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History of Mass Spectrometric Techniques

In its history, mass spectrometry has passed through fascinating scientific epochs of development and supplied important contributions to the world view in quite different fields of science (especially in the life sciences, environmental science and technology, material and nuclear sciences, geosciences, cosmochemistry,[1] planetary and forensic sciences) and in basic studies in chemistry and physics.

Mass spectrometry is more than 100 years old and has yielded basic results and profound insights for the development of atomic physics. The rapid development of nuclear physics, in particular, would be unthinkable without the application of mass spectrometric methods. Mass spectrometry has contributed to conclusive evidence for the hypothesis of the atomic structure of matter. So far mass spectrometry has supplied specific results on the structure of the nucleus of atoms. Nobel prizes have been awarded to a number of scientists (Thomson, Wien, Aston, Paul, Fenn and Tanaka) associated with the birth and development of mass spectrometry, or in which mass spectrometry has aided an important discovery (e.g., for the discovery of fullerenes by Curl, Kroto and Smalley).

Relevant preliminary work for the development of mass spectrography started with Goldstein's discovery of anode rays, which are positive charged gas-phase ions, in gas discharge in the mid-1980s. The experimental arrangement of Goldstein's glow discharge tube as the simplest possible ion source is shown in Figure 1.3 and was firstly published in the '*Sitzungsbericht der Königlich-Preußischen Akademie der Wissenschaften*' in 1886.[2] Goldstein's method for generating positively charged ions in a gas discharge was used in the early mass analysis measurements of Wien,[3] Thomson[4] and Aston.[5] In 1898 Wien analyzed the anode rays by magnetic deflection and found that these rays carried a positive charge. The schematic of a Wien velocity filter with *EB* configuration (*E* – electrical sector field and *B* – magnetic sector field) is shown in Figure 1.4. In this experimental arrangement, the deflection of positively charged ions in a magnetic field is compensating by a superimposed deflection in an electrical field. For ions which are transmitted through a Wien

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Inorganic Mass Spectrometry: Principles and Applications J. S. Becker

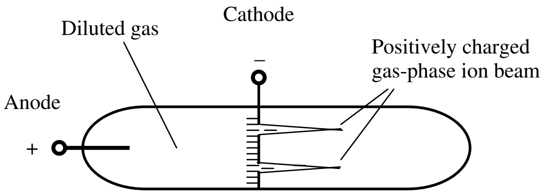

Figure 1.3 Goldstein's glow discharge tube (1886) for generation of positively charged ions. (C. Brunnée, Int. J. Mass. Spectrom. Ion Proc. 76, 125 (1987). Reproduced by permission of Elsevier.)

velocity filter it is valid that the electrical force (e E) that acts on an ion is equal the Lorentz force (e v B):

$$\mathrm{e}\,E = \mathrm{e}\,v\,B \tag{1.1}$$

The velocity of the ion (v) can be described then as the ratio of electrical field force (E) and magnetic field force (B):

$$v = E/B \tag{1.2}$$

$$\text{with} \quad v = \sqrt{2\mathrm{e}V/m} \tag{1.3}$$

The Wien velocity filter possesses a high sensitivity and allows analysis over a mass range (using a high accelerating voltage V), but with increasing mass the mass resolution decreases.[3] For his discovery Wien was honoured with the Nobel Prize in 1911.

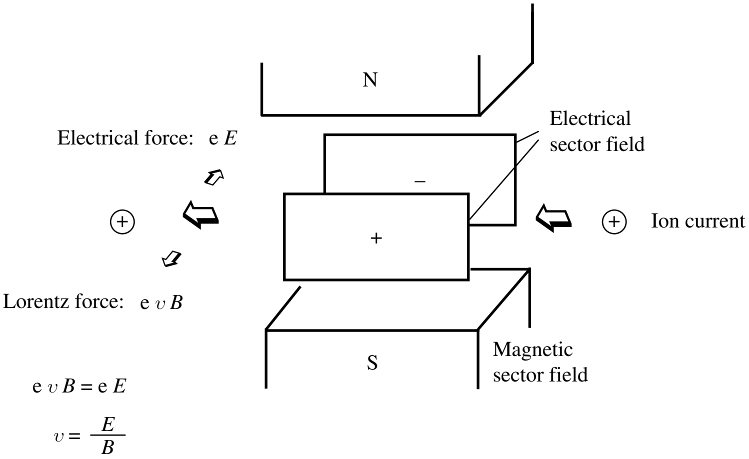

Figure 1.4 Schematic of a Wien velocity filter with EB configuration: combination of electric (E) and magnetic (B) field (Wien,1898). (C. Brunnée, Int. J. Mass. Spectrom. Ion Proc. 76, 125 (1987). Reproduced by permission of Elsevier.)

Just 11 years after Goldstein's first publication, Thomson discovered the electron and determined its mass-to-charge (m/z) ratio (in 1897). 'In recognition of the great merits of his theoretical and experimental investigations on the conduction of electricity by gases,' Thomson was honoured in 1906 with the Nobel prize 'for discovery of the electron and determination of its m/z ratio'. Thomson began his investigations of positive rays in 1907 and found that there was a 'different type of positive ions for each element'.[4]

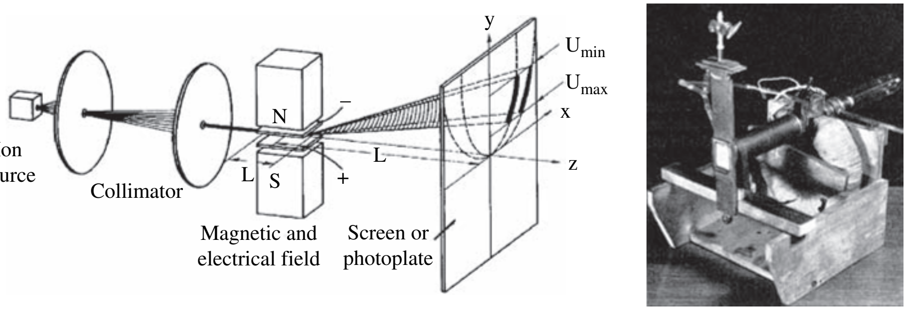

Figure 1.5 *Parabola mass spectrograph constructed by J. J. Thomson (1910) with a discharge tube as ion source, a superimposed electrical field and a magnetic field oriented parallel to it for ion separation, and a photoplate for ion detection. (H. Kienitz (ed.), Massenspektrometrie (1968), Verlag Chemie, Weinheim. Reproduced by permission of Wiley-VCH.)*

The real development of mass spectrometry goes back to 1910 when Thomson[6] found that neon consisted of two different isotopes with masses of 20 and 22 and so he discovered the isotopes of an element with the same chemical behaviour, but different isotope masses. This was the birth of the discovery of isotopes of elements by mass spectroscopy, whereby the history of isotopes is connected with the history of mass spectrometry. However, for mass spectrometry the most important instrumental development was Thomson's first parabola mass spectrograph (1907 and the improved version in 1910, see Figure 1.5). In this parabola mass spectrograph the positively charged ions (positive rays) were formed in a discharge tube. The direction of ion bundle was determined by two apertures. The ions were then deflected by a superimposed electrical field and a magnetic field oriented parallel to it, whereby ions with equal mass, but different energy (and velocity) were detected using an ion-sensitive photoplate in a parabola. In a later work in 1913, Thomson analyzed by means of his parabola mass spectrograph, the line at mass 22 together with the expected more intense line at mass 20 in the mass spectrum of neon. The first mass spectrum that demonstrated two stable isotopes of neon with masses of 20 and 22 and an isotope ratio of about 9 : 1, is shown in Figure 1.6. After the discovery of the neon isotopes by mass spectrography, Thomson tried to separate them by distillation. A few years later Aston[6] found a further very low-abundance neon isotope (of roughly 0.3 %) with a mass of 21 u. With the discovery of isotopes of elements by Thomson in 1910 together with investigations by Mosley[7] on the X-ray line spectra of elements, basic knowledge was obtained about a property of a chemical element which is determined by the atomic number, but not by the mass number. Thomson is accepted as the father of mass spectroscopy today (his fundamental discovery of isotopes by mass spectrometry and the development of first mass spectrograph was, however, not honoured by a Nobel Prize).

In several experiments Thomson also introduced molecules such as $COCl_2$ and hydrocarbons into the discharge ion source of the parabola mass spectrograph and observed the formation of

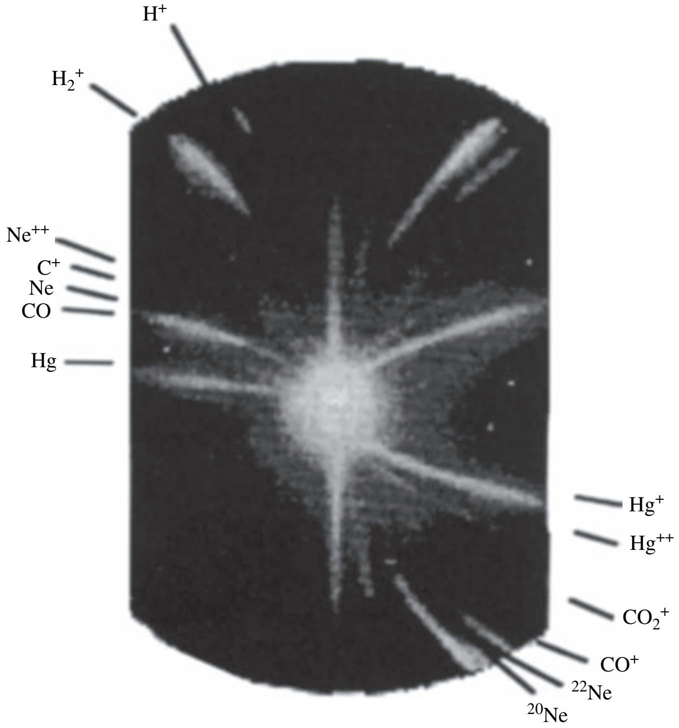

Figure 1.6 *Mass spectrum of neon with masses 20 and 22 u measured by J. J. Thomson (1913) using his parabola mass spectrograph is shown in Figure 1.5. (H. Kienitz (ed.), Massenspektrometrie (1968), Verlag Chemie, Weinheim. Reproduced by permission of Wiley-VCH.)*

many parabolas, revealing the formation of a variety of positively charged fragments (e.g., those corresponding to $COCl_2^+$, CO^+, C^+, O^+, etc.). Because the photoplate, as an ion-sensitive detector, has different sensitivities for the various ions, a quantitation of the relative intensities of the ions was not possible at that time. Especially for mixtures of hydrogen and oxygen, varying in composition over wide ranges, there was little difference in the intensities of the H_2^+ and O_2^+ ions on the photographic plate. Thomson replaced the photographic plate by a Wilson tilted electroscope and Faraday cylinder behind a parabolic slit. By changing the magnetic field and taking 10 s measurements, Thomson demonstrated the first mass spectrum as a plot of the ion current as a function of the mass-to-charge (m/z) ratio. Using the electrical detection system, he was able to achieve more accurate proportions of hydrogen and oxygen content in a given mixture compared to his measurements by photographic ion detection.

Aston, with experience in chemistry as well as physics, began working at the Cavendish Laboratory in 1909 on separating isotopes using mass spectrography. He started to assist Thomson in his study on positive rays. Together they improved on Thomson's original apparatus.

A quite different type of mass spectrometer – the first 180° magnetic sector field mass spectrometer (see Figure 1.7), with directional focusing of ions for isotope analysis, was constructed by Dempster, independently of other instrumental developments in mass spectrometry, in 1918.

Dempster also introduced a monoenergetic source – the electron bombardment ion source – into mass spectrometry[8] and analyzed ions of constant energy, which were extracted from the ion source (A) and were accelerated through a slit into the magnetic sector field. The positive single charged ions were separated in the 180° magnetic sector field (B) according to their mass and could be directed by changing their accelerating voltage or the power of the magnetic sector field on the exit slit. Ions starting with divergence in their direction from the entrance slit of the magnetic sector field were focused on the exit slit. This means that this semicircular uniform magnetic sector field arrangement was the first instrument with directional focusing. The separated ions were collected in a Faraday cup (C) and subsequently measured electrometrically using an electrometer (D). Dempster[8] measured curves for the ion current by gradually changing the magnetic field strength. For selected isotopes maximum ion intensities were observed, whereby the height of a selected maximum was proportional to the abundance of the isotope. With this apparatus (see Figure 1.7) Dempster discovered, in 1920, the isotopes of magnesium and later lithium, potassium and zinc.

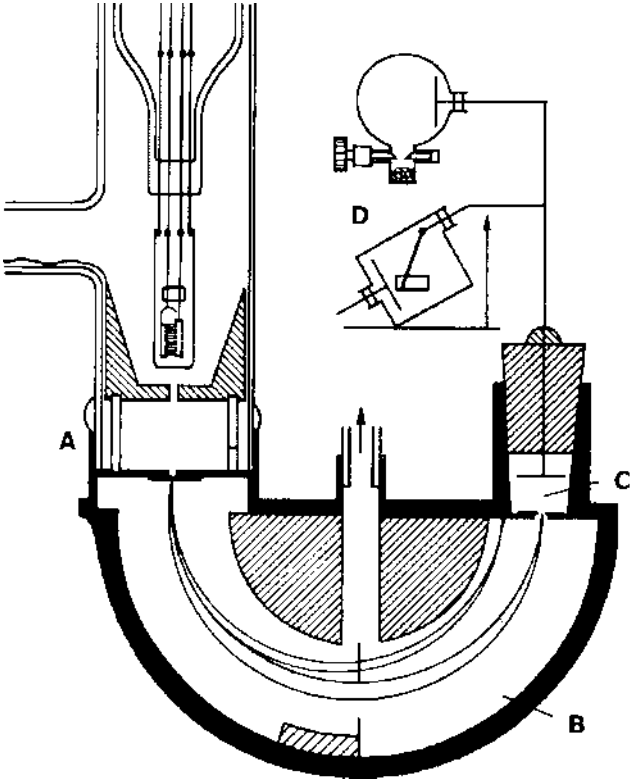

Figure 1.7 *Mass spectrometer from A. J. Dempster (1918). A – ion source; B – electromagnet; C – Faraday cup; D – electrometer. (H. Kienitz (ed.), Massenspektrometrie (1968), Verlag Chemie, Weinheim. Reproduced by permission of Wiley-VCH.)*

The typical mass spectrum of magnesium with three stable isotopes of masses 24 u, 25 u and 26 u using this magnetic sector field mass spectrometer with an electrometer for ion detection is shown in Figure 1.8. Dempster's mass spectrometer was of a simpler design that Aston's mass spectrograph, but could not be used for precise mass measurements. On the other hand, this magnetic sector field mass spectrometer was better suited than Aston's mass spectrograph for measuring the relative abundances of the ionic species and was used for initial investigations of electron impact processes in gases.

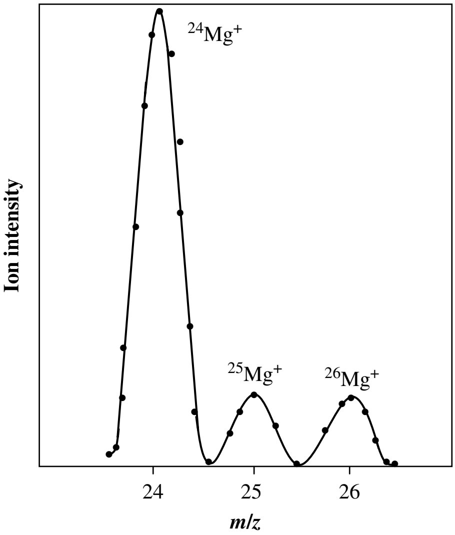

Figure 1.8 *Mass spectrum of magnesium with masses 24u, 25u and 26u (Dempster 1921). (H. Kienitz (ed.), Massenspektrometrie(1968), Verlag Chemie, Weinheim. Reproduced by permission of Wiley-VCH.)*

Another way of focusing ions was applied by Aston in his first mass spectrograph developed in 1919 (Figure 1.9). This mass spectrograph contained a separation of electrical and magnetic fields and used ion detection with an ion-sensitive photoplate.[9] The ions formed in a discharge tube were directed using two diaphragms. The ion beam passing through an electric and subsequent magnetic field was separated according to the difference in mass, and ions with different velocities (kinetic energy) flew on different pathways, but were focused at one point of the photoplate. Aston's instrument was the first mass spectrograph with velocity focusing of ions. Mass spectrographs developed between 1915 and 1920 were ultilized for two different applications: one was concerned with the precise determination of masses, and the other with measuring the relative abundances of isotopes. The mass spectrograph developed by Aston with photographic ion detection was applied mainly for measurements of isotope masses to a precision of 0.1 %, but it was not suited for accurate determination of the relative isotope abundances. In Figure 1.10, mass spectra of different inorganic and organic gases (BF_3, SiF_4, CH_3Br, SO_2 and AsH_3), recorded by Aston in 1920, are presented. Apart from the detection of isotopes of matrix elements (e.g., both boron isotopes at masses 10 u and 11 u or monoisotopic fluorine at mass 19 u), also several impurity elements were detected, for example, C, N, and O at masses 12 u, 14 u and 16 u in the mass spectrum of BF_3, or Hg in the mass spectrum of SO_2 and AsH_3 as contaminant from mercury diffusion pumps applied in the instrument. Furthermore, fragment ions were detected by studying mixtures of light hydrocarbons. Since this time $^{12}C^{16}O^+$ and $^{12}C^{16}O_2{}^+$ ions at masses 28 u and 44 u have been used as reference points for the interpretation of mass spectra and for the calibration of mass scales at light masses. It should be noted that the term 'mass spectrum' was introduced by F. W. Aston in 1920. At this

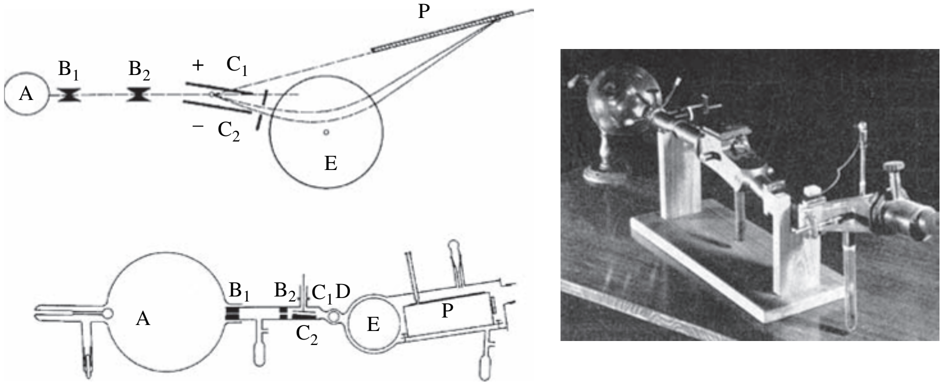

Figure 1.9 Mass spectrograph from F. W. Aston (1919/20). A – ion source (discharge tube); B_1, B_2 – slits; C_1, C_2 – plates of condensator; D – valve; E – magnet; P – photoplate for ion detection. (H. Kienitz (ed.), Massenspektrometrie (1968), Verlag Chemie, Weinheim. Reproduced by permission of Wiley-VCH.)

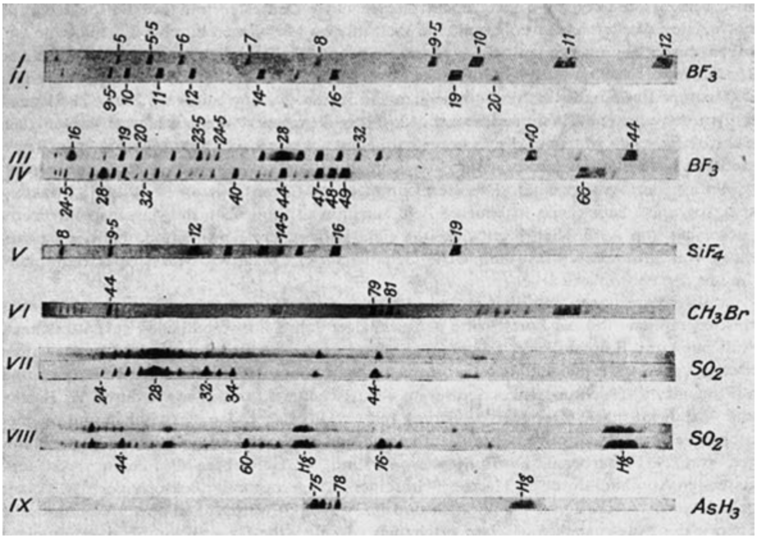

Figure 1.10 Mass spectra of different gases measured by F. W. Aston in 1920. (H. Kienitz (ed.), Massenspektrometrie (1968), Verlag Chemie, Weinheim. Reproduced by permission of Wiley-VCH.)

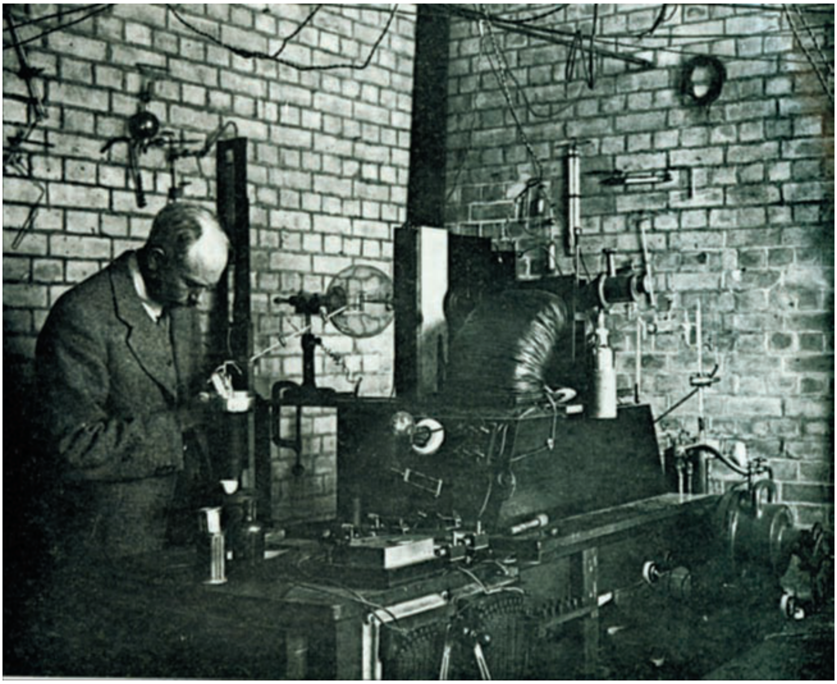

Figure 1.11 *F. W. Aston with second mass spectrograph (1922).*

time mass spectrometers were capable of precise mass determinations and measurement of relative abundances of ions, but could also perform valuable electron impact studies.

In 1921, Aston began to build an improved mass spectrograph. Aston's second mass spectrograph (see Figure 1.11)[10] used curved plates to produce its electric field, so that deflected particles would always be midway between the plates. Aston built the batteries for these plates himself, and developed a large, heavy magnet, capable of producing a powerful magnetic field of 1.6 tesla.

At the beginning of mass spectrometry development, two significant discoveries were made. Firstly, the existence of stable isotopes, which is the basis of mass spectroscopy, was discovered by J. J. Thomson. Secondly, a significant discovery of mass spectrography – made by F. W. Aston – was that the masses of all isotopes are not simple multiples of a fundamental unit, but are characterized by its mass defect. The mass defect ($\Delta m = \mathrm{m_a} - A\mathrm{m_u}$) ($\mathrm{m_a}$ – atomic mass, $\mathrm{m_u}$ – atomic mass unit and A – mass number of the isotope) as a function of the atomic number (Z) is presented in Figure 1.12. In 1923 Aston measured mass defects of a multitude of isotopes.[11] By precise determination of the masses of isotopes using mass spectrometry, the experimental evidence for the mass defect of isotopes was obtained and subsequently Einstein's equivalence principle between mass and energy was confirmed. This mass – energy relation postulated by Einstein was first proved experimentally in 1932 by Bainbridge[12] by measuring the masses of the nuclei involved in the following nuclear reaction of hydrogen $^{1}\mathrm{H}$ with lithium $^{7}\mathrm{Li}$:

$$^{1}\mathrm{H} + {}^{7}\mathrm{Li} \rightarrow 2\,{}^{4}\mathrm{He} + \mathrm{Q} \tag{1.4}$$

For this experiment Bainbridge used the high-precision mass spectrograph he had developed by combining a Wien filter with a 180° magnetic analyzer.[13]

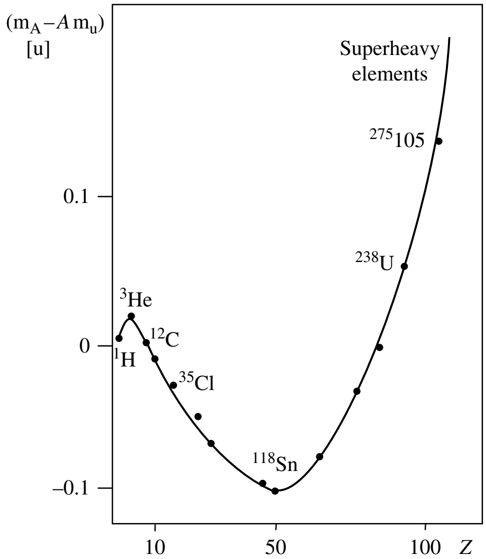

Figure 1.12 *Mass defect as a function of atomic number.*

With the 180° mass spectrometer with electrometric ion detection developed by Dempster serving for the precise electrometric measurements of isotopic abundances and the mass spectrograph created by Aston with an ion-sensitive photoplate for the exact mass determination of isotopes, a multitude of measurements were carried out for the characterization of naturally occuring stable isotopes of chemical elements. In Figure 1.13, the mass spectra of Cd and Nd measured by Dempster in 1935[14] using a photographic plate for ion detection are shown. Since the beginning of mass spectrography many other stable isotopes have been discovered and studied mass spectrometrically. By 1933 183 isotopes of 66 elements had been discovered. Of the 283 isotopes of 83 elements detected by 1948, 202 isotopes of 71 elements were found by Aston. Therefore Aston is accepted as the actual 'father of the isotopes'. For his discovery, by means of his mass spectrograph, of isotopes in a large number of non-radioactive elements and for his formulation of the 'whole-number rule' Aston was awarded a Nobel Prize in 1922.

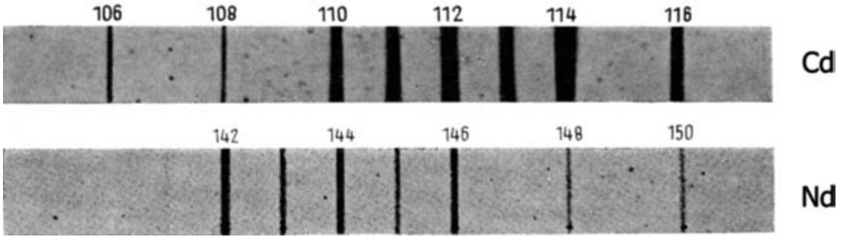

Figure 1.13 *Mass spectra of Cd and Nd measured by Dempster (1935). (H. Kienitz (ed.), Massenspektrometrie (1968), Verlag Chemie, Weinheim. Reproduced by permission of Wiley-VCH.)*

In 1937, Aston built his third mass spectrograph with an improved magnetic sector field. The slit system for focusing charged ion beams could now be adjusted externally and a more sensitive photographic plate from the Ilford Photographic Company was used. The mass resolution of Aston's final mass spectrograph was about 20 times greater than his first, and this instrument was about 100 times more accurate in the mass determination of separated ions.

Progress in mass spectrometric development was demonstrated, in particular, by a significant improvement in the resolving power of instruments (or mass resolution: $R = m/\Delta m$, if Δm is the smallest mass difference for which two mass lines with masses m and $m + \Delta m$ are resolved) and the sensitivity of the analytical method. Whereas in Thomson's parabolic mass spectrometer the resolving power was only 15, Dempster's 180° magnetic mass spectrometer and Aston's first mass spectrograph had a mass resolution of 100 and 130, respectively. The resolving power was significantly increased to 2000 in Aston's third mass spectrograph. Subsequently, theoretical and practical developments in ion optics enabled further improvements to be made to mass spectrometers and mass spectrographs with respect to resolving power, sensitivity and detection limits of elements. In the 1930s Barber[15] and Stevens[16] theoretically and experimentally studied the effect of the directional focusing of ions in magnetic fields after a deflection of 180°. Hughes and Rojanski[17] demonstrated the directional focusing properties of the electrical field of a cylindrical condenser if the deflection angle is 127°. Herzog and Mattauch[18] generalized the calculations for other deflection angles and Henneberg[19] studied the directional focusing properties of electrical and magnetic fields. The first suggestion of applying directional focusing and velocity focusing simultaneously was published by Dempster and Bartky[20] in 1929. Relevant work on the theory of the ion optical system of mass spectrometry was done in the middle of the thirties and focused on the development and construction of powerful double-focusing mass spectrographs, for example by Mattauch and Herzog[21] in 1934. The practical application of the construction of a double-focusing mass spectrometer was completed in 1936 on the basis of theoretical work on ion optics in instruments with significantly improved mass resolution for the precise determination of isotopes masses by Mattauch and Herzog.[21] This special combination of a 31.8° electrical field and a 90° magnetic field (Mattauch–Herzog geometry) allowed – by the double focusing of ion beams along a 25 cm long photoplate – an improvement of mass resolution of up to 6500. This type of mass spectrometer initiated a new era of so-called high-resolution instruments. Independently of Mattauch and Herzog, Dempster[14] in Chicago, and Bainbridge and Jordan[22] at Harvard University developed instruments with double-focusing properties for ion beams over a small mass range detected on the ion-sensitive photoplate. Whereas in Dempster's mass spectrograph[14] with a 90° deflection condenser and 180° magnetic sector field, a mass resolution of 1000 was observed, Bainbridge and Jordan's apparatus[22] with a 127° deflection condenser followed by a 60° magnetic field allowed a mass resolution of 10 000. In the following years Dempster, Bainbridge, Mattauch and coworkers used double-focusing mass spectrometry to measure a multitude of doublets from which the exact masses of isotopes were determined.[23] The applied ion optical system is unique in providing double focusing simultaneously for ions of all masses. The special feature of this system, namely that on a plane ion detector (e.g., photoplate) the separated ions beams are registered over a relatively large mass range, opened up the application field of multi-element analysis of inorganic solid samples.

Significant progress in inorganic mass spectrometry was made with the introduction of the spark ion source by Dempster in 1934[14,24] for the direct solid analysis of electrical conducting solids (e.g., metals, alloys or graphite). The application of a pulsed radio-frequency (rf) spark source combined with a double-focusing mass spectrograph using Mattauch–Herzog geometry and an ion-sensitive photographic plate for quasi-simultaneous detection of separated ion beams meant that the multi-element trace analysis of nearly all chemical elements even in non-conducting solid samples was possible with detection limits down to the 0.1 μg g^{-1} concentration range.[25]

Double-focusing mass spectrometers with high mass resolution are rather bulky and expensive instruments so that the development of single magnetic sector field mass spectrometers was of significance in the following years.

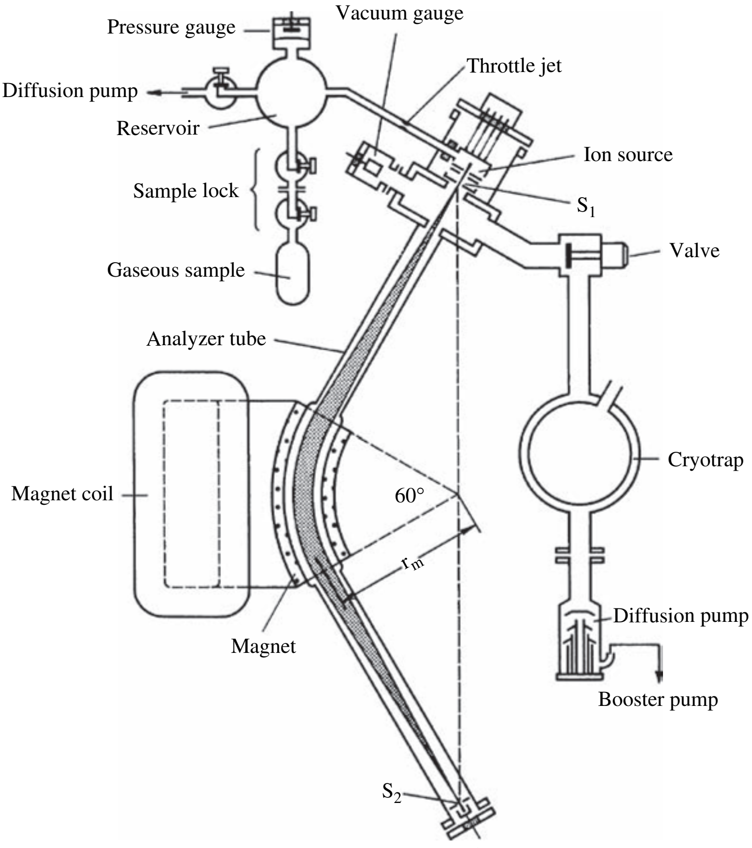

Figure 1.14 *Schematic of a 60° magnetic sector field mass spectrometer (Nier's mass spectrometer, 1940); S_1 – entrance slit; S_2 – exit slit. (H.Kienitz (ed.), Massenspektrometrie (1968), Verlag Chemie, Weinheim. Reproduced by permission of Wiley-VCH.)*

In 1940 Nier[26] designed a new type of sector field mass spectrometer – a single-state 60° sector field instrument – which was significantly simpler and cheaper in comparison to double-focusing sector field instruments of similar capability. Figure 1.14 shows the experimental arrangement of the Nier 60° magnetic sector field mass spectrometer. A schematic of a commercial 60° magnetic sector field mass spectrometer (type CH4, Atlas MAT) for analysis of gases is illustrated in Figure 1.15.

Nier's instrumentation, in comparison to the mass spectrometers existing at that time in 1934, was well developed and was extensively used for a quite different application during the Manhattan Project (1940–1945): for separation of uranium isotopes. It is well known that the ^{235}U isotope

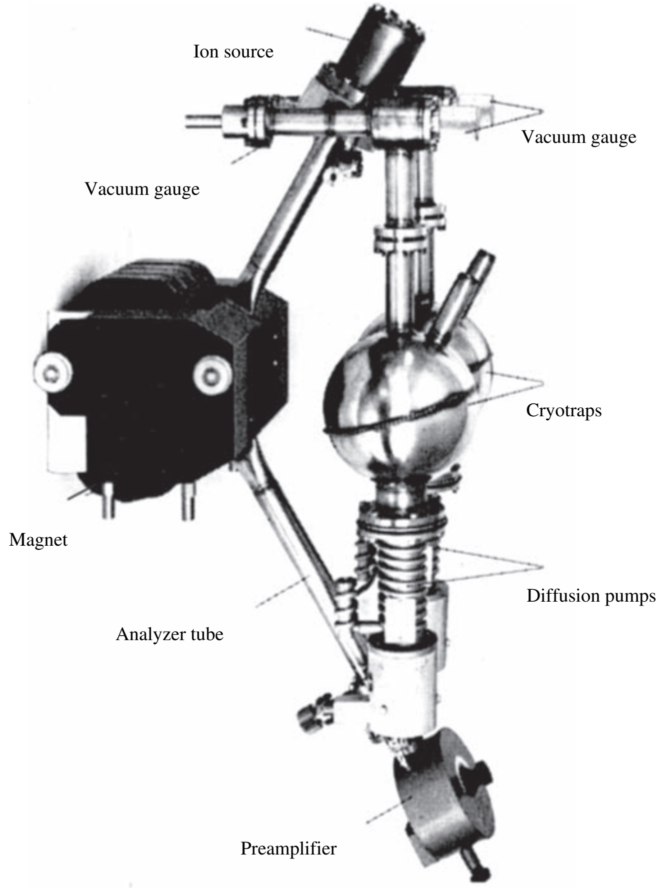

Figure 1.15 *Commercial 60° magnetic sector field mass spectrometer (Type CH4, Atlas MAT) for analysis of gases. (H. Kienitz (ed.), Massenspektrometrie (1968), Verlag Chemie, Weinheim. Reproduced by permission of Wiley-VCH.)*

is responsible for the process of fission by neutrons used in nuclear weapons and nuclear power plants. Using this apparatus Nier had already separated μg quantities of ^{235}U from uranium of natural isotope composition (^{235}U isotope abundance: 0.72 %) in 1940.[26] Nier, Booth, Dunning, and Grosse[27] proved in a similar way the practicability of ^{235}U fission using slow neutrons. In 1939, Alvarez and Cornog[28] had already used the 100 inch Berkeley cyclotron as a mass spectrograph in order to measure the rare ^{3}He with an abundance of 10^{-7} % in natural helium. In 1941, Lawrence and coworkers began to convert the 37 inch Berkeley cyclotron to a large mass spectrograph for isotope separation of uranium isotopes. By the end of 1941, using this mass spectrograph, uranium was separated, whereby the rare isotope ^{235}U with a natural abundance of 0.72 % was enriched to 3 %. An ion beam current of 5 μA was received at the ion collector for ^{235}U^{+}, ten times as large as that used by Nier and coworkers. At the beginning of 1942, 0.2 mg of material isotopically enriched to 30 % ^{235}U was obtained. With some further design changes, ion source modifications, and different collectors, a new unit was installed in the 37 inch magnet in early 1942 (the mass separator was named 'Calutron': *Cal*fornia *U*niversity Cyclo*tron*). The successful application of the Calutron for the isotopic separation of uranium was a precondition for the construction of more efficient electromagnetic separation devices (e.g., at Clinton and Oak Ridge, Tennessee) for the separation of ^{235}U with high enrichment. Solomon[29] noted that in 1945, 3 kg of ^{235}U was produced per day as nuclear material by electromagnetic separation in the USA. After the end of the Second World War the Calutron mass separator was also used for the magnetic separation of other highly enriched stable isotopes which could be applied for a multitude of scientific applications, such as isotope dilution analysis or tracer experiments in biology, medicine, geology, chemistry, material research, forensics and in other fields.

An important application of mass spectrometry in geoscience was the evidence of the ß-decay of ^{87}Rb obtained by Mattauch in 1937 as the fundamental decay process in the well-known Rb–Sr age dating method in geochronology. In continuation of the work by Strassman and Walling[30] in 1938, Ahrens[31] published his results on the development and application of the Rb–Sr geochronological method in 1949, based on the β-decay of ^{87}Rb in ^{87}Sr ($t_{1/2} = 4.88 \times 10^9$ years). The Rb–Sr age dating method was improved by the careful chemical separation of analytes (Rb and Sr) from matrix elements by the ion exchange technique introduced in 1953 by Aldrich.[32] In addition, the development, in particular, of thermal ionization mass spectrometry (TIMS) opened up the possibility of more precise isotope ratio measurements for studying the fine variation of isotope abundances in Nature. Today it is well known that the nuclear decay of naturally occurring radionuclides (e.g., $^{87}\mathrm{Rb} \rightarrow ^{87}\mathrm{Sr}$; $^{187}\mathrm{Re} \rightarrow ^{187}\mathrm{Os}$; $^{176}\mathrm{Lu} \rightarrow ^{176}\mathrm{Hf}$; $^{232}\mathrm{Th} \rightarrow ^{208}\mathrm{Pb}$; $^{235}\mathrm{U} \rightarrow ^{207}\mathrm{Pb}$ and $^{40}\mathrm{K} \rightarrow ^{40}\mathrm{Ca}$) results in a small to large variation of the isotope composition of the elements. These isotopic variations in nature determined by mass spectrometry are the results of naturally occurring decay processes and supply information on the age of minerals and geological formation. With further instrumental developments of sector field mass spectrometers, a major new area of application was improved in the 1950s and 1960s – geochronology for age dating of geological samples and minerals.

Although the physicist Nier was interested mainly in isotope research, including earth and planetary science, he was also aware of the importance of mass spectrometry for chemical analysis of organic compounds, especially for the quick and reliable analysis of complex hydrocarbon mixtures in oil refineries. So a new area of mass spectrometry began in 1942 with the construction of the first commercial mass spectrometer for organic analysis. Financial support for the production of commercial mass spectrometers by the Consolidated Engineering Corporation was indeed provided by the oil industry (Atlantic Refining Corporation). The first mass spectrometers were of the 180° deflection type (Consolidated Engineering Corporation model 21–101 instruments). This was the beginning of the large-scale application of mass spectrometry in analytical chemistry. Due to a series of physical and technical improvements to the vacuum system, ion optics, ion source developments (e.g., of the 'Nier-type' electron impact ion source, which allowed more homogeneous energy distribution of the ions formed) and electronics, single sector field instruments become dominant.[33] These magnetic sector field instruments can reach a mass resolution of a few thousands and were used for separation of ion beams with relatively low ion energy spread (at eV range).

For separation of ion beams with a wide energetic spread (at keV range) double focusing mass spectrometers are necessary. A further technical development to the high-resolution double-focusing mass spectrometer with Mattauch–Herzog geometry was proposed by Ewald[34] in 1946. This instrumentation allowed mass spectrometric measurements with mass resolutions of 30 000–50 000. In the fifties, mass spectrometry was improved by additional theoretical work (investigation of imaging properties for different field arrangements and calculation of imaging errors) by Ewald and Liebl[35] and Hintenberger and König,[36] which resulted in the development of mass spectrometers with high mass resolution. Of special importance, also for inorganic mass spectrometry, and still applied today in modern mass spectrometers, is the double-focusing mass spectrometer constructed by Johnson and Nier in 1952,[37] which employed an electrostatic analyzer symmetrically and a magnetic analyzer asymmetrically and thus allowed a large divergence angle while maintaining second-order directional focusing. Quisenberry *et al.*[38] enlarged this instrument and consequently increased the mass resolution to 75 000, which is of significance for the high-precision mass determination of isotopes. The first commercial double-focusing mass spectrometer was introduced by Kratos in 1957.

Basic investigations in mass spectrometry[39,40] continue to influence instrumental developments. The first application in ion cyclotron resonance mass spectrometry (ICR-MS) was described by Sommer, Thomas and Hipple in 1949.[41] Free radicals were also mass spectrometrically studied by G. C. Eltenton.[42]

Improvements in solid mass spectrometry after the Second World War focused on the development of several types of ion source and mass analyzers. For example, the fundamentals of secondary ion mass spectrometry had already been described by the observation of secondary ions by Thomson in 1910:[5] 'I had the occasion . . . to investigate the secondary Canalstrahlen produced when primary Canalstrahlen strike against a metal plate.' Significantly later in 1949, the first instrumental arrangement for secondary ion mass spectrometric measurements was reported by Herzog and Viehböck.[43] The idea of applying secondary ions for surface analysis was developed in 1950 at the RCA Laboratories, Princeton, where Honig[44] presented results of early SIMS studies.

The evolution in mass spectrometry in the forties and fifties was determined by the requirements of chemical analysis in industry and focused on the development of dynamic mass spectrometers (so-called 'non-magnetic' mass spectrometers). By replacing the heavy magnet, for example, by a quadrupole analyzer, not only was a significant decrease in weight, size and price of the instruments achieved, but faster scanning of electrical fields and shorter analysis time was also possible. Finnigan introduced the first commercial quadrupole mass spectrometer in 1968. Although quadrupole mass spectrometers are not as accurate and precise as double-focusing sector field mass spectrometers they are fast, and today they are the most widely used mass analyzers in organic and inorganic mass spectrometry, for the latter especially by coupling them to an inductively coupled plasma source. Yost and Enke built the first triple quadrupole mass spectrometer as an important tandem mass spectrometric instrument for structure analyses in 1978,[45] and this design was introduced commercially on the analytical market by Finnigan and Sciex in 1982.

The instrumental development of a quadrupole ion trap, which can trap and analyze ions separated by their m/z ratio using a 3D quadrupole radio-frequency electric field, was initiated by Paul and coworkers in the fifties.[46–48] The advantage of Paul's quadrupole ion trap is the reduction of instrumental size at high mass resolution, high sensitivity and the possibility of analyzing compounds at high masses (~100 000 Da), for example proteins and large biomolecules. Furthermore, collision-induced dissociation using a collision gas in the ion trap can solve the interference problems by isobaric ions in mass spectrometry. Finnigan MAT introduced an ion trap system for GC-MS in 1983. 'For the invention of the separated oscillatory field method and its use in the hydrogen maser and other atomic clocks . . . (and) for the development of the ion trap technique' Paul was honoured with the Nobel Prize in 1989.

Another type of dynamic mass spectrometer is the time-of-flight (ToF) analyzer. In 1946, Stephens presented his concept of the linear time-of-flight mass spectrometer (ToF-MS) as the simplest mass separation technique at an American Physical Society meeting in Cambridge, MA.[49] Cameron and Eggers first published the design and showed mass spectra for linear ToF-MS in

1948.[50] At the same time, Goudsmit demonstrated improved mass determination by ToF-MS with an accuracy to the third decimal place for xenon isotopes.[51,52] Progress in the development of the linear ToF by the Bendix Corporation was made by Wiley and McLaren[53] during the fifties. Both designed the first commercial time-of-flight mass spectrometer – the Bendix instrument (Detroit, Michigan) – which was produced in 1958. In a time-of-flight analyzer ions acted upon by the same electrical impulse acquire velocities inversely proportional to their mass, so that they pass the same distance through a field-free space to the detector in a different time. Due to the advantages of the time-of-flight analyzer: unlimited mass range, high ion transmission (there are no slits) very high recording speed (10 000 mass spectra per second) and simplicity of flight tube, this type of dynamic mass spectrometer attained increasing popularity in the following decades. The direct coupling of gas chromatography (GC) and ToF-MS was achieved in the mid-fifties by McLafferty[54] and Gohlke.[55,56] GC-MS became one of the most important hyphenated routine methods and ushered in a new era in bioorganic analysis since biological and medical samples were now also increasingly analyzed with respect to, for example, hormones and steroids.

Time-of-Flight mass spectrometers in combination with a pulsed ion source were used in inorganic mass spectrometry (e.g., ToF-SIMS), but more frequently in organic mass spectrometry. Because of their high sensitivity and ability to detect all separated ion beams ToF analyzers have been used with liquid chromatographic systems for the identification of organic compounds of high molecular weight. In order to improve the mass resolution from several hundred to about 1000, an ion reflector – the so-called reflectron introduced by Mamyrin in 1974[57,58] – was added to the linear ToF. The reflectron compensates for possible differences in the flight times of ions to be analyzed resulting from their kinetic energies.

The development of laser ionization mass spectrometry was started by Honig and Woolston in 1963[59] with studies of laser beam solid surface interaction and ion formation processes. Due to the pulse character of laser-induced ions, ToF analyzers were coupled to laser ion sources in the seventies and produced commercially as LAMMA-500 and later LAMMA-1000 and 2000 (Leybold-Heraeus, Cologne, Germany).

In 1974, Comarisov and Marshall[60] developed Fourier transform ion cyclotron resonance mass spectrometry (FTICR-MS). This technique allows mass spectrometric measurements at ultrahigh mass resolution ($R = 100\,000–1\,000\,000$), which is higher than that of any other type of mass spectrometer and has the highest mass accuracy at attomole detection limits. FTICR-MS is applied today together with soft ionization techniques, such as nano ESI (electrospray ionization) or MALDI (matrix assisted laser/desorption ionization) sources.

Major progress in inorganic mass spectrometry was made possible by the development of inductively coupled plasma mass spectrometry in 1980 by Houk, Fassel and co-workers[61] and by Date and Gray[62] and especially with the commercial introduction of inductively coupled plasma mass spectrometry in 1983. Since that year, ICP-MS has experienced exponential growth and today plays the dominant role among the inorganic mass spectrometric techniques for trace, ultratrace and isotope analysis.[63,64] The coupling of a laser ablation system to ICP-MS was proposed by Gray[65] in 1985 and has been commercially available on the analytical market since 1990. Nowadays, LA-ICP-MS is the most versatile and sensitive solid mass spectrometric technique in direct trace, ultratrace and surface analysis and is extremely useful for isotope ratio measurements.

Two recently developed mass spectrometric techniques have had a major impact on the analysis of large biomolecules: matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS) and electrospray ionization mass spectrometry (ESI-MS). MALDI-MS was first introduced by Karas and Hillenkamp[66] and Tanaka *et al.*[67] in 1988 and has experienced an exponential development. It has become a widespread soft ionization technique for bioorganic samples, especially large biomolecules. Fenn and co-workers[68] first published the successful soft ionization technique for large synthetic polymers, and subsequently proteins, using ESI-MS in the late 1980s. An important feature of this technique was the transfer of analytes directly from solution to the gas phase ions with high charge states.[69] Fenn and Tanaka (together with Wüthrich) received the Nobel Prize for chemistry in 2002 in recognition of their contribution to the characterization of biomolecular macromolecules and to mass spectrometry and nuclear resonance spectroscopy (NMR). MALDI and ESI are soft ionization techniques which, combined with low-cost mass analyzers (quadrupole, ion trap or ToF mass spectrometers) or more expensive FTICR-MS, are routinely used today for the analysis of proteins, peptides, synthetic polymers, small oligonucleotides, carbohydrates and lipids. In addition, the multiple-charging phenomenon enables large macromolecules to be detected in mass spectrometers of modest mass-to-charge ratio range. Further solution-based ionization methods, like thermospray and other liquid inlet sources, enables molecules to be introduced directly into a mass spectrometer from chromatographic and electrophoretic separation systems.

Today there are a number of mass spectrometer companies producing a wide variety of different types of quadrupole-based, sector field and ToF instruments for quite different applications in the trace, ultratrace, isotope and surface analysis of inorganic materials and for the structural analysis of organic and bioorganic compounds. Mass spectrometry for the structural analysis of organic compounds including large biomolecules is described elsewhere.

Detailed accounts of the history of mass spectrometry and the detection of isotopes are given by Ewald and Hintenberger,[70] de Bievre,[10] Kienitz,[71] Brunneé,[72,73] Duckworth *et al*.,[74] de Laeter[1] and Budzikiewicz and Grigsby.[75]

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