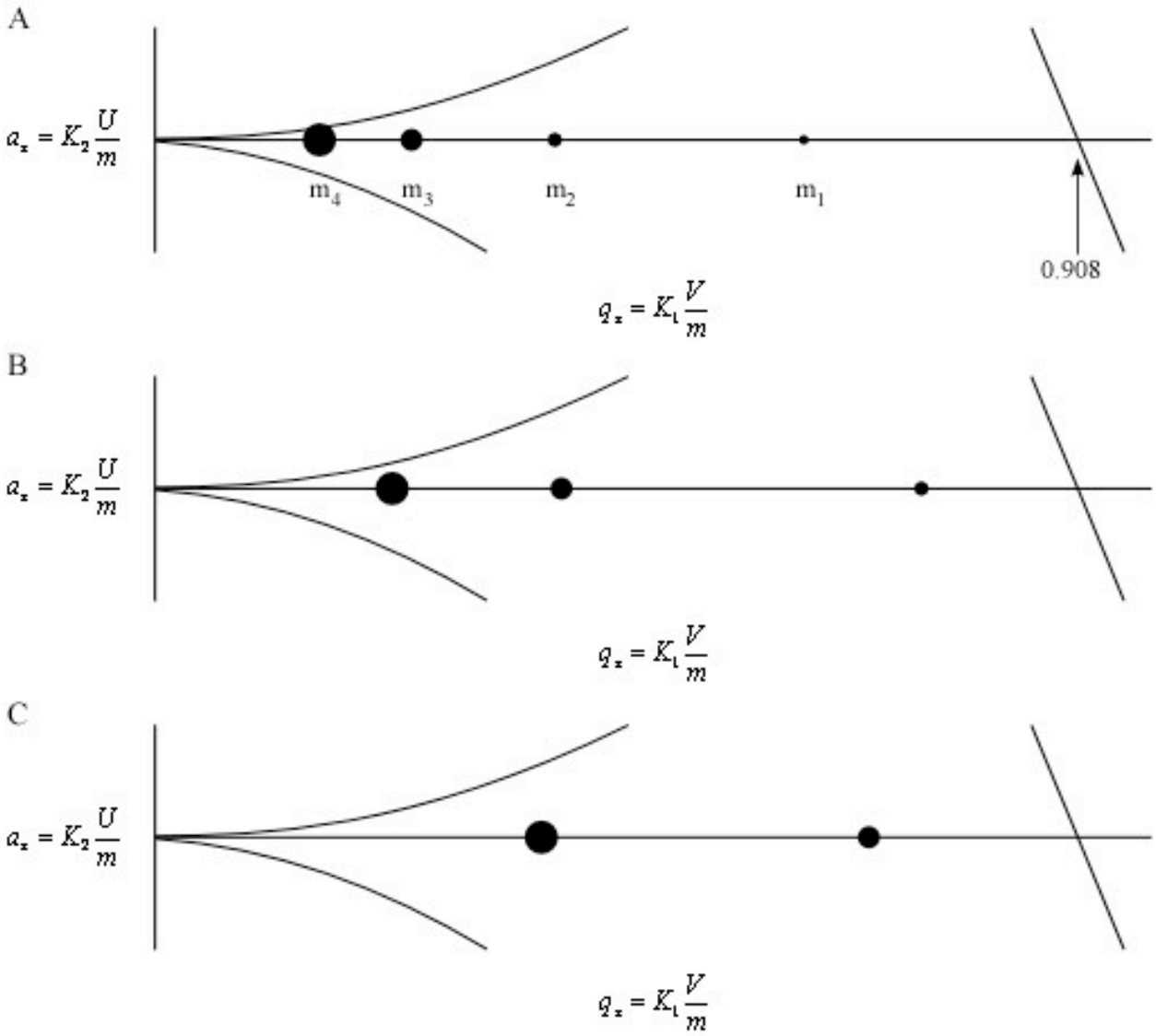


Figure 4-15 A Stability Diagram During a Sample Scan

The stability diagram above at A, B, and C was the result of taking a snapshot of the ac voltage during the scan and placing each mass at its corresponding q_z values for that particular voltage. In this mode of operation, the lightest masses (m_1) are always ejected from the trap (Figure 4-15 B) before the heaver masses (m_2). The heaviest masses (m_3 and m_4) still remain in the trap at point C. To eject these ions, a very large ac voltage is necessary. This voltage is so high that it becomes extremely difficulty to eject ions over a m/z value of 650. Since it is impractical to apply such high voltages to the electrode and its

circuits, a new method of operation needed to be discovered so the ion trap could analyze more massive molecules.

As a result, resonance ejection was developed to extend the mass range of the ion trap to a m/z value of 70,000. Under normal scanning conditions, ions oscillate at a given frequency depending on their q_z value which is a function of its mass, charge, and the amplitude of the ac voltage. This frequency is referred to as the ions secular frequency. It was discovered that an ac voltage applied to the end cap electrodes would only affect one secular frequency. The effected ion's oscillation in the z direction would increase linearly until it was ejected from the trap. Resonance ejection can be conceptualized as a "hole" inside the stability diagram at any chosen q_z value. Then the ac voltage of the ring electrode can be altered so any mass can have the same q_z value as the "hole" and exit the trap in the z direction (Figure 4-16). This mode of operation not only extended the mass analyzer's mass range, but it also made it possible to eject ions from the trap in any order. Before this mode of operation existed, it was only possible to eject the ions in order from lightest to heaviest. Figure 4-17 illustrates how it is possible to eject the heaviest ion (m_4) before the lighter ion (m_3).

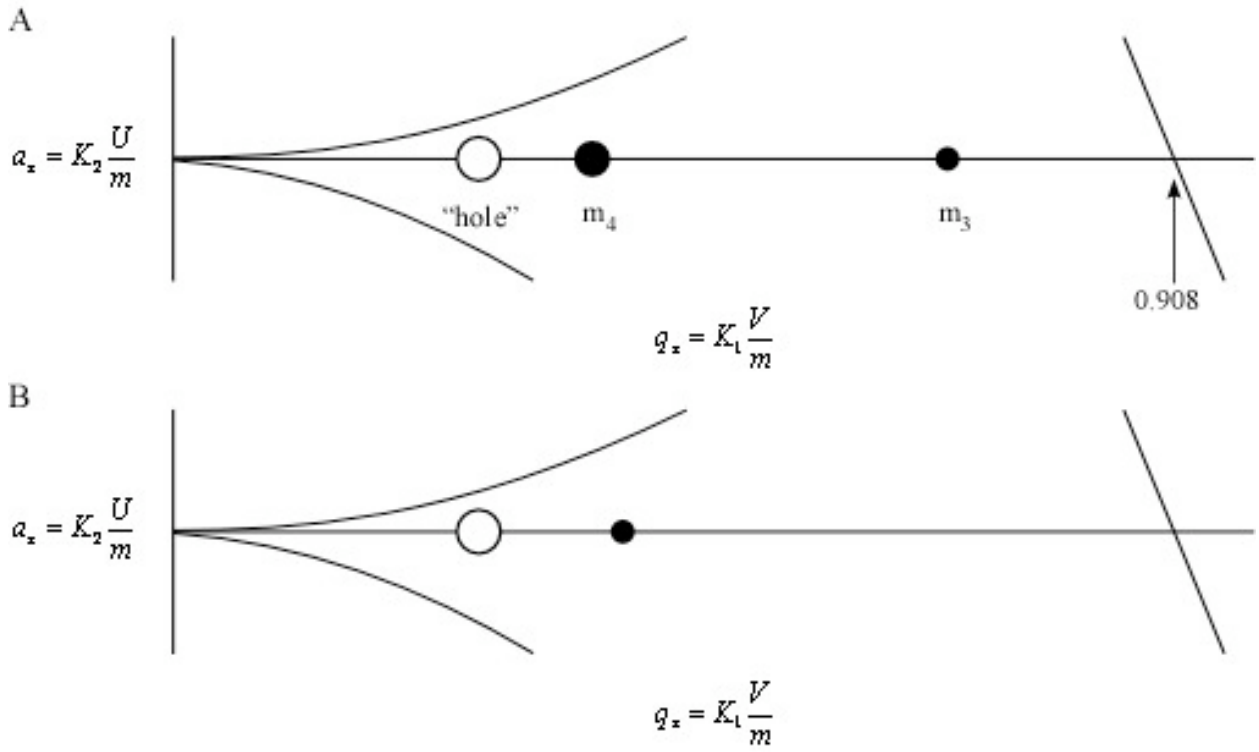
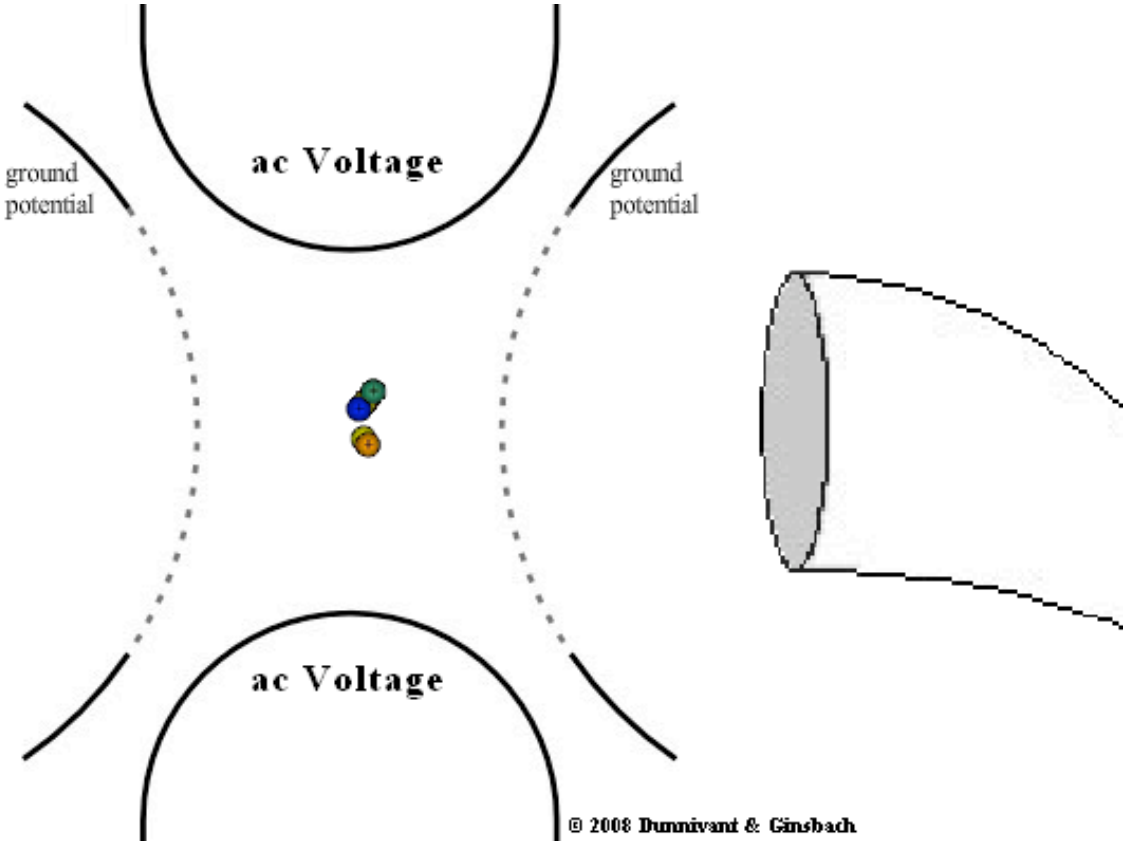


Figure 4-16 A Sample Resonance Ejection Scan

The resonance ejection mode of operation is one reason why the ion trap is such a valuable tool. It not only greatly extends the mass range of the mass analyzer, but it also increased its applications in tandem spectroscopy. The ability to isolate any given mass under 70,000 amu is an extremely powerful tool. Through the use of both modes of operation, the ion trap has become a valuable tool in performing many specialized mass separations.

View Animation 4.5 at this time for an illustration of how an ion trap mass filter contains and ejects ions of given mass to charge ratios.



Animation 4.5 Illustration of an Ion Trap Mass Filter.

4.2.6.4 *Time-of-Flight (TOF) mass filter:* While time-of-flight mass filters were one of the first modern MS systems to be developed, they had limited use due to their need for very fast electronics to process the data. Developments in fast electronics and the need for mass filters capable of resolving high mass ranges (such as in geological analysis of isotopes) has renewed interest in time of flight systems.

Entry into the TOF mass filter is considerably different than with other mass filters. The entry has to be pulsed or intermittent in order to allow for all of the ions entering the TOF to reach the detector before more ions are created. With sources that operate in a pulsing fashion such as in ICP or direct insertion of the sample, the TOF functions easily as a mass analyzer. In sources that continual produce ions such as an ICP, the use of a TOF is a bit more difficult. In order to use a TOF system with these continuous sources, an electronic gate

must be used to create the necessary pulse of ions. The gate changes the potential on an accelerator plate to only allow ions to enter the TOF mass filter in pulses. When the slit has a positive charge, ions will not approach the entryway to the mass analyzer and are retained in the ionization chamber. When all of the previously admitted ions have reached the detector, the polarity on the accelerator(s) is again changed to negative and ions are accelerated toward the slit(s) and into the TOF mass analyzer. This process is repeated until several scans of each cation peak has been measured. (This type of ionization and slit pulsing will be shown in the animation below).

Prior to developing the mathematics behind TOF separations a simple summary is useful. Mass to charge ratios in the TOF instrument are determined by measuring the time it takes for ions to pass through the "field-free" drift tube to the detector. The term "field-free" is used since there is no electronic or magnetic field affecting the ions. The only force applied to the ions occurs at the repulsion plate and the acceleration plate(s) where ions obtain a constant kinetic energy (KE). All of the ions of the same mass to charge ratio entering the TOF mass analyzers have the same kinetic energy and velocity since they have been exposed to the same voltage on the plates. Ions with different mass to charge ratios will have velocities that will vary inversely to their masses. Lighter ions will have higher velocities and will arrive at the detector earlier than heavier ones. This is due to the relationship between mass and kinetic energy.

$$KE = mv^2/2$$

The kinetic energy of an ion with a mass m and a total charge of q = ze is described by:

$$mv^2/2 = qV_S = zeV_S$$

where V_S is potential difference between the accelerator plates, z is the charge on the ion, and e is the charge of an electron (1.60×10^{-19} C). The length (d) of the drift tube is known and fixed, thus the time (t) required to travel this distance is

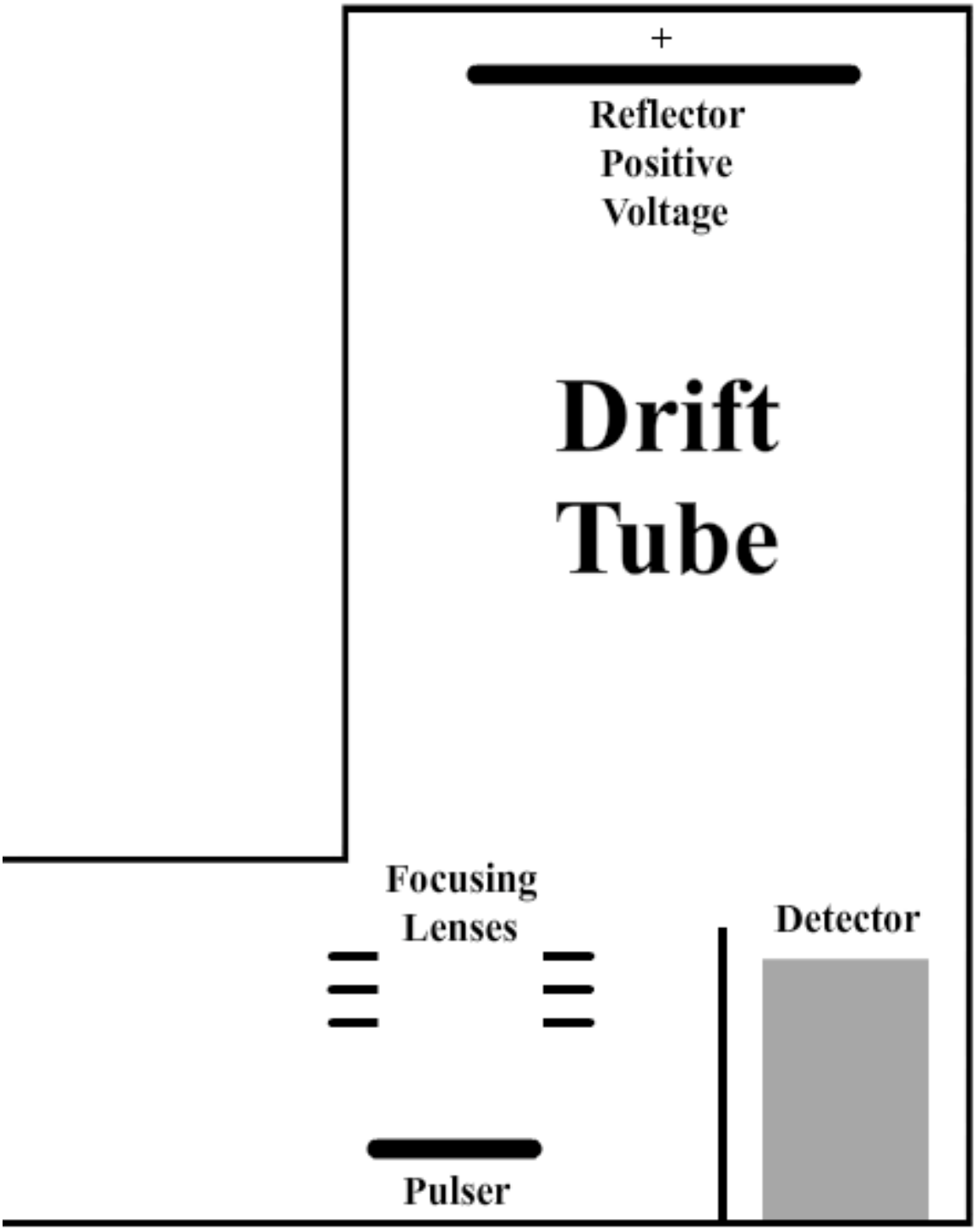
$$t = d/v \ .$$

By solving the previous equation for v and substituting it into the above equation we obtain

$$t^2 = \frac{m}{z}\left(\frac{d^2}{2V_S e}\right) \ .$$

In a TOF mass analyzer, the terms in parentheses are constant, so the mass to charge of an ion is directly related to the time of travel. Typical times to traverse the field-free drift tube are 1 to 30 ms.

Advantages of a TOF mass filter include their simplicity and ruggedness and a virtually unlimited mass range. However, TOF mass filters suffer from limited resolution, related to the relatively large distribution in flight times among identical ions (resulting from the physical width of the plug of ions entering the mass analyzer).



Animation 4.6 illustrations how a pulsed accelerator plate/slit acts as a gate for a reflectiveTOF mass filter system.

Animation 4.6. Illustration of a TOF Mass Filter.

4.2.6.5 *Double Focusing Systems:* The magnetic sector MS described earlier is referred to as a single-focusing instrument since it only uses the magnetic component to separate ion mass to charge ratios. This can be improved by adding a second electrostatic-field based mass filter, and is referred to as double focusing. A magnetic field instrument focuses on the distribution of translational energies imparted on the ions leaving the ionization source as a means of separation. But in doing so, the magnetic sector instruments broaden the range of kinetic energies of the ions, resulting in a loss of resolution. If we combine both separation techniques by passing the ions separately through an electrostatic (to focus the kinetic energy of the ion packet) and magnetic field (to focus the translational energies of the ion packet), we will greatly improve our resolution. In fact, by doing this we can measure ion masses to within a few parts per million (precision) which results in a resolution of ~2500. Compare this to the unit resolutions (28 versus 29 Daltons) discussed at the beginning of this section (under resolution). On the downside, these instruments can be costly.

4.2.6.6 *Tandem Mass Spectroscopy:* Mass spectroscopy is commonly referred to as a confirmatory technique since there is little doubt (error) in the identity of an analyte. To be even more certain of an analyte's identify, two or even three, mass spectrometers can be used in series (the output of one MS is the input of another MS). Subsequent MS systems will select for a specific ion from the second MS and separate the masses in this peak for further identification. This technique allows for unit resolution or better in the first MS, subsequently separating the masses of a given peak in the second and third MS, and identified based on a three to four decimal place mass. You should be able to see the confirmatory nature of this technique. Mass filters of choice for use in tandem include magnetic sector, electrostatic, quadrupole, and ion trap systems.

4.2.7 Detectors:

Once the analytes have been ionized, accelerated, and separated in the mass filter, they must be detected. This is most commonly performed with an electron multiplier (EM), much like the photoelectron multipliers used in optical spectroscopy. In MS systems, the electron multiplier is insensitive to ion charge, ion mass, or chemical nature of the ion (as a photomultiplier is relatively insensitive to the wavelength of a photon). The EMs in ICP-MS systems are usually discrete dynodes EMs since these can be easily modified to extend their dynamic range.

A continuous EMs is typically horn shaped and are made of glass that is heavily doped with lead oxide. When a potential is placed along the length of the horn, electrons are ejected as ions strike the surface. Ions usually strike at the entrance of the horn and the resulting electrons are directed inward (by the shape of the horn), colliding sequentially with the walls and generating more and more electrons with each collision. Potentials across the horn can range from high hundreds of volts to 3000 V. Signal amplifications are in the 10 000 fold range with nanosecond response times. Animation 4-7 illustrates the response of a continuous electron multiplier as ions, separated in a mass filter, strike its surface.

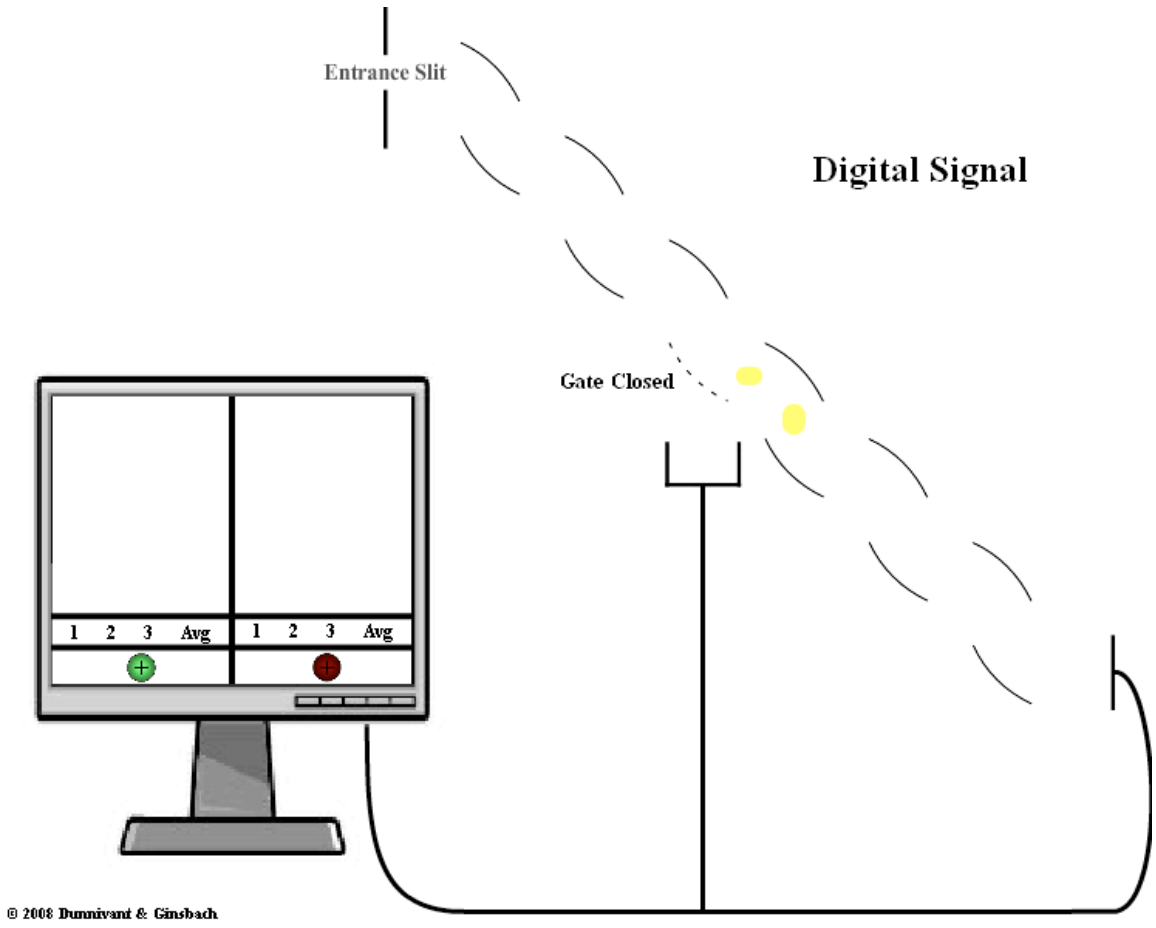
Animation 4.7. Illustration of a Continuous-Dynode Electron Multiplier.

A standard discrete electron multiplier is shown in Animation 4.8 is actually a connected series of phototubes. In a discrete system each dynode is held at a +90 V potential as compared to immediately adjacent dynodes. As a cation hits the first cathode, one or more electrons are ejected and pulled toward the next cathode. These electrons eject more and more electrons as they go forward producing tens to hundreds of thousands of electrons and amplifying the

signal by a factor of 10^6 to 10^8. This allows for extremely low detection limits in the parts per billion (ppb) to parts per trillion ranges (ppt). Such an EM is shown in Animation 4.8.

Animation 4.8 Illustration of a Standard Discrete-Dynode Electron Multiplier.

In order to extend the dynamic range of an EM to cover relatively high analyte concentration (in the ppm range), some manufactures have incorporated two EM detector in one by including a switch that allows high signals to be counted in a digital manner in order to prevent the overload of signal, and use analogue counting to analyze low concentration samples. Such an EM detector is illustrated in Animation 4.9.



Animation 4.9 Illustration of a Dual (Gated) Discrete-Dynode Electron Multiplier.

Another form of MS detector is the Faraday Cup with counts each ion entering the detector zone. These detectors are less expensive but provide no amplification of the signal and are not used in typical instruments due to their poor detection limits.

One of the latest detectors to reach the market is a microchannel plate, a form of an array transducer also called an electro-optical ion detector (EOID). The EOID is a circular disk that contains numerous continuous electron multipliers (channels). Each channel has a potential applied across it and each cation reaching the detector will generate typically up to 1000 electrons. The electrons produce light as they impinge on a phosphorescent screen behind the disk containing the channels. An optical array detector, using fiber optic technology, records the flashes of light and produces a two dimensional resolution of the ions. The advantage of an EOID is their ability to greatly increase the speed of mass determinations by detecting a limited range of masses simultaneously, thus reducing the number of discrete magnetic field adjustments required over a large range of masses. The positioning of the dispersed beam of cations is easier to visualize for a magnetic sector MS, but the EOIDs have applications in most mass filter systems. Unfortunately, EOIDs have not been adapted as rapidly as expected by instrument manufacturers.

4.3 Summary

Mass spectrometry detection greatly expands the applications of ICP system in the analysis of metals. Not only can more elements be analyzed, as compared to FAAS, FAES, and ICP-AES, but isotopic data can be collected. A variety of sample introduction techniques and mass filters make the ICP-MS a diverse instrument. But increased capabilities and lower detection limits come

with a relatively high price tag. For example, a basic ICP-MS costs in the range of $70-80 thousand while a basic ICP-MS with reaction cell-quadrupole technology costs around $150 thousand; high-resolution instruments can cost as high as $600 thousand or more, and some are not even commercially available.

Mass spectrometry is in a constant and rapid state of development. In this Etextbook, we have focused on the basic mass analyzers, such as the quadrupole, ion trap, time of flight and magnetic sector (double focusing) designs. Recent technological advances have allowed for the development of two upcoming instruments; a new magnetic sector mass analyzer (Walder, et al., Journal of Analytical Atomic Spectrometry, 1992, 7, 571-575) and orbital trap (Makarov, Analytical Chemistry, 2000, 72(6), p.1156). The new magnetic sector instrument relays on a new sector design referred to as the Mattauch-Herzog geometry. Although the resolution is relative low (~500) for a high-end instrument, this mass filter allows for the monitoring of multiple masses at the exact same time by using a multi-collector-Faraday based detector. The advantage of this system is that high accuracy in isotopic ratios that can be obtained. The orbital trap instrument is an electrostatic ion trap capable of resolution values (R_s) approaching 200 000. While these instruments carry a high price tag, they greatly increase the normal capabilities of the instrument.

Additional recent breakthroughs in mass spectrometry include the drastic lowering of detection limits. A new technique referred to as nanostructured initiator MS (NIMS) is being used in research-grade instruments to measure biological metabolites. Utilization of these systems with a laser-based systems produces detection limits are easily at the attomole (10^{-18}) amounts. Specific molecules in the yoctomole (10^{-24}) levels have even been detected (Nature, 2007, 449, 1003). These systems make the ppb and ppt detection limits discussed in this Etextbook seem trivial. It is likely that similar detection limits will soon be achieved for ICP-based instruments.

A summary of resolution and price for commercially available instruments is given in the following table.

Table 4.2 Summary of Mass Filter Features. Source: Personal Communiqué David Koppenaal, Thermal Scientific & EMSL, Pacific National Laboratory.

Type of Mass Filter	**Resolution**	**Detection Limit**	**Approximate Instrument Price**
Routine Mass Filters Coupled with ICP			
Single Quadrupole with a collision / reaction cell (CRC)	250-500	low ppb – high ppt	$150 000 - $200 000
Ion Trap (no longer available)	1 000 – 10 000	ppb	$400 000 - $500 000
Time of Flight	3000 – 10 000	high ppt	$300 000 - $400 000
Double Focusing	10 000 – 20 000	mid to high ppt	$750 000 - $1 000 000
Fourier Transform	200 000 – 1 000 000	ppb	Not commercially available
New Mass Filters			
Magnetic Sector / Multi-collector with the Mattauch-Herzog Geometry	~500	high ppb	$350 000 - $400 000
Orbital Trap (Electrostatic Ion Trap)	150 000 – 200 000	ppb	$600 000 (currently only available with HPLC; possibly soon to be available with ICP)