This article will give a short overview of the most common MS instruments and their working principles. However, this is not intended to be an exhaustive presentation of all possible techniques and variants. For more details we refer readers to dedicated literature on MS (1–3).

**Quadrupole Systems**

**Introduction.** Both quadrupole and ion trap systems use radio frequency (rf) and direct current (dc) voltages ($V_{rf}$ and $V_{dc}$).
ions will succeed in passing through this mass filter depends on their m/z value.

When \( V_{\text{rf}} > V_{\text{dc}} \), the low mass ions are lost in, for example, the x-direction because they readily follow the rapidly fluctuating rf potential and collide with the rods, such that only the heavier ions pass through (quadrupole working as high pass filter). At the same time, in the y-direction, the heavy atoms are lost because of their inertia towards the fast altering rf field (that is, quadrupole working as a low pass filter). The combination of both yields a stability window defined by the frequency \( \omega \) of \( V_{\text{rf}} \) and the ratio \( V_{\text{rf}}/V_{\text{dc}} \).

Working principle. In a quadrupole mass spectrometer (4) the rf and dc potentials are applied to four rods arranged in a square array (Figure 1). Ideally, rods with hyperbolic cross-sections should be used; however, in practice more economical cylindrical rods give results that are more than sufficient for most applications. Opposite rods are electrically connected. Application of voltages on these pairs of rods creates a hyperbolic field within the rods given by

\[
\Phi = (V_{\text{dc}} + V_{\text{rf}} \cos \omega t) \frac{x^2 - y^2}{r_0^2}
\]

resulting in a force on the ion at position \((x, y)\) proportional to the distance from the axis \((z)\) of the quadrupole. Whether

where \( r_0 \) is the distance between the rods.

When the known function of the electric field is substituted in the equations of motion we obtain the so-called Mathieu equations:

\[
\frac{d^2 x}{dt^2} = \frac{e}{m r_0} (V_{\text{dc}} + V_{\text{rf}} \cos \omega t) x = 0
\]

\[
\frac{d^2 y}{dt^2} = \frac{e}{m r_0} (V_{\text{dc}} + V_{\text{rf}} \cos \omega t) y = 0
\]

For a given quadrupole instrument, \( r_0 \) is a fixed value and the frequency of the rf potential \( \omega \) is constant. These equations are solved numerically and plotted (Figure 2) using two parameters:

\[
a = \frac{4eV_{\text{dc}}}{mw^2r_0^2}
\]

\[
a = \frac{2eV_{\text{rf}}}{mw^2r_0^2}
\]

All areas in the plot where \( x \) and \( y \) are smaller than \( r_0 \) (that is, the ion stays within the rods), represent a stable path through the mass spectrometer. The two experimental variables are the potentials \( V_{\text{rf}} \) and \( V_{\text{dc}} \). In most experiments the ratio \( V_{\text{dc}}/V_{\text{rf}} \) is constant. This defines a line in the a-q plot (see Figure 2). All ions with an m/z value that fits with points on this line within a stable region will move through the mass spectrometer. The intersection with the edges of the stability region defines the window of m/z values that are stable. Generally, the ratio \( V_{\text{dc}}/V_{\text{rf}} \) is chosen such that a 1 Da window is selected resulting in unit resolution over the entire mass range. Modern quadrupole
instruments have an upper mass limit between 3000 and 4000 Da. The separation of ions in a quadrupole does not depend on the kinetic energy of the ions entering the analyzer or the initial spatial distribution of the ions. However, the residence time between the rods has to be long enough to allow for the rf potential to influence them; that is, the residence time must be longer than the period of the rf voltage. This poses limits on the kinetic energy of the ions leaving the ion source/LC interface and entering the quadrupole to approximately 100 eV. Also, collision energies used in tandem MS instruments employing quadrupoles are limited to approximately 100 eV for the same reason (see the “Tandem Instruments” section).

Pros

• Energy and spatial distribution of ions produced in the source and entering the mass analyzer are not critical (important for coupling to LC because LC-MS interfaces generally produce ions with a relatively wide energy and spatial distribution)
• simple scanning method \( V_{dc}/V_{rf} = C^e \)
• low potentials allow relatively high pressures and simple vacuum systems
• low cost
• easy to couple multiple quadrupoles to one another or other MS analyzers (see the “Tandem Instruments” section).

Cons

• Low-resolution systems, typically 1 Da
• mass range limited to approximately m/z 4000.

Applications

• General low-resolution MS instrument
• molecular weight determination.

Ion Traps

Introduction. Together with the quadrupole instruments, ion traps are among the most widespread mass analyzers. Their small size and inherent tandem MS capabilities make quadrupole ion traps or “quistors” ideal for benchtop applications and MS experiments.

Working principle. The fundamental working principles of the ion trap (5) are the same as previously described for the linear quadrupole in the "Quadrupole Systems" section. One can describe a quistor as a linear quadrupole bent to a closed loop. The outer rod forms a ring, and the inner rod is reduced to a mathematical point in the center of the trap. The top and bottom rods form end-caps above and below the ring electrode (see Figure 3). These end-caps are perforated to allow the injection and detection of ions. Within this three-dimensional quadrupole, the ions travel on a Lissajous figure-shaped path. Similar equations of motion as used for the quadrupole are used to describe the behavior of ions in a quistor, except that \( r \) and \( z \) are used instead of \( x \) and \( y \).

Ions of different mass are stored together in the trap and released one at a time by scanning the applied voltages. Ions of selected mass can be ejected through the end-caps and detected by applying an rf voltage with a frequency corresponding to the characteristic frequency of the ion moving through the ion trap, or by scanning the amplitude of the applied rf voltage.

By allowing a \( 10^{-3} \) torr pressure of gas (often He), the motion of ions in the trap is dampened and the ions move closely around the center of the trap. This avoids ion loss by collisions with the electrodes and improves the resolution because all ions remain in a small space (limited spatial distribution), and field imperfection is minimal at the center of the trap. Without the damping gas, ions have a tendency to increase the radius of their motion because of the electrostatic repulsion of equally charged particles. As He or H\(_2\) is used in the trap, this makes ion traps natural detectors for coupling with gas chromatography (GC) in which the ions are formed by electron ionization (EI) with a short pulse of electrons in the ion trap. When applied in LC-MS, the ions are formed outside the ion trap and then transported into the cell for mass analysis.

Pros

• Energy and spatial distribution of ions produced in the source and entering the mass analyzer are not critical (important for coupling with LC because LC-MS interfaces generally produce ions with a relatively wide energy and spatial distribution)
• low potentials allow relatively high pressures and simple vacuum systems
• low cost
• small instruments (most systems fit on a benchtop)
• inherent tandem MS capabilities (see the “Tandem Instruments” section).

Cons

• Low-resolution systems, typically 1 Da; however, using specific scan methods higher resolutions can be obtained.

Applications

• General low-resolution MS instrument
• molecular weight determination.

Time-of-Flight Analyzers

Introduction. The initial idea of measuring the mass of an ion by its flight time was put forward by Stephens in 1946 (6, 7). The very simple concept makes time-of-flight (TOF) an
attractive method, but high demands on electronics and limited resolution constrained its applications. The technique was improved with the introduction of an electrostatic reflector (8). Enhanced ion optics to focus the ion beam from the LC-MS source into a pusher made coupling with LC available, while the development of fast electronics further improved the results of these instruments. When the ion-beam focusing lenses are replaced by a mass spectrometer (quadrupoles, sectors), TOF analyzers are readily incorporated in tandem MS instruments.

**Working principle.** The basic working principle of a TOF mass spectrometer involves measuring the flight time of an ion through the mass spectrometer (9, 10). Because the dimensions of the mass spectrometer are known, as is the energy of the ion, a straightforward calculation is required to obtain the m/z value of the ion.

We give the ion a well-defined kinetic energy by acceleration of the ion in a known electrostatic field. The kinetic energy is given by

\[ \frac{mv^2}{2} = qV \]  

(7)

Where the charge is

\[ q = ze \]  

(8)

The flight time of the ion through the mass spectrometer is

\[ t = \frac{d}{v} \]  

(9)

Substituting v yields

\[ \frac{m}{z} = t^2 \left( \frac{2Ve}{d^2} \right) \]  

(10)

For a given setting of V and a given apparatus (d is fixed) the value between brackets is a constant. Measurement of the flight time, t, yields the m/z value.

As a defined start/stop signal is essential for the time measurement, the ion input must be pulsed. This requires the introduction of some kind of pulsing device to convert the continuous flow of an LC system to a discrete series of ion packets. Often this is performed by focusing the ion beam orthogonal to the flight tube and using a pulsed electric field to push the ions into the TOF analyzer. This complies both with the limitations on energy and spatial distribution. The ion beam has little or no radial velocity component, and a well-focused beam orthogonal to the TOF analyzer has a well-defined position.

The correctness of the time measurement immediately influences the accuracy of the mass assignment. Also, the initial kinetic energy and spatial distribution of the ions is important. Variations of the kinetic energy or position of the ion when entering the acceleration region will influence the energy of the ions when starting their flight through the flight tube. These variations themselves will result in variations in the measured flight time and m/z value reducing the mass resolution of the system. As the energy and spatial distribution of most LC interfaces is not well defined, special measures must be taken in order to get good resolution using TOF instruments. The introduction of a reflector in the flight tube and the use of orthogonal injection techniques improved the mass spectrometric resolution by controlling or compensating for the initial energy spread and spatial distributions.

The electronics of the detector must be capable of recording the complete mass spectrum within the flight time of the ions (typically in the 1–100 μs range), with peak widths in the nanosecond range. Current state-of-the-art electronics use detectors with GHz sampling rates. Even at these high speeds, detectors are still a limiting factor on the resolution of TOF instruments (resolutions from 10,000 to 20,000 are routinely obtainable), given that all other components and experimental parameters are tuned to an optimum. Note that no instrumental parameter limits the detection of high-mass ions. Theoretically the highest detectable mass is only determined by the observed flight time. In practice, production and stability of the ions and response differences of the detector for different masses are the limiting factors for the detection of high m/z values.

**Pros**

- High scan rate (as high as 20,000 scans/s) allows for the detection of narrow/transient chromatographic signals
- high resolution when reflectron and high-speed electronics are used
- virtually no limit on mass range
- high sensitivity, no ion loss because of scanning.

**Cons**

- Strict demands on initial energy and spatial distribution of ions
- high-performance electronics needed
- low resolution in linear mode.

**Applications**

- High-resolution measurement using reflectron
- high-sensitivity measurements
- detection of transient signals (narrow chromatographic peaks).

**Sector Instruments**

**Introduction.** The very first mass spectrometer used by Sir J.J. Thomson was a sector instrument; that is, he used the same physical forces still applied in modern instruments. When studying the nature of cathode rays (electrons) he applied magnetic and electric fields to a beam of electrons and thus obtained an estimate for the m/e value of the charged particles in these beams (11). The modern descendants of Thomson’s devices are now highly sophisticated mass spectrometers working at high resolution, often in complex set-ups.
using multiple sectors (magnetic or electrostatic), and other mass analyzers (quadrupoles, TOF).

**Working principle.** Two types of sectors can be encountered in sector instruments: magnetic and electric, abbreviated respectively as B and E. For an ion (charge \( \text{ze} \)) moving in a magnetic field (B), we know that the charged particle moves on a circular path (radius \( r_m \)), where the centrifugal force equals the force of the magnetic field on the ion.

\[
ze B v = \frac{m v^2}{r_m} \tag{11}
\]

which yields

\[
m v = \text{ze} B r_m \tag{12}
\]

Note that the magnetic field works as a momentum \((mv)\) separator. If we want ions with equal mass and charge to follow the same path \((r_m)\) through the fixed magnetic field \((B)\), the momentum (or for a given mass the velocity \(v\) or kinetic energy \(m v^2/2\)) must be constant.

If we give the ions a known kinetic energy by accelerating them in an electric field \((V_a)\), we know that

\[
\frac{m v^2}{2} = \text{ze} V_a \tag{13}
\]

When we substitute velocity into the previous equation, we can measure the \(m/z\) value of an ion as a function of the experimental parameters \(B\) and \(V_a\).

\[
\frac{m}{z} = \frac{\text{ze} B r_m^2}{2 V_a} \tag{14}
\]

The kinetic energy of the ions depends on their initial energy and spatial distribution before acceleration. Therefore, an electrostatic sector is introduced. When the ions move through a radial electrical field, their path is determined by

\[
\frac{m v^2}{r_e} = \frac{\text{ze} V_e}{d} \tag{15}
\]

where \(V_e\) is the potential applied on the curved plates, \(d\) the distance between both plates, and \(r_e\) the radius of the path the ions follow in the electric field. For a given geometry, \(r_e\) and \(d\) are fixed, and the setting of \(V_e\) now selects the kinetic energy \(m v^2/2\).

As the ions move with the same velocity through both the magnetic and electrostatic sectors, we can equate the velocities used for electric and magnetic sectors that yield

\[
\frac{\text{ze} B r_m}{m} = \sqrt{\frac{\text{ze} V_a}{md}} \tag{16}
\]

From this equation we can measure a mass spectrum by scanning the magnetic field \((B)\) and the electrostatic field \((V_e)\)

\[
\frac{m}{z} = \frac{\text{ze} V_e B^2 r_m^2}{V_e d} \tag{17}
\]

From this equation we see that \(m/z\) is independent of the initial acceleration potential \((V_a)\). However, by stating that the final velocity after acceleration is equal to the velocity in the electrostatic sector, we obtain an instrument-defined correlation between the acceleration potential and the electric field strength \((V_e/d)\) in the electrostatic sector

\[
V_a = \frac{V_e d}{2d} \tag{18}
\]

In a double-focusing magnetic sector mass spectrometer, both a magnetic and electrostatic sector are used. Proper combination of both analyzers yields an instrument that corrects for the spatial and velocity (energy) heterogeneities of the incoming ions. Several different geometries are used (see Figure 4). These instruments give mass spectra with high resolution (greater than 10,000), high accuracy of mass and a wide mass range (greater than 15,000 Da). Both can be increased (resolution to \(100,000\) and mass range to greater than \(100,000\) Da), but at the cost of sensitivity loss because of reduced voltages and narrower slit openings. These instruments are used most often in fundamental studies.

To reduce the energy spread of the ion beam and improve ion extraction, the ion source is operated at high voltage (as high as 10 kV). This high energy allows high-energy collision-induced dissociation (CID) studies. However, these high voltages yield practical problems when coupled to an LC system. At the pressures used in LC-MS techniques, such as thermospray and electrospray, arcing is a serious problem, although good commercial solutions are available.
Pros
- High resolution and mass accuracy
- high-energy CID
- tandem MS experiments are possible.

Cons
- Expensive instruments
- scan speeds limited by hysteresis and heating of the magnets
- limited sensitivity, especially at high resolution
- LC-MS coupling technically demanding (sparking in the source)
- complex instruments.

Applications
- High-resolution measurements
- fundamental MS studies (for example, studies using fragmentation in the different field free regions.)

Fourier Transform Instruments

Introduction. The Fourier transform mass spectrometer (12) is the current version of the ion cyclotron resonance (ICR) mass spectrometer. Though being the nec plus ultra (nothing is higher) in terms of resolution (in excess of $10^6$), detection efficiency (one-molecule detection [13]), scans speed and the MS capabilities, its technical demands, especially in terms of vacuum technology, and its high price limit its use mostly to fundamental studies.

Working principle. As in sector instruments, a magnetic field is used to curve the motion of the ions. However, the applied magnetic field $B$ is so intense that the radius of the ion’s trajectory becomes smaller than the inner dimensions of the mass spectrometer, effectively trapping the ions on a circular path inside the ICR cell. An electric potential on the trapping plates prevents the ions from escaping laterally (Figure 5).

The ions circle in the ICR cell with an angular velocity given by

$$\omega = 2\pi v = \frac{zeB}{m}$$  \hspace{1cm} (19)

The mass spectrum is given by

$$\frac{m}{z} = \frac{eB}{\omega}$$  \hspace{1cm} (20)

For a magnetic field of $\pm 5$ T and a mass range of 15–1500 amu, radio frequencies in the kHz to MHz range result. When a radiofrequent potential is applied to the emitter plates (Figure 5), ions with the corresponding angular frequency will absorb energy and their trajectory radius will increase. Thus, ions first randomly distributed over the circular path will become focused into a packet of ions circling together. Once the ion trajectory comes close enough to the receiver plates, an “image current” will be induced that can be detected. Scanning the frequency will yield a signal if an ion with the corresponding $m/z$ value is present. This method can be thought of as pushing the keys of a piano one-by-one and listening to hear a note (that is, a string is present — ion of corresponding $m/z$ in the ICR). A faster method involves hitting the piano with a big hammer and listening to all the notes produced, and from that deriving which strings are present. In the ICR, this is done by exciting all ions present using a fast sweep of frequencies over a broad range. The receiver plates pick up the signals of all the ions present in the cell. This complex signal can be reduced to its component frequencies by Fourier transformation. The individual frequencies can then be converted to corresponding $m/z$ values by the equation given above. Note that the ions are not destroyed by the detection. Because they remain in the ICR cell, they can be reobserved (ion stability experiments) or fragmented for use in a second MS experiment (tandem MS).

At high frequencies/low $m/z$ detection is limited by the speed of the digitizers; at low frequencies/high $m/z$ the amplifiers and low frequency noise in electronics limits the mass range. The dynamic range is limited by the maximum number of ions that the ICR cell can hold. About $10^6$ ions are allowed in the cell. Larger numbers result in repulsion between ions and, subsequently, lower resolution.

Collisions with residual gas in the ICR cell reduce the amplitude of the cyclotron motion of the ions. As such, a high vacuum must be used ($10^{-8}$ torr). This poses a technical challenge when coupling with LC interfaces; however, successful couplings have been made (14). Because of the number of calculations needed for Fourier transform, dedicated high-performance computers are needed to cope with the data flow generated by an LC separation.

Pros
- Unsurpassed resolution
- high detection efficiency
- detection is not destructive (ion stability experiments)
- inherent tandem MS capabilities.

**Cons**
- High price, both in purchase and use (cooling of superconducting magnets)
- High vacuum, difficult to couple with high pressure ion sources (LC-MS)
- Demanding on computing facilities, problems with fast signal (narrow LC peaks).

**Applications**
- Extreme high-resolution measurements
- Fundamental ion chemistry studies
- Detection of single ions.

**Tandem Instruments**
Tandem mass spectrometry employs two or more stages of mass spectrometric analysis. Each mass spectrometer might scan, select one ion, or transmit all ions. In between two MS experiments, the ions can be subjected to different actions: collision with neutral or reactive gases; collision with surfaces; interaction with light, electrons, or other ions; acceleration; deceleration; neutralization; decomposition, and so forth. Selection from these scanning or nonscanning MS analyzers and the different actions on the ions between the analyzers yields a panoply of possible tandem MS experiments. Describing all of them is far beyond the scope of this text. Therefore, focus will be put on the most-used instruments and scanning methods.

**Tandem MS Scanning Methods**

**Product ion scan.** This is one of the most widespread scanning modes in MS-MS, often called “daughter ion scanning.” The first mass analyzer (MS1) is used to select an ion, called the precursor or parent ion, which is provided with extra energy in a reaction region to induce fragmentation. This energy can be high (kEV range) or low (eV range), and various techniques can be used to provide it. The most common method is to collide the precursor ion with an inert gas (often a noble gas) introduced into the reaction region, here called the “collision cell.” This process is termed collision-activated dissociation (CAD), and is the technique used in this study. Collisions with a solid surface result in surface-induced fragmentation. Alternatives include excitation of the ions by photon absorption using, for example, a laser, resulting in photodissociation, or the use of an electron beam to excite the ions. The excited ions fall apart into a charged fragment ion, the product ion, and one or more neutral parts. The product ions are then sampled into the next mass filter (MS2) scanning over the m/z range of interest and detected yielding a product ion spectrum (See Figure 6).

**Precursor ion scan.** In terms of activity of the mass filters, this scanning mode, also named “parent ion scan,” is the mirror image of the product ion scan. MS1 scans while MS2 is fixed at a chosen m/z value. Because there is only one response at the detector when a precursor of the selected ion passes through MS1, here the precursor ions of a selected product are detected (see Figure 7). This method can be applied to detect the nucleotides present in a more or less complex mixture. Selecting in MS2 a fragment typical for the presence of a phosphate moiety (PO₄⁻, m/z 79 in ES⁻), and scanning MS1 yields only a signal for those precursor ions bearing a phosphate group, thus reducing the interference (chemical noise) of other compounds in the mixture (15).

**Constant neutral loss.** When both analyzers are scanned with a fixed mass difference (MS1 higher than MS2), only those ions that lose that specific mass in the collision cell will be detected (see Figure 8). This feature provides another opportunity to detect products of a specific class containing similar structural features. Nucleosides are detected as a group by their loss of the (2′-deoxy)-ribose moiety (Δ = 116), which is characteristic for (2′-deoxy)-nucleosides; however, a whole range of losses can be used: (Δ = 18 for water, Δ = 44 for carbon dioxide, Δ = 46 for NO₂, and so forth). As for precursor ion scanning, constant neutral loss (CNL) enhances data by reducing chemical noise.

A related technique is constant neutral gain (CNG), essentially the same scan technique as CNL, but MS1 is a constant mass difference below MS2. For this technique to be applicable, the ions of interest passing through the collision cell...
should interact with the gas present there. Obviously, this requires some kind of reactivity of the collision gas, and the inert gases used for the techniques mentioned above are useless.

**Single/multiple reaction monitoring.** The selectivity of mass selection can be used to enhance the detection limits in analytical procedures. By fixing MS1 on the mass-to-charge ratio of interest, the signal at the detector is improved. The simple reason for this phenomenon is that practically all the ions of interest will be detected, whereas in scanning MS1 an important fraction of the ions of interest is lost. To eliminate interference from isobaric ions and the isotopic contribution of lighter analytes, one can select, after fragmentation, a product ion characteristic for the analyte of interest using MS2, thus removing the interference. A single reaction is monitored, yielding a highly selective detection with high sensitivity because of the removal of chemical noise. Selecting two or more characteristic ions is possible as well; this technique is called “multiple reaction monitoring” (MRM) (see Figure 9).

**Triple Quadrupole Instruments**
A triple quadrupole instrument uses two quadrupole MS analyzers for the actual MS experiments and a third quadrupole in rf-only mode, which transmits all incoming ions from MS1 to MS2 (16). This second intermediate quadrupole (in some commercial instruments higher multipole are applied) is placed in a partially closed area filled with a collision gas. In the majority of experiments a neutral gas, a noble gas is often used.

These instruments have all the advantages of the quadrupoles (as described earlier). Because both MS experiments are separated in space — that is, MS1 and MS2 are two different mass analyzers (for comparison see “Ion Traps” and “Fourier Transform Instruments”) — both mass spectrometers can be scanned simultaneously. This allows CNL and CNG experiments.

**Pros**
- Unit resolution tandem MS experiments
- relatively low price
- ease of operation
- high sensitivity in MRM experiments
- allows parent ion scanning, CNL and CNG.

**Cons**
- Limited to MS2 experiments.

**Applications**
- General tandem MS instrument
- sensitive detection system (MRM).

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**Quadrupole–TOF Instruments**

**Introduction.** The quadrupole orthogonal acceleration time-of-flight instrument is derived from triple quadrupole instruments. The last quadrupole is replaced by a TOF analyzer, often equipped with a reflectron. The collision cell is used to fragment the precursor ions and to decelerate the ions before orthogonal acceleration into the TOF analyzer. As the TOF analyzer is an obligatory scanning device, all tandem MS experiments requiring a nonscanning MS2 are excluded for a Q-TOF instrument. Also, experiments requiring parallel scanning of MS1 and MS2 are impossible (CNL and CNG). However, because of its fast scanning, intelligent software applications and dynamic experiments can overcome this potential handicap and produce results similar to, or even more informative than, precursor ion scanning, CNL, and CNG.

**Pros**
- High-resolution product ion spectra
- high sensitivity because of high transmission in MS2 (TOF).

**Cons**
- Parent ion scans and CNL/CNG require extra software.

**Applications**
- Proteomics.

**Ion Storage Systems**
In both ion traps and Fourier transform MS instruments, ions can be selected and stored in the MS, fragmented, and the product ions analyzed by a second MS experiment using the same mass analyzer; that is, the two (or more) successive MS experiments are separated in time instead of space (two different MS analyzers). Being an advantage for some types of
experiments (M S¹ is possible), M S-M S experiments in which M S1 scans and M S2 selects a specific product ion are impossible.

Pros
• Both ion traps and Fourier M S instruments have inherent tandem M S capabilities.

Cons
• Not all tandem M S experiments are possible.

Applications
• Proteomics.

Combinations with Sector Instruments

Introduction. Because most sector instruments use more than one sector, it is possible to analyze fragment ions that are formed in the field-free regions before and in between the sectors. Although widely used, the scanning methods are rather complex and resolutions are not very good, depending on the scan method used. As a result of the high ion velocities used in these instruments, high-energy CID spectra are generally obtained (collisions in the keV region).

Multiple sector instruments. By adding extra sectors to the instrument (E or B), performance as a tandem M S dramatically increases. Several different configurations are built and used. The most successful instruments appear to be of the EBE and BEB configuration. In these configurations, several different combinations of sectors and choice of reaction region can be made. Using EBE, the first two sectors can be used as a high-resolution M S selecting the precursor ion, and E analyzes the product ions. Using the BEB configurations, with B as M S1, the last two sectors can work as a high-resolving M S2 that yields product ion spectra with high resolution. Further extension to a four-sector instrument EBEB allows both M S1 and M S2 to be run at high resolution.

These complex instruments are often equipped with extra acceleration and deceleration lens stacks in between the sectors in order to control collision energies. They find their application mostly in fundamental ion chemistry and physics studies.

Sectors combined with quadrupoles. As quadrupoles are cheaper than sectors, the addition of quadrupoles to a sector instrument is more cost effective than adding extra sectors. Using quadrupoles also allows low-energy CID without another acceleration for M S analysis using a sector.

Sectors combined with TOF. Sectors have been combined with TOF measurements; however, these instruments are mostly built for fundamental studies and have few applications in the LC-M S field.

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