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 (FTICR)*

The ICR instrument, also called a **Penning ion trap**, uses a magnetic field to trap and store ions. As shown in Fig. 9.25, six conducting plates arranged as a cube serve as the ion trap. The cubic cell is about 100 mm on a side, is under 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 (radians/s); e, the charge on electron (coulombs); B, the magnetic field (tesla); z, the charge on the ion; m, the mass of the ion; v, the velocity of the ion; and r, the radius of orbit.

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

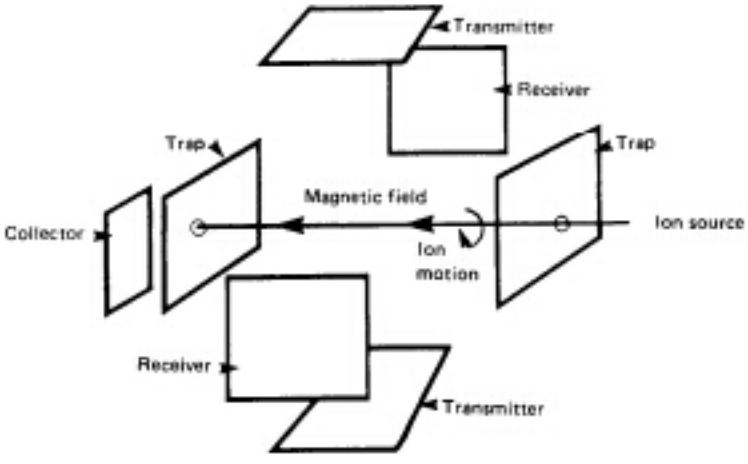

Figure 9.25 "Exploded" view of an ICR ion trap. The ICR has been the primary mass analyzer used in FTMS, both alone and in newer "hybrid" FTMS instruments.

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 application of the Fourier transform (FT). The use of an ICR ion trap and Fourier transformation is called Fourier transform ion-cyclotron resonance mass spectrometry (FTICRMS) 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 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 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 quadrupole ion trap, a more complex design, and high instrument cost.

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.

9.2.4. Detectors

Most mass spectrometers measure one m/z value at a time. A single channel ion detector is used for these instruments, either an **dectron multiplier** or a **Faraday cup**. TOF, ion trap, and FTICR mass spectrometers have the ability to extract ions with many m/z values simultaneously, so simultaneous detection of these ions is desirable. One approach to multiple ion detection has been to use multiple detectors. Multiple detectors are also used for high-resolution magnetic sector MS instruments designed for very precise isotope ratio determination and for quantitative analysis using isotope dilution. Instruments with

multiple detectors are called "multicollectors". New detector developments in array detectors hold the promise of simultaneous m/z measurement over a wide mass range.

9.2.4.1. *Electron Multiplier (EM)*

The most common detector used for ions in mass spectrometers is the electron multiplier (EM). The EM is very similar in concept to the photomultiplier tube for optical detection. It is very sensitive and has fast response. The EM is based on the dynode, which has a surface that emits electrons when struck by fast-moving electrons, positive ions, negative ions, or neutrals. A **discrete-dynode EM** uses a series of 12–24 dynodes, each biased more positively than the preceding dynode. A collision releases several electrons from the dynode surface. These electrons are then accelerated to a second such surface, which, in turn, generates several electrons for each electron that bombards it. This process is continued until a cascade of electrons (an amplified current) arrives at the collector. The process is shown schematically in Fig. 9.26. Typically, one ion can produce 10^5 electrons or more; this ratio of electrons measured per ion is referred to as the gain. The gain of the detector can be adjusted, with operating gains of 10^4 – 10^8 used, depending on the application. Figure 9.26(b) shows a commercial discrete-dynode electron multiplier. A **continuous-dynode EM**, also called a channel electron multiplier (CEM) uses a continuous glass tube, either lead-doped or coated on the inside with a conductive surface of high electrical resistance, such as those shown in Fig. 9.27. A potential difference is applied across the tube ends so that the potential varies in a linear manner along the tube. Each incident ion releases electrons that are accelerated and strike the tube again, resulting in the same cascade effect seen in the discrete-dynode EM. The curved or coiled form is designed to reduce electrical noise by preventing positive ions from returning upstream.

A disadvantage to dynode-based detectors is that the number of secondary electrons released depends on the type of incident primary particle, its angle and energy. The dependence of the number of secondary electrons emitted on incident energy is shown for electron impact in Fig. 9.26(c); the same plot for ion impact would be similar. Therefore, they can exhibit *mass discrimination* due to differences in ion velocity. Heavy ions from quadrupole mass analyzers and from QIT mass analyzers impact the dynode surface at lower velocities than light ions. EM detectors for these instruments must be designed to overcome the difference in velocities, often by accelerating the ions prior to them striking the first electron-emitting dynode. An excellent source of information on how discrete dynode electron multipliers work is the SGE website at www.sge.com, which describes their ETP electron multipliers. Similarly, the Burle Technologies website at www.burle.com provides technical information on their Channeltron® continuous-dynode electron multiplier.

9.2.4.2. *Faraday Cup*

The least-expensive ion detector is the Faraday cup, a metal or carbon cup that serves to capture ions and store the charge. The resulting current of a few microamperes is measured and amplified. The cup shape decreases the loss of electrons from the metal due to ion impact. The Faraday cup is an absolute detector and can be used to calibrate other detectors. The current is directly proportional to the number of ions and to the number of charges per ion collected by the detector. Unlike dynode-based detectors, the Faraday cup does not exhibit mass discrimination. The detector does have a long response time, which limits its utility. The Faraday cup detector is used for making very accurate measurements in isotope-ratio MS, where the ion currents do not change rapidly. The

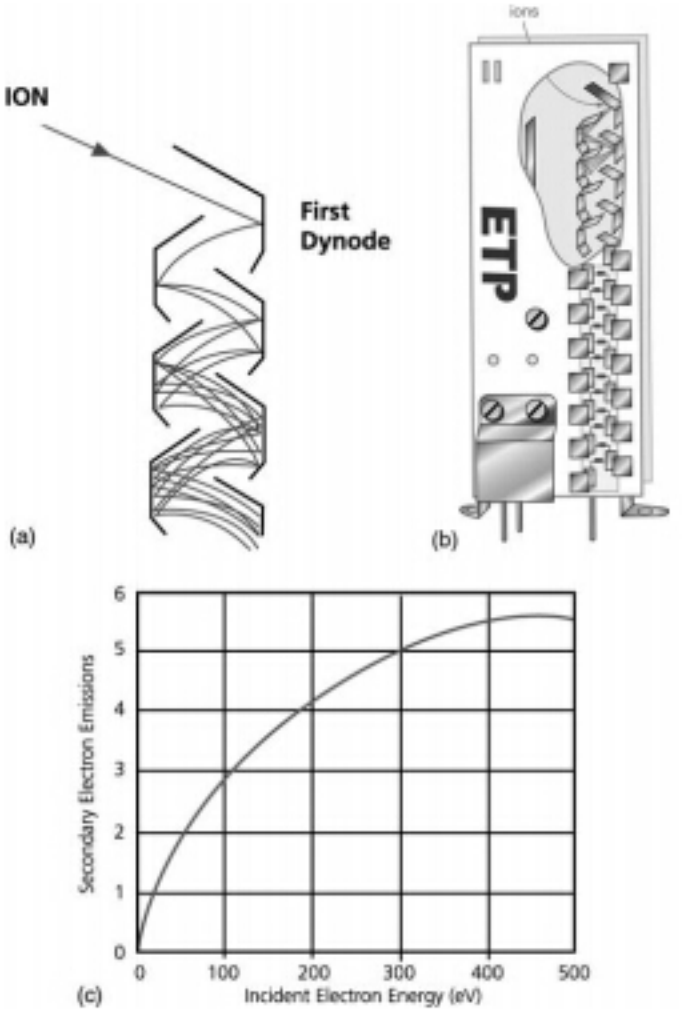

Figure 9.26 (a) A schematic discrete-dynode electron multiplier, showing the electron gain at each successive dynode after impact of an ion on the first dynode surface. The electron cascading process results in gains of up to 10^8 being achieved with approximately 21 dynodes. (b) An ETP electron multiplier schematic showing the position of the dynodes in the detector. (c) Dependence of the number of secondary electrons emitted on impact energy. [Images courtesy of SGE, Inc. (Austin, TX) and ETP Electron Multipliers Pty Ltd, a division of SGE (Sydney, Australia). (www.etpsci.com and www.sge.com).]

Faraday cup detector has no gain associated with it, unlike dynode-based detectors. This limits the sensitivity of the measurement.

High-precision isotope ratio mass spectrometers are designed with combinations of multiple Faraday cup detectors and multiple miniature electron multipliers (used as ion counters) for simultaneous isotope measurement. For example, the TRITON and NEPTUNE multicollector mass spectrometers from Thermo Electron Corporation can be configured with up to nine Faraday cups and eight ion counters to detect 17 ion beams simultaneously. Details of these instruments can be found at www.thermo.com. The use of multicollector instruments improves precision by two to three orders of

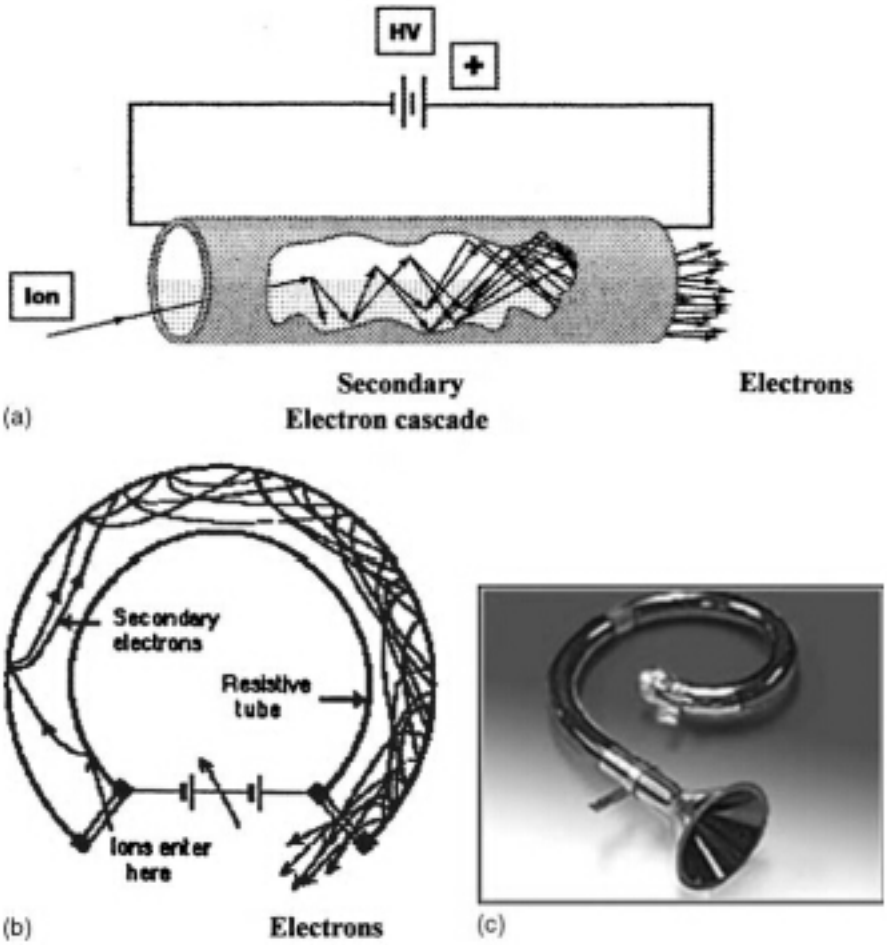

Figure 9.27 (a) A schematic channel electron multiplier (CEM), consisting of a glass or interior-coated ceramic tube that emits secondary electrons upon ion impact. (b) A schematic curved CEM. The curved shape minimizes ion feedback noise. (c) Photo of the Channeltron® electron multiplier, showing the curved glass tube without the associated electronics. [Courtesy of BURLE Electro-Optics (www.burle.com).]

magnitude over a single collector magnetic sector instrument, and this high precision is needed for isotope ratio measurements.

9.2.4.3. *Array Detectors*

The microchannel plate is a spatially resolved array detector formed of 10^5-10^7 continuous-dynode electron multipliers, each only 10–100 μm in diameter. This detector is used in focal plane mass spectrometers as a replacement for photograph plate detectors and is used in some TOFMS instruments.

The *focal plane camera* (FPC), still in initial development, consists of an array of 31 Faraday cups, each 145 μm wide. Up to 15 m/z values can be measured simultaneously. This detector shows improved precision compared with single channel detectors and has the ability to measure fast transient signals such as those from laser ablation. The detector design is described in the references by Barnes et al. and Knight et al. cited in the bibliography.