Steps in Atomic Mass Spectrometry

- Atomization
- Conversion of substantial fraction of atoms formed into ions
- Separating ions formed based on their mass-to-charge (m/z) ratio
- Counting the ions produced of a given m/z with some sort of transducer (*i.e.*, detection)

Components of a Mass Spectrometer

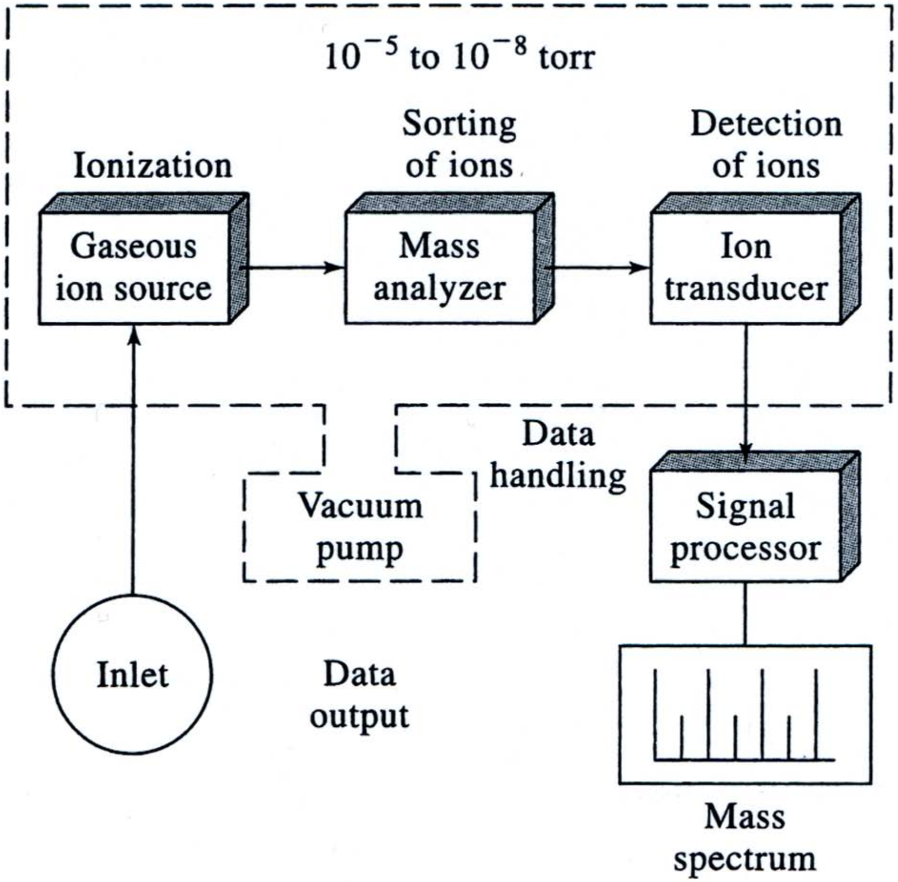


FIGURE 11-1 Components of a mass spectrometer.

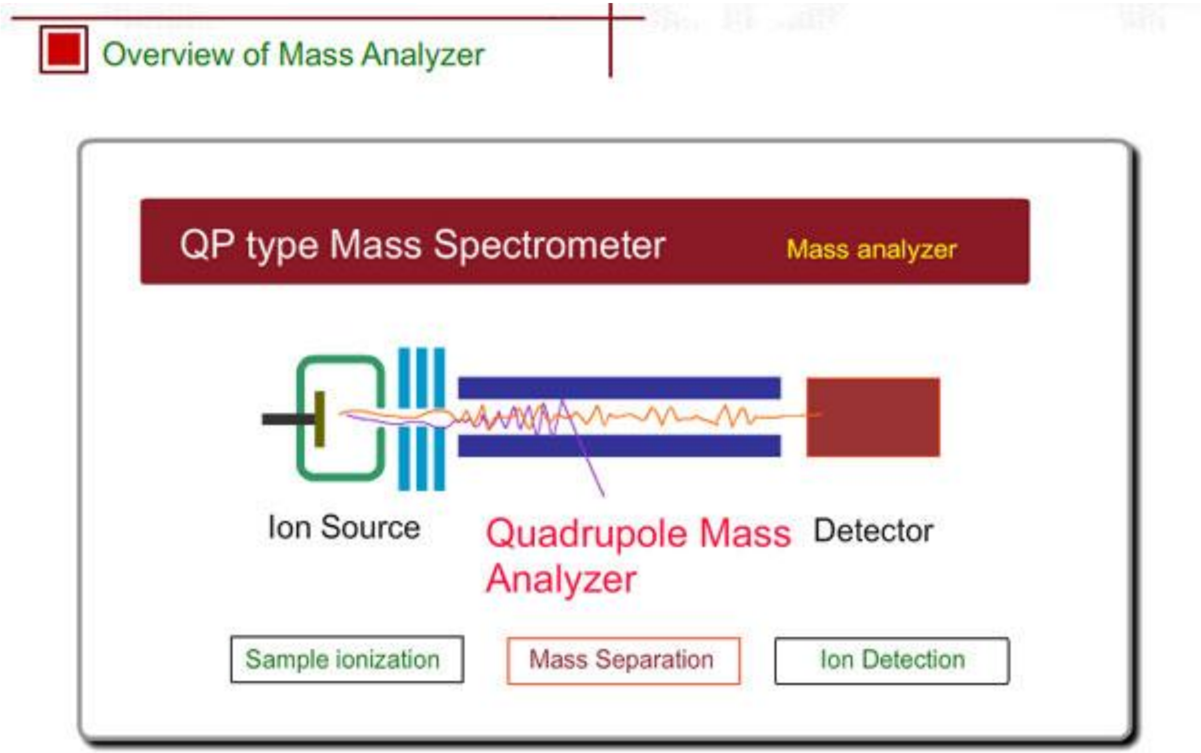
Chapter 20 - Molecular Mass Spectrometry

Read pp. 550-570   Problems: 20-2,5,6,7,11,12,13

MS is probably the most widely applicable of all the analytical tools available.

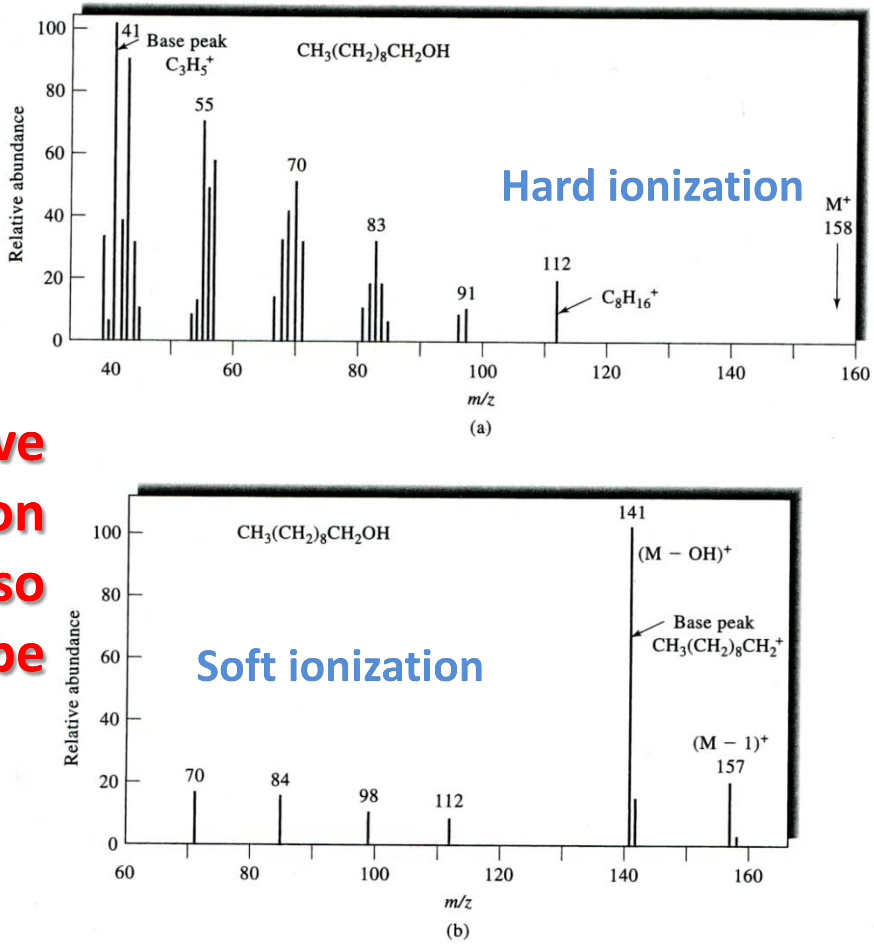
1. Elemental composition of samples of matter.
2. Structures of inorganic, organic and biological molecules.
3. Qualitative and quantitative composition of complex samples.
4. Structure and composition of solid surfaces.
5. Isotopic ratios of atoms in samples.

Overview of a Mass Analyzer



Mass Spectrum

Spectral features depend on method of ionization!



Hard ionization

Soft ionization

FIGURE 20-2 Mass spectrum of 1-decanol from (a) a hard ionization source (electron impact) and (b) a soft ionization source (chemical ionization).

Most ideal to have the molecular ion to remain intact so $M^{\bullet+}$ can be determined.

Ion Sources – The Starting Point

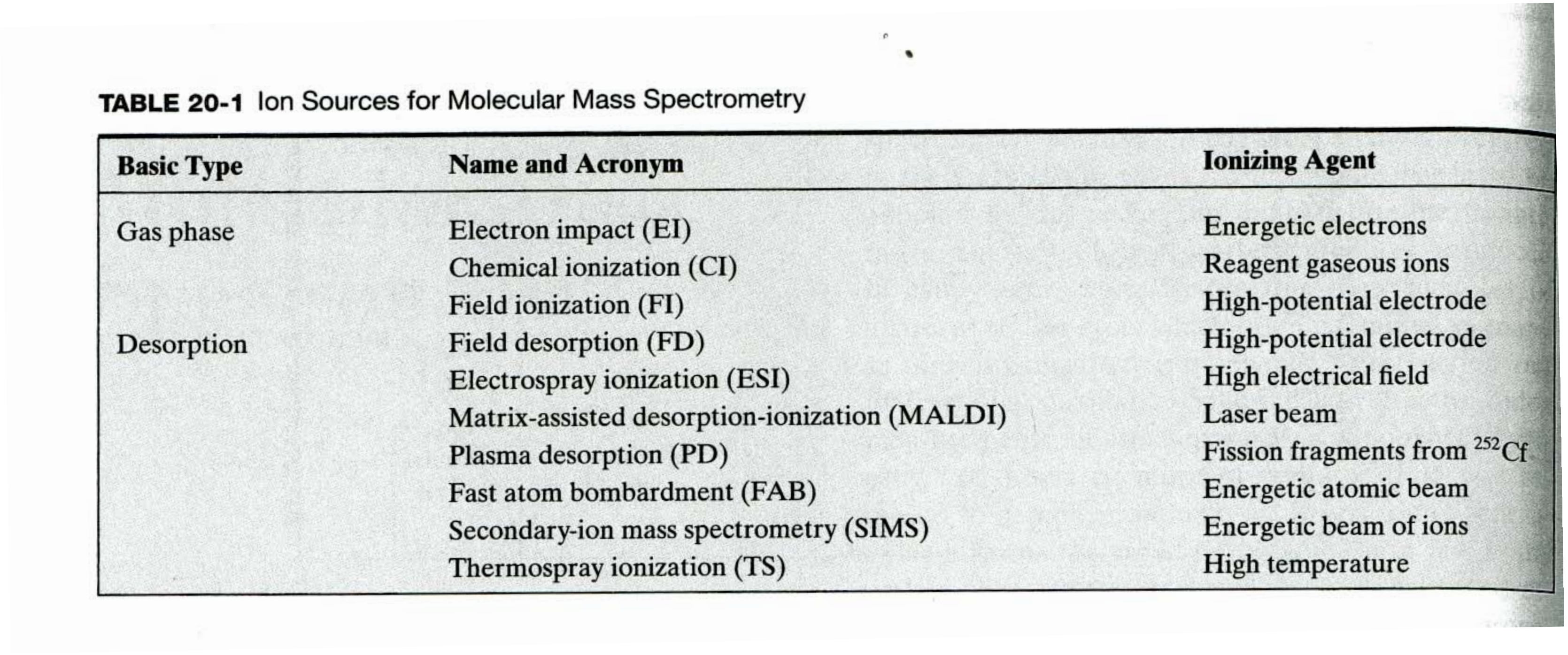


TABLE 20-1 Ion Sources for Molecular Mass Spectrometry

Basic Type	Name and Acronym	Ionizing Agent
Gas phase	Electron impact (EI)	Energetic electrons
	Chemical ionization (CI)	Reagent gaseous ions
	Field ionization (FI)	High-potential electrode
Desorption	Field desorption (FD)	High-potential electrode
	Electrospray ionization (ESI)	High electrical field
	Matrix-assisted desorption-ionization (MALDI)	Laser beam
	Plasma desorption (PD)	Fission fragments from ^{252}Cf
	Fast atom bombardment (FAB)	Energetic atomic beam
	Secondary-ion mass spectrometry (SIMS)	Energetic beam of ions
	Thermospray ionization (TS)	High temperature

Formation of gaseous ions. Gas phase sources – sample is vaporized and then ionized. 10^3 Da limit. Desorption sources – sample is converted directly to gaseous ions. Applicable to non-volatile and thermally unstable samples. 10^5 Da limit.

Electron Impact Ionization - Hard

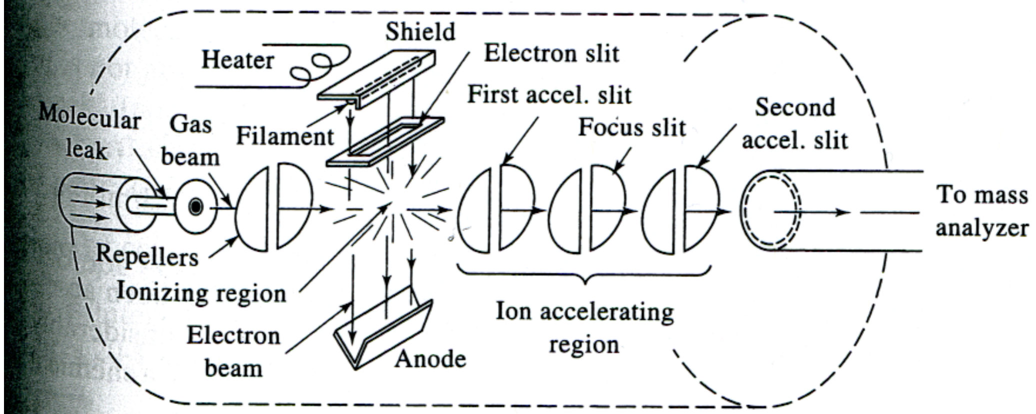


FIGURE 20-3 An electron-impact ion source. (Adapted from R. M. Silverstein and F. X. Webster, *Spectrometric Identification of Organic Compounds*, 6th ed., p. 4, New York: Wiley, 1998. Reprinted with permission of John Wiley & Sons, Inc.)

$$M + e^{-} \rightarrow M^{\bullet +} + 2e^{-}$$

Energetic electron beam causes molecules to lose an electron (become ionized) due to electrostatic repulsion.

Electron Impact Spectra

Complex mass spectra are useful for compound identification.

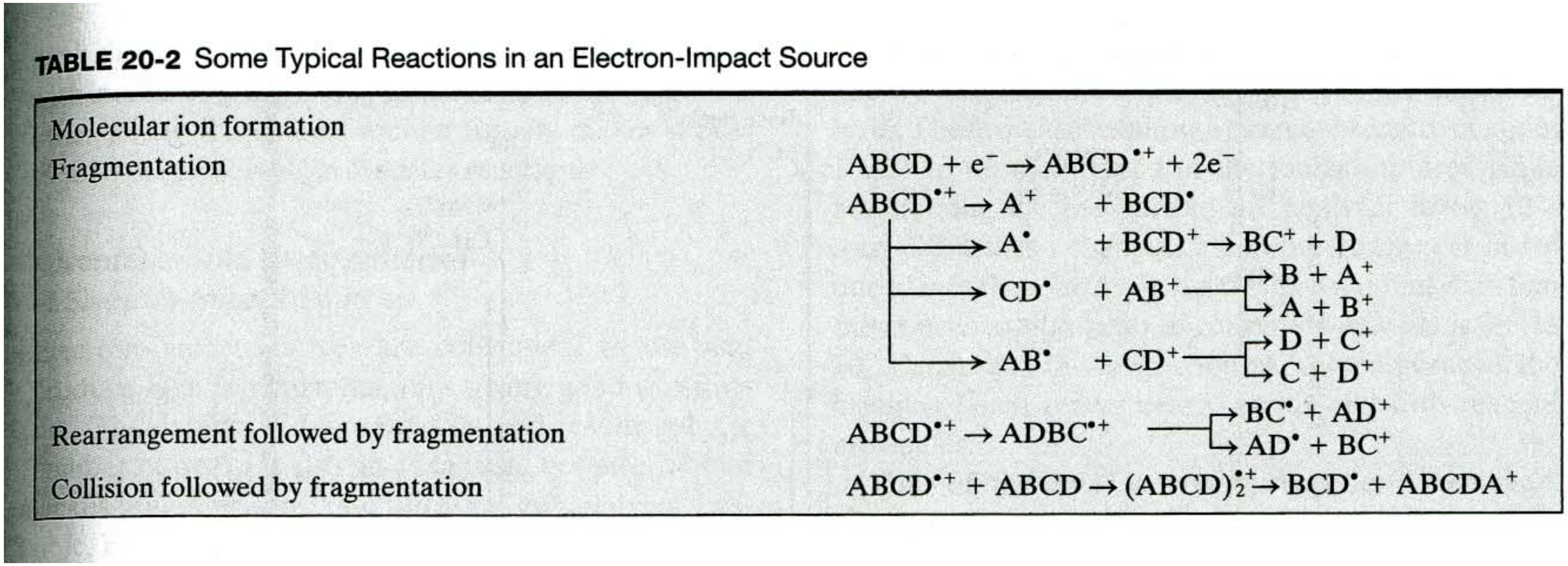


TABLE 20-2 Some Typical Reactions in an Electron-Impact Source

Molecular ion formation	$ABCD + e^- \rightarrow ABCD^{\bullet +} + 2e^-$
Fragmentation	$ABCD^{\bullet +} \rightarrow A^+ + BCD^\bullet$
	$\rightarrow A^\bullet + BCD^+ \rightarrow BC^+ + D$
	$\rightarrow CD^\bullet + AB^+ \rightarrow B + A^+$ $\rightarrow A + B^+$
	$\rightarrow AB^\bullet + CD^+ \rightarrow D + C^+$ $\rightarrow C + D^+$
Rearrangement followed by fragmentation	$ABCD^{\bullet +} \rightarrow ADBC^{\bullet +} \rightarrow BC^\bullet + AD^+$ $\rightarrow AD^\bullet + BC^+$
Collision followed by fragmentation	$ABCD^{\bullet +} + ABCD \rightarrow (ABCD)_2^{\bullet +} \rightarrow BCD^\bullet + ABCDA^+$

Interaction with the electron beam ionizes the molecule but it also leaves the molecule in a highly excited vibrational and rotational state. Relaxation occurs by extensive fragmentation giving a large number of positive ions of various masses that are less than the mass of the molecular ion.

Typical Electron Impact Mass Spectra

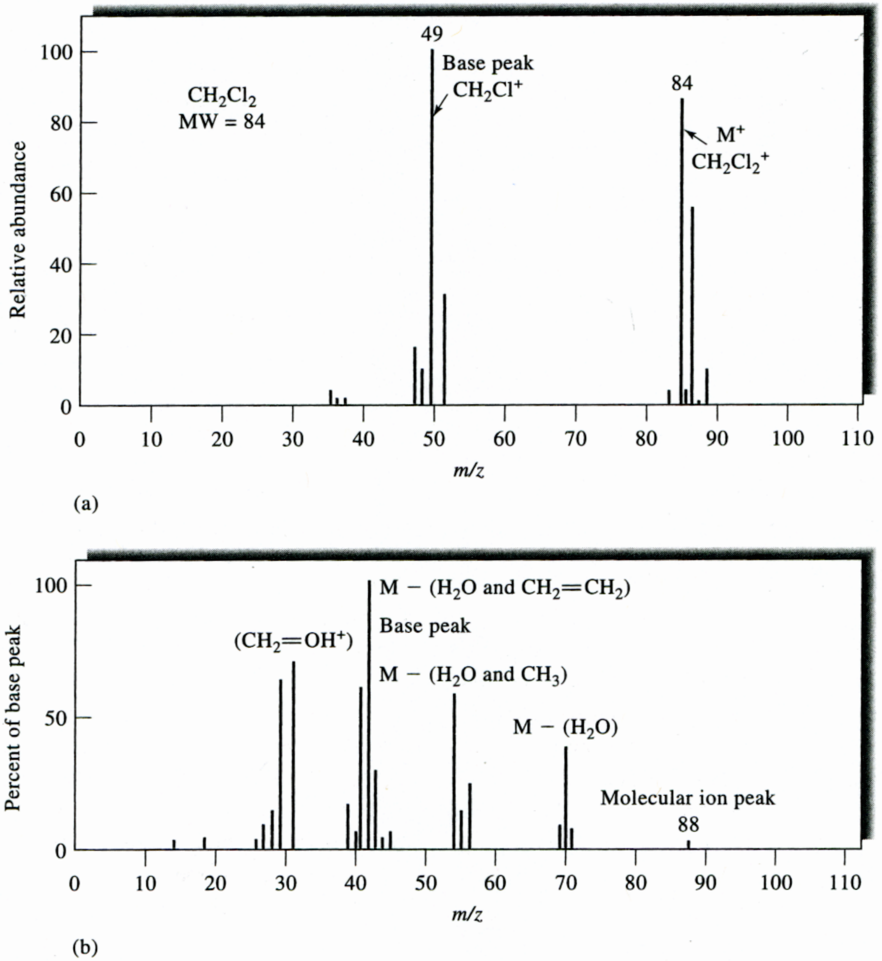
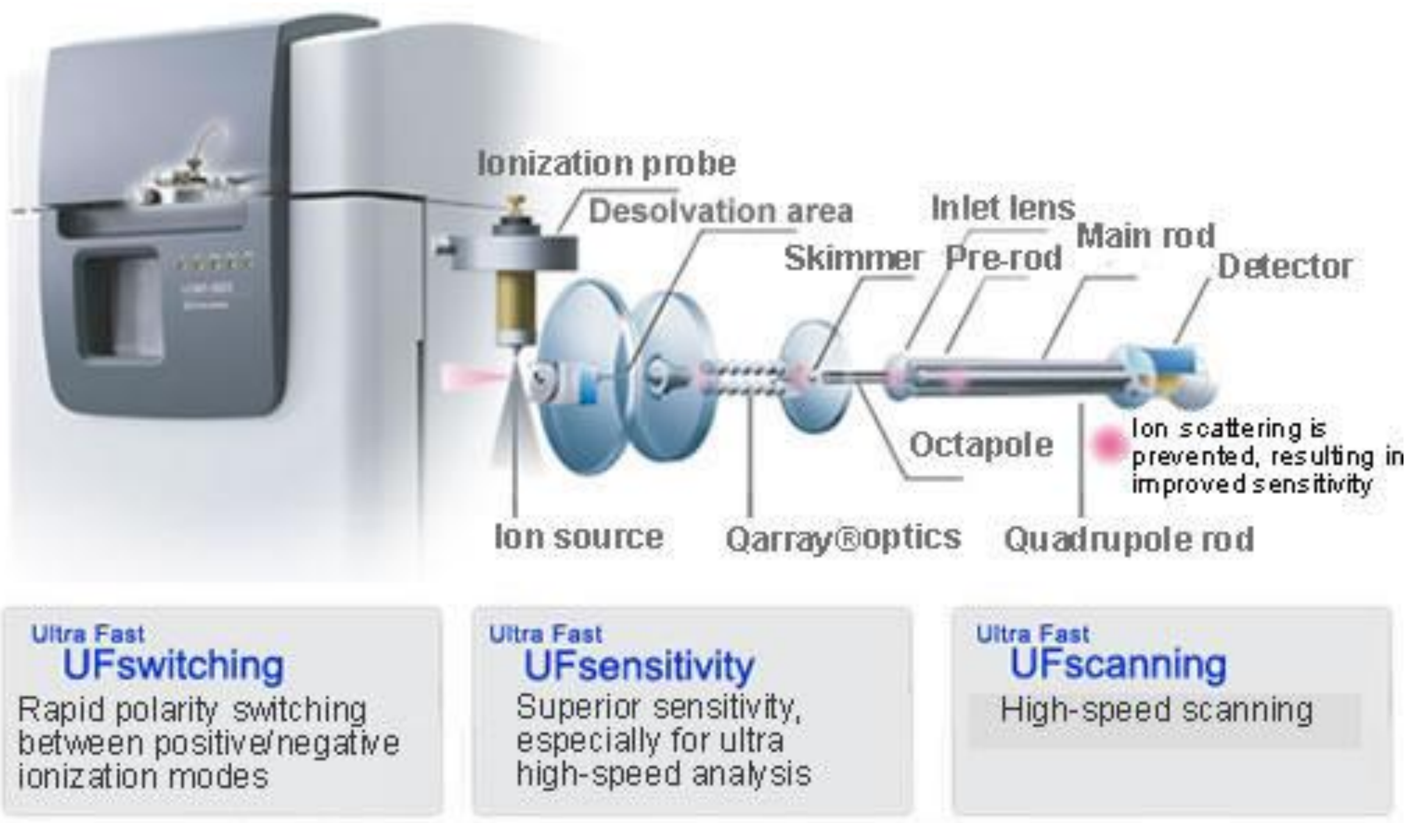


FIGURE 20-4 Electron-impact mass spectra of (a) methylene chloride and (b) 1-pentanol.

LC-MS Instrument



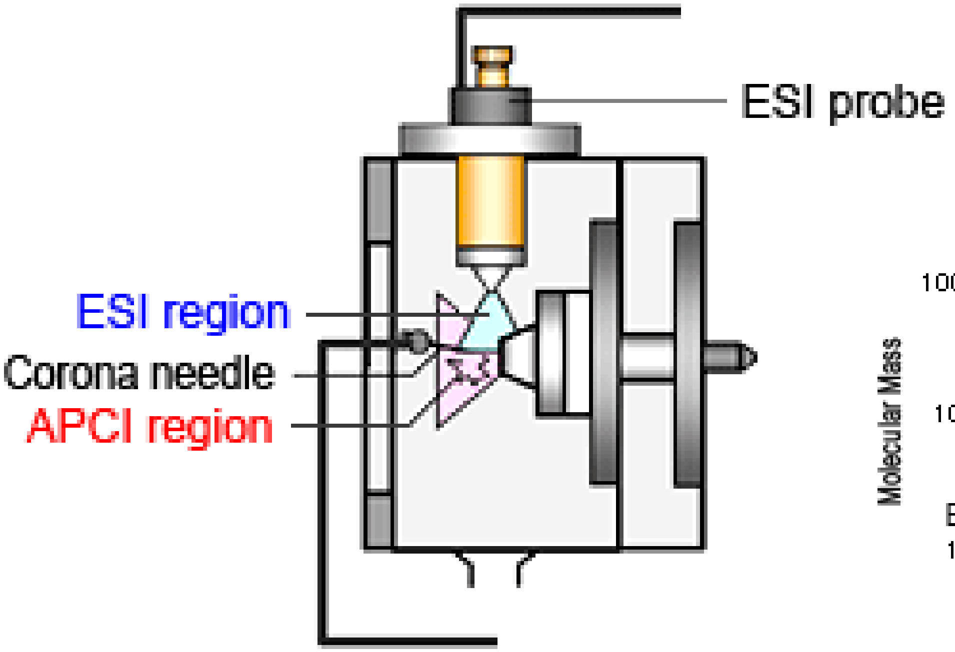
Ion scattering is prevented, resulting in improved sensitivity

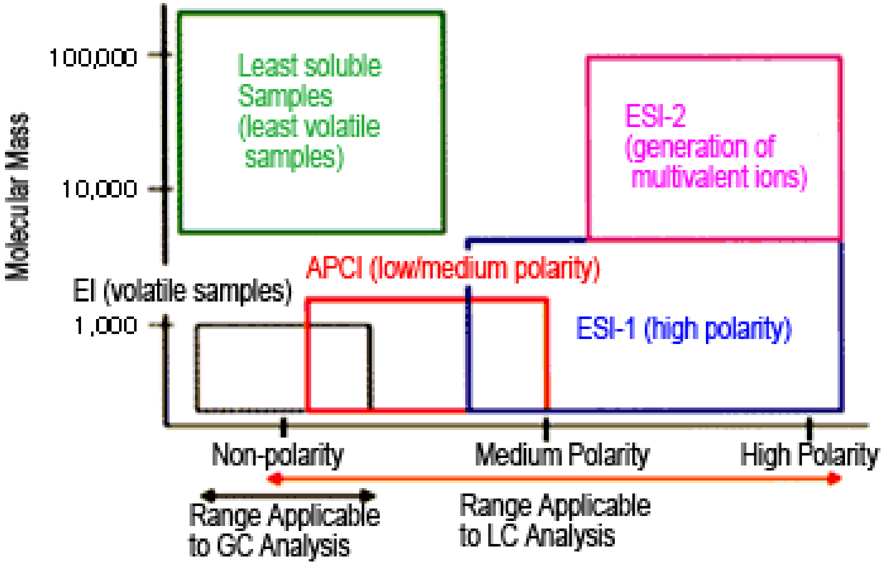
Ultra Fast
UFswitching
Rapid polarity switching between positive/negative ionization modes

Ultra Fast
UFsensitivity
Superior sensitivity, especially for ultra high-speed analysis

Ultra Fast
UFscanning
High-speed scanning

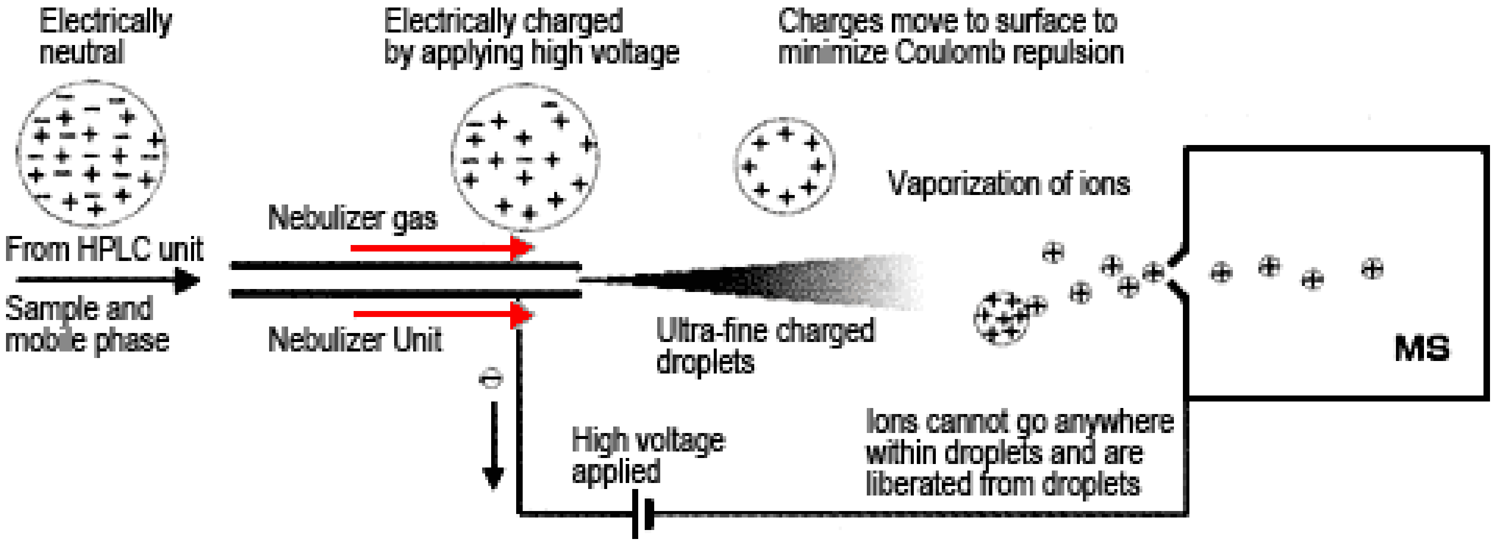
Dual Ion Source for LC-MS
(ESI and APCI)





Shimadzu Scientific Instruments

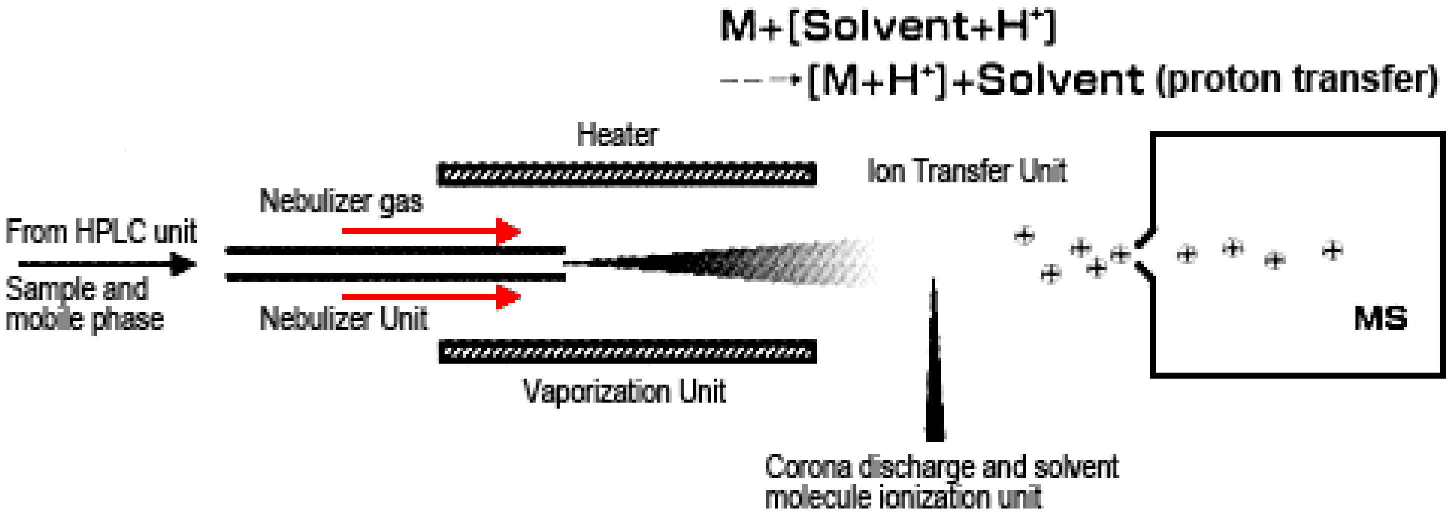
Electrospray Ionization (ESI)



ESI draws sample solutions to the tip of a capillary tube, where it applies a high voltage of about 3 to 5 kV. A nebulizer gas flows from outside the capillary to spray the sample. This creates a fine mist of charged droplets with the same polarity as the applied voltage. As these charged particles move, the solvent continues to evaporate, thereby increasing the electric field on the droplet surface. When the mutual repulsive force of the charges exceeds the liquid surface tension, then fission occurs.

Since most of the generated ions are protonated molecules (or deprotonated molecules), complicated fragment ions are not generated. This makes it easy to determine the molecular mass of compounds. It generates multivalent ions, depending on the compound, even if a compound has a molecular mass of 10,000, for example, ions with a valence of 20 would only have an m/z ratio of 501

Atmospheric Pressure Chemical Ionization (APCI)

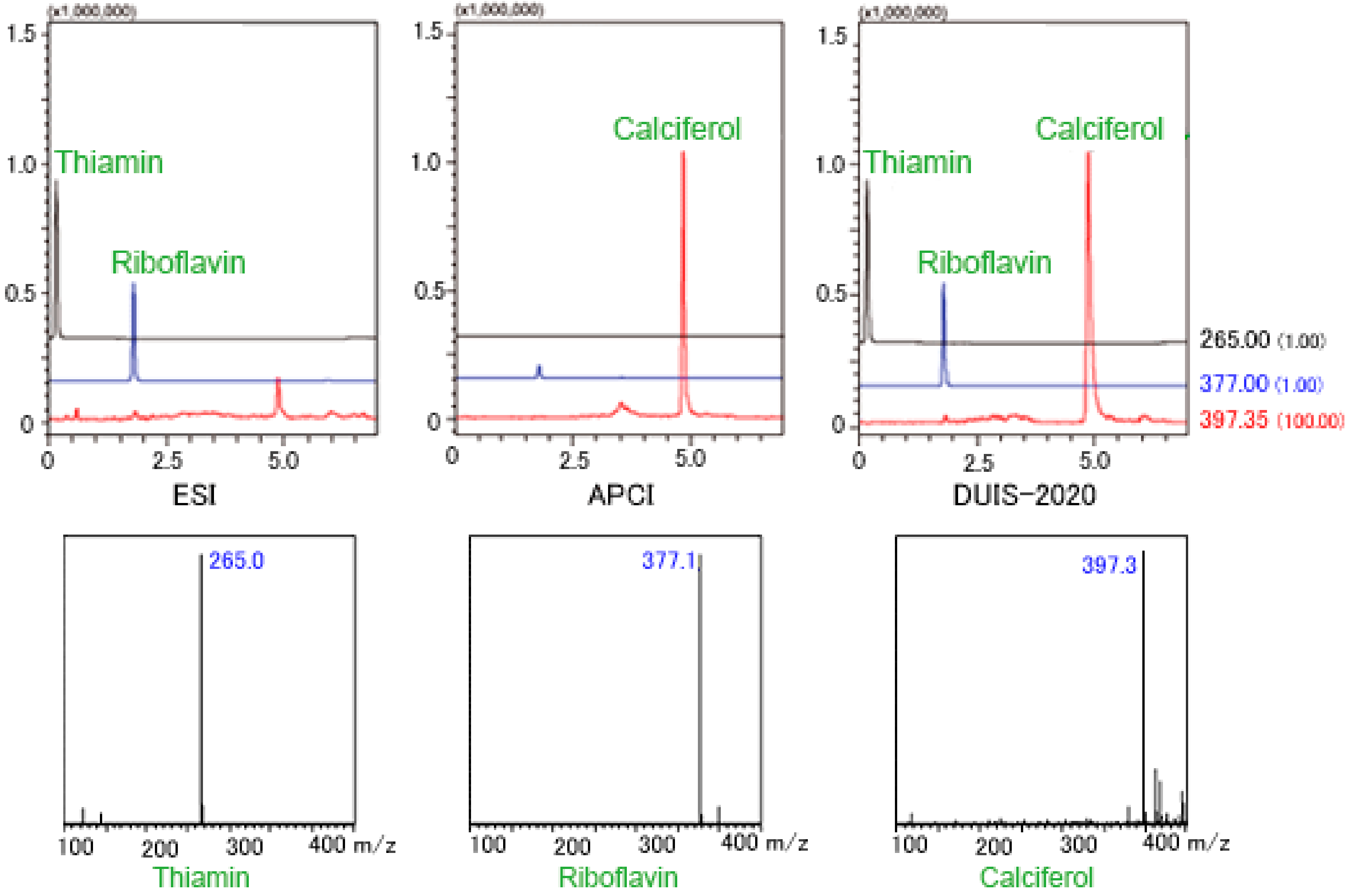


$$M + [Solvent + H^+] \dashrightarrow [M + H^+] + Solvent \text{ (proton transfer)}$$

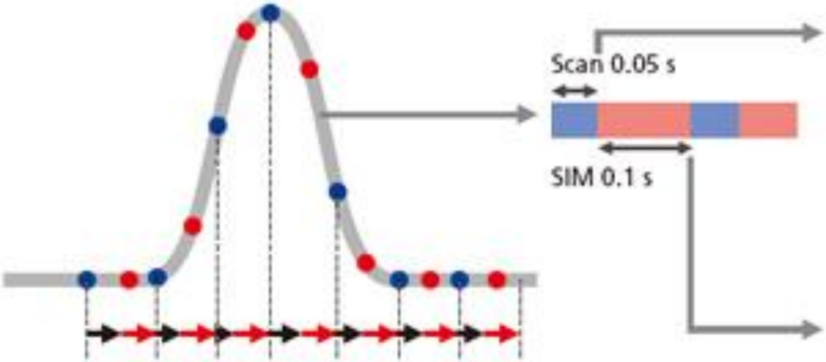
APCI vaporizes solvent and sample molecules by spraying the sample solution into a heater (heated to about 400 °C) using a gas, such as N_2. Solvent molecules are ionized by corona discharge to generate stable reaction ions.

Protons are transferred between these reaction ions and sample molecules (ion-molecule reaction) to ionize sample molecules by either adding or removing a proton. These ion-molecule reactions are known to involve several patterns, such as proton-transfer reactions and electrophilic addition reactions. As with ESI, mainly protonated molecules (or deprotonated molecules) are detected.

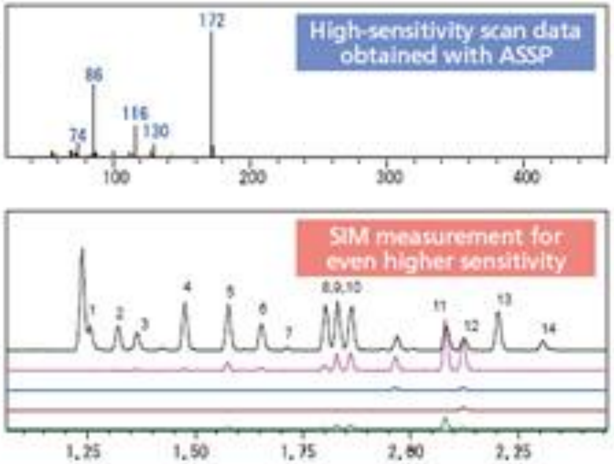
Dual ESI and APCI



Fast Scanning Speeds



Scan/SIM simultaneous data acquisition



1: Alanine, 2: Sarcosine, 3: Glycine, 4: *alpha*-Aminobutyric acid, 5: Valine, 6: *beta*-Aminoisobutyric acid, 7: Norvaline, 8: Leucine, 9: allo-Isoleucine, 10: Isoleucine, 11: Threonine, 12: Serine, 13: Proline, 14: Asparagine each derivatized compound

Simultaneous Scan/SIM data acquisition in amino acid analysis using Fast-GC/MS

20,000 amu/s

Chemical Ionization - Soft

$$CH_4 + e^- \rightarrow CH_4^+ + 2e^-$$

$$CH_4^+ + CH_4 \rightarrow CH_5^+ + CH_3$$

$$CH_5^+ + MH \rightarrow MH_2^+ + CH_4$$

Spectra contain mainly the molecular ion peak (M+1) – most abundant!! There is no extensive fragementation.

MALDI Ionization

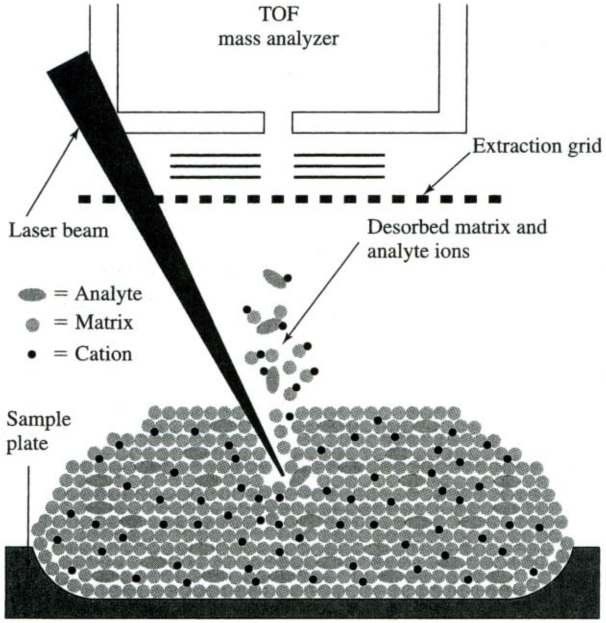
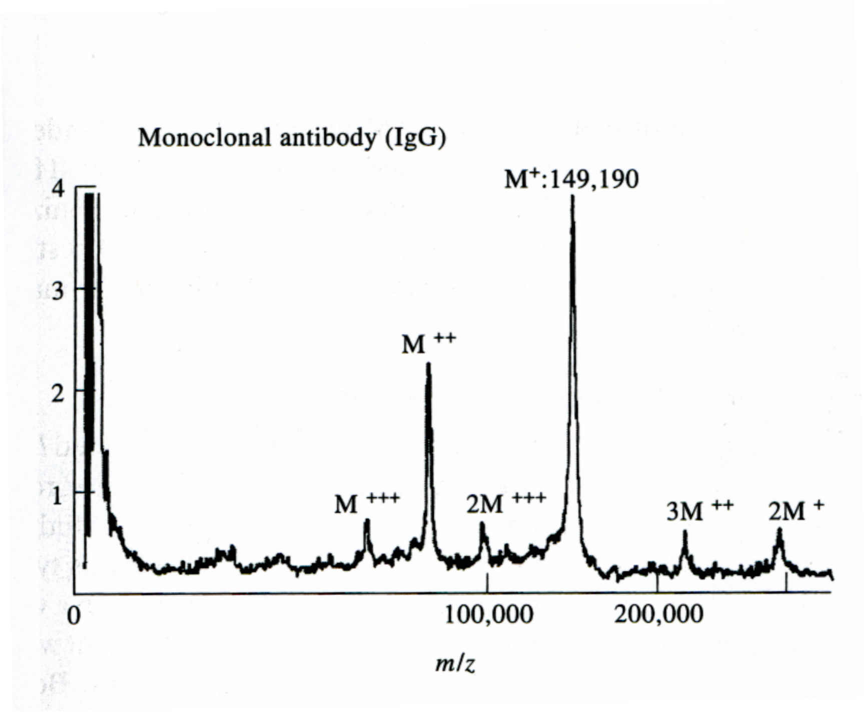
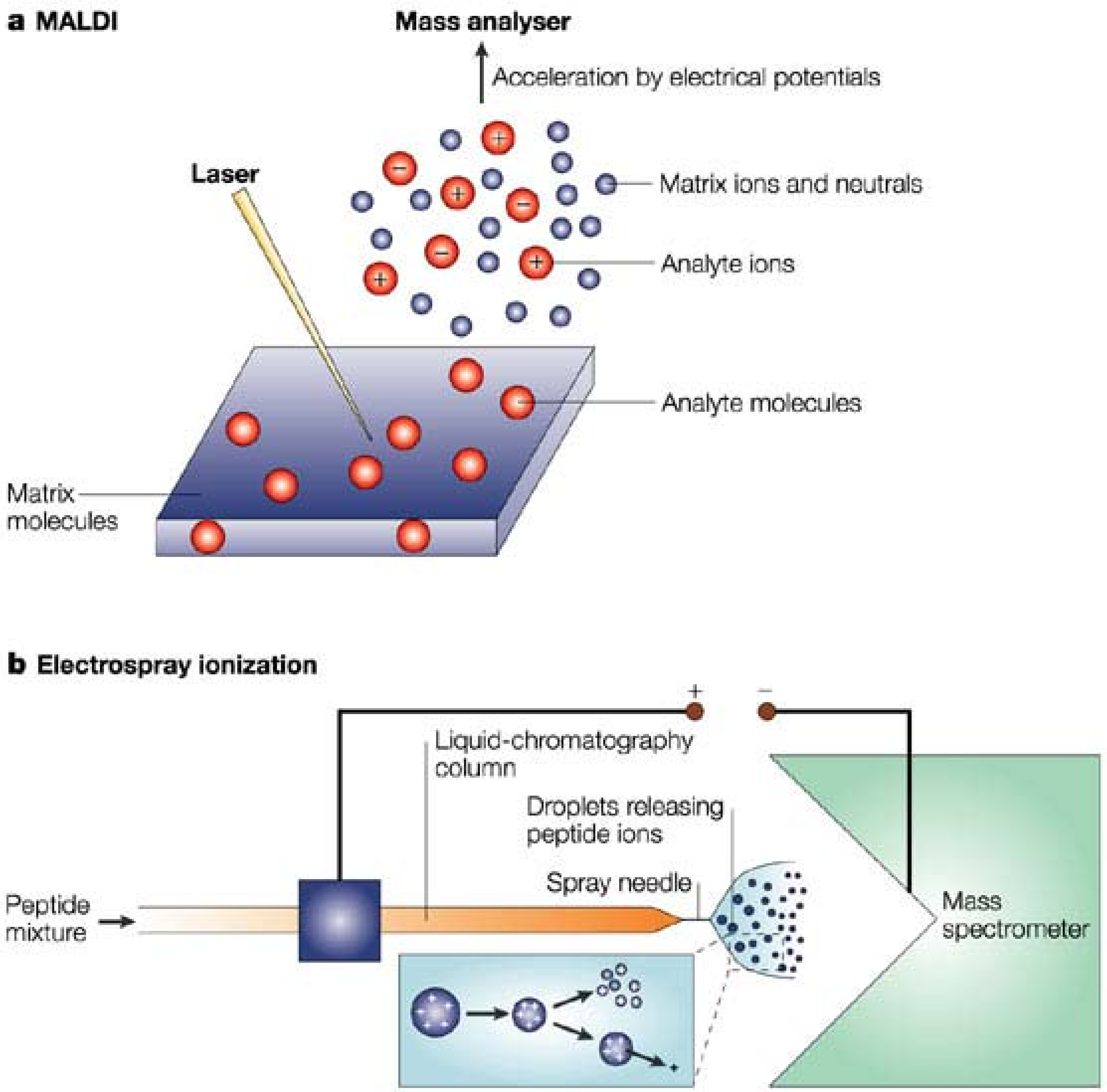


FIGURE 20-7 Diagram of the MALDI process. The analyte is uniformly dispersed in a matrix and placed on a metal sample plate. A pulsed laser beam strikes the sample causing desorption of a plume of matrix, analyte, and other ions. The analyte can be protonated, be deprotonated, or form adducts before entering the TOF analyzer.



Atom transfer reactions happen in the matrix to give multiply charged.



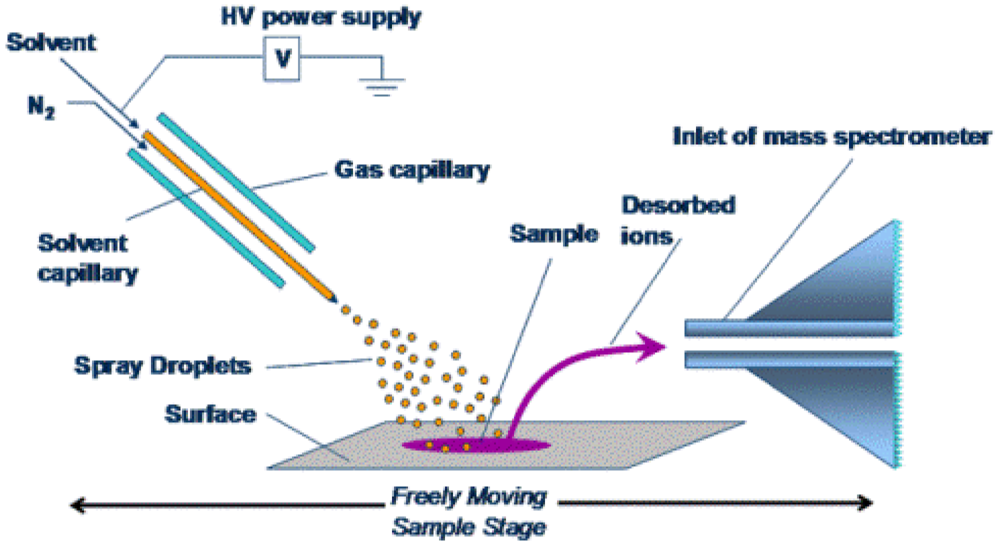
Nature Reviews Molecular Cell Biology **5**, **699-711 (September 2004)**

Nature Reviews | Molecular Cell Biology

Desorption Electrospray Ionization (DESI)

This proprietary technology was first published by Dr. R. Graham Cooks' group in *Science* (**Mass Spectrometry Sampling Under Ambient Conditions with Desorption Electrospray Ionization**, *Science*, 2004, 306, 471-473).

Desorption Electrospray Ionization (DESI) is carried out by directing pneumatically assisted electrosprayed droplets onto a surface to be analyzed at atmospheric conditions. Ions are produced from the sample originally present on the surface. The resulting mass spectra are similar to normal ESI mass spectra. The contents of the solvent spray, the gas flow rate, the amount of applied voltage, the spray angle and the ion uptake angle, as well as the various distances in aligning the spray, sample and mass spectrometer are all variables which can be studied to achieve an optimal mass spectrum for a particular type of sample.



Using DESI, high quality mass spectra have already been obtained for a wide range of molecules by directly interrogating a diverse range of surfaces. For example, explosive agents, chemical warfare simulants, amino acids, peptides, proteins, commercially available drug molecules, alkaloids, terpenoids and steroids have all been successfully ionized using DESI.

Electrospray Ionization MS Data

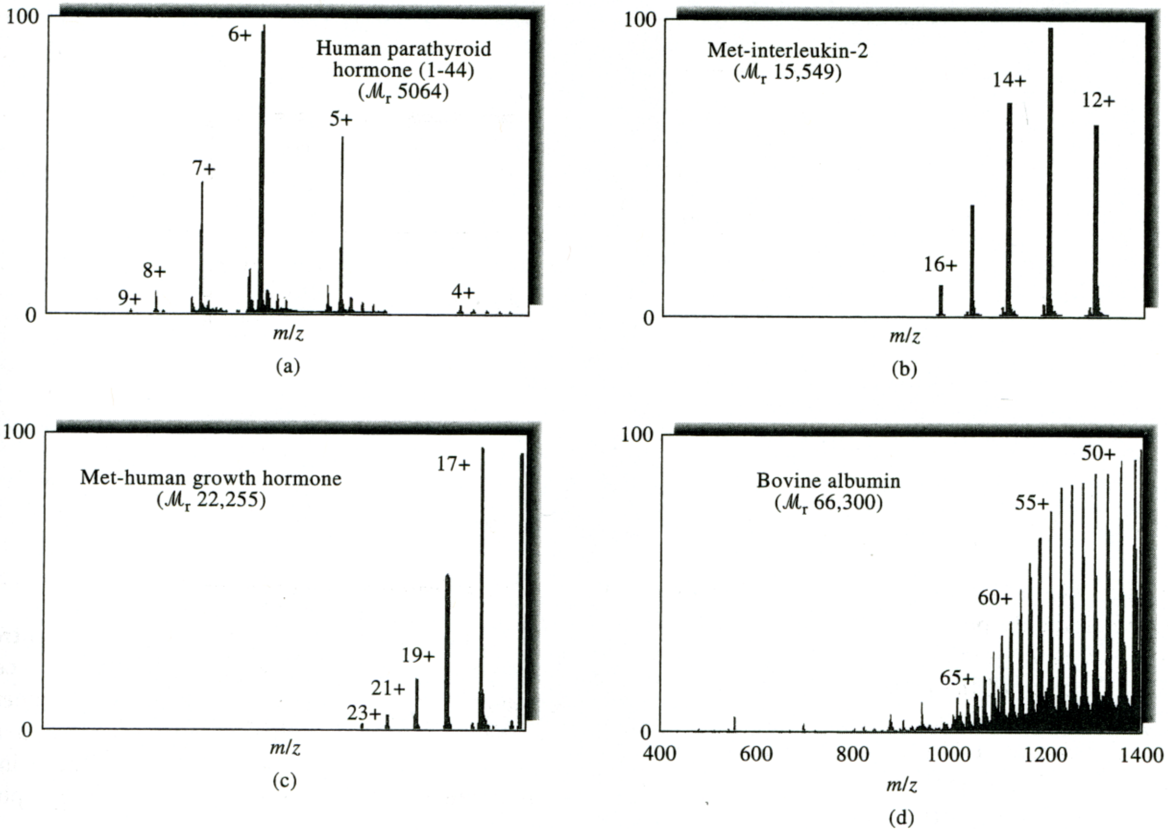


FIGURE 20-10 Typical electrospray mass spectra of proteins and peptides. The numbers above the peaks represent the molecular charge associated with each peak. (From R. D. Smith et al., *Anal. Chem.*, **1990**, *62*, 882. Copyright 1990 American Chemical Society.)

Types of Mass Spectrometry

(i) quadrupole, (ii) time-of-flight and (iii) double focusing sector

Mass spectrometers produce ions and separate them according to their charge.

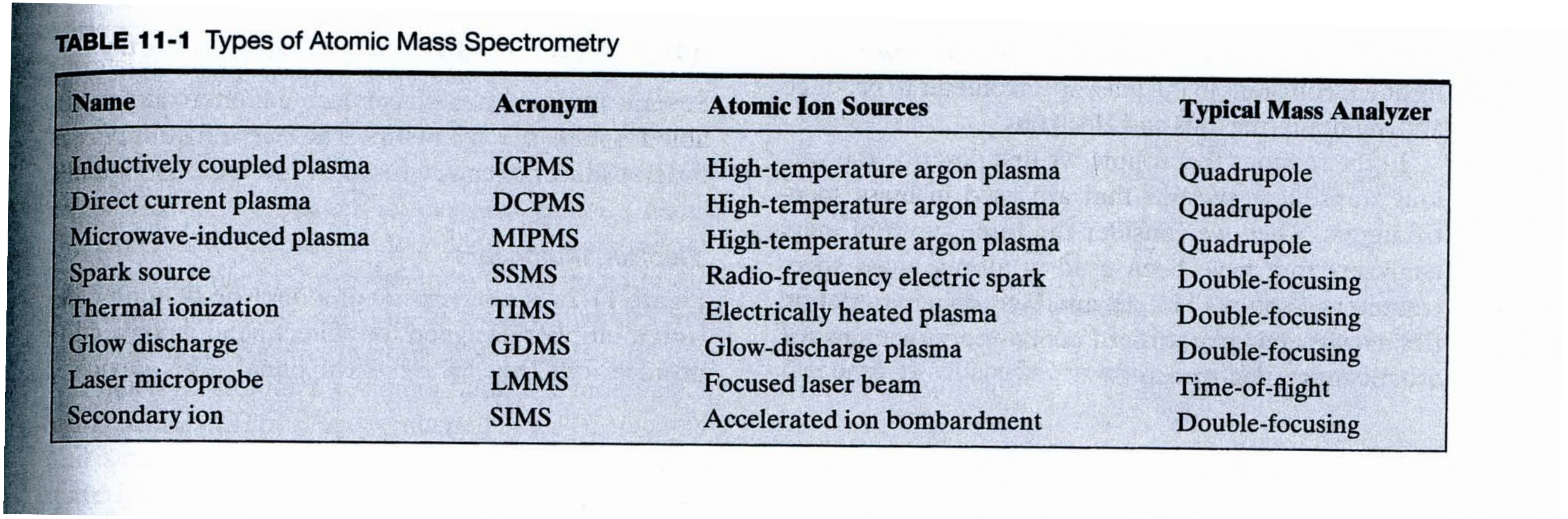
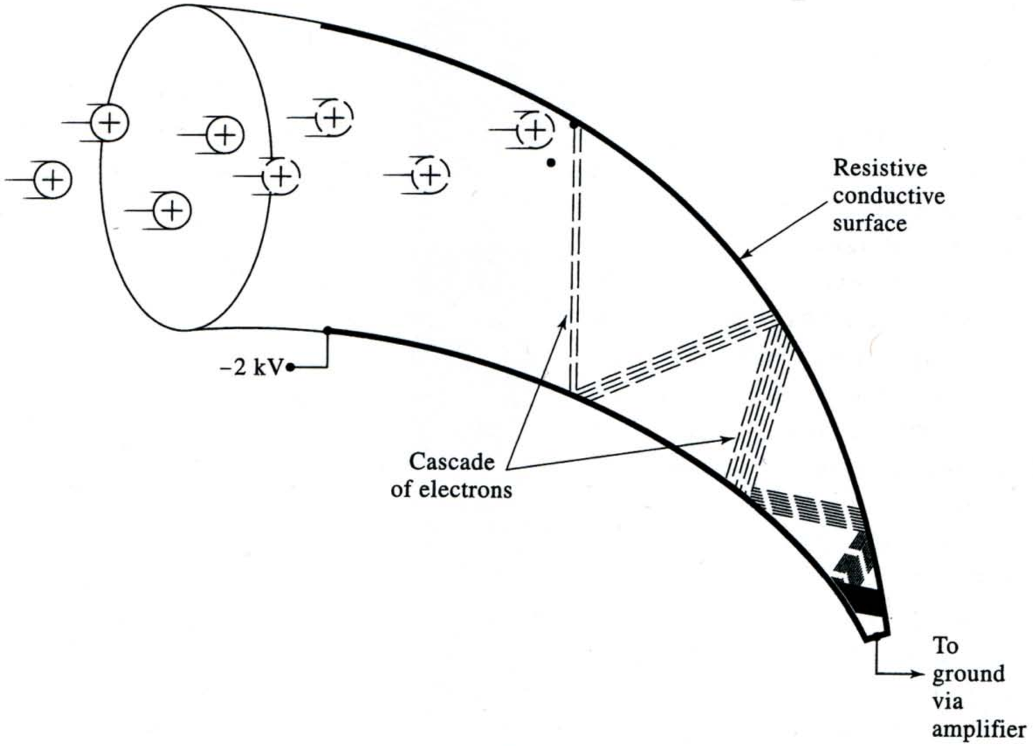


TABLE 11-1 Types of Atomic Mass Spectrometry

Name	Acronym	Atomic Ion Sources	Typical Mass Analyzer
Inductively coupled plasma	ICPMS	High-temperature argon plasma	Quadrupole
Direct current plasma	DCPMS	High-temperature argon plasma	Quadrupole
Microwave-induced plasma	MIPMS	High-temperature argon plasma	Quadrupole
Spark source	SSMS	Radio-frequency electric spark	Double-focusing
Thermal ionization	TIMS	Electrically heated plasma	Double-focusing
Glow discharge	GDMS	Glow-discharge plasma	Double-focusing
Laser microprobe	LMMS	Focused laser beam	Time-of-flight
Secondary ion	SIMS	Accelerated ion bombardment	Double-focusing

Detectors for Mass Spectrometry



(b)

FIGURE 11-2 (a) Discrete-dynode electron multiplier. Dynodes are kept at successively higher voltages via a multistage voltage divider. (b) Continuous-dynode electron multiplier. (Adapted from J. T. Watson, *Introduction to Mass Spectrometry*, 3rd ed., pp. 334–35, New York: Raven Press, 1997. With permission.)

Electron multiplier – 20 dynodes, Gain = 10^7

Rugged, reliable and fast response time

Detectors for Mass Spectrometry

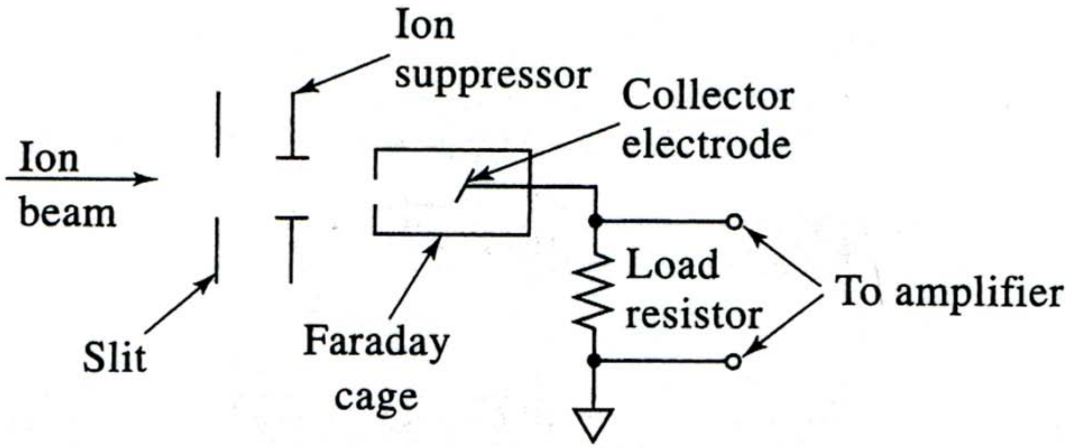


FIGURE 11-3 Faraday cup detector. The voltage on the ion suppressor plates is adjusted to minimize differential response as a function of mass.

Faraday cup is simple and inexpensive. Response is independent of the energy, mass and chemical nature of the ion.

Mass Analyzers - Quadrupole

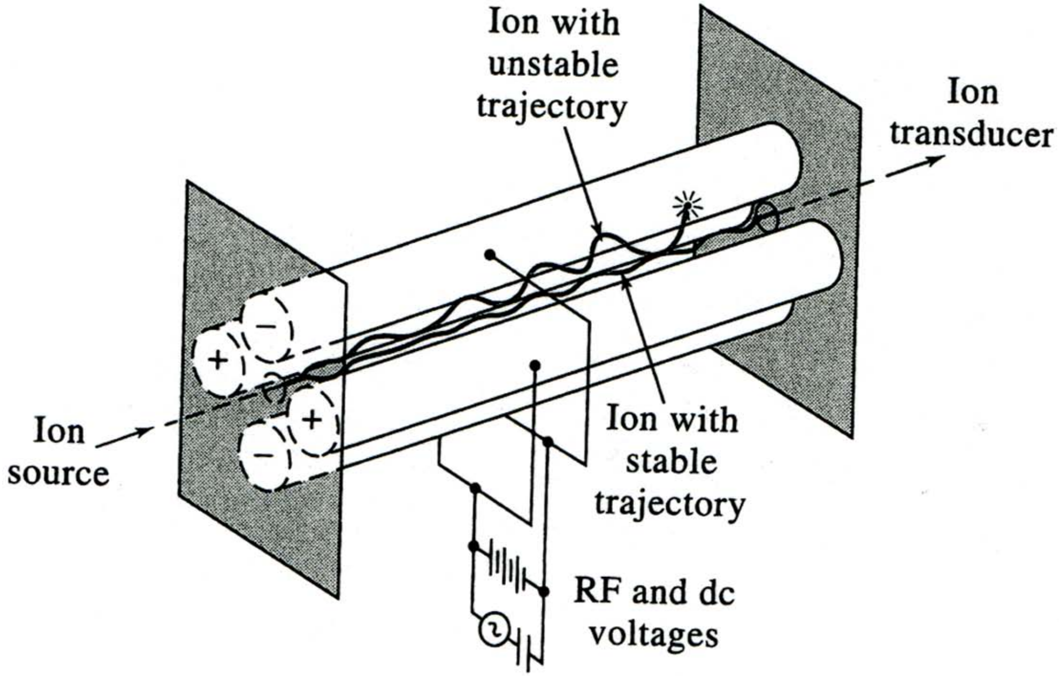


FIGURE 11-6 A quadrupole mass spectrometer.

Whether a positive ion strikes the rod depends on the rate of movement of the ion along the z-axis, its m/z ratio, and the frequency and magnitude of the ac signal.

Mass Analyzers – Time-of-Flight

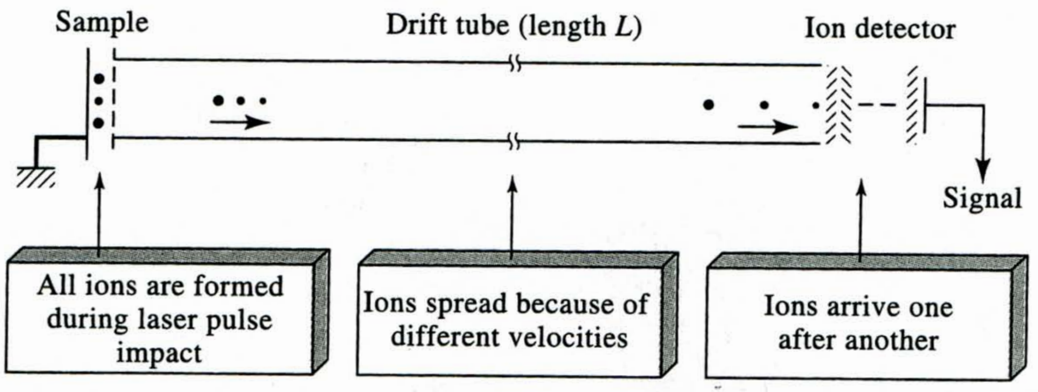


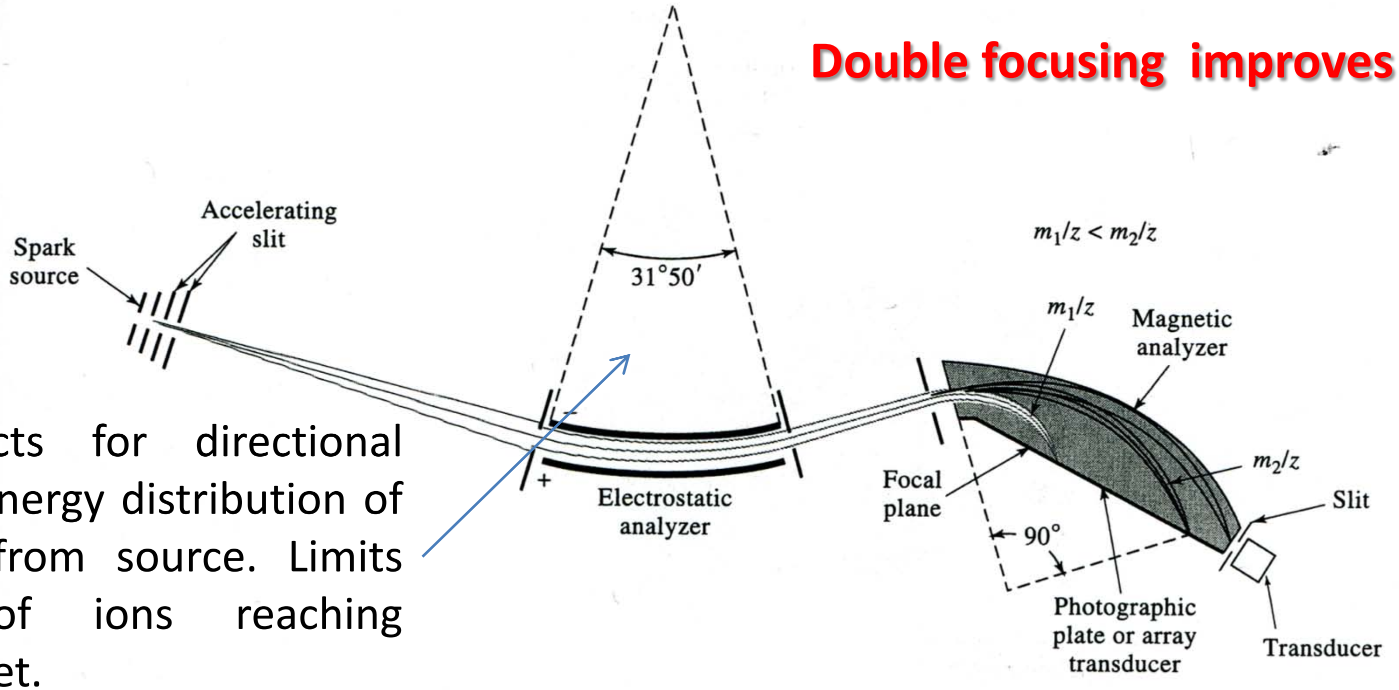
FIGURE 11-10 Principle of a TOF mass spectrometer. A spatially tightly bunched group of ions produced by a laser probe is accelerated into the drift tube where separation occurs. (From A. H. Verbueken, F. J. Bruynseels, R. Van Grieken, and F. Adams, in *Inorganic Mass Spectrometry*, p. 186, F. Adams, R. Gijbels, and R. Van Grieken, eds., New York: Wiley, 1988. With permission.)

$zeV = KE = \frac{1}{2}(mv^2)$ $t_f = L/v = L\,(m/2zeV)^{1/2}$

(+) ions produced by pulsing a sample with e- or photons (~25 kHz and 0.25 ms). Ions are accelerated into the flight tube with a pulsed electric field ~10^4 V. ***Lighter elements arrive at the detector earlier, heavier elements later. Advantages – ruggedness, unlimited mass range, rapid data acquisition rate.***

Mass Analyzers – Double Sector

Double focusing improves resolution!



Corrects for directional and energy distribution of ions from source. Limits KE of ions reaching magnet.

FIGURE 11-11 Mattauch-Herzog-type double-focusing mass spectrometer. Resolution >10^5 has been achieved with instruments based on this design.

$$m/z = (B^2r^2e)/2V$$

Usually ions are sorted by holding V and r constant, and sweeping B.