Mass Spectrometry in Five Parts
Stoll, Che380

Part I – General Idea, Important Terms

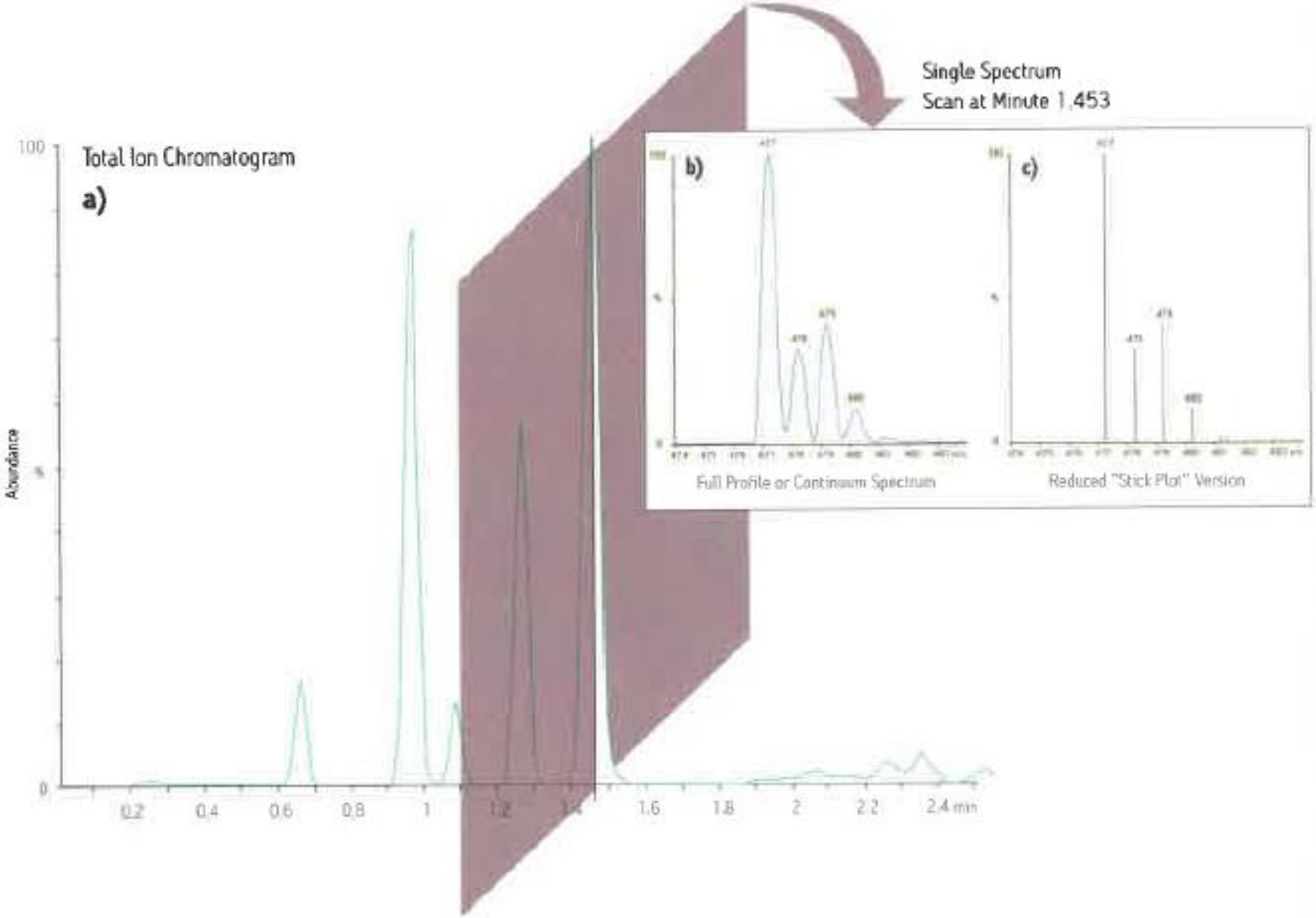


Figure 2: a) Increasing abundance in the total ion current (TIC) is represented as it changes over time in a chromatographic-like trace. b) Each digital slice of a peak represents the ions at that time making up the ion current often referred to as a profile or continuum acquisition. The x or 'time' axis is now the mass-to-charge ratio (m/z) the ability to resolve neighboring ions in the spectrum (such as isotopes) is readily seen. c) A profile spectrum is often reduced to a 'stick plot' represented by centroids dropped from each peak apex reducing the size of the stored file in favor of the increased resolution information.

Balogh, M. (2009) *The Mass Spectrometry Primer*, Waters Corporation.

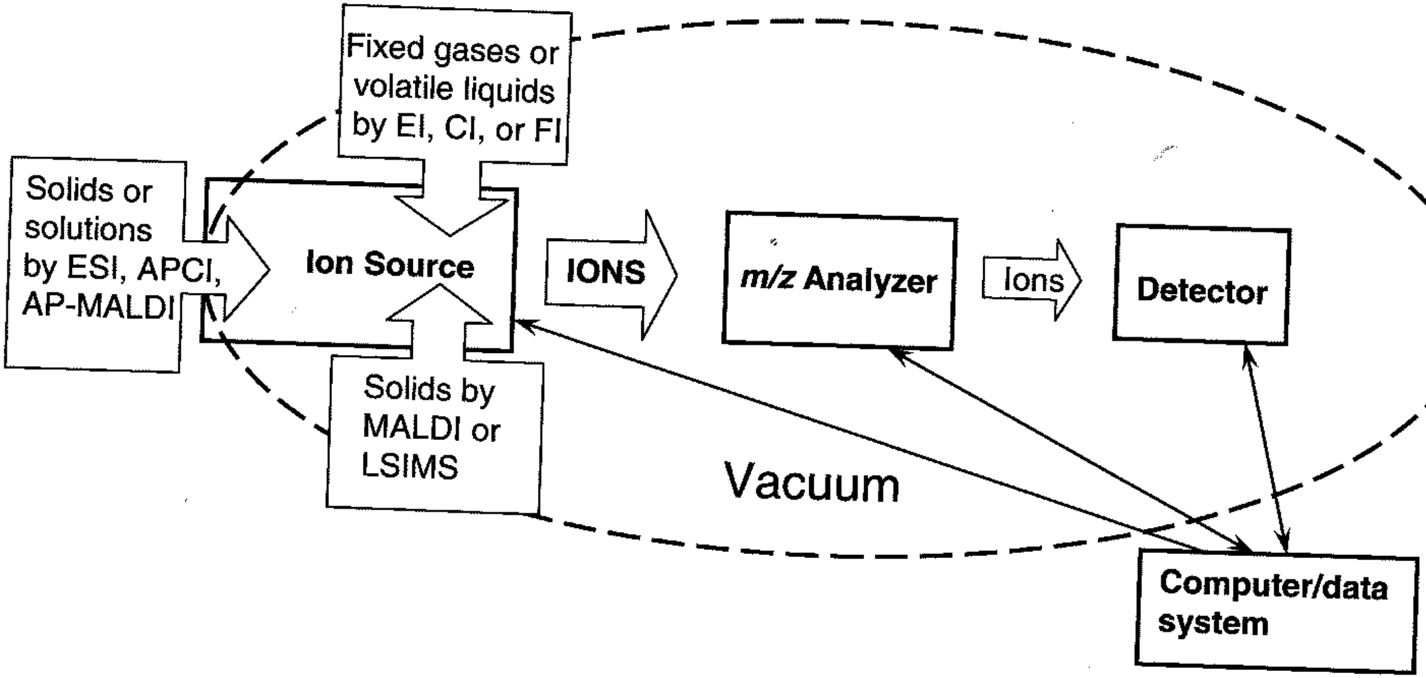


Figure 1-1. ***This conceptual illustration of the mass spectrometer shows the major components of mass spectrometer, i.e., sample inlets (dependent on sample and ionization technique; ion source (origin of gas phase ions); m/z analyzer (portion of instrument responsible for separation of ions according to their individual m/z values); detector (generates the signals that are a recording of the m/z values and abundances of the ions); vacuum system (the components that remove molecules, thereby providing a collision-free path for the ions from the ion source to the detector); and the computer (coordinates the functions of the individual components and records and stores the data).***

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

Early 1900s

Replica of an early mass spectrometer

http://en.wikipedia.org/wiki/Mass_spectrometry

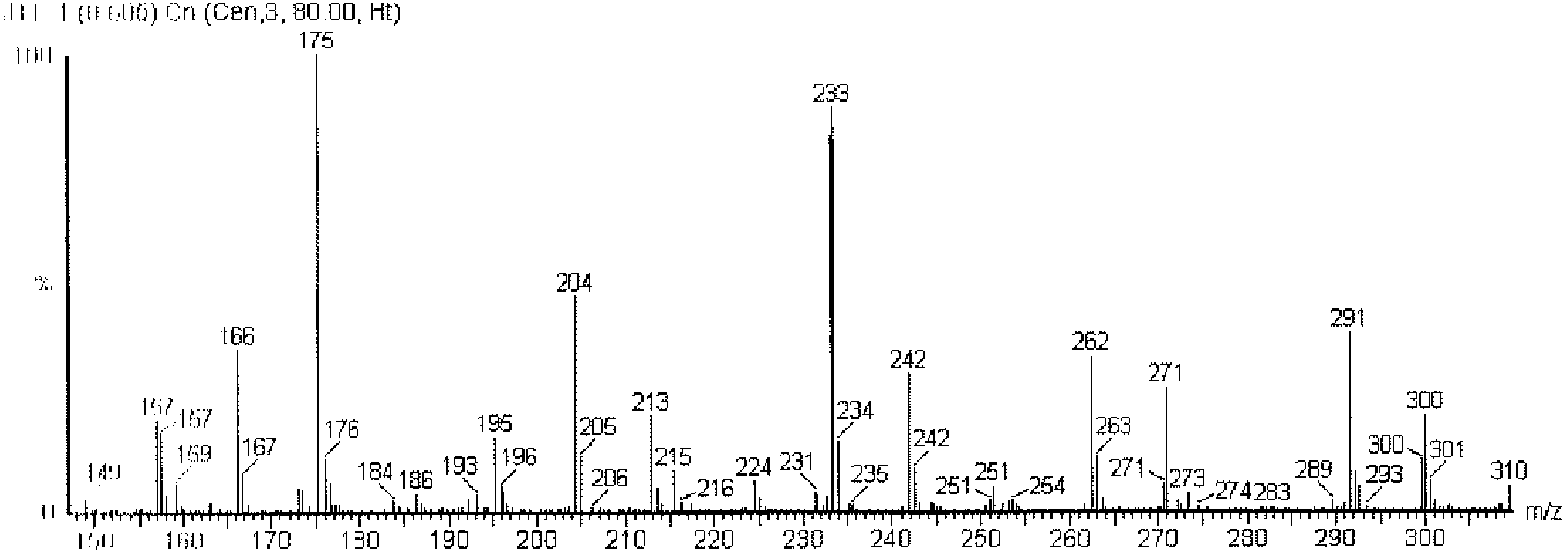
1980s

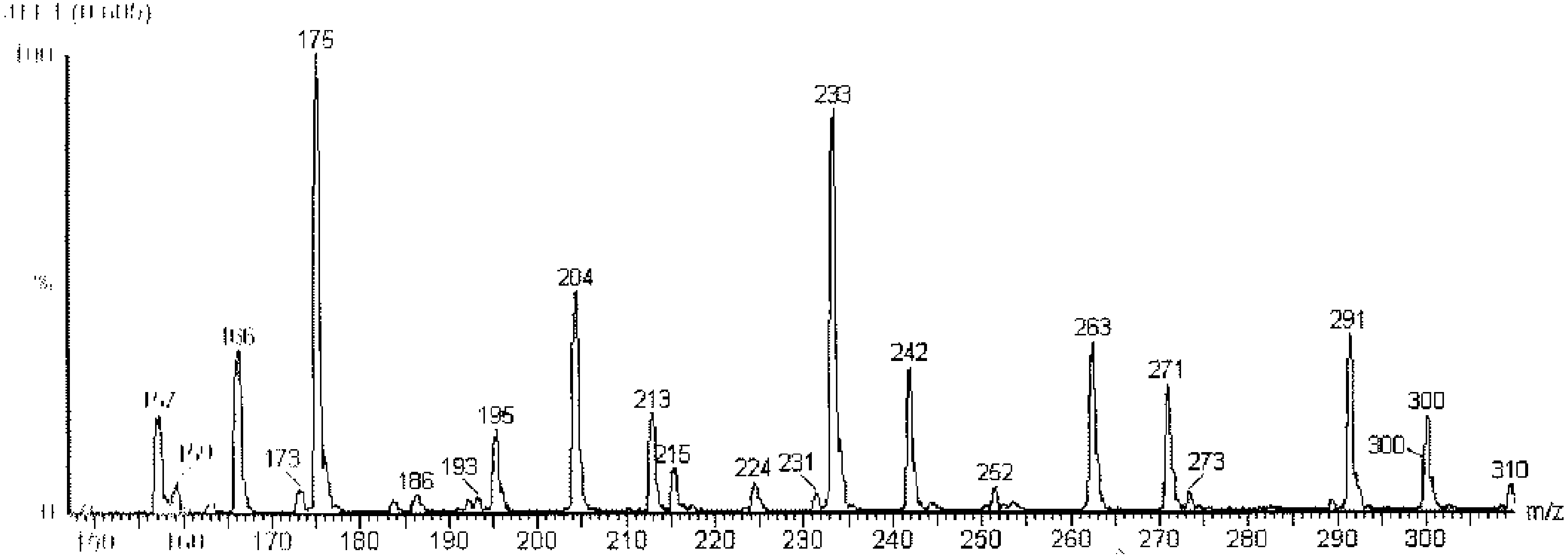
The instrument Fenn and his colleagues used to develop ESI is on display at the Chemical Heritage Foundation Museum in Philadelphia, PA

http://en.wikipedia.org/wiki/John_Fenn_(chemist)

2013

http://www.waters.com/waters/en_US/ACQUITY-QDa-Mass-Detector-for-Chromatographic-Analysis/nav.htm?cid=134761404&locale=en_US





Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

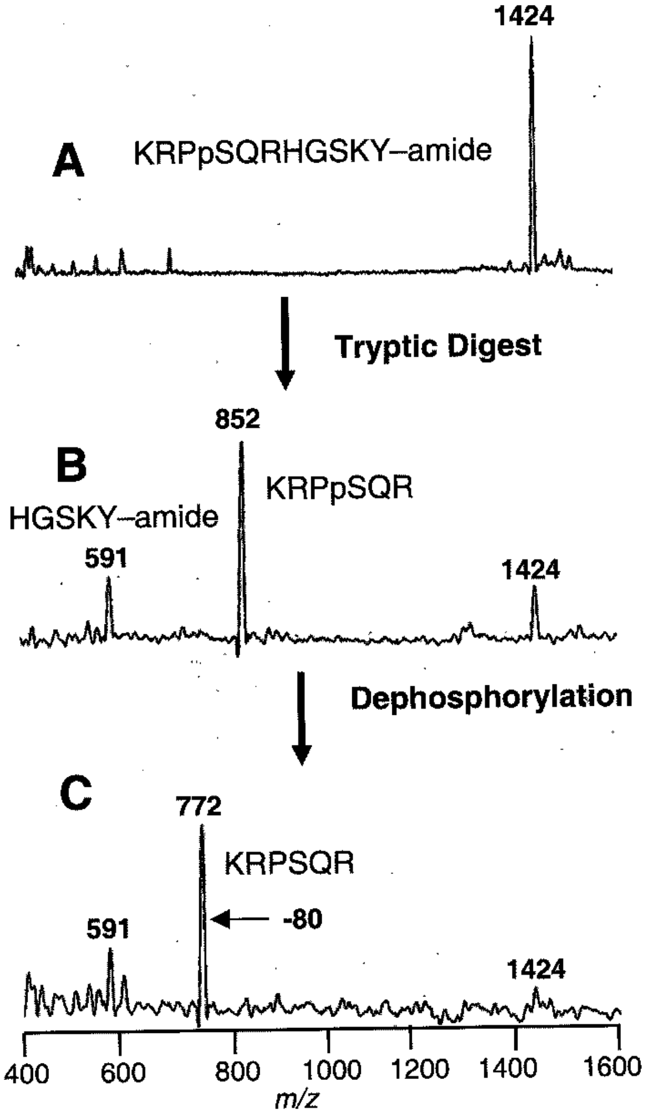


Figure 1-26. ***MALDI mass spectrum of phosphopeptide before (A) and after (B) treatment with trypsin in an effort to map the location of the phosphate group. (C): MALDI spectrum of tryptic digest after treatment with phosphatase.*** *Reprinted from Liao P-C, Leykam J, Andrews PV, Gage DA, and Allison J "An approach to locate phosphorylation sites in proteins by MALDI" Anal. Biochem. 1994, 219, 9-20, with permission from Academic Press.*

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

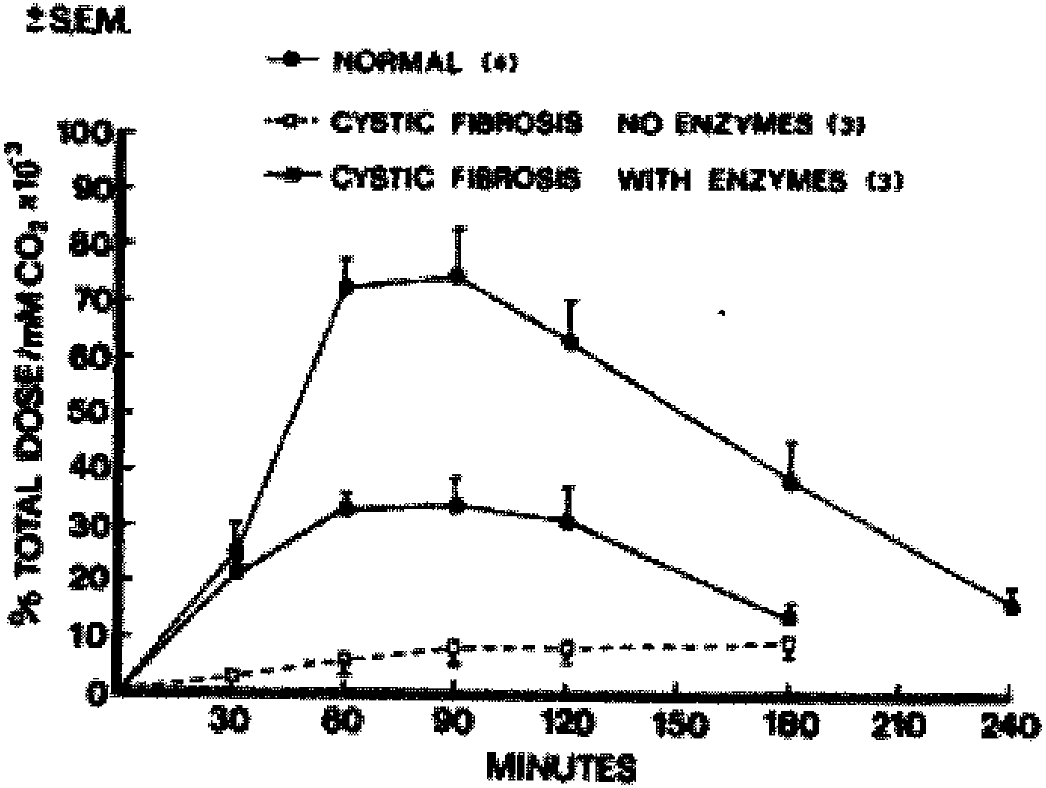


Figure 1-27. **Plot of excess $^{13}CO_2$ beyond natural abundance in the breath of normal vs cystic fibrosis patients following an oral dose (10 mg kg^{-1}) of 1-^{13}C-trioctanoin.** *Reprinted from Barr RG, Perman JA, Schoeller DA, and Watkins JB "Breath tests in pediatric gastrointestinal disorders: new diagnostic opportunities" Pediatrics 1978, 62(3), 393–401, with permission from the American Academy of Pediatrics.*

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

Centroid vs. Profile Data

Mass Accuracy

Mass Resolution

Resolving Power

Monoisotopic Mass

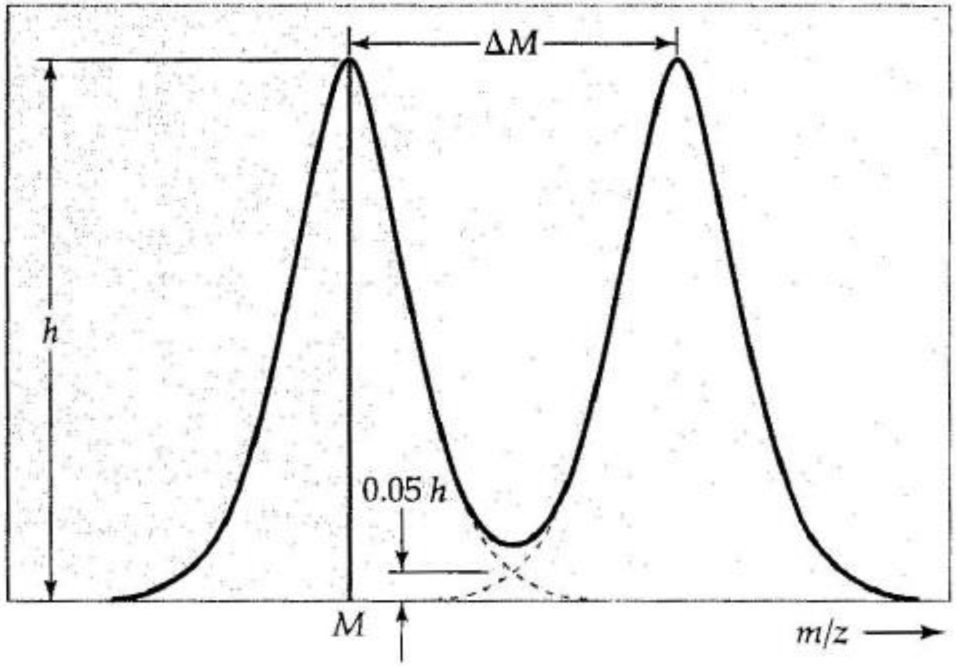


Figure 12.6 from Rubinson and Rubinson, *Contemporary Instrumental Analysis*

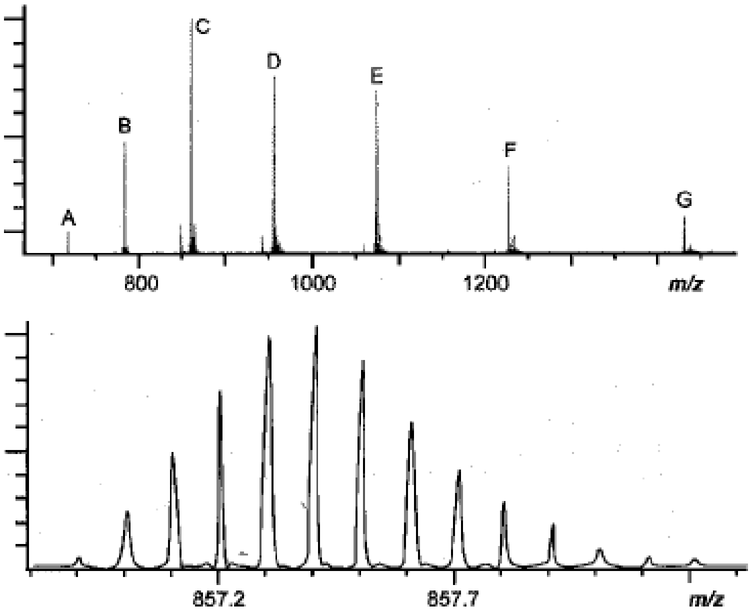


Figure 2-47.* *(Top) ESI mass spectrum of ubiquitin obtained with an FTICR mass spectrometer at low resolving power (top) and at high resolving power (Bottom) in the vicinity of m/z 857 (peak C in top spectrum). *Data provided by I. Jon Amster, Department of Chemistry, University of Georgia, Athens, GA, USA.*

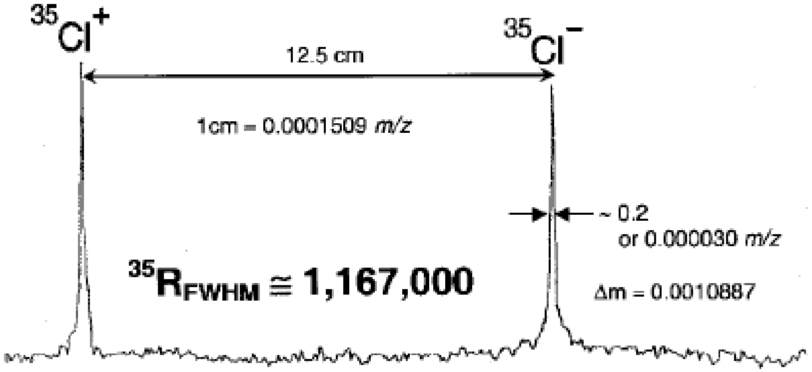
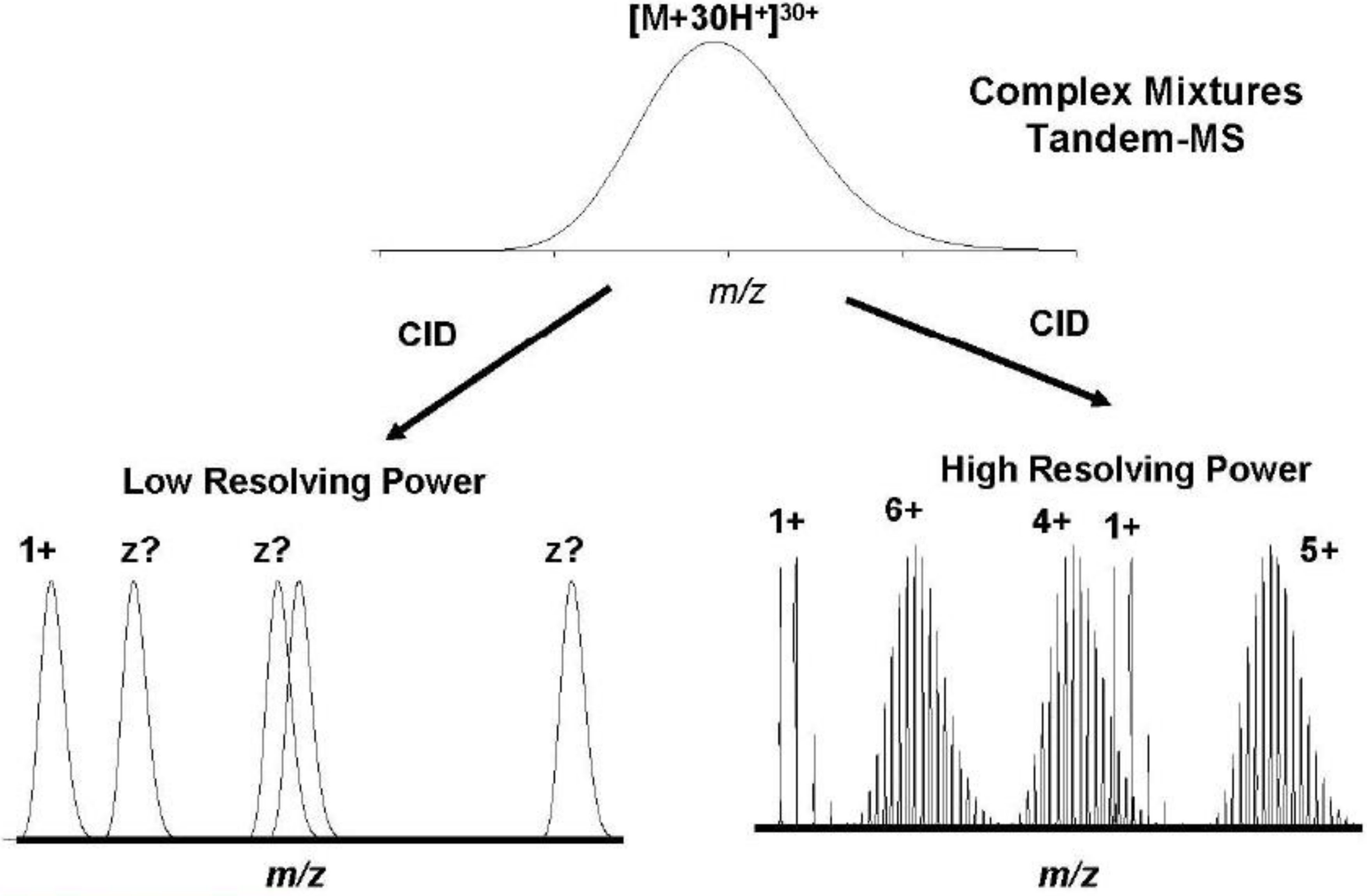


Figure 2-46.* *Segment of mass spectrum in the region of the nominal m/z 35 showing a resolving power >1,000,000 (FWHM) using FTMS. The peaks represent the positive and negative ions of ^{35}Cl that have a difference in mass equal to the mass of two electrons (~0.15 millimass units). The instrument was switched from positive-ion detection mode to negative-ion detection mode during the scan between the two peaks. *Courtesy of Spectrospin AG.*

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

What else does direct charge-state determination facilitate?



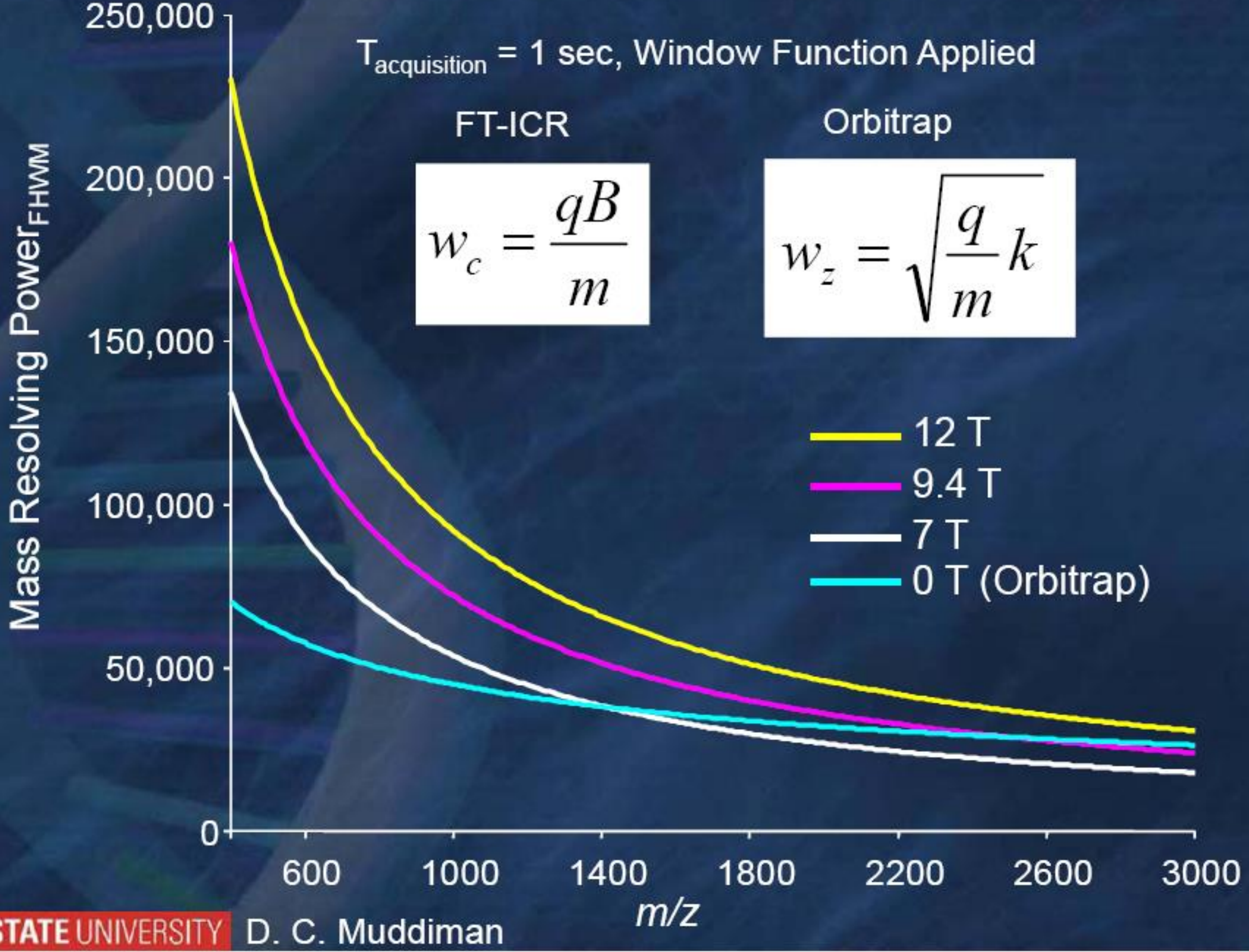
Complex Mixtures
Tandem-MS

Low Resolving Power

High Resolving Power

Resolving Power in FT-ICR and Orbitrap Mass Spectrometry

can you ever have too much peak capacity?



$T_{acquisition}$ = 1 sec, Window Function Applied

FT-ICR

$$w_c = \frac{qB}{m}$$

Orbitrap

$$w_z = \sqrt{\frac{q}{m}k}$$

FT-ICR and Orbitrap MS at *m/z* = 600
Bringing Clarity to Complex Mixture Analysis

IonTrap*

TOF

Orbitrap

7T FT-ICR

12 T FT-ICR

-Renoir
Two Sisters

TOF

Orbi

12T

Part II – Ionization Methods

Method	Acronym	Ionization Due to…	Advantages	Disadvantages	Main Applications
Electron					
Chemical					
Photo					
Electrospray					
Matrix Assisted Laser Desorption					

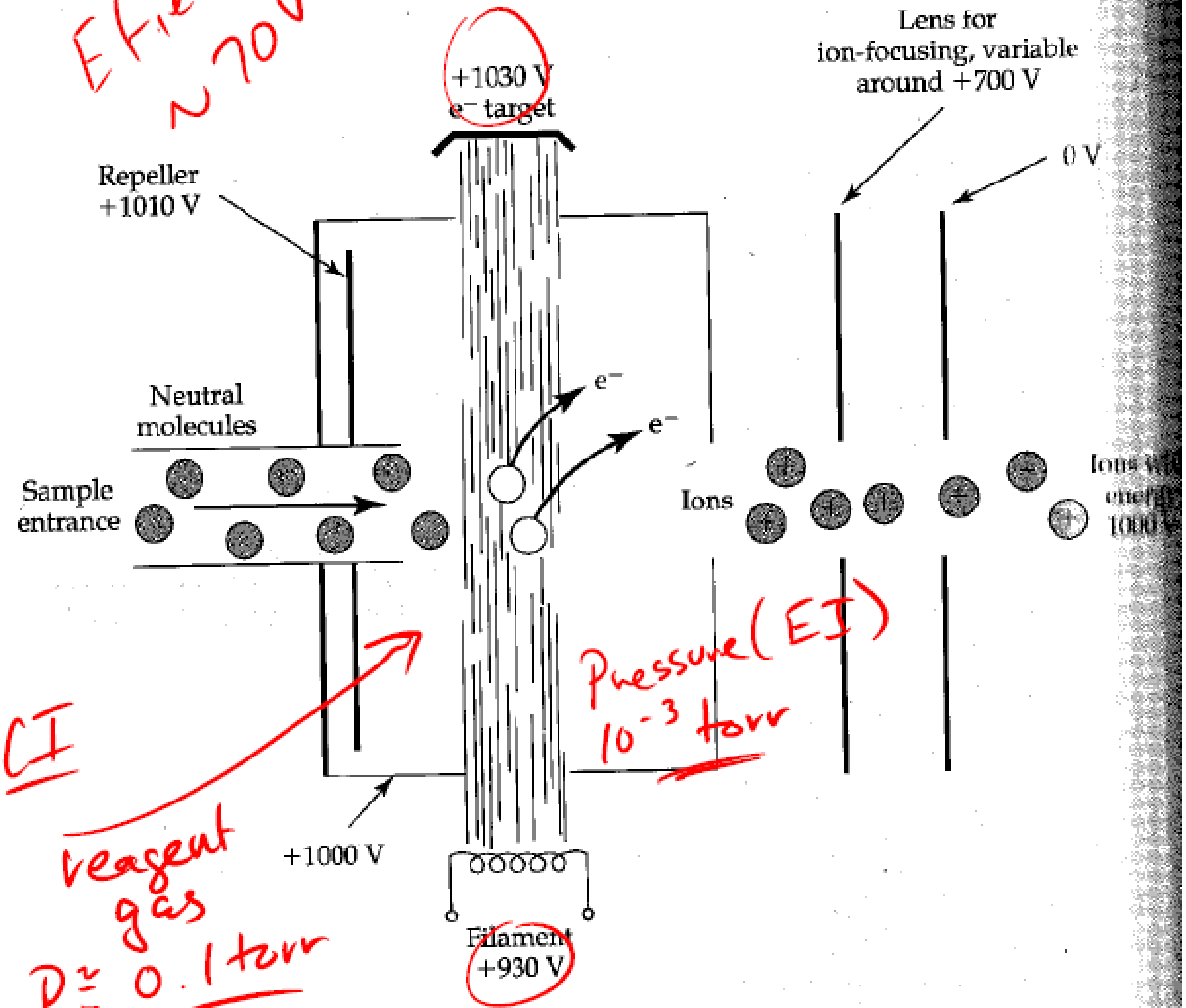


FIGURE 12.16 ▶
Diagram of the operation of an electron-impact ion source.
Neutral molecules are vaporized into the chamber. A beam of electrons passes through the vapor, causing positive ions to form. The ions are repelled out of the chamber, focused, and admitted into the mass analyzer. The potentials shown in the figure are such that the ions will enter the mass analyzer with kinetic energies thermally distributed around an average E_k of 1000 eV. Notice that although the electron beam is accelerated by 100 V, both electrodes are held at a high enough potential so that the electrons will be driven into and through the ionization chamber. Some sources have magnets placed so that the electrons of the beam will cross the chamber with helical paths. This makes the effective ionization path much longer.

E field
~70V

CI

reagent
gas
$P \cong 0.1$ torr

Pressure (EI)
10^{-3} torr

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[2] One exception is high-resolution mass determinations, which are limited by the quality of the mass separation.

$$M + e^- \longrightarrow M^{\bullet +} + e^- + e^-$$

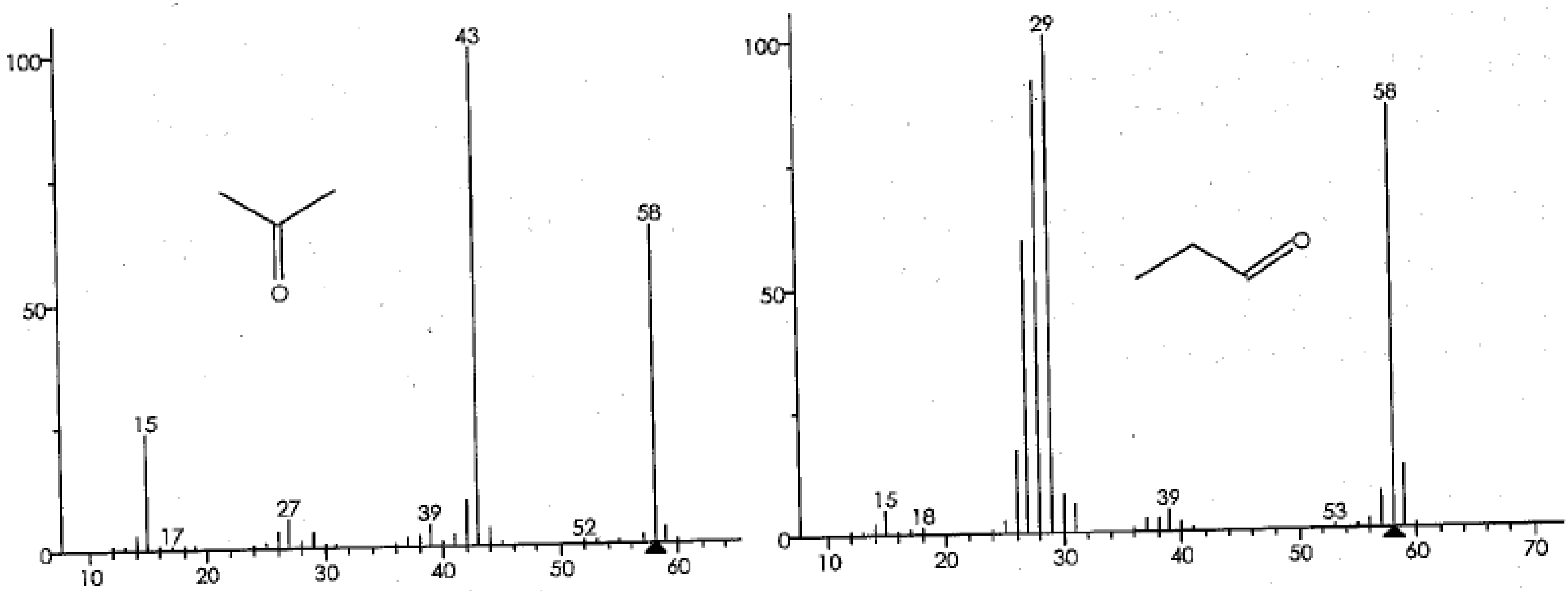
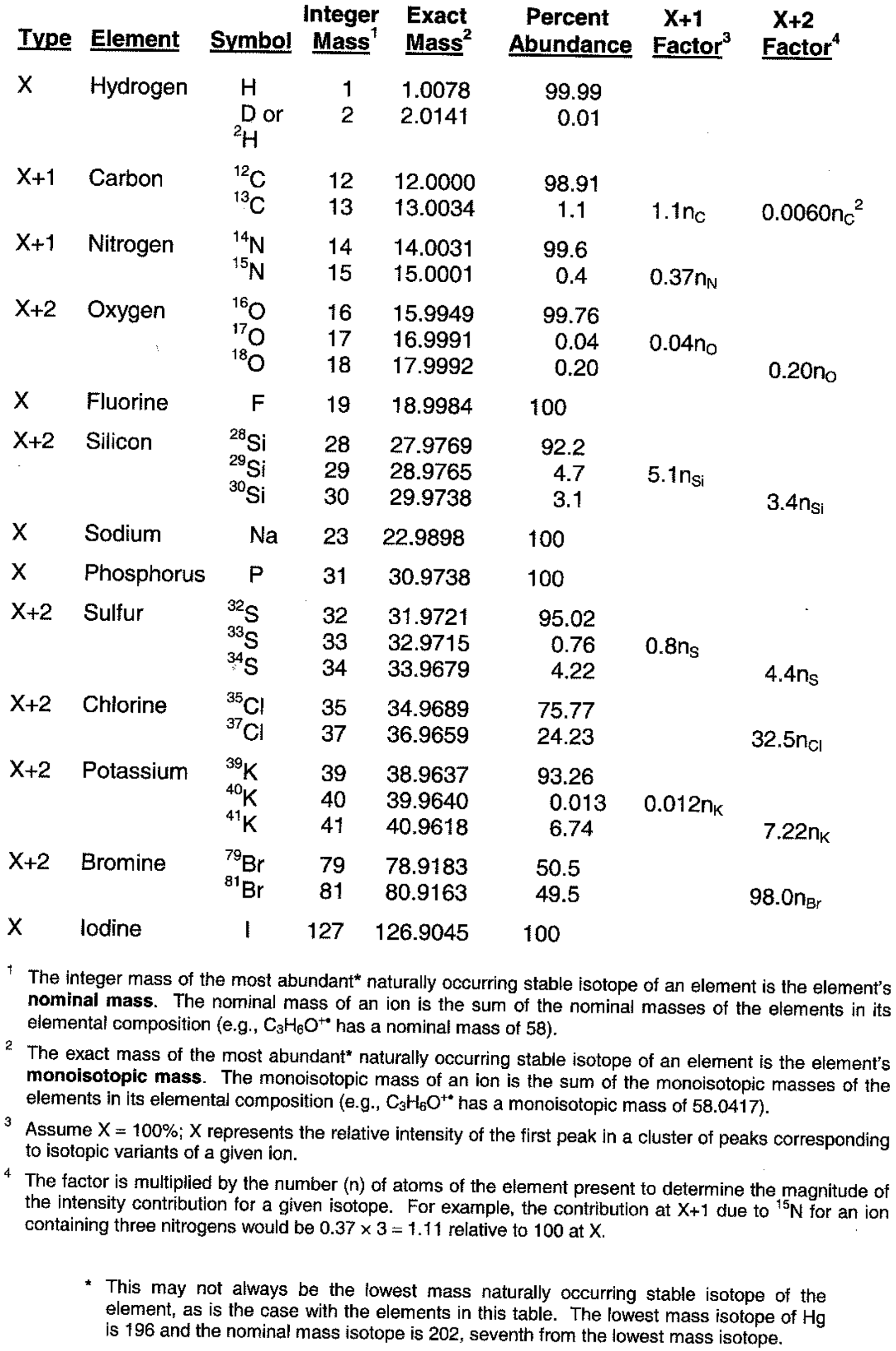


Figure 1-16. **EI mass spectrum of acetone (left) and propionaldehyde (right). Both compounds have an elemental composition of C_3H_6O and a nominal mass of 58.**

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*



Type	Element	Symbol	Integer Mass[1]	Exact Mass[2]	Percent Abundance	X+1 Factor[3]	X+2 Factor[4]
X	Hydrogen	H	1	1.0078	99.99		
		D or ^{2}H	2	2.0141	0.01		
X+1	Carbon	^{12}C	12	12.0000	98.91		
		^{13}C	13	13.0034	1.1	$1.1n_C$	$0.0060n_C^2$
X+1	Nitrogen	^{14}N	14	14.0031	99.6		
		^{15}N	15	15.0001	0.4	$0.37n_N$	
X+2	Oxygen	^{16}O	16	15.9949	99.76		
		^{17}O	17	16.9991	0.04	$0.04n_O$	
		^{18}O	18	17.9992	0.20		$0.20n_O$
X	Fluorine	F	19	18.9984	100		
X+2	Silicon	^{28}Si	28	27.9769	92.2		
		^{29}Si	29	28.9765	4.7	$5.1n_{Si}$	
		^{30}Si	30	29.9738	3.1		$3.4n_{Si}$
X	Sodium	Na	23	22.9898	100		
X	Phosphorus	P	31	30.9738	100		
X+2	Sulfur	^{32}S	32	31.9721	95.02		
		^{33}S	33	32.9715	0.76	$0.8n_S$	
		^{34}S	34	33.9679	4.22		$4.4n_S$
X+2	Chlorine	^{35}Cl	35	34.9689	75.77		
		^{37}Cl	37	36.9659	24.23		$32.5n_{Cl}$
X+2	Potassium	^{39}K	39	38.9637	93.26		
		^{40}K	40	39.9640	0.013	$0.012n_K$	
		^{41}K	41	40.9618	6.74		$7.22n_K$
X+2	Bromine	^{79}Br	79	78.9183	50.5		
		^{81}Br	81	80.9163	49.5		$98.0n_{Br}$
X	Iodine	I	127	126.9045	100		

[1] The integer mass of the most abundant* naturally occurring stable isotope of an element is the element's **nominal mass**. The nominal mass of an ion is the sum of the nominal masses of the elements in its elemental composition (e.g., $C_3H_6O^{+\bullet}$ has a nominal mass of 58).

[2] The exact mass of the most abundant* naturally occurring stable isotope of an element is the element's **monoisotopic mass**. The monoisotopic mass of an ion is the sum of the monoisotopic masses of the elements in its elemental composition (e.g., $C_3H_6O^{+\bullet}$ has a monoisotopic mass of 58.0417).

[3] Assume X = 100%; X represents the relative intensity of the first peak in a cluster of peaks corresponding to isotopic variants of a given ion.

[4] The factor is multiplied by the number (n) of atoms of the element present to determine the magnitude of the intensity contribution for a given isotope. For example, the contribution at X+1 due to ^{15}N for an ion containing three nitrogens would be 0.37 × 3 = 1.11 relative to 100 at X.

* This may not always be the lowest mass naturally occurring stable isotope of the element, as is the case with the elements in this table. The lowest mass isotope of Hg is 196 and the nominal mass isotope is 202, seventh from the lowest mass isotope.

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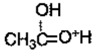
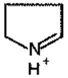
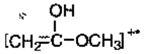
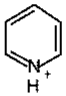
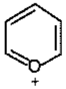
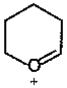
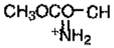
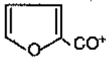
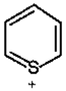
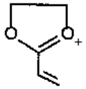
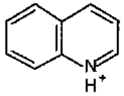
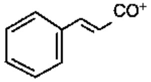
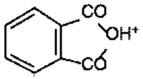
Common Fragment Ions

m/z	Ion	Origin
29	HCO^+	Aldehydes
30	$CH_2NH_2^+$	Amines
31	$H_2C{=}\overset{+}{O}H$ CH_3O^+	Alcohols Methyl esters
36	$HCl^{+\bullet}$	Chloro compounds
43	$C_3H_7^+$ CH_3CO^+	Propyl ion Acetyl groups
47	CH_3S^+	Sulfides
49	CH_2Cl^+	Chloro compounds
55	$C_4H_7^+$	Alkyl groups
57	$C_4H_9^+$ $C_2H_5CO^+$	Alkyl groups Acylium ion
58	 $[H_2CC\overset{\diagup H}{O}CH_3]^{+\bullet}$	Ketones with a γ-hydrogen
59	$[COOCH_3]^+$	Methyl esters
61	 $CH_3\overset{OH}{\overset{\vert}{C}}{=}O^+H$	Esters of high molecular weight alcohols
70		Pyrrolidines
74	 $[CH_2{=}\overset{OH}{\overset{\vert}{C}}{-}OCH_3]^{+\bullet}$	Methyl esters with a γ-hydrogen
77	$C_6H_5^+$	Aromatics
78	$C_5H_4N^+$	Pyridines and alkyl pyrroles
80		Pyrroles
80(82)	$HBr^{+\bullet}$	Bromo compounds
81		Furans
		Aliphatic chain with two double bonds
83	$C_6H_{11}^+$ $CHCl_2^+$	Cyclohexanes or hexenes Chloro compounds
85		Tetrahydropyranyl ethers
88	 $CH_3OCO{-}\underset{\overset{\Vert}{^{+}NH_2}}{C}H$	Amino acid esters
91	$C_7H_7^+$	Aromatic hydrocarbons with side chains
92	$C_7H_8^{+\bullet}$	Benzyl compounds with a γ-hydrogen
95		Furyl-CO-X
97		Alkyl thiophenes
99		Ethylene ketals of cyclic compounds (steroids)
104	$C_8H_8^{+\bullet}$	Alkyl aromatics
105	$C_6H_5CO^+$ $C_8H_9^+$	Benzoyl compounds Aromatic hydrocarbons
106		Amino benzyl
107	$C_7H_7O^+$	Phenolic hydrocarbons
117	$C_9H_9^+$	Styrenes
128	$HI^{+\bullet}$	Iodo compounds
130		Indoles
131		Cinnamates
149		Dialkyl phthalates (rearrangement)

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

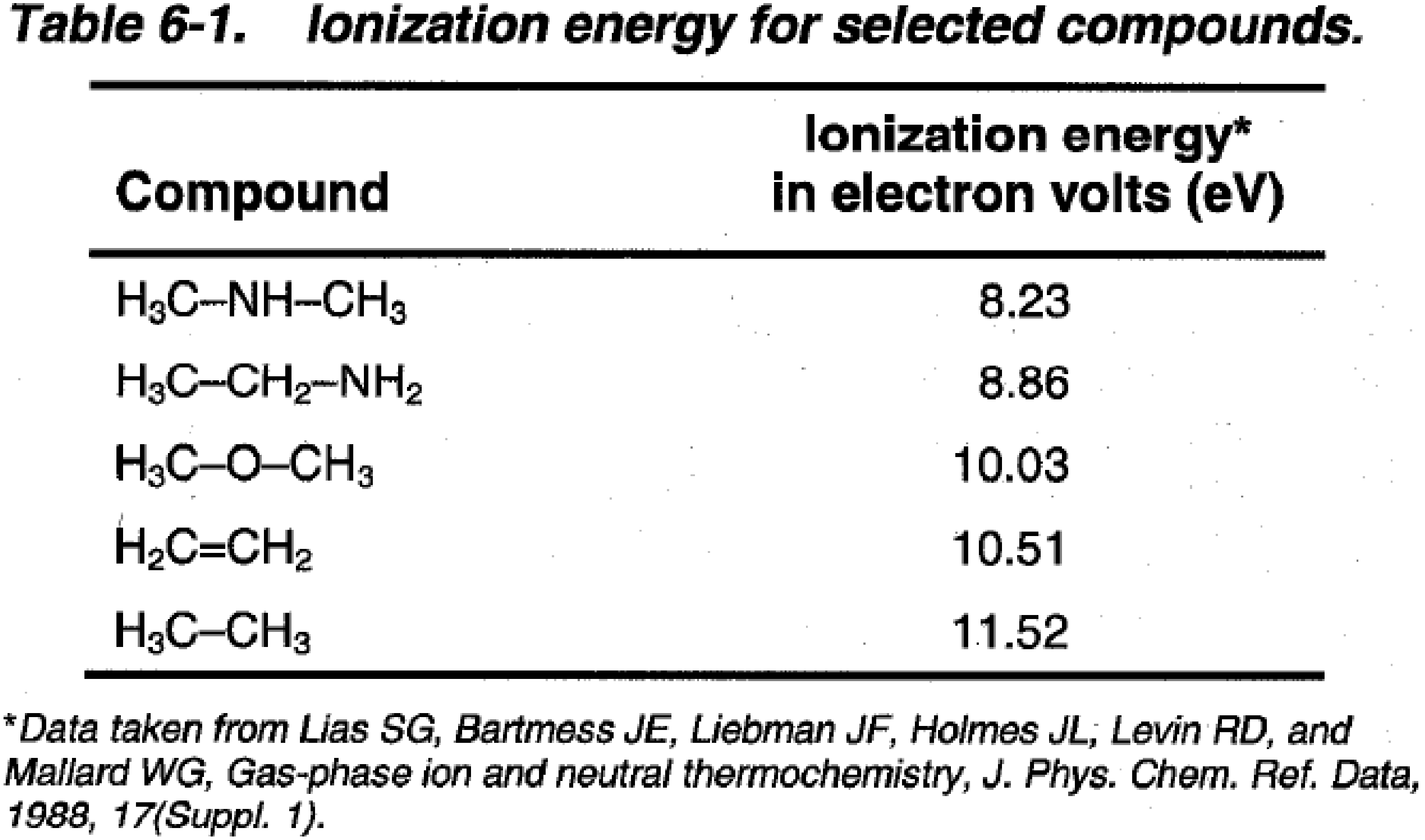


Table 6-1. Ionization energy for selected compounds.

Compound	Ionization energy* in electron volts (eV)
$H_3C{-}NH{-}CH_3$	8.23
$H_3C{-}CH_2{-}NH_2$	8.86
$H_3C{-}O{-}CH_3$	10.03
$H_2C{=}CH_2$	10.51
$H_3C{-}CH_3$	11.52

**Data taken from Lias SG, Bartmess JE, Liebman JF, Holmes JL, Levin RD, and Mallard WG, Gas-phase ion and neutral thermochemistry, J. Phys. Chem. Ref. Data, 1988, 17(Suppl. 1).*

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

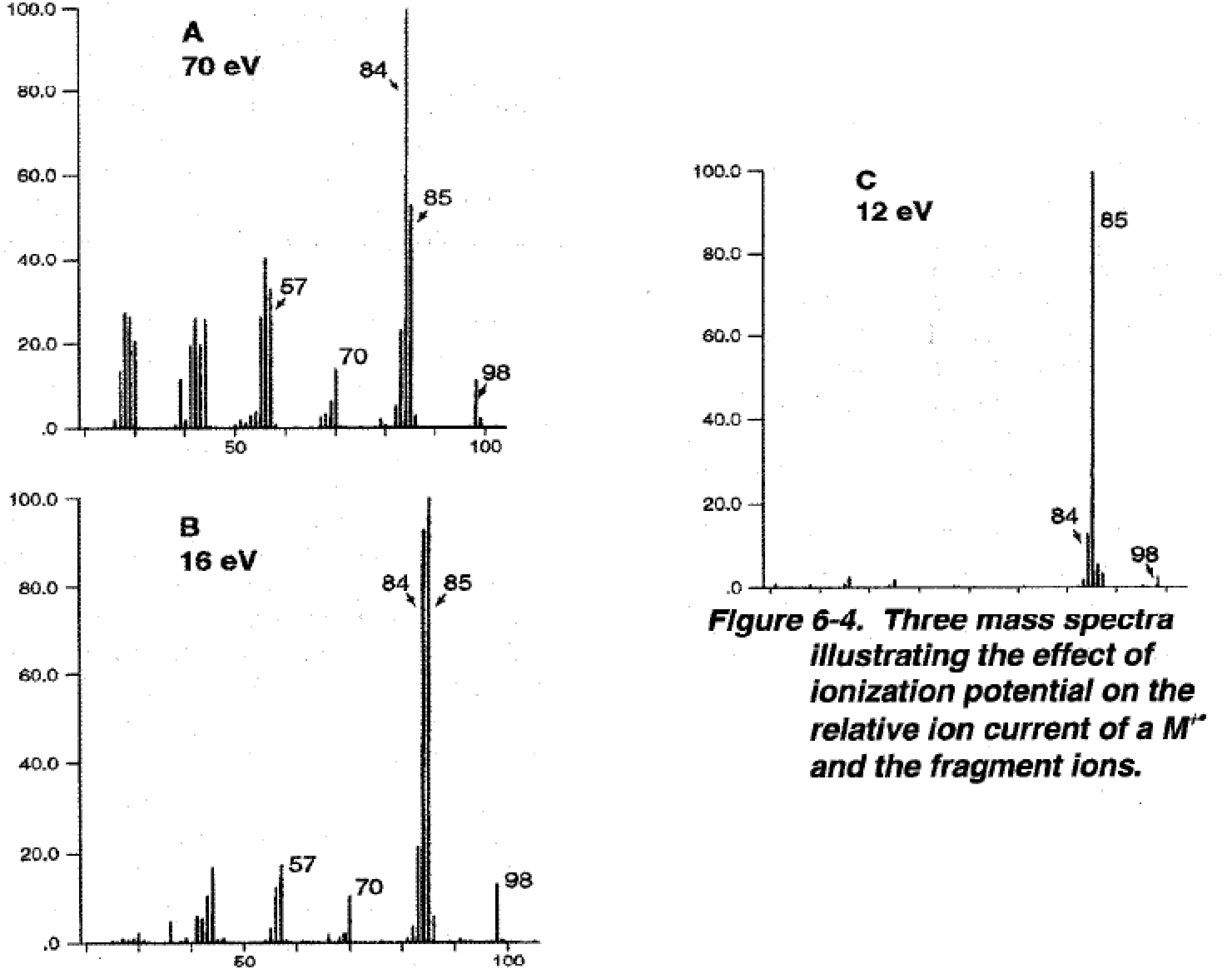
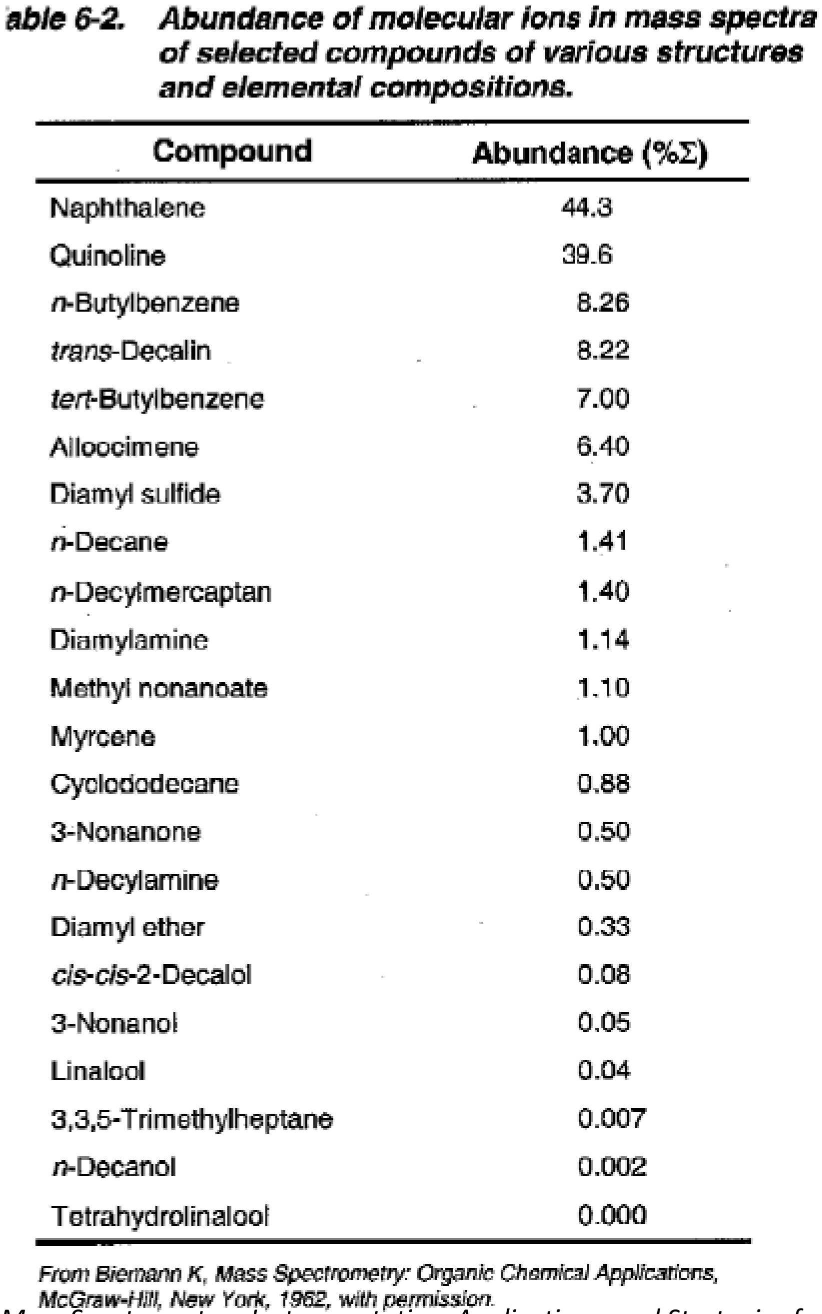


Figure 6-4. Three mass spectra illustrating the effect of ionization potential on the relative ion current of a $M^{+\bullet}$ and the fragment ions.

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*



able 6-2. Abundance of molecular ions in mass spectra of selected compounds of various structures and elemental compositions.

Compound	Abundance (%Σ)
Naphthalene	44.3
Quinoline	39.6
n-Butylbenzene	8.26
trans-Decalin	8.22
tert-Butylbenzene	7.00
Alloocimene	6.40
Diamyl sulfide	3.70
n-Decane	1.41
n-Decylmercaptan	1.40
Diamylamine	1.14
Methyl nonanoate	1.10
Myrcene	1.00
Cyclododecane	0.88
3-Nonanone	0.50
n-Decylamine	0.50
Diamyl ether	0.33
cis-cis-2-Decalol	0.08
3-Nonanol	0.05
Linalool	0.04
3,3,5-Trimethylheptane	0.007
n-Decanol	0.002
Tetrahydrolinalool	0.000

From Biemann K, Mass Spectrometry: Organic Chemical Applications, McGraw-Hill, New York, 1962, with permission.

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

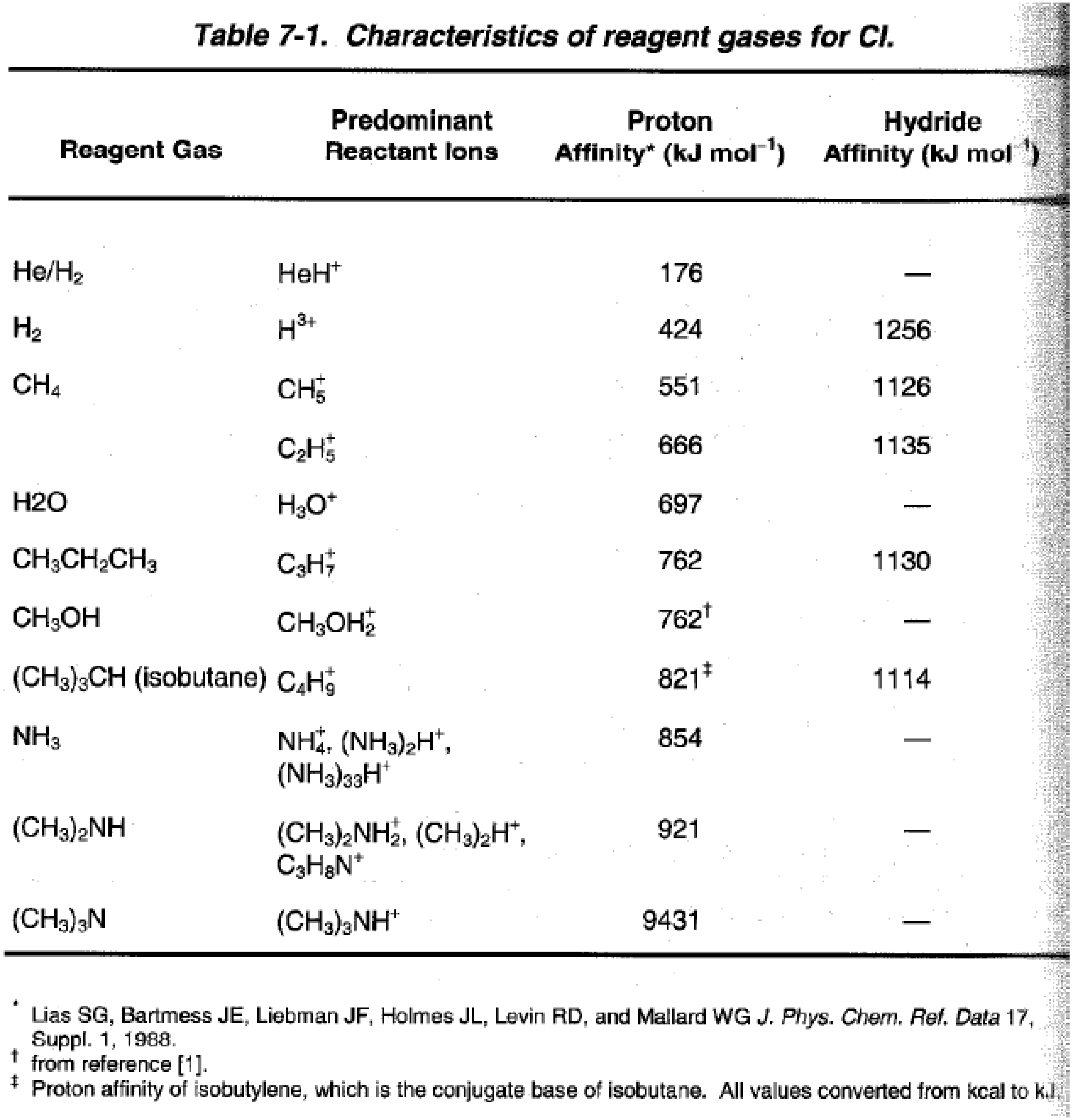


Table 7-1. Characteristics of reagent gases for CI.

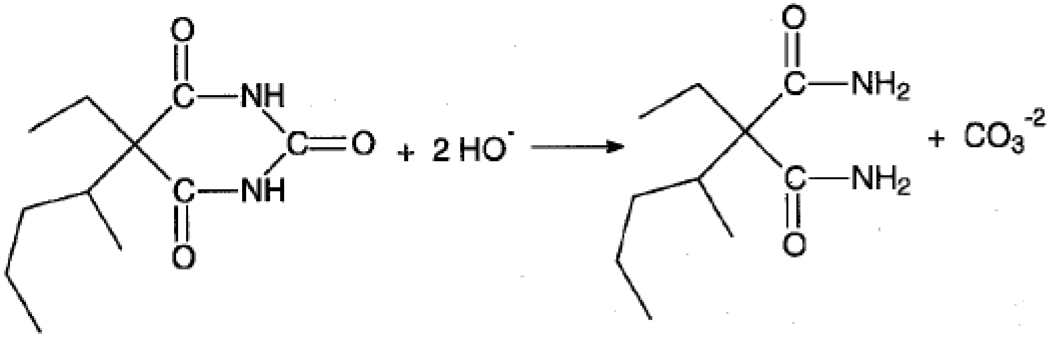
Reagent Gas	Predominant Reactant Ions	Proton Affinity* (kJ mol^{-1})	Hydride Affinity (kJ mol^{-1})
He/H_2	HeH^+	176	—
H_2	H^{3+}	424	1256
CH_4	CH_5^+	551	1126
	$C_2H_5^+$	666	1135
H2O	H_3O^+	697	—
$CH_3CH_2CH_3$	$C_3H_7^+$	762	1130
CH_3OH	$CH_3OH_2^+$	762†	—
$(CH_3)_3CH$ (isobutane)	$C_4H_9^+$	821‡	1114
NH_3	NH_4^+, $(NH_3)_2H^+$, $(NH_3)_{33}H^+$	854	—
$(CH_3)_2NH$	$(CH_3)_2NH_2^+$, $(CH_3)_2H^+$, $C_3H_8N^+$	921	—
$(CH_3)_3N$	$(CH_3)_3NH^+$	9431	—

* Lias SG, Bartmess JE, Liebman JF, Holmes JL, Levin RD, and Mallard WG *J. Phys. Chem. Ref. Data* 17, Suppl. 1, 1988.

† from reference [1].

‡ Proton affinity of isobutylene, which is the conjugate base of isobutane. All values converted from kcal to kJ.

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*



Pentobarbital (III)

Malonamide of Pentobarbital (IV)

Scheme 1-6

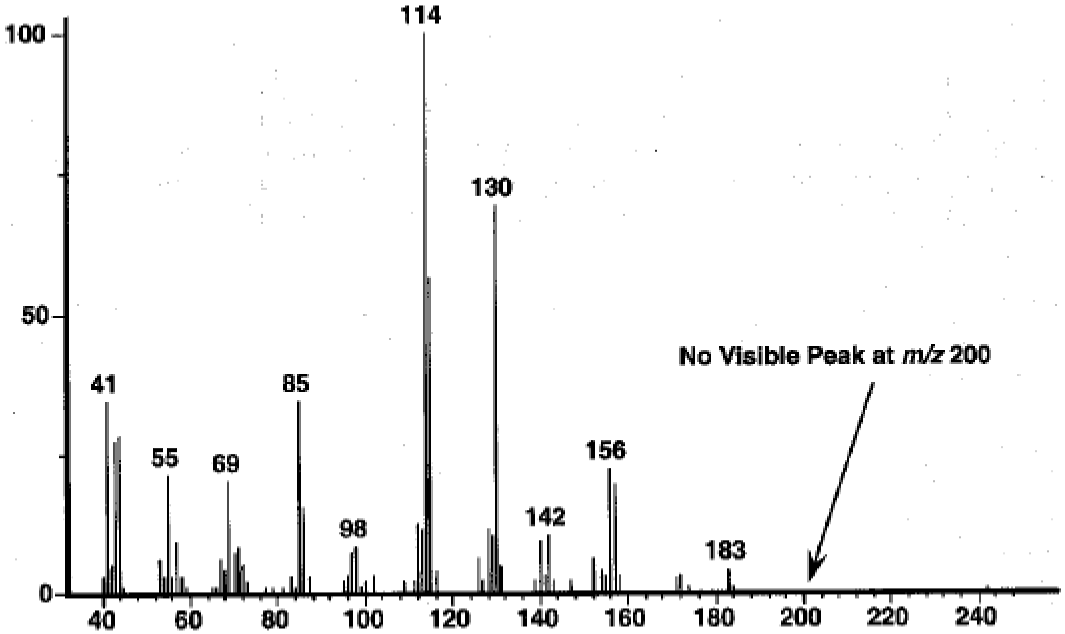


Figure 1-22. EI mass spectrum of the malonamide (IV) of pentobarbital.

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

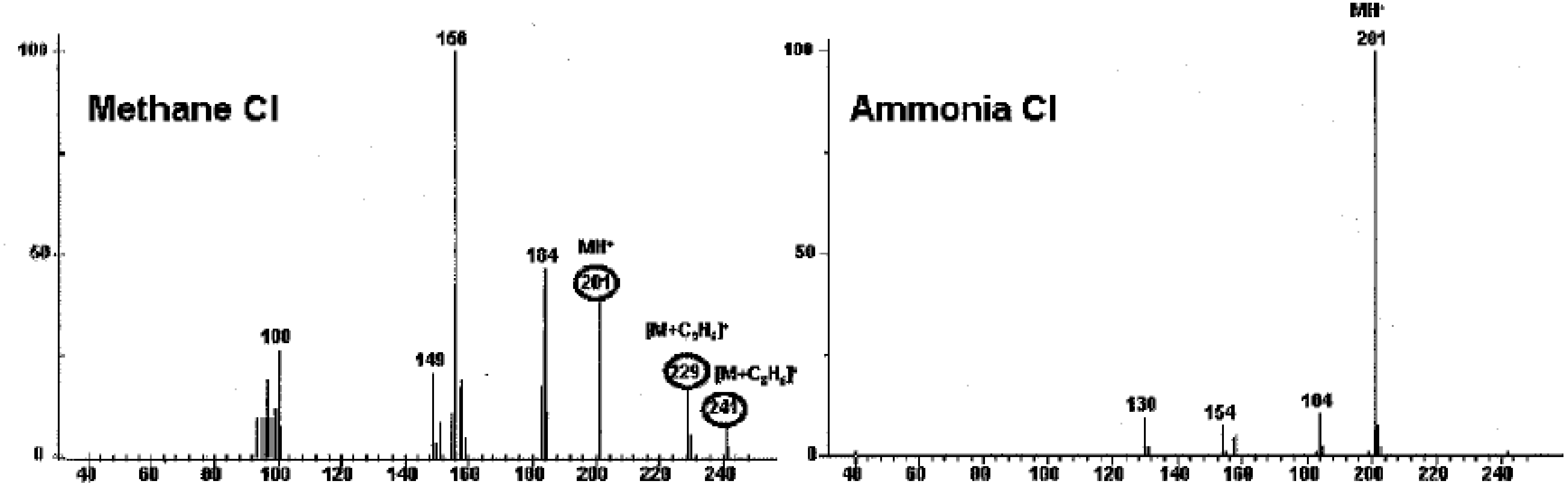
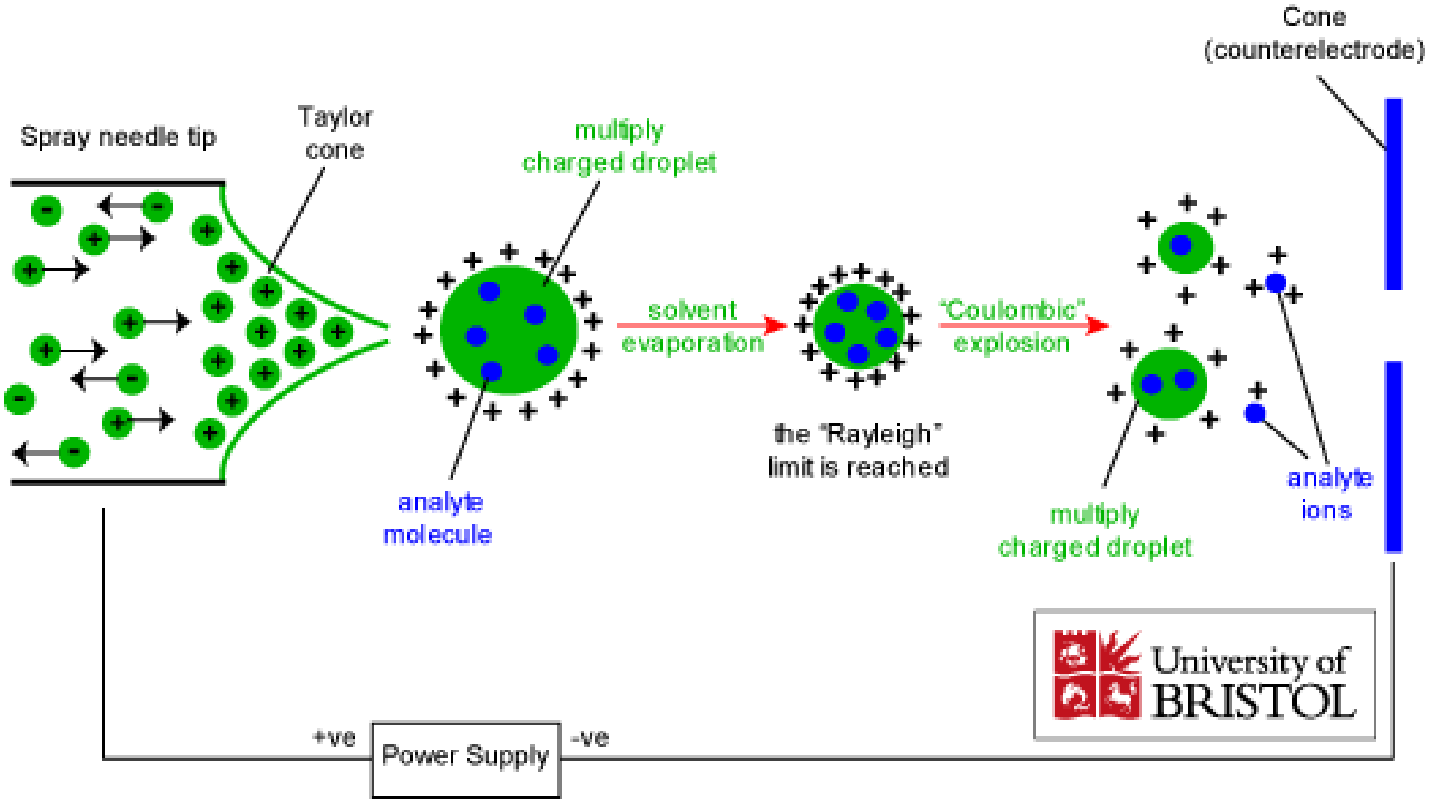


Figure 1-23. CI spectra of the malonamide of pentobarbital using methane (panel A) or ammonia (panel B) as reagent gas.

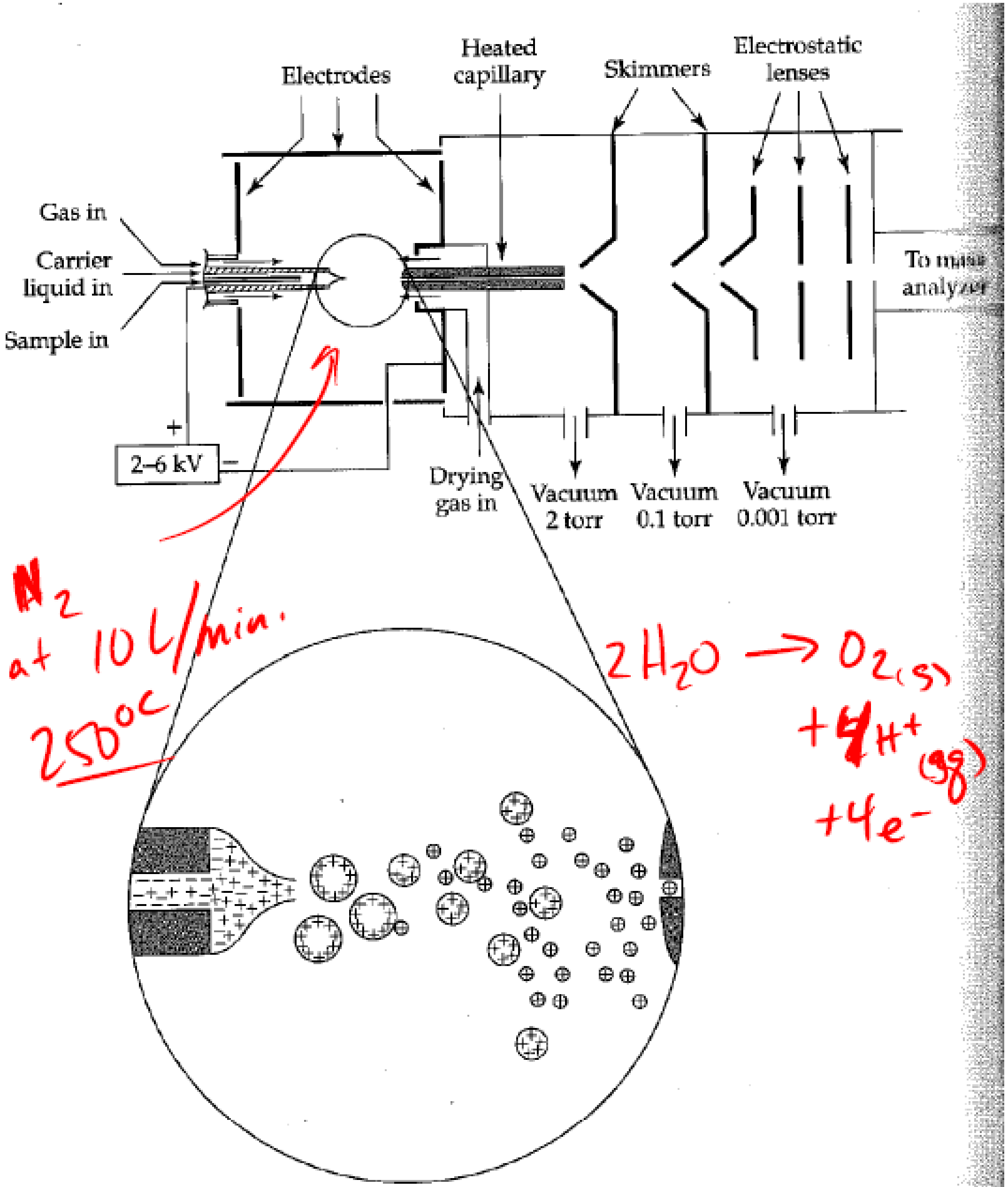
Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*



http://www.chm.bris.ac.uk/ms/images/esi-mechanism.gif

FIGURE 12.17 ▶ Illustration of the major components of an electrospray ionization source.

Shown is the triple-layer needle from which the solvent emerges. The liquid takes the shape of a **Taylor cone** as it comes under the influence of the flow and the electrostatic field pulling on the ions immersed in the liquid. (The force on the ions drags the liquid along while the surface tension tries to pull it into a sphere.) The conditions of flow, ion concentration, solvent, and voltage must be set carefully to achieve a stable condition. Illustrated here is operation in the positive ion mode. Negative ions can also be selected. The net ion charge that flies off with the droplets is replenished by metal ions generated electrochemically from the metal tip. The capillary into which the droplets fly is heated to aid solvent evaporation. Differential pumping through a number of stages brings the atmospheric pressure system into the vacuum level needed for effective mass separation.



N_2 at 10 L/min. 250°C

$2H_2O \rightarrow O_{2(g)} + 4H^+_{(aq)} + 4e^-$

Fig. 12.17 Rubinson and Rubinson *Contemporary Instrumental Analysis*

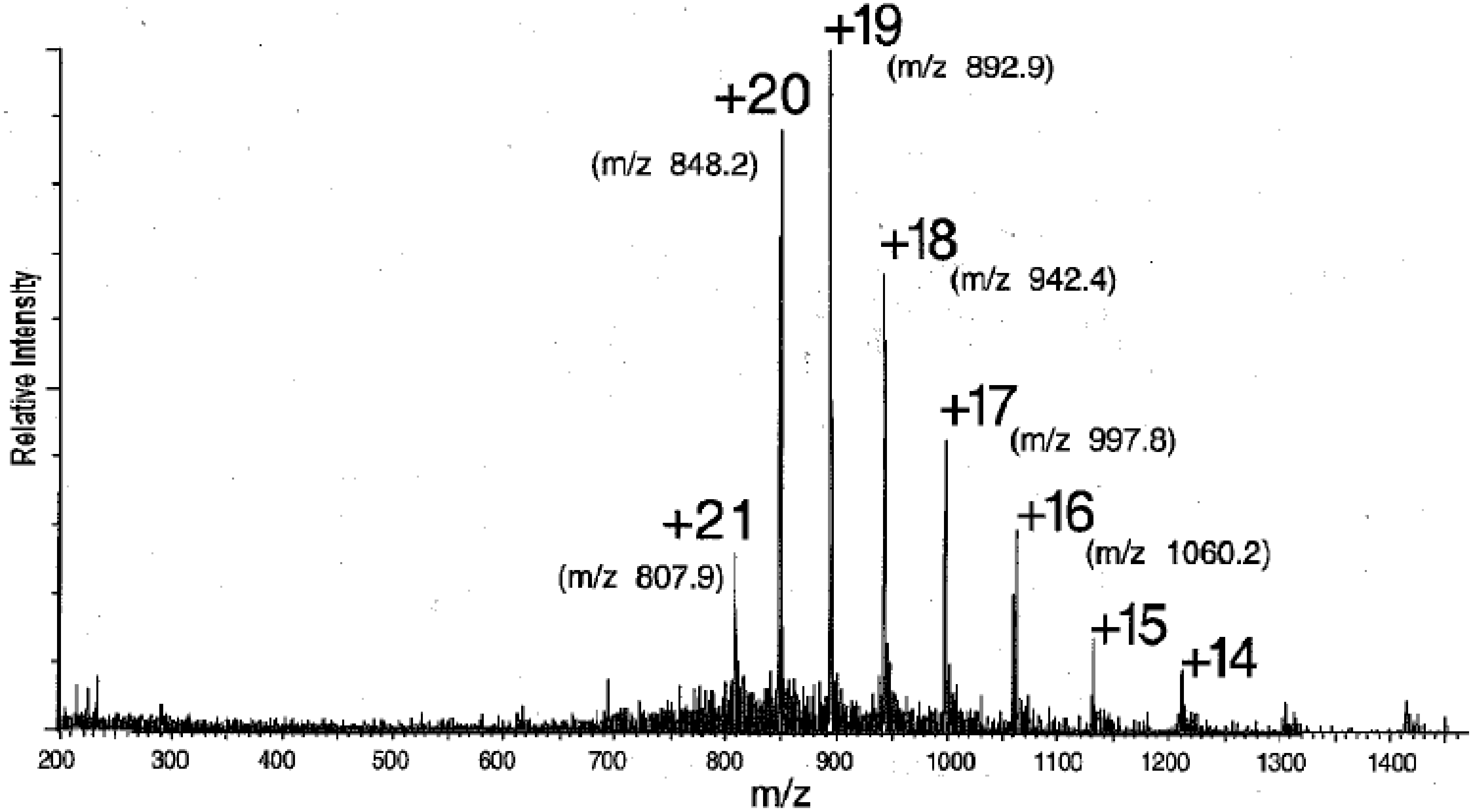


Figure 8-6. ***ESI mass spectrum of 10 pmol horse heart myoglobin (reported average mol. wt = 16,951.5 Da; experimentally determined as 16,951.0 Da) obtained with a low-resolution quadrupole mass spectrometer.*** *Data provided courtesy of James Bradford, Graduate Assistant, in the Macromolecular Structure Facility at Michigan State University, East Lansing, MI.*

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

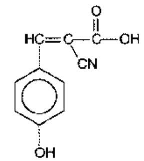
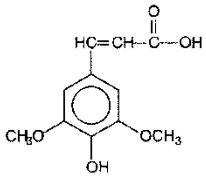
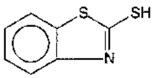
Matrix	Application	Structure	Matrix Solution
α-cyano-4-hydroxy cinnamic acid (α-CHCA)	First choice for small proteins and peptides (<10 kDa)		10 mg mL^{-1} in 50:50:0.3 water/ acetonitrile/TFA
3,5-Dimethoxy-4-hydroxy cinnamic acid (Sinapinic acid)	First choice for heavy proteins (>10 kDa)		10 mg mL^{-1} in 70:30:0.3 water/ acetonitrile/TFA 10 mg mL^{-1} in 50:50:0.3 water/ acetonitrile/TFA if sample contaminated
2-Mercapto-benzothiazole (MBT)	Unusually fine crystals/even distribution on plate Good for peptidoglycans Also good for heavy proteins		10 mg mL^{-1} in 1:1:1 ethanol (EtOH)/ tetrahydrofuran (THF)/water

Figure 9-1. ***Structures and properties of representative compounds used as MALDI matrices.***

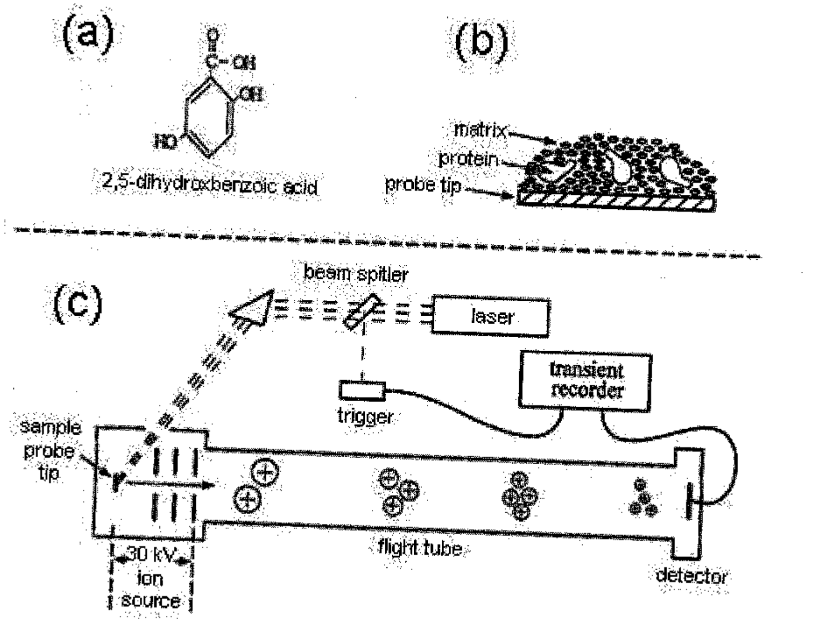


Figure 9-2. ***Schematic diagram of a MALDI TOF instrument (c). A solid deposit of analyte/matrix mixture is conceptually represented on a sample plate (b). Laser radiation is focused onto the sample spot on the plate to effect ionization.***

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

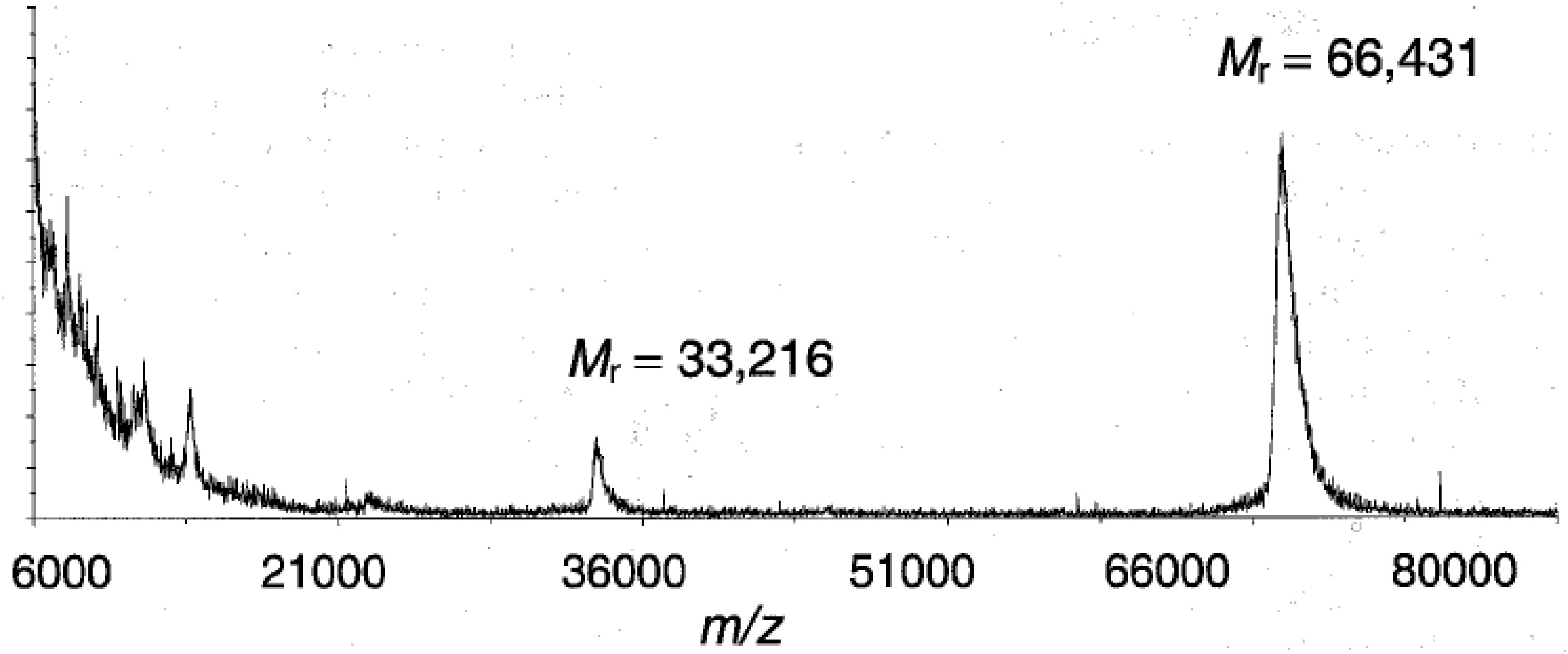


Figure 9-5. MALDI TOF mass spectrum of bovine serum albumin from a matrix of sinapinic acid. *Data obtained by Dr. Robin Hood, Visiting Scientist in the Department of Biochemistry, Michigan State University, East Lansing, MI.*

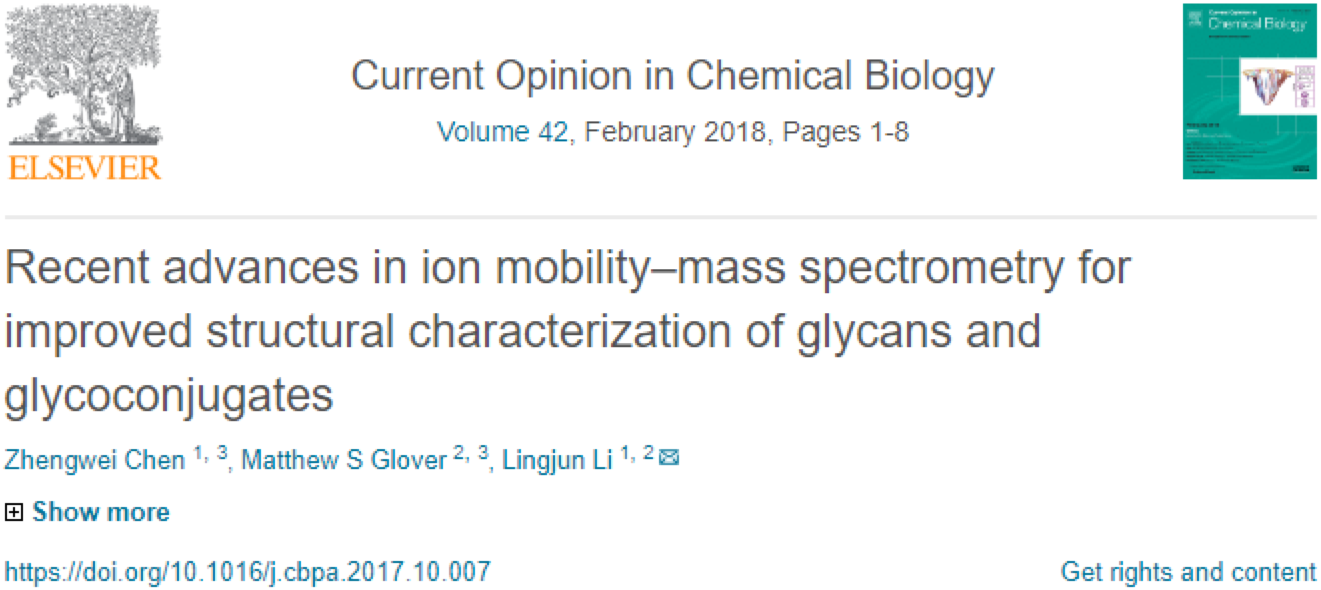
Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

https://www.youtube.com/watch?v=sAJ9FiuxUhA

Waters MALDI MS

http://www.waters.com/waters/en_US/MALDI-SYNAPT-G2-Si-Mass-Spectrometry/nav.htm?cid=134740700

Agilent IM-QTOF
https://www.youtube.com/watch?v=UuV1xtiI7Qw



Current Opinion in Chemical Biology
Volume 42, February 2018, Pages 1-8

Recent advances in ion mobility–mass spectrometry for improved structural characterization of glycans and glycoconjugates

Zhengwei Chen [1, 3], Matthew S Glover [2, 3], Lingjun Li [1, 2] ✉

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https://doi.org/10.1016/j.cbpa.2017.10.007

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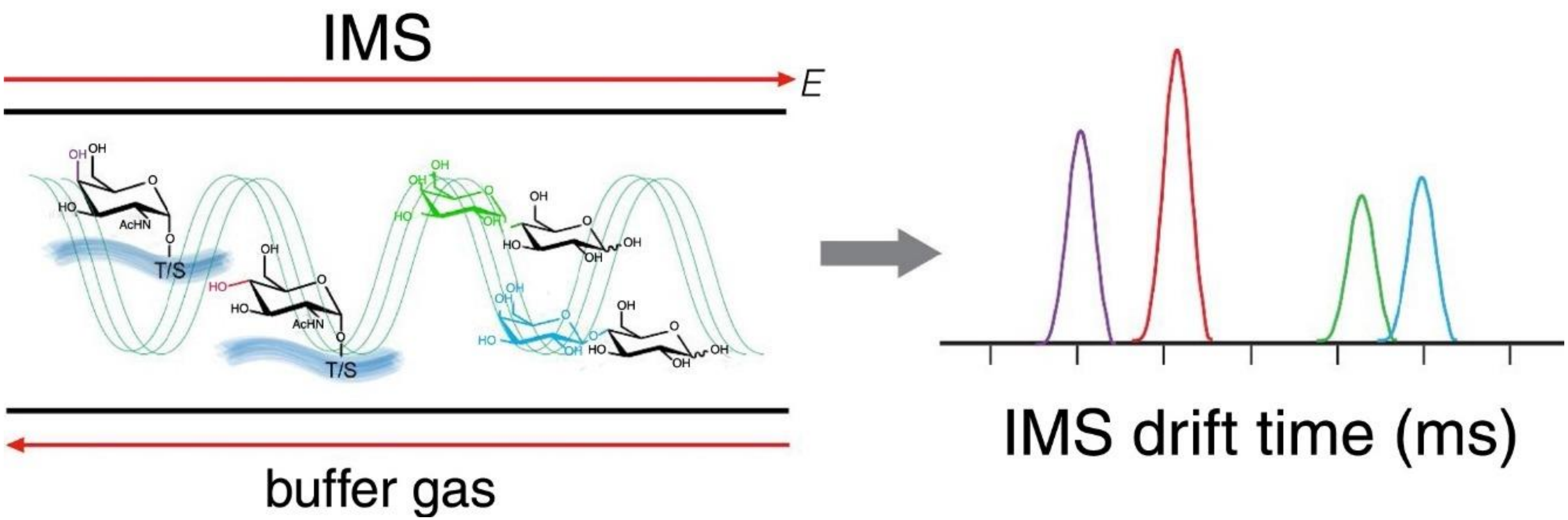


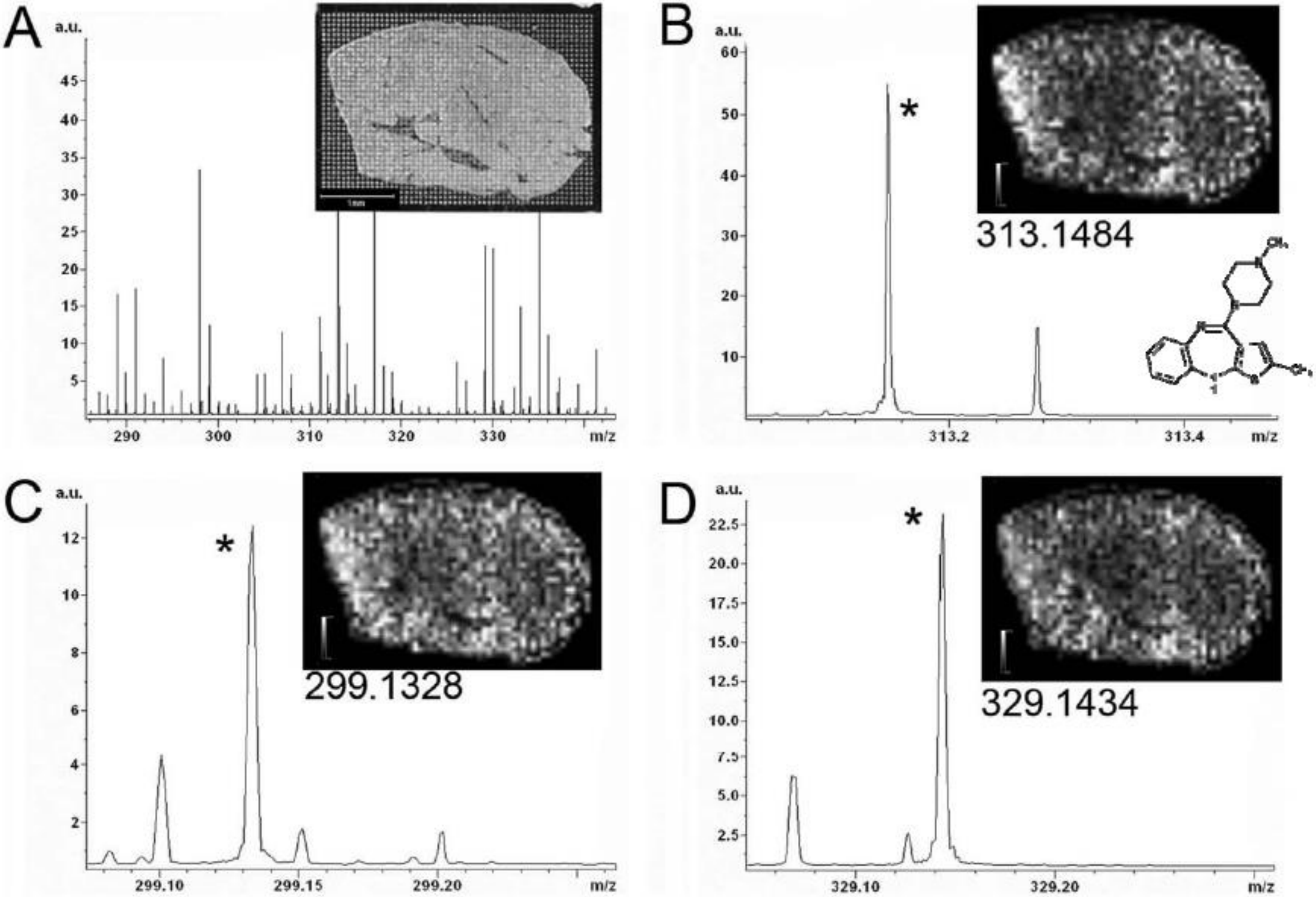


Figure 1. FTICR images from a liver of a rat dosed with 8 mg/kg olanzapine (2 h postdose). (A) Average of all spectra collected from matrix spots on the tissue (inset image). The *m/z* region of the average spectrum in the regions of protonated molecule of (B) olanzapine, (C) desmethyl metabolite, and (D) hydroxymethyl metabolite. Ion images of each marked peak is inset to each spectrum.

Caprioli, R. et al., *Analytical Chemistry, Vol. 80, No. 14, July 15, 2008*

Part III – Mass Analyzers

	Analyzer Type			
Figure of Merit	**Magnetic Sector**	**Quadrupole**	**TOF**	**ICR**
m/z Range (Da/charge)				
Mass Resolution (Da)				
Resolving Power				
Mass Accuracy (ppm)				
Linearity (Orders of Magnitude)				
Scan Speed				
Acquisition				
Chief Attribute				
Cost ($k)				
Typical Application				

Types of Mass Analyzers – Sectors (Magnetic/Electrostatic)

Initial Ion Acceleration

$$KE = zeV = \frac{1}{2}mv^2$$

Electrostatic

Magnetic

ET

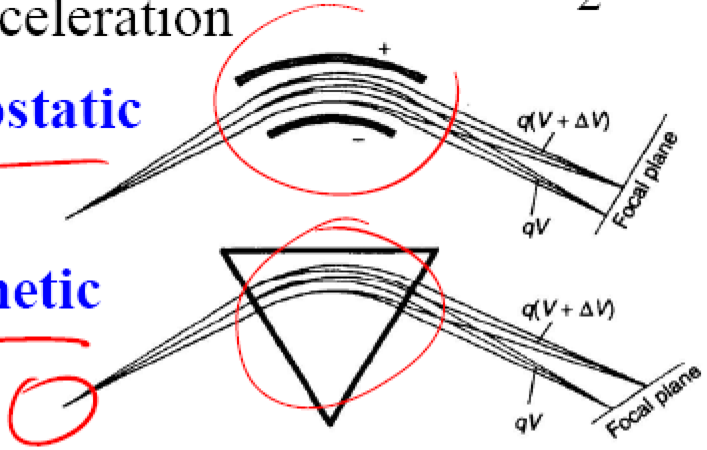


Figure 2.43
Energy dispersion in an electric sector (*top*) and in a magnetic sector (*bottom*)

Electrostatic

$$\frac{m}{z} = \frac{reE}{v^2}$$

Magnetic

$$\frac{m}{z} = \frac{B^2r^2e}{2V}$$

Double Focusing

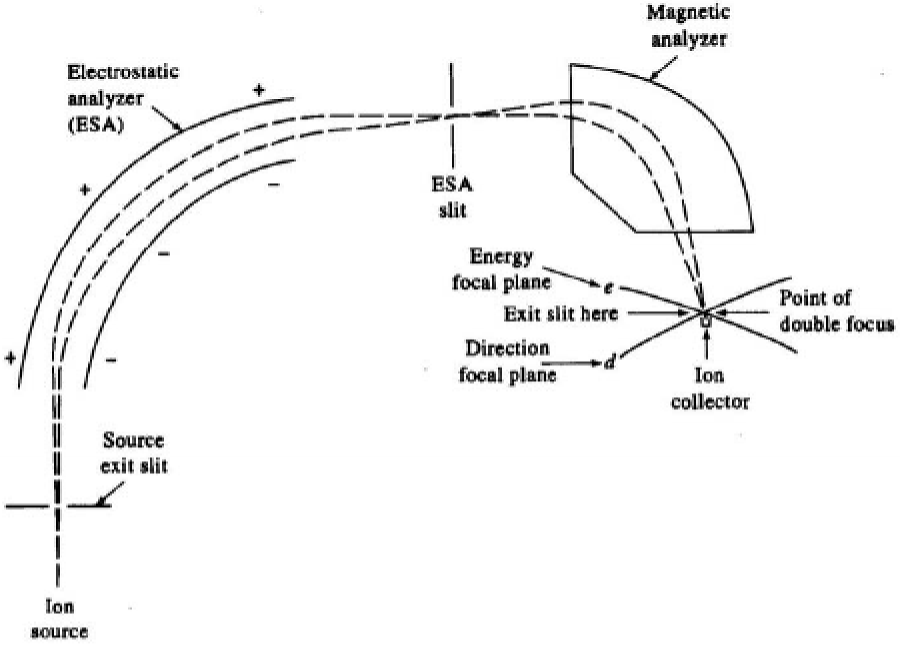


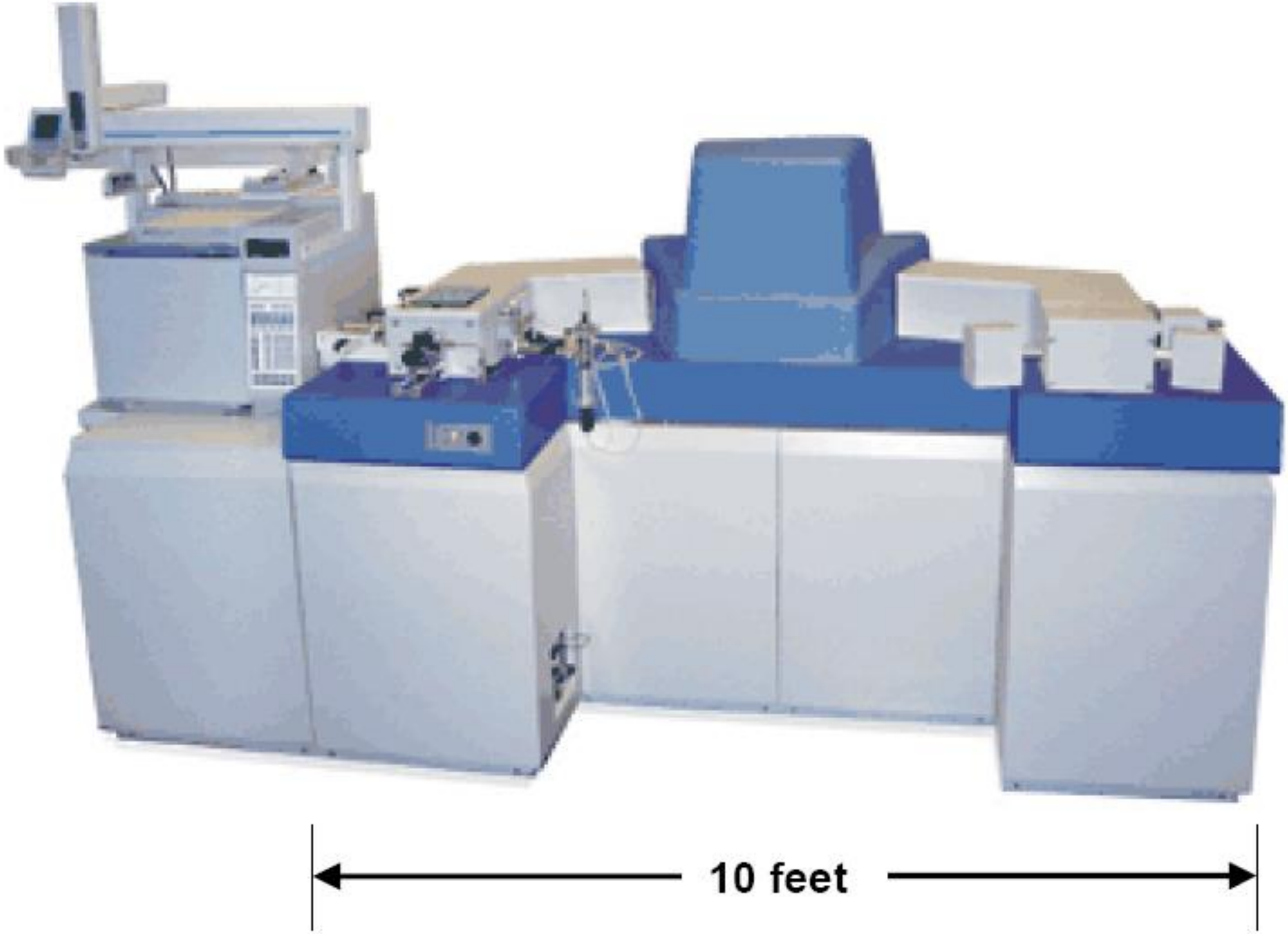
Figure 20-13 Nier-Johnson design of a double-focusing mass spectrometer.

The m/z spectrum is obtained by changing the magnitude of B or E

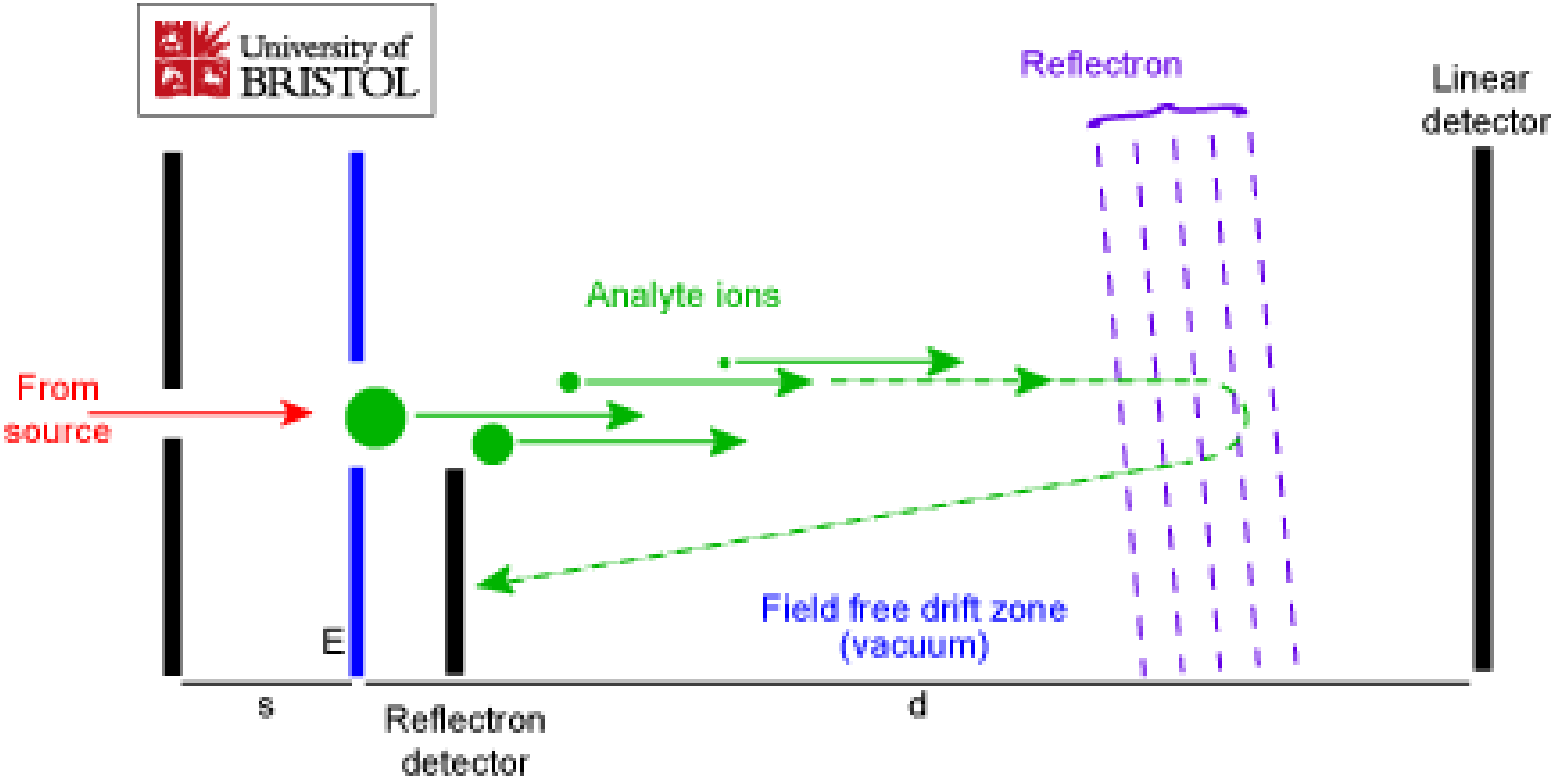
Hoffman and Stroobant, *Mass Spectrometry*

Skoog, Holler, and Nieman, *Instrumental Analaysis*

Commercial Double-Focusing Mass Spectrometer



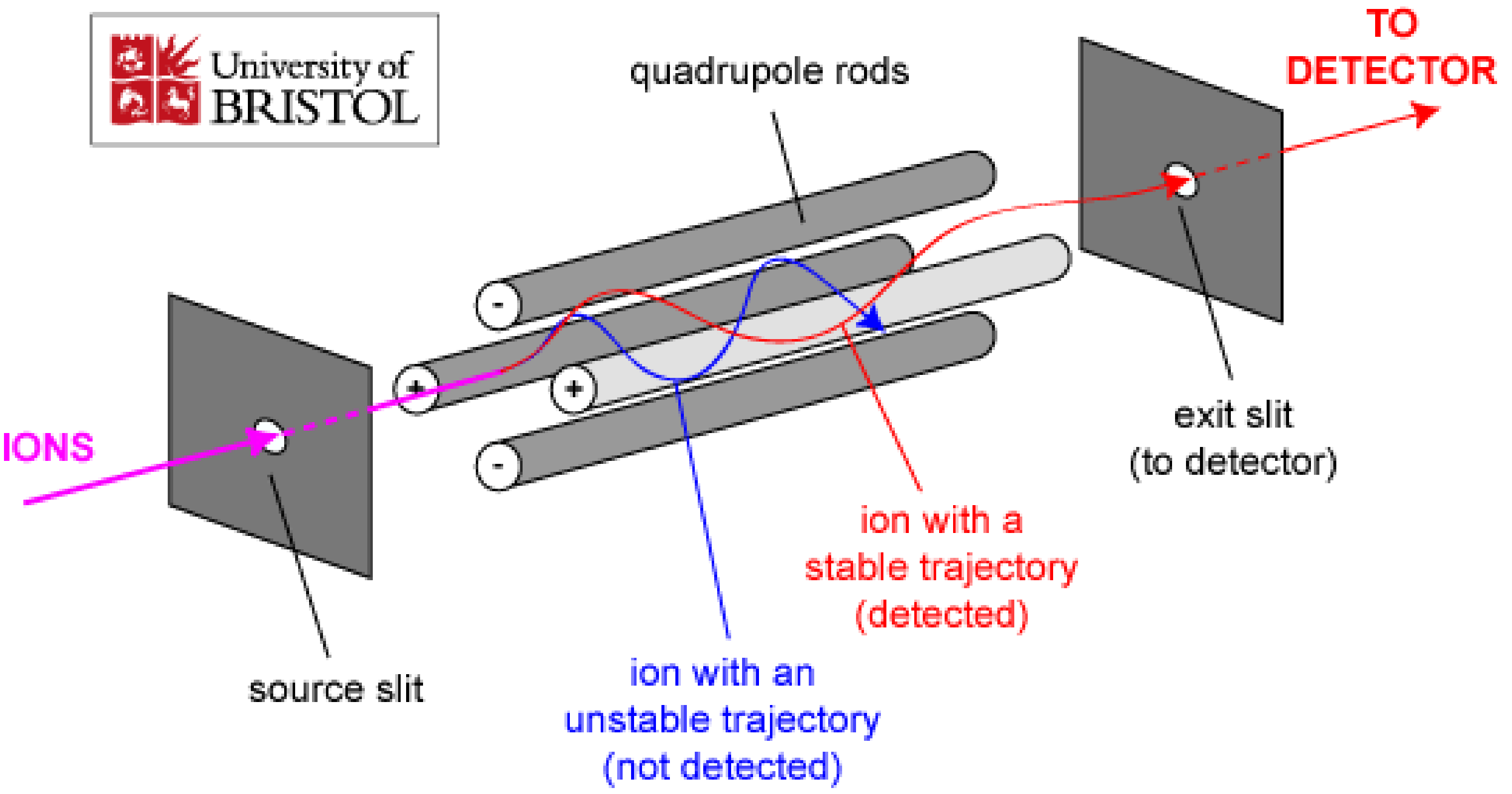
Types of Mass Analyzers – Time-of-Flight (TOF)



http://www.chm.bris.ac.uk/ms/theory/tof-massspec.html

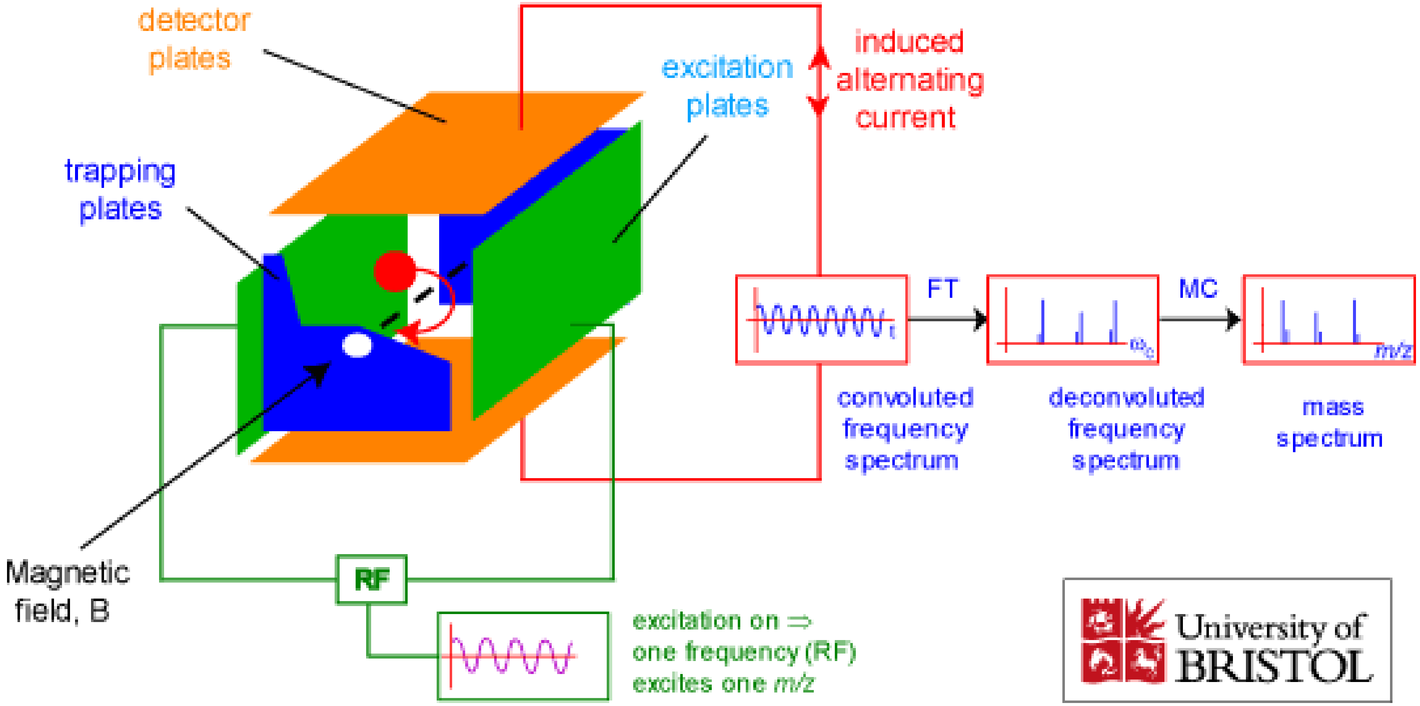
https://www.youtube.com/watch?v=BFuZaIi-zDk

Types of Mass Analyzers – Quadrupole (Single Quad)



http://www.chm.bris.ac.uk/ms/images/quad-schematic2.gif
https://www.youtube.com/watch?v=IowMQnI6Rxc

Types of Mass Analyzers – Fourier Transform Ion Cyclotron Resonance (FTICR)



http://www.chm.bris.ac.uk/ms/images/fticr-schematic.gif

http://youtu.be/a5aLlm9q-Xc

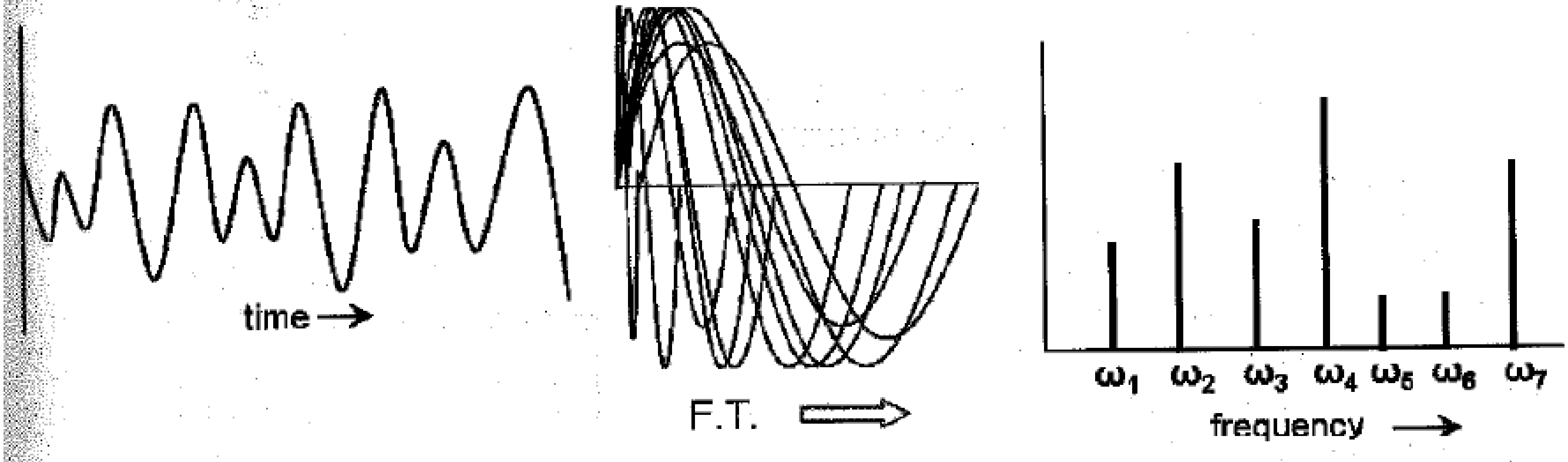


Figure 2-44. **Concept of Fourier transform (FT) in converting a complex signal from the time domain to the frequency domain.**

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

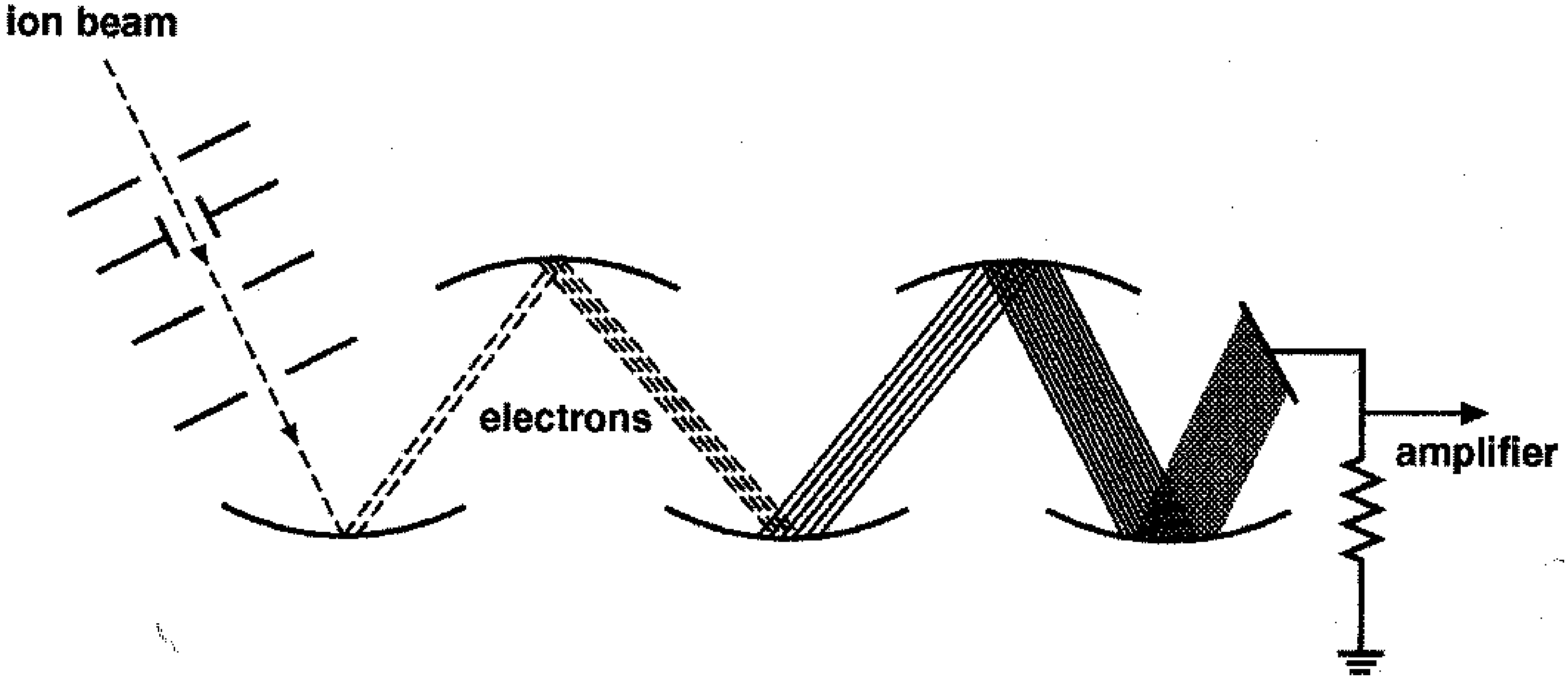


Figure 2-56. Conceptual diagram of a discrete-dynode electron multiplier.
From McFadden, WH, Techniques of GC/MS, Wiley-Interscience, New York, 1973, with permission.

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

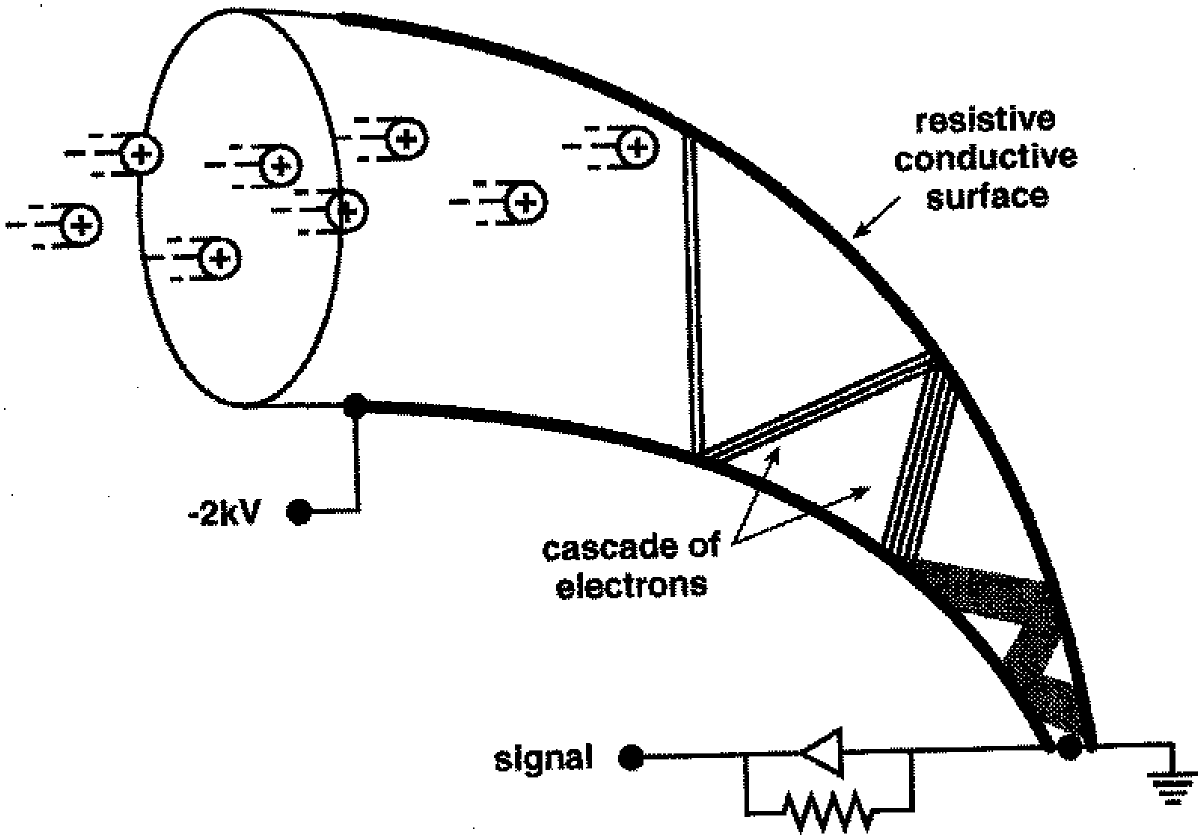


Figure 2-57. ***Conceptual diagram of a continuous-dynode electron multiplier; the field gradient along the conductive internal surface of the cornucopia attracts the cascading electrons toward the preamplifier.***

Watson, J. T.; Sparkman, O. D. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation, 4th ed.; John Wiley and Sons, 2007.*

Part IV – Tandem Mass Spectrometry

The Reference

Yost, R. A. and C. G. Enke (1979). "Triple quadrupole mass spectrometry for direct mixture analysis and structure elucidation." Anal. Chem. 51(12): 1251A-1252A, 1256A, 1258A, 1260A, 1262A.

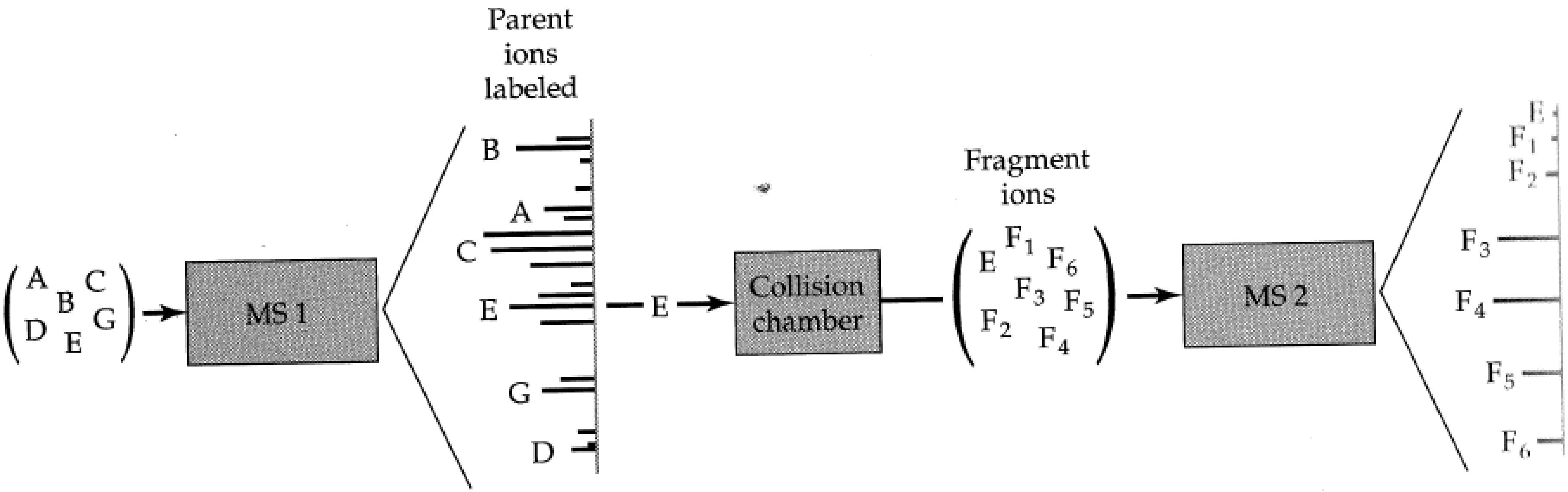


FIGURE 12.7 ▲

Illustration of the operation of a MS/MS system.

The sample mixture of molecules with molecular masses B > A > C > E > G > D can be separated, but with the parent ions and their fragments overlapping. The first mass separator is set to select a single parent ion, which is passed into the collision chamber where it undergoes fragmentation through collisions with a gas such as argon or helium. For example, suppose E is selected. The surviving parent ion E and ion fragments F_1–F_6 pass into a second mass separator, which produces a mass spectrum of E and its fragmentation products.

Rubinson, K. A.; Rubinson, J. F. *Contemporary Instrumental Analysis*; Prentice Hall: Upper Saddle River, 2000.

Triple Quadrupole Tandem Mass Spectrometer

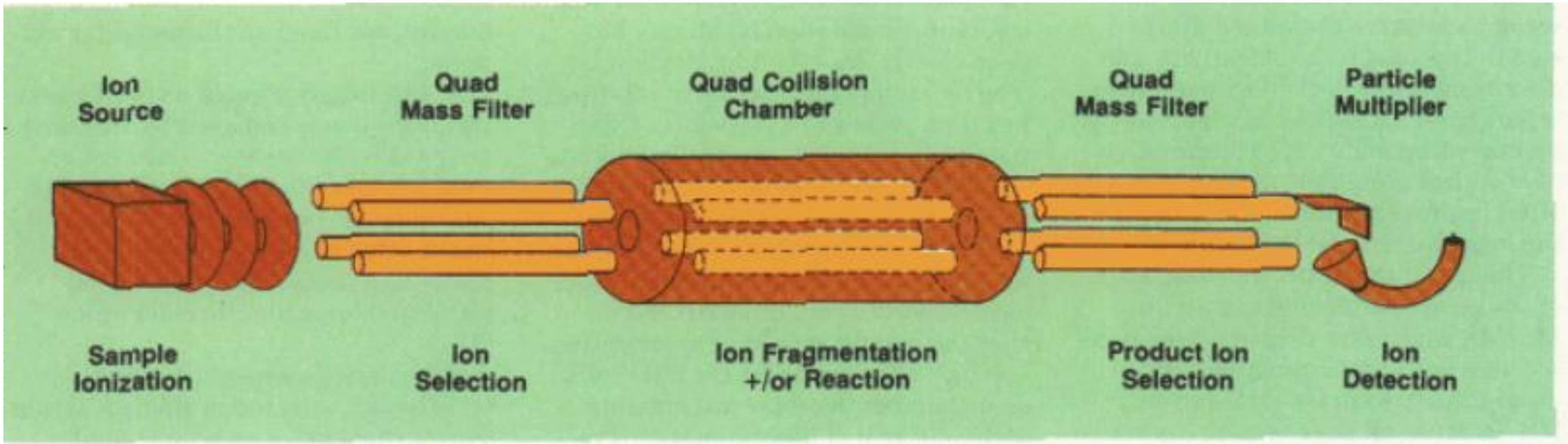


Figure 1. Conceptual diagram of the triple quadrupole mass spectrometer showing each component and its function.

- Particularly simple and efficient approach to selecting ion fragments.
- Fragmentation caused by Collision-induced dissociation (CID).

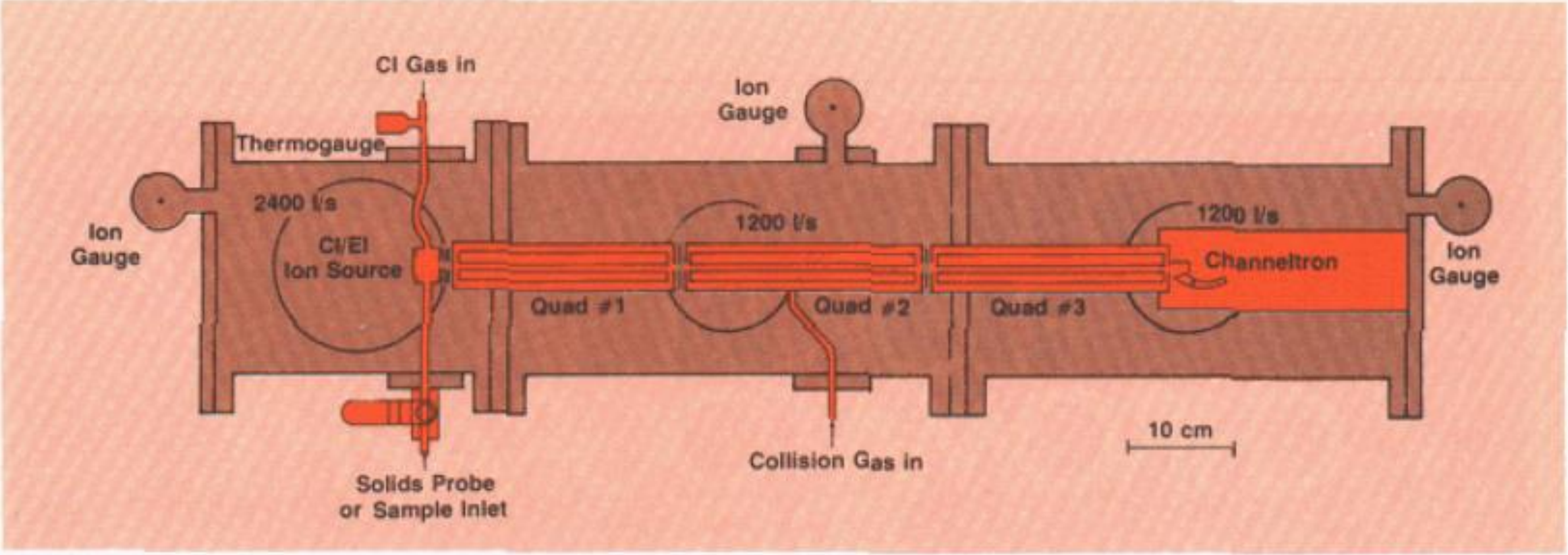


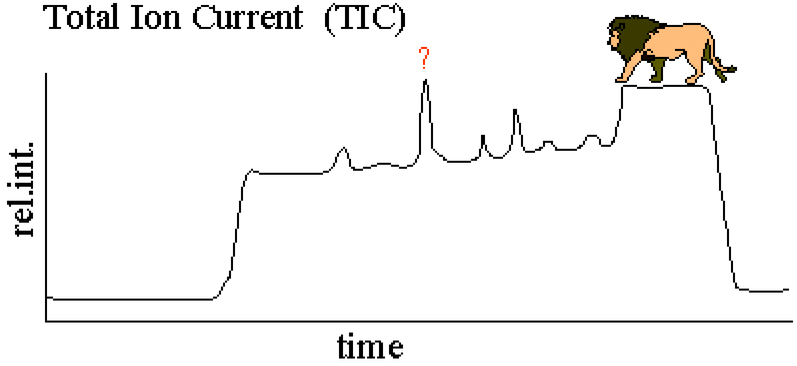
Figure 5. Scale drawing (top view) of triple quadrupole mass spectrometer

A scale drawing of the triple quadrupole spectrometer constructed at Michigan State University.

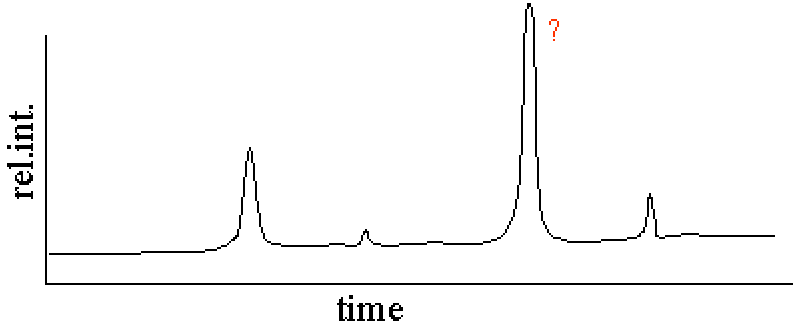
Modes of Operation

1. Normal Mass Spectrometry
   - 2nd and 3rd quadrupoles in RF-only mode
2. Scan for fragments of parent ion
   - 1st quadrupole select specific ion while 3rd quadrupole scans for fragments
3. Fragment Ion Measurement
   - 1st quadrupole select specific ion while 3rd quadrupole measures a specific fragment ion
4. Fragment Reaction
5. Specific Neutral Mass Loss
   - Scanning both mass filters with a fixed difference in mass (example following)

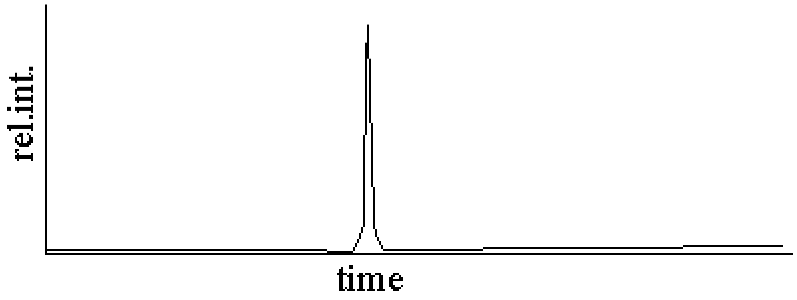
Total Ion Current (TIC)



Selected Ion Monitoring (SIM)



Selected Reaction Monitoring (SRM)

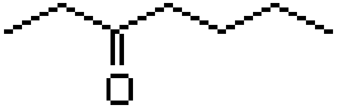


http://www.ionsource.com/tutorial/msquan/intro.htm; accessed 10/18/2010

Mixture Analysis

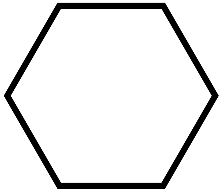
Example: solution containing 3-heptanone, *n*-heptanal, *n*-octane, cyclohexane, and 2-pentanone all in equal concentrations.

114 g/mol



114 g/mol

114 g/mol



84 g/mol

Mixture Spectrum after fragmentation

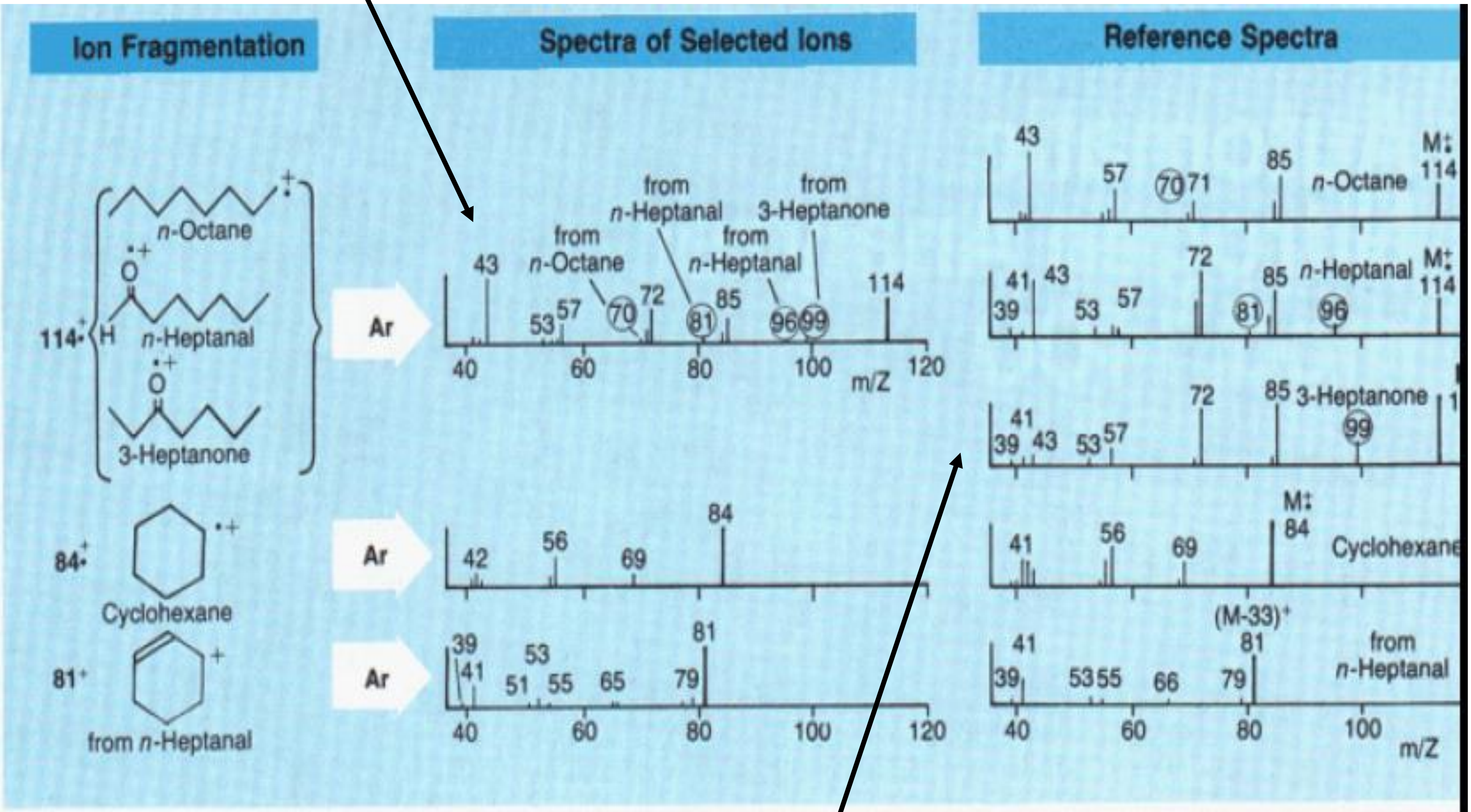


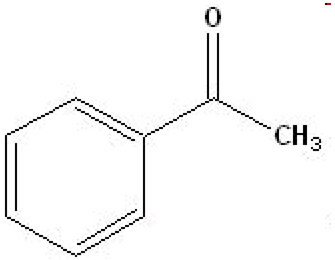
Figure 3. Comparison of CID spectra of selected ions in the EI spectrum of a five component mixture with reference CID spectra from pure components

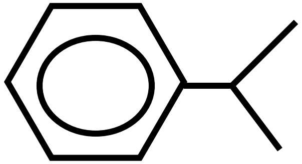
Fragmentation Reference Spectra

Structure Elucidation

Example:

Same molar weight but they have a difference fragmentation spectra thus we can tell them apart using triple quadrupole mass spectroscopy.





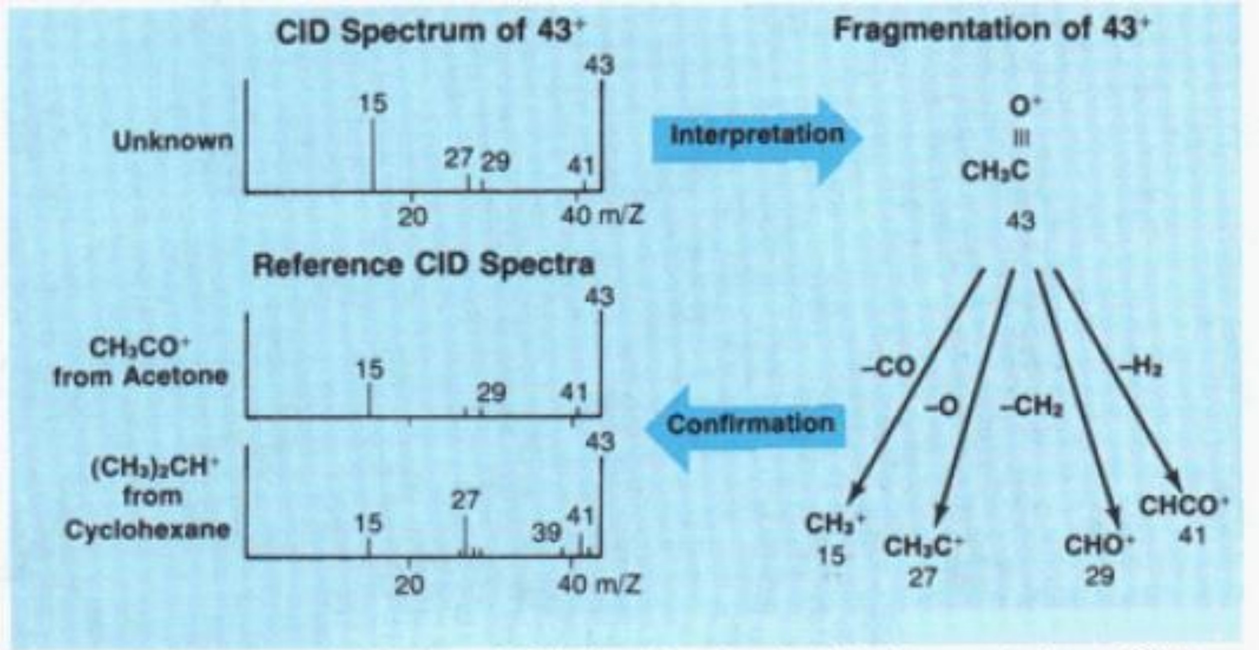
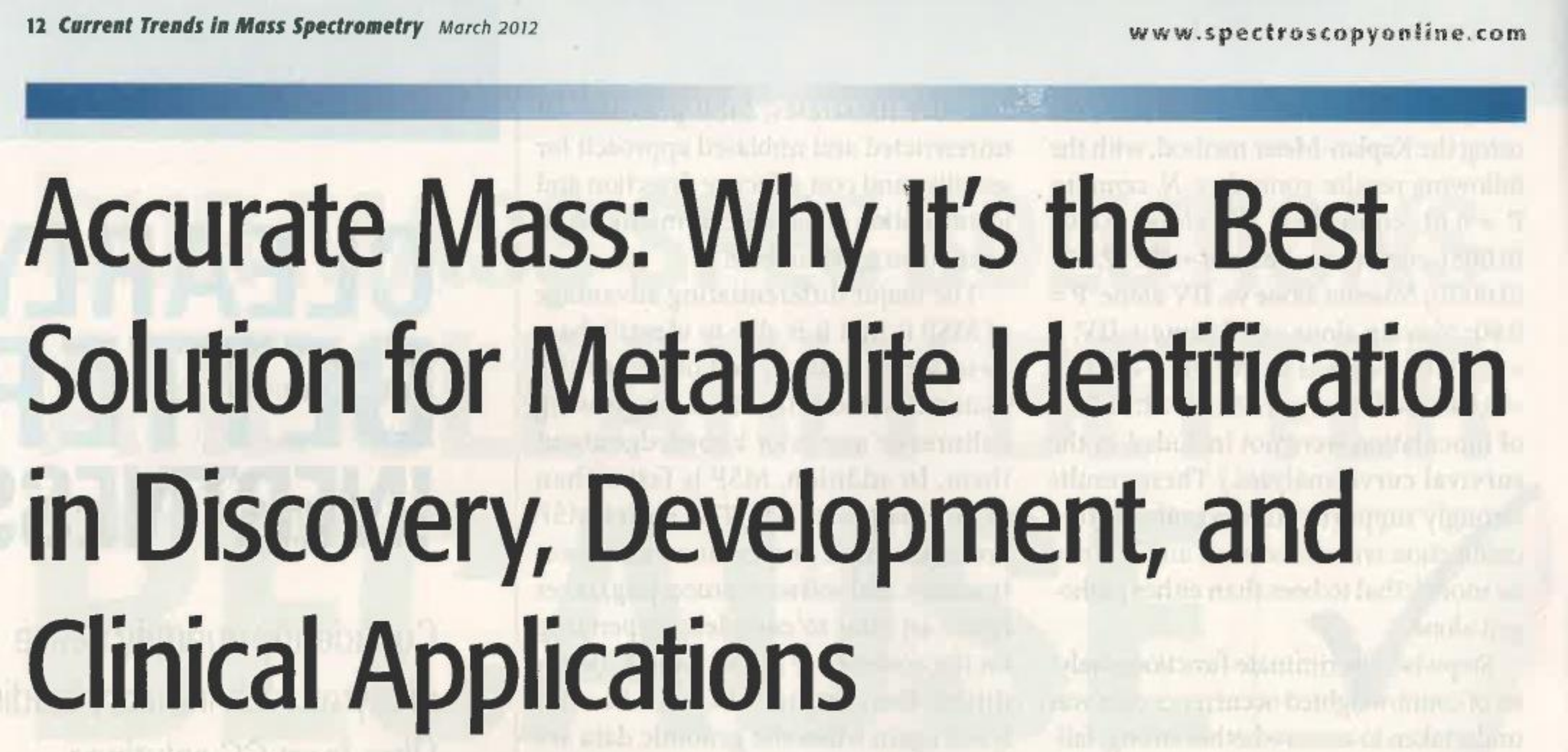


Figure 4. Structure elucidation of 43^+ functional moiety by interpretation of CID spectrum and comparison with reference CID spectra

Part V – Applications

Accurate Mass



12 *Current Trends in Mass Spectrometry* March 2012 www.spectroscopyonline.com

Accurate Mass: Why It's the Best Solution for Metabolite Identification in Discovery, Development, and Clinical Applications

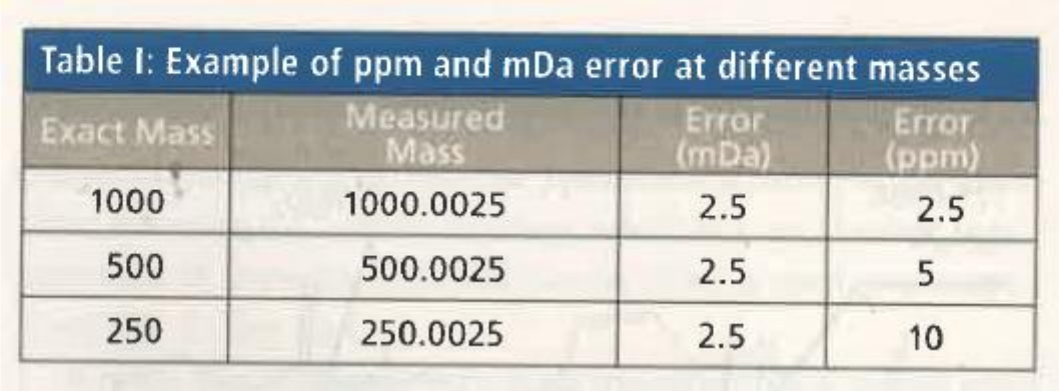


Table I: Example of ppm and mDa error at different masses

Exact Mass	Measured Mass	Error (mDa)	Error (ppm)
1000	1000.0025	2.5	2.5
500	500.0025	2.5	5
250	250.0025	2.5	10

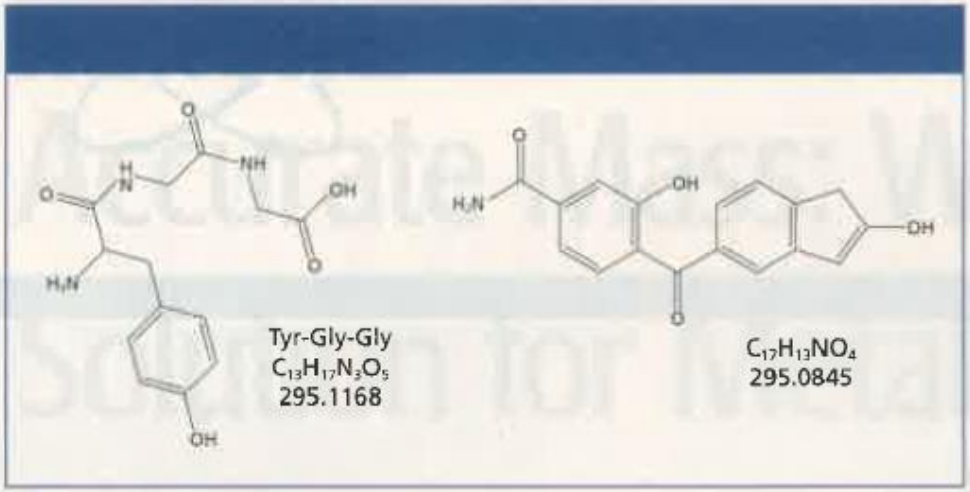


Figure 1: Example of a tripeptide and a possible xenobiotic with similar nominal mass.

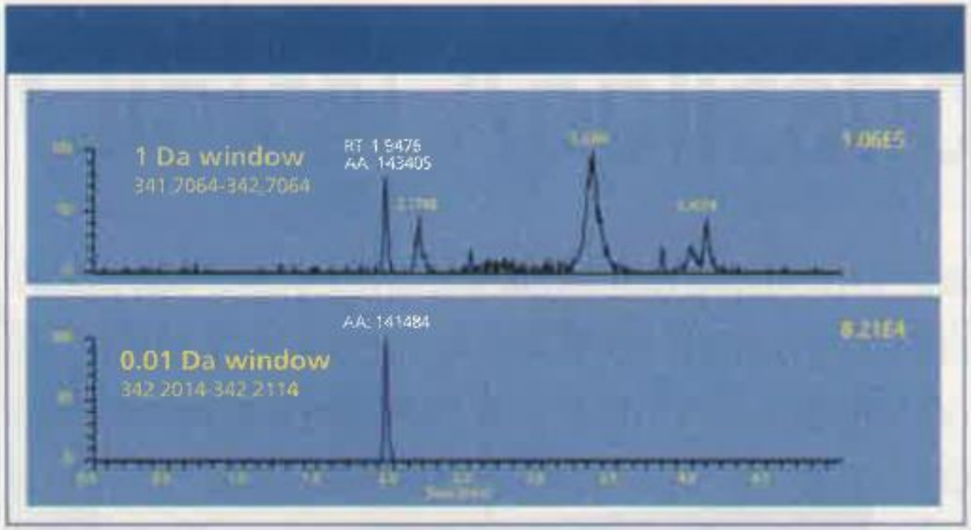


Figure 2: Two extracted ion chromatograms from the same data file. The top trace is generated using a 1-Da wide window. The bottom trace is from using a 10-mDa wide window.

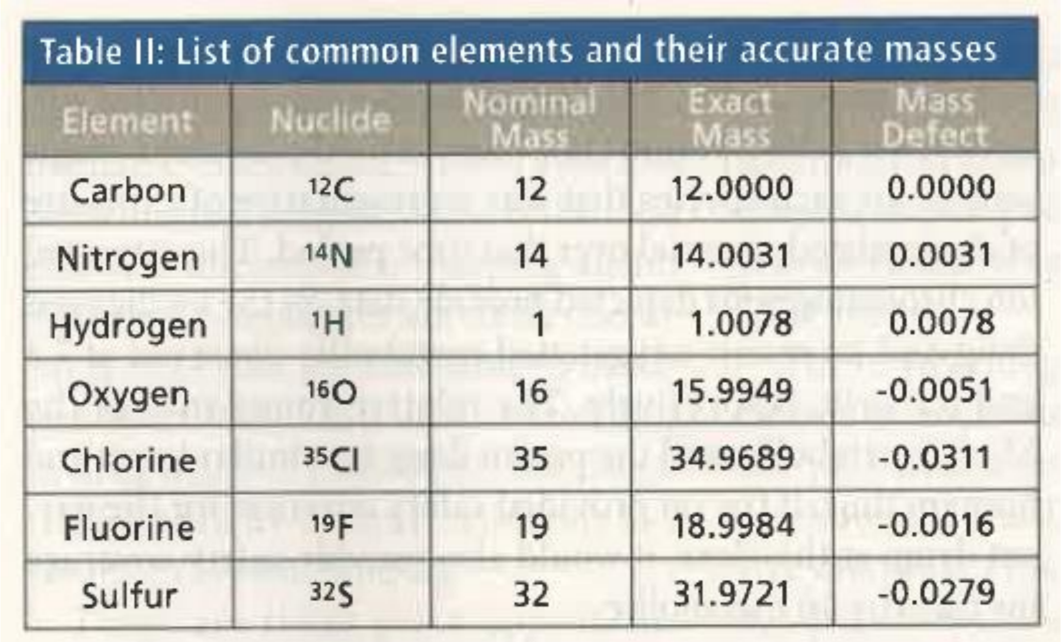
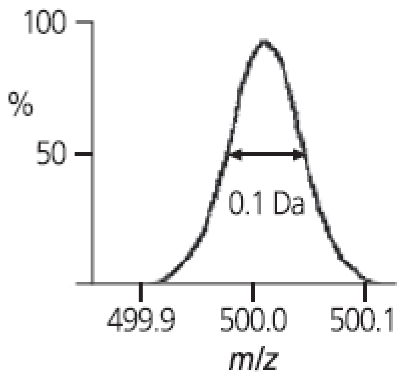


Table II: List of common elements and their accurate masses

Element	Nuclide	Nominal Mass	Exact Mass	Mass Defect
Carbon	^{12}C	12	12.0000	0.0000
Nitrogen	^{14}N	14	14.0031	0.0031
Hydrogen	^{1}H	1	1.0078	0.0078
Oxygen	^{16}O	16	15.9949	-0.0051
Chlorine	^{35}Cl	35	34.9689	-0.0311
Fluorine	^{19}F	19	18.9984	-0.0016
Sulfur	^{32}S	32	31.9721	-0.0279

http://www.chemcalc.org/

Figure 1: Mass accuracy determination and the FWHM method for determining resolution for a mass spectrometer measured at a given ion.



True mass = 400.0000

Measured mass = 400.0020

Difference = 0.0020 or 2 mmu

Error = $\frac{0.002}{400} \times 10^6 = 5$ ppm

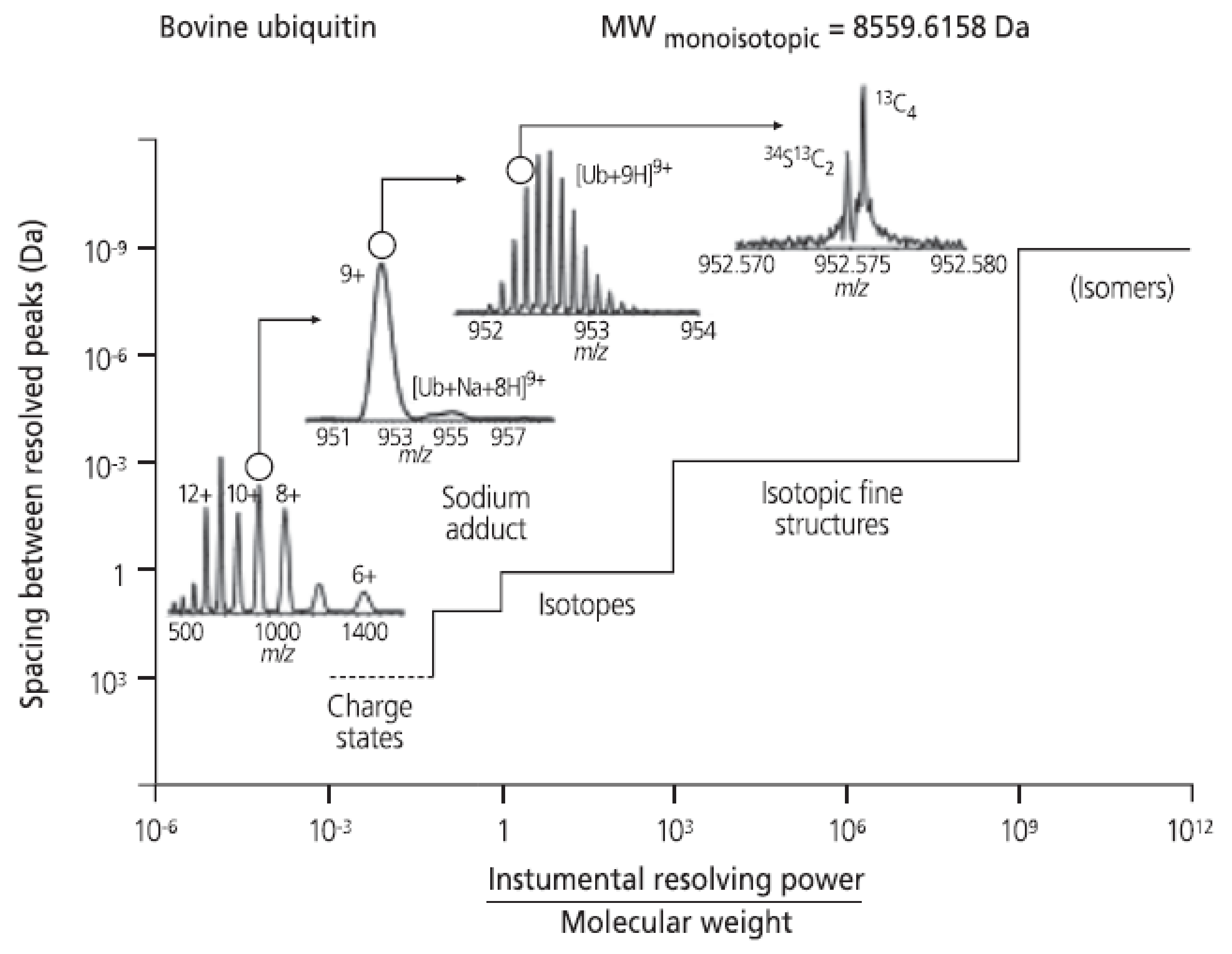
Mass = 500

Peak width (@ 50%) = 0.1

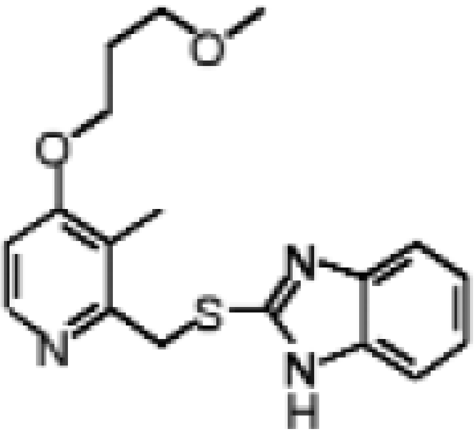
Resolution (FWHM) $\frac{500}{0.1} = 5000$

Balogh, M. LC-GC Europe, 17(3), 152–159 (2004)

Figure 2: The need for informational spacing to increase (instrumental resolving power) between ion peaks and associated isotopes as informational demand increases. (Reprinted with permission from reference 7.)

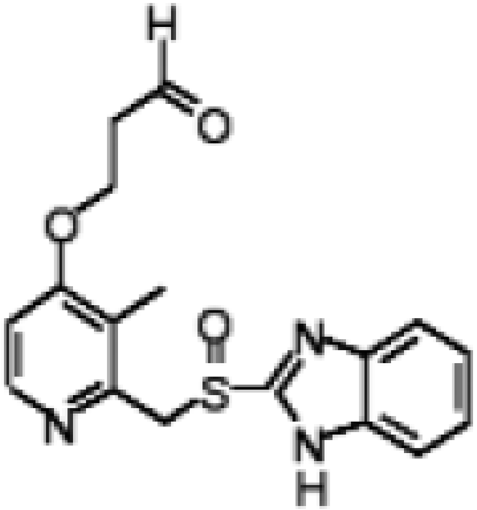


Balogh, M. LC-GC Europe, 17(3), 152–159 (2004)



Sulphide

m/z 344.1433 (2.3 ppm)



Aldehyde

m/z 344.1069 (1.5 ppm)

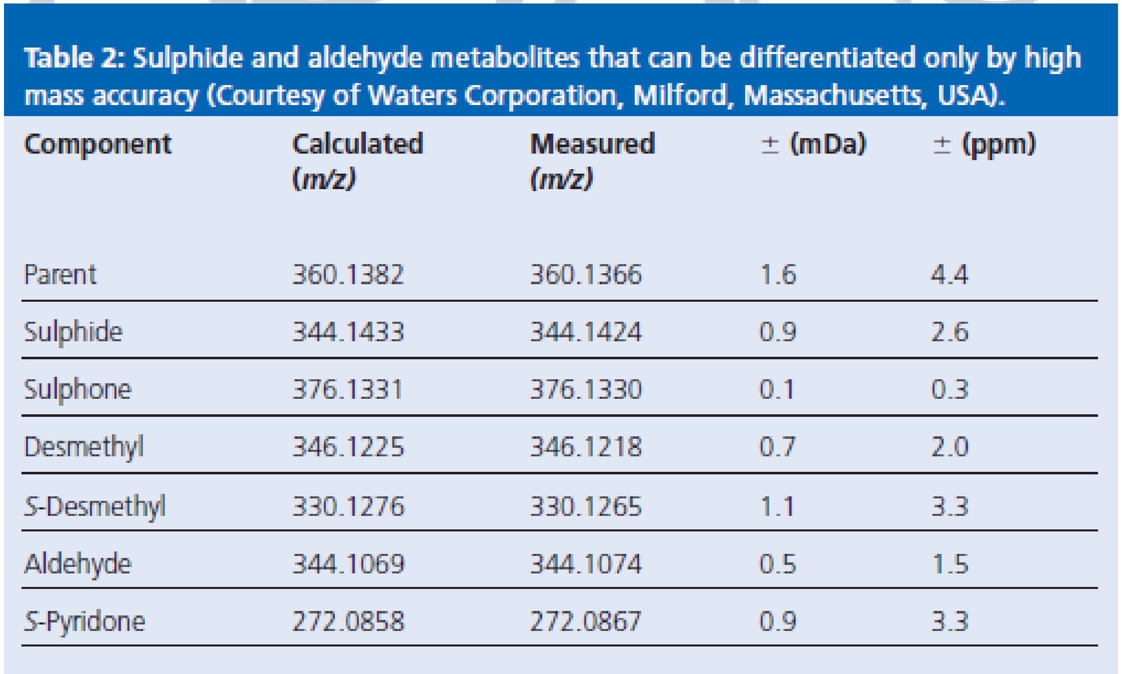
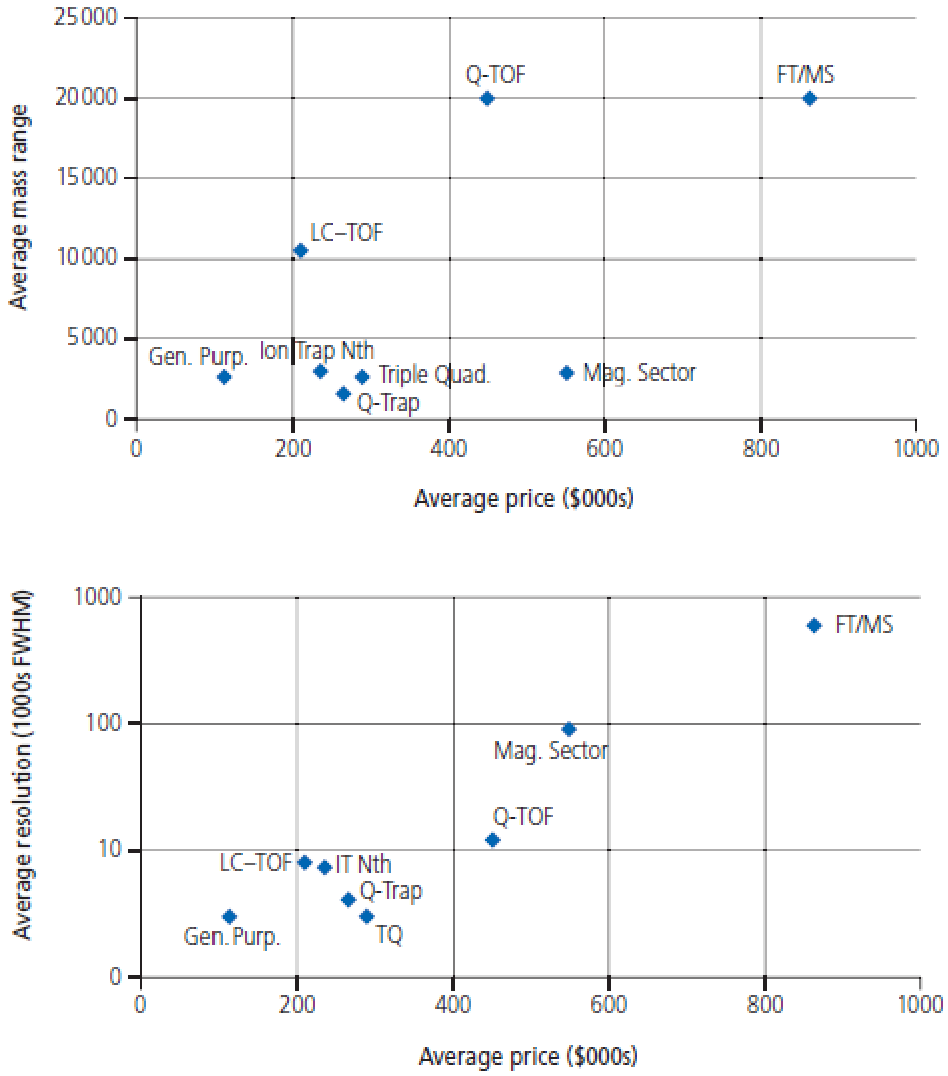


Table 2: Sulphide and aldehyde metabolites that can be differentiated only by high mass accuracy (Courtesy of Waters Corporation, Milford, Massachusetts, USA).

Component	Calculated (*m/z*)	Measured (*m/z*)	± (mDa)	± (ppm)
Parent	360.1382	360.1366	1.6	4.4
Sulphide	344.1433	344.1424	0.9	2.6
Sulphone	376.1331	376.1330	0.1	0.3
Desmethyl	346.1225	346.1218	0.7	2.0
S-Desmethyl	330.1276	330.1265	1.1	3.3
Aldehyde	344.1069	344.1074	0.5	1.5
S-Pyridone	272.0858	272.0867	0.9	3.3

Balogh, M. LC-GC Europe, 17(3), 152–159 (2004)

Figure 5: Differentiated by overall cost (and complexity), the combination of quadrupole technology and TOF appears to deliver the best capability, especially in terms of performance (fragmentation for structural characterization, quantitative capabilities and sensitivity). (Reprinted with permission from reference 1.)



Balogh, M. LC-GC Europe, 17(3), 152–159 (2004)

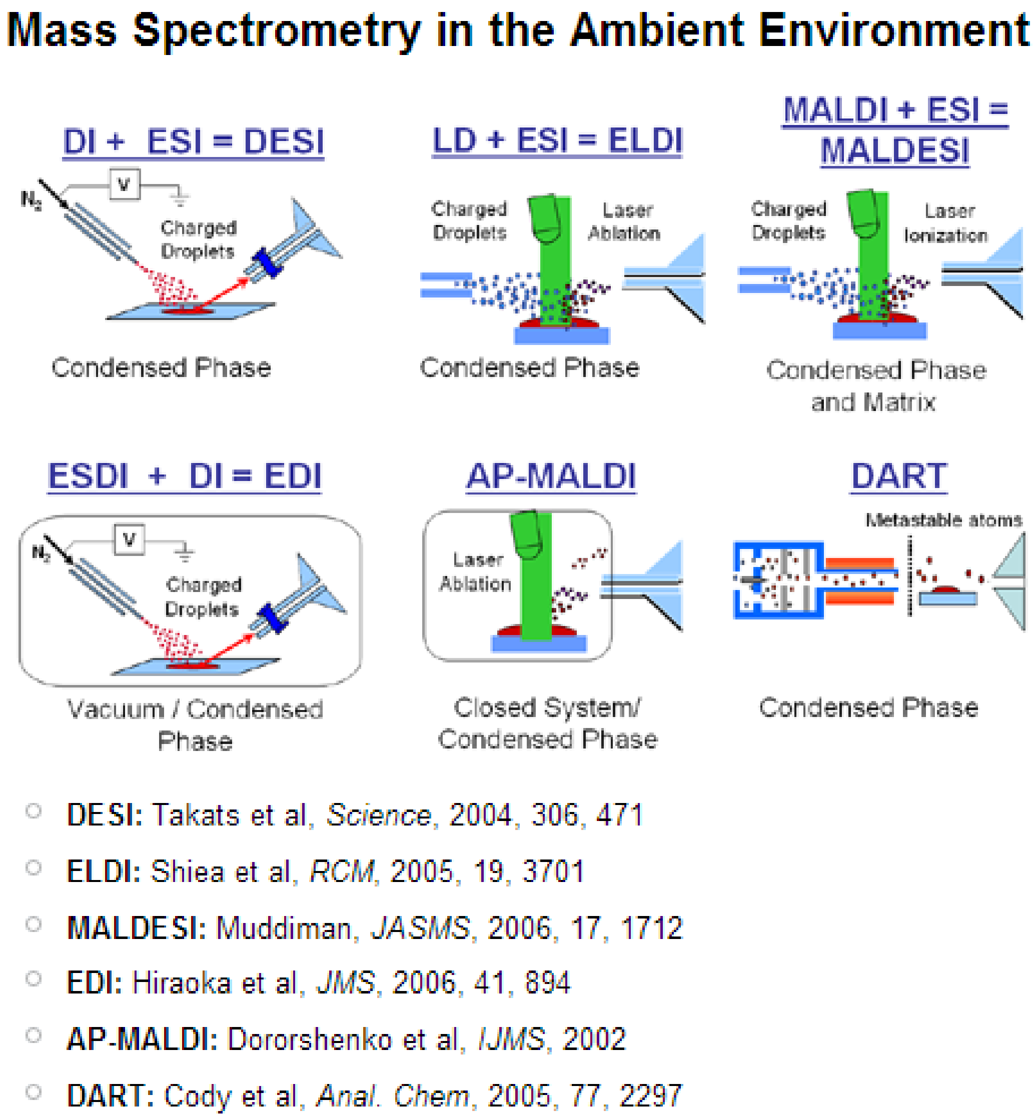
1. Draw the mass spectra you expect to observe for benzyl alcohol if you analyze it to different ways:

a. Using an EI source with a quadrupole mass analyzer

b. Using an ESI source with a TOF mass analyzer

Ambient Ionization Methods

http://aston.chem.purdue.edu/research/ambient-ionization-methods



Mass Spectrometry in the Ambient Environment

DI + ESI = DESI

Condensed Phase

LD + ESI = ELDI

Condensed Phase

MALDI + ESI = MALDESI

Condensed Phase and Matrix

ESDI + DI = EDI

Vacuum / Condensed Phase

AP-MALDI

Closed System/ Condensed Phase

DART

Condensed Phase

○ **DESI:** Takats et al, *Science*, 2004, 306, 471

○ **ELDI:** Shiea et al, *RCM*, 2005, 19, 3701

○ **MALDESI:** Muddiman, *JASMS*, 2006, 17, 1712

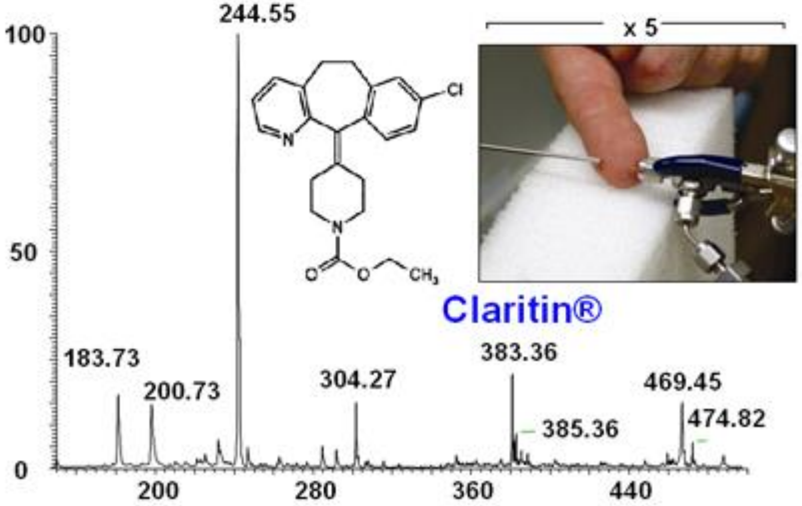
○ **EDI:** Hiraoka et al, *JMS*, 2006, 41, 894

○ **AP-MALDI:** Dororshenko et al, *IJMS*, 2002

○ **DART:** Cody et al, *Anal. Chem*, 2005, 77, 2297

DESI analysis on skin for drug monitoring

Human skin 50 minute after ingestion of 10 mg Claritin®



http://aston.chem.purdue.edu/research/ambient-ionization-methods

http://cen.acs.org/articles/87/i21/Silver-Lining-Melamine-Crisis.html