

History of Mass Spectrometry of Organic Molecules

Lutz Alder

Introduction

What we use in pesticide residue analysis today

Our instruments are triple quadrupoles, TOFs or orbitraps made by Agilent, Bruker, Sciex, Thermo or Waters.

But where are the roots of mass spectrometry?



Outline

1. First mass spectrometers
2. Generation of vacuum
3. Ion detection and ion recording
4. Mass spectral library search
5. The beginning of hyphenated techniques (GC-MS)
6. GC- and LC-MS interfaces
7. Tandem mass spectrometry

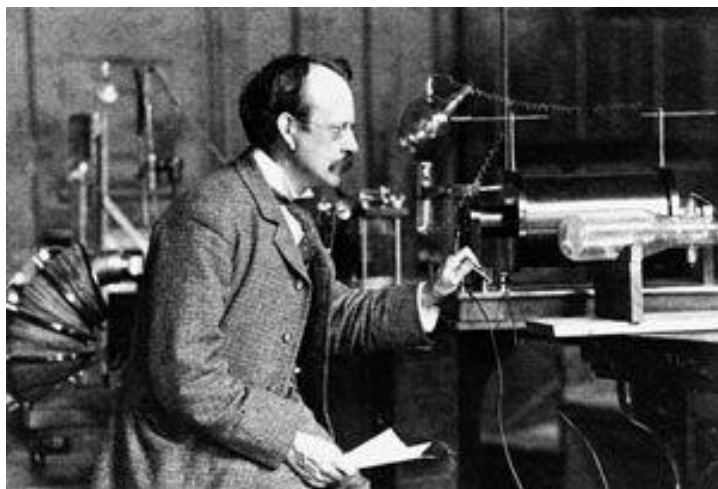
Unfortunately nothing about high resolution MS or fragmentation of organic molecules

1. FIRST MASS SPECTROMETERS

From the beginning until
commercial production

First Mass Spectrometers – The year 1910

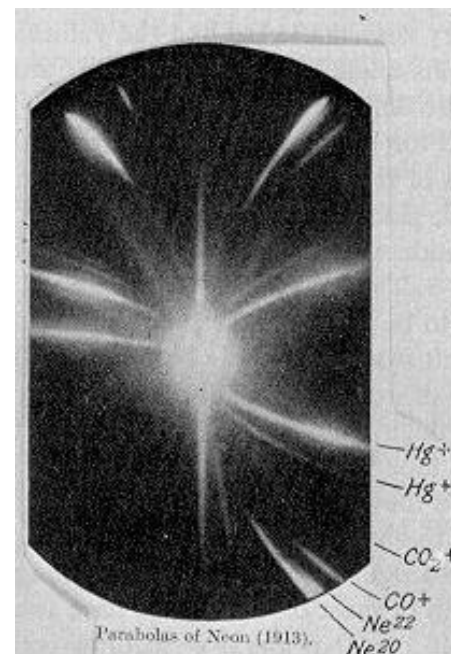
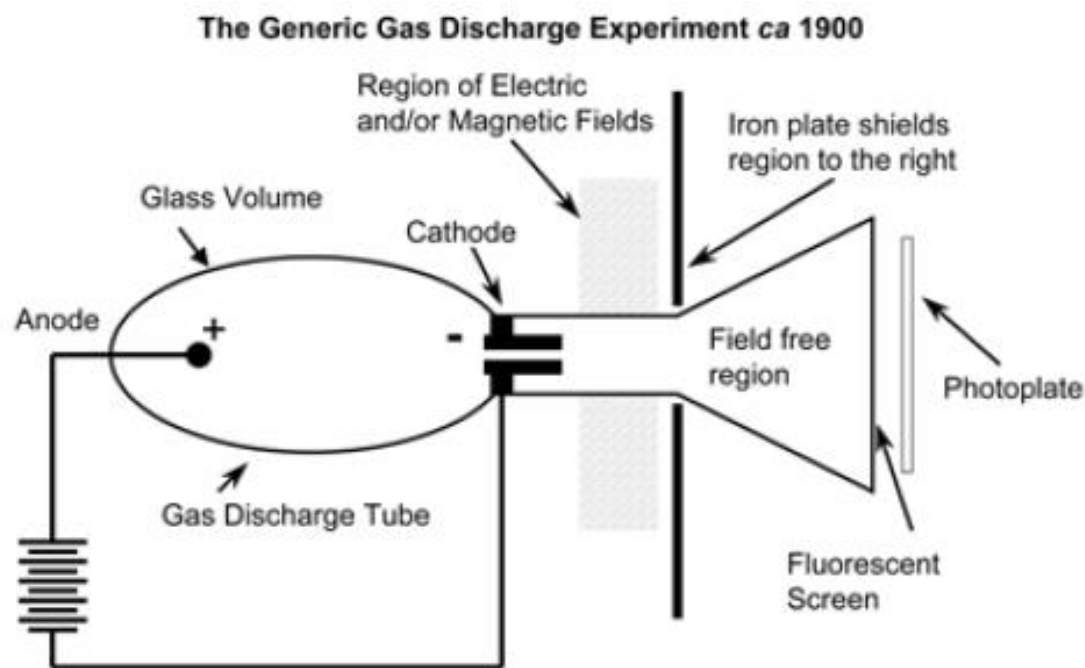
Sir Joseph John Thomson's detection of neon isotopes



Thomson worked at the University of Cambridge (UK). He used glow discharge for ionisation. Cations of neon are accelerated to the cathode and passed a hole. The deflection by parallel electric and magnetic fields showed that neon was actually composed of two isotopes.

Nobel Prize for physics in 1906

© Science Museum Pictorial



First parabola mass spectra were obtained 1910

Resolution: 10

Source:
https://en.wikipedia.org/wiki/History_of_mass_spectrometry

First Mass Spectrometers

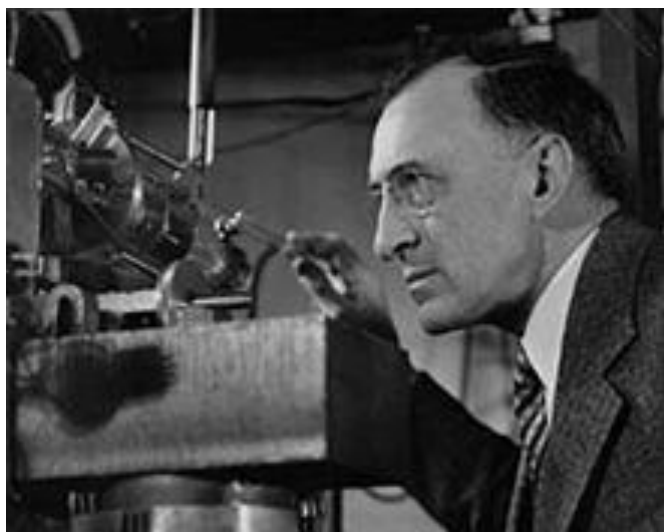
J J Thomson's vision published in 1913

... one of the main reasons for writing this book was the hope that it might induce others, and especially chemists, to try this method of analysis. I feel sure that there are many problems in chemistry which can be solved with far greater ease by this than by any other method.



First Mass Spectrometers – The year 1918

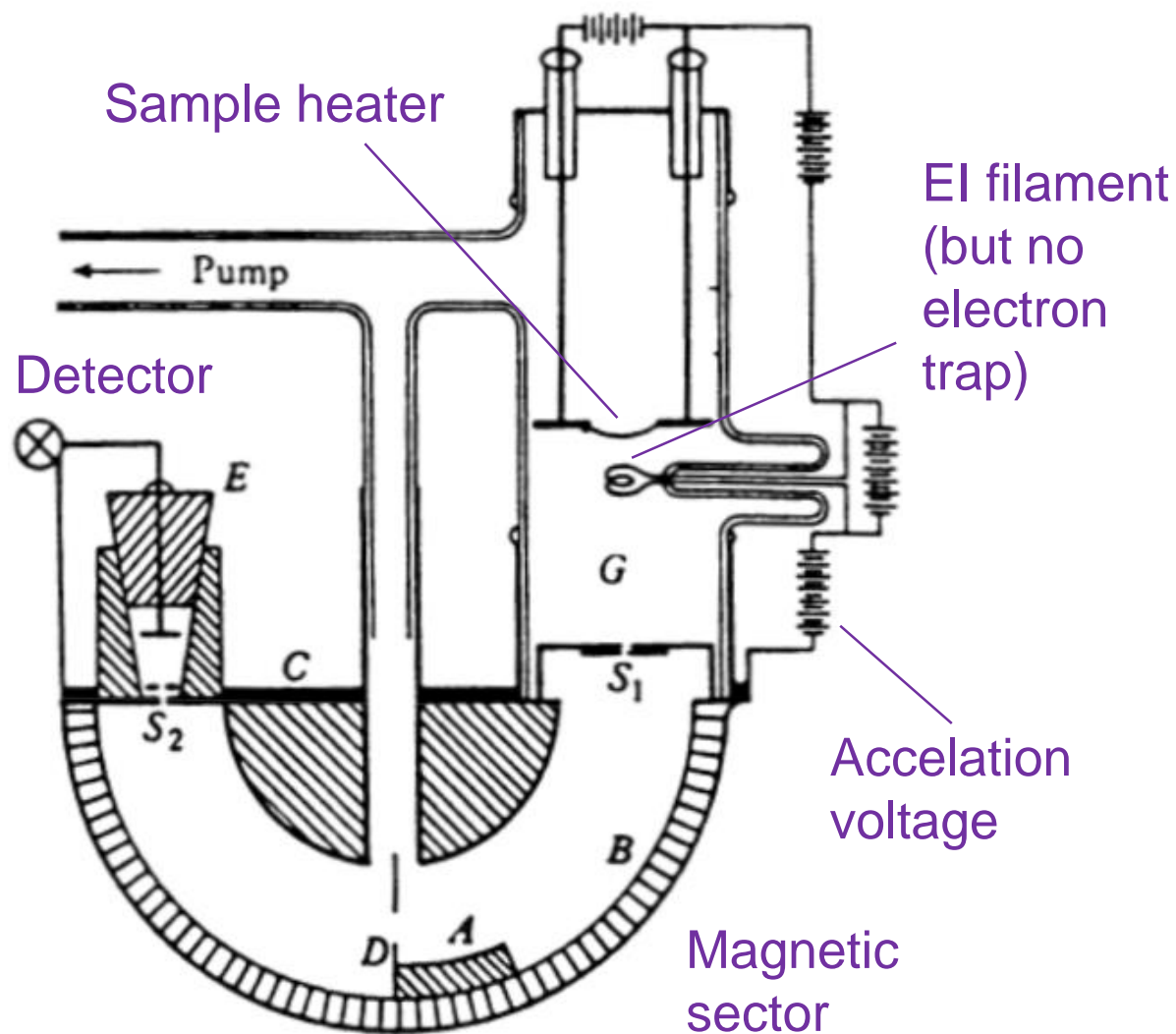
Arthur Jeffrey Dempster: The first MS with thermal ionization and electron impact as well as ion detection without photo plate



Source: Wikipedia

Dempster was born in Toronto and worked at the University of Chicago. He obtained better resolution by smaller differences in the energy (speed) of ions.

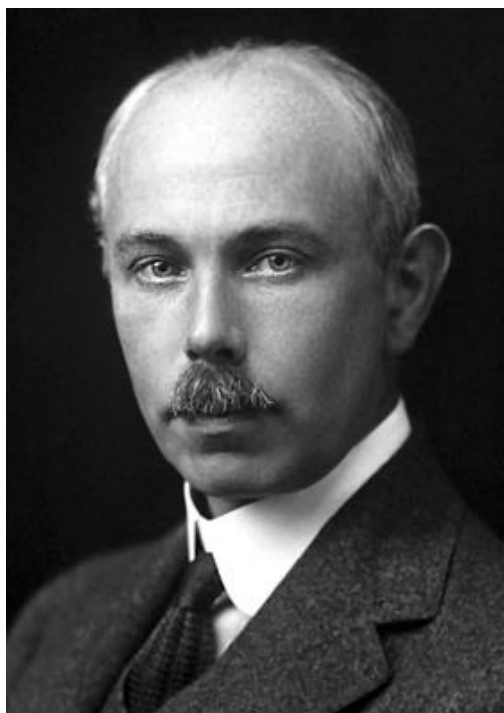
Instead of glow discharge he used thermal ionization to produce ions. He first time separated uranium isotopes (^{235}U / ^{238}U).



Dempster's MS with 180° magnetic sector built in 1918
(Source: https://en.wikipedia.org/wiki/Arthur_Jeffrey_Dempster)

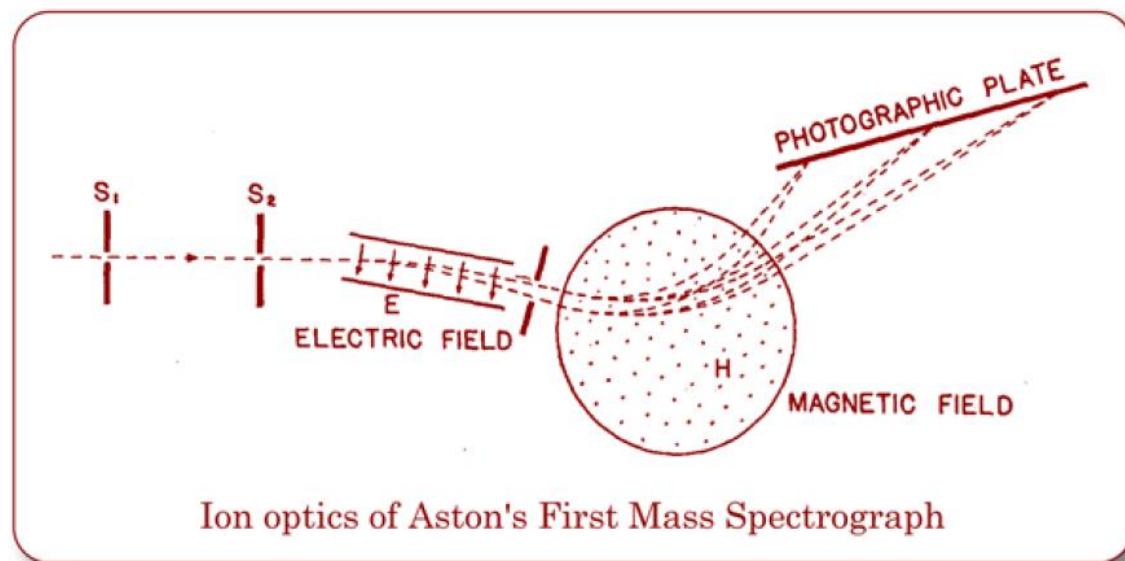
First Mass Spectrometers – The year 1919

Francis William Aston separated electric and magnetic fields

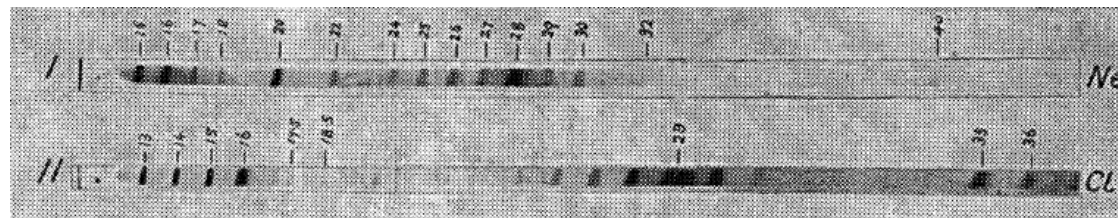


Source: Wikipedia

In 1909, Aston became a research assistant of Thomson. He also used glow discharge for ionisation. However, he separated electric fields (to obtain ions of equal kinetic energy) and magnetic fields and obtained a **Resolution of 2000** in his 3rd MS. Nobel Prize in chemistry in 1922

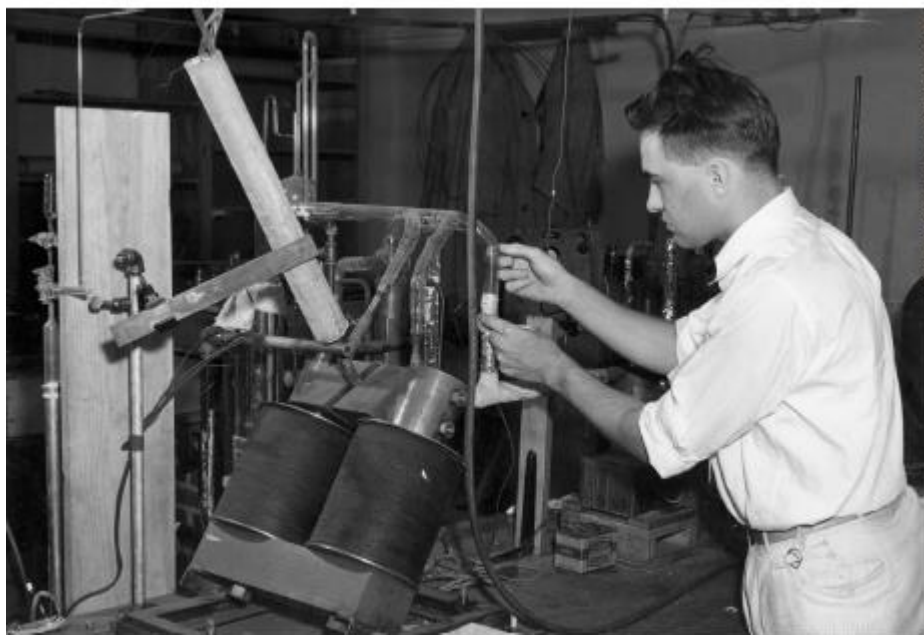


Replica of the 3rd mass spectroeter of J. J. Thomson and Aston build in 1937 (Source: Wikipedia)



First Mass Spectrometers – The year 1940

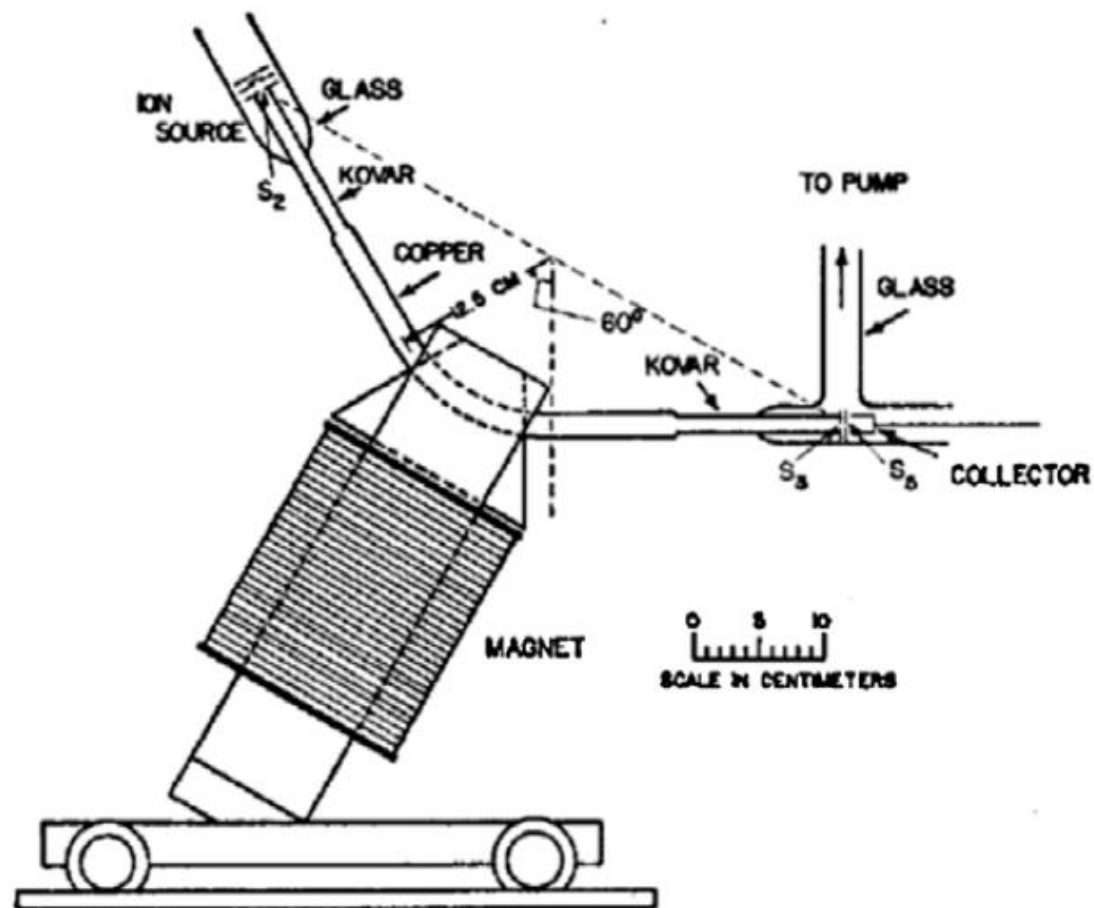
Alfred Otto Carl Nier: Introduction of an simple, rugged and cheap 60° magnetic sector instrument with EI ion source built in series



Nier with one of his early mass spectrometers.

The 60° deflection required smaller electromagnets ($\ll 2$ tons) with less powerful power supply ($\ll 5$ kW).

In the Manhattan project about 100 mass spectrometers of this type were build for Site K-25 in Tennessee.

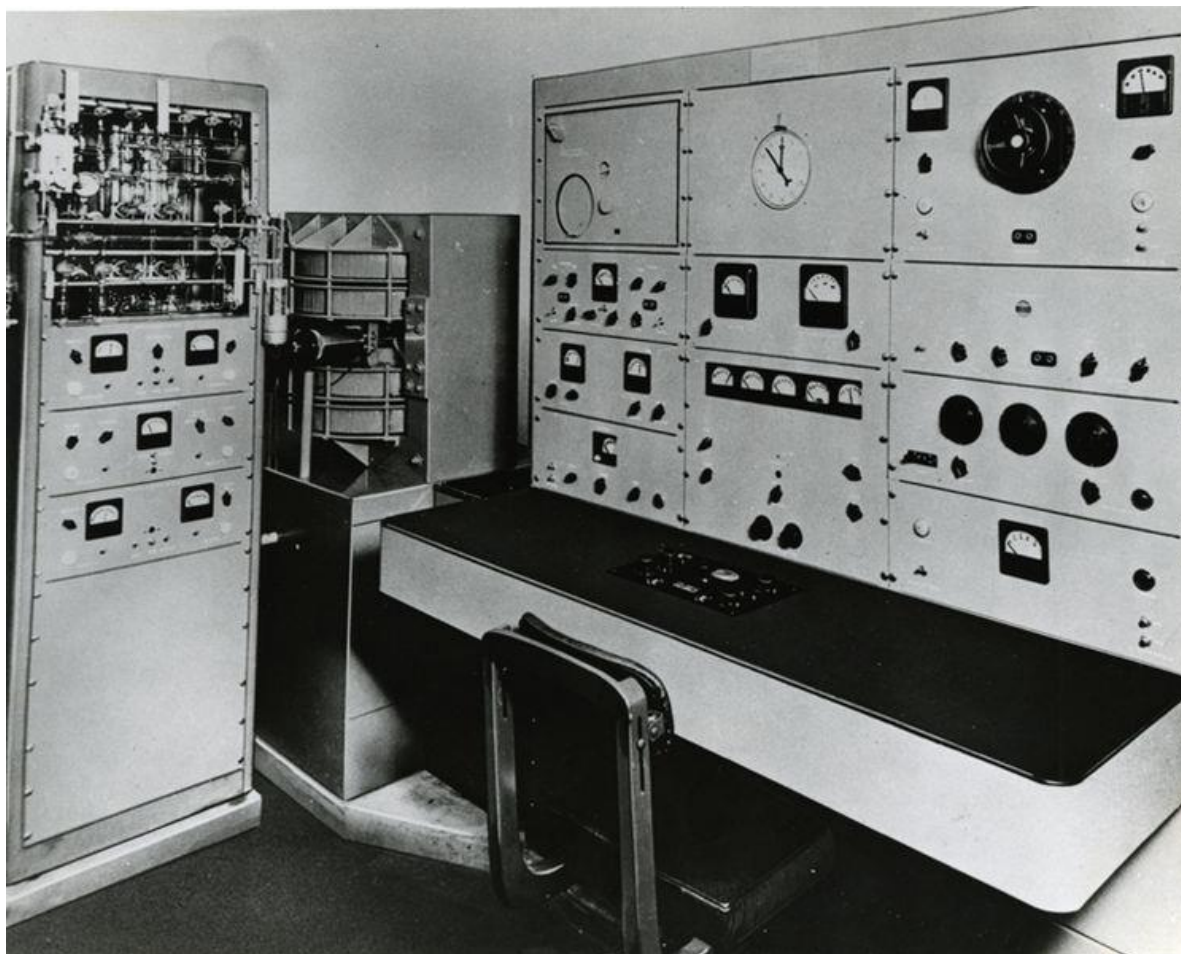


Nier's construction published in 1940 used an ion path made from copper combined with parts made from glass

(Source: Intern J Mass Spectrom 349– 350 (2013) 9– 18)

First Mass Spectrometers

The Spring of Organic Mass spectrometry started December 1942: The Consolidated Electrical Engineering (CEC) model 21-101



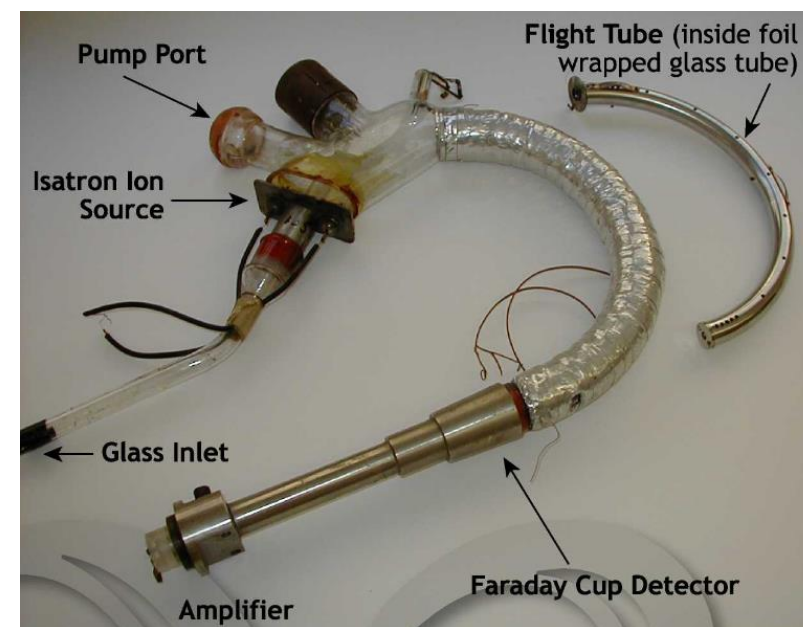
Picture of first commercial instrument (CEC 21-101), which is based on Dempster's 180° geometry
Source: https://commons.wikimedia.org/wiki/File:CEC_Model_21-101_mass_spectrometer_PP2008.038.004.jpg

Technical specification

Mass range: 16 -71 amu

(later versions 10 – 160 amu)

Scan speed: 20 min/spec



Ion path of CEC 21-102

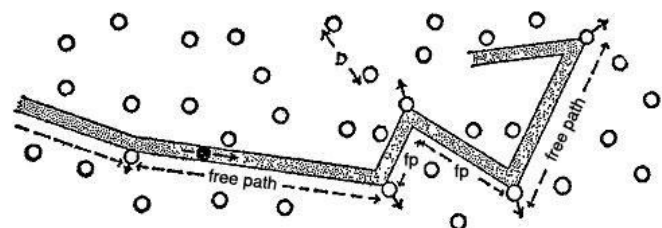
Source: <http://msr.dom.wustl.edu/pubs-misc/cec-103c.pdf>

2. GENERATION OF VACUUM

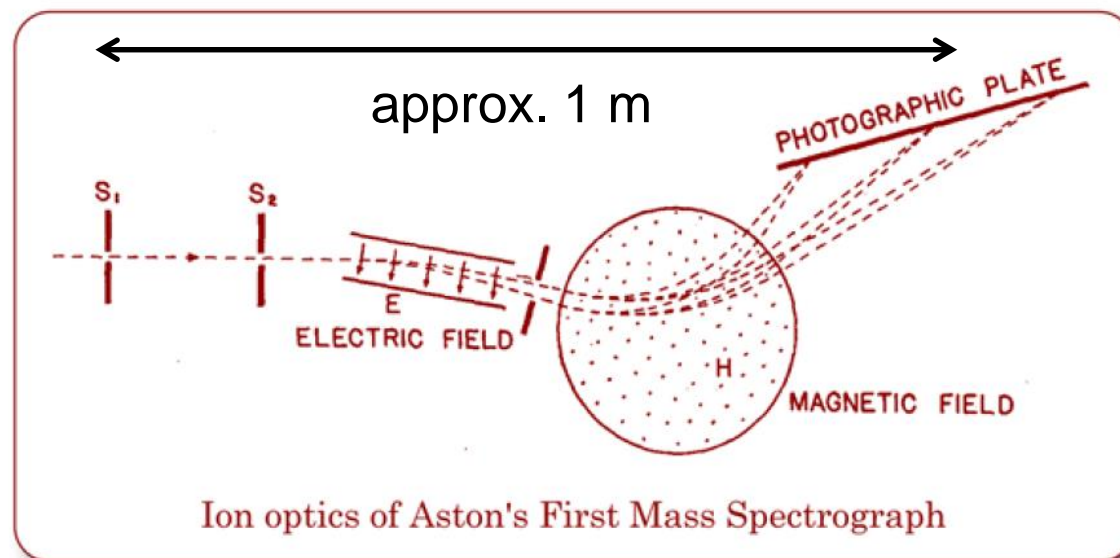
Generation of vacuum

Why we need vacuum?

In the mass spectrometer ions want to fly straight forward without collisions!



Mean free path of a gas molecule



Mean free path

From Wikipedia, the free encyclopedia

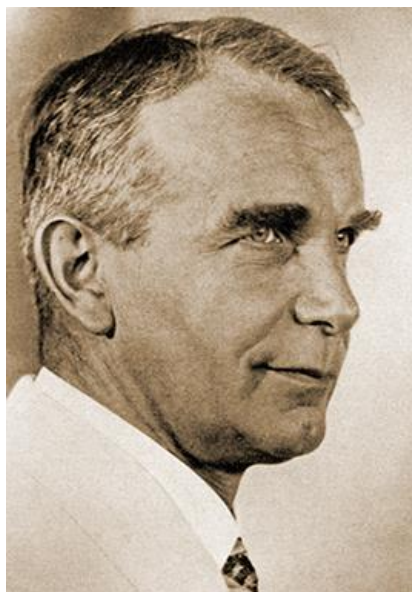
In [physics](#), the **mean free path** is the average distance traveled by a moving particle (such as an [atom](#), a [molecule](#), a [photon](#)) between successive impacts (collisions),^[1] which modify its direction or energy or other particle properties.

The following table lists some typical values for air at different pressures at room temperature.

Vacuum range	Pressure in hPa (mbar)	Pressure in mmHg (Torr)	Molecules / cm ³	Molecules / m ³	Mean free path
Ambient pressure	1013	759.8	2.7×10^{19}	2.7×10^{25}	68 nm ^[2]
Low vacuum	300 – 1	$225 - 7.501 \times 10^{-1}$	$10^{19} - 10^{16}$	$10^{25} - 10^{22}$	0.1 – 100 μ m
Medium vacuum	$1 - 10^{-3}$	$7.501 \times 10^{-1} - 7.501 \times 10^{-4}$	$10^{16} - 10^{13}$	$10^{22} - 10^{19}$	0.1 – 100 mm
High vacuum	$10^{-3} - 10^{-7}$	$7.501 \times 10^{-4} - 7.501 \times 10^{-8}$	$10^{13} - 10^9$	$10^{19} - 10^{15}$	10 cm – 1 km
Ultra-high vacuum	$10^{-7} - 10^{-12}$	$7.501 \times 10^{-8} - 7.501 \times 10^{-13}$	$10^9 - 10^4$	$10^{15} - 10^{10}$	1 km – 10^5 km
Extremely high vacuum	$<10^{-12}$	$<7.501 \times 10^{-13}$	$<10^4$	$<10^{10}$	$>10^5$ km

Generation of vacuum

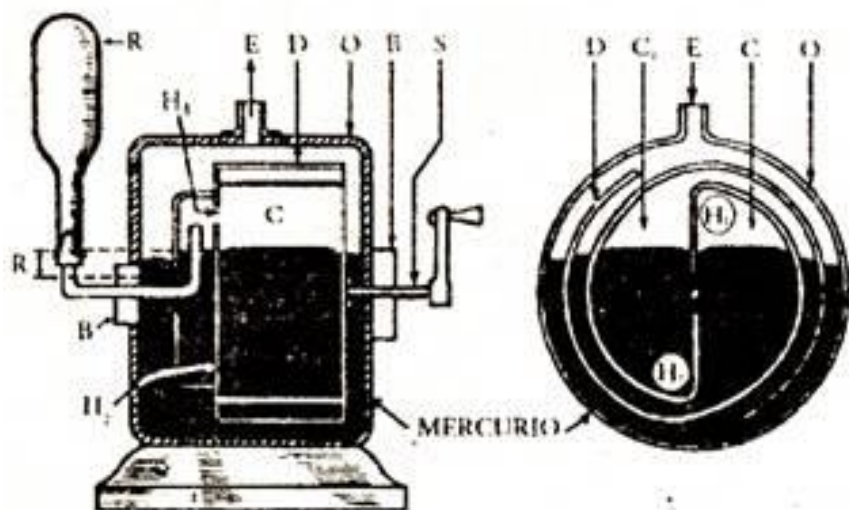
Aston used Gaede's rotary mercury pump driven by hand



Wolfgang Gaede developed 1909 the rotary mercury pump



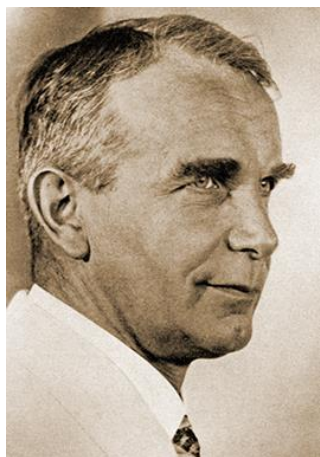
Aston with his 2nd MS



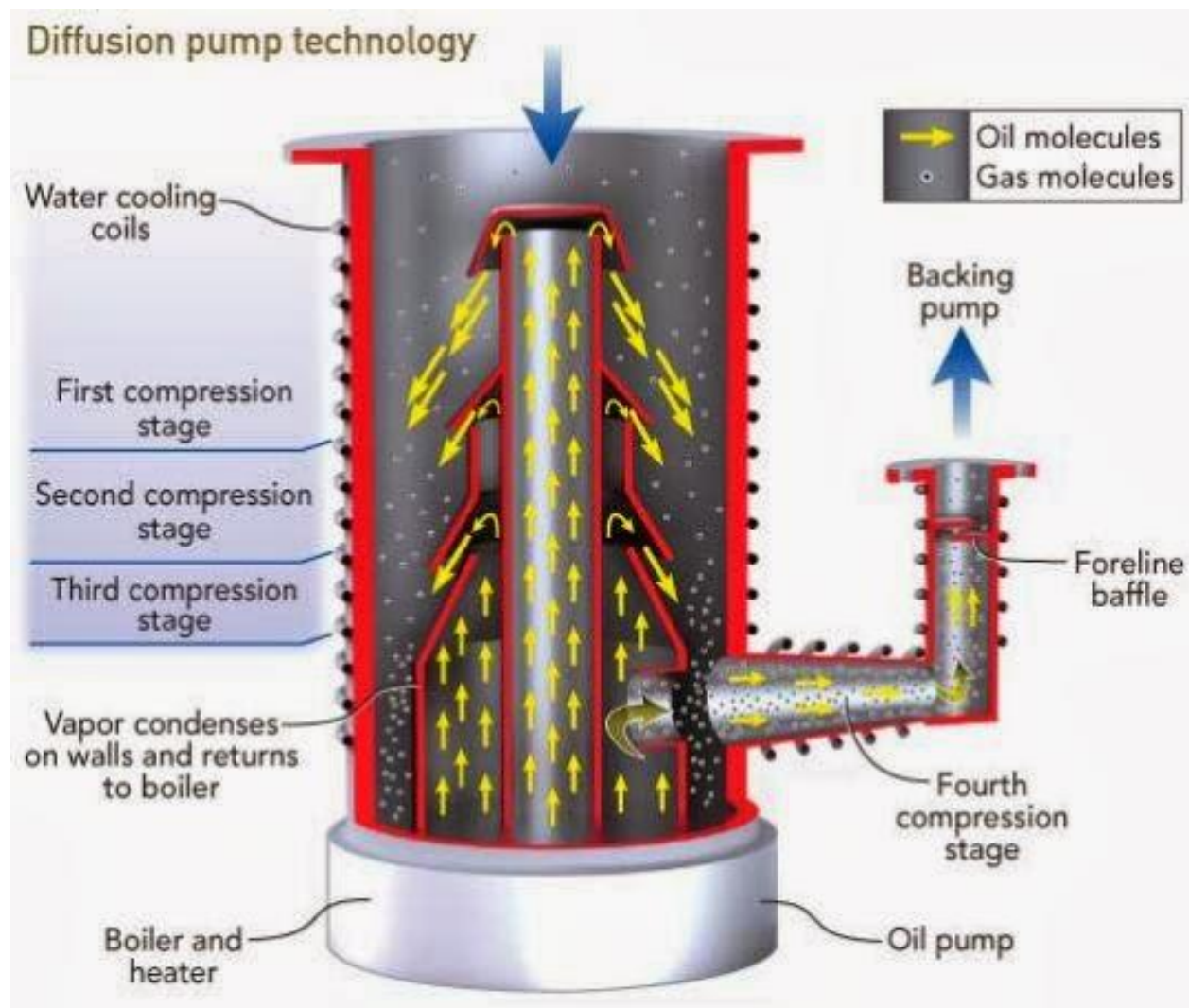
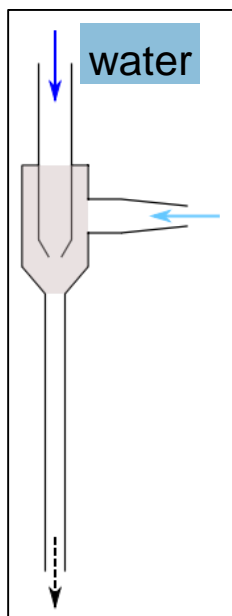
Gaede's mercury pump
© The Yale Peabody Museum

Generation of vacuum

In 1913 Gaede also developed the quicksilver diffusion pump which was improved by Irving Langmuir



Wolfgang Gaede



Irving Langmuir, USA

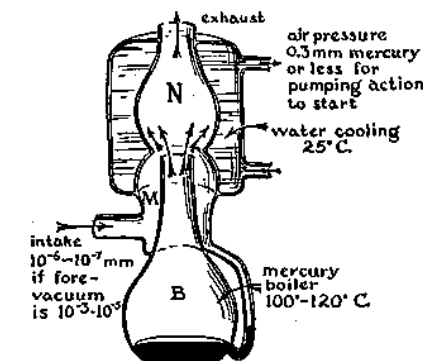
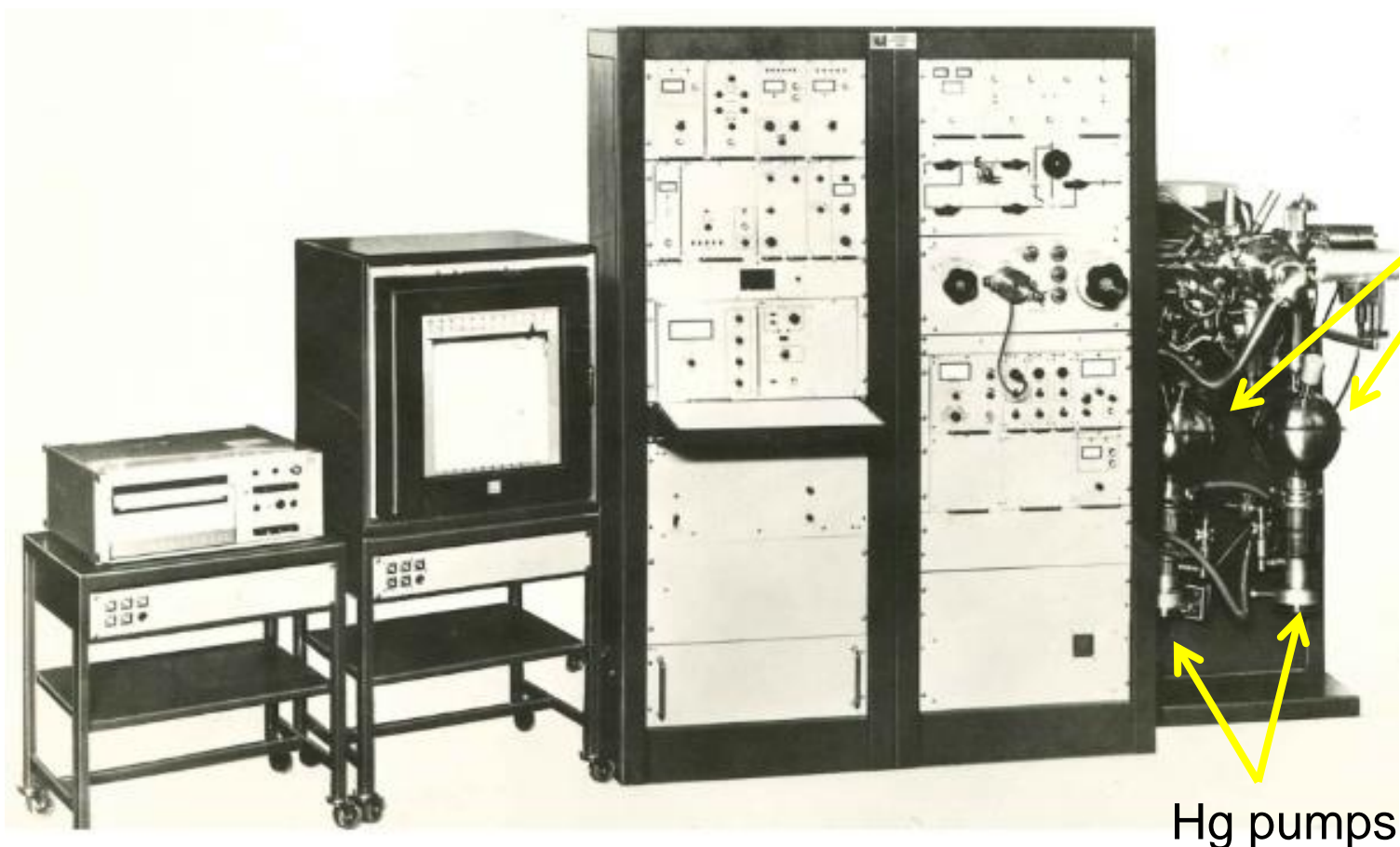


Fig. 5. Diagrammatic sketch of Langmuir's diffusion pump.

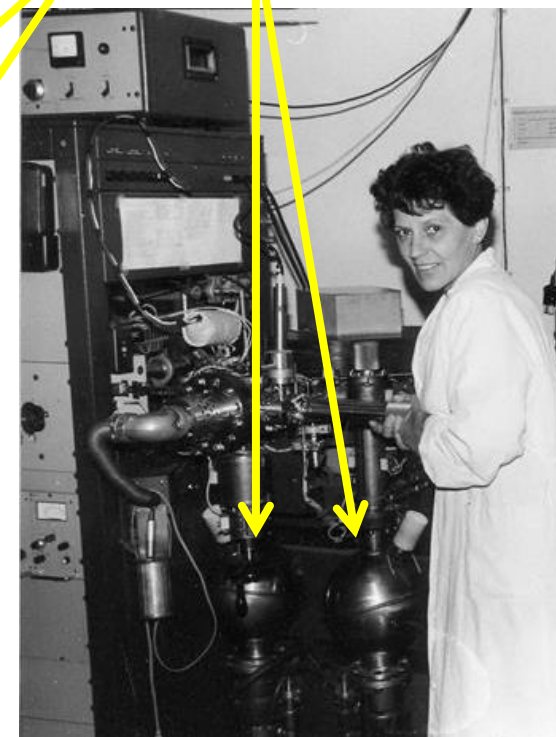
Later quicksilver was replaced by oil. Metrovick (UK) developed pumps with oil base on hydrocarbons (Apiezon A + B) in 1928.

Generation of vacuum

Quicksilver diffusion pumps required baffles cooled with liquid nitrogen



Baffles filled with liquid nitrogen



The Varian MAT CH5 introduced in 1967 was the first MS without radio bulbs (using semiconductor technology). The vacuum was produced with two Hg diffusion pumps.

(picture taken from: http://apps.thermoscientific.com/media/SID/IOMS/PDF/niagara2011/1_Huebschmann_History_of_MS_in_Bremen.pdf)

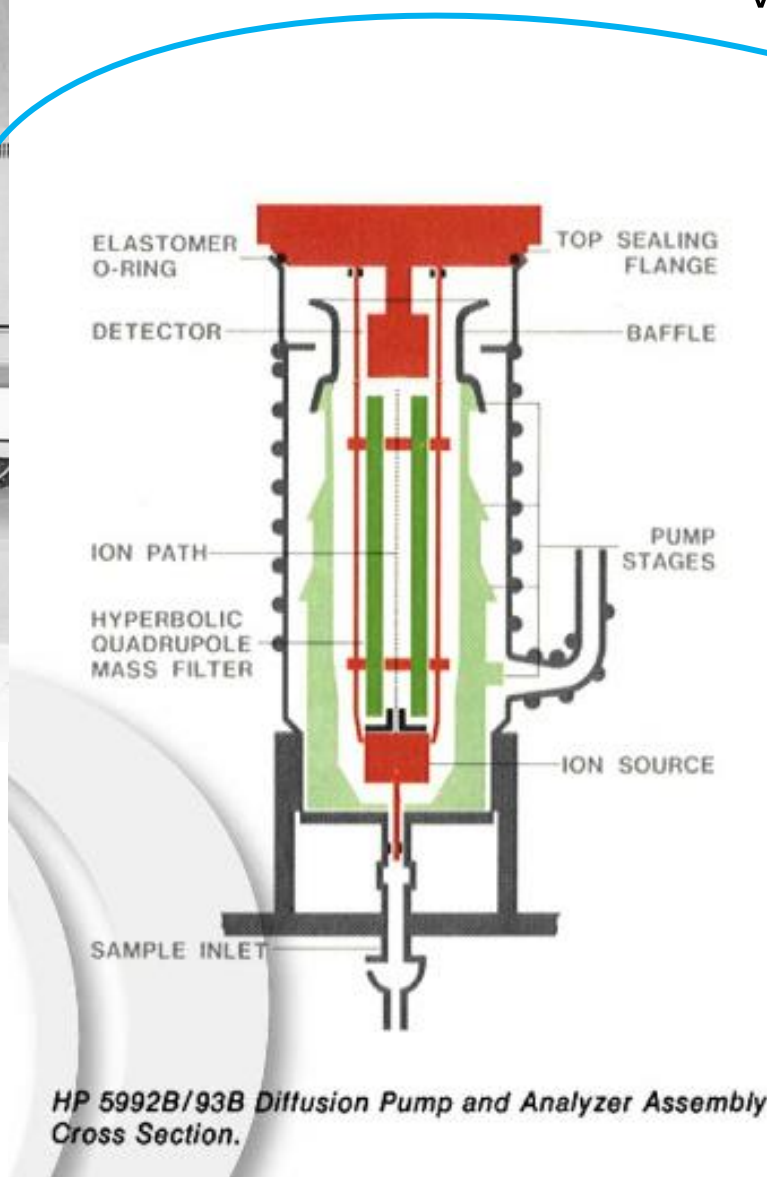
Generation of vacuum

Shortest way to vacuum: The MS installed in a oil diffusion pump

Vertical installation of quadrupole



HP 5993B GC-MS installed in 1984 at Humboldt University in Berlin (private photograph)



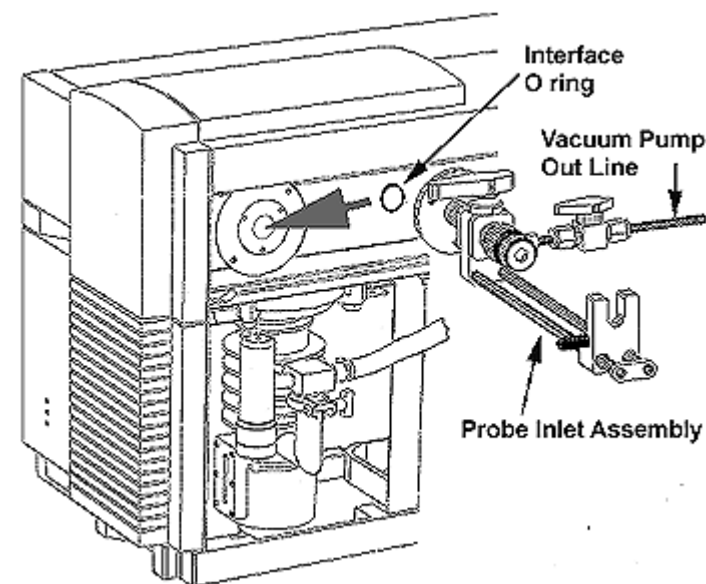
HP 5992B/93B Diffusion Pump and Analyzer Assembly Cross Section.



Picture taken from: <http://www.asms.org/docs/history-posters/hp5992.pdf?sfvrsn=2>

Generation of vacuum

Oil diffusion pumps were installed at least until 2010



The oil diffusion of Agilent's 5975 MSD allows a column flow of not more than 1.5 mL He/min and no CI mode.

Generation of vacuum

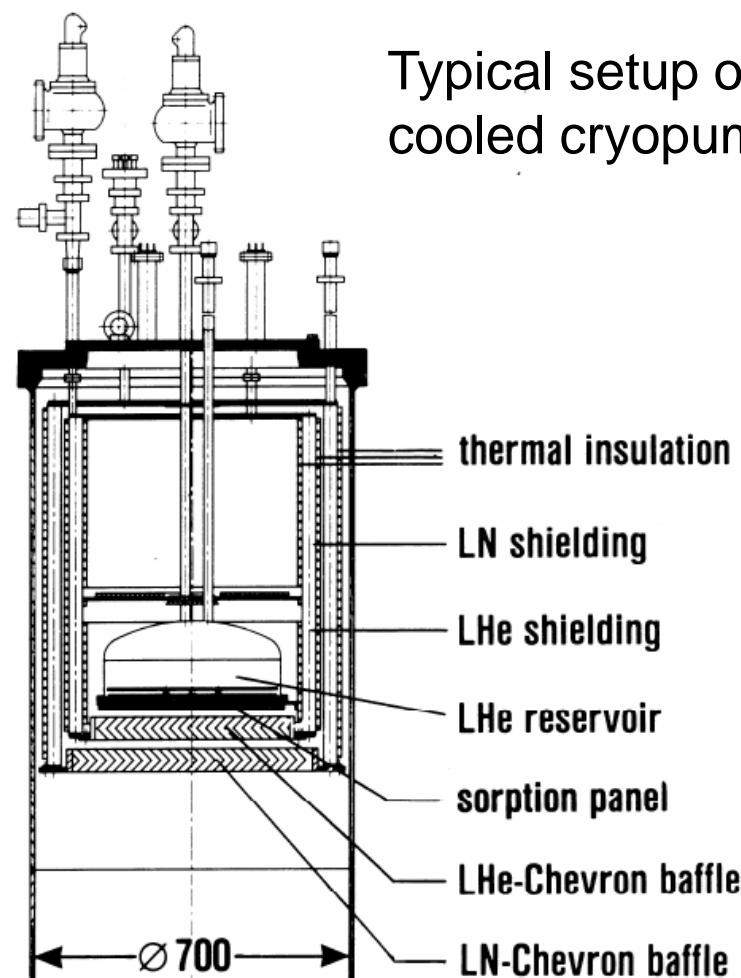
Sciex API III TripleQuad: Best pumping speed obtained using a cryopump filed with liquid helium



The large open cryoarray and cryopump allowed an effective pumping speed of greater than 100,000 L/s!

Disadvantage:

Need of liquid helium. Venting of the system for baking out 2 – 4 times in a month.



Typical setup of a helium-cooled cryopump

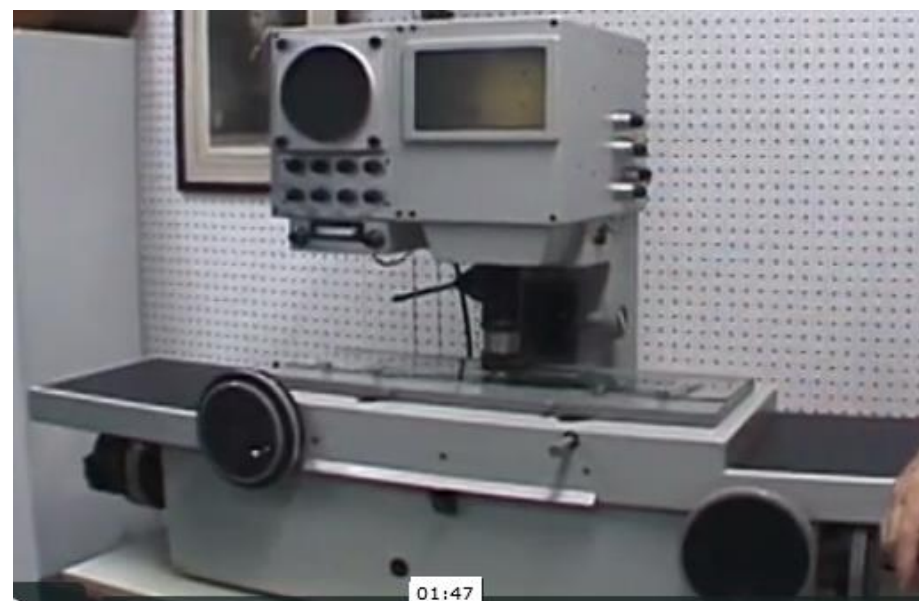
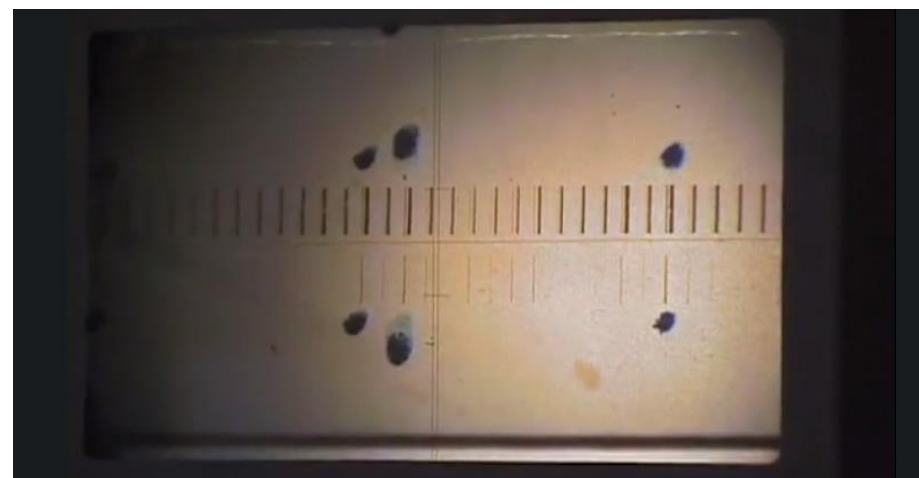
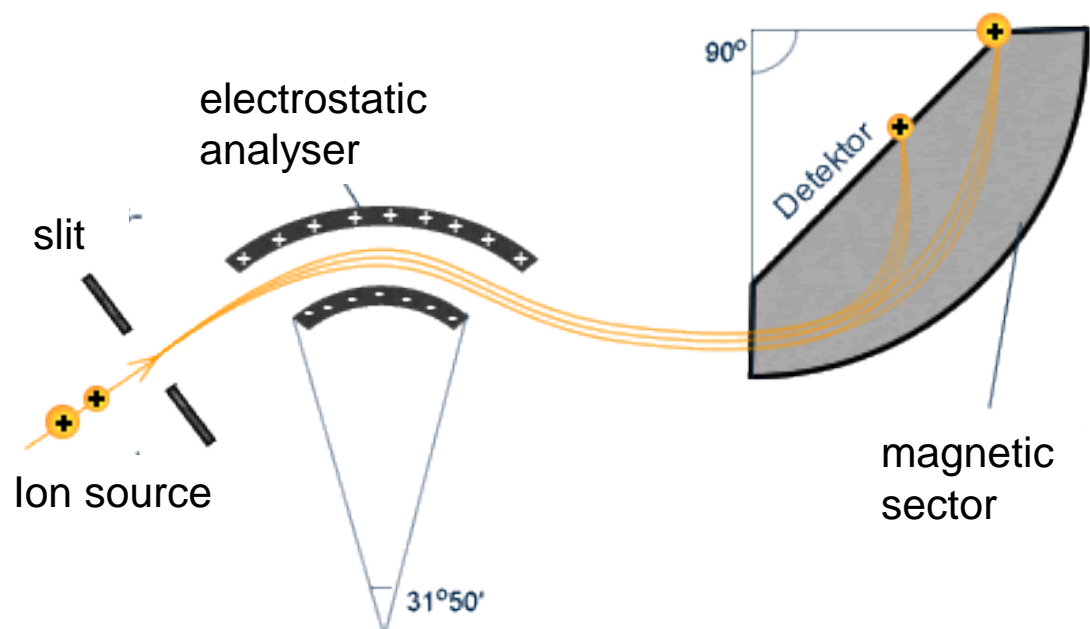
One turbomolecular pump of the 6500 Qtrap offers < 1000 l/s



3. ION DETECTION AND ION RECORDING

Ion detection and recording

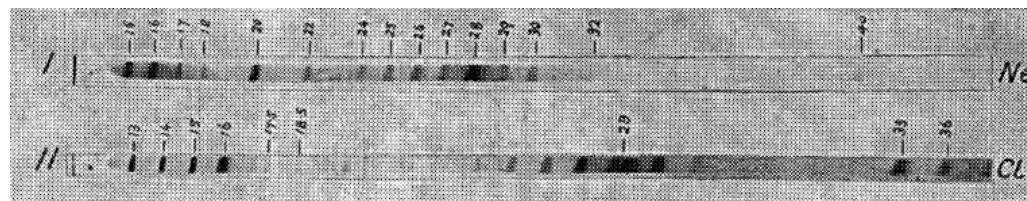
Photo plates of a Mattauch-Herzog double focusing mass spectrograph



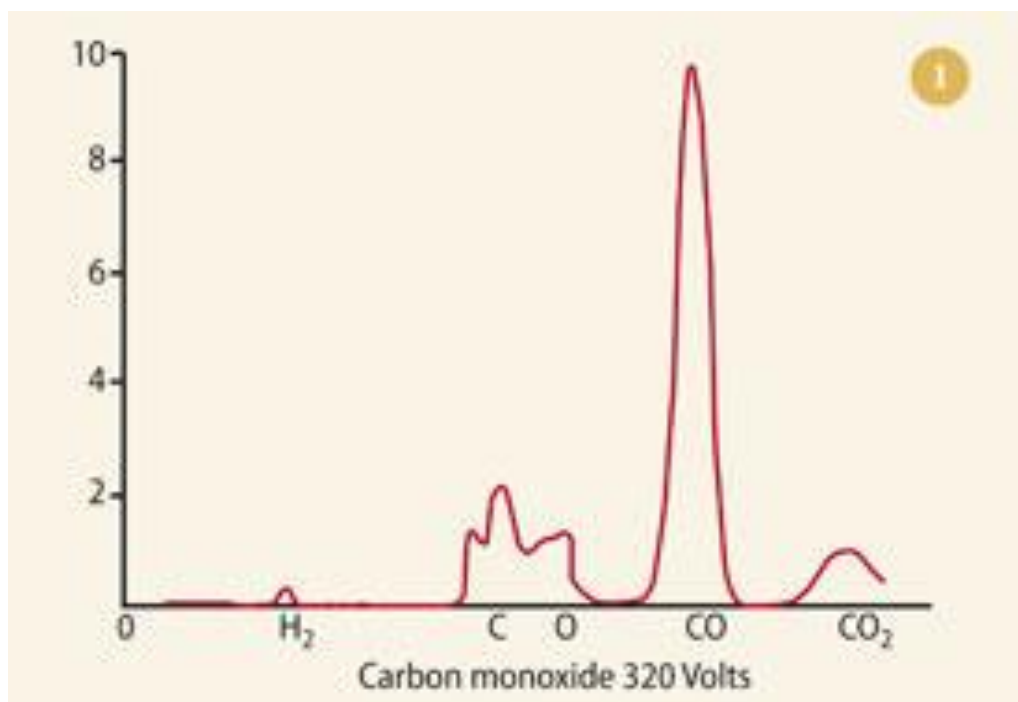
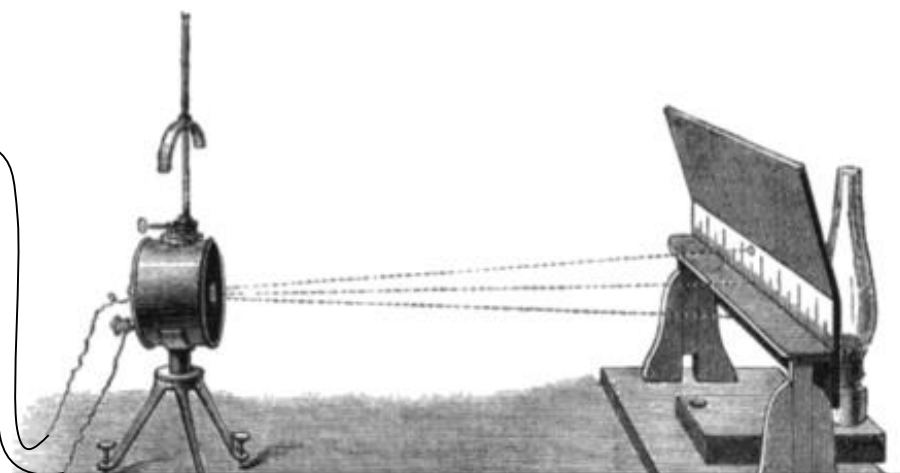
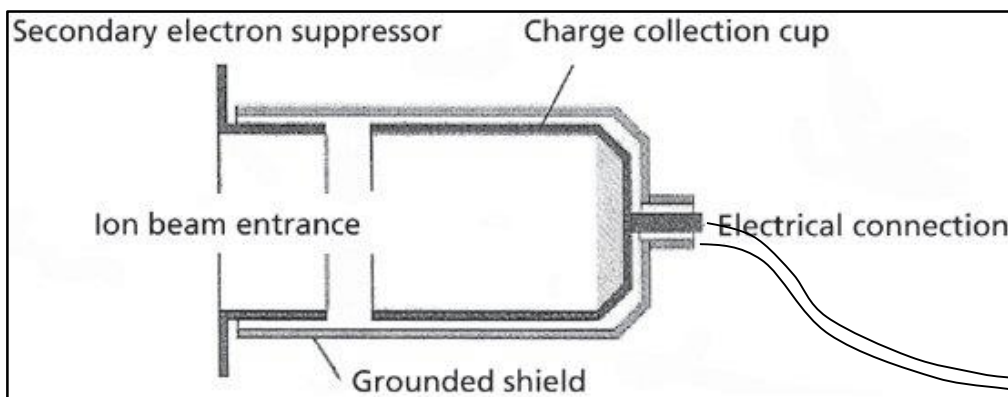
Ion detection and recording

The Faraday cup used by J. J. Thomson in the first scanning instrument

Thomson was dissatisfied with his photographic method of recording “spectra”.



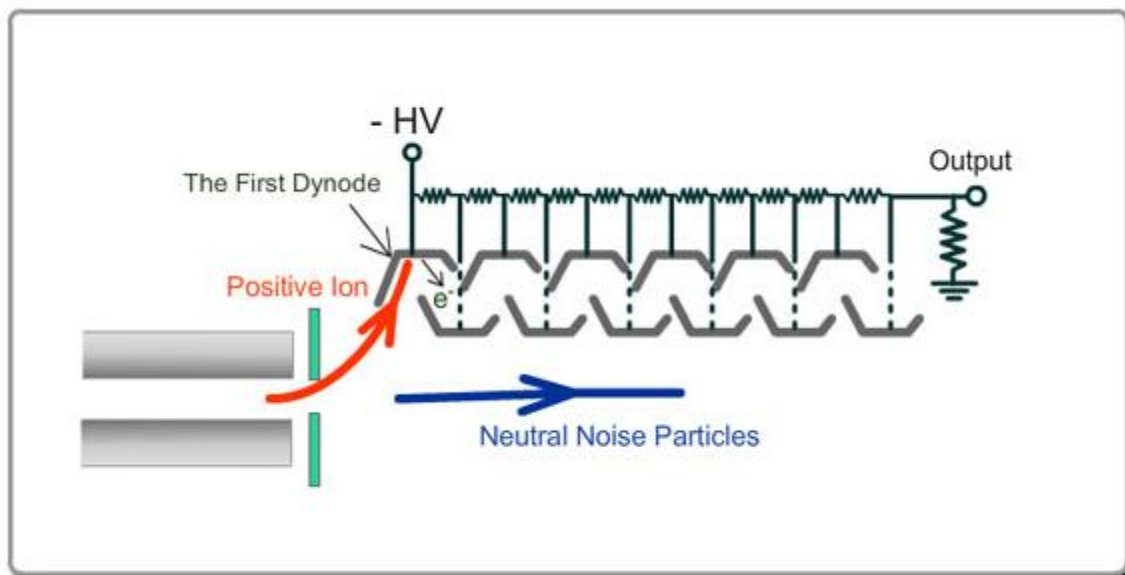
The Faraday cup: Not more than a simple tin can placed at the focal point of ion beam



Mass spectrum of carbon monoxide (CO)
Thomson's plots of ion intensity against relative mass, first published in 1912, were the world's first mass spectra.

Ion detection and recording

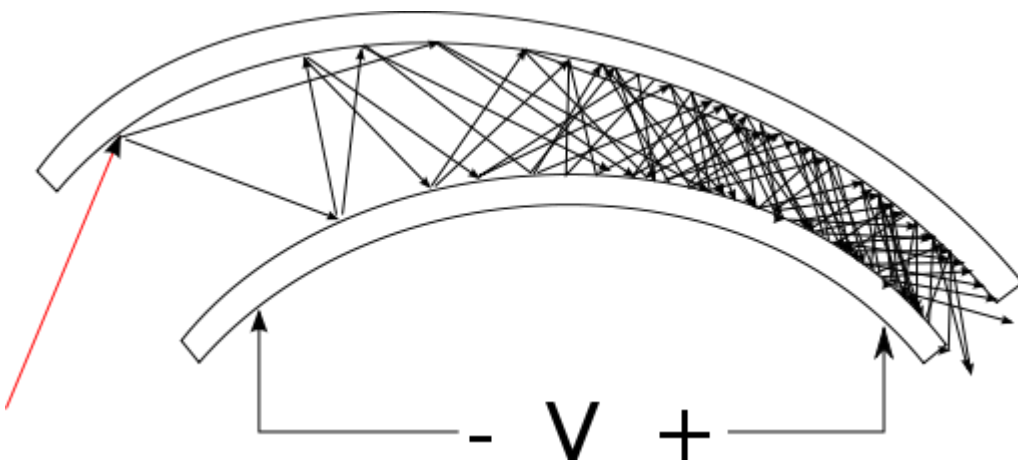
1955: Introduction of the electron multiplier



Principle of 12 discrete dynode secondary electron multiplier, first time supplied with MS 5 of Metrovick in 1955 (earlier than in the US instruments).

In MAT CH-6 we had a multiplier with 18 dynodes

Picture from: www.shimadzu.com/an/structure_electron.html



Modern continuous dynode multiplier with semiconducting surface

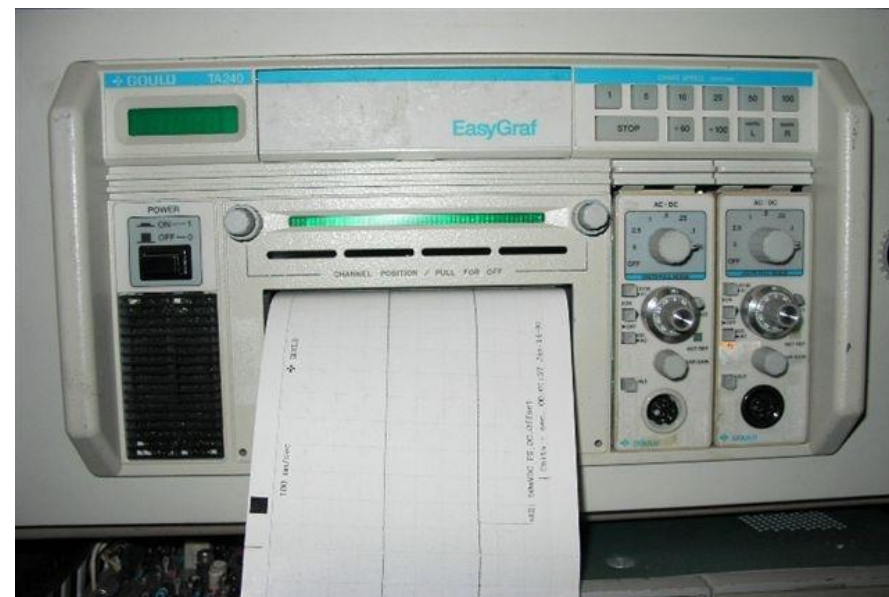
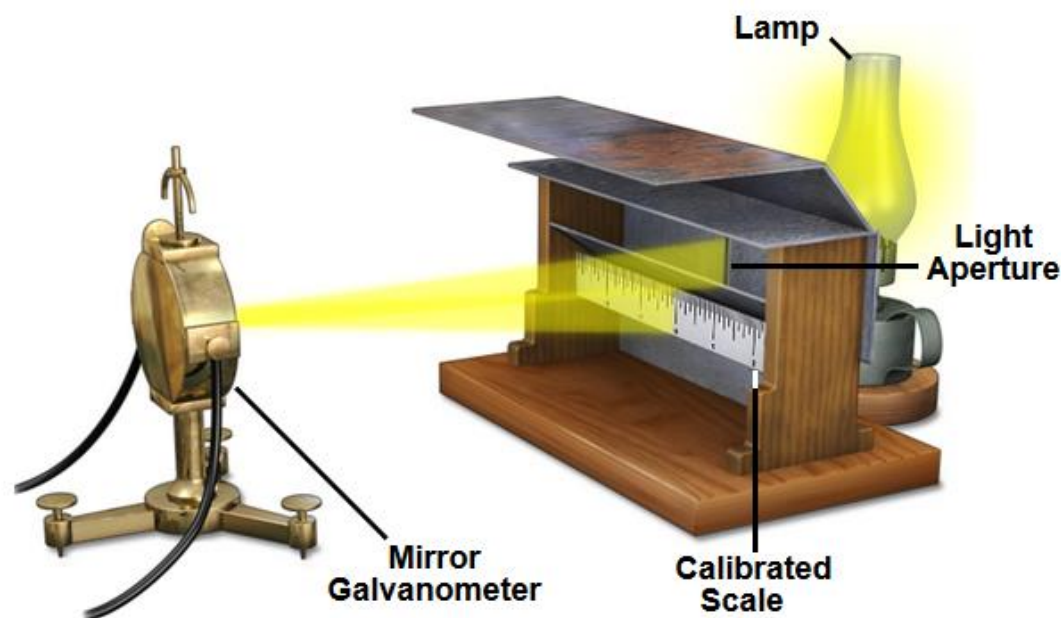
Picture from: en.wikipedia.org/wiki/Electron_multiplier



HP5970 multiplier

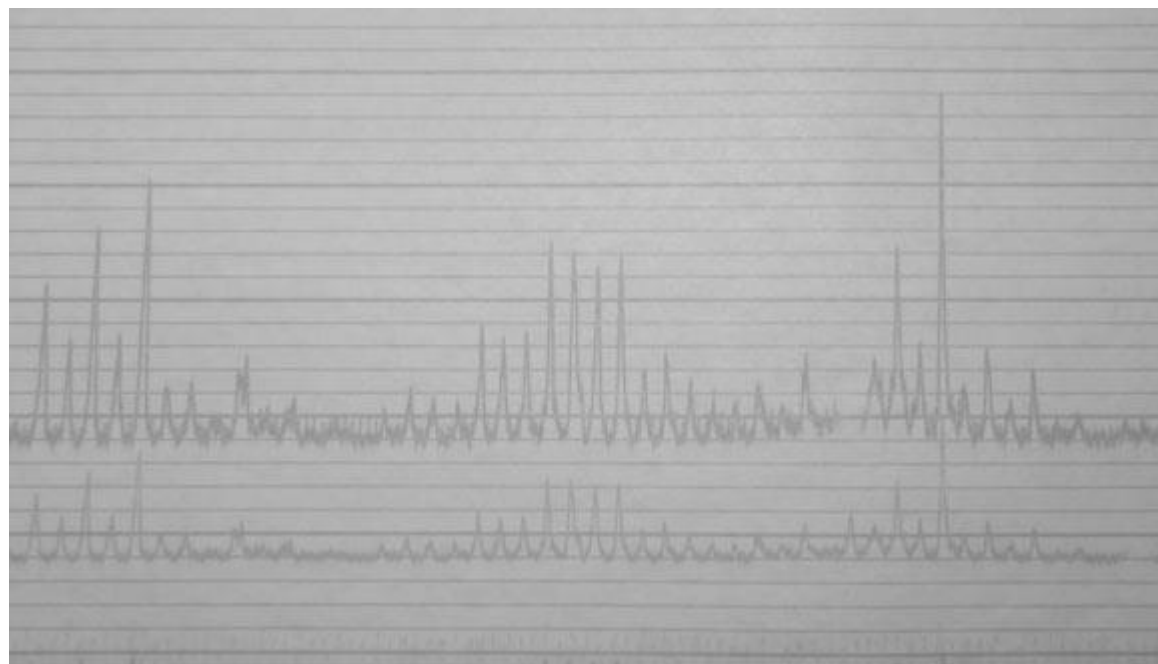
Ion detection and recording

Registration of spectra with an oscillographic chart recorder on light sensitive paper used with MAT CH-6 in Berlin until 1990



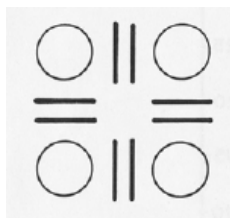
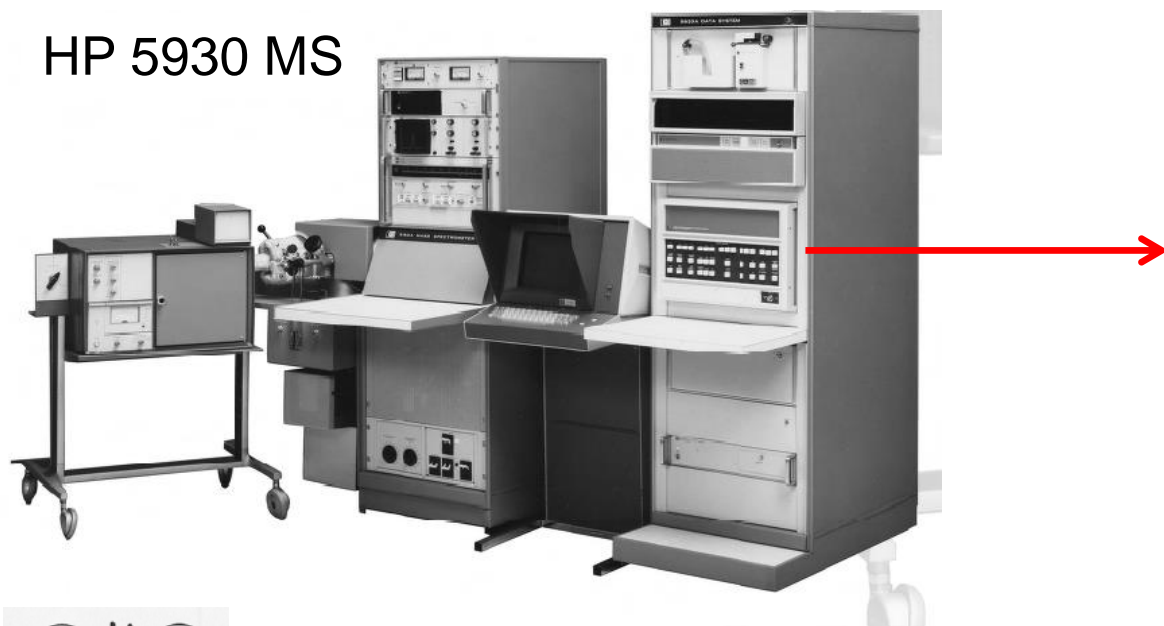
Mirror galvanometer developed by Lord Kelvin

Two traces of a mass spectrum recorded with an oscillographic chart recorder. The mass axis on each spectrum had been manually marked!



The computer of the first quadrupole of Hewlett-Packard (1971)

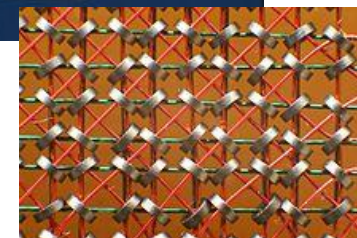
HP 5930 MS



(More precisely the 5930 had an dodecapole mass filter)

Available programs

- Scan
- Plot
- Tabulate
- Search (in library)
- Print



HP 2100A minicomputer

- 8 kB magnetic-core RAM (options up to 32 kB)
- 1 MHz processor
- Software on magnetic cassette
- Assembler language
- With CRT screen

(Source of all: www.asms.org/docs/history-posters/hp5932a_data-system_reduced.pdf?sfvrsn=2)

4. MASS SPECTRAL LIBRARY SEARCH

Mass spectral library search

The first library of spectra: The 'Cornu-Massot' published 1966

COMPOUND NAME	MASS SPECTRUM	C	H	D	Br	Cl	F	I	N	O	P	S	Si	Di	M/E
DODECANAL No 1 12AC3 M=184 T=0.24	57 43 41 55 82 68 69 56 29 44 12 24 1	12	24	1	57
TETRADECANAL No 1 13AC3 M=217 T=0.16	57 43 41 55 82 69 71 68 83 29 14 28 1	14	28	1	57
1 CYCLOPENTYL 2 DECYLDODECANE No 980 1 M=378 B=0.52	57 43 41 55 83 69 97 71 236 237 27 54	27	54	57
2 2 DIMETHYLPENTANE No 18 1 M=100 B=1.20	57 43 41 56 85 29 27 39 15 55 7 16	7	16	57
2 2 DIMETHYL PENTANE No 167 1 M=100 B=1.07	57 43 41 56 85 29 27 39 15 55 7 16	7	16	57
DI.TERT.BUTYL.PEROXIDE No 1689DM4 M=146 T=0.80	57 43 41 58 29 73 146 15 28 27 8 18 2	8	18	2	57
4 N PROPYLHEPTADECANE No 593 1 M=282 B=1.01	57 43 41 71 29 55 85 98 56 69 20 42	20	42	57
5 8 DIETHYLDODECANE No 1538 1 M=226	57 43 41 71 55 85 98 56 197 39 16 34	16	34	57
4 9 DI N PROPYLDODECANE No 1467 1 M=254 H=1.05	57 43 41 71 55 85 98 69 211 56 18 38	18	38	57
3 METHYLEICOSANE No 1656 1 M=296 H=0.81	57 43 41 71 56 55 85 69 42 70 21 44	21	44	57
3 METHYLEICOSANE No 1472 1 M=296 H=0.37	57 43 41 71 56 55 85 69 267 42 21 44	21	44	57

Figure 4. A partial listing of the reference spectra in A. Cornu and R. Massot (1966), Compilation of Mass Spectral Data (Table 4), which lists spectra in the order of most intense peak in the spectrum.

The very popular Eight-Peak-Index

3rd edition 1983: 66,000 entries

Volume 1: Sorted by molecular weight and molecular formula – Search for spectra of known compounds

Volume 2: Sorted by base peak – Search for compounds based on spectra

An invaluable resource from The Royal Society of Chemistry

Eight Peak Index of Mass Spectra, 3rd Edition

The Eight Peak Index of Mass Spectra is the world's largest printed index of mass spectral data. An excellent aid for identifying unknown compounds, it's also a convenient single point of entry to the various full mass spectral collections and mass spectral information appearing in scientific journals.

This new index contains the eight most abundant ions in 66,720 mass spectra, covering 52,332 compounds indexed by molecular weight, elemental composition and most abundant ions. Contains twice as many spectra as the previous addition.

The Eight Peak Index of Mass Spectra can be used for the identification of unknown compounds by

simply comparing mass spectral data of the unknown with the equivalent data of known compounds contained in the Eight Peak Index.

CAS Registry Numbers

A special feature of the Eight Peak Index is the CAS Registry Number assigned to each unique compound. This number can be used to access information concerning that compound in a multitude of manual and computer readable files. It's a useful link to other information sources.

Source of Data

The Eight Peak Index is published by the Mass Spectrometry Data Cen-

tre. Sources of the spectra are as follows: Imperial Chemical Industries, general mass spectrometry literature, American Petroleum Institute/Thermodynamics Research Centre, the American Society for Testing and Materials, the Dow Chemical Company, the Mass Spectrometry Data Centre, John Wiley and Sons Inc., and the NIH/EPA System.

Indexing System

Seven bound books are indexed in the following ways:

Volume 1, Parts 1 and 2—Molecular weight sub-indexed on formula. Spectra appear in ascending mol. wt. order, sub-indexed on number of carbon hydrogen, oxygen atoms, etc. For use with KNOWN mol. wt. or formula, UNKNOWN spectra.

Volume 2, Parts 1 and 2—Molecular weight sub-indexed on fragment ion m/z values. Spectra appear in ascending mol. wt. order. For each mol. wt, spectra are grouped in increasing m/z of the most abundant ion, UNKNOWN formula.

Volume 3, Parts 1, 2, and 3—Fragment ion m/z values of the two most abundant ions. Spectra appear in ascending order of m/z of the most abundant ion followed by that same m/z of the 2nd most abundant ion, while maintaining an ascending m/z for the most abundant ion. For use with KNOWN spectral values, UNKNOWN mol. wt. or formula.

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1442 A • ANALYTICAL CHEMISTRY, VOL. 57, NO. 13, NOVEMBER 1985

Mass spectral library search

First NBS (NIH) data base published in 1978 allowed retrieval via modem

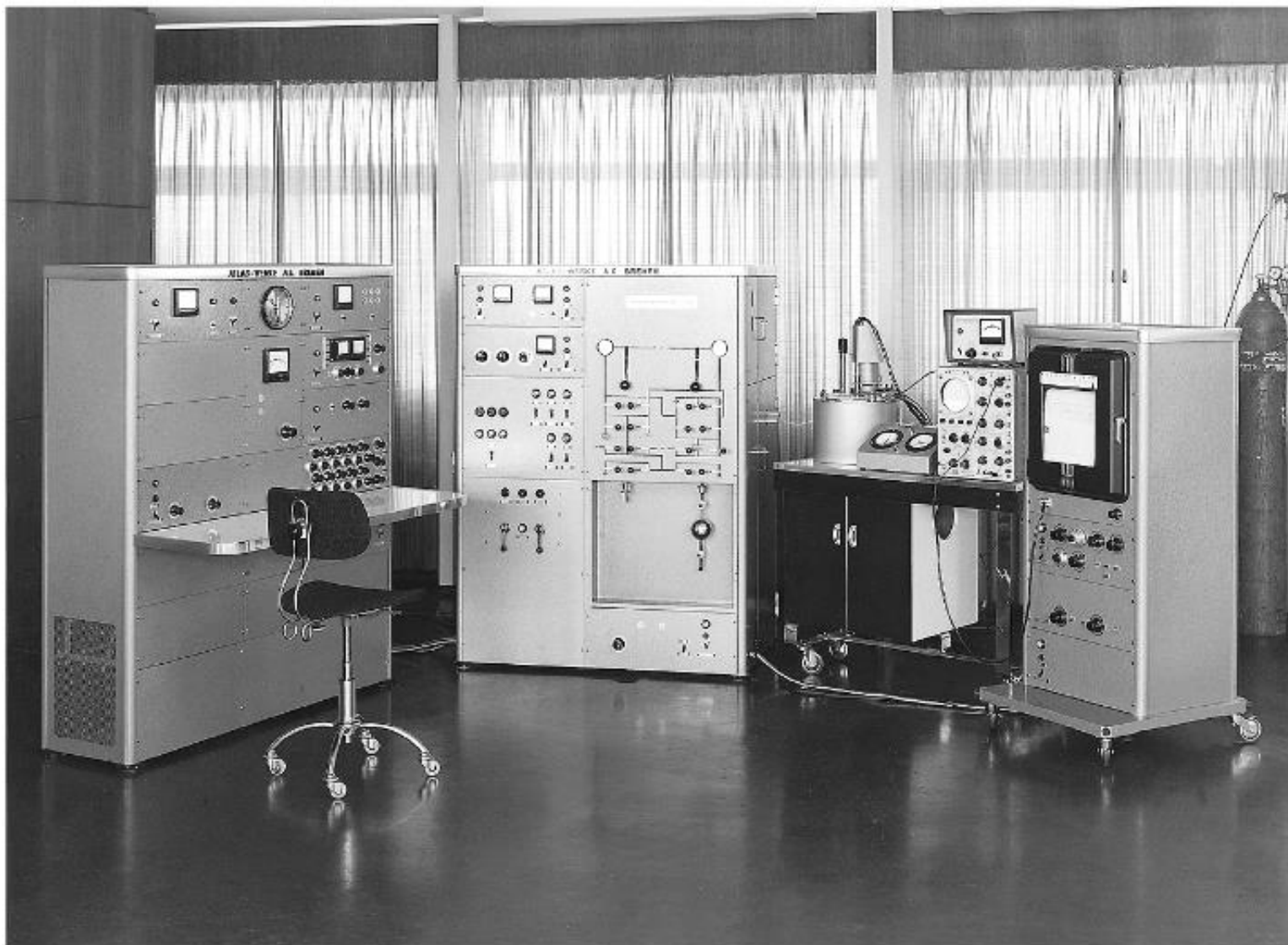
4. Eight Peak Index of Mass Spectra , 1st ed. (Atomic Weapons Research Establishment, 1970)	Mass Spectrometry Data Centre*	17,124	Examine spectra for obvious numerical errors	Maximum of three listed for spectra obtained under the most dissimilar conditions	Computer-readable version of compilation available
5. Eight Peak Index of Mass Spectra , 2nd ed. (Atomic Weapons Research Establishment, 1974)	Mass Spectrometry Data Centre*	31,101	Examine spectra for obvious numerical errors	Maximum of three listed for spectra obtained under the most dissimilar conditions	Computer-readable version of compilation available
6. Registry of Mass Spectral Data (3 volumes) (Stenhagen, Abrahamsson, & McLafferty, 1974)	Wiley-Interscience	18,806	Automated error checking and evaluation	List quality duplicates	Search algorithms developed for collection at Cornell
7. National Standard Reference Data Series (U.S. National Bureau of Standards) NSRDS-NBS-63: EPA/NIH Mass Spectral Data Base (5 volumes) (Heller & Milne, 1978)	U. S. Government Printing Office	25,556	Automated error checking and evaluation	Duplicate spectra culled	Interactive via modem connection
8. EPA-NIH Mass Spectral Data Base , Supplement 1 (Heller, Milne, & Gevantman, 1980)	U. S. Government Printing Office	8,807	Automated error checking and evaluation	Duplicate spectra culled	Interactive via modem connection
9. Eight Peak Index of Mass Spectra , 3rd ed. (Atomic Weapons Research Establishment, 1983)	Mass Spectrometry Data Centre*	66,720	Automated error checking and evaluation	Maximum of three listed for spectra obtained under the most dissimilar conditions	Computer readable version of compilation available



My first modem installed in 1990 had a bit rate of 56 kbit/s!

5. THE BEGINNING OF HYPHENATED TECHNIQUES (GC-MS)

The beginning of hyphenated techniques (GC-MS)
MAT CH4 (launched 1958) – The GC was regarded as curiosity



1967
> 400 units installed
Applications
Coffee aroma
Perfumes
Cigarette smoke
MAT expanded

GC-CH4
Launch atACHEMA as
curiosity

Picture from:

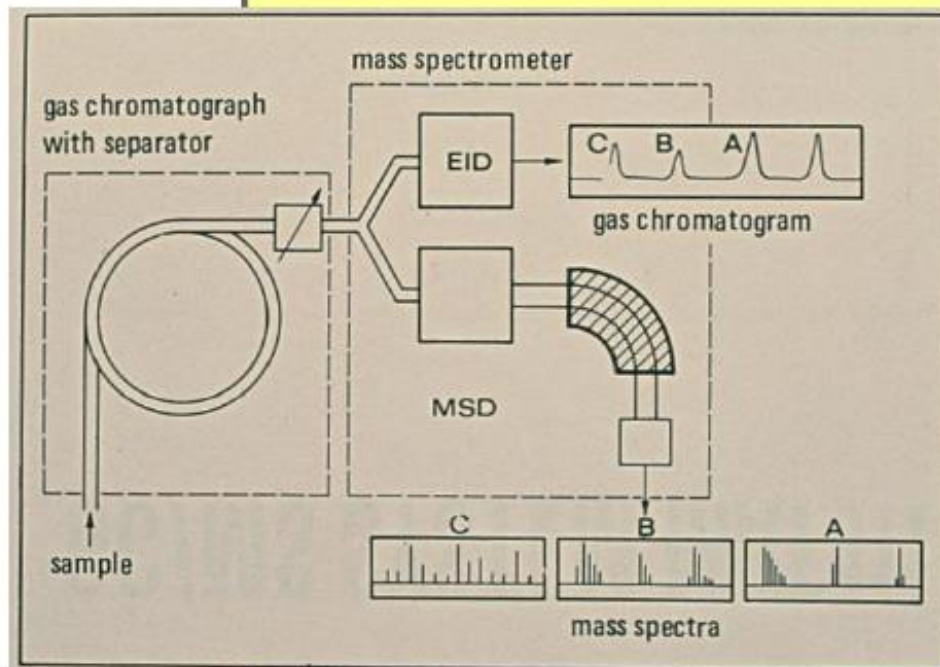
http://apps.thermoscientific.com/media/SID/IOMS/PDF/niagara2011/1_Huebschmann_History_of_MS_in_Bremen.pdf

The beginning of hyphenated techniques (GC-MS)

MAT 111 Gnome: first routine GC-MS with magnetic sector (1971)



- Resolution **1 000**
- Single focussing



- GC-MS sensitivity specs
 - **30 ng** Methylstearate for a full spectrum
 - On Varian Aerograph packed column
 - 2 detectors EID (chro) and MSD (spectra)

Neue Empfindlichkeits-Spezifikationen

Massenbereich 1 bis 1000
Messbereich: linear und logarithmisch
Auflösungsvermögen: bis zu 1000/10% Teil
Empfindlichkeit: Aquantitative Messungen mit 0,5 bis 100 ng
Methylnol, löslich in die Säule, oder 2-µg/ml Chloroform bei
Grenzauflösung



GC/MS-System **MAT 111** =GNOM=

Picture from:

http://apps.thermoscientific.com/media/SID/IOMS/PDF/niagara2011/1_Huebschmann_History_of_MS_in_Bremen.pdf

The beginning of hyphenated techniques (GC-MS) MAT 112 – GC/HRMS used for doping control

Anal Chem 46 (1976) 310A:

Varian MAT Mass Spectrometry in Action Innsbruck 1976



For the second time in the history of the Olympic Games the GC/MS technique has been applied among other safeguards to assure fair competition. Again, a Varian MAT GC/MS system was chosen to prevent the use of such drugs which are against the regulations of the International Olympic Committee (IOC). Every day, urine samples selected at random from the athletes were screened by GC and thin layer chromatography. "Suspicious" samples were subject to identification by means of the Varian MAT 112 GC/MS system. Of all analytical methods only the unique GC/MS technique allows most effectively the unambiguous identification of organic compounds especially the commonly used drugs. Generally, all peaks detected by GC analysis belong to normal metabolic products.

MS is the only method to make sure that none of the GC peaks indicates the presence of a drug listed by the IOC.

The specificity of the GC/MS technique makes it a very powerful method for the solution of such chemical problems involved in legal matters.

For more information about the entire Varian MAT GC/MS system line of instruments and what they can do to help you please contact:



VARIAN MAT GmbH
Postfach 14 40 62
2800 Bremen 10

CIRCLE 227 ON READER SERVICE CARD

310 A • ANALYTICAL CHEMISTRY, VOL. 48, NO. 3, MARCH 1976

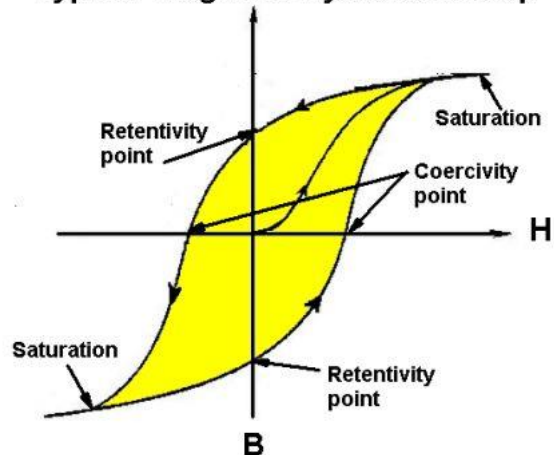
At the 1976 Innsbruck Winter Olympics, 356 drug samples are analyzed by GC and TLC. Positive samples are confirmed by GC-MS using a Varian MAT 112!



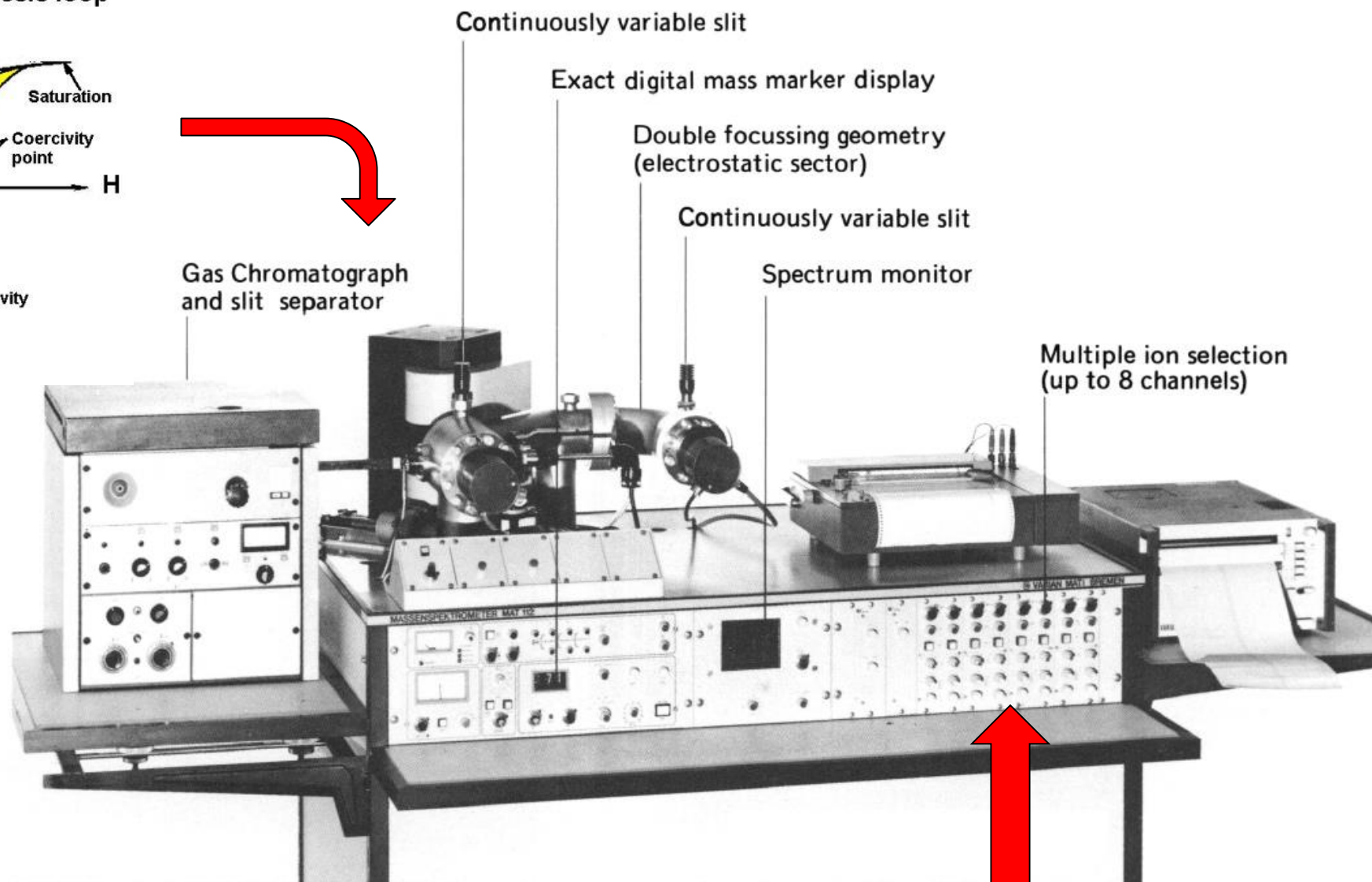
The beginning of hyphenated techniques (GC-MS)

VARIAN MAT 112 (1975): Selected ion monitoring using a double focusing sector field instrument

Typical magnetic hysteresis loop



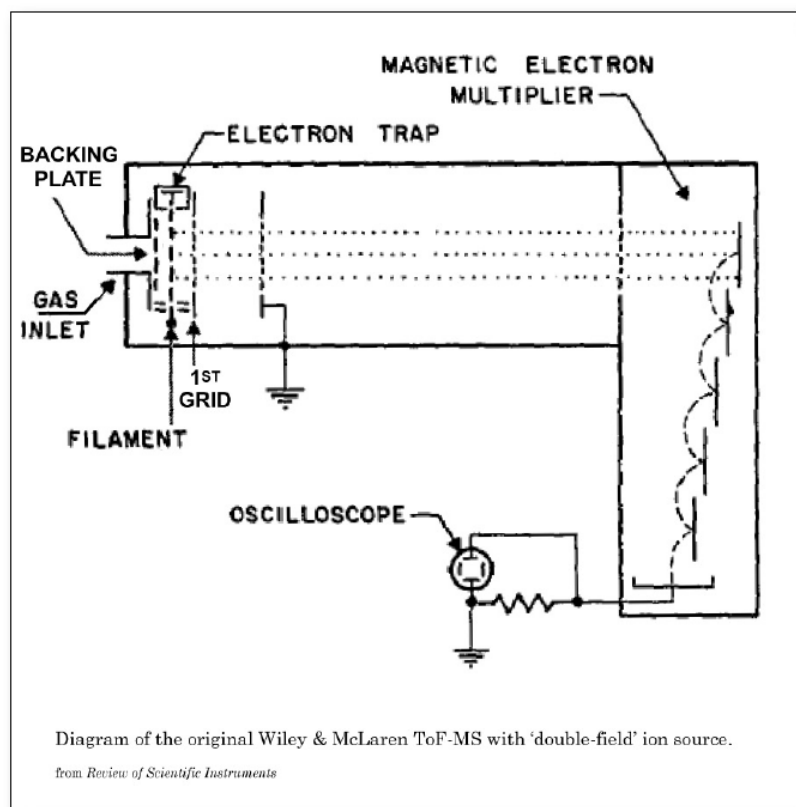
It is impossible to jump to selected ions with a magnet.



Up to 8 ions were monitored by changing the acceleration and ESA voltages

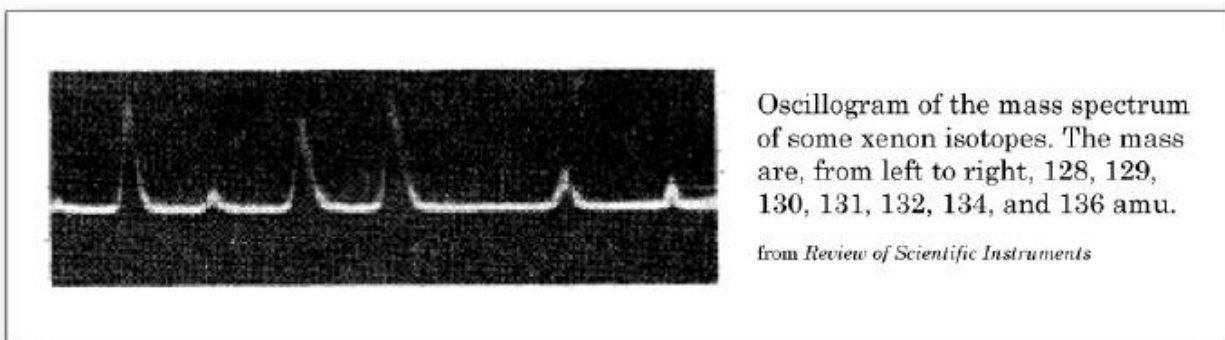
The beginning of hyphenated techniques (GC-MS)

The first commercial Time-of-Flight mass spectrometers (ca. 1956)



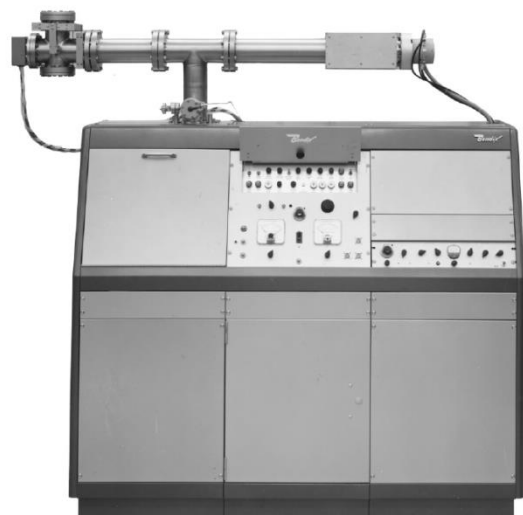
Special features of the Bendix TOF 12-101A:

- Pulsed ion source and constant acceleration voltage of 2.8 kV
- 1.7 m flight tube
- Mass range 1 to 1800
- 0.1 GHz multiplier
- Resolution approx. 700 (= 134 amu/0.2 amu)
- Recording of spectra on an oscilloscope



The picture shows the xenon isotopes.

In the early '70s sales of TOF instruments declined and production was stopped.



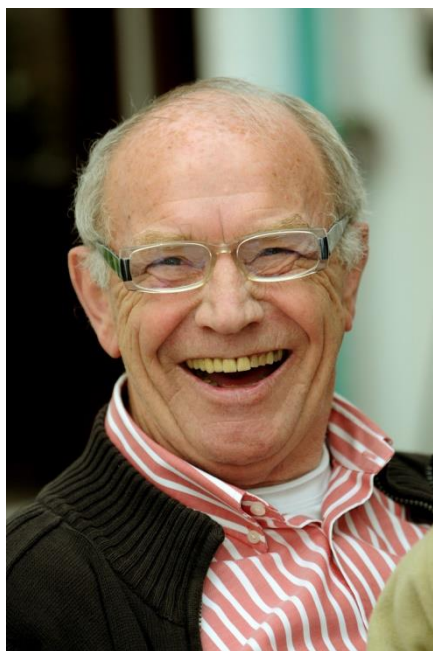
Bendix Model 12-101A; ca 1961

Bendix model 12-101A, ca. 1961

(all pictures taken from:
<http://www.asms.org/docs/history-posters/bendix-tof.pdf?sfvrsn=2>

The beginning of hyphenated techniques (GC-MS)

The Quadrupole Mass Analyser developed by Wolfgang Paul



Wolfgang Paul,
University of Bonn
Nobel Price in 1989

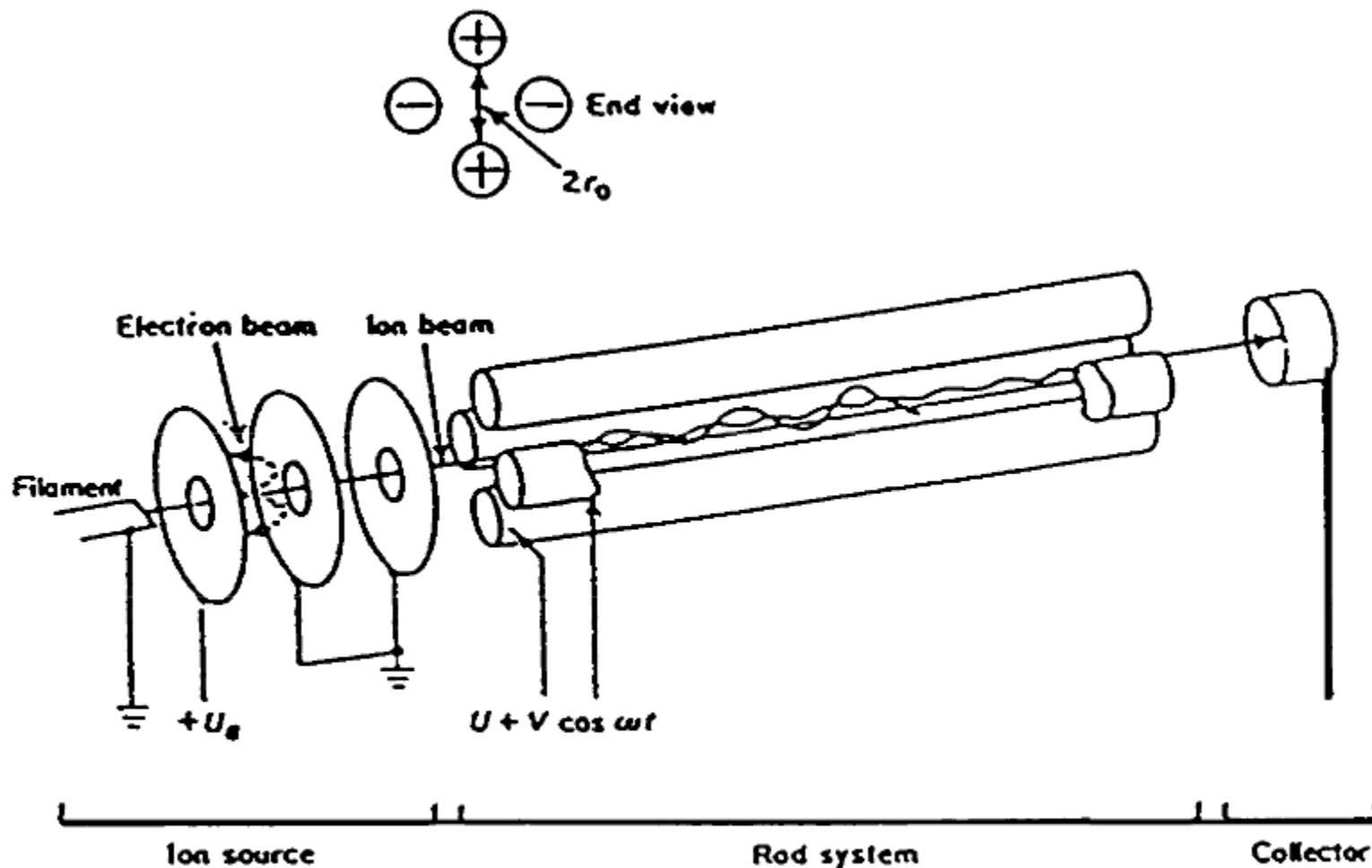


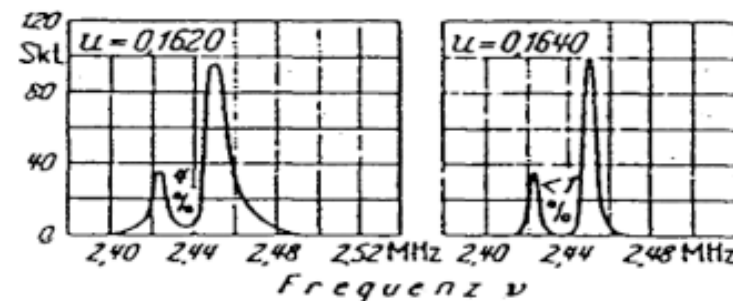
Figure 4. Schematic view of the quadrupole mass spectrometer or mass filter.

Top:

Schematic view of a quadrupole mass spectrometer

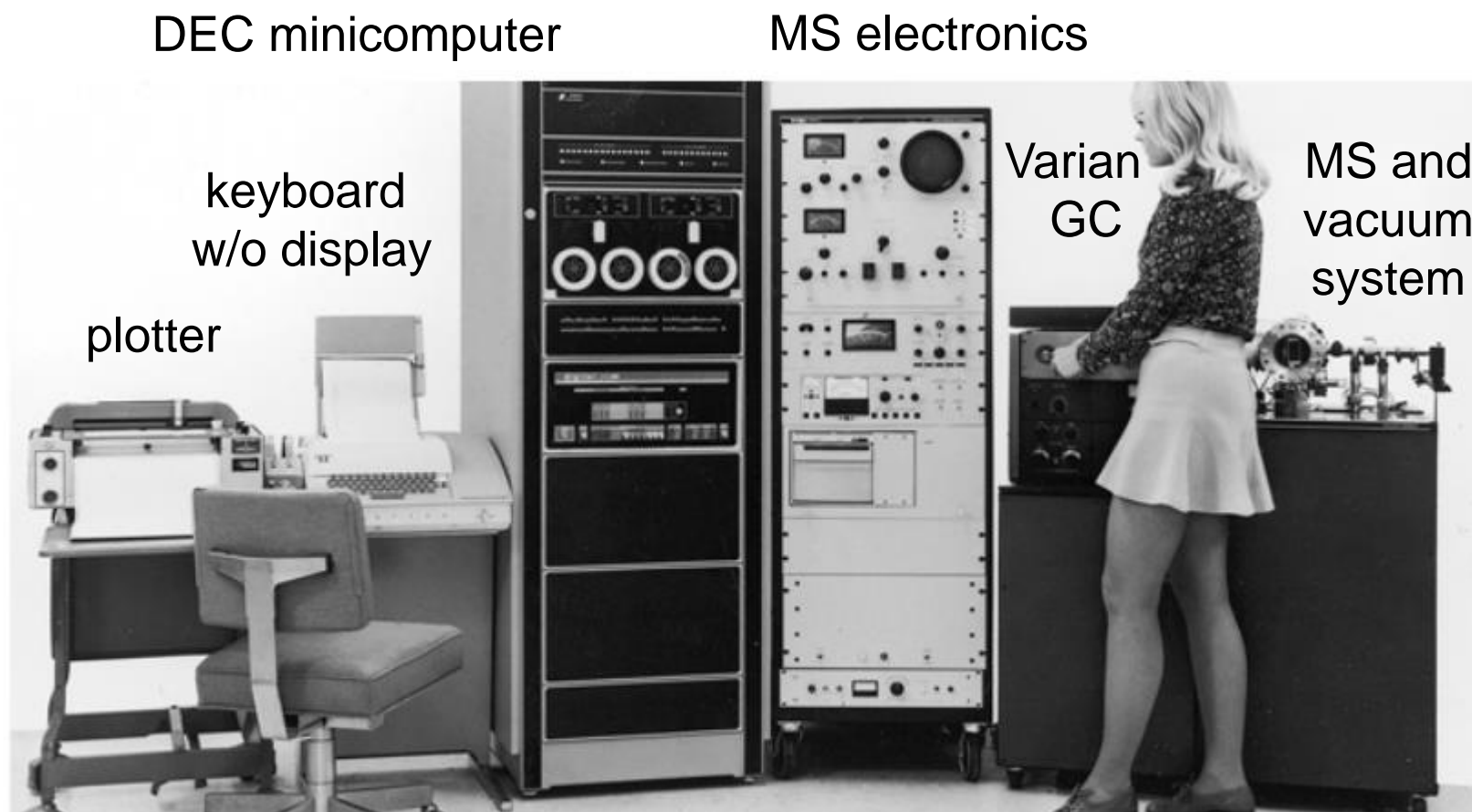
Bottom:

First mass spectrum of rubidium published by Paul in 1954 (Source: Nobel Price Lecture 1989)



The beginning of hyphenated techniques (GC-MS)

Finnigan model 1015 – the first commercial quadrupole GC-MS system launched 14 years after Paul's publication (1968)



Robert E. Finnigan, an ex-cold war engineer established Finnigan Instrument Corporation, in January 1967

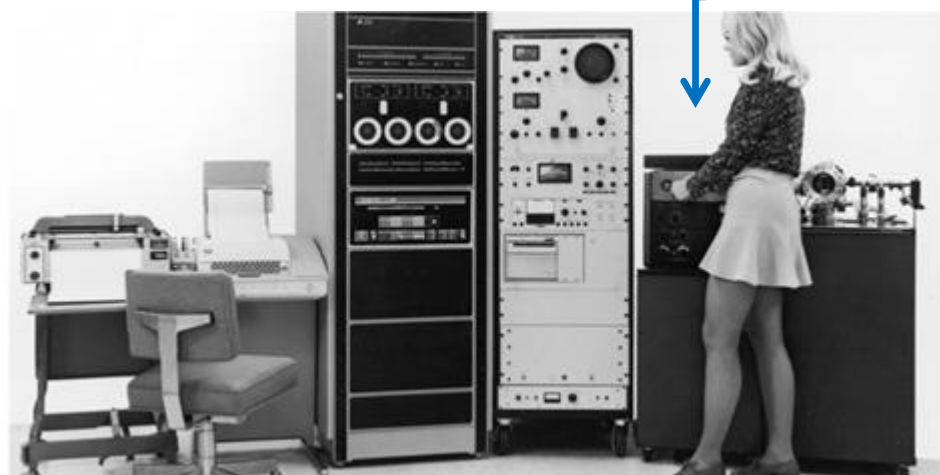
A Finnigan Instrument Corporation Model 1015 GC/MS/DS. From left to right: a minicomputer from Digital Equipment; part of the quadrupole mass spectrometer; the remainder of the mass spectrometer electronics console and gas chromatograph. Image courtesy of Robert Finnigan.

Price: 100,000 \$

(Source: <https://littlemsandsailing.files.wordpress.com/2015/03/finnigan-1015-bob-finnigan.pdf>)

6. GC- AND LC-MS INTERFACES

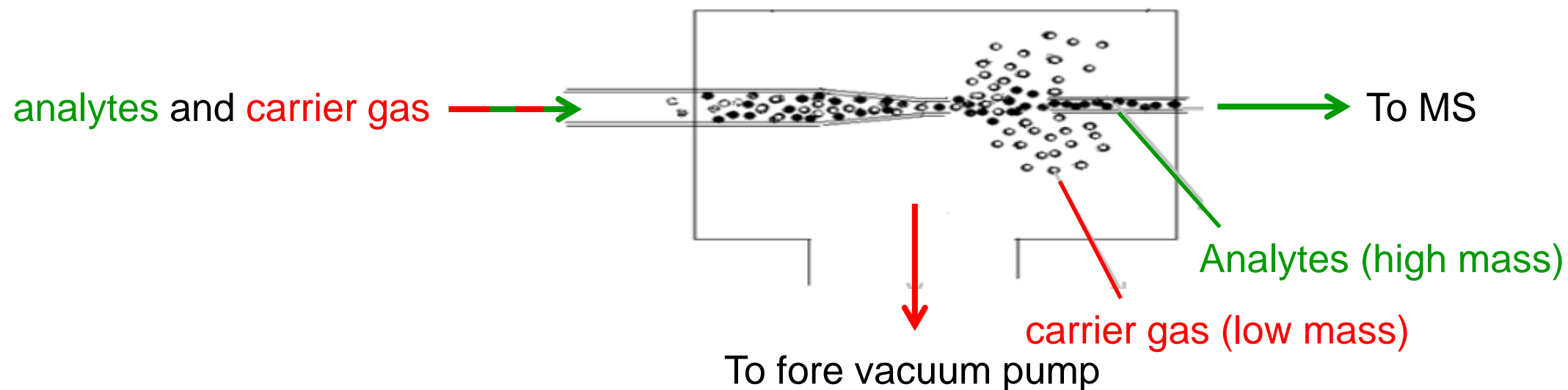
Interfacing a Varian Aerograph with packed columns to the finnigan model 1015



Varian Aerograph:
Typical column flow from packed column:
> 20 ml/min

Finnigan 1015 MS:
Typical pumping speed was 10% of
modern instruments

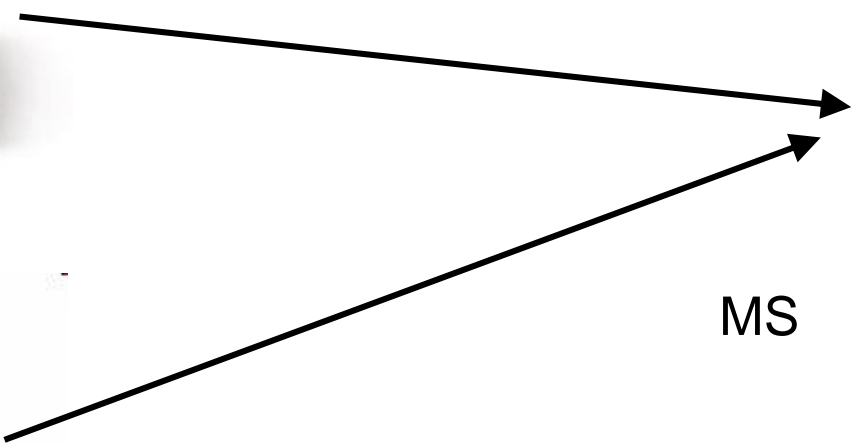
Most often used:
The **Ryhage jet separator**



Challenges of combining LC to MS (compared to capillary GC-MS)

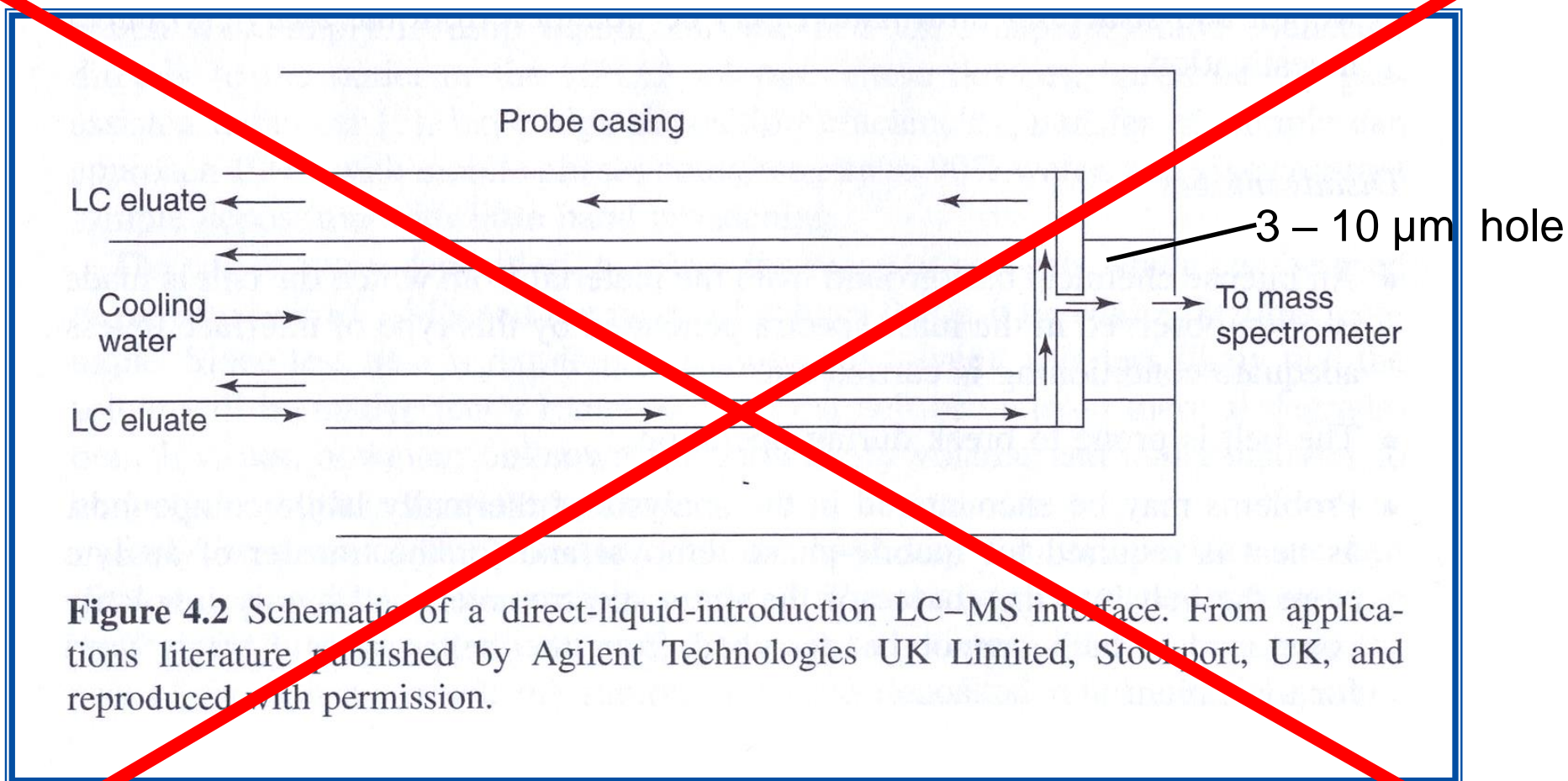


Molecular mass of mobile phase: 2 amu (H_2) or 4 amu (He)
Purity of mobile phase: 99.999%
Additives to mobile phase: no
Gas flow per minute: 1-5 mL
EI ionization: possible



Molecular mass of mobile phase: ≥ 32 amu (CH_3OH)
Purity of mobile phase: $< 99\%$
Additives to mobile phase: yes (salts)
Flow rate of liquid: $> 100 \mu L/min$
Resulting gas flow per minute: > 70 mL (up to 1200 mL/min)
EI ionization: impossible in the presence of solvent

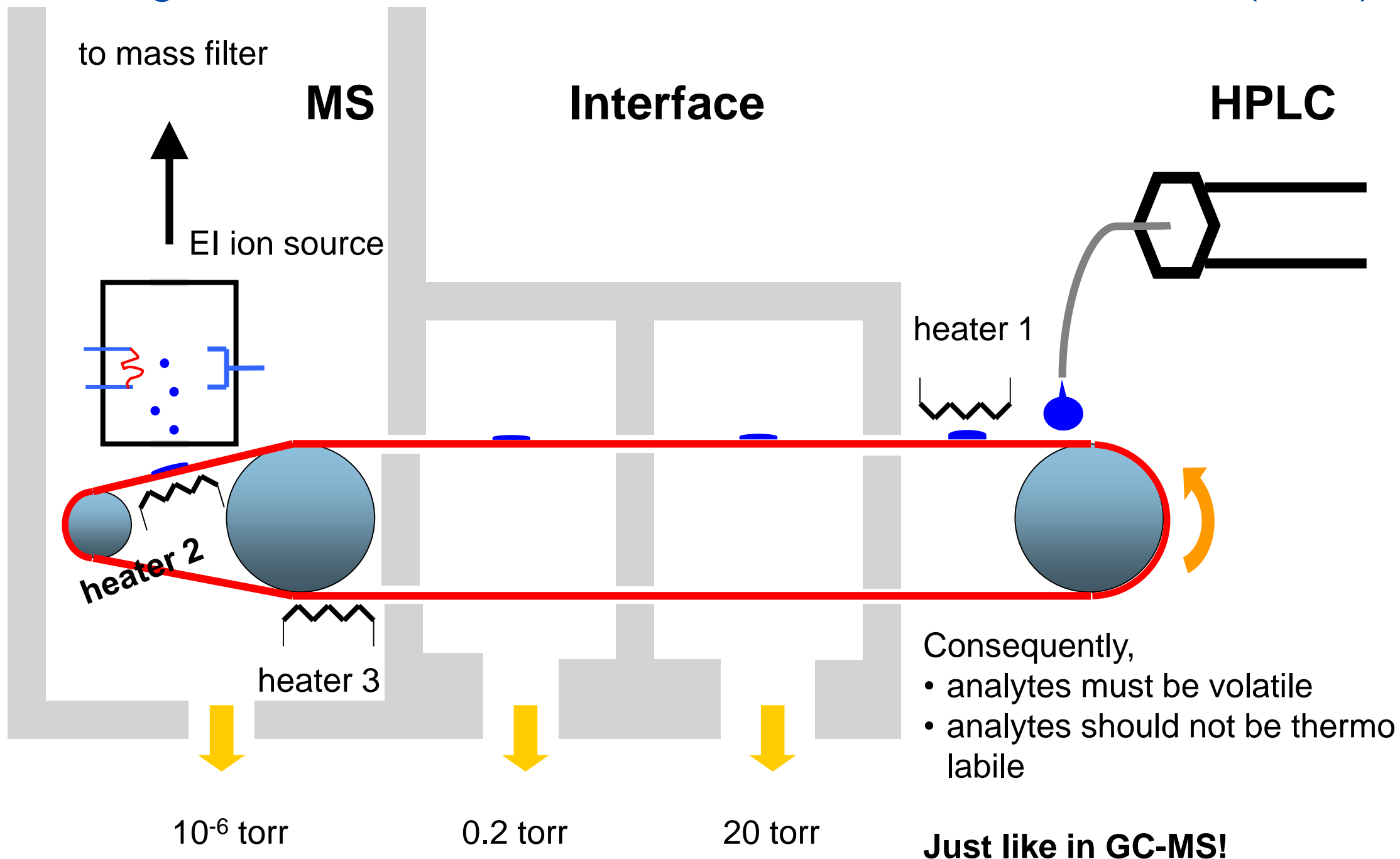
Direct liquid injection: Never used in trace analysis



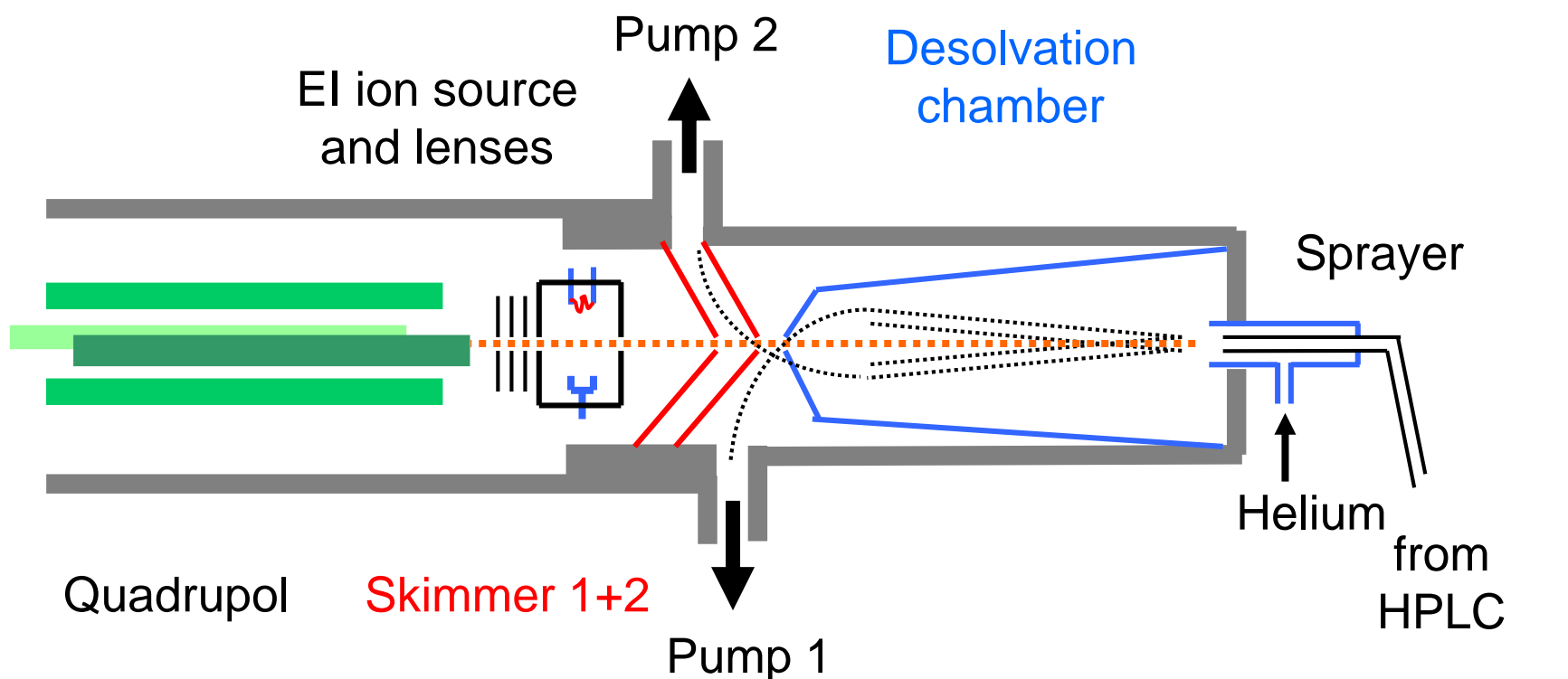
Developed by Tal'Rose et al. in the USSR and by McLafferty in the USA.

Was commercially available from Hewlett-Packard

Moving belt interface – The 1st commercial LC-MS interface (1977)



Particle beam interface: The jet separator for liquids (1984)



Consequently, analytes

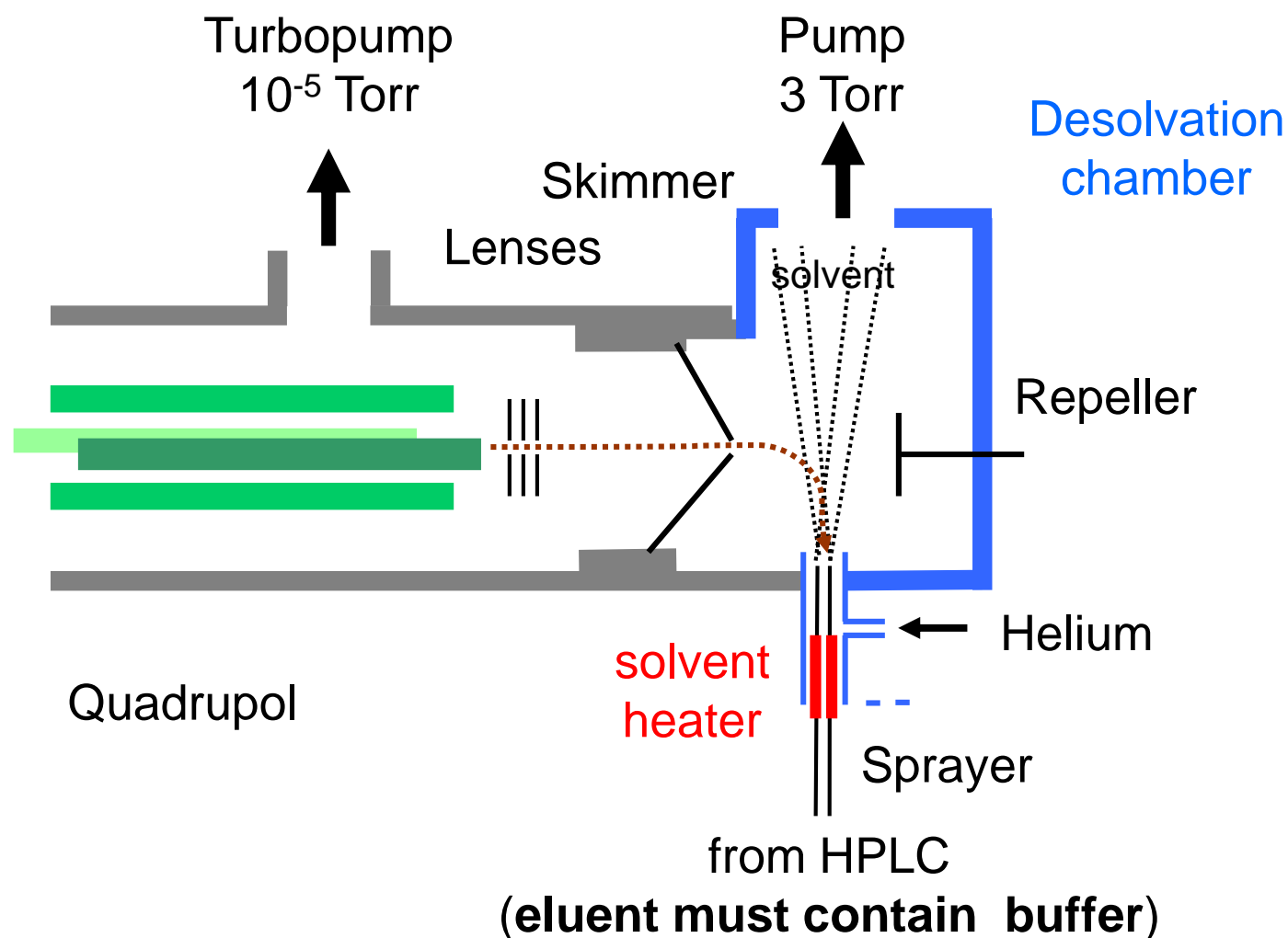
- must **not** be volatile
- **but** must have significant higher mass than solvent

Main problem: many analyte molecules are lost; low sensitivity

HP 5989 MS ('Engine')



Thermospray: Halfway to atmospheric pressure ionization

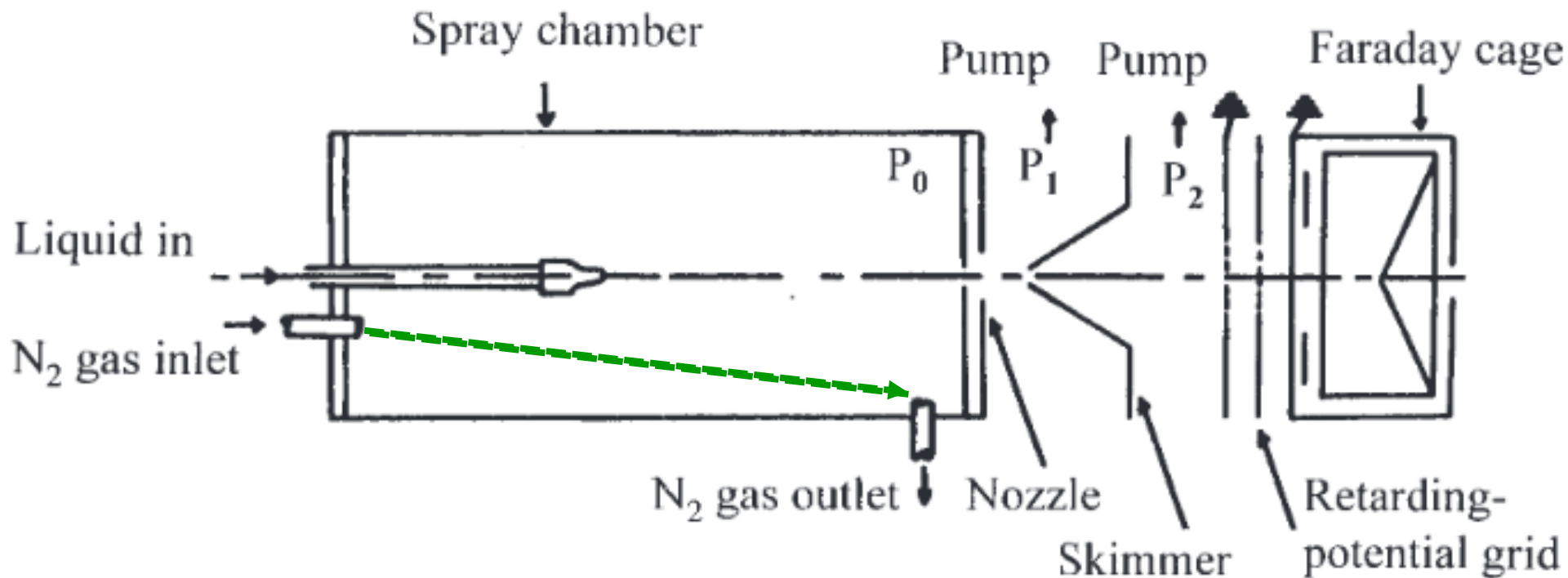


Main problem: analyte molecules must form adducts with buffer ions as NH_3 (and solvent should not)

HP 5989 MS ('Engine')



The first electrospray ionization experiment published by Malcom Dole in 1968

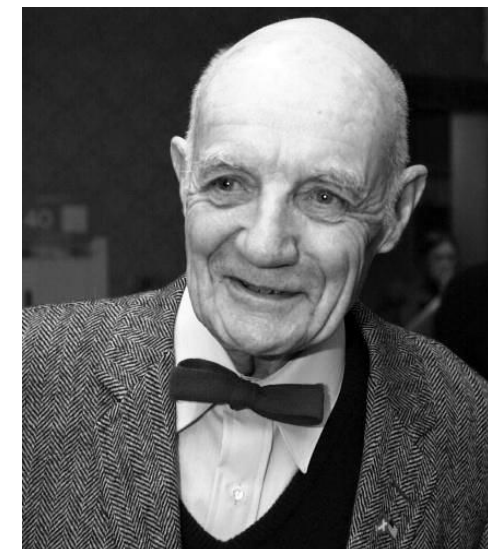
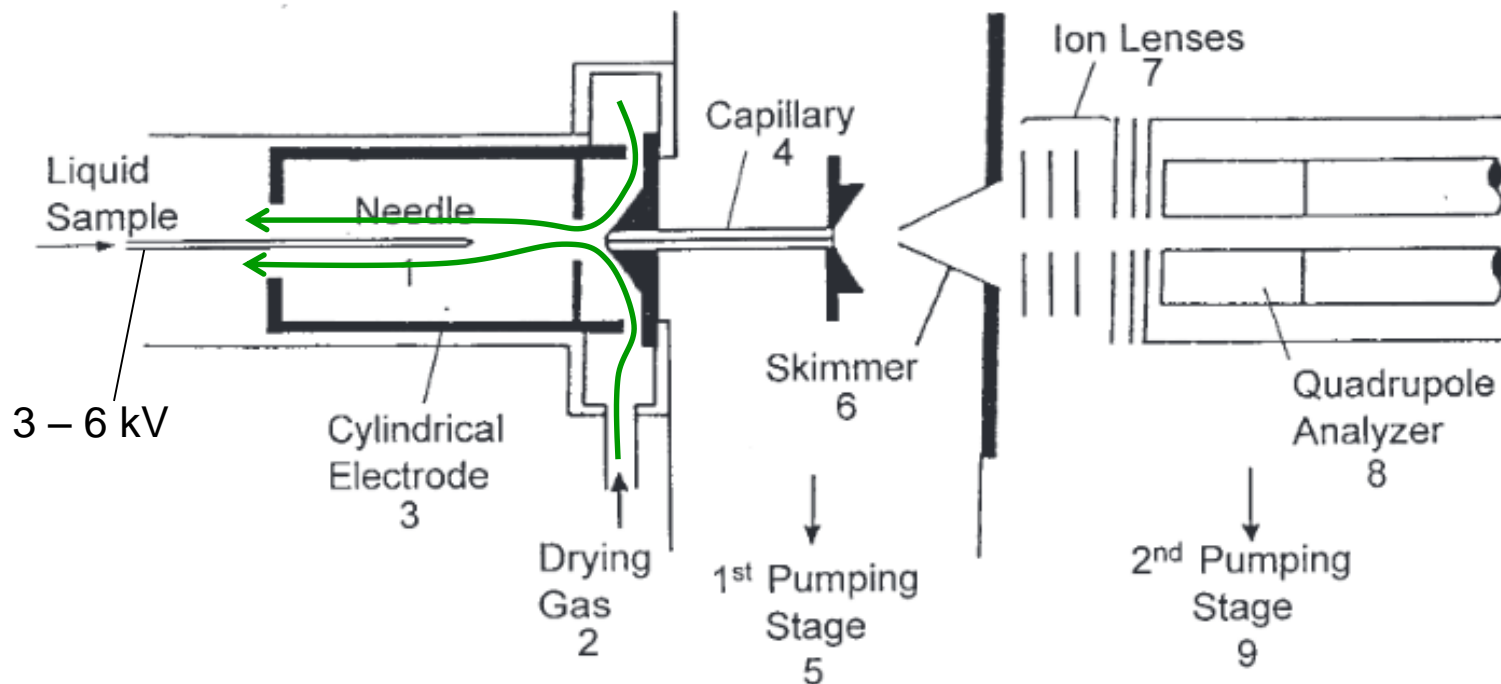


The number of ions produced was very low because of high concentration of solvent vapor at the end of the chamber.

(Picture from https://masspec.scripps.edu/mshistory/timeline/time_pdf/Fenn_ESI.pdf)

GC- and LC-MS interfaces

Fenn's electrospray ionization source with counter-current flow of nitrogen as drying gas



John B. Fenn
Nobel Prize in 2002

Schematic diagram of the second ESI-MS apparatus build by Fenn in Yale. It features the important counter current flow of drying gas

(Picture from http://www.nobelprize.org/nobel_prizes/chemistry/laureates/2002/fenn-lecture.pdf)

GC- and LC-MS interfaces

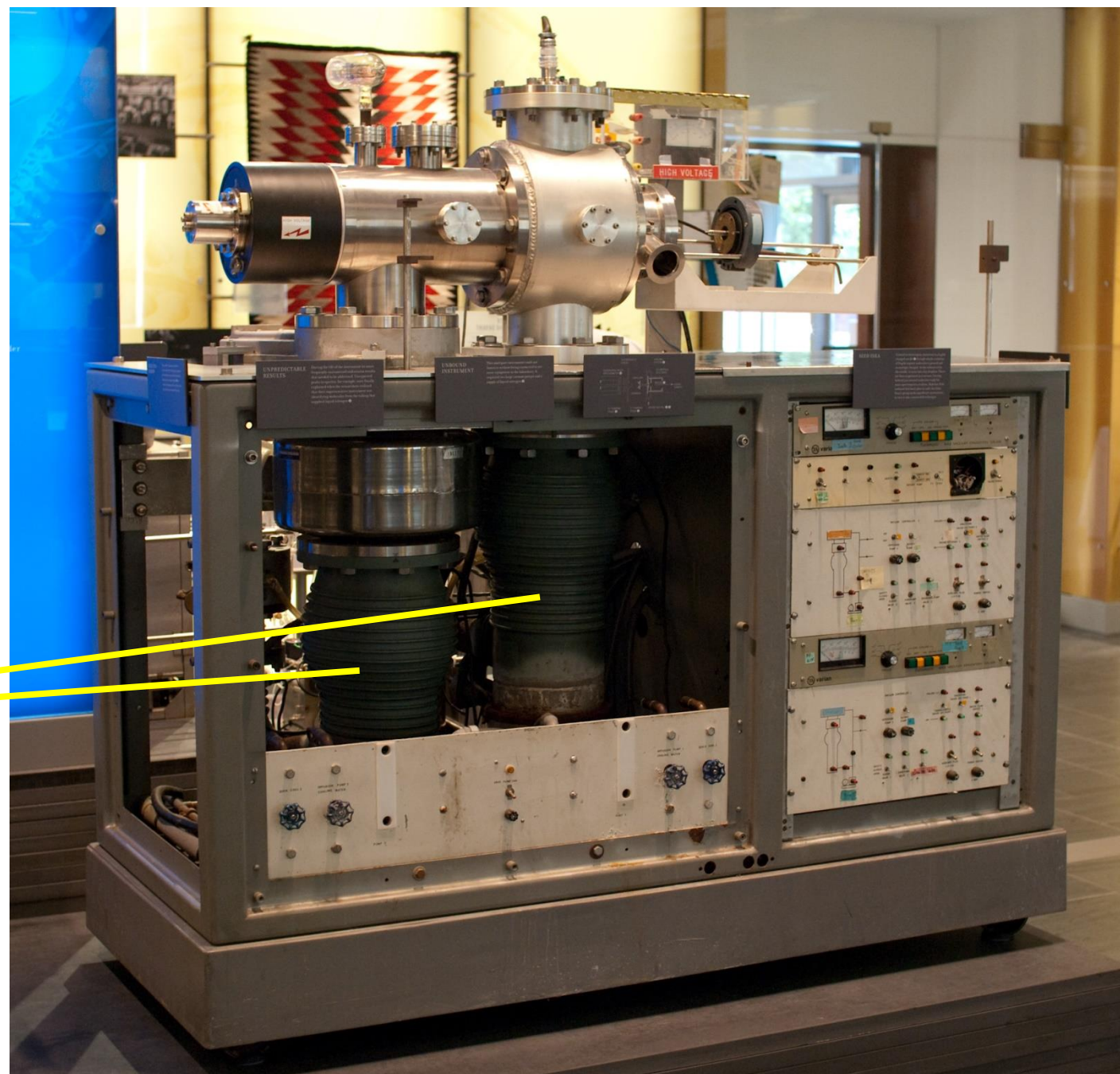
Fenn's home made MS instrument used for electrospray

Single quadrupole mass spectrometer used for John Fenn's work on electrospray ionization (1982 – 1988)

(Picture from:

https://en.wikipedia.org/wiki/History_of_mass_spectrometry)

Pretty large oil diffusion pumps



7. TANDEM MASS SPECTROMETRY

Tandem mass spectrometry

The birth of tandem mass spectrometry in 1973

Anal. Chem., 1973, 45 (12), pp 1023A–1031A

Design and Performance of a Mass-analyzed Ion Kinetic Energy (MIKE) Spectrometer

J. H. Beynon, R. G. Cooks, J. W. Amy, W. E. Baitinger, and T. Y. Ridley
Department of Chemistry, Purdue University, West Lafayette, Ind. 47907

Ion kinetic energy spectrometry allows the study of both unimolecular and bimolecular reactions and is a unique source of information on thermochemistry, molecular structure, isotopic quantitation, and reaction dynamics

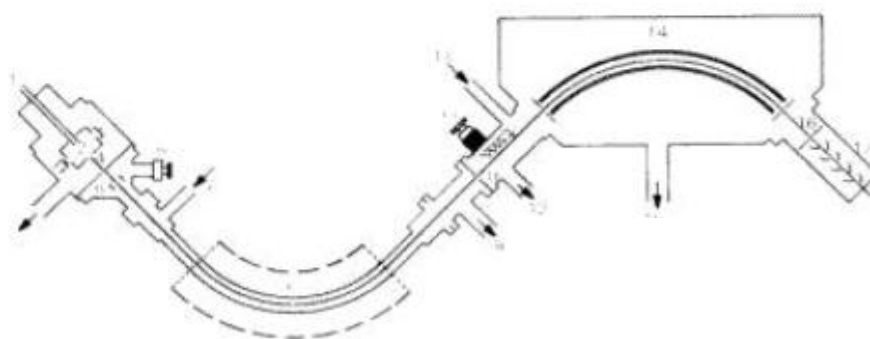


Figure 1. Ion optical arrangement used in MIKE of pumping and sample introduction ports

The double focusing mass spectrometer with BE configuration used for MIKES

Analytical determinations of a

Product ion spectrum obtained from methyl benzoate

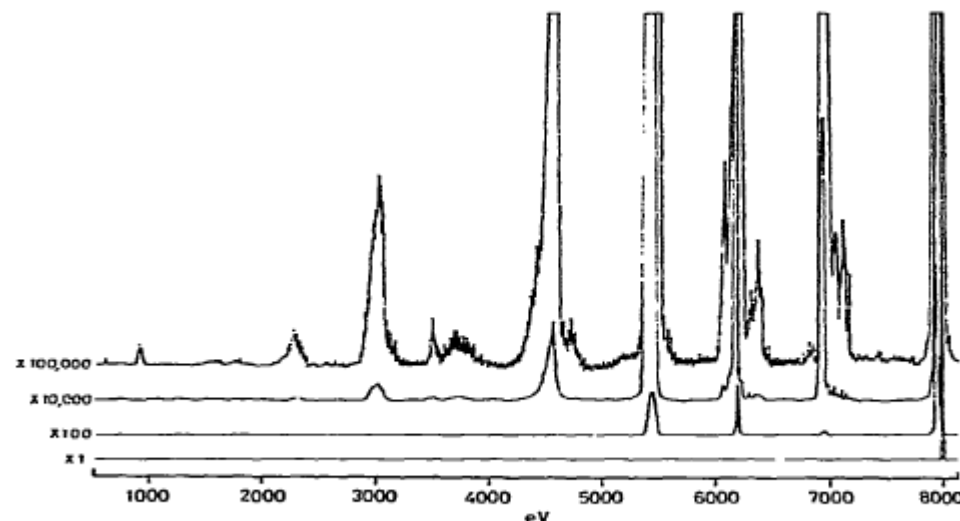
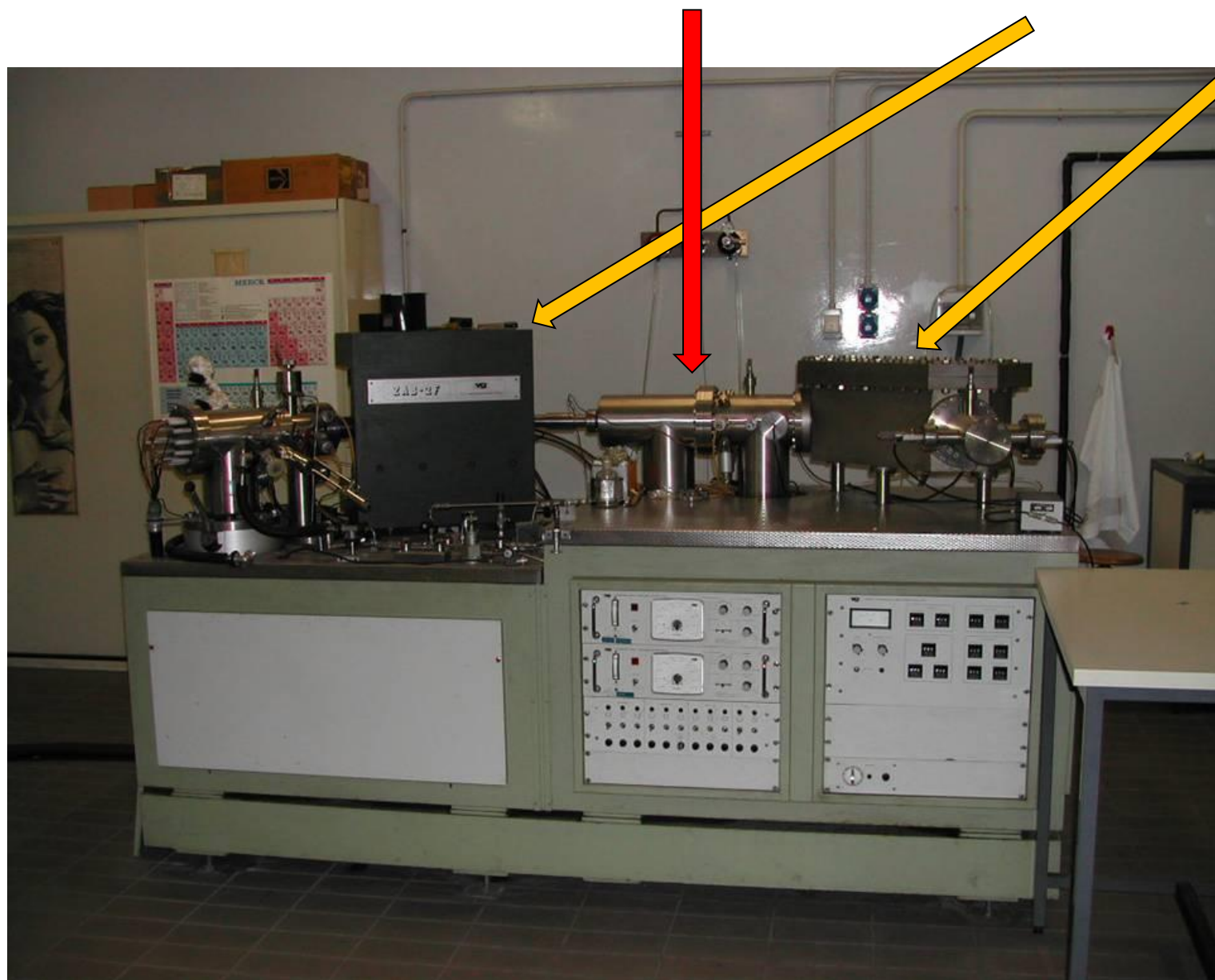


Fig. 12. A complete mass-analysed unimolecular ion kinetic energy spectrum obtained on the molecular ion of methyl benzoate.

Tandem mass spectrometry

The first commercial tandem MS/MS was introduced in 1978

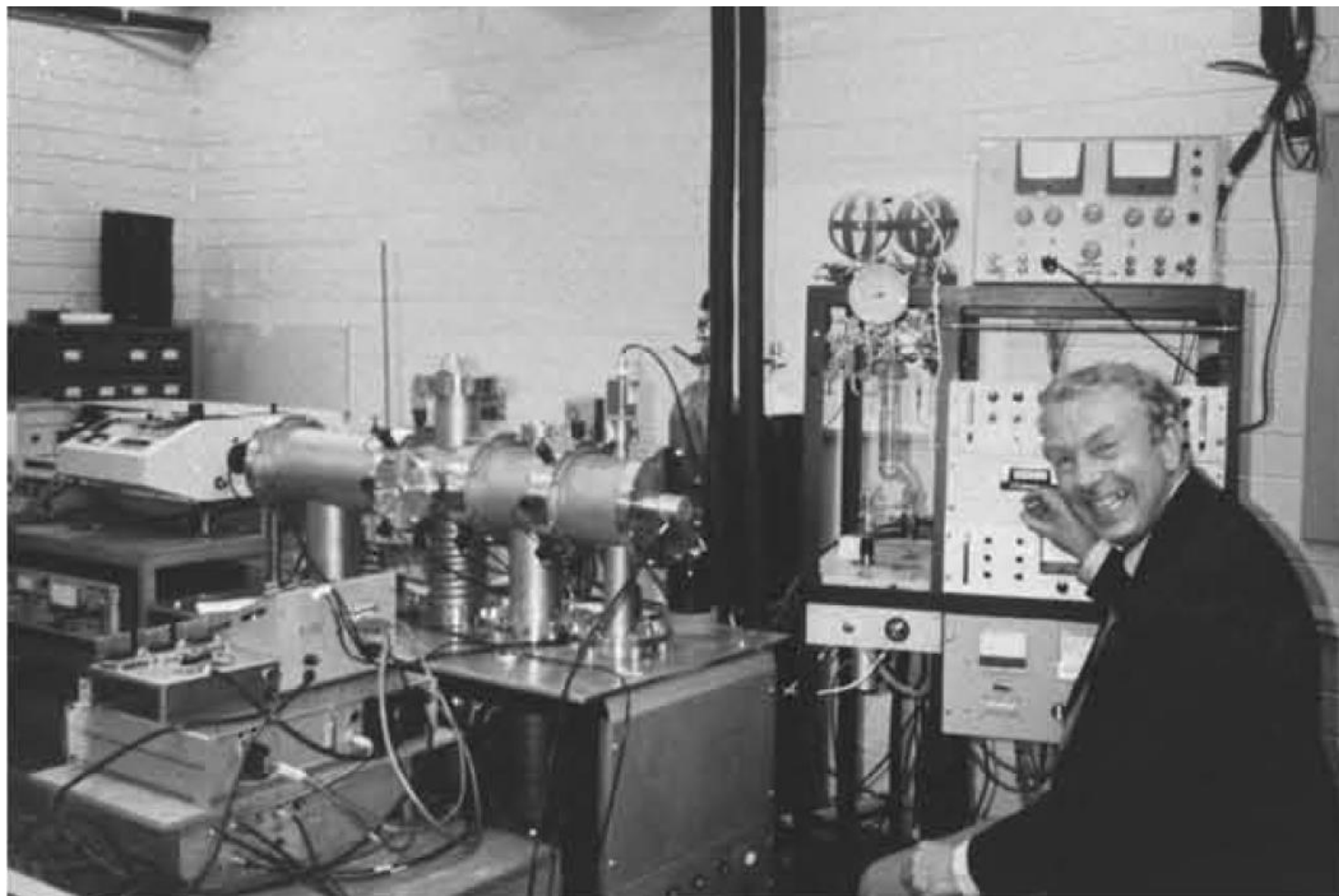
Micromass ZAB-2F with large collision cell between magnet and electrostatic analyser



The instrument was designed in co-operation with J. H. Beynon from Purdue University (USA)

Tandem mass spectrometry

The first tandem quadrupole instrument was used to study photo dissociation



J. Morrison at La Trobe University in Australia with his home made tandem quadrupole. (about 1975)

The potential of triplequats as highly selective mass analyser was recognized by Christi Enke, who added the RF only quadrupole as collision cell (published 1978).

8. WHERE THE EXPERTS ARE COMING FROM

Where the MS branches of companies are coming from?

year	Agilent	Bruker	Thermo	Sciex	Waters
2000-1995	Hewlett Packard became Agilent 1999	Bruker Daltonik GmbH		API 2000 1997	VG was aquired by Waters
1995-1990		Mobile GC-MS EM 640	Thermo Electron 1990		VG became micromass
1990-1985	HP 5989 Engine with CI/NCI			First MS/MS API III 1989	VG lauched the AutoSpec
1985-1980		Launch of MM1 (mobile MS)	Finnigan MAT 1981		
1980-1975	HP 5990 bench-top GC/MS 1976	Bruker-Franzen Analytik 1980	Quadrupole MAT 44	First MS 1978	VG introduced ZAB 2F
1975-1970	First MS with data system HP 5930/5932		First GC-MS MAT 111 Gnome		VG startedwith small MS
1970-1960	First GC 1965		Varian MAT CH 5/6 1967		Key personnel from AEI went to VG
1960-1950			MAT CH4 (400 units)		Metrovic became AEI
1950-1940			Atlas MAT founded 1947 in Bremen		Metrovick sold first MS in 1946

For further reading

A History of European Mass Spectrometry (ed. By K.R. Jennings), published by IM Publications LLP (UK), ISBN 978-1-906715-04-5

K.S. Sharma “Mass spectrometry—The early years”,
Intern J Mass Spectrom 349– 350 (2013) 3 – 8

J. Griffiths “A Brief History of Mass Spectrometry”, Anal Chem 80 (2008) 5678–5683

B A Thompson “Atmospheric Pressure Ionization and Liquid Chromatography/Mass Spectrometry - Together at Last”, J Am Soc Mass Spectrom 9 (1998) 187-193

The historical posters prepared by the American Society for Mass Spectrometry (for their 50th anniversary) found online at <http://www.asms.org/publications/historical>

Mass spectrometry - the early days

<http://www.rsc.org/Education/EiC/issues/2010May/MassSpectrometryTheEarlyDays.asp>

Origins of tandem mass spectrometry

<http://www.asms.org/docs/history-posters/tandem-ms-poster-2012.pdf?sfvrsn=2>

Thank you for listening

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Senior Fellow

Federal Institute for Risk Assessment

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Timeline (modified from Wikipedia)

1913

Thomson is able to separate particles of different mass-to-charge ratios. He separates the ^{20}Ne and the ^{22}Ne isotopes, and he correctly identifies the $m/z = 11$ signal as a doubly charged ^{22}Ne particle.[27]

1919

Francis Aston constructs the first velocity focusing mass spectrograph with mass resolving power of 130.

1922

Aston is awarded the Nobel Prize in chemistry "for his discovery, by means of his mass spectrograph, of isotopes, in a large number of non-radioactive elements, and for his enunciation of the whole-number rule."

1931

Ernest O. Lawrence invents the cyclotron.

1934

Josef Mattauch and Richard Herzog develop the double-focusing mass spectrograph.

1936

Arthur J. Dempster develops the spark ionization source.

1937

Aston constructs a mass spectrograph with resolving power of 2000.

1943

Westinghouse markets its mass spectrometer and proclaims it to be "A New Electronic Method for fast, accurate gas analysis".

1946

William Stephens presents the concept of a time-of-flight mass spectrometer.

1954

A. J. C. Nicholson (Australia) proposes a hydrogen transfer reaction that will come to be known as the McLafferty rearrangement.[28]

1959

Researchers at Dow Chemical interface a gas chromatograph to a mass spectrometer.

1964

British Mass Spectrometry Society established as first dedicated mass spectrometry society. It holds its first meeting in 1965 in London.

1966

F. H. Field and M. S. B. Munson develop chemical ionization.

1968

Malcolm Dole develops electrospray ionization.

1969

H. D. Beckey develops field desorption.

1974

Comisarow and Marshall develop Fourier Transform Ion Cyclotron Resonance mass spectrometry.

1976

Ronald MacFarlane and co-workers develop plasma desorption mass spectrometry.

1984

John Bennett Fenn and co-workers use electrospray to ionize biomolecules.

1985

Franz Hillenkamp, Michael Karas and co-workers describe and coin the term matrix-assisted laser desorption ionization (MALDI).

1987

Koichi Tanaka uses the “ultra fine metal plus liquid matrix method” to ionize intact proteins.

1989

Wolfgang Paul receives the Nobel Prize in Physics "for the development of the ion trap technique".

1999

Alexander Makarov presents the Orbitrap mass spectrometer.[29]

At the 1976 Innsbruck Winter Olympics, 356 drug samples are analyzed ...

(http://www.kawasaki-m.ac.jp/soc/mw/journal/en/2007-e12-2/01_kremenik.pdf)

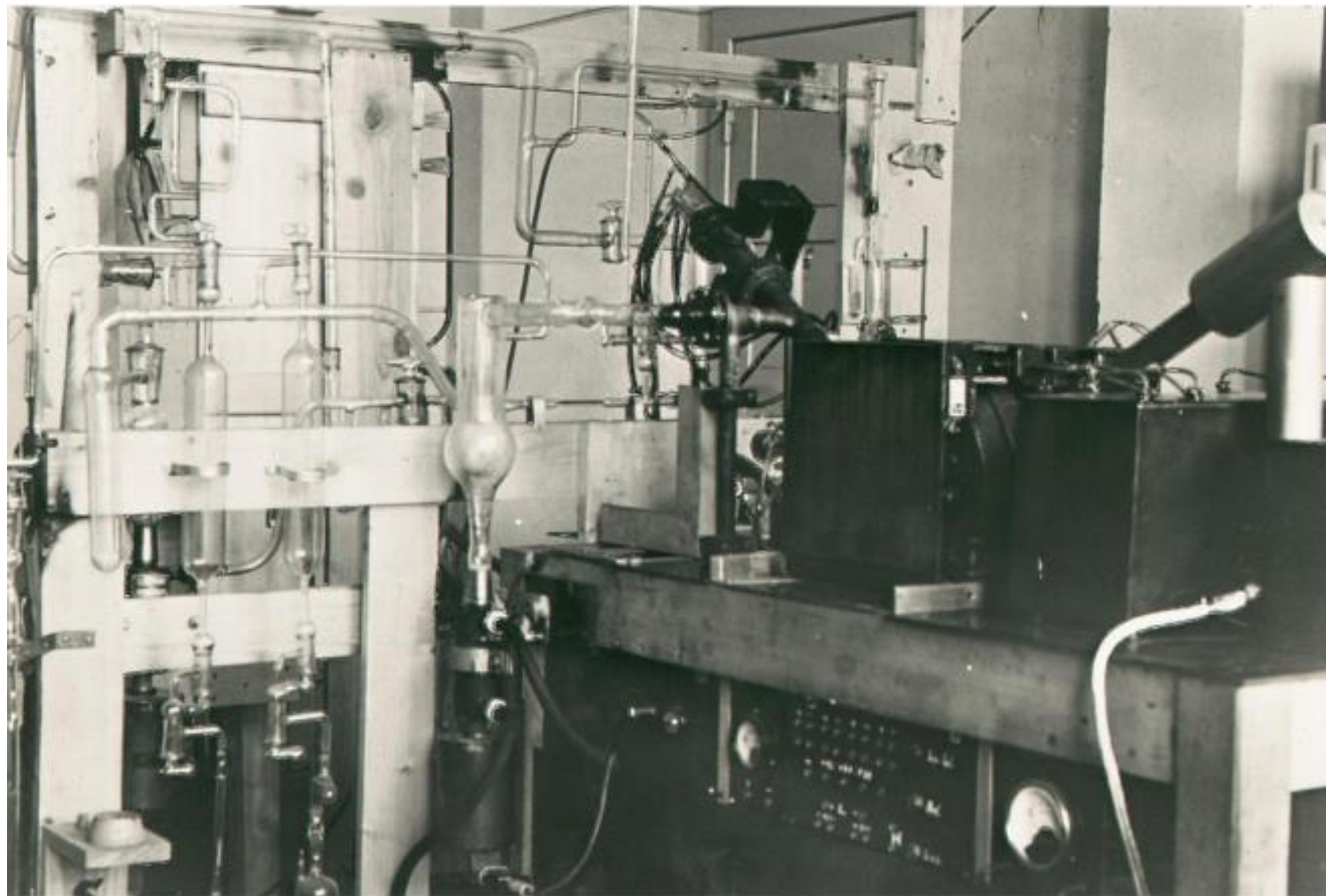
<http://pubs.acs.org/doi/abs/10.1021/ac60367a750?journalCode=ancham>

Mass spectrometry at 1965 at IAEA in Seibersdorf



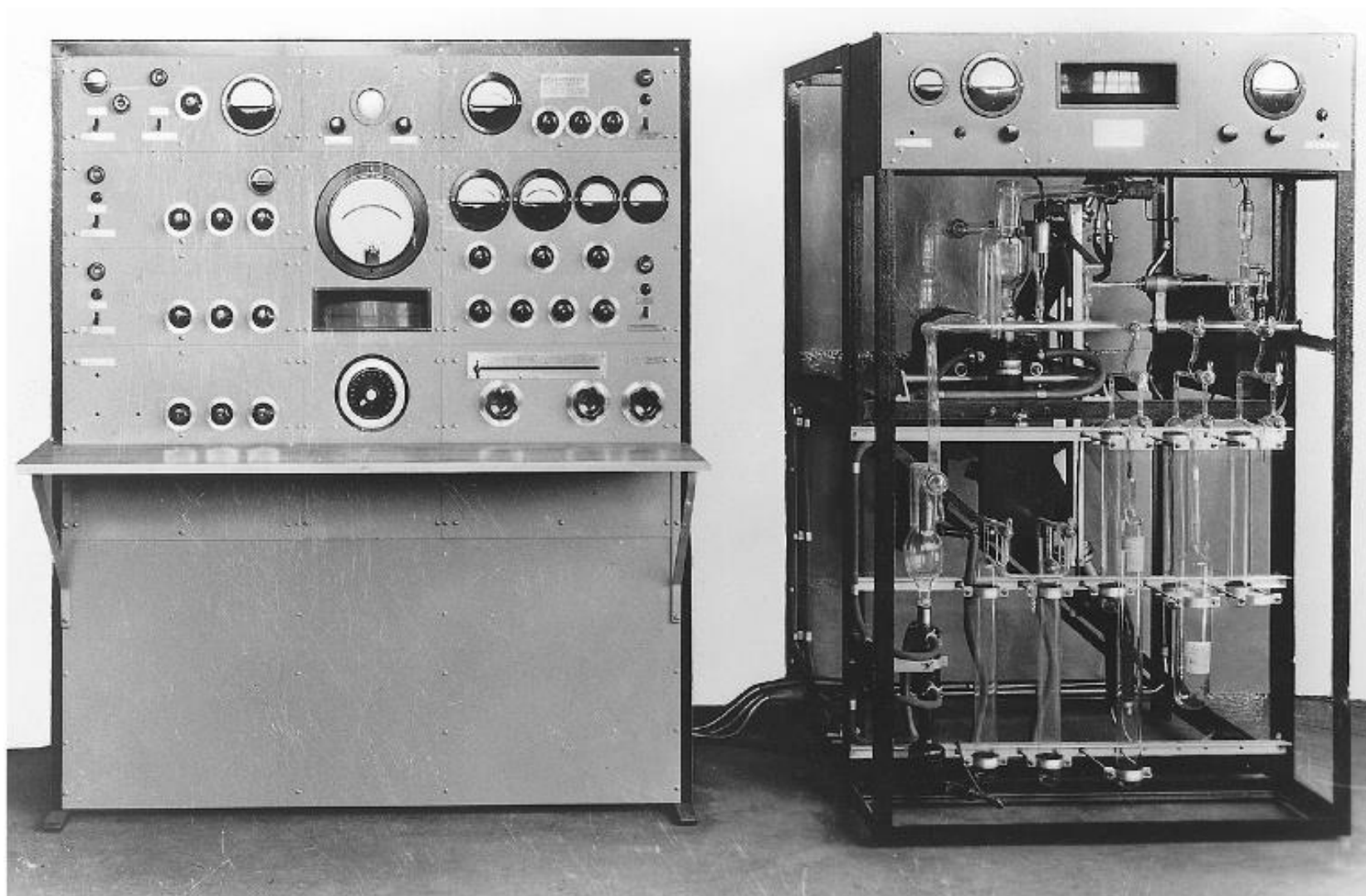
A mass spectrometer being used to find the nitrogen content of plants fed with fertilizer, photographed at the International Atomic Energy Agency (IAEA) in 1963. Photo by courtesy of International Atomic Energy Agency (IAEA), published on Flickr under a Creative Commons (CC BY-SA 2.0) licence

The beginning of mass spectrometry in Bremen in 1948



First prototype of a mass spectrometer build by Jenckel in a cellar of a hospital.

CH3 – The first commercial product from Atlas-MAT (1952)

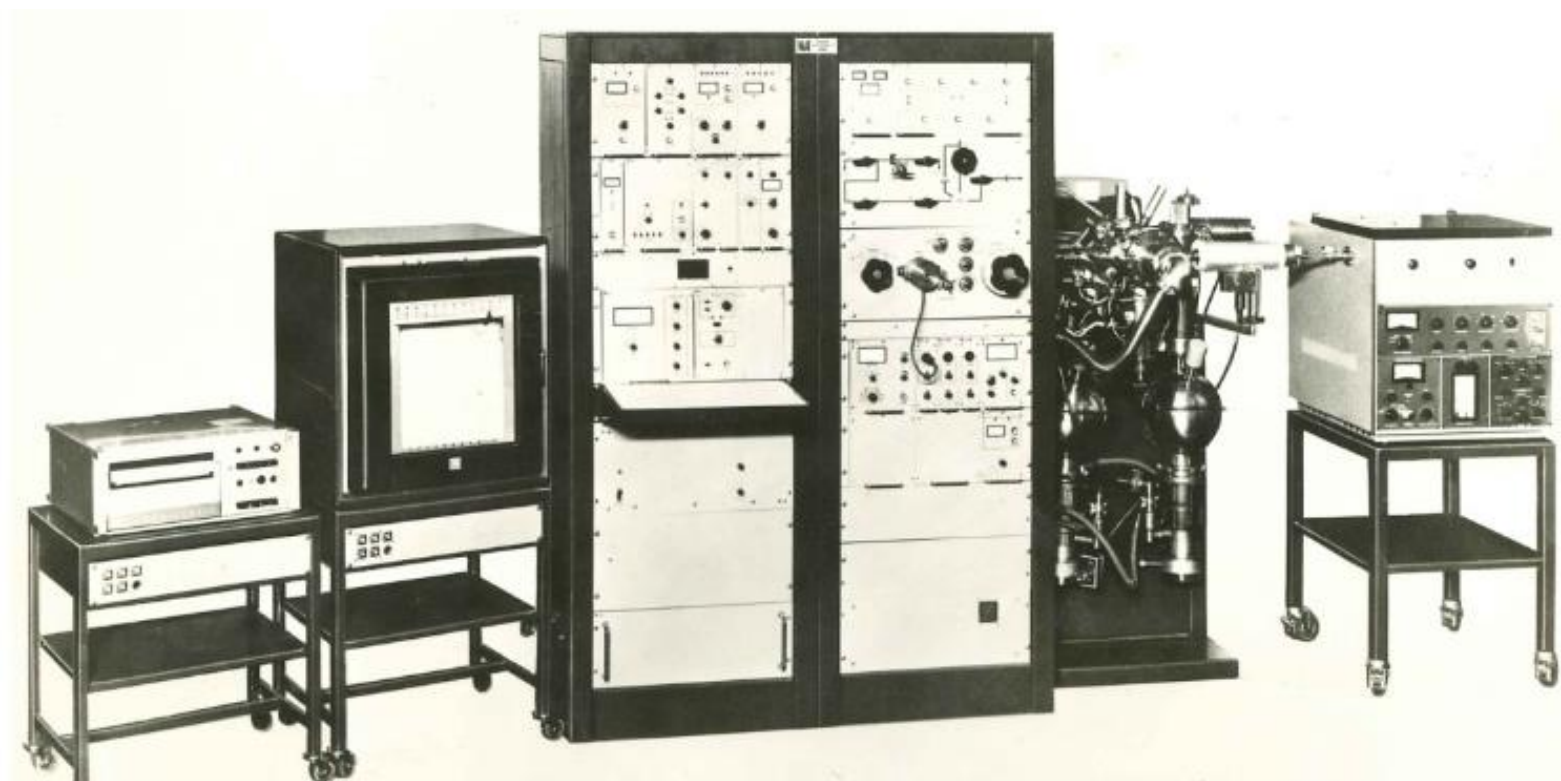


1952
Exhibited at the
Achema show in
Frankfurt

Resolution **300**

1954
Sales volume
100.000\$ per
year.
Not enough for a
division with 20
people

MAT CH5/CH6 (1967): first time controlled with transistors and without radio bulbs



For routine analysis
Single focussing
GC coupling
Double focussing
optional

Resolution
> 10 000
> 30 000 CH5-DF

MAT 44 (1977) First Quadrupole MS from MAT

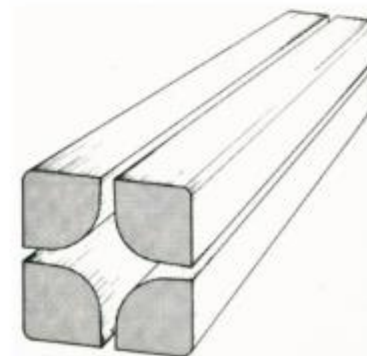
MAT



Resolution
> 4 000 (10% val.)
@ 1166/1167 Da

Sensitivity
1 ng Me-Stearate
S/N 20:1
(CI 1 ng BZP 50:1)

Data System
SS 200
64 k memory
4.7 Mb Dual Floppy
Disk storage



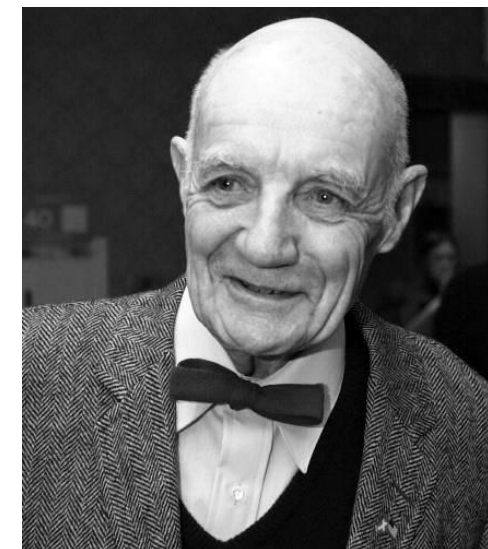
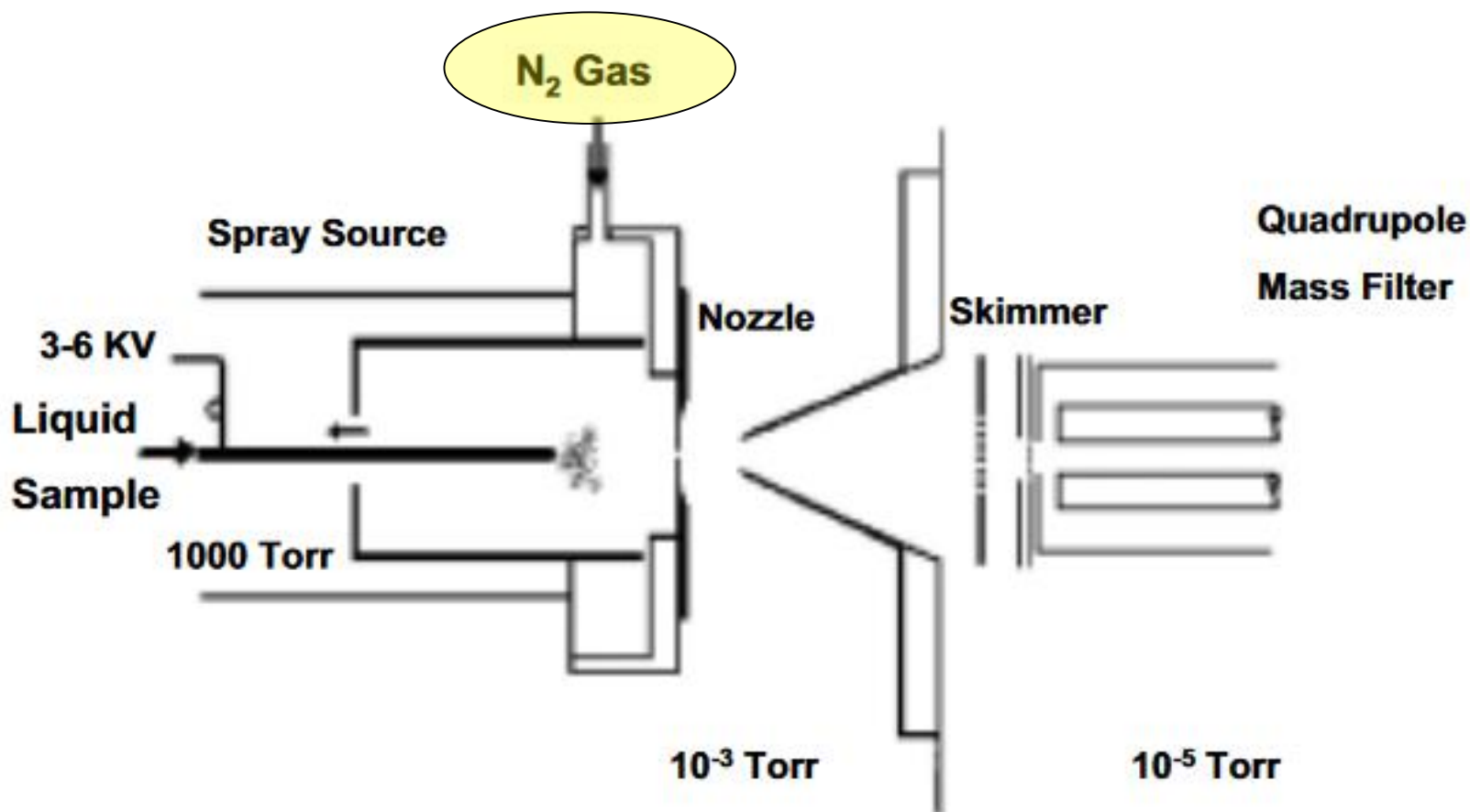
Mass spectrometer at late 1940s



© National physical laboratory

GC- and LC-MS interfaces

Fenn's first electrospray ionization source (with weak counter-current flow of gas)



John B. Fenn
Nobel Prize in 2002

The first electrospray ion source built at Yale University. Sample solution was sprayed from the hypodermic needle into a counter-current flow of dry nitrogen, which provided the needed thermal energy.

(Source: http://www.nobelprize.org/nobel_prizes/chemistry/laureates/2002/fenn-lecture.pdf)

Past, present and future of LC-MS

Step 1:

Development of selective interfaces or ionization techniques



VG 7070