**Figure 9.21**   A commercial reflectron TOF mass analyzer, the Pegasus III from LECO. The analyzer is shown with sample introduction from a GC. [Diagram courtesy of LECO Corporation (www.leco.com).]

The rapid collection of the entire mass spectrum made possible by the TOF makes it ideal for interfacing with a chromatograph. It is especially useful when combined with fast GC, which requires the rapid collection of hundreds of mass spectra. For example, the LECO Pegasus 4D GC-TOFMS collects the entire mass range from 1 to 1000 Da in 170 μs and collects up to 500 mass spectra/s. (A detailed description of this instrument can be found at www.leco.com.)

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 radio frequency (RF) voltage and a constant direct current (DC) voltage applied to a set of four precisely machined parallel metal rods (Fig. 9.22). This results in an 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 electrical source oscillating at RFs. 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 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; cheaper circular cylindrical rods are often used instead of hyperbolic rods.

(a)   (b)
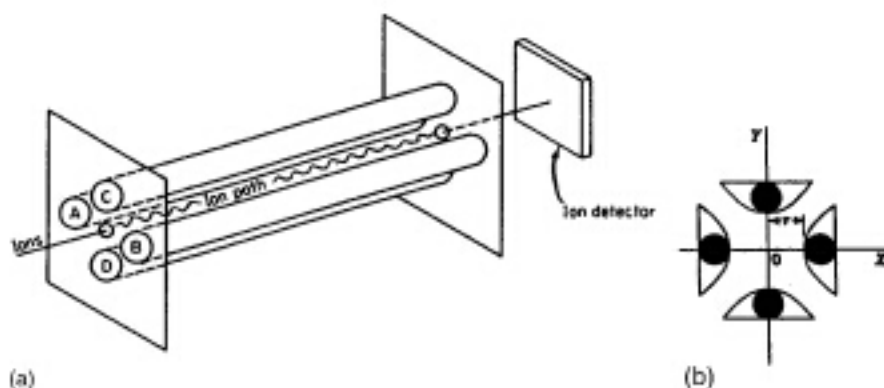
Figure 9.22 (a) Transmission quadrupole mass spectrometer. Rods A and B are tied together electrically, as are Rods C and D. The two pairs of rods, AB and CD, are connected both to a source of direct potential and a variable RF excitation such that the RF voltages are 180° out of phase. (b) The geometry of the rods.

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 Fig. 9.22(b). 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}, the amplitude of the voltage of the RF field; f, the frequency of oscillation of the RF field (rad/s); r, the half the distance between the inner edges of opposing poles such as A and B as shown in Fig. 9.22(b); and t, 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 Eqs. (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 Eqs. (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.

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 molecular weight 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 are also used in MS-MS systems as mass analyzers and ion lenses. 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 of acceptance 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 GC-MS and LC-MS instruments with quadrupoles are small enough to fit on a benchtop. 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** mass spectrometer discussed in Section 9.2.3.5.

9.2.3.4. *MS-MS and MS^n Instruments*

Many analytical questions require the mass spectrometrist to obtain more information about the structure of fragment ions or about ion–molecule reactions than can be obtained from the initial ionization of an analyte. In such cases, the technique of MS-MS, also called tandem MS may be useful. MS-MS is a mass spectral technique that uses two (or more) stages of mass analysis combined with a process that causes a change in mass of the ion of interest, such as dissociation into lighter fragment ions by collision with an inert gas or conversion into a heavier ion by reaction with a neutral molecule.

The stages of mass analysis may be performed by two physically separate mass analyzers, such as two quadrupoles coupled in series; this type of arrangement for MS-MS is called "tandem in space". Figure 9.23 shows a quadrupole MS-MS instrument with three quadrupoles for "tandem in space" analysis. Alternatively, ion traps, discussed in Sections 9.2.3.5 and 9.2.3.6, may be used to perform MS-MS experiments within the same mass analyzer; this type of MS-MS experiment is called "tandem in time".

Using Fig. 9.23, we will look at a simple MS-MS experiment. For example, an analyte may be ionized as usual by the ion source. One ion of a particular m/z value is
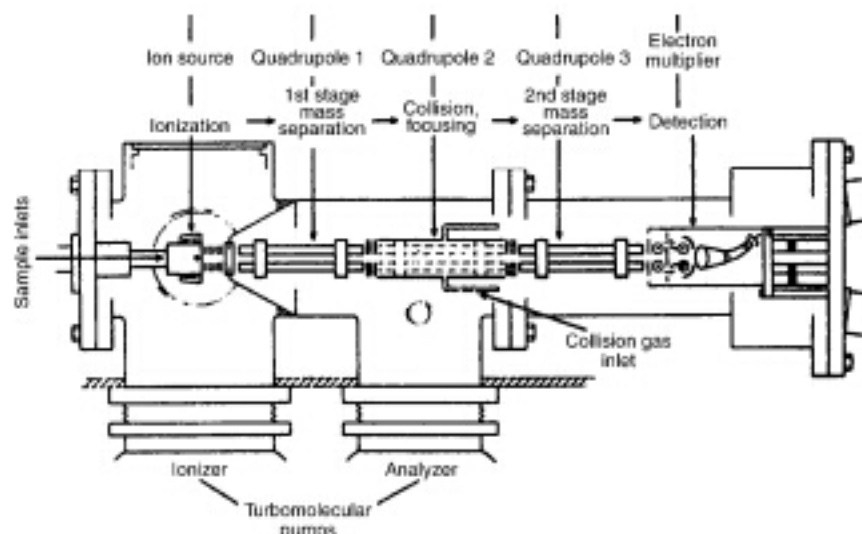
Figure 9.23 A commercial quadrupole tandem MS-MS instrument. [Courtesy of Thermo Electron Corporation (www.thermo.com).]

of interest. This ion is called the **precursor** ion. The precursor ion is selected by the first quadrupole, which is operating as a mass analyzer. The precursor ion enters the second quadrupole. This second quadrupole is the reaction region and acts as a collision cell and ion lens, not as a mass analyzer. An inert gas may be added in this region to cause collision-induced fragmentation of the precursor ion into lighter product ions or a reactive reagent gas may be introduced to form heavier product ions through ion–molecule reactions. The second quadrupole also serves to focus the product ions; that is:

$$M^+_{precursor} \longrightarrow M^+_{product}$$
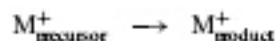
where the precursor and product ions have different m/z values. The product ions then undergo mass analysis as usual in the third quadrupole. This type of design, where the first and third quadrupoles are used for mass analysis and the center quadrupole is used for collision and focusing, is often abbreviated as a QqQ design, to indicate that there are only two stages of mass analysis symbolized by the capital Q.

 If we had an instrument with three mass analyzers, the fragmentation process could be repeated before final analysis. A precursor ion is selected, fragmented, a given product ion is selected and fragmented again before mass analysis of its product ions; that is:

$$M^+_{precursor} \longrightarrow M^+_{product\ 1} \longrightarrow M^+_{product\ 2}$$
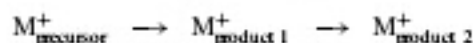
where all three ions have different m/z values. This is an example of MS-MS-MS or MS^3; the number of steps can be increased to give an MS^n experiment. It is not practical to build "tandem in space" instruments with large numbers of mass analyzers; three or four is the upper limit. Commercial MS-MS instruments are limited to two mass analysis stages. Ion trap instruments are used for higher order experiments. In general, $n = 7$ or 8 is a practical upper limit in ion trap instruments.

 Tandem mass spectrometers have been built with three quadrupoles as shown in Fig. 9.23, and with other combinations of sector and TOF mass analyzers. Electric and magnetic sector analyzers have been combined with quadrupoles and with TOF analyzers.
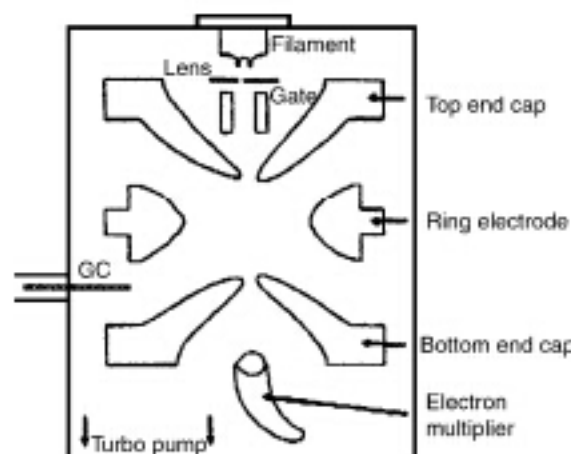
9.2.3.5.   *Quadrupole Ion Trap*

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 two commercial types of ion traps in use in MS, the *quadrupole ion trap* (QIT) and the *ion cyclotron resonance* trap (ICR).

The QIT mass spectrometer is also called a **Paul 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 ICR trap discussed in the next section. The QIT is shown schematically in Fig. 9.24. 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 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

Figure 9.24   Cross-section of a quadrupole ion trap 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 and van der Greef, used with permission.)