Chapter 5
Basic Mass Spectrometry

Continued

5.5 Common Mass Filters (Mass Analyzers)

Mass analyzers separate the molecular ion and its fragments by ion velocity, mass, or mass to charge ratio. A number of mass filters/analyzers are available for GC, LC and CE interfaces, but not all are commercially 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 common ones.

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

$$Rs = m/\Delta m$$

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 (0.0001) to low resolution instruments that only require unit resolution (28 versus 29 Daltons). Resolution values for commonly available instruments can range from 500 to 500 000.

Before introducing the various types of mass analyzers, remember our current location of the mass analyzer in the overall MS system. The analyte has been ionized, underwent fragmentation, been accelerated, and in some cases focused to a focal point with a velocity towards the mass analyzer. Now the packet of ion fragments needs 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 text. But, first a controversy in the literature needed to be addressed with respect to how a mass filter actually separates ion fragments.

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 oscillation in an oscillating electrical field). These differences may seem semantic but some MS users insist on their clarification. For the discussions below, in most cases, mass to charge will be used for all mass analyzers.

5.5.1 *Magnetic sector mass filter:* It has been known for some time that the trajectory of a point charge, in our case a positively charged molecular ion or fragment, 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

$$KE = 1/2\, mv^2 = zeV \qquad Eqn\ 5.1$$

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 in EI and CI, 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 ion's path, the magnetic force (F_M) and the centripetal force (F_C), are described by

$$F_M = B\, z\, ev \qquad Eqn\ 5.2$$

and

$$F_C = (mv^2)/r \qquad Eqn\ 5.3$$

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

$$B\ z\ e\ v = (mv^2)/r \qquad \text{Eqn 5.4}$$

which upon rearrangement yields

$$v = (V\ z\ e\ r) / m \qquad \text{Eqn 5.5}$$

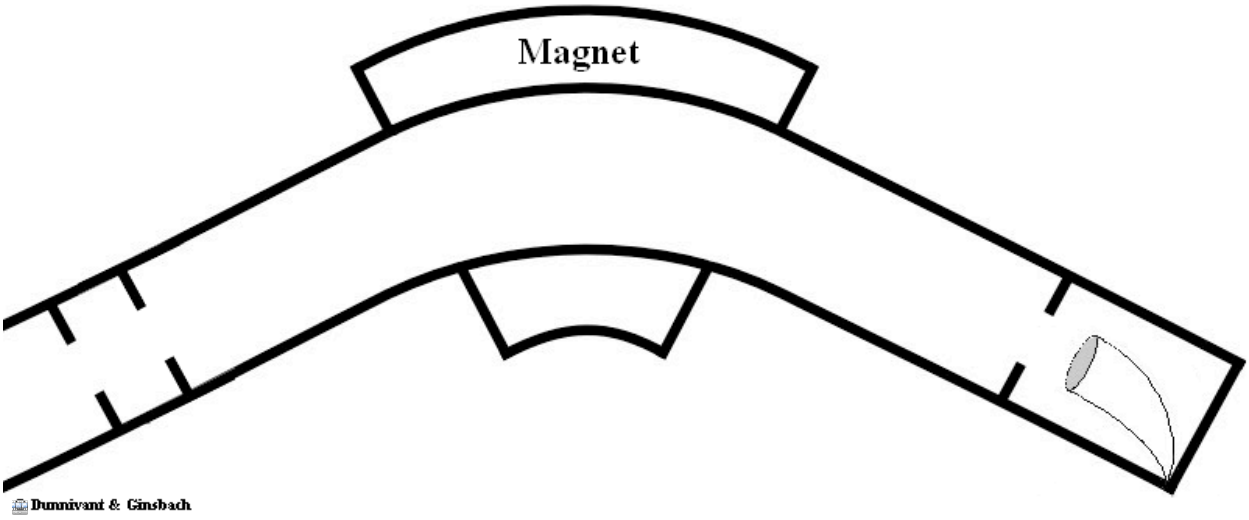
Substituting this last equation into our first KE equation yields

$$m/z = (B^2\ r^2\ e) / 2V \qquad \text{Eqn 5.6}$$

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.

However, it is difficult to quickly vary the magnetic field strength. The resulting slow scan rate is especially problematic with capillary column GCs since the peak width is narrow. Using a magnetic sector instrument could complicate identification of a compound if two or more peaks emerge from the GC during a single scan, especially in the relatively fast elution of peaks from a capillary column GC. Generally, several complete mass to charge scans are desired for accurate analyte identification. This 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 ion fragments, as opposed to sweeping the field strength. 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 5.5 below. Although B and r are normally held constant, this modern design is difficult to illustrate, so we will illustrate a magnetic sector MS where B, the magnetic field, is varied to select for different ions. As a particular peak (compound) enters the MS from a GC, it is ionized/fragmented by an EI in the animation. The ions are then 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 5.5. Illustration of a Magnetic Sector MS. Go to the book's web page, download, and play An_5_4_Mag_Field.mov

While magnetic sector mass filters were once the only tool 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 double-focusing instruments (Section 5.5.6).

5.5.2 *Quadrupole mass filter:* Quadrupole mass filters have become the most common type of MS used 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 GC applications and to some extent in LC systems because they are able to operate at a relatively high pressure (5×10^{-5} torr). 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/trajectory within the oscillating electrical field.

A quadrupole system consists of four rods that are arranged 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). 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 dc 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, and is commonly referred to as being 180˚ out of phase (Figure 5.9).

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

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

and Eqn 5.7

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

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 in the above equation ranges from 0 to 3000 volts.

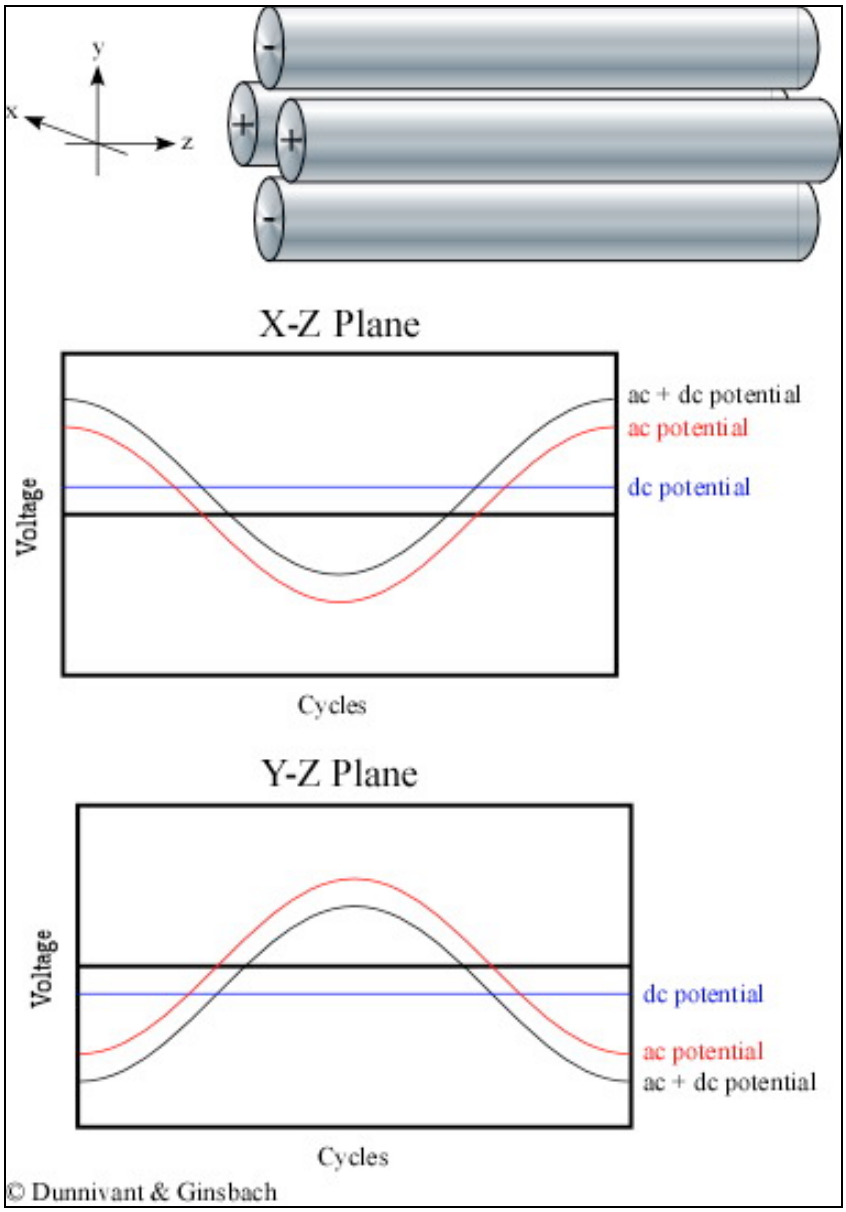


Figure 5.10 AC and DC Potentials in the Quadrupole MS.

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 pair of rods. 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 out 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 5.11).

Now look at the other pair of rods and the converse of the ac/dc potentials. 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 pass mass 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.* Different ions possess a stable trajectory at different magnitudes and reach the detector at different times during a sweep of the ac/dc magnitude range. The graph of the combined effect, shown in Figure 5.10c, is actually a simplification of the actual stability diagram.

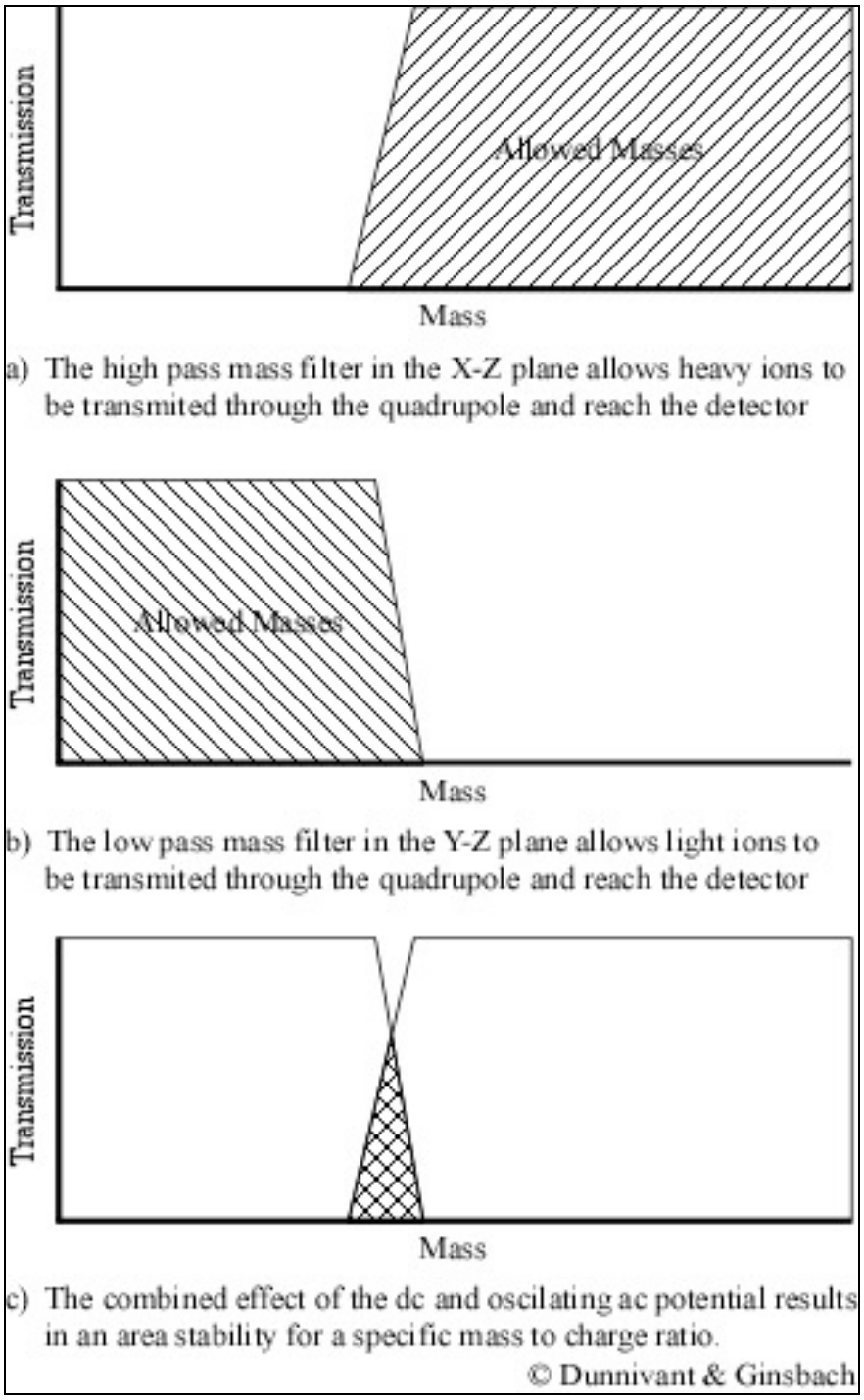


Figure 5.11 A “Conceptual” Stability Diagram

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 5.12. 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 5.12. 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 5.12). 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 5.12 is equivalent to shifting the position of the high and low pass mass filters with respect to the x axis illustrated in Figure 5.11. Even though the mass is not changing for the stability diagram discussed here, the mass that has a stable trajectory is altered.

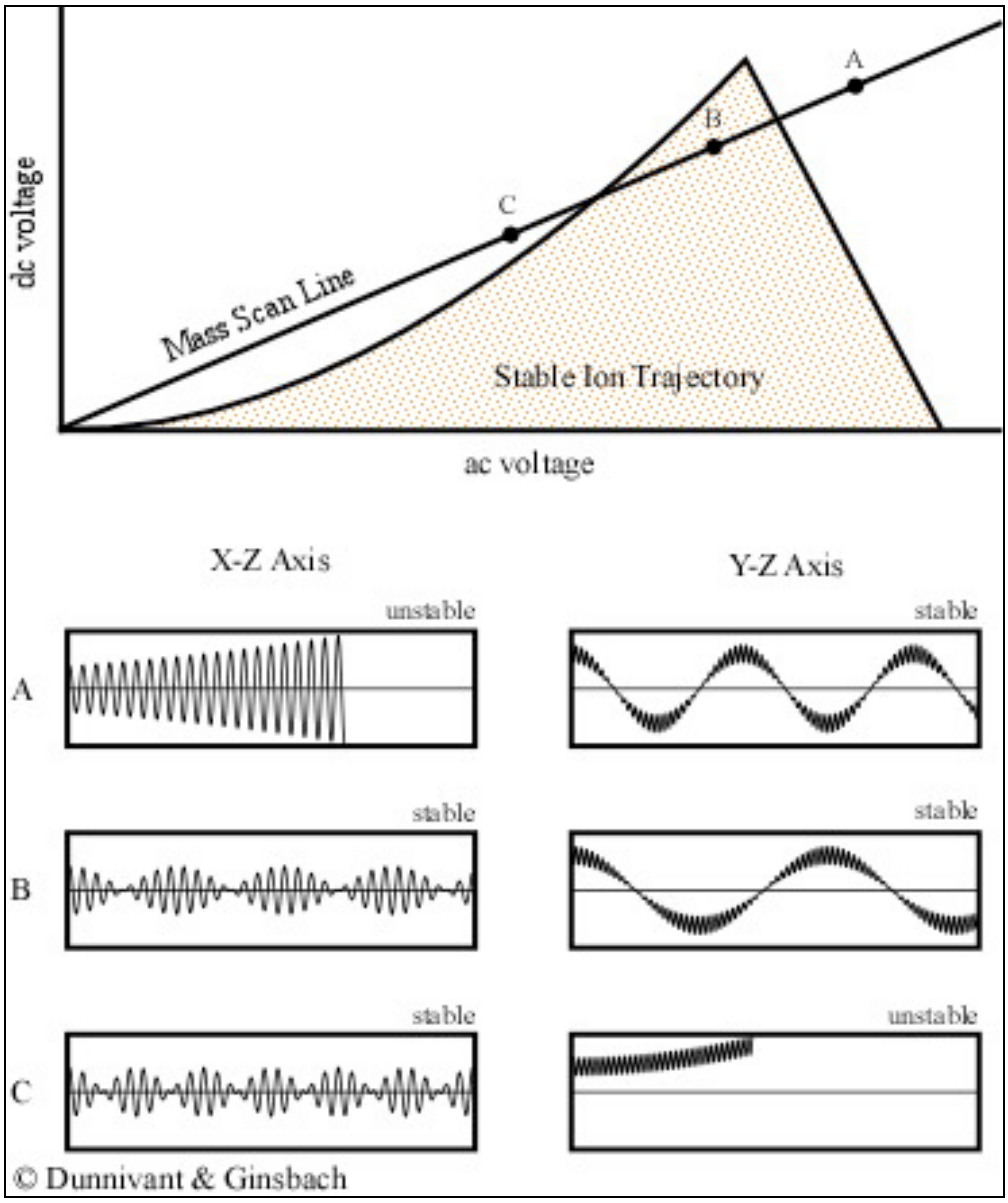


Figure 5.12 Stability Diagram for a Single Ion Mass. Used with permission from the Journal of Chemical Education, Vol. 75, No. 8, 1998, p. 1051; copyright © 1998, Division of Chemical Education, Inc.

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/rod. The motion of the particle in the Y axis is stable because the combination of the ac potential as well as the negative dc potential yields a stable trajectory. 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 using a force balance approach. This derivation requires a complex understanding of differential equations and is beyond the scope of an introductory text, but it can be explained graphically (Figure 5.13). The parameters in the axes are explained below the figure.

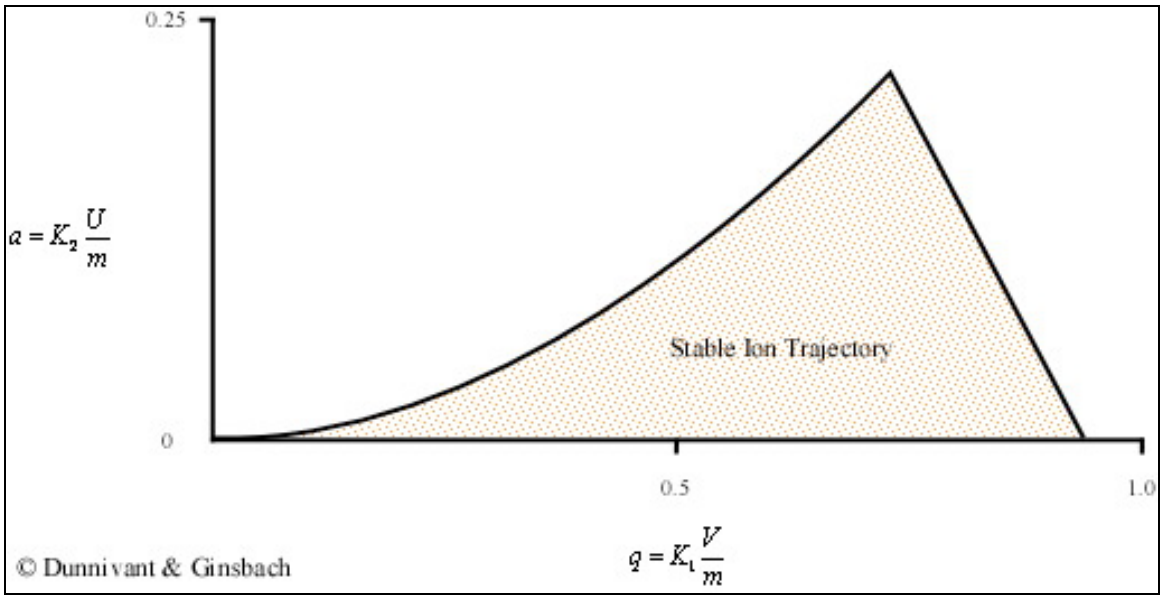


Figure 5.13 The General Stability Diagram

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 above. 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, we 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* and allows a sweep of mass to charge ranges. 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:

$$K_1 = \frac{2e}{r^2\omega^2} \qquad \textit{Eqn 5.8}$$

$$K_2 = \frac{4e}{r^2\omega^2} \qquad \textit{Eqn 5.9}$$

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 for almost all cases. The distance from the center of the quadrupole (r) is carefully controlled by the manufacturing process and an Einzel 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 5.13) is illustrated where there is an inverse relationship between the two. Figure 5.12 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 5.12 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 5.14). The resolution can be improved when the slope of the mass line is increased. 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) voltage. As a result, the line intersects a little below this point allowing the quadrupole to obtain unit resolution.

Once the resolution has been determined, the ratio of the ac to dc potential is left unchanged throughout the scan process. Again, to perform a scan, the magnitude of the ac and dc voltages is altered while their ratio stays constant. This places a different mass to charge 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 5.14. By scanning throughout a voltage range, the quadrupole is able to create the majority of mass spectra produced in today's chemical laboratories. But it should be noted that quadrupole mass filters have a upper limit of approximately 650 amus.

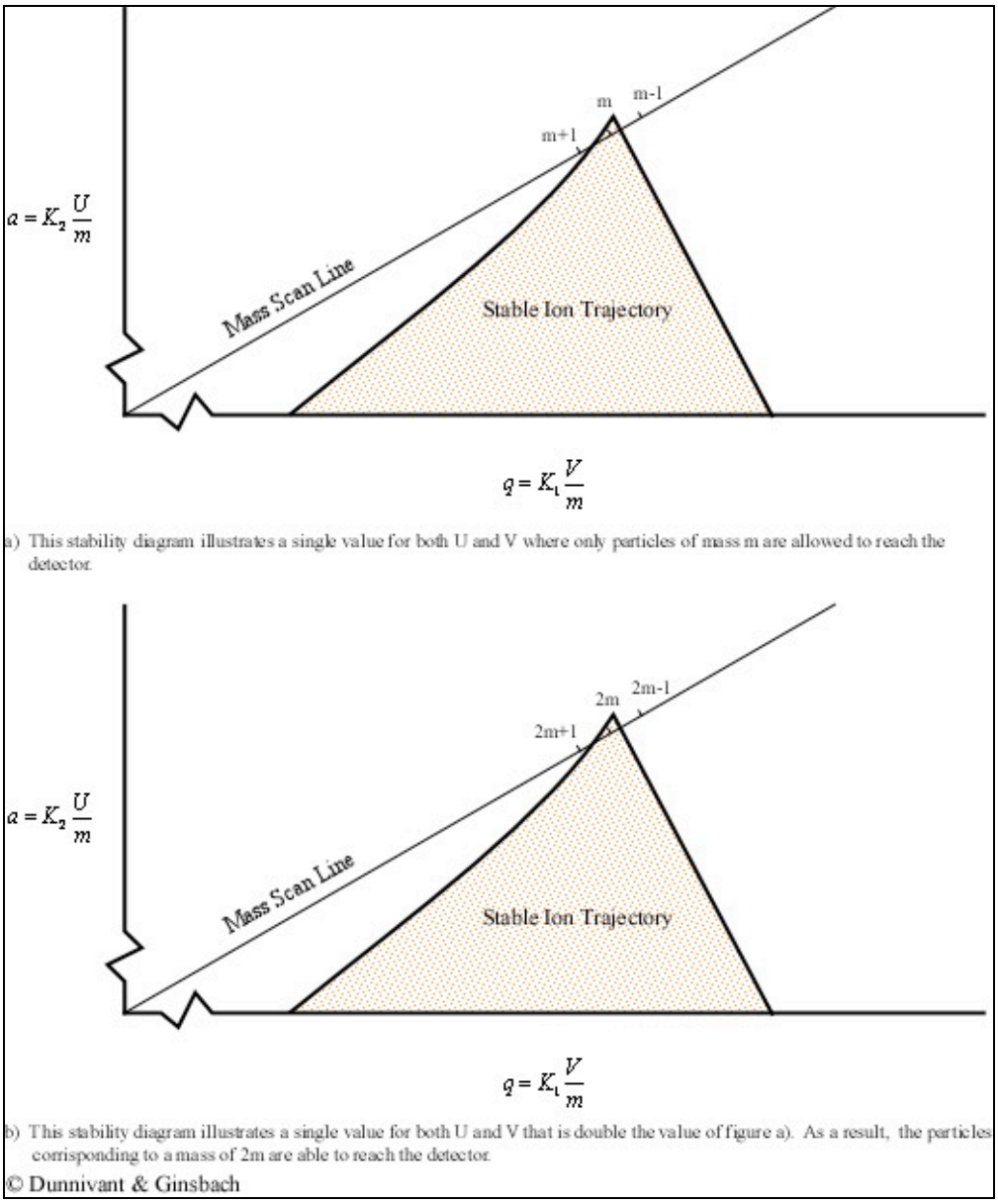


Figure 5.14 Quadrupole Mass Scan. Used with permission from the Journal of Chemical Education, Vol. 63, No. 7, 1998, p. 621; copyright © 1986, Division of Chemical Education, Inc.

Now that we have given a detailed description of the factors influencing the movement of a charged particle through the quadrupole, it is advantageous to summarize the entire process as a physicist would do in the form of a force balance. This is the origin of the governing equation where the French scientist E. Mathieu balanced the equations for the motion of ionized particles to the potential forces (electrical potentials) encountered in a quadrupole mass analyzer. This six-parameter differential equation, known as the Mathieu equation, is represented by

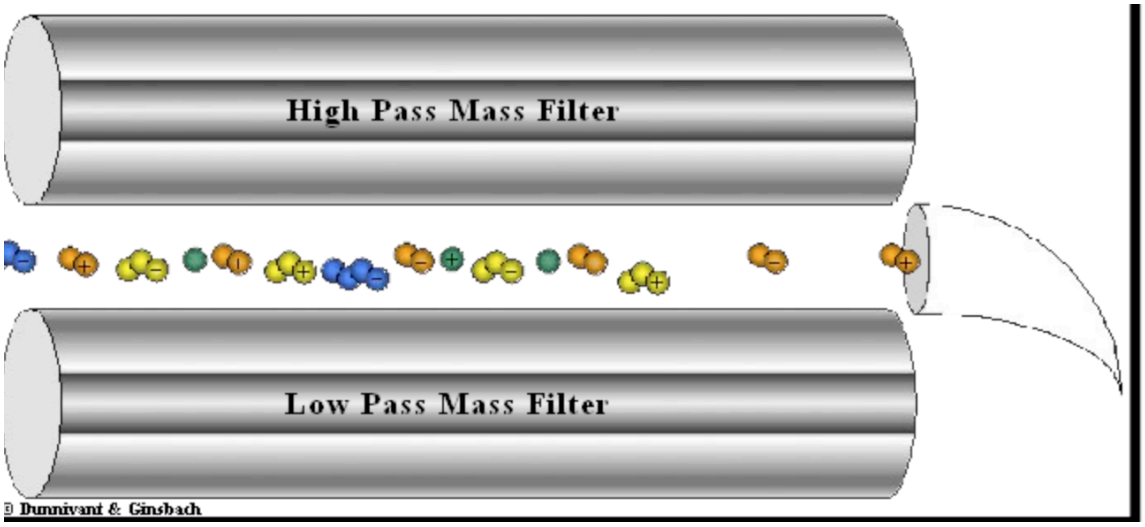
$$\frac{d^2u}{d\xi^2} + [a_u + 2qCos2\xi]u = 0 \qquad \text{Eqn 5.10}$$

where

$$a = \frac{4eU}{\omega^2 r_0^2 m} \quad \text{and} \quad q = \frac{2eV}{\omega^2 r_0^2 m}$$

and where *u* is either the x or y directional coordinate, ξ is the redefining of time (t/2), *e* is the charge of the ion, U is the magnitude of the dc potential, ω is the angular frequency (2pf) of the applied ac waveform, r_o is the distance from the center axis (the z axis) to the surface of any electrode (rod), *m* is the mass of the ion, and V is the magnitude of the applied ac or radio frequency waveform. By using the reduced terms, *a* and *q*, the six-parameter equation (*e, w, r_o, m, U, and V*) can be simplified to a two-parameter equation (involving *a* and *q*). Thus, when the two opposing forces are balanced, the movement of a charged particle in an electrical field, the particle will pass through the quadrupole and strike the detector.

View Animation 5.5 for an illustration of how the trajectory of ions of different masses are changed during a mass scan.



Animation 5.6. Illustration of a Quadrupole Mass Filter. Go to the book's web page, download, and play An_5_6_Quad.mov

5.5.3 *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 several thousand m/z units) to unit resolution in commonly encountered instruments. The ion trap is also an extremely sensitive instrument which 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 (section 5.5.7).

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 5.15). 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.

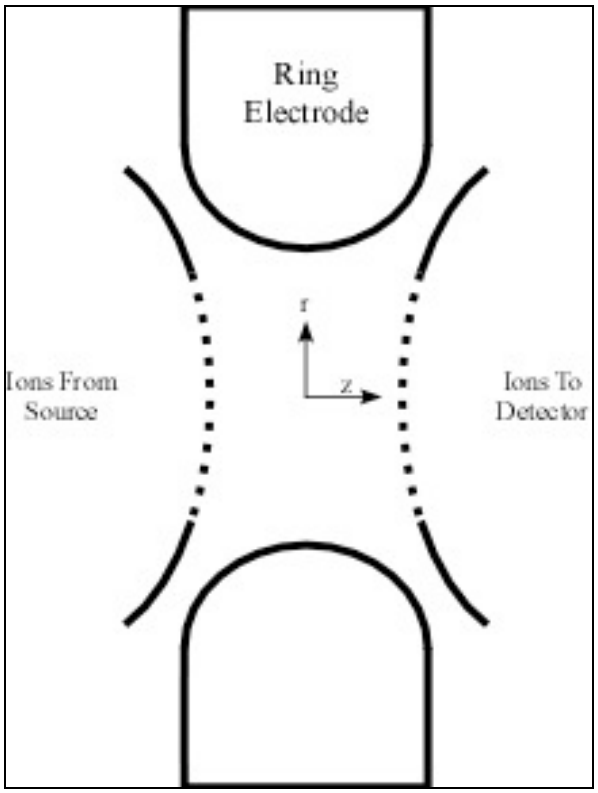


Figure 5.15 A Cross Section of the Ion Trap

After the sample molecules have been ionized by the 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 mass spectrometry (Section 5.5.4). 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 ion to oscillate in both the r and z direction (Figure 5.16). 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.

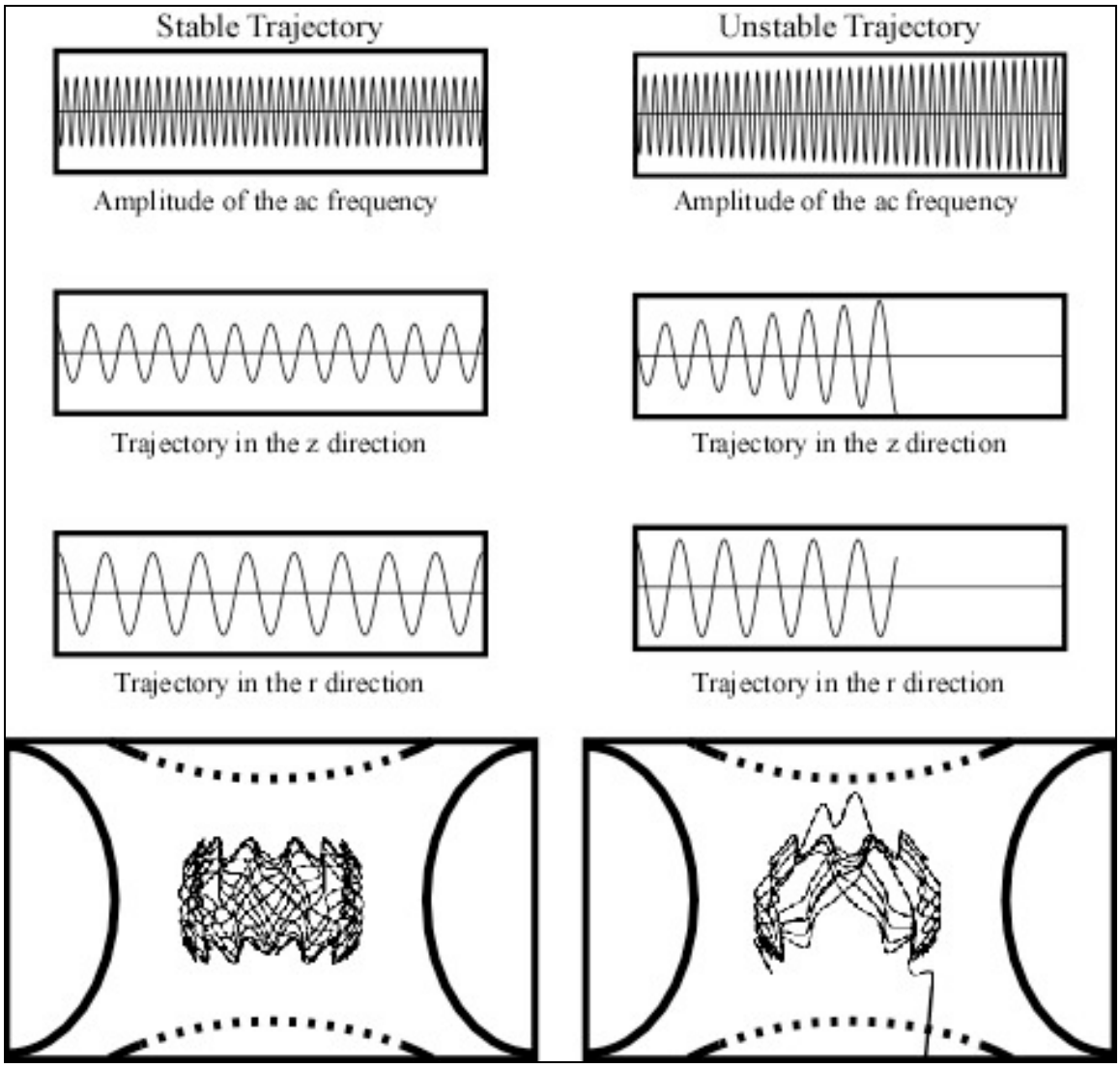


Figure 5.16 The Trajectories of a Single Mass Within the Electrical Field. Figure 6 from Wong and Cooks, 1997. Reprinted with permission of Bioanalytical Systems, Inc., West Lafayette, IN.

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 5.17.

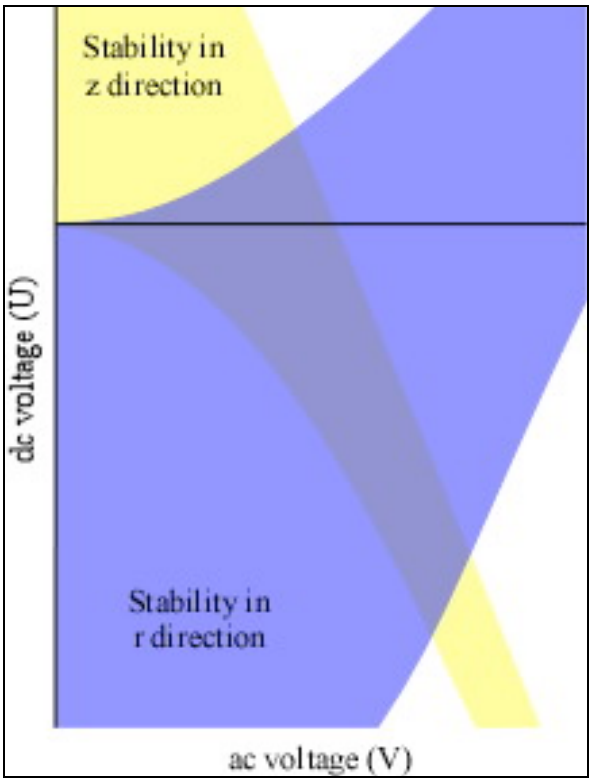


Figure 5.17 A Single Mass Stability Diagram for an Ion Trap. Adapted from Figure 5 from Wong and Cooks, 1997. Reprinted with permission of Bioanalytical Systems, Inc., West Lafayette, IN.

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 are 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 direction 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 5.18). As with the linear quadrupole mass filter, the solution here is simplified from a six-variable problem to a simpler two-variable problem.

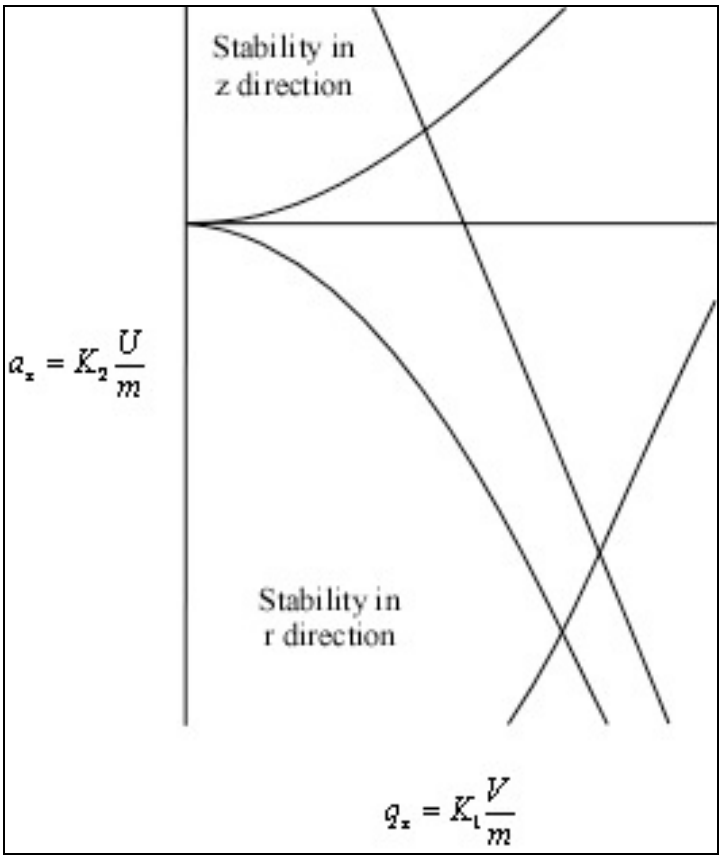


Figure 5.18 A General Stability Diagram. Adapted from Figure 5 from Wong and Cooks, 1997. Reprinted with permission of Bioanalytical Systems, Inc., West Lafayette, IN.

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:

$$K_1 = \frac{4e}{r_0^2 \omega^2} \qquad \textit{Eqn 5.11}$$

$$K_2 = \frac{-8e}{r_0^2 \omega^2} \qquad \textit{Eqn 5.12}$$

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 5.19 is identical to Figure 5.18 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. 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.

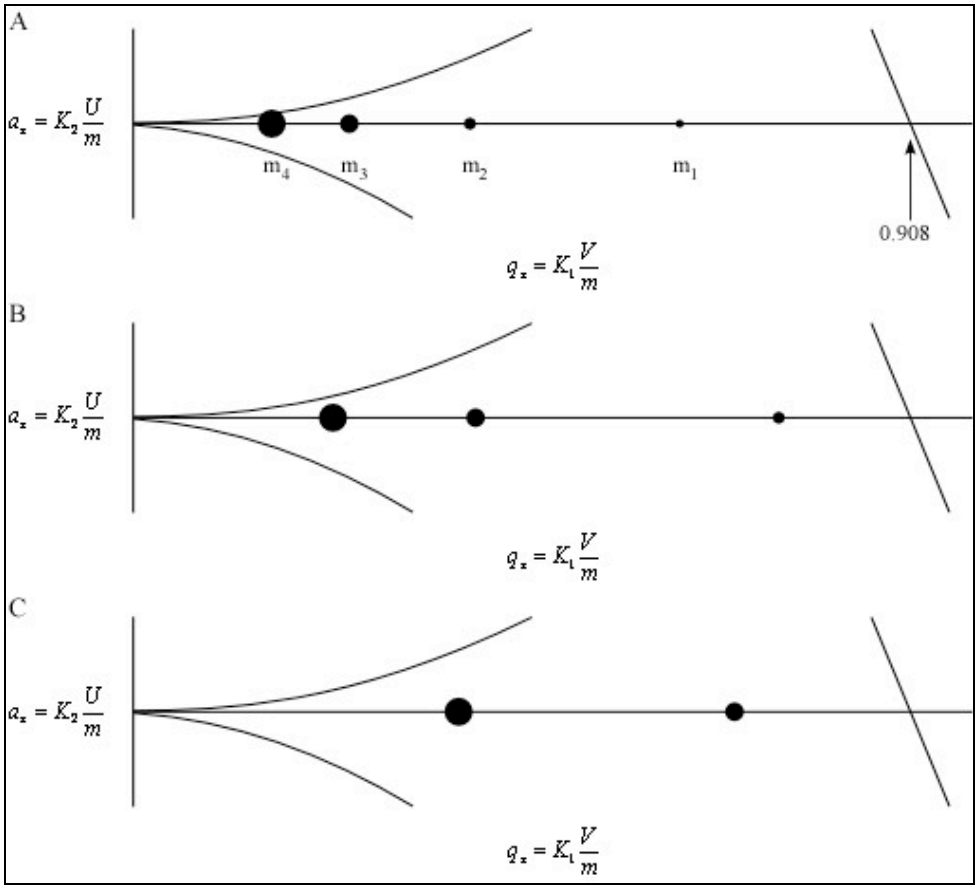


Figure 5.19 A Stability Diagram During a Sample Scan

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 15.19 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 several thousand. 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 ion's secular frequency. It was discovered that an ac voltage applied to the end cap electrodes would only affect one ion's 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 5.20). 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 5.20 illustrates how it is possible to eject the heaviest ion (m_4) before the lighter ion (m_3).

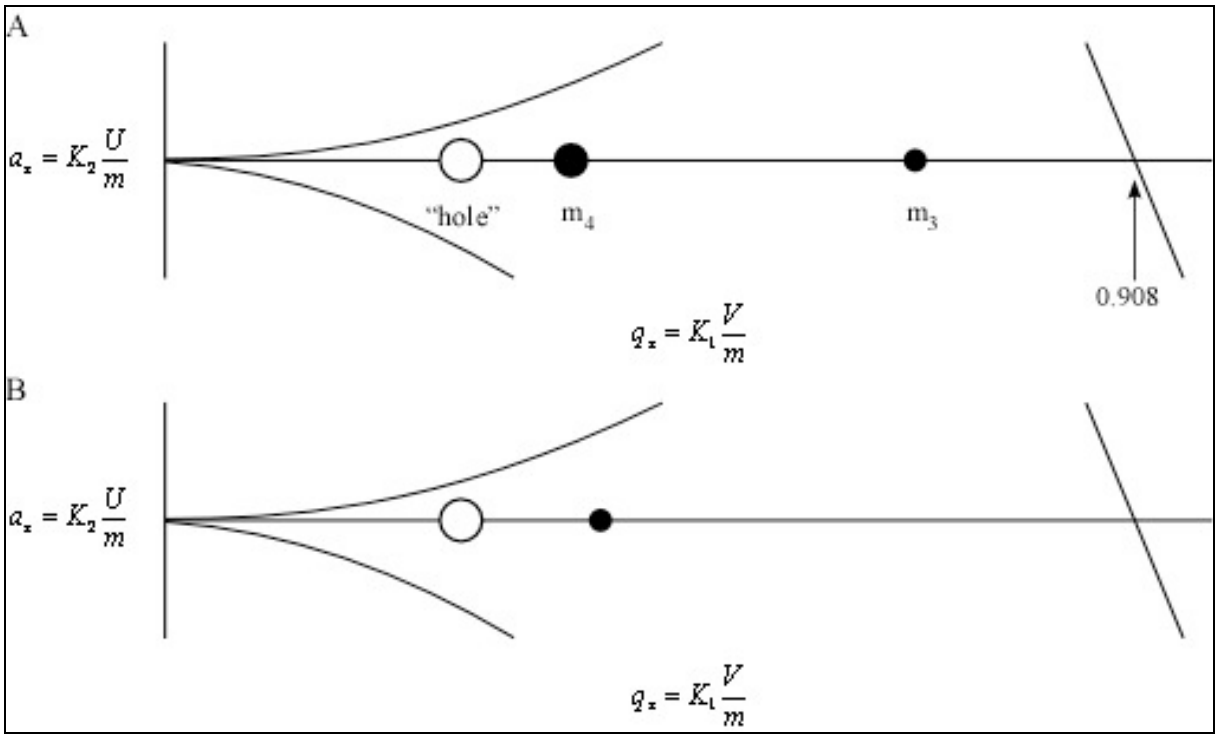
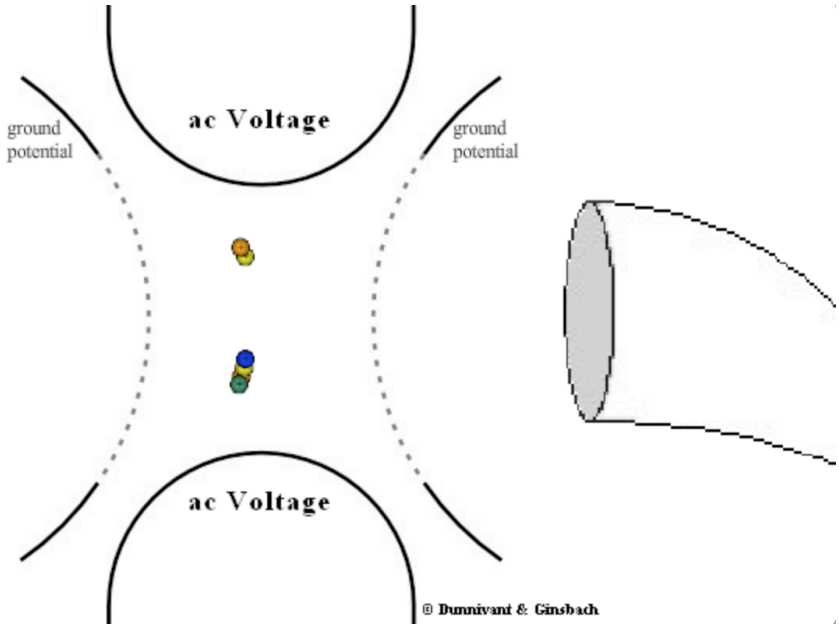


Figure 5.20 A Sample Resonance Ejection Scan

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 (section 5.5.8). The ability to isolate any given mass under several thousand 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 5.7 at this time for an illustration of how an ion trap mass filter contains and ejects ions of given mass to charge ratios.



Animation 5.7. Illustration of an Ion Trap Mass Filter. Go to the book's web page, download, and play An_5_7_Ion_Trap.mov

5.5.4 *Time-of-Flight (TOF) mass filter:* While time-of-flight mass filters were one of the first 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 MALDI systems) has renewed interest in time of flight systems. TOF is used exclusively with MALDI systems and also has other applications, as in HPLC where high molecular weight compounds are encountered.

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 MALDI or field desorption, the TOF functions easily as a mass analyzer. In sources that continually produce ions such as a GC system or an EI source, the use of a TOF is 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 chromatographic peak have been measured. (This type of ionization and slit pulsing will be shown in the animation below). The other way to interface EI with TOFs is to operate the EI source in a pulsing mode. This is

achieved by maintaining a constant negative polarity on the accelerator plate/slit, and pulsing the EI source. This method can also periodically introduce packets of ions into the TOF mass filter.

Whichever type of ionization and entry into the TOF mass filter is used the remainder of the process is the same. 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 similar 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.

$$KE = mv^2/2 \qquad \text{Eqn 5.13}$$

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

$$mv^2/2 = q\,V_S = z\,e\,V_S \qquad \text{Eqn 5.14}$$

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

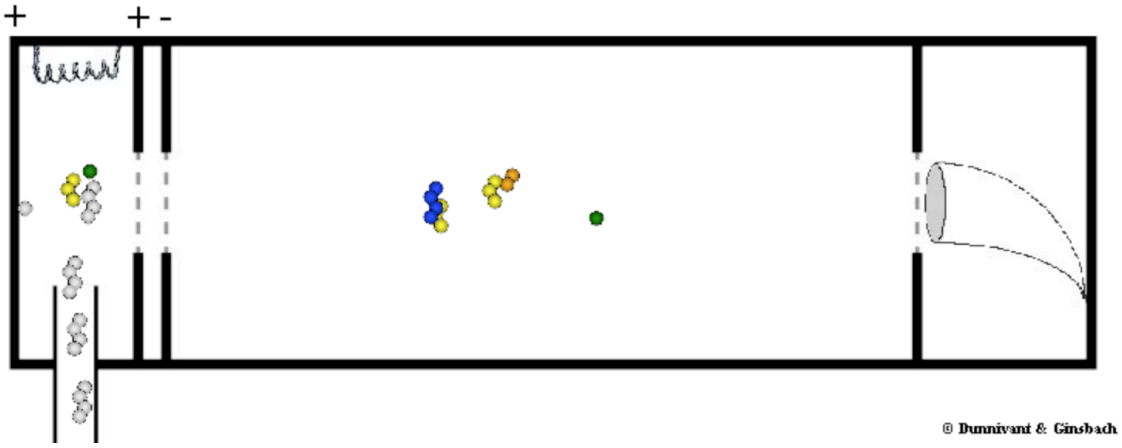
$$t = d/v \qquad \text{Eqn 5.15}$$

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

$$t^2 = \frac{m}{z}\left(\frac{d^2}{2V_s e}\right) \qquad \text{Eqn 5.16}$$

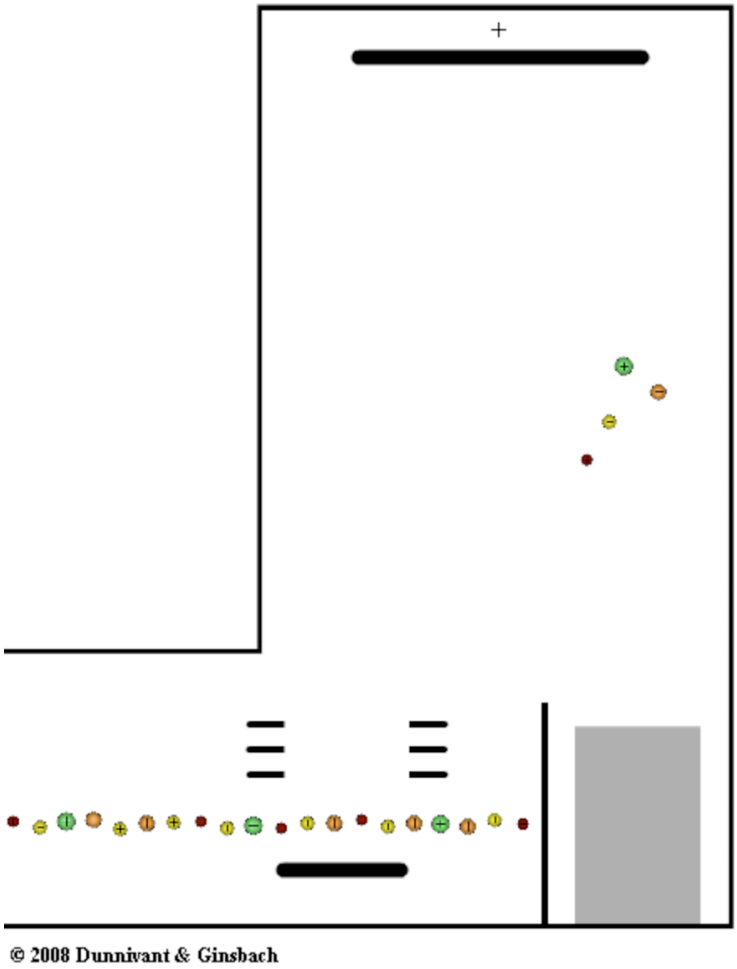
In a TOF mass analyzer, the terms in parentheses are constant, so the mass to charge of an ion is directly related to the time of travel. Typical times to traverse the field-free drift tube are 1 to 30 ms.

Advantages of a TOF mass filter include their simplicity and ruggedness and a virtually unlimited mass range. Additionally, virtually all ions produced in the ionization chamber enter the TOF mass filter and traverse the drift tube. 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 5.8 illustrates how a pulsed accelerator plate/slit acts as a gate for a TOF mass filter system.



Animation 5.8. Illustration of a Traditional TOF Mass Filter. Go to the book's web page, download, and play An_5_8_Linear_TOF.mov

Animation 5.9 illustrations how a pulsed accelerator plate/slit acts as a gate for a reflective TOF mass filter system. (The system shown is actually for the analysis of metal isotopes with an Inductively Coupled Plasma (ICP), but the reflective TOF works the same for organic analytes.



Animation 5.9. Illustration of a Reflective TOF Mass Filter. Go to the book's web page, download, and play An_5_9_Ref_TOF.mov

Ion Mobility Mass Spectrometry:

If you have been in an airport recently you have seen or your luggage has been analyzed by an Ion Mobility Spectrometer (IMS). Although originally developed by Earl W. McDaniel of Georgia Institute of Technology in the 1950s, IMS systems have gained popularity recently due to their versatility—they can designed for specific classes of compounds, they have excellent detection limits, and they can be manufactured to be light-weight and mobile.

The basic design is similar to the TOF mass filter. Important differences are that they use an easier ionization source, they can be operated at atmospheric pressure and therefore do not necessarily require pressurized gases or high vacuum pumps, and as a result of their atmospheric pressure sample introduction they have good detection limits. Samples are introduced at atmospheric pressure and ionized by corona discharge, atmospheric pressure

photoionization (APPI), electrospray ionization (ESI), or a radioactive source such as a small piece of ^{63}Ni or ^{241}Am, similar to the those used in ionization smoke detectors or GC electron capture detectors. The ionized analytes are then introduced to the drift tube by a gate valve similar to the one described earlier in this section for TOF mass filters. However, the IMS drift tube is different in that it can be operated at atmospheric pressure and is a counter current environment. The analytes travel from left to right in the one-meter drift tube due to a 10-30 kV potential difference between the inlet and exit. As the analytes are mobile due to the potential they travel through a buffer gas that is passed from right to left in the drift tube (and atmospheric gases are commonly used). Separation of different analytes is achieved due to each ion having a different mass, charge, size and shape (the ion mobility). As the ions are electrically drawn toward the detector, the ion's cross sectional area strikes buffer gases and its velocity is reduced based on its size and shape. Larger ions will collide with more buffer gas and be impeded, travel slower, and arrive at the detector after longer times in the drift tube. Detectors for IMS are usually relatively simple Faraday cups but better detection limits can be obtained with an EM.

The most common use of IMS is for volatile organic molecules. IMS has been expanded for use in gas, liquid, and super critical fluid chromatography.

5.5.5 *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 field (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.

5.5.6 Fourier Transform Ion Cyclotron – Mass Spectrometry: (by Nicole James)

Developed by Alan G. Marshall and Melvin B. Comisarow at the University of British Columbia, the use of FT-ICR MS first began in 1974 with approximately 235 instruments in use by 1998. FT-ICR MS has higher mass resolution and accuracy than any other MS system and can detect multiple mass-to-charge ratio

ions simultaneously. However, FT-ICR MS can be prohibitively expensive at $1-2 million for a standard instrument.

The general steps of an FT-ICR MS experiment are: (1) ion formation outside of the detector; (2) ion focusing and accumulation; (3) transportation of ions into a Penning trap; (4) selection of ions based on mass-to-charge ratio and ejection of these ions from the Penning trap; (5) excitation; (6) detection; (7) fast Fourier transform of the digital time-domain signal; (8) conversion of frequency to mass-to-charge ratio.

Ion-Cyclotron Motion

If a moving ion is exposed to a uniform magnetic field, it is subject to a force dependent on the mass, charge and velocity of the ion. If an ion does not collide with another particle and hit off its natural course, the magnetic field will bend the ion's path into a circular orbit.

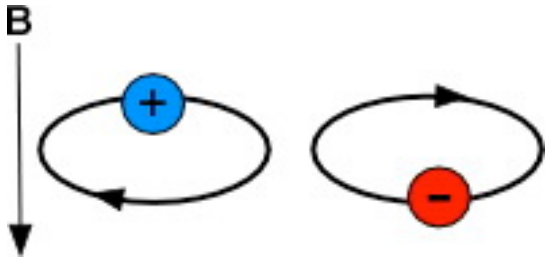


Figure 5.21a Illustration of a particle in a magnetic field.

The motion of the ion can be described by the equation below, where *w* is the unperturbed ion cyclotron frequency, B_0 is the magnetic field in Tesla, q is the charge in Coulombs, and *m* is the mass in micrograms.

$$w = \frac{qB_o}{m}$$

This equation can be rearranged into the following equation where *v* is the velocity, and *z* is the charge of the ion in units of elemental charge (e.g., +1, +2, etc).

$$v = \frac{w}{2\pi} = \frac{1.5356 \text{ x } 10^7 \text{ } B_o}{m/z}$$

It is important to note that the above equation is dependent on only the mass-to-charge ratio of the ion and not its velocity. This makes ion-cyclotron resonance especially useful in mass spectrometry, as one does not need to focus translational energy—which requires longer experiment times, larger apparatus and more powerful electronics—in order to obtain high-accuracy results.

The radius of the circle an ion makes when exposed to the magnetic field can be found by the equation below, where *r* is radius in meters, and *T* is the temperature in Kelvin:

$$r = \frac{1.3365 \text{ x } 10^{-6}}{zB_0} \sqrt{mT}$$

One can see from the above equation that an ion with a mass of 100 amu and a charge of +1 in a magnetic field of 1 Tesla at room temperature (298 K) would have a radius of 0.2 mm; the same ion with triple the magnetic field (3 T) at room temperature would have a radius of 0.077 mm. Thus, ions can be easily confined to a relatively small orbit by a reasonable magnetic field; this is called ion trapping and is vital to ICR-MS because the longer (approximately 1s) experiment times require one to be able to retain the ions in a designated space. Additionally, a 3T magnetic field is easily attainable for commercially available electronics. The largest FT ICR MS built as of 2010 can attain a magnetic field of 15T, allowing one to confine an ion with an m/z value of 60,000.

Ion Cyclotron Excitation and Detection

A number of ions at a specific mass-to-charge ratio spinning in an ion-cyclotron orbit does not, itself, generate an observable electric signal, because (a) the ions were randomly placed (i.e, incoherent; ions are spread throughout the radio of orbit) as they began orbiting, meaning that an ion at a specific position will have its charge cancelled out by an ion half an orbit away from it, leaving no net electrical current, and (b) the radius of the orbits are generally too small to be detectable, even if all ions were in the same phase. Thus, ions must be excited in order to be detected.

Particles in an ion-cyclotron orbit can be excited by applying an oscillating or rotating uniform electric field at or near the frequency of ions of a given mass-to-charge ratio. This excitation can be used for three purposes: (1) accelerating the ions into a larger orbital radius for detection, (2) accelerating the ions to a larger orbital that is ejected from the ion trap, and (3) increasing the kinetic energy of an ion to the point that it further ionizes or reacts with another molecule. For the purposes of this text, excitation in order to accelerate the ions for detection is most significant.

Applying an oscillating or rotating radio-frequency electric field in resonance with (at the same frequency as) a specific m/z value or range applies a force on the ion(s) that continuously enlarges the circular orbit of the ion(s) at one point—in other words, the orbiting ions begin to spiral outward. Ions of different types will spiral outward at different rates. The post-excitation orbit for

an ion excited for a period of time, *t*, is shown in the following equation, where E_0 is the applied electric field and B_0 is the magnetic field:

$$r = \frac{E_0 t}{2B_o}$$

The fact that the above equation is independent of the mass-to-charge ratio of the ion means that all ions can be excited by a radio-frequency electric field to enlarged ion-cyclotron orbits for detection. This simultaneous detection vastly decreases both the time an experiment will take and the amount of analyte required.

When a group of ions with the same mass-to-charge ratio are excited, they are pushed off-axis due to their spiraling nature. By pushing the ions off axis, not all ions have a "partner" ion half a cycle away—the ions are considered to be "cohered." A cohered packet of orbiting ions causes a difference in current between opposing detection plates within the ion trap; this differential current can be modeled as an "image" current opposing the current on the detection plates; this image current is proportional to the number of coherent orbiting ions. This is the ICR signal; the ICR signal increases linearly with increasing ion-cyclotron radius after excitation and with increasing ion charge. Throughout most of the frequency range possible on the instrument, the signal-to-noise ratio (S/N) is proportional to the differential current observed. The number of ions required for a S/N ratio of 3:1 on a standard instrument using standard parameters is approximately 190 ions. Other detection processes have been designed to such high accuracy and detection that they are able to detect a single ion and have been used to corroborate the theory that protons and anti-protons do, in fact, have the same mass (Gabrielse et al, 1990).

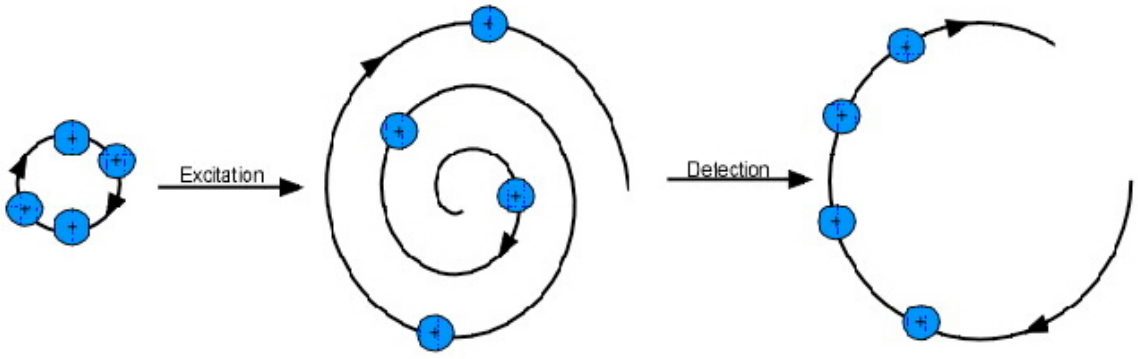


Figure 5.21b Excitation and Detection of an Ion.

The Penning Trap

The most common ion trap used in FT-ICR MS is the Penning trap, designed in the 1950s by Hans Georg Dehmelt, who named it after Frances Michel Penning for his work on the Penning gauge. The ion-cyclotron motion induced by a radial magnetic field contains ions radially, but it is necessary to add an axial electric field in order to trap the ions axially. Thus, the motion of an ion inside a Penning trap is essentially the combination of three distinct motions: the cyclotron, “magnetron” (a component of ion-cyclotron motion), and the axial motion. The axial containment is accomplished by introducing two “end-cap” electrodes. The end-cap electrodes are coupled by capacitance, which allows for a nearly perfect rf electric field to be used for the ion-cyclotron excitation without any negative effects on other electronics. Opposing plates with an electric field applied across them within the Penning trap are used as detector plates.

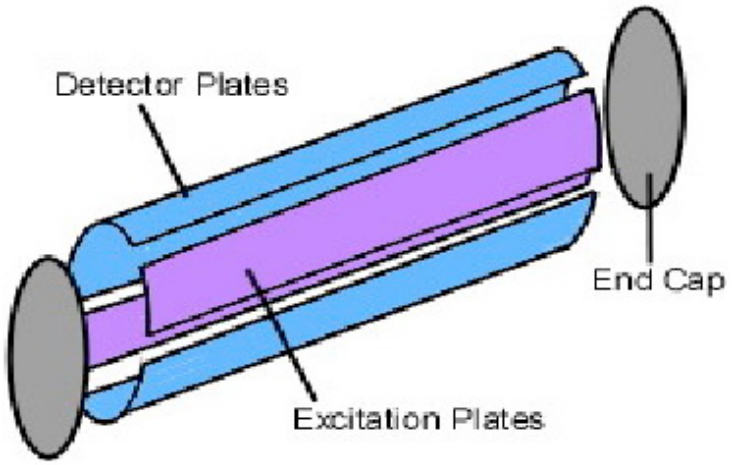


Figure 5.21c Diagram of a Penning Trap.

Analysis of Results

The signal detected by an experiment is in units of current per time. To extract mass-to-charge data, one must apply a Fourier transform. In general, a Fourier transform (FT) takes a time-based signal and converts it into a frequency-based plot. Since the initial function is a function of time, it is typically called the *time domain*; the frequency plot is called the frequency domain, or the *frequency domain representation* of the initial function. More specifically, the Fourier transform uses the fact that almost any function can be degraded into a sum of sine and cosine waves; each component sine and/or cosine wave represents a periodic component of the data. By finding each component sine or cosine wave, one can make a frequency plot by representing a specific sine or cosine wave as a peak on a plot of amplitude versus the frequency of the wave. The sharper the

peak, the more “exact” the periodicity is; in most real-life applications, the peak will be somewhat broad—not just a vertical line.

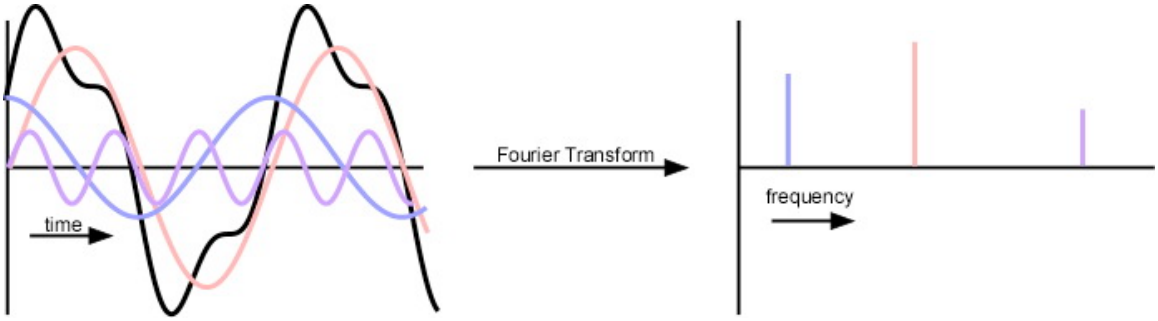


Figure 5.21d Graphic Representation of the Fourier-Transform Process where a time domain signal is transformed to a frequency output.

A Fourier-transform of the (time-domain) ICR response results in a frequency plot that can be mass-corrected to result in a mass spectrum. Obtaining this mass spectrum with most other types of MS would have required sweeping slowly across the entire range of mass-to-charge ratios; being able to quickly and simultaneously detect all mass-to-charge ratios decreases the time, effort and supplies that must be used to test a sample. In addition, the greatly increased resolution means that FTICR-MS will continue being an extremely powerful instrument.

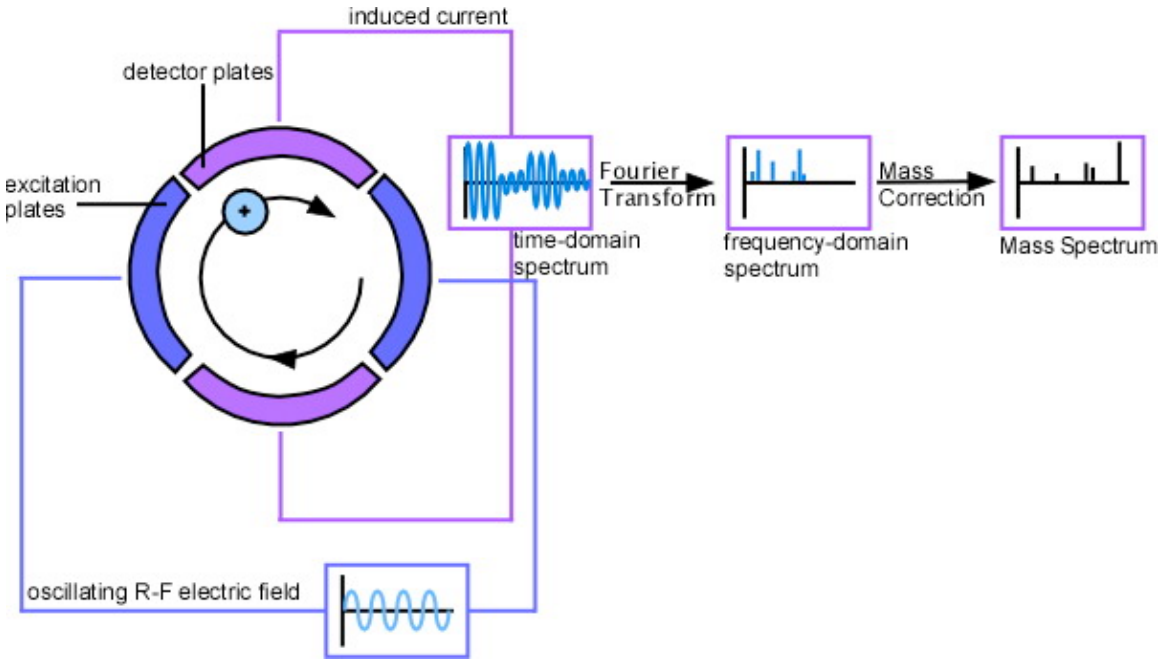


Figure 5.21e Overall Schematic of an Ion Cyclotron Mass Spectrometer.

5.5.7 Orbitrap Analyzers (by Nicole James)

Designed in 2005 by Alexander Makarov, the Orbitrap mass spectrometer features a mass resolution of up to 150,000, high mass accuracy (2-5ppm, compared with approximately 20ppm for quadrapole systems), a mass-to-charge ratio range of 6,000 and a dynamic range larger than 1,000.

The Orbitrap works similarly to an FT ICR-MS: all ions are identified simultaneously by reading an image current of oscillations that are unique to a given mass-to-charge ratio and a Fourier transform is applied to the data to isolate individual signals. However, the Orbitrap requires no magnet, no RF field, and no excitation sequence. Despite this, Orbitrap systems generally cost at least $600,000.

Ions are first ionized by a given source; given the large m/z range, Orbitrap systems are often used to study biological molecules such as proteins, peptides, oligsaccharides—consequently, one of the most common ionization methods is ESI. The ions are then transported to a storage cell, generally a storage quadrapole, which is kept at a vacuum near 10^{-3} mbar. A series of transfer lenses gradually increases the electric field experienced by the ions until they are at the level of the Orbitrap.

After ions have been transferred into the Orbitrap, the system uses only electrostatic (DC) fields. The Orbitrap itself is composed of an outer “barrel“ electrode, an inner “spindle” electrode, and two endcap electrodes. Upon introduction into the Orbitrap, stable ion trajectories will result in orbiting around the center electrode while also oscillating in the z-direction. The motion in the z-direction can be described as an harmonic oscillator, which is described in equation 5.5.6.1, where ω is oscillation frequency, z is the ion charge, m is the ion mass and k is the field curvature.

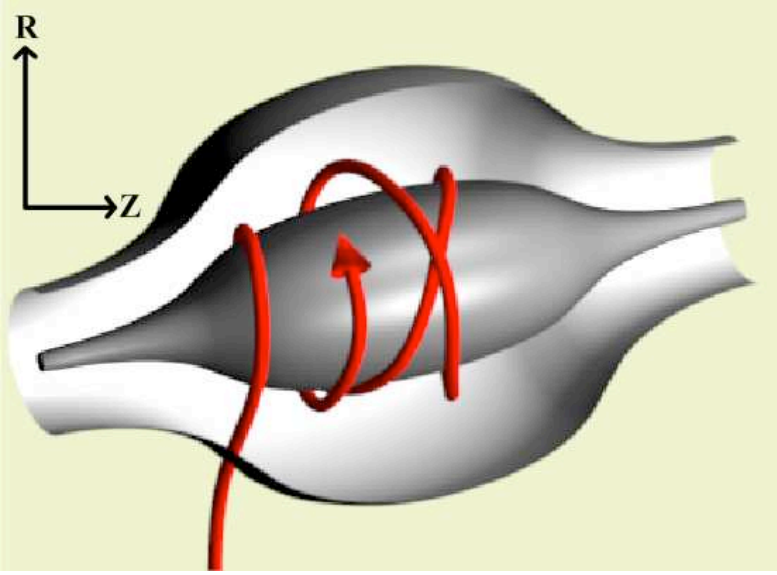


Figure 5.22 The Orbitrap (reprinted from WikiPedia via the *GNU Free Documentation License*)

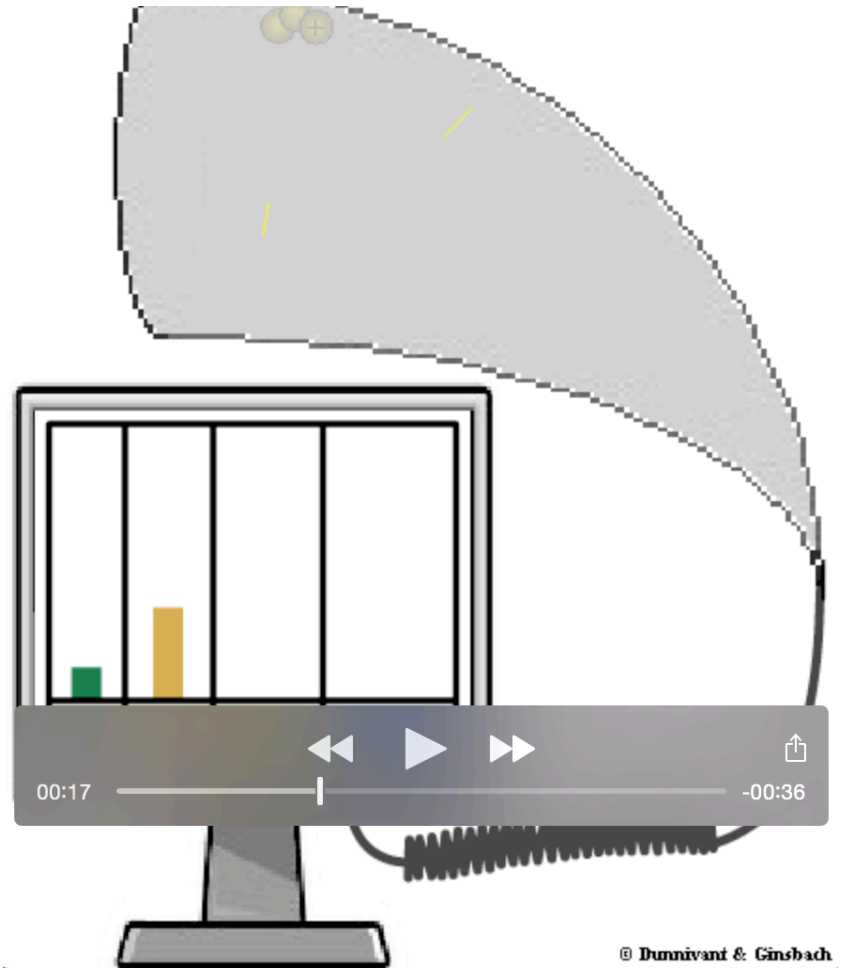
While the frequency of orbiting the central electrode is also dependent on the ion's mass-to-charge ratio, this frequency is also dependent on the ion's energy and when it was introduced into the Orbitrap, whereas oscillations in the z-direction are independent of energy and any initial parameters. The oscillations in the z-direction are read by the image current produced on the end-cap electrodes. While all ions of a given mass to charge ratio oscillate in phase for hundreds of thousands of oscillations, small imperfections in the Orbitrap or orbital shape, along with occasionally collisions with background gas molecules (despite the 10^{-10}mbar vacuum) can result in the loss or displacement of some ions, ultimately resulting in a slow decrease in the intensity of the signal until it is completely lost in instrument noise. This results in a free induction decay (FID), similar to that which is acquired in NMR analysis. A Fourier Transform of the FID results in a mass spectrum.

5.5.8 *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). Most often a soft ionization source, such as chemical ionization, is used in the first MS and allows for selection of the molecular ion in the first MS, while a harder ionization is used in the second MS to create fragments. A subsequent MS will select for a specific ion fragment from the second MS and further fragment it for identification. This technique allows a molecular ion (or ion fragment) to be isolated in the first MS, subsequently fragmented in the second and third MS, and identified based on its final fragment pattern. You should be able to see the confirmatory nature of this technique.

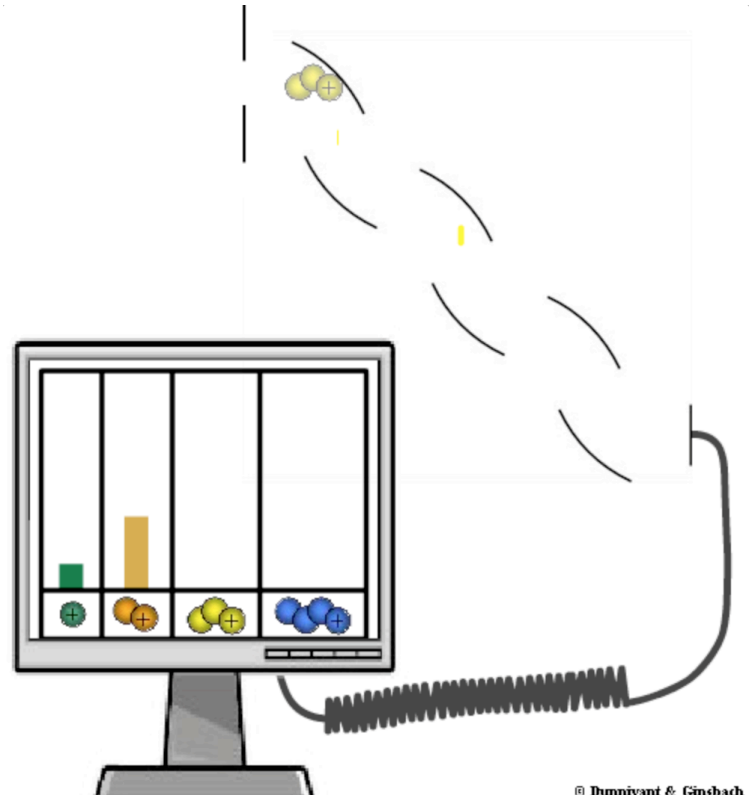
Mass filters of choice for use in tandem include magnetic sector, electrostatic, quadrupole, and ion trap systems. In the absence of HPLC or GC introduction, tandem MS offers many of the same advantages of a single GC-MS or HPLC-MS system but it is much faster since the analyst does not have to wait on the chromatography portion of the analysis. For example, chromatograph separations take from minutes to hours prior to entry into a MS, while tandem MS systems (without GC) require only milliseconds. But of course, this saving in time is considerably more expensive than simple chromatographic-based MS systems.

5.6 Ion Detectors

Once the analytes have been ionized, accelerated, and separated in the mass filter, they must be detected. This is most commonly completed with an electron multiplier (EM), much like the ones 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). EMs for MS systems can be a series of discrete dynodes as in the photomultiplier or they can be continuous in design. Most commonly, continuous EMs are used. Continuous EMs are horn shaped and are typically 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. Electrical 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 1.10 illustrates the response of a continuous electron multiplier as ions, separated in a mass filter, strike its surface.



Animation 5.10. Illustration of a Continuous-Dynode Electron Multiplier. Go to the book's web page, download, and play An_5_10_Con'tDetector.mov



Animation 5.11. Illustration of a Discrete-Dynode Electron Multiplier. Go to the book's web page, download, and play An_5_11_Descrete_EM.mov

Another form of MS detector is the Faraday Cup that 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.

5.7 Three-Dimensional Aspects of GC-MS

Typical chromatographic peaks were illustrated in earlier chapters. But as each chromatographic peak enters the MS it is fragmented and separated into a series of ion fragments. When graphed together on an x, y, and z plot, the x-axis represents time and traces the arrival of each compound at the chromatographic detector and the z-axis represents the total detector response that is related to analyte concentration. The mass-to-charge spectrum of each chromatographic peak is represented by a series of lines that are parallel to the y-axis and show the arrival of molecular fragments at the MS detector. Again, detector response and concentration are represented by the height of each peak. This is illustrated for one chromatographic peak in Figure 5.22.

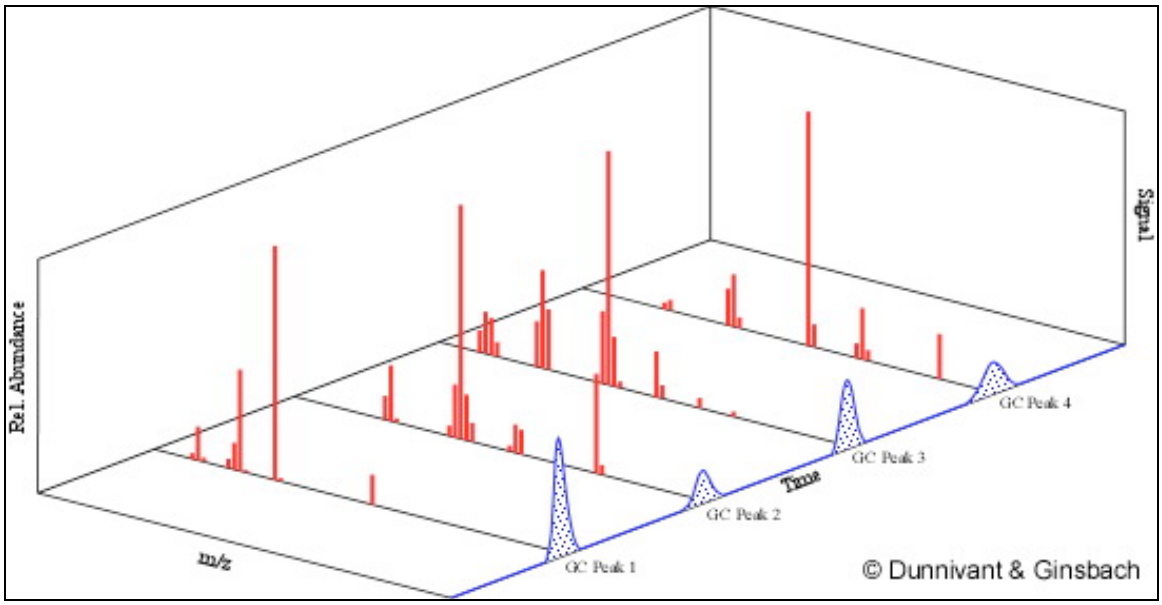


Figure 5.23. The Three-Dimensional Nature of a GC-MS Analysis.

5.8 Summary

In this chapter we illustrated the utility of combining chromatography and MS systems. A variety of possible components provide for interesting instruments that can be used to analyze a broad range of analytes. Hard and soft ionizations techniques provide for the determination of the molecular weight of the analyte, as well as unique fragmentation patterns for confirmational identification of an unknown chemical structure. More inexpensive instruments, such as quadrupole and time of flight mass spectrometers, allow only unit resolution of ions while double focusing instruments yield the determination of differences with resolution of four decimal points in masses. Mass spectrometry, like NMR, is one of the most powerful techniques available to chemists and it is becoming more and more important. While most of the instruments presented in the chapter have detection limits in the sub parts per million range, extremely lower detection limits (10^{-15} moles) have been obtained in research-grade instruments.

A summary of mass filters and their characteristics is given below in Table 5.2.

Table 4.2 Summary of Mass Filter Features. Source: Company Literature and 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			
Ion Mobility	50	Low ppm	$40,000
Single Quadrupole	250-500	low ppb – high ppt	$80 000 - $100 000
Ion Trap	1 000 – 10 000	ppb	$250 000 - $300 000
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 Ion Cyclotron	200 000 – 1 000 000	ppb	$2 000 000 +
New Mass Filters			
Magnetic Sector / Multi-collector with the Mattauch-Herzog Geometry	~500	high ppb	$350 000 - $400 000
Proton Transfer Reaction Ionization Chamber	Depends on type of mass filter	ppt	$120 000
Orbital Trap (Electrostatic Ion Trap)	150 000 – 200 000	ppb	$600 000 (currently only available with HPLC)

5.9 Questions

1. Why are most mass filters maintained at a low pressure?

2. List the common ways samples are introduced into a MS system.

3. How can solid samples be introduced into a MS?

4. Draw and explain how the interface between a GC and a MS works.

5. Why do capillary columns, versus packed columns, work best for MS interfaces?

6. Explain the difference between hard and soft ionization in GC-MS.

7. Why does soft ionization reduce the fragmentation of analytes in GC-MS?

8. Write the chemical reactions occurring when methane is used in soft ionization.

9. Draw and explain how the interface between a LC and a MS works.

10. What is the major problem with interfacing LC (ESI) to MS?

11. Explain how MALDI works. What types of samples is it commonly used for. What type of MS is it commonly coupled with?

12. Draw and explain how the interface between a CE (ESI) and a MS works.

13. Explain resolution with respect to mass filters. Give relevant resolution numbers.

14. Draw and explain how a magnetic sector mass filter works.

15. Draw and explain (in detail) how a quadrupole mass filter works.

16. The governing equation of the quadrupole mass filter consists of a six-parameter differential equation. Which two parameters are used to control the mass filter?

17. What is the purpose of the dc voltage in the quadrupole MS?

18. What is the purpose of the ac cycle in the quadrupole MS?

19. How does the low mass and high mass filters work to create a stable cation region in the quadrupole MS?

20. Explain the mass scan line in the quadrupole MS figures.

21. What is the purpose of sweeping the dc-ac voltages?

22. Extend the concepts of a linear quadrupole mass filter, explained above, to explain how the quadrupole ion trap mass filter works.

23. How is the mass range of a quadrupole ion trap mass filter extended?

24. Explain the concept of resonance ejection in ion trap mass filters.

25. Draw and explain how a time-of-flight mass filter works.

26. Contrast traditional TOF and ion mobility MS.

27. Draw and explain how a PTR-MS works.

28. Give a brief explanation of how an Ion Cyclotron works.

29. Draw and explain how a double focusing mass filter works. What are its advantages?

30. What is tandem mass spectrometry?

31. What types of detectors are used in mass spectrometry?

32. Use the date in Table 5.2 to contrast the various types of mass filters. Which is the most economical? Which has the best mass resolution?

5.10 References

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