MASS SPECTROMETERS

APPLICATIONS OF MASS SPECTROMETRY

Mass spectrometers precisely determine the masses of ionized atoms or molecules with extreme sensitivity (1,2). Such investigations allow the following measurements.

The Identification of Atoms or Molecules

From a reasonably resolved mass spectrum, the original atoms or molecules (see Fig. 1) are identified by determining their atomic or molecular weight precisely. From such a mass spectrum the binding energies of different isotopes of one or of several elements are also determined (3,4) if the mass-resolving power $m/\Delta m$ of the mass analyzer is large enough (see also the section "The Magnetic Ion Trap Mass Spectrometer").

The Investigation of Macromolecules

The mass analysis of macromolecules is helpful for investigating very large biomolecules (see Fig. 2) and also atomic or molecular clusters. The goal of such investigations is to precisely determine the molecular weight.

The Determination of the Structure of Molecules

To understand the structure of complex organic molecules one can isolate ions of one specific mass in a first-stage mass analyzer, fragment this ion by gas collisions in some intermediate gas cell, and analyze the mass spectrum of the molecule fragments in a second-stage mass analyzer. This (MS/MS) technique (5) is used, for instance, in the amino acid sequencing of proteins (6).

The Measurement of Isotopic Distributions

When some isotopes of a certain element decay radioactively, the isotopic intensity distribution reveals the age of the sample. Some of the isotopes exist only in very small quantities while others are abundantly available. For this reason it is very important to use a mass analyzer that provides for a rather small mass cross-contamination from one mass to the next. The system must be designed properly for this purpose, and it must have a very good vacuum to reduce residual gas scattering of the most abundant ion species (see Fig. 3). Especially low mass cross-contamination is achieved by using high-energy ions accelerated in tandem accelerators (7). In

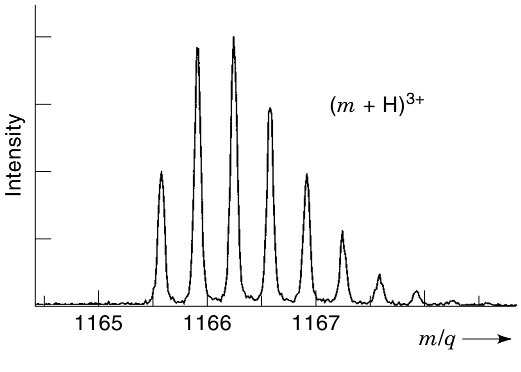

Figure 1. Mass spectrum of β-chain insulin of mass $m \approx 3494.9$ u, recorded as $(m + \mathrm{H})^{3+}$, that is, with one proton attached. This mass spectrum was recorded in a time-of-flight mass spectrometer (see Fig. 9) of mass resolving power $m/\Delta m = 17000$ (FWHM), that is, measured as the full line width at half maximum. Since carbohydrate molecules all contain about one ^{13}C-atom for every one hundred ^{12}C-atoms there is a mass multiplet of ions for every molecule. When the molecule is large, the probability is high that it contains one or several ^{13}C-atoms. Thus, the most abundant molecule is usually not the one that contains only ^{12}C-atoms.

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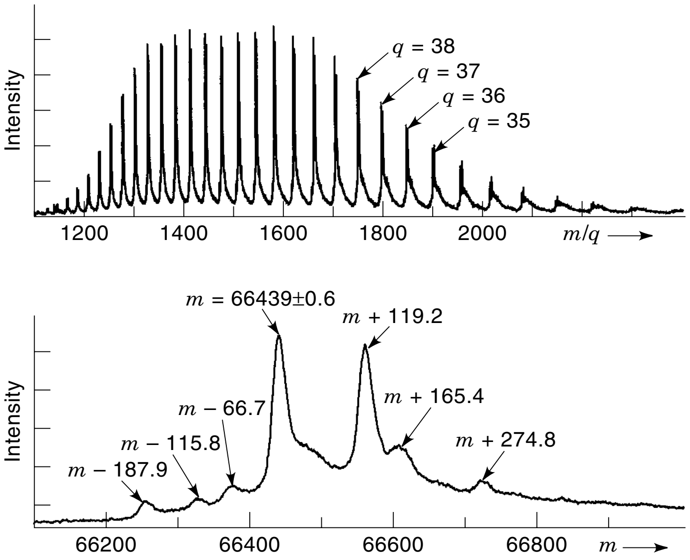

Figure 2. The mass spectrum of ≈30 to ≈55 times charged ions of albumin. This molecule has a molecular weight of about (66,439 ± 0.6) u. The time-of-flight mass spectrometer used for this investigation had only a mass resolving power $m/\Delta m \approx 12{,}000$ so that individual ion masses could not be separated from each other. Also shown is the mathematical combination of all of these mass distributions, from which one determines the molecular mass of albumin with certain adducts with a precision of only 10 ppm. The main adducts here had a mass of $m_1 = 119.2$ u.

such systems, for instance, the isotopic ratio $^{14}C/^{12}C$ can be investigated. This is important because ^{14}C, which has a half-life of 5730 years, is constantly produced in the earth's atmosphere by the sun, so that the $^{14}C/^{12}C$ ratio is a good measure for the age of old natural products, such as wood or bones.

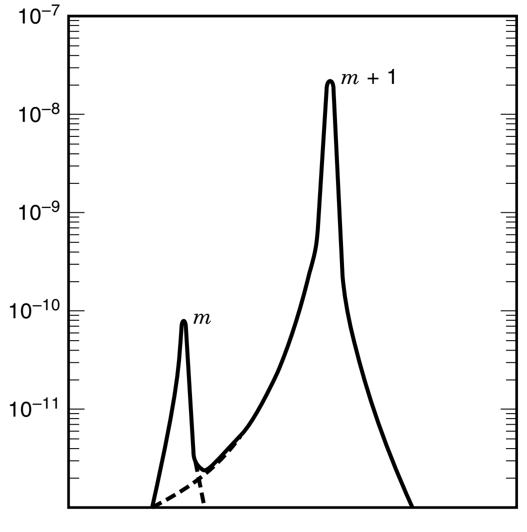

Figure 3. Mass cross-contamination caused by the tails of an intense neighboring mass line. The shown spectrum was recorded by a rather good sector field mass analyzer that had a (FWHM) mass-resolving power of $m/\Delta m \approx 5000$ and was operated at a pressure of only a few times 10^{-8} mbar.

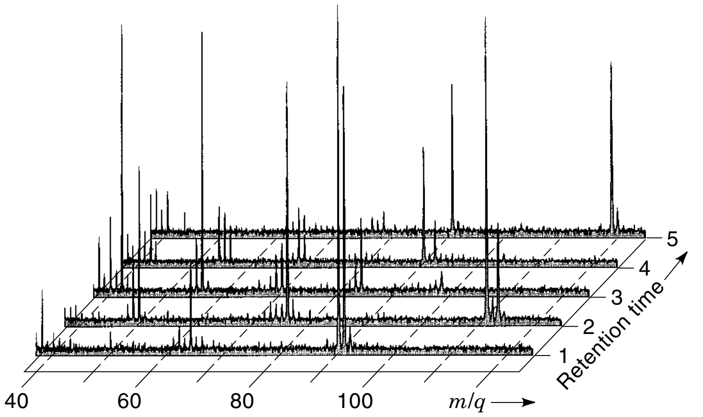

Figure 4. The record of a GC/MS investigation of traces of about 10^{-12} g of (1) toluene, (2) chlorobenzene, (3) nonane, (4) chloroheptane, and (5) *t* butylbenzene. For such a measurement several thousand or 10,000 mass spectra are recorded of the chromatograph effluent, and each mass spectrum is characteristic of the effluent at a specific time. For clarity, however, here only one mass spectrum is shown for each GC peak. A typical record, as shown here, requires several hundred seconds and in some cases up to a few thousand seconds because one must wait until the substance with the longest retention time leaves the gas chromatograph.

The Detection of Small Amounts of Specific Atoms of Molecules

To investigate the pollution, for instance, of water or air samples one can use the high sensitivity and specificity of mass spectrometers and combine them with the selectivity of gas chromatographs (GC/MS), liquid chromatographs (LC/MS), or of complex but powerful capillary zone electrophoresis (CZE) systems. In such chromatographs the molecules are separated according to their chemical adsorption properties (8), that is, simultaneously injected chemically different molecules leave the chromatograph successively. A specific substance is identified in such a system by the mass spectrum of the chromatograph's effluent recorded at a specific time (see Fig. 4).

FUNDAMENTALS OF MASS SPECTROMETRY

The very diverse applications described are all united by the use of the same instrumentation. Thus it is necessary to describe the mass spectrometric techniques in some detail.

An atomic or a molecular ion to be mass analyzed is characterized by

1. its mass m measured in *mass units* u, that is, the mass of one-twelfth of a ^{12}C-atom;
2. its charge q measured in *charge units,* that is, the negative value of the charge of one electron or ≈1.6022×10^{-19} C;
3. its kinetic energy $K = qV$ measured in electron volts where V is the potential difference by which the ion has been accelerated; and
4. its velocity v measured in kilometers per second or in millimeters per microsecond (9) is given by

$$v \approx 9.82269\sqrt{\frac{2K}{m}} \tag{1}$$

The numerical multiplier is found from $c/\sqrt{m_u} \approx 299{,}792{,}458/\sqrt{931{,}494{,}300}$ where c is the velocity of light in millimeters per microsecond and m_u is the energy equivalent of one mass unit in electron volts.

MASS ANALYZERS

To distinguish ions of different masses, the electromagnetic fields used can either provide a lateral dispersion, that is, a mass-dependent beam deflection or a longitudinal dispersion, that is, a mass-dependent flight-time difference. In the second case one must use a chopped and bunched ion beam, whereas in the first case bunched ion beams and dc beams can be used.

Laterally Dispersive Mass Analyzers

Laterally dispersive mass analyzers consist mainly of a magnetic deflecting field of flux density B measured in Tesla (T). In a magnetic flux density B, nonrelativistically fast ions ($v \ll c$) of mass m, energy K, and charge q move along radii ρ measured in millimeters according to the expression

$$B\rho \approx \frac{\sqrt{2Km}}{9.82269q} \tag{2}$$

Usually the ions produced are all accelerated by the same potential difference V_0 so that their kinetic energies are all $K_0 = qV_0$. Thus their velocities $v_0 \approx 10\sqrt{2K_0/m}$ are also the same. However, because of the ionization process, the ions always have an energy spread $\pm\Delta K$ which is usually smaller than 1 eV.

When ions of different masses $m = m_0 \pm \Delta_m$ and of a range of energies $K = K_0 \pm \Delta K$ enter into a magnetic sector field, the ions are finally separated from the beam axis by $\pm[(x_B|m)(\Delta m/m_0) + (x_B|K)(\Delta K/K_0)]$ with $(x_B|m) = (x_B|K)$ for a given magnetic field. Here $\pm(x_B|m)(\Delta m/m_0)$ determines the desired mass separation between ions of masses $m_0 + \Delta m$ and $m_0 - \Delta m$, and $(x_B|K)(\Delta K/K_0)$ causes a detrimental beam widening because of the continuous distribution of ion energies from $K_0 - \Delta K$ to $K_0 + \Delta K$. This energy spread also causes the ions to diverge from the ion source at angles of divergence given by

$$\alpha_0 = \pm\frac{v_i}{v_0} = \pm\sqrt{\frac{\Delta K}{K_0}} \tag{3}$$

because the velocity distribution of the unaccelerated ions is isotropic.

For a given magnetic field this widening of a mass line caused by the ions' energy distribution is unavoidable. However, for a combination of two or more sector fields, one can arrange the fields such that the energy dispersions compensate for each other, and the overall mass dispersion is $(\overline{x}|m)\Delta m \neq 0$. For a two-sector field system there are two possible arrangements (see Fig. 5):

1. The first solution uses an electrostatic sector field in addition to the magnetic sector which is dimensioned so that the forwardly calculated energy dispersion $(\vec{x}_E|K)(\Delta K/K_0)$ of the electrostatic sector field is equal to the backward calculated energy dispersion $(\overleftarrow{x}_B|K)$ $(\Delta K/K_0)$ of the magnetic sector field (9,10), as indicated in Fig. 5(a). Because the electrostatic sector field has no mass dispersion, the mass dispersion of the magnetic sector field is also the mass dispersion of the full system.

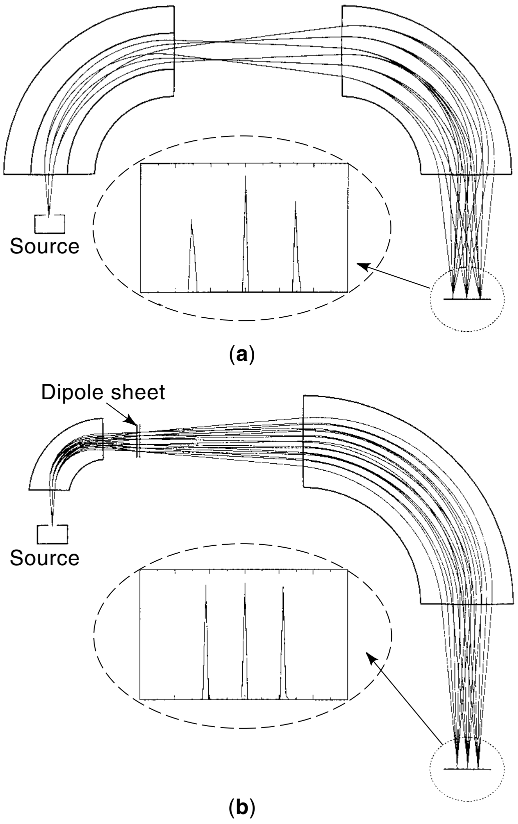

Figure 5(a) and (b). Ion trajectories are shown in two types of angle and energy focusing mass spectrometers which in the example shown both use the same geometry for the final magnetic sector-field mass analyzer. In Fig. 5(a) this magnetic sector field is preceded by (9,10) an electrostatic sector field and in Fig. 5(b) by a magnetic sector field placed at a different potential (10). It is assumed here that the ions are accelerated in a dipole sheet between the two stages. Note that in both systems 18 ion trajectories are shown characterized by two energies and three masses which leave the ion source at three different angles of inclination. For both systems there are also only three beams at the end (characterized by the three ion masses) independent of the angles at which the ions left the ion source and independent of the energy of these ions.

2. The second solution uses a small magnetic sector field to compensate for the energy dispersion of the main magnetic sector (11), as indicated in Fig. 5(b). When the two sector magnets operate at different potentials and the energies K_1 and K_2 denote the ion energies in the two fields, one must postulate that the forwardly calculated energy dispersion $(\vec{x}_{B1}|K)(\Delta K/K_1)$ of the first magnetic sector field equals the backward calculated energy dispersion $(\overleftarrow{x}_{B2}|K)(\Delta K/K_2)$ of the second sector field (11). However, such a combination of two sector fields is useful only for $K_1 \neq K_2$ because only in this case the mass dispersions of the two sector magnets do not cancel each other for the case of a vanishing energy dispersion.

Comparing the two solutions, one sees that the overall mass dispersion is a little larger for the first case than for the second. The mass cross-contamination, however, is lower for the second solution (11) because the two momentum analyzers are used in series whereas only one momentum analyzer exists for the first solution (10).

Longitudinally Dispersive Mass Analyzers

Laterally dispersive mass analyzers have proven to be effective and powerful tools exhibiting the lowest mass cross-contamination of all known mass analyzers. However, longitudinally dispersive systems are becoming more and more popular because they are mechanically simpler. There are three types of such systems:

1. high-frequency mass analyzers (12,13,14) in which low mass ions pick up higher speeds than high mass ions within one frequency cycle. Thus, low mass ions swing in this field with larger amplitudes that can become larger than the electrode separation.
2. mass spectrometers in which ions circulate in a homogeneous magnetic field (15–17) or in race tracks (3,9).
3. time-of-flight mass analyzers (18–23) in which the mass-dependent flight times are observed directly for ions that have started simultaneously.

High-Frequency Mass Analyzers. High-frequency mass analyzers cause ions of energies of a few electron volts to swing in electric ac fields of some 100 V/mm and frequencies of $\nu \approx$ 1 MHz. Because low mass ions swing with larger amplitudes than high mass ions, ions of too low mass are intercepted by the electrodes and only high mass ions survive. Adding a dc potential to the electrodes (see Figs. 6 and 7) also eliminates the heaviest ions (12,13) so that only ions within a small range of masses move along stable trajectories. There are two basic configurations of such mass analyzers.

The Quadrupole Ion Trap. The *quadrupole ion trap* uses rotationally symmetrical, hyperbolically shaped electrodes (see Fig. 6). Into such a *trap* ≈10 eV ions are introduced which then under the action of the high-frequency field mainly swing up and down between the two electrodes of the two-surface hyperboloids of Fig. 6. If the ac voltage is increased over time, the amplitudes of these swings also increase, and ions of higher and higher masses impinge on the electrodes or if appropriate holes are provided (14), leave the trap and can be recorded on some sensitive ion detector. By varying the voltages on these electrodes appropriately over time or during different time intervals, ions over a wide mass range or over a deliberately narrowed one can be made to move along stable orbits. One very useful MS/MS sequence requires that during the time interval Δt_1 the voltages are chosen so that stable ion motion is guaranteed only for ions of one particular molecule mass m_0, whereas during the time interval Δt_2 the voltages are chosen so that ions of a range of masses all perform stable motions. Though, at the beginning of this time interval Δt_2, only ions of mass m_0 are in the trap, these ions fragment because of collisions with residual gas atoms. With properly chosen ac and dc voltages, these fragments are all stored in the trap. Then during the time interval Δt_3, the voltages are scanned so that the mass range for the ions that perform stable motion is constantly decreased. Thus a mass spectrum is recorded of the fragment ions which become unstable successively according to their mass values.

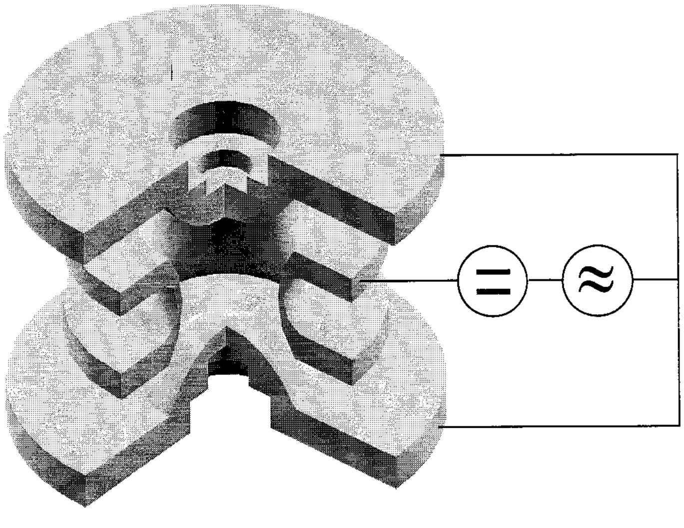

Figure 6. In the ion trap shown the ions can swing in the rotationally symmetrical quadrupolar ac field. If the dc power supply is left off, only ions above a certain mass move along stable orbits. The addition of a dc power supply also provides a limit for the high mass ions. In all cases the ion motion is mainly up and down in the figure shown here.

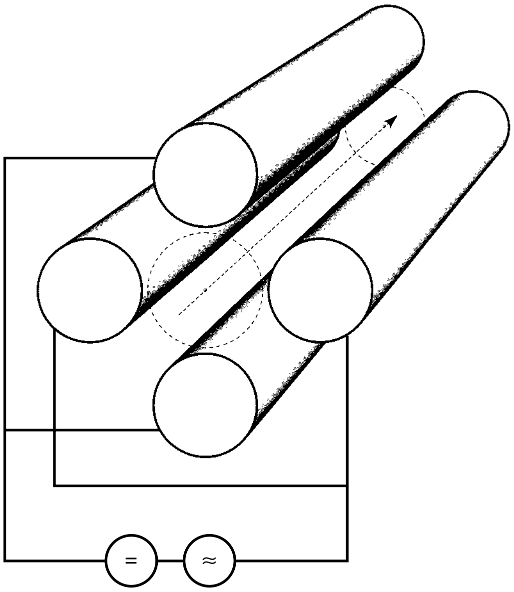

Figure 7. The quadrupole mass filter. Under the action of ac and dc fields, low energy ions swing laterally between the electrodes shown, and they move with constant velocity in the direction of the z-axis. Analogously to the ion motion in an ion trap, here also a pure ac field would allow only ions above a certain mass to move along stable orbits, whereas an added dc field would make the trajectories of the heavier ones unstable.

The Quadrupole Mass Filter. A second well-established high-frequency mass analyzer consists of four rod-like electrodes (see Fig. 7) with ≈10 eV ions injected along the quadrupole axis. For appropriate ac and AD voltages of several 100 V, only ions within a very small mass range pass this *mass filter* (12,13), that is, move in the z-direction about 0.1 mm in each high-frequency period and at the same time swing transversally between the electrodes with amplitudes of about 5 mm. At the end, a mass spectrum is recorded in an ion detector if the ac and dc amplitudes are scanned appropriately over time.

The Magnetic Ion Trap Mass Spectrometer. A mass spectrometer of very high mass-resolving power $R = m/\Delta m$ is a system in which ions move in a magnetic flux density B along radii ρ according to Eq. (2) with a velocity v according to Eq. (1). Thus the flight time per turn in microseconds is given by

$$\bar{t} \approx 2\pi \frac{\rho}{v} \approx 0.0651212 \frac{m}{B} \tag{4}$$

where B is in Tesla and m is in mass units. This flight time is independent of the ion energy K. There are several ways to determine this flight time per turn.

1. If the radius ρ is large enough, one can determine the time $\bar{t}$ directly for one turn by small pulsed beam deflectors (15). In principle, this method is also applicable for many turns (9).
2. One can amplify the potentials induced on electrodes close to the ion path (see Fig. 8). After a Fourier analysis these induced voltages reveal mass specific frequencies $\nu = 1/\bar{t}$ and thus the desired mass spectrum (3,16).
3. If the radius ρ is small enough, one can superimpose a high frequency electrostatic field to the magnetic one and register the finally left ions in the system by accelerating them axially out of the magnetic field. In this case the ions' azimuthal velocities are transformed into axial velocities that can be measured by a time-of-flight technique (17) which identifies the ions in resonance.

All these systems deliver rather high mass resolving powers of $m/\Delta m \geq 100{,}000$ or more which can be used for molecule mass analysis (16) or for the determination of nuclear mass defects (24) and other basic information like the CPT invariance (25). Note here that the mass resolving power of such systems is proportional to the number of rotations of the ion cloud and that the mass resolving power per turn can be rather small (16,17). Thus for a given experimental time it is advantageous to increase the magnetic flux density as much as possible. Note also that for $B = 7$ T, singly charged 100 eV ions of 100 u would move along circles of radius $\rho \approx 2.057$ mm with $\bar{t} \approx 0.930$ μs.

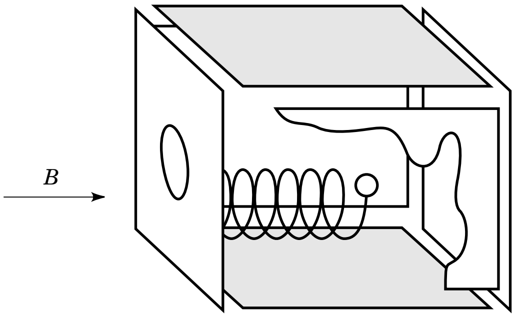

Figure 8. A Fourier transform mass analyzer that uses a high field magnetic solenoid (14). The mass-resolving power increases with an increased magnetic flux density B.

Instead of having ions move along circles in a homogeneous magnetic field, one can also arrange a number of magnetic and/or electrostatic sector fields into a *race track* with intermediate field-free regions (3,9,18) and then determine the flight time $\bar{t}$ per turn via Fourier transform techniques. In principle this flight time $\bar{t}$ depends on the ion mass and also on the ion energy. However, there are still two ways to achieve high mass-resolving power:

1. reduce the energy spread in the ion beam either by an electron cooler (3) for high energy ions or by gas collisions (26) for low energy ions.
2. introduce magnetic and/or electrostatic quadrupole lenses into the ring and excite them so that the overall system is energetically isochronous (9,18), that is, faster ions are sent around the ring along properly elongated trajectories.

Both race track systems have been used successfully for mass measurements of stable (14) and of short-lived nuclei (4).

Time-of-Flight Mass Analyzers

A different approach is a time-of-flight (TOF) mass spectrometer (MS) into which a bunch of ions of different masses is injected and the ion arrival is recorded at some downstream ion detector (see Fig. 9). Differing from all scanning mass analyzers, there is no limit in a TOF-MS on the mass values of the ions under investigation. Therefore TOF-MS systems are powerful tools for the investigation of large biomolecules or cluster ions.

The ion source for a TOF system requires that all ions of equal mass start from some point at the same time. This is guaranteed by

1. a pulsed ion acceleration in which a pulsed electric field acts on some cloud of ions. If all of these ions are stationary initially and then are accelerated in the z-direction, they all reach a properly placed ion detector simultaneously if their masses are the same. In other words, *they will be bunched* because the ions that start from $z_0 + \Delta z$ receive a little less energy than those that start from $z_0 - \Delta z$, but the first ones must also travel a little further (18,19). There are three ways to implement this method:
   a. introduce ions at a specific z_0, and wait until they move apart to different z-values because of their thermal energies (19). In this case the final ion positions z are correlated to their initial energies which improves the bunching properties considerably.
   b. store (20) the ions in the potential well caused by a beam of electrons of energy K_0. Depending on the electron beam current I_e, the potential in the middle of the beam is $V_e \approx 15200(I/\sqrt{U_0})$. For $U_0 = 70$ eV and $I = 0.0005$ A, one thus finds that $V_e \approx 0.75$ V. In this case the final bunch length is usually determined by the "turnaround time," that is the time in which an ion that moved initially in the $-z$-direction has reversed its velocity.
   c. introduce a low energy ion beam perpendicularly to the z-direction, that is, the direction of the pulsed ion acceleration (21). In this arrangement some "ion stor-

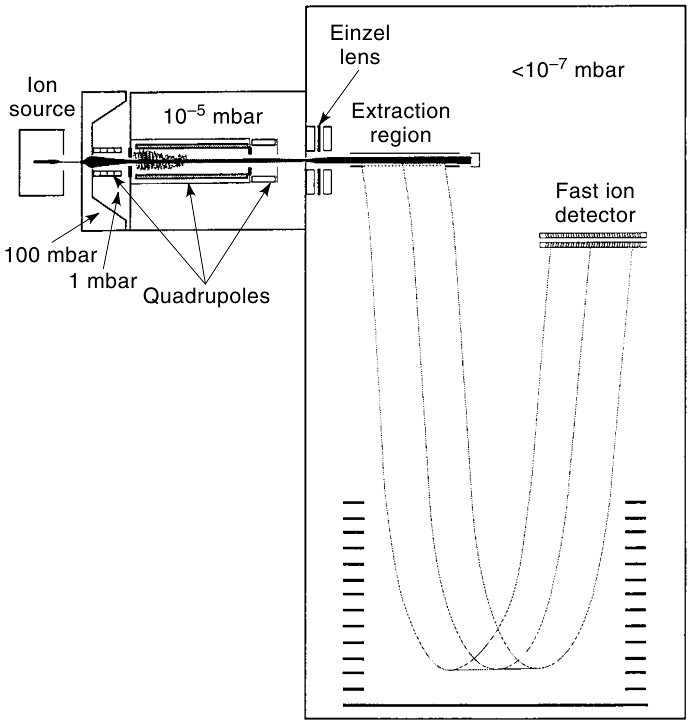

Figure 9. A time-of-flight mass analyzer for heavy molecules. Note the folded flight path in the z-direction and the large ion mirror used (23). Also note the orthogonal ion injection in the x-direction and the pulsed ion acceleration in the z-direction (21). The electrospray ion source (31) forms charged droplets and sends them into the vacuum system where in flight they evaporate all the solvent, so that highly charged ions remain. Then these ions are passed through three quadrupoles the last of which is powered in a dc mode and focuses the 10eV ions into the extraction region. The other two are two gas-filled ac only quadrupoles the first of which *heats* the ions to boil off any molecule adducts or to fragment the main molecule (6), and the second of which because of its different gas pressure *cools* the ions by gas collisions. This procedure works continuously so that finally the ions all have more or less the same velocity in the x-direction before being pulse accelerated orthogonally in the z-direction.

age" is also achieved because it takes a relatively long time for the ions to perpendicularly traverse the region from which they are then accelerated. Most importantly, however, there is almost no ion motion in the z-direction initially. Thus the "turnaround time" is reduced compared to 1(b).

For such a pulsed ion acceleration, the final energy distribution in the bunched ion beam is large, for instance, $\Delta K \approx 100$ eV.

2. a pulsed ion generation which is, for instance, the case for the laser ionization of a sample. A very good method is (20) to embed some organic material into a matrix, for instance one of glycerol, so that each molecule to be investigated is surrounded only by matrix molecules. Irradiating this sample by a short intense laser pulse releases such molecules as ions. This method is called *matrix-assisted laser desorption and ionization* (MALDI). The performance of this technique is improved by accelerating these ions in an electrostatic field that is switched on shortly after the laser pulse (19).

The time focus (19,21) achieved by pulsed ion acceleration is a good technique for achieving reasonable mass-resolving powers for a so-called *linear TOF-MS*. One can improve the simultaneous arrival of ions of equal mass by using this time focus as the source for a folded-flight-path TOF-MS (18,20). In such a system the ions are reflected by some *electrostatic ion mirror* in an energy isochronous manner, that is, so that the more energetic and thus faster ions reach the final ion detector only via a properly dimensioned detour (18,23) achieved by their deeper penetration into the reflector field. One can also say: *to first order the overall flight time becomes independent of the ions' energy spread* ΔK. Investigating q-times charged ions of energy ($K_0 \pm \Delta K$) that enter a homogeneous repeller field E this condition of isochronicity postulates that

$$L_1 + L_2 = \frac{4qE}{K_0} \tag{5}$$

where L_1 and L_2 denote the lengths of the field-free regions between the ion source and the repeller field and between the repeller field and the final ion detector, respectively. In this case the overall flight time is $t + \Delta t$ with $\Delta t/t = (\Delta K/K_0)^2/8 + \ldots$. Using an ion reflector composed of two regions (23) of properly dimensioned field strengths or a grid-free ion reflector (18,20) that produces a properly dimensioned field region, the performance of such a TOF-MS can even be improved, so that finally only much smaller effects proportional to $(\Delta K/K_0)^3$ remain.

ION SOURCES

Many different ion sources have been developed for different mass spectrometers and different applications. Only in a few cases this ion formation can occur inside a mass analyzer, as for instance inside of an "ion trap." In most cases an external ion source is used that consists of two parts: the ionization device and the ion accelerating and beam-forming device.

Electron Impact Ion Sources

Energetic electrons ionize vaporized atoms or molecules by collisional impact. The electron energy here must be large enough that at least one electron in the shell of the atom or molecule in question is removed. Optimally, (2,27) beams of electrons of 70 eV or 80 eV are used with currents of usually a few 100 μA. In many cases these beams are held together by magnetic fields of perhaps 0.01 T produced easily by permanent magnets. This magnetic field usually confines the electron beam to diameters ≤ 2 mm and at the same time elongates the electron path thus increasing the overall ionization probability for a given electron current. Usually the ions are pulled from the ionization region through some narrow orifice by an accelerating electrode at a potential of some 100 V or even 1000 V. However, the ions often are also pushed toward this orifice by some relatively large pusher electrode at a potential of a few volts.

Plasma Ion Sources

In a plasma ions already exist and only need to be extracted. However, electrostatic fields cannot penetrate deeply into a conductive plasma and thus ions can be extracted only from the plasma surface which consequently is depleted of ions to some depth after a very short time. Thus a pulsed ion acceleration that extracts ions from a replenished *plasma surface* is especially effective (28). As one should expect, the extracting field strength shapes the plasma surface and thus greatly influences the ion optical properties of the extracted ion beam.

Thermal Ion Sources

If the ionization energy I_p for some atom under consideration is smaller than the work function W of a substrate, the atoms leave this substrate partially as ions. The ratio between ionized and neutral atoms evaporating from a filament heated to a temperature T is given by

$$\frac{N^+}{N^0} = \exp\frac{W - I_p}{kT} \tag{6}$$

where $k = 8.62 \times 10^{-5}$ is the Boltzmann constant measured in electron volts per K. Re and also W or Ta substrates have large work functions which cause them to efficiently remove one electron from evaporating alkali atoms, that is Li, Na, K, Rb, Cs, Fr and from some earth alkali atoms during evaporation. With Rb or Sr on 2500 K hot Re, and $I_p(\text{Rb}) = 4.18$ eV or $I_p(\text{Sr}) = 5.7$ eV one finds that $N^+/(N^0 + N^+)$ equals 100% or 85% if the work function of the Re surface is assumed to be 6.1 eV. However, other atoms, for instance, U are also ionized with some efficiency (2,27). Similarly, one can also attach one electron to atoms with large electron affinities (for instance, Br) if they are evaporated from a substrate that has a very low work function, for instance, LaB_6.

This simple ionization technique is improved considerably if the substrate forms the inner surface of a hot cavity (29). In this case most elements are ionized with efficiencies of about 1%. The reason for this enhancement is that the ions are extracted through a small hole in this cavity whereas the atoms stay in the cavity and thus get another chance to be ionized.

Laser Ion Sources

As one might expect, one can directly ionize specific isotopes by high-power lasers of some resonant frequencies. However, often one uses only lasers of broader frequency bands and thus ionizes all isotopes of a specific element simultaneously (30). In some cases one also uses the property of a finely focused laser beam to produce a small plasma at some surface as, for instance, for the previously mentioned MALDI sources (22).

Electrospray Ion Sources

A very interesting ion source for high mass biomolecules uses the electrospray technique (31). In one of these ion sources a very dilute solution of the molecules of interest is sprayed in fine droplets into some gas at about 1 bar. Then the gas and these droplets are sucked through a small orifice into a vacuum vessel where the droplets will evaporate most of the solvent and thus rapidly decrease in size. If there were only one molecule in the droplet there is only one molecule left at the end when all the solvent has evaporated. Because the droplets were multiply charged from the beginning, as is the case in the spray from any waterfall, the final molecule is multiply charged (see Figs. 1 and 4).

CONCLUSION

Mass spectrometry began as a special technique to determine the isotopic distribution of all elements (9), but it has grown into a very general, sensitive, and specific analytical technique for ionized atoms or molecules. For this reason mass spectrometers have been used in very diverse applications from nuclear physics to pharmacology. The fastest growing application certainly is the analysis of biomolecules and the trace detection of organic molecules.

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