Summary of the characteristics of different mass analyzers

All mass spectrometers combine ion formation, mass analysis, and ion detection. This discussion is concerned with how various mass analyzers are used to separate ions according to their mass-to-charge ratio. Each mass analyzer has its own special characteristics and applications and its own benefits and limitations. The choice of mass analyzer should be based upon the application, cost, and performance desired. **There is no ideal mass analyzer that is good for *all* applications.** For an excellent and more complete discussion of mass analyzers, see "The Ideal Mass Analyzer: Fact or Fiction?" (Curt Brunnee, <u>Int. J. Mass Spectrom. Ion Proc.</u> 76 (1987), 125-237.

Note that different mass analyzers use different resolution definitions. See <u>"How Resolution is Defined"</u> for a discussion of this topic.

Note also that a complete discussion of MS/MS methods is beyond the scope of this essay, but some comments about MS/MS are provided here in the context of comparing different mass analyzers strengths and weaknesses.

General: The effect of electromagnetic fields on ions

All commonly used mass analyzers use electric and magnetic fields to apply a force on charged particles (*ions*). The relationship between force, mass, and the applied fields can be summarized in Newton's second law and the Lorentz force law:

$\mathbf{F}$ = m$\mathbf{a}$ (Newton's second law)

$\mathbf{F}$= e($\mathbf{E}$+ $\mathbf{v}$ x $\mathbf{B}$) (Lorentz force law)

where

- $\mathbf{F}$ is the force applied to the ion,
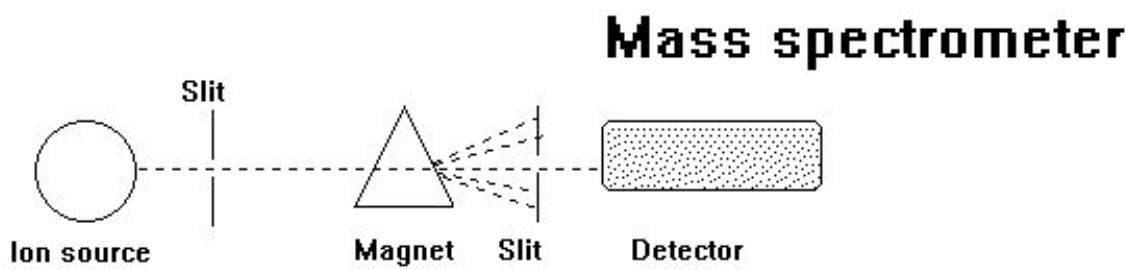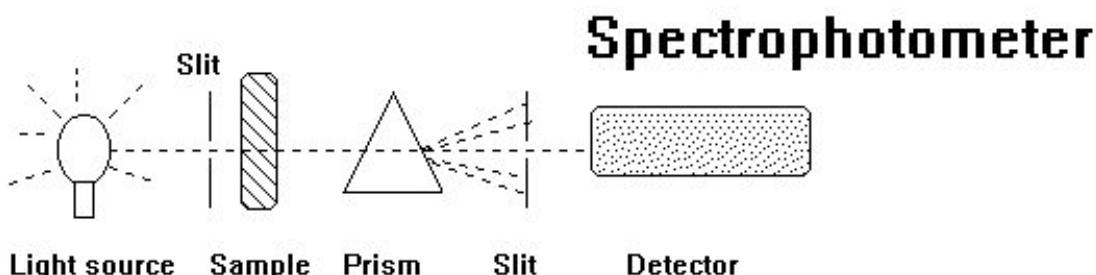- m is the mass of the ion,
- $\mathbf{a}$ is the acceleration,

- . **e**is the ionic charge,
- . **E** is the electric field
- . **v x B**is the vector cross product of the ion velocity and the applied magnetic field

From Newton's second law, it is apparent that the force causes an acceleration that is mass-dependent, and the Lorentz force law tells us that the applied force is also dependent on the ionic charge. Therefore, it should be understood that mass spectrometers separate ions according to their *mass-to-charge ratio* (*m/z*) rather than by their mass alone.

Scanning Mass Analyzers

A scanning mass analyzer is analogous to the equipment used in optical spectroscopy for analyzing the color content of visible light. In optical spectroscopy, one starts with visible light which is composed of individual colors (different wavelengths of light) that are present at different intensities. A prism separates the light into its different wavelengths, and a slit is used to select which wavelength reaches the detector. The different wavelengths are then swept (scanned) across the detector slit and the light intensity is recorded as a function of time (wavelength).

In scanning mass spectrometry, one starts with a mixture of ions having different mass-to-charge ratios and different relative abundances. Electromagnetic fields separate the ions according to their mass-to-charge ratios, and a slit is used to select which mass-to-charge ratio reaches the detector. The different mass-to-charge ratios are then scanned across the detector slit and the ion current is recorded as a function of time (mass).

Spectrophotometer

Light source   Sample   Prism   Slit   Detector

Mass spectrometer

Ion source   Slit   Magnet   Slit   Detector

Both magnetic sector and quadrupole mass spectrometers can be "jumped" from one target mass to another instead of scanning over a given mass range. This *selected ion monitoring (SIM)*method is used to improve sensitivity for quantitative analysis ad target compound identification by monitoring only the masses of interest for specific compounds. In contrast to scanning analyses, no time is wasted making measurements of the baseline noise between peaks or measuring ions that are not relevant to the analysis. However, this is only useful when the target masses are known in advance.
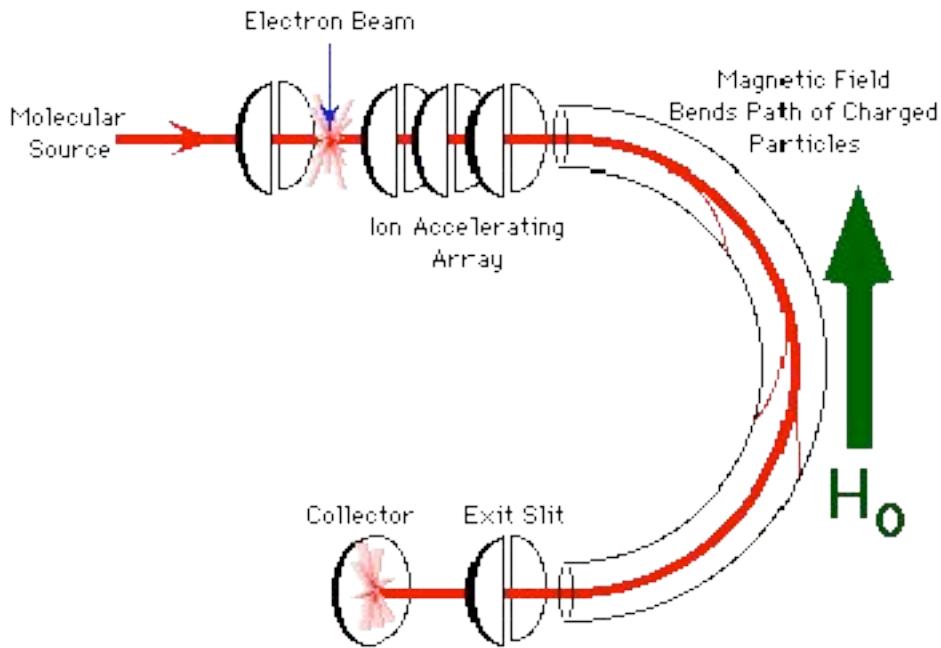
Magnetic Sector Mass Spectrometers

Principal of operation

The analogy between scanning mass spectrometry and scanning optical spectroscopy is most apparent for magnetic sector mass spectrometers.

In a magnetic deflection mass spectrometer, ions leaving the ion source are accelerated to a high velocity. The ions then pass through a **magnetic sector** in which the magnetic field is applied in a direction perpendicular to the direction of ion motion. From physics, we know that when acceleration is applied perpendicular to the direction of motion of an object, the object's velocity remains constant, but the object travels in a circular path. Therefore, the magnetic sector follows an arc; the radius and angle of the arc vary with different ion optical designs.

A magnetic sector alone will separate ions according to their mass-to-charge ratio. However, the resolution will be limited by the fact that ions leaving the ion source do not all have exactly the same energy and therefore do not have exactly the same velocity. This is analogous to the *chromatic aberration* in optical spectroscopy. To achieve better resolution, it is necessary to add an **electric sector** that focuses ions according to their kinetic energy. Like the magnetic sector, the electric sector applies a force perpendicular to the direction of ion motion, and therefore has the form of an arc.

A schematic representation of the JEOL MStation double-focusing mass spectrometer is shown below. For historical reasons, this is referred to as a "reverse-geometry" magnetic sector mass spectrometer, which means that the magnetic sector precedes the electric sector,

The simplest mode of operation of a magnetic sector mass spectrometer keeps the accelerating potential and the electric sector at a constant potential and varies the magnetic field. Ions that have a constant kinetic energy, but different mass-to-charge ratio are brought into focus at the detector slit (called the 'collector slit") at different magnetic field strengths.

The dependence of mass-to-charge ratio on the electric and magnetic fields is easily derived. All ion formed in the ion source are accelerated to a kinetic energy, T of:

$$T = eV = \frac{mv^2}{2}$$

Solving for the velocity, v, we get:

$$v = \sqrt{\frac{2eV}{m}}$$

From the Lorentz force law, the magnetic field applies a force evB that must be equal to the centripetal force mv**2/r as the ions move in an arc through the magnetic sector:

$$evB = \frac{mv^2}{r}$$

Substituting for v, we arrive at the working equation for a magnetic sector mass spectrometer:

$$\frac{m}{e} = \frac{B^2 r^2}{2V}$$

As mentioned previously, the electric sector is usually held constant at a value which passes only ions having the specific kinetic energy., V. Therefore the parameter that is most commonly varied is B, the magnetic field strength. The magnetic field is usually scanned exponentially or linearly to obtain the mass spectrum. A magnetic field scan can be used to cover a wide range of mass-to-charge ratios with a sensitivity that is essentially independent of the mass-to-charge ratio.

An alternative is to hold B constant and scan V. The electric sector potential tracks the accelerating voltage. This has the advantage that the electric field is not subject to hysteresis, so the relationship between mass-to-charge ratio and accelerating voltage is a simple linear relationship. The disadvantage of an accelerating voltage (electric field) scan is that the sensitivity is roughly proportional to the mass-to-charge ratio.

The maximum ion transmission and sensitivity occur at the maximum working accelerating voltage for a given magnetic sector mass spectrometer. The effective mass range of the mass spectrometer can be increased by decreasing the accelerating voltage, with a sensitivity that is roughly proportional to the accelerating voltage.

Focal-plane (array) detectors can detect a range of masses simultaneously. This provides a multi-channel advantage that can improve the sensitivity for magnetic sectors, and detection limits can be improved if the analysis is limited by the analyte ion current instead of the chemical background level. This is the case for experiments such as MS/MS, electrospray ionization, and field desorption. Array detectors can be used with pulsed ionization methods, but the array detectors

for commercial magnetic sector mass spectrometers can only detect a portion of the entire mass range at any given instant.

The resolving power of a magnetic sector mass spectrometer is determined by the slit widths. Higher resolution is obtained by decreasing the slit widths, and thereby decreasing the number of ions that reach the detector.

Linked scans, in which the magnetic and electric fields are scanned together, can be used to perform MS/MS experiments (product, precursor, and neutral loss) with a double focusing mass spectrometer.

Benefits

Double focusing magnetic sector mass analyzers are the "classical" model against which other mass analyzers are compared.

- Classical mass spectra
- Very high reproducibility
- Best quantitative performance of all mass spectrometer analyzers
- High resolution
- High sensitivity
- High dynamic range
- Linked scan MS/MS does not require another analyzer
- High-energy CID MS/MS spectra are very reproducible

Limitations

- Not well-suited for pulsed ionization methods (e.g. MALDI)
- Usually larger and higher cost than other mass analyzers
- Linked scan MS/MS gives either limited precursor selectivity with unit product-ion resolution, or unit precursor selection with poor product-ion resolution

Applications

- All organic MS analysis methods
- Accurate mass measurements
- Quantitation
- Isotope ratio measurements

Quadrupole Mass Spectrometers

Principal of Operation

The quadrupole mass analyzer is a "mass filter". Combined DC and RF potentials on the quadrupole rods can be set to pass only a selected mass-to-charge ratio. All other ions do not have a stable trajectory through the quadrupole mass analyzer and will collide with the quadrupole rods., never reaching the detector.

A crude schematic of a quadrupole mass filter is shown below:
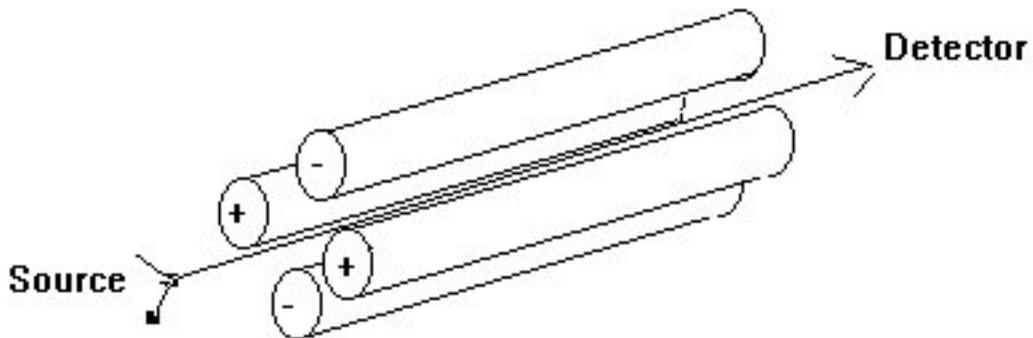
A derivation of the working equations for a quadrupole mass analyzer is beyond the scope of this discussion, but it is based upon a second-order differential equation known as the Mathieu equation. See R. E. March, R. J. Hughes and J. F. Todd, "Quadrupole Storage Mass Spectrometry", volume 102 of *Chemical Analysis,* Wiley, 1989 for a good description of the theory behind both quadrupole mass filters and quadrupole ion traps.

The operation of a quadrupole mass analyzer is usually treated in terms of a *stability diagram* that relates the applied DC potential (U) and the applied RF potential (V(t)) and the RF frequency (omega) to a stable vs. unstable ion trajectory through the quadrupole rods. A qualitative representation of a stability diagram for a given mass m is shown below: a and q are parameters that are proportional to *U/m* and *V/m* respectively:
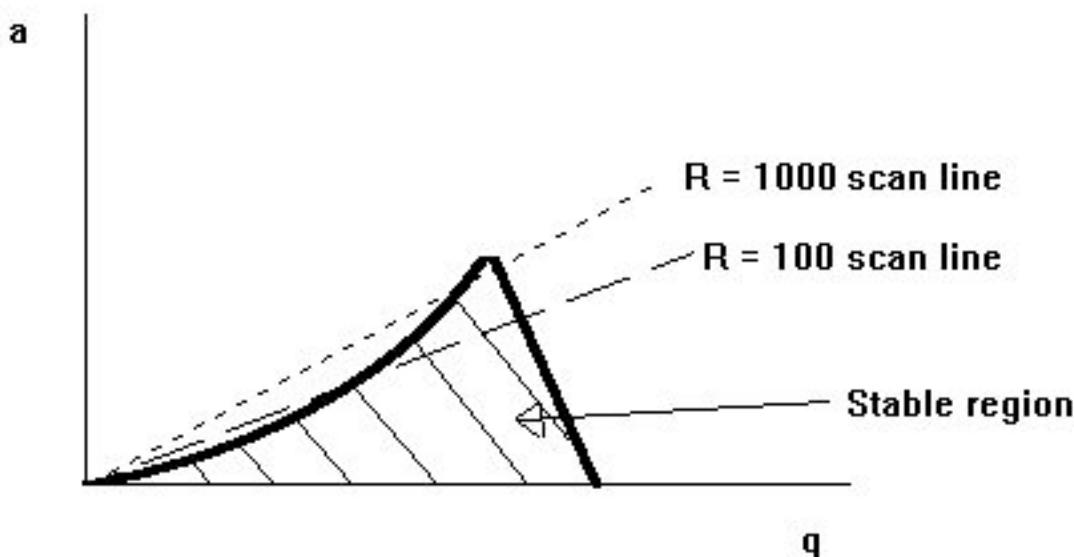
Changing the slope of the scan line will change the resolution. Increasing the resolution decreases the number of ions that reach the detector (the region at the apex of the stable region that is bounded by the scan line). Good resolution also depends on the quality of the machining for the quadrupole rods.

Quadrupole rods can have other functions besides their use as a mass filter. An RF-only quadrupole will act as an ion guide for ions within a broad mass range. For example, the collision region of a triple quadrupole mass spectrometer uses an RF ion guide. A DC-only quadrupole is used as a lens element in some ion optic designs (such as JEOL's magnetic sector mass spectrometers).

Benefits

- Classical mass spectra
- Good reproducibility
- Relatively small and low-cost systems
- Low-energy collision-induced dissociation (CID) MS/MS spectra in triple quadrupole and hybrid mass spectrometers have efficient conversion of precursor to product

Limitations

- Limited resolution
- Peak heights variable as a function of mass (mass discrimination). Peak height vs. mass response must be 'tuned'.
- Not well suited for pulsed ionization methods

.   Low-energy collision-induced dissociation (CID) MS/MS spectra in triple quadrupole and hybrid mass spectrometers depend strongly on energy, collision gas, pressure, and other factors.

Applications

.   Majority of benchtop GC/MS and LC/MS systems
.   Triple quadrupole MS/MS systems
.   Sector / quadrupole hybrid MS/MS systems

Time-of-Flight Mass Analyzers

Principal of Operation

Linear

A time of flight mass spectrometer measures the mass-dependent time it takes ions of different masses to move from the ion source to the detector. This requires that the starting time (the time at which the ions leave the ion source) is well-defined. Therefore, ions are either formed by a pulsed ionization method (usually matrix-assisted laser desorption ionization, or MALDI), or various kinds of rapid electric field switching are used as a 'gate' to release the ions from the ion source in a very short time.

Recall that the kinetic energy of an ion leaving the ion source is:

$$T = eV = \frac{mv^2}{2}$$

The ion velocity, v, is the length of the flight path, L, divided by the flight time, t:

$$v = \frac{L}{t}$$

Substituting this expression for v into the kinetic energy relation, we can derive the working equation for the time-of-flight mass spectrometer:

$$\frac{m}{e} = \frac{2Vt^2}{L^2}$$

or, rearranging the equation to solve for the time-of-flight:

$$t = L\sqrt{\frac{m}{e}\frac{1}{2V}}$$

Reflectron

The ions leaving the ion source of a time-of-flight mass spectrometer have neither exactly the same starting times nor exactly the same kinetic energies (recall the "chromatic aberrations" discussed for magnetic sector mass spectrometers). Various time-of-flight mass spectrometer designs have been developed to compensate for these differences. A reflectron is an ion optic device in which ions in a time-of-flight mass spectrometer pass through a "mirror" or "reflectron" and their flight is reversed.

A linear-field reflectron allows ions with greater kinetic energies to penetrate deeper into the reflectron than ions with smaller kinetic energies. The ions that penetrate deeper will take longer to return to the detector. If a packet of ions of a given mass-to-charge ratio contains ions with varying kinetic energies, then the reflectron will decrease the spread in the ion flight times, and therefore improve the resolution of the time-of-flight mass spectrometer.

A curved-field reflectron ensures that the ideal detector position for the time-of-flight mass spectrometer does not vary with mass-to-charge ratio. This also results in improved resolution for time-of-flight mass spectrometers.

Pulsed
Laser

Deflector

Target

Acceleration
and ion focus

Detector

Reflectron
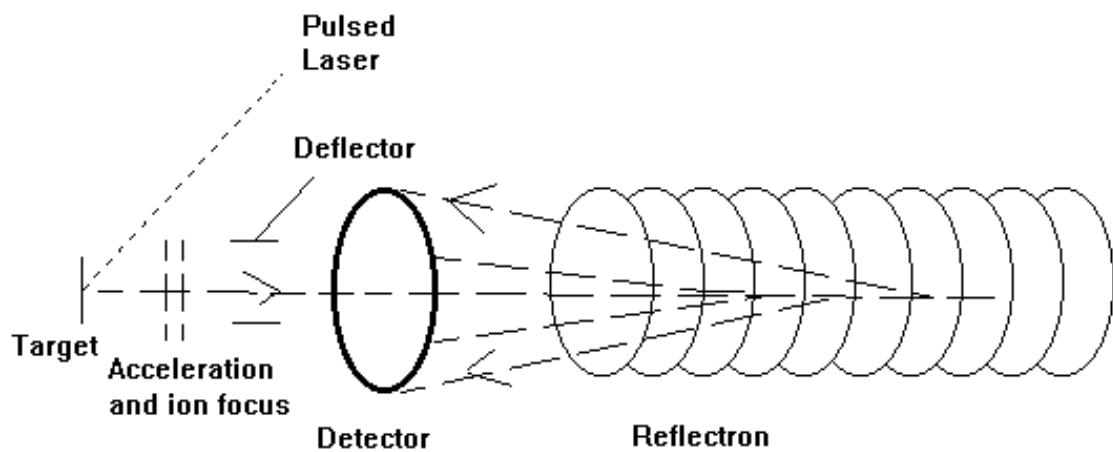
Benefits

- . Fastest MS analyzer
- . Well suited for pulsed ionization methods (method of choice for majority of MALDI mass spectrometer systems)
- . High ion transmission
- . MS/MS information from post-source decay
- . Highest practical mass range of all MS analyzers

Limitations

- . Requires pulsed ionization method or ion beam switching (duty cycle is a factor)
- . Fast digitizers used in TOF can have limited dynamic range
- . Limited precursor-ion selectivity for most MS/MS experiments

Applications

- . Almost all MALDI systems
- . Very fast GC/MS systems

Trapped-Ion Mass Analyzers

There are two principal trapped-ion mass analyzers: three-dimensional quadrupole ion traps ("dynamic" traps), and ion cyclotron resonance mass spectrometers ("static" traps). Both operate by storing ions in the trap and manipulating the ions by using DC and RF electric fields in a series of carefully timed events. This provides some unique capabilities, such as extended MS/MS experiments, very high resolution, and high sensitivity. The tradeoff is that trapping the ions for long periods of time (milliseconds to *days*) provides plenty of time for the ions fall apart spontaneously (unimolecular decomposition), to experience undesirable interactions with other ions (space charge effects), neutral molecules (ion-molecule reactions), or perturbations in the ion motion due to imperfect electric fields. This can lead to artifacts and unexpected changes in the mass spectrum (so called "non-classical mass spectra").

Ion Cyclotron Resonance

Principal of Operation

Ions move in a circular path in a magnetic field. The *cyclotron frequency* of the ion's circular motion is mass-dependent. By measuring the cyclotron frequency, one can determine an ion's mass.

The working equation for ICR can be quickly derived by equating the centripetal force (m**v****2/r) and the Lorentz force e**v****B** experienced by an ion in a magnetic field:

$$\frac{mv^2}{r} = evB$$

Solving for the angular frequency (omega), which is equal to **v**/r :

$$\omega = \frac{v}{r} = \frac{eB}{m}$$

A group of ions of the same mass-to-charge ratio will have the same cyclotron frequency, but they will be moving independently and out-of-phase at roughly thermal energies. If an *excitation pulse* is applied at the cyclotron frequency, the "resonant" ions will absorb energy and be brought into phase with the excitation pulse. As ions absorb energy,the size of their orbit also increases.

The packet of ions passes close to the receiver plates in the ICR cell and induces *image currents* that can be amplified and digitized. The signal induced in the receiver plates depends on the number of ions and their distance from the receiver plates.

If several different masses are present, then one must apply an excitation pulse that contains components at all of the cyclotron frequencies. This is done by using a rapid frequency sweep ("chirp"), an "impulse" excitation, or a tailored waveform. The image currents induced in the receiver plates will contain frequency components from all of the mass-to-charge ratios. The various frequencies and their relative abundances can be extracted mathematically by using a *Fourier transform* which converts a time-domain signal (the image currents) to a frequency-domain spectrum (the mass spectrum).

A schematic representation of a cubic FTICR cell is shown below:
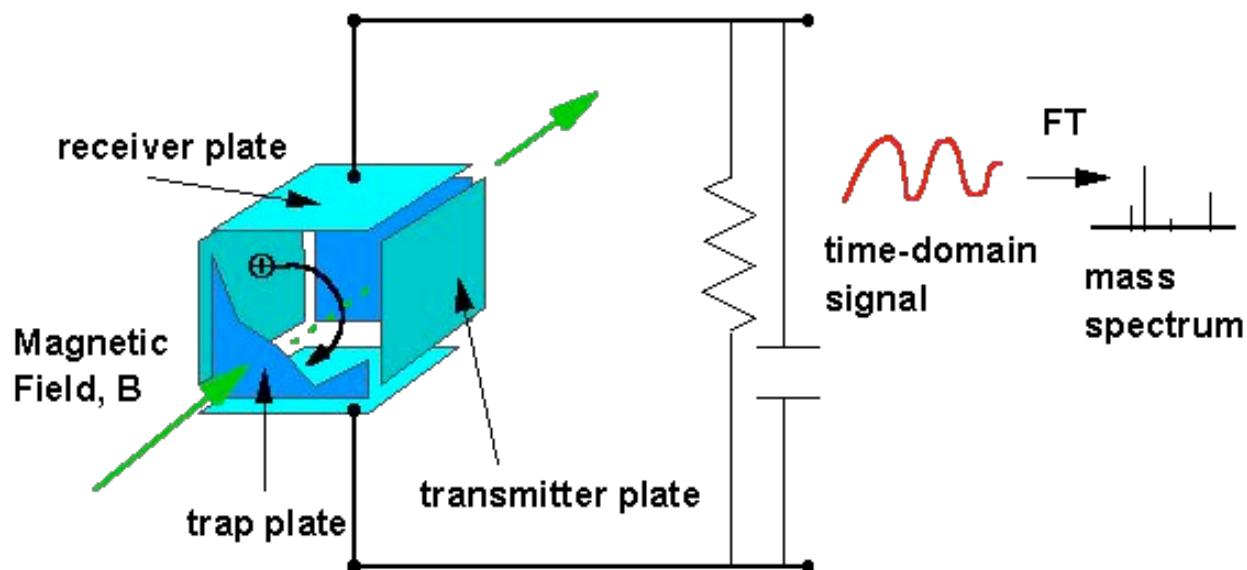
The cubic ICR cell consists of three pairs of parallel plates. The functions of the excitation and receiver plates are apparent from the preceding discussion. A small potential is applied to the trapping plates to keep the ions contained within the ICR cell because the magnetic field does not constrain the ion motion along the direction of the applied magnetic field. Beside the cubic cell, many other ICR cell designs have been evaluated, and each has its own special characteristics.

Excitation events can be used to increase the kinetic energy of ions, or to eject ions of a given mass-to-charge ratio from the cell by increasing the orbital radius until ions are lost by collisions with the cell plates.

The background pressure of an FTICR should be very low to minimize ion-molecule reactions and ion-neutral collisions that damp the coherent ion motion. A variety of *external ion source*

designs have been developed to deal with this problem, and each design has its own performance characteristics.

Most FTICR mass spectrometers use superconducting magnets, which provide a relatively stable calibration over a long period of time. Although some mass accuracy can be obtained without internal calibrant, mass accuracy and resolution are inversely proportional to m/z, and the best accuracte mass measurements require an internal calibrant.

Unlike the quadrupole ion trap, the FTICR mass spectrometer is not operated as a scanning device.

Benefits

- The highest recorded mass resolution of all mass spectrometers
- Powerful capabilities for ion chemistry and MS/MS experiments
- Well-suited for use with pulsed ionization methods such as MALDI
- Non-destructive ion detection; ion remeasurement
- Stable mass calibration in superconducting magnet FTICR systems

Limitations

- Limited dynamic range
- Strict low-pressure requirements mandate an external source for most analytical applications
- Subject to space charge effects and ion molecule reactions
- Artifacts such as harmonics and sidebands are present in the mass spectra
- Many parameters (excitation, trapping, detection conditions) comprise the experiment sequence that defines the quality of the mass spectrum
- Generally low-energy CID, spectrum depends on collision energy, collision gas, and other parameters

## Applications

- Ion chemistry
- High-resolution MALDI and electrospray experiments for high-mass analytes
- Laser desorption for materials and surface characterization

Quadrupole Ion Traps

Principal of Operation

Ions are dynamically stored in a three-dimensional quadrupole ion storage device. The RF and DC potentials can be scanned to eject successive mass-to-charge ratios from the trap into the detector (*mass-selective ejection*). The theory of the ion trap is beyond the scope of this essay, and the reader is again referred to R. E. March, R. J. Hughes and J. F. Todd, "Quadrupole Storage Mass Spectrometry", volume 102 of *Chemical Analysis,*Wiley, 1989 for a good description of the theory behind both quadrupole mass filters and quadrupole ion traps.
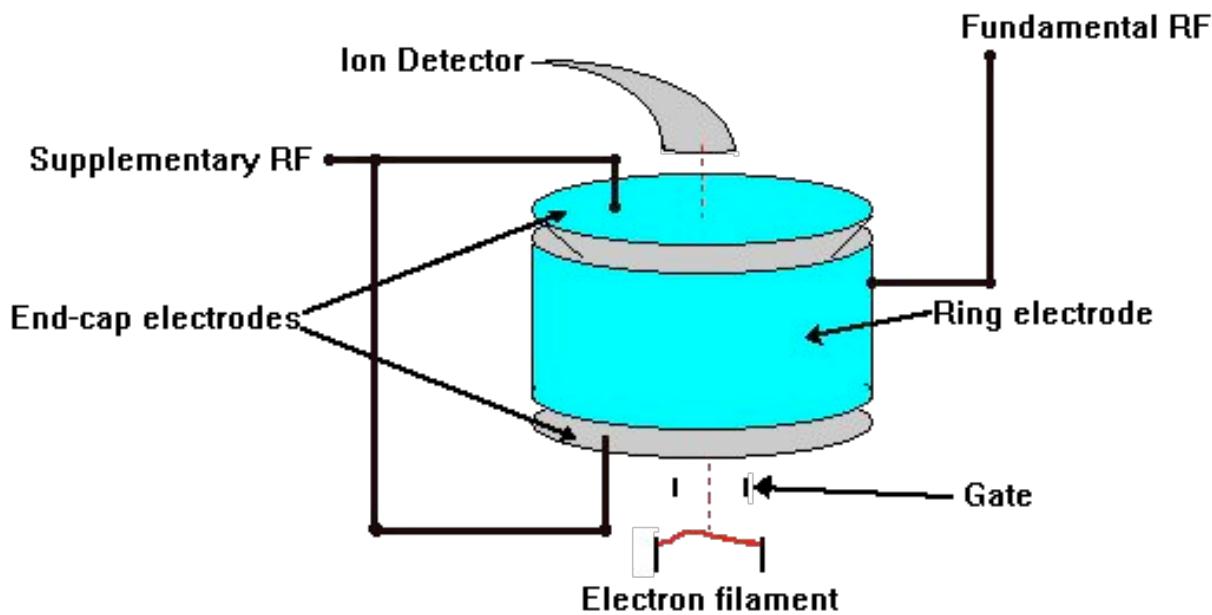
Ions are formed within the ion trap or injected into an ion trap from an external source. The ions are dynamically trapped by the applied RF potentials (a common trap design also makes use of a "bath gas" to help contain the ions in the trap). The trapped ions can be manipulated by RF events analogous to the events in FTICR to perform ion ejection, ion excitation, and mass-selective ejection. This provides MS/MS and MS/MS/MS... experiments analogous to those performed in FTICR.

Space-charge effects (ion-ion repulsion) severely limit the inherent dynamic range of the ion trap. This is usually handled by auto-ranging. That is, a pre-scan is performed to determine the ion current, and then the ionizing electron current is adjusted to reduce the number of ions formed to within the working range. This can be done wherever the ion formation event can be manipulated to control the number of ions formed (such as in electron ionization).

The ions contained within the ion trap can react with any neutral species present. "Self-CI" refers to the case when analyte ions react with analyte neutrals within the trap, and this can produce concentration-dependent changes in the mass spectrum. Such effects can be reduced by injecting ions into the trap from an external source, but ion transmission and trapping losses can lead to reduced sensitivity compared to ion traps that form ions within the trap.

Researchers have demonstrated high resolution and high mass range in specially designed ion trap systems. However, these extended capabilities have not been made generally available in commercial ion trap systems.

Benefits

- High sensitivity
- Multi-stage mass spectrometry (analogous to FTICR experiments)
- Compact mass analyzer

Limitations

- Poor quantitation
- Very poor dynamic range (can sometimes be compensated for by using auto-ranging)
- Subject to space charge effects and ion molecule reactions
- Collision energy not well-defined in CID MS/MS
- Many parameters (excitation, trapping, detection conditions) comprise the experiment sequence that defines the quality of the mass spectrum

Applications

- Benchtop GC/MS, LC/MS and MS/MS systems
- Target compound screening
- Ion chemistry