9.2.3 Mass Analyzers

classes of analyzers:

The mass analyzer is at the core of the mass spectrometer. Its function is to differentiate among ions according to their mass-to-charge ratio. There are a variety of mass analyzer designs. *Magnetic sector* mass analyzers employing narrow metal slits to isolate individual *m/z* ions and *quadrupole* mass analyzers are scanning instruments; only ions of a given mass-to-charge ratio pass through the analyzer at a given time. The *m/z* range is scanned over time. Other mass analyzers allow simultaneous transmission of all ions; these include *TOF*, *ion trap*, and *ion cyclotron resonance (ICR)* mass analyzers as well as *dispersive magnetic* mass analyzers. Tandem mass spectrometers are instruments with several mass analyzers in sequence; these allow the selection of one ion in the first analyzer (the precursor ion), collisional fragmentation or decomposition of that ion or its reaction with a vapor reagent in a second element using 4, 6, or 8 rods to focus and confine the precursor ions in the second stage (often called a "collision cell") and mass determination of these products in a third quadrupole, TOF, or magnetic sector analyzer stage.

9.2.3.1 Magnetic and Electric Sector Instruments

The principle of operation of a simple **single-focusing magnetic sector** mass analyzer was described briefly in Section 9.1. An ion moving through a magnetic field B will follow a circular path with radius r (Equation 9.6). Changing B as a function of time allows ions of different m/z values to pass through the fixed radius flight tube sequentially. This scanning magnetic sector sorts ions according to their masses, assuming that all ions have a +1 charge and the same kinetic energy. A schematic of a 90° sector instrument is shown in Figure 9.17. A variety of other magnetic mass spectrometers are shown in Figure 9.18; some of these will be discussed later. The sector can have any apex angle, but 60° and 90° are common. It can be demonstrated that a divergent beam of ions of a given m/z will be brought to a focus by passing through a sector-shaped magnetic field, as shown by the three ion paths in Figure 9.17.

A **dispersive magnetic sector** mass analyzer does not use a flight tube with a fixed radius. Since all ions with the same kinetic energy but different values of m/z will follow paths with different radii, advantage can be taken of this. The ions will emerge from the magnetic field at different positions and can be detected with a position-sensitive detector such as an array detector. Examples of dispersive magnetic sector systems are shown in Figure 9.18c and d.

A single-focusing instrument such as the system shown in Figure 9.18b has the disadvantage that ions emerging from the ion source do not all have exactly the same velocity. This is due to several factors. The ions are formed from molecules that have a Boltzmann distribution of energies to begin with. The ion source has small variations in its electric field gradient, causing ions formed in different regions of the source to experience different acceleration. Also, when fragmentation occurs, kinetic energy is released. This results in a distribution of velocities and adversely affects the resolution of the instrument by broadening the signal at the detector.

However, ions in a radial electrostatic field also follow a circular trajectory. The electrostatic field is an *electric sector* and separates ions by kinetic energy, not by mass (Figure 9.19). The ion beam from the source can be made much more homogeneous with respect to velocities of the ions if the beam is passed through an electric sector before being sent to the mass analyzer. The electric sector acts as an energy filter; only ions with a very narrow kinetic energy distribution will pass through.

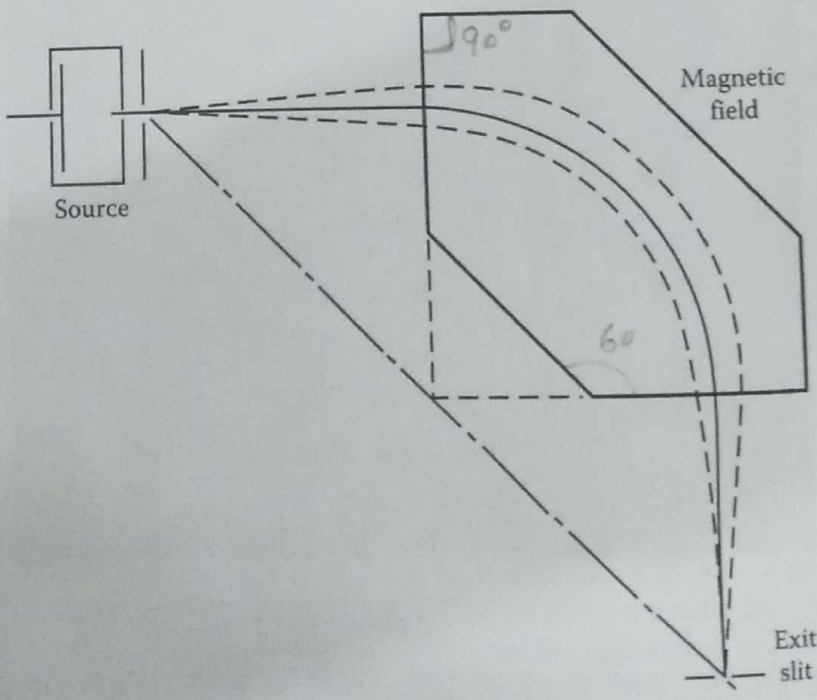

Figure 9.17 A 90° magnetic sector mass spectrometer. (From Ewing, G.W., Mass spectrometry, in Ewing, G.W. (ed.), *Analytical Instrumentation Handbook*, 2nd edn., Marcel Dekker, Inc., New York, 1997. Used with permission.)

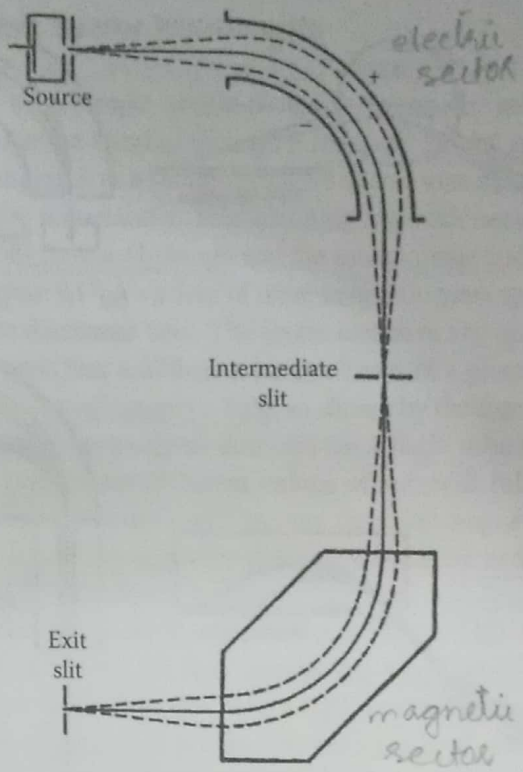

Figure 9.20 A Nier–Johnson double-focusing mass spectrometer. (From Ewing, G.W., Mass spectrometry, in Ewing, G.W. (ed.), *Analytical Instrumentation Handbook*, 2nd edn., Marcel Dekker, Inc., New York, 1997. Used with permission.)

Most magnetic sector instruments today combine both an electric sector and a magnetic sector. Such instruments are called double-focusing mass spectrometers. One common commercial double-focusing design is the Nier–Johnson design (Figure 9.20), introduced in 1953; this design is also used with the ions traveling in the opposite direction in "reverse" Nier–Johnson geometry. A second common design using two sectors is the Mattauch–Herzog dispersive design, shown in Figures 9.18c and 9.22.

Mass ranges for magnetic sector instruments are in the m/z 1–1,400 range for single-focusing instruments and m/z 5,000–10,000 for double-focusing instruments. Very high mass resolution, up to 100,000, is possible using double-focusing instruments.

Double-focusing sector field instruments of the Nier–Johnson and Mattauch–Herzog designs are used in ICP-MS instruments (ICP-sector field MS or ICP-SFMS, also referred to as high-resolution ICP-MS or HR-ICP-MS) as well as in organic MS instruments. In atomic MS, the ICP-SFMS instruments offer high sensitivity, high resolution, very low noise, and very low detection limits—on the order of $<1 \times 10^{-15}$ g/L (i.e., less than 1 fg/mL or less than one part per quadrillion [ppq]) for most elements. The Thermo Fisher Scientific Element XR, introduced in 2005 (Figure 9.21), uses a reverse Nier–Johnson geometry with the magnetic sector first for directional focusing and then an electric sector for energy focusing of the ion beam. The instrument is a single ion collector and is available as an ICP-MS or GDMS. The instrument has three mass resolution settings: low, $m/\Delta m \approx 300$; medium, $m/\Delta m \approx 3{,}000$; and high, $m/\Delta m \approx 10{,}000$. Medium resolution and high resolution can separate isobaric interferences of analyte ions from polyatomic ions. Examples include $^{80}Se^+$ from $^{40}Ar_2^+$ and $^{56}Fe^+$ from $^{40}Ar^{16}O^+$. Interferences and examples are discussed in detail in Chapter 10. The Element is equipped with 2 detectors, a secondary EM and a Faraday detector for a linear dynamic range of 12 orders of magnitude Figure 9.22. This permits detection of sub-part-per-quadrillion to % concentrations. The detectors are described in Section 9.2.4.

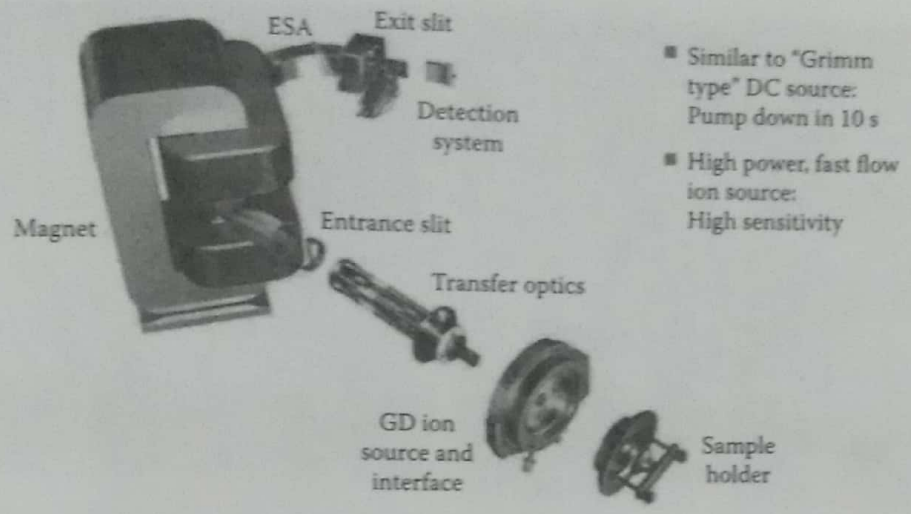

Figure 9.21 The reverse Nier–Johnson geometry of the Thermo Scientific Element with a GD source. (© Thermo Fisher Scientific. www.thermofisher.com. Used with permission.)

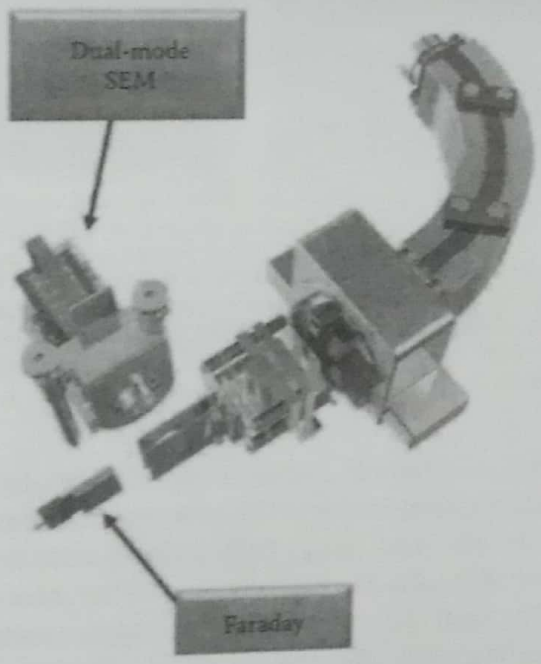

Figure 9.22 The dual detectors on the Thermo Scientific Element MS. (© Thermo Fisher Scientific. www.thermofisher.com. Used with permission.)

In 2011, SPECTRO Instruments GmbH (www.spectro.com, www.ametek.com) introduced the first simultaneous ICP-MS, the SPECTRO MS, based on Mattauch–Herzog geometry and using a novel direct charge detector (Section 9.2.4) placed in the focal plane of the magnet occupying the location of the photoplate shown in Figure 9.18c. The instrument consists of a novel ion optic (Figure 9.23a) and a double-focusing Mattauch–Herzog spectrometer (Figure 9.23b) with an entrance slit (which defines resolution), a 31.5° electrostatic analyzer (ESA), a drift length with energy slit, and a 90° magnetic field sector with the detector attached at the focal plane. The assembled instrument is shown in Figure 9.24.

The novel ion optic consists of a curved ESA (not to be confused with the ESA in the mass spectrometer), an Einzel lens and a quadrupole doublet. The ESA separates ions of a defined kinetic energy, which have been extracted by a prefilter, from neutrals, particles, and photons. The ions are

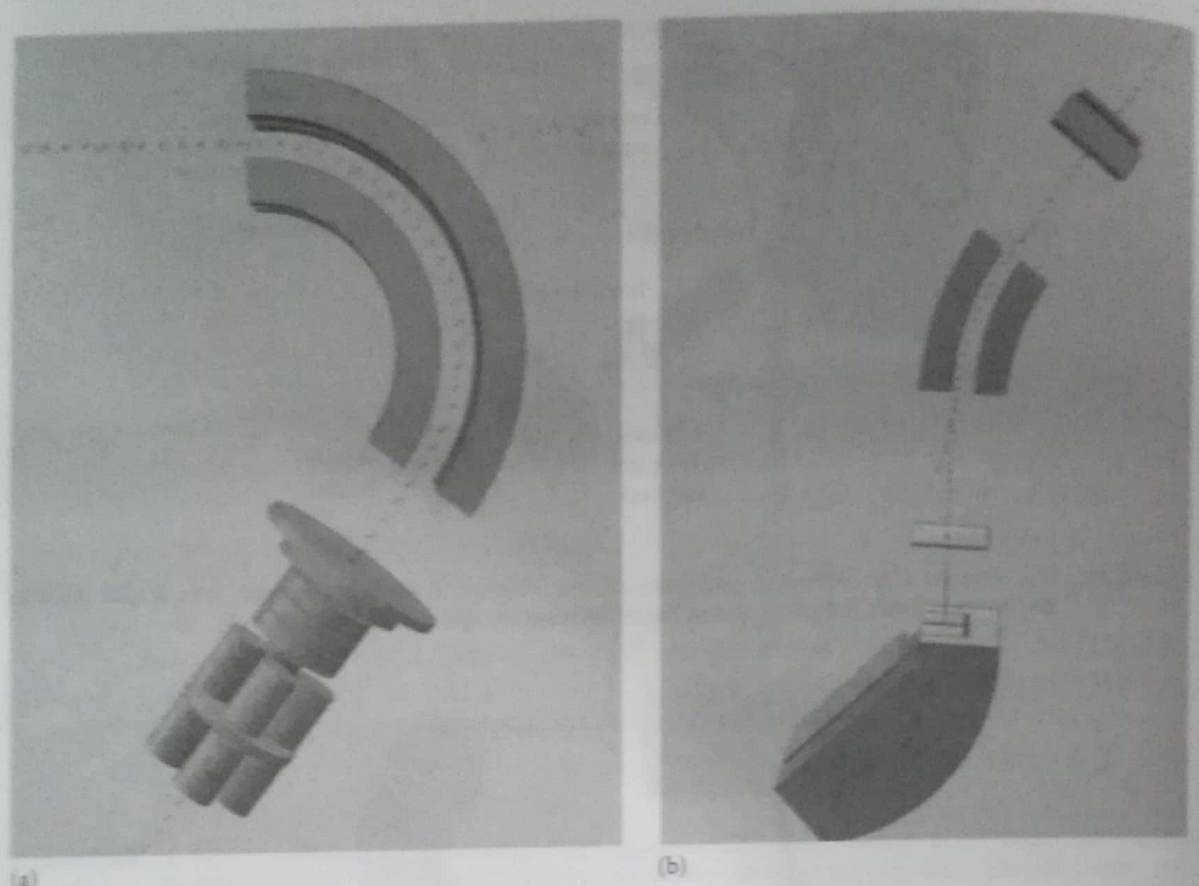

Figure 9.23 (a) The ion optic in the SPECTRO MS. Ions of a defined kinetic energy are introduced into the curved ESA (top). An Einzel lens focuses the ions (middle) into a quadrupole doublet (bottom). (b) The Mattauch–Herzog geometry of the SPECTRO MS. (Courtesy of SPECTRO Analytical Instruments, Inc., AMETEK® Materials Analysis Division. www.spectro.com, www.ametek.com. Used with permission.)

focused by the Einzel lens into a quadrupole doublet, which changes the shape of the ion beam from round to rectangular to match the entrance slit of the mass spectrometer.

The ESA sector reduces the ion beam energy band width to achieve high-resolution *m/z* separation in the magnetic field. The Mattauch–Herzog geometry of the mass spectrometer focuses all the ions, separated by *m/z*, onto the focal plane at the exit of the magnet using a fixed setting for the ESA and a permanent magnet (see Section 9.2.4).

This enables the use of a flat surfaced array detector. No scanning is required, resulting in a fully simultaneous determination of all the elements (5–240 amu) and fully utilizing the continuous ion beam produced by the ICP. Because the entire spectrum is recorded at once, it is possible to go back and retrieve concentration data for any element in any sample at anytime.

The major disadvantage of double-focusing MS systems for elemental analysis is their high cost compared to quadrupole-based systems.

9.2.3.2 *Time-of-Flight Analyzer*

A TOF analyzer does not use an external force to separate ions of different *m/z* values. Instead, pulses of ions are accelerated into an evacuated field-free region called a drift tube. If all ions have the same kinetic energy, then the velocity of an ion depends on its mass-to-charge ratio, or on its mass, if all ions have the same charge. Lighter ions will travel faster along the drift tube than heavier ions and are detected first. The process is shown schematically in Figure 9.25.

Figure 9.24 Cutaway view of the SPECTRO MS, showing the ICP torch box upper left and the ion optic to the right of the torch box, leading to the mass spectrometer on the left under the torch box. (Courtesy of SPECTRO Analytical Instruments, Inc., AMETEK® Materials Analysis Division. www.spectro.com, www.ametek.com. Used with permission.)

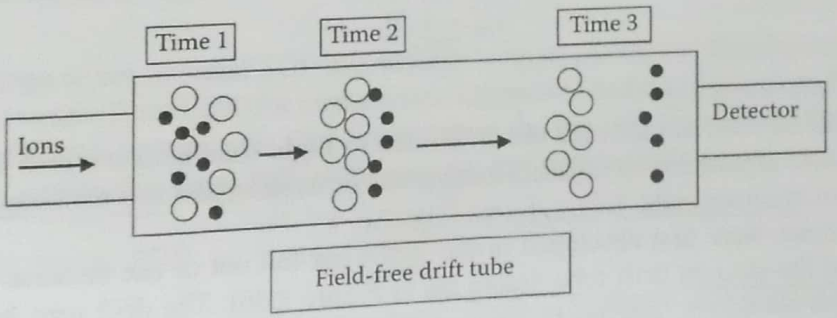

Figure 9.25 A pulse of ions of two different *m/z* values enters the field-free drift tube of a TOF mass spectrometer at time 1. The large white circles have *m/z* > the small dark circles. As they travel down the tube, the lighter ions move faster and, by time 3, have been separated from the heavier ions.

Extraction field and V:

A schematic TOF mass spectrometer is shown in Figure 9.26. The drift tube in a TOF system is approximately 1–2 m in length. Pulses of ions are produced from the sample using pulses of electrons, secondary ions, or laser pulses (e.g., MALDI). Ion pulses are produced with frequencies of 10–50 kHz. The ions are accelerated into the drift tube by a pulsed electric field, called the ion-extraction field, because it extracts (or draws out) ions into the field-free region. Accelerating voltages up to 30 kV and extraction pulse frequencies of 5–20 kHz are used.

Ions are separated in the drift tube according to their velocities. The velocity of an ion, v, can be expressed as

$$v = \sqrt{\frac{2zV}{m}} \tag{9.10}$$

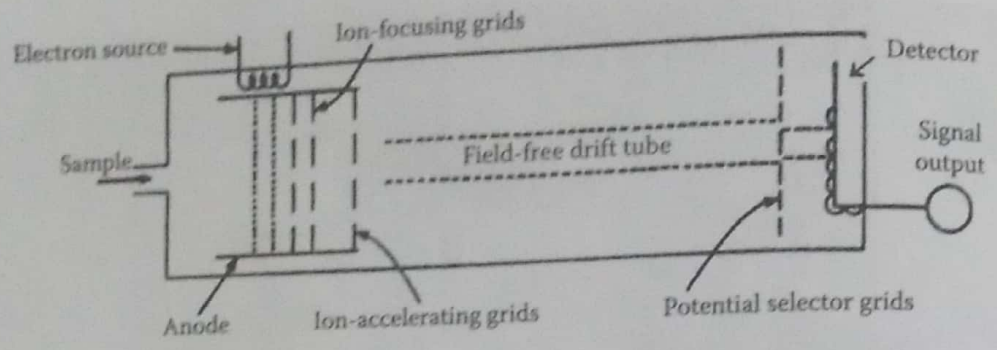

Figure 9.26 Schematic TOF mass spectrometer.

where V is the accelerating voltage. If L is the length of the field-free drift tube and t is the time from acceleration to detection of the ion (i.e., the flight time of the ion in the tube):

$$v = \frac{L}{t} \tag{9.11}$$

and the equation that describes ion separation is

$$\frac{m}{z} = \frac{2Vt^2}{L^2} \tag{9.12}$$

The flight time, t, of an ion is

$$t = L\sqrt{\frac{m}{2zV}} \tag{9.13}$$

time difference:

Equation 9.13 can be used to calculate the difference in flight time between ions of two different masses. Actual time separations of adjacent masses can be as short as a few nanoseconds, with typical flight times in microseconds. Disadvantage:

TOF instruments were first developed in the 1950s but fell out of use because of the inherent low resolution of the straight drift tube design (as in Figure 9.26). The drift tube length and flight time are fixed, so resolution depends on the accelerating pulse. Ion pulses must be kept short to avoid overlap of one pulse with the next, which would cause mass overlap and decrease resolution. Interest in TOF instruments resurfaced in the 1990s with the introduction of MALDI and rapid data acquisition methods. The simultaneous transmission of all ions and the rapid flight time means that the detector can capture the entire mass spectral range almost instantaneously. Reflectron:

The resolution of a TOF analyzer can be enhanced by the use of an ion mirror, called a **reflectron**. The reflectron is used to reverse the direction in which the ions are traveling and to energy-focus the ions to improve resolution. The reflectron's electrostatic field allows faster ions to penetrate more deeply than slower ions of the same m/z value. The faster ions follow a longer path before they are turned around, so that ions with the same m/z value but differing velocities end up traveling exactly the same distance and arrive at the detector together. The use of a curved field reflectron permits the focusing of ions over a broad mass range to collect an entire mass spectrum from a single laser shot. In a reflectron TOF, the ion source and the detector are at the same end of the spectrometer; the reflectron is at the opposite end from the ion source. The ions traverse the drift tube twice, moving from the ion source to the reflectron and then back to the detector. A schematic of a commercial reflectron TOF mass analyzer is shown in Figure 9.27.

9.2.3.3 *Quadrupole Mass Analyzer*

The quadrupole mass analyzer does not use a magnetic field to separate ions. The quadrupole separates ions in an electric field (the quadrupole field) that is varied with time. This field is created using an oscillating RF voltage and a constant DC voltage applied to a set of four precisely machined parallel metal rods (Figure 9.31). This results in an alternating current (AC) potential superimposed on the DC potential. The ion beam is directed axially between the four rods.

The opposite pairs of rods A and B, and C and D, are each connected to the opposite ends of a DC source, such that when C and D are positive, A and B are negative. The pairs of electrodes are then connected to an oscillating RF electrical source. They are connected in such a way that the potentials of the pairs are continuously 180° out of phase with each other. The magnitude of the oscillating voltage is greater than that of the DC source, resulting in a rapidly oscillating field. The RF voltage can be up to 1200 V while the DC voltage is up to 200 V. The rods would ideally be hyperbolic instead of circular in cross section, with their hyperboloid axes pointed toward the center of the rod array, to provide a more uniform field. Under these conditions, the potential at any point between the four poles is a function of the DC voltage and the amplitude and frequency of the RF voltage. The shape of the rods varies with different manufacturers;

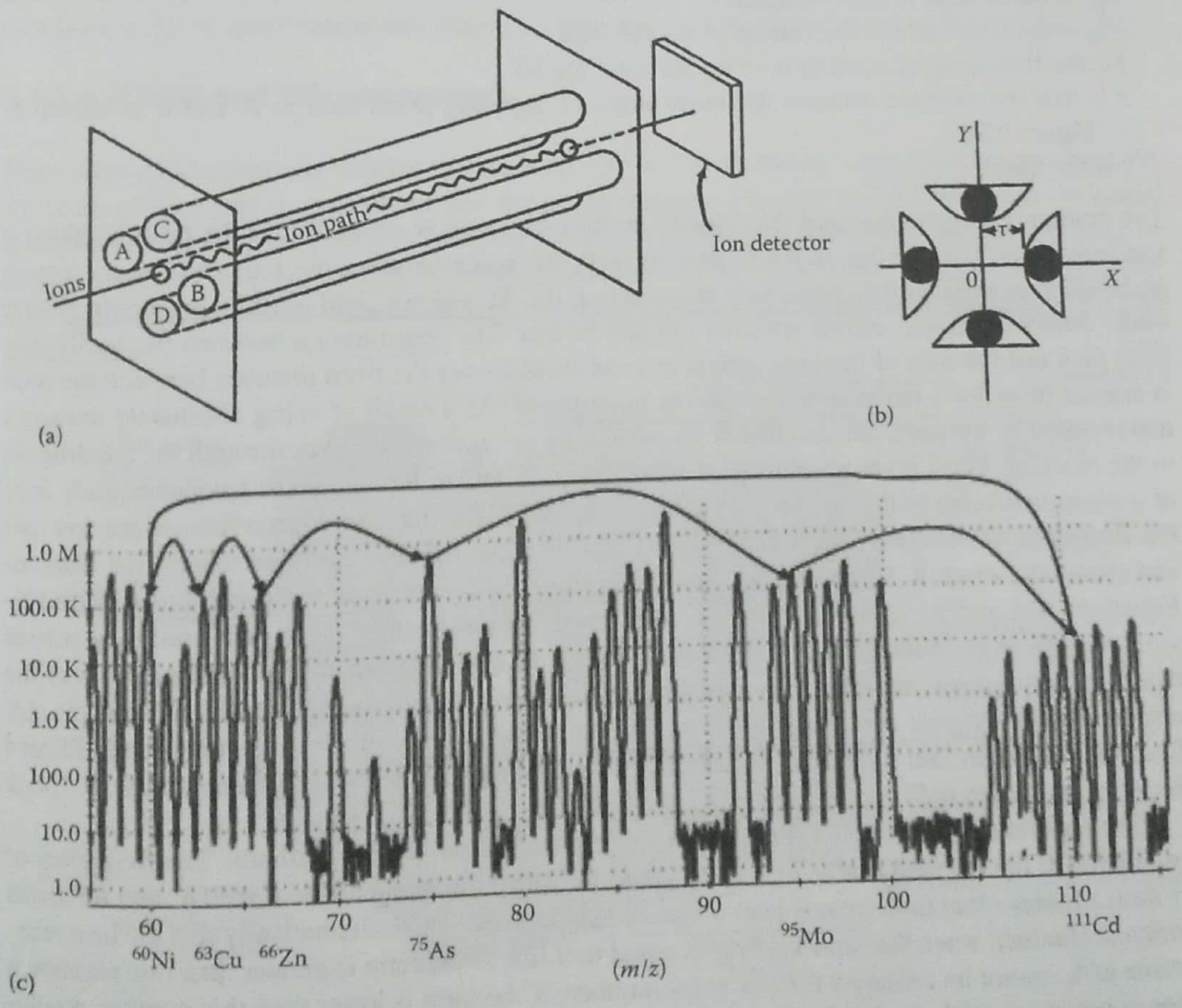

Figure 9.31 (a) Transmission quadrupole mass spectrometer. Rods A and B are tied together electrically, as are Rods C and D. The two pairs of rods, AB and CD, are connected both to a source of direct potential and a variable RF excitation such that the RF voltages are 180° out of phase. (b) The geometry of the rods. (c) Sequential detection of elements by peak hopping.

cheaper circular cylindrical rods are often used instead of hyperbolic rods. Agilent Technologies manufactures the only hyperbolic quadrupole used in ICP-MS.

An ion introduced into the space between the rods is subjected to a complicated lateral motion due to the DC and RF fields. Assume that the x-direction is the line through the midpoint of the cross sections of rods A and B; the y-direction is the line through the midpoint of the cross sections of rods C and D, as shown in Figure 9.31b. The forward motion of the ion in the z-direction (along the axis between the rods) is not affected by the field. The following equations describe the lateral motion of the ion:

$$\frac{d^2x}{dt^2} + \frac{2}{r^2(m/z)}(V_{DC} + V_{RF}\cos 2\pi ft)y = 0 \tag{9.14}$$

$$\frac{d^2y}{dt^2} + \frac{2}{r^2(m/z)}(V_{DC} + V_{RF}\cos 2\pi ft)x = 0 \tag{9.15}$$

where

V_{DC} is the voltage of the DC signal
V_{RF} is the amplitude of the voltage of the RF field
f is the frequency of oscillation of the RF field (rad/s)
r is half the distance between the inner edges of opposing poles such as A and B as shown in Figure 9.31b
t is the time

The motion is complex because the velocity in the x-direction is a function of the position along y and *vice versa*. In order for an ion to pass through the space between the four rods, every time a positive ion is attracted to a negatively charged rod, the AC electric field must be present to push it away; otherwise, it will collide with the rod and be lost. The coordination between the oscillating (AC) field and the time of the ion's arrival at a rod surface over the fixed distance between the rods is critical to an ion's movement through the quadrupole. As a result of being alternately attracted and repelled by the rods, the ions follow an oscillating or "corkscrew" path through the quadrupole to the detector. For a given amplitude of a fixed ratio of DC to RF at a fixed frequency, only ions of a given m/z value will pass through the quadrupole. If the mass-to-charge ratio of the ion and the frequency of oscillation fit Equations 9.14 and 9.15, the ion will oscillate toward the detector and eventually reach it. If the m/z value and the frequency do not meet the conditions required by Equations 9.14 and 9.15, these ions will oscillate with an increasingly wide path until they collide with the rods or are pulled out by the vacuum system. In any case, the ions will not progress to the detector. Only a single m/z value can pass through the quadrupole at a given set of conditions. In this respect, the quadrupole acts like a filter and is often called a mass filter. One m/z value is filtered from the ion beam and passed to the detector; the elements are measured sequentially by "peak hopping" as shown in Figure 9.31c.

The separation of ions of different m/z can be achieved by several methods. The frequency of oscillation of the RF field can be held constant while varying the potentials of the DC and RF fields in such a manner that their ratio is kept constant. It can be shown mathematically that the best resolution is obtained when the ratio V_{DC}/V_{RF} is equal to 0.168. If the ratio is greater than this number, a stable path cannot be achieved for any mass number; if the ratio is lower than this number, resolution is progressively lost.

The resolution of the system is dependent on the number of oscillations an ion undergoes in the drift chamber. Increasing the rod lengths, therefore, increases resolution and extends the use of the system to higher MW compounds. Increasing the frequency of the RF field can bring about this

same improvement. The rod diameter is also important. If the diameter is increased, the sensitivity is greatly increased, but then the mass range of the system is decreased. The manufacturer must come to a compromise with these factors when designing an instrument for analytical use. The resolution achievable with the quadrupole mass spectrometer is approximately 1000; the *m/z* range for a quadrupole mass analyzer is 1–1000 Da. As with other mass spectrometers, the sample must be available in the gas phase and must be ionized.

Quadrupole mass analyzers are found in most commercial ICP-MS instruments, in most GC-MS instruments (Chapter 12) and in many LC-MS instruments (Chapter 13). Quadrupoles or higher number multipole rod arrays are also used in both organic and inorganic MS/MS systems as mass analyzers or collision cells, respectively. This use will be described in Section 9.2.3.4.

Although the quadrupole mass analyzer does not have the range or resolution of magnetic sector instruments, it is very fast. It can provide a complete mass spectrum in less than 100 ms. This property and its wide angle for acceptance of ions make it suitable for coupling to transient signal sources such as those from chromatography or laser ablation. In addition, the quadrupole mass analyzer is inexpensive, compact, and rugged. Most ICP-MS, GC-MS, and LC-MS instruments with quadrupoles are small enough to fit on a benchtop. Figure 9.32 shows the cutaway view of the smallest benchtop ICP-MS. Quadrupoles are the most common mass analyzer in commercial use. The term **transmission quadrupole** mass spectrometer is sometimes used for this mass analyzer to avoid confusion with the **quadrupole ion trap (QIT)** mass spectrometer discussed in Section 9.2.3.5.

9.2.3.5 *Quadrupole Ion Trap*

An **ion trap** is a device where gaseous ions can be formed and/or stored for periods of time, confined by electric and/or magnetic fields. There are three commercial types of ion traps in use in MS, the QIT; the Orbitrap, which uses a spiral trajectory that oscillates along a 1D linear axis; and the ICR trap.

The QIT mass spectrometer is also called a **Paul ion trap, a 3D ion trap** or, more commonly, just an ion trap. This analyzer uses a quadrupole field to separate ions, so "quadrupole" is used in the name to distinguish this system from the Orbitrap and ICR traps discussed in the next section. The QIT is shown schematically in Figure 9.34. A ring-shaped electrode and two end cap electrodes, one above and one below the ring-shaped electrode, are used to form a 3D field. A fixed frequency RF voltage is applied to the ring electrode while the end caps are either grounded or under RF or DC voltages. Ions are stored in the trap by causing them to move in stable trajectories between the electrodes under the application of the field. This is done by varying the potentials, so that just before an ion collides with an electrode, the potential changes sign and repels the ion. Ions with a very broad range of *m/z* values can be stored simultaneously in the ion trap.

Ionization of the sample can take place outside of the ion storage area of the ion trap; such external ionization is required for LC-MS using an ion trap and may be used for GC-MS. Alternatively, ionization can take place inside the ion storage area; this internal ionization approach can be used for GC-MS. Inert gas may be introduced into the trap after initial ionization for MS/MS experiments using collision-induced dissociation.

Ions are extracted from the trap by changing the amplitude of the ring electrode RF. As the amplitude increases, the trajectory of ions of increasing *m/z* becomes unstable. These ions move toward the end caps, one of which has openings leading to the detector. Ions of a given *m/z* value pass through the end cap sequentially and are detected.

The use of various RF and DC waveforms on the end caps allows the ion trap to selectively store precursor ions for MS/MS experiments or to selectively store analyte ions while eliminating

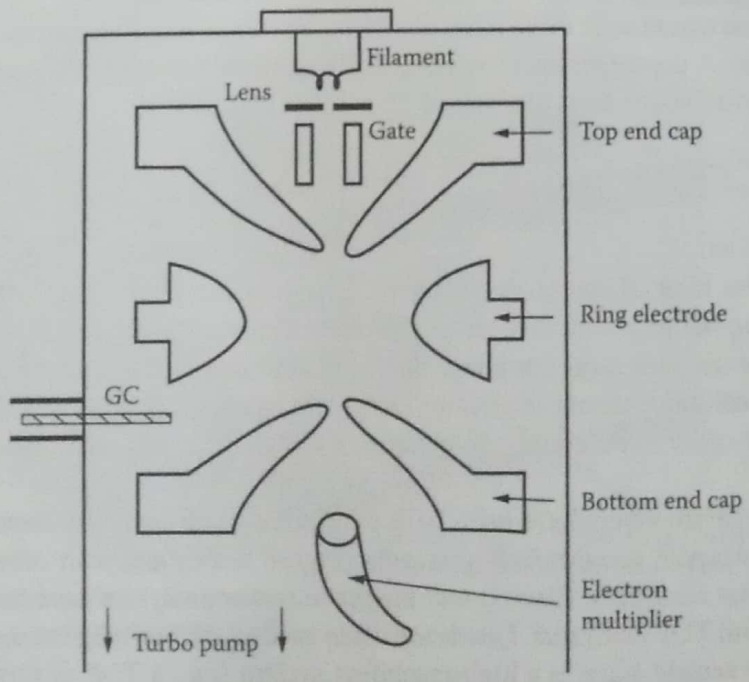

Figure 9.34 Cross section of a QIT mass spectrometer. This schematic shows a gas-phase sample introduced from a GC and ionized inside the trap by electrons from the filament. (From Niessen, W.M.A. and van der Greef, J., *Liquid Chromatography–Mass Spectrometry*, Marcel Dekker, Inc., New York, 1992. Used with permission.)

ions from the matrix. This can result in improved detection limits in analysis. The ion trap has limitations. Because the stored ions can interact with each other (a space–charge effect), thereby upsetting stability of trajectories, the concentration of ions that can be stored is low. This results in a low dynamic range for ion trap mass spectrometers. Trace level signals from a target analyte ion at one mass can be destabilized by the presence of great excesses of contaminant ions, even if these are of sufficiently different mass to be well resolved from the ion of interest. Ion trap MS instruments are less forgiving of "dirty samples" than are quadrupoles, which "throw away" such unwanted ions as they are measuring the target ion. The stored ion interaction also limits the accuracy of the mass-to-charge ratio measurement. Resolution of commercial QIT mass spectrometers is on the order of 0.1–1, with an m/z range of 10–1000.

9.2.3.6 Fourier Transform Ion-Cyclotron Resonance

The ICR instrument, also called a **Penning ion trap**, uses a magnetic field to trap and store ions. As shown in Figure 9.35, six conducting plates arranged as a cube serve as the ion trap. The cubic cell is about 100 mm on a side, is under very high vacuum ($<10^{-8}$ torr), and is located inside a strong magnetic field produced by a superconducting magnet. Sample is introduced into the cell and ionized by an external ion source such as an electron beam passing through the trap. Ions in the presence of a magnetic field move in circular orbits perpendicular to the applied field, at a frequency called the cyclotron frequency:

$$\omega_c = \frac{z}{m}(eB) = \frac{v}{r} \tag{9.16}$$

where

ω_c is the frequency of rotation of ions (rad/s)
e is the charge on electron (Coulombs)
B is the magnetic field (Tesla)
z is the charge on the ion
m is the mass of the ion
v is the velocity of the ion
r is the radius of orbit

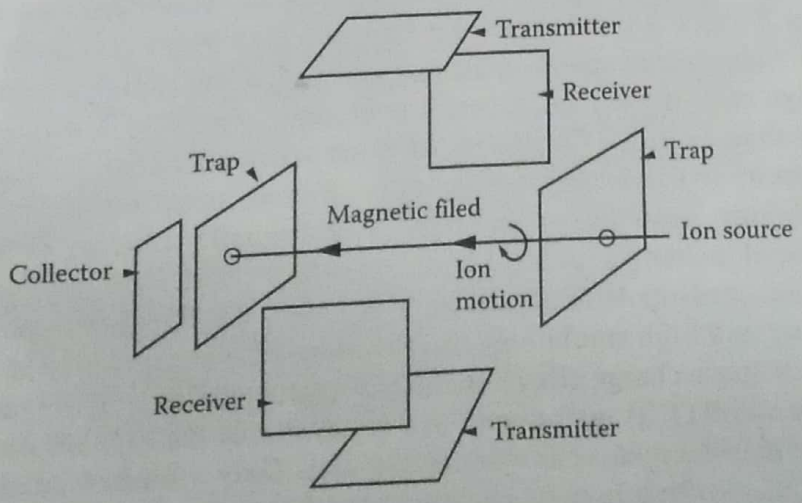

Figure 9.35 "Exploded" view of an ICR ion trap. The ICR has been the primary mass analyzer used in FTMS, both alone and in newer "hybrid" FTMS instruments.

The frequency of motion of an ion depends on the inverse of its *m/z* in a fixed magnetic field. Mass analysis is performed by applying an RF pulse of a few milliseconds duration to the transmitter plates. The RF pulse provides energy to the ions, causing them to move in larger circular orbits at the same frequency. For a given *m/z* value, a pulse at a frequency of ω_c causes all ions of that *m/z* value to absorb energy and increase their orbit of rotation. When the RF pulse is off, the motion of the ions is detected by current induction in the receiver plates. As a group of positive ions approaches the receiver plate, its charge attracts electrons to the inside surface of the plate. As the group recedes, the electrons are released. This induced current, called an "image current," is a sinusoidal signal with frequency ω_c. The larger the orbit, the larger is the induced current. The frequency provides the *m/z* information about the ion and the current amplitude depends on the number of ions of that *m/z* value, providing information about the concentration of ions.

It would be possible to scan the RF and measure the magnitude of the image current at each *m/z* value to obtain the mass spectral information but the process would be very slow. Instead, an RF pulse is used that contains a range of frequencies. The range of frequencies is chosen to excite the desired *m/z* range. When the pulse is off, all of the exited ions induce image currents in the receiver plates as they rotate. The output current, which contains all of the frequency and magnitude information from all of the ions present, can be converted mathematically to a mass spectrum by the application of the Fourier transformation. The use of an ICR ion trap and Fourier transformation is called FTICR-MS or just FTMS. As of early 2003, this was the only type of FTMS instrument commercially available.

There are several advantages to the ICR. One is that the ion detection is nondestructive. Therefore, signals can be accumulated by averaging many cycles, resulting in greatly improved S/N and signal-to-background as well as very low detection limits. Detection of attomoles of analyte is possible. Frequency can be measured very accurately, so the mass accuracy and resolution of these FTMS systems can be very high, on the order of 1 ppb for a mass of 100 Da. In order to acquire sufficient information to achieve such high resolutions by the FT process, the data must be acquired over a longer period. In order that collisions with residual gas atoms in the ICR trap do not remove the ions during this period, it must be operated at very high vacuum (e.g., $<10^{-8}$ torr), if such high resolution is to be attained. The ICR can also be used for MS/MS and MS^n experiments, by storing precursor ions and fragmenting them in the trap using a collision gas, lasers, or ion beams. An advantage of the FTMS system is that it is nondestructive, so ions at all stages of an MS^n experiment can be measured. A QIT instrument expels ions to be analyzed, so only ions in the final step can be measured.

The major disadvantages of the ICR are a limited dynamic range due to the same space charge effect described for the QIT, a more complex design, and high instrument cost, resulting from the need for extremely high vacuum operation and high field superconducting magnets.

Despite the high cost of the FTICR instrument, new "hybrid" FTMS instruments costing significantly more than 1 million US dollars were introduced commercially in 2003 because of their ability to determine the structure of proteins. Protein structure determination is critical to fundamental biology, genomics, proteomics, and the understanding of drug–biomolecule interactions for development of pharmaceuticals. "Hybrid" FTMS instruments combining either an ion trap or quadrupole(s) on the front end with the FTICR on the back end exhibit both high sensitivity and high resolution. The diversion of nontarget ions in the earlier stages greatly reduces their space charge effects in the ICR trap, enabling it to operate at its maximum capability. Ion trap and FTICR instruments are not available for ICP-MS due to the large Ar^+ intensity (from the plasma) relative to the analyte ions. Only a limited number of ions can be stored in the ion trap, resulting in poor sensitivity for the analytes compared to other ICP mass spectrometer designs.