Ionization schemes and techniques in FT- ICR MS: From commercial towards customized solutions

EU_FT-ICR_MS
2nd Advanced User School
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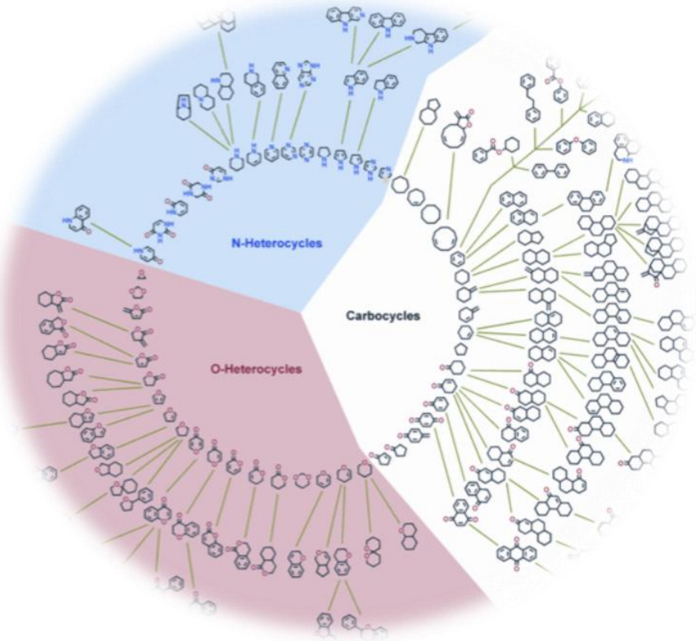
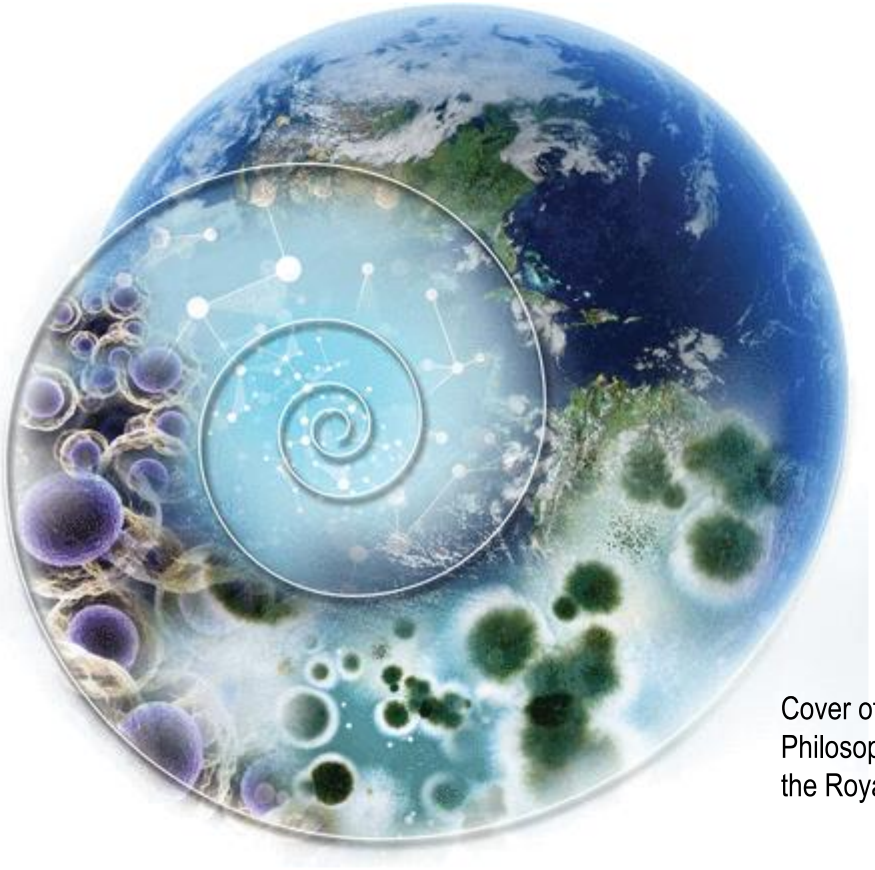
Outline

- **Introduction and Motivation**
    - Chemical Space, Selectivity of Ionization Techniques, Overview of Schemes and Concepts
- **Vacuum Ionization**
    - Electron Impact and Photoionization
    - Laser Desorption Ionization and Allied Techniques
- **Atmospheric Pressure Ionization**
    - Electrospray Ionization, Atmospheric Pressure Chemical/Photo/Laser Ionization
    - Other Concepts and Combination, Applications
- **Summary**

Motivation

Complexity of organic mixtures – The chemical space



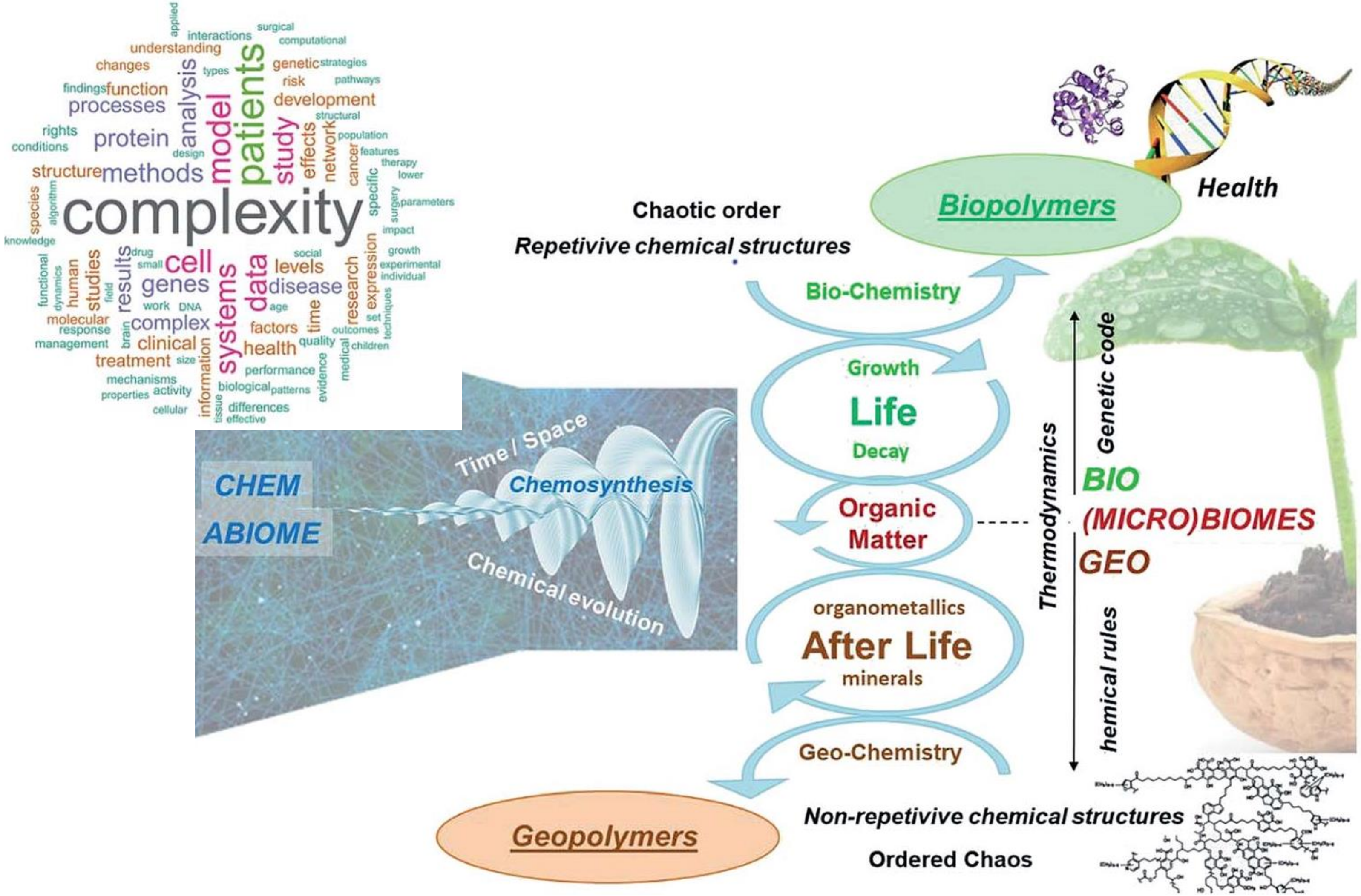


Cover of Vol. 375, 2109,
Philosophical Transactions of
the Royal Society A, Dec. 2017

Estimated number of organic molecules with MW < 500: 10^{62}

Bohacek, R. S., McMartin, C., and Guida, W. C. (1996), Med. Res. Rev. 16, 3–50

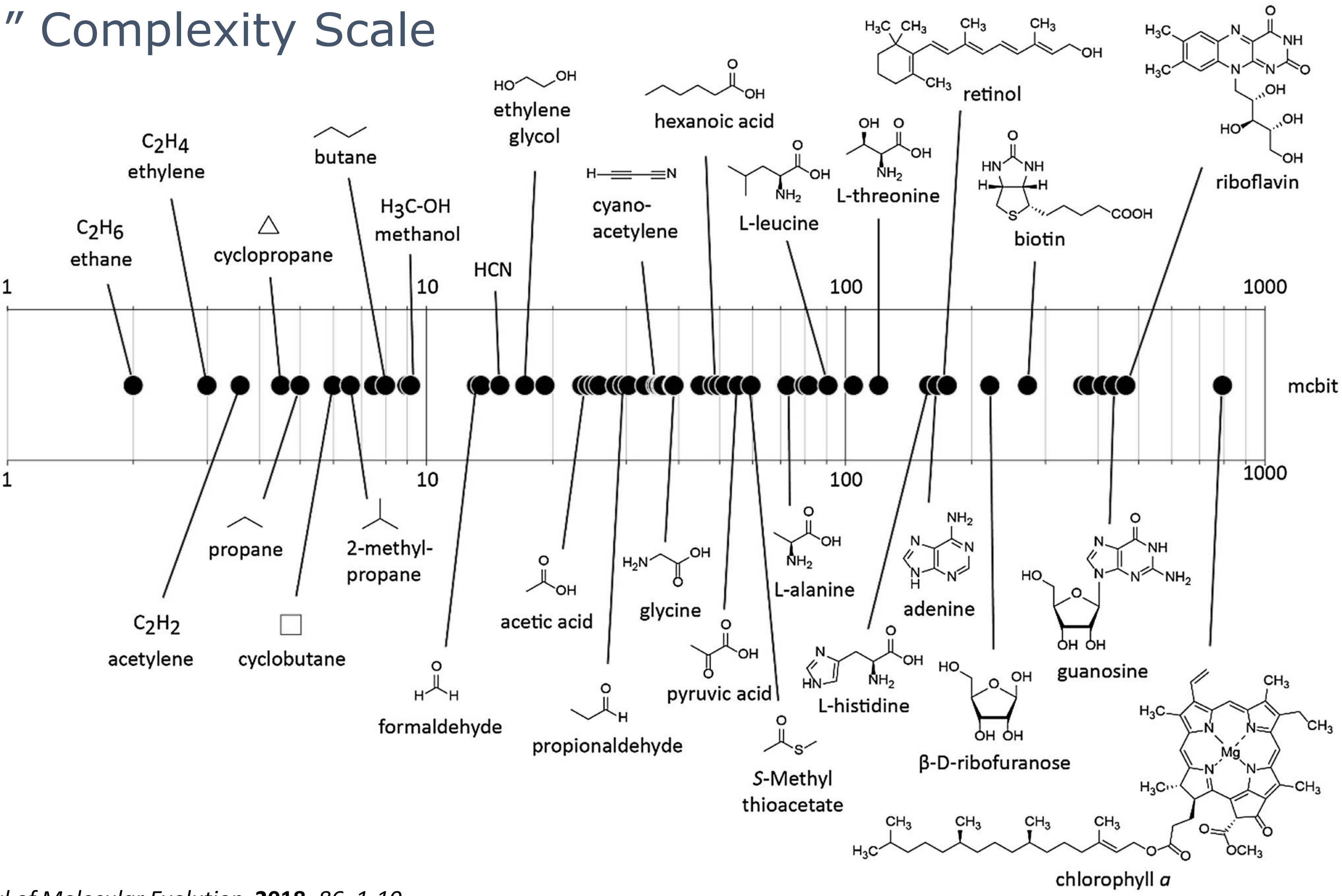
What are Complex Mixtures?



Schmitt-Kopplin et al., *Faraday Discussions*, **2019**, *218, 9-28*

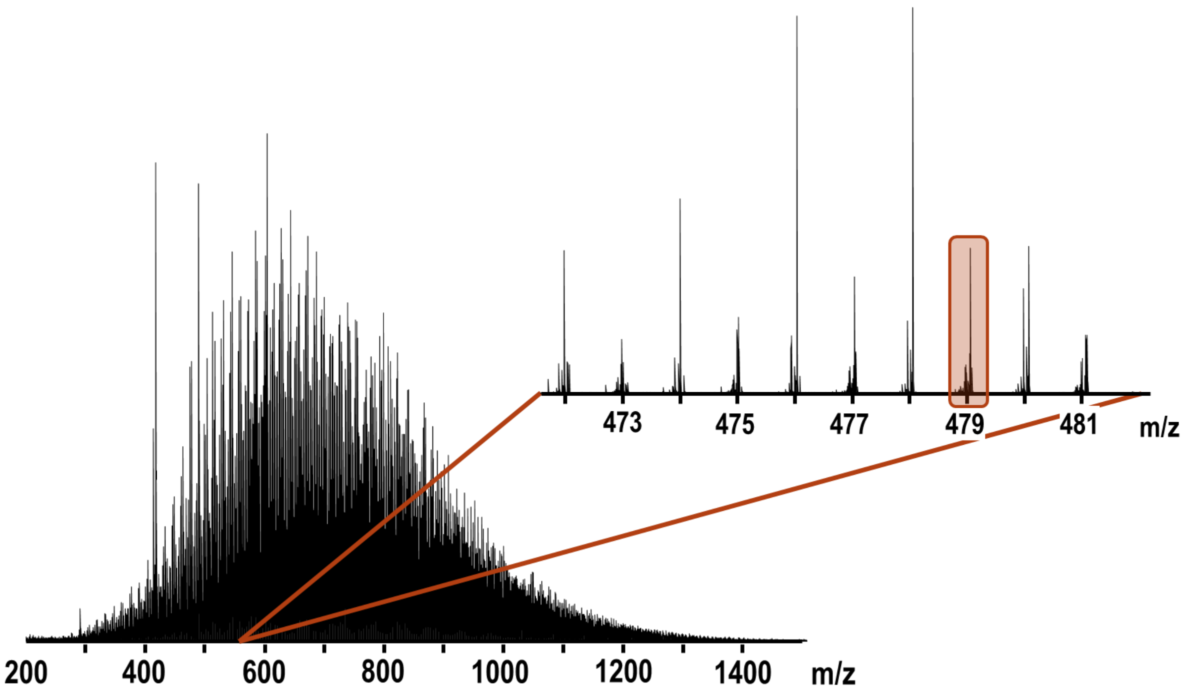
Chemical Complexity

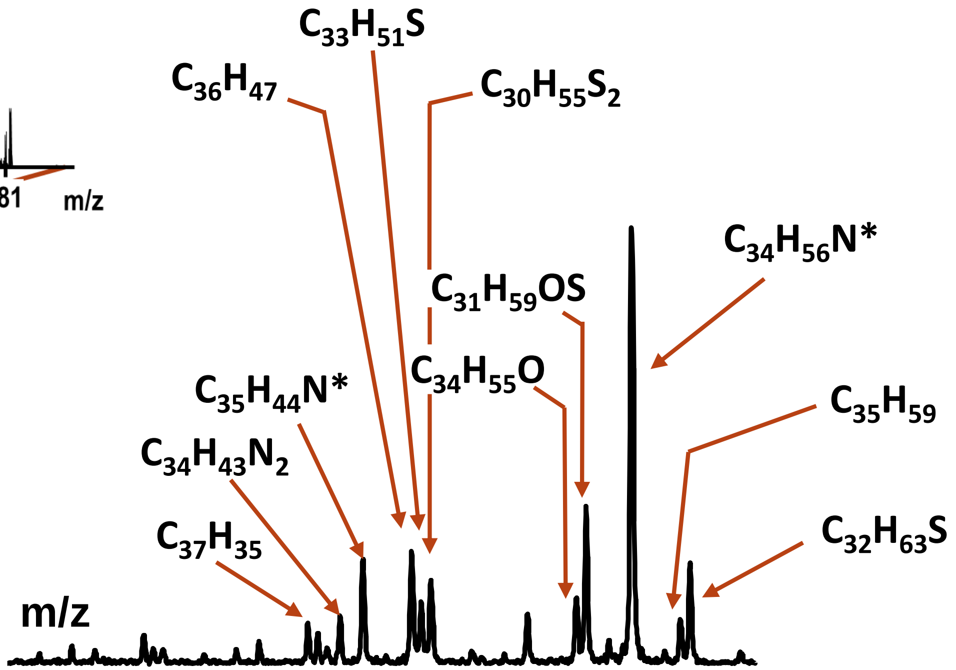
“Universal” Complexity Scale



Thomas Böttcher, *Journal of Molecular Evolution*, **2018**, *86, 1-10*

Why High-Resolution Mass Spectrometry?

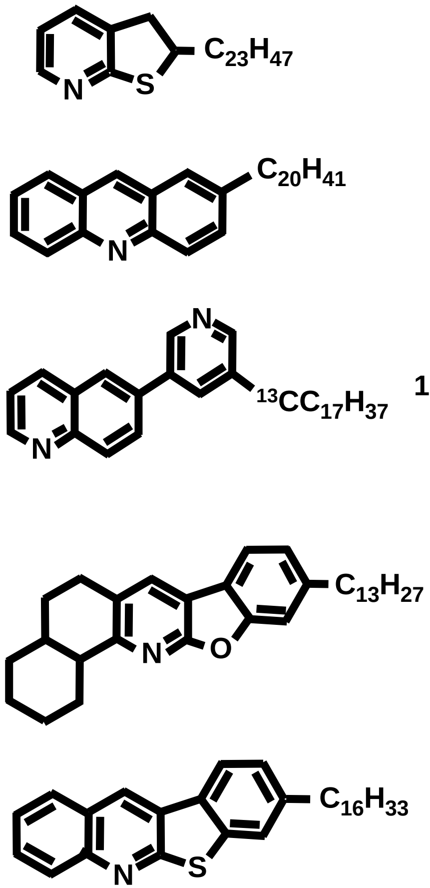




Every $C_cH_hN_nO_oS_s$ mass is unique!

Mass defect =
Atom mass – nearest integer mass

What can high-resolution mass spectrometry do for us?



459.3899
$C_{30}H_{53}NS$

459.3865
$C_{33}H_{49}N$

459.3695
$^{13}CC_{31}H_{46}N_2$

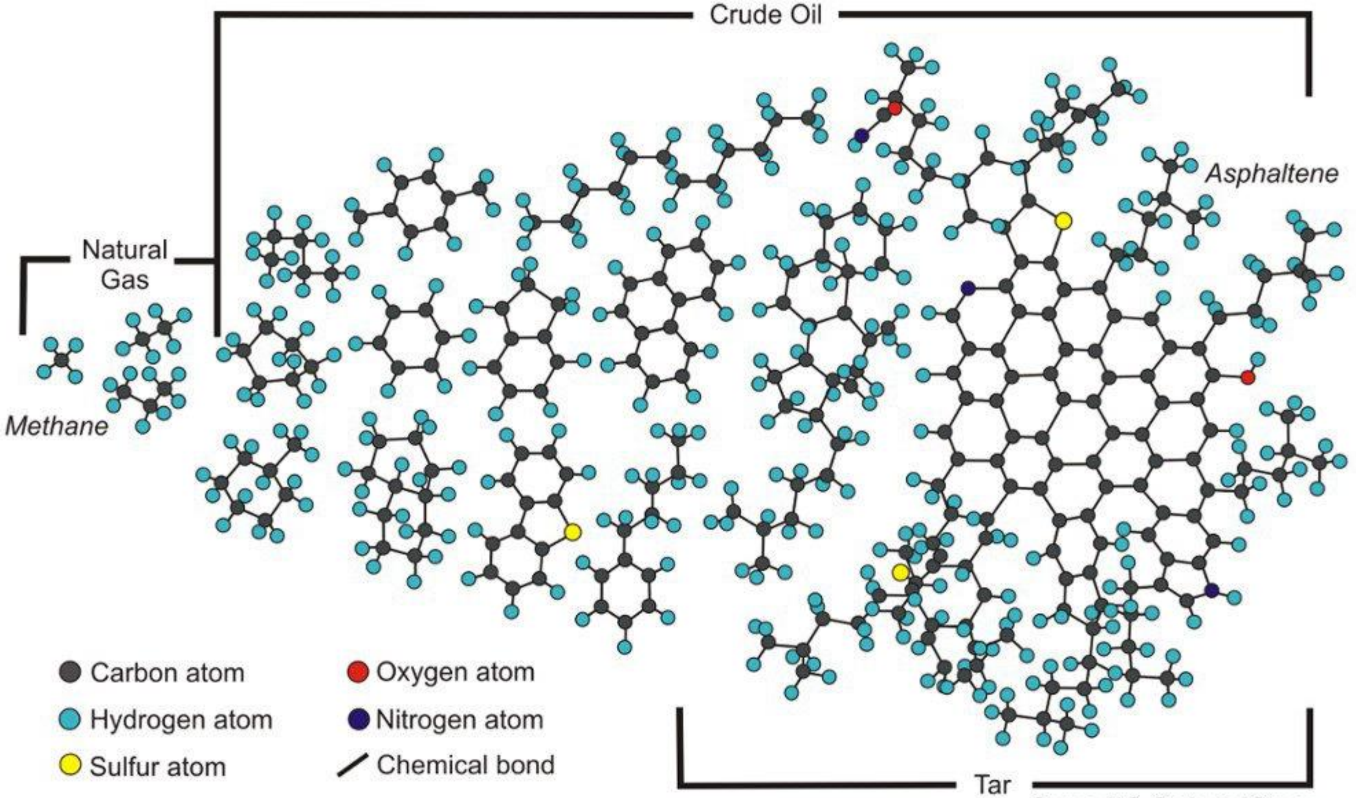
459.3501
$C_{32}H_{45}NO$

459.2960
$C_{31}H_{41}NS$

Doublet	m_2-m_1	$\frac{m_2}{m_2-m_1}$
SH_4/C_3	3.4 mDa	135,000
$C_2H_3/^{13}CN$	17.0 mDa	27,000
O/CH_4	36.4 mDa	13,000
H_{12}/C	93.9 mDa	5,000

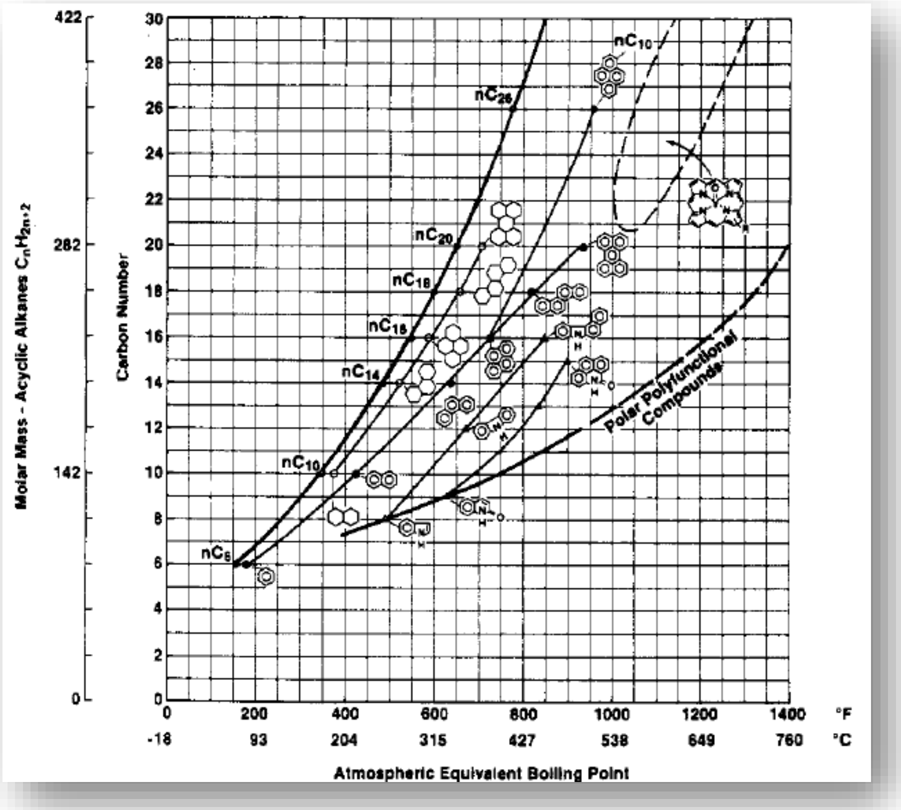
Rodgers, R., Presentation at Mag Lab Summer School 2009

Complex Mixtures – Example: Petroleum



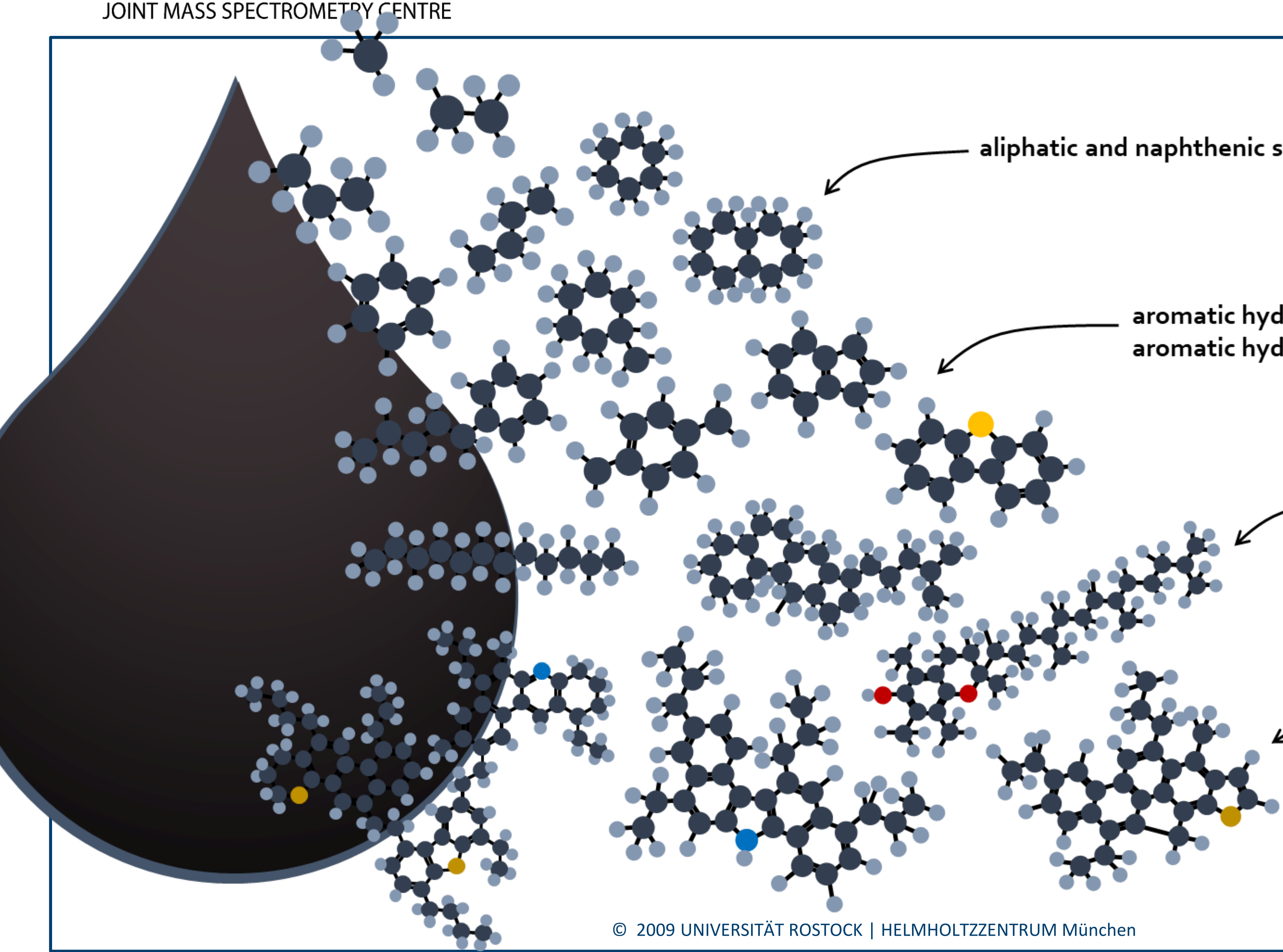
Source: U.S. Geological Survey

Boduszynski continuum



- Petroleum (fossil/**biomass/pyrolysis**): an complex mixture with continuum of chemical functionalities

Complex Mixtures – Example: Petroleum



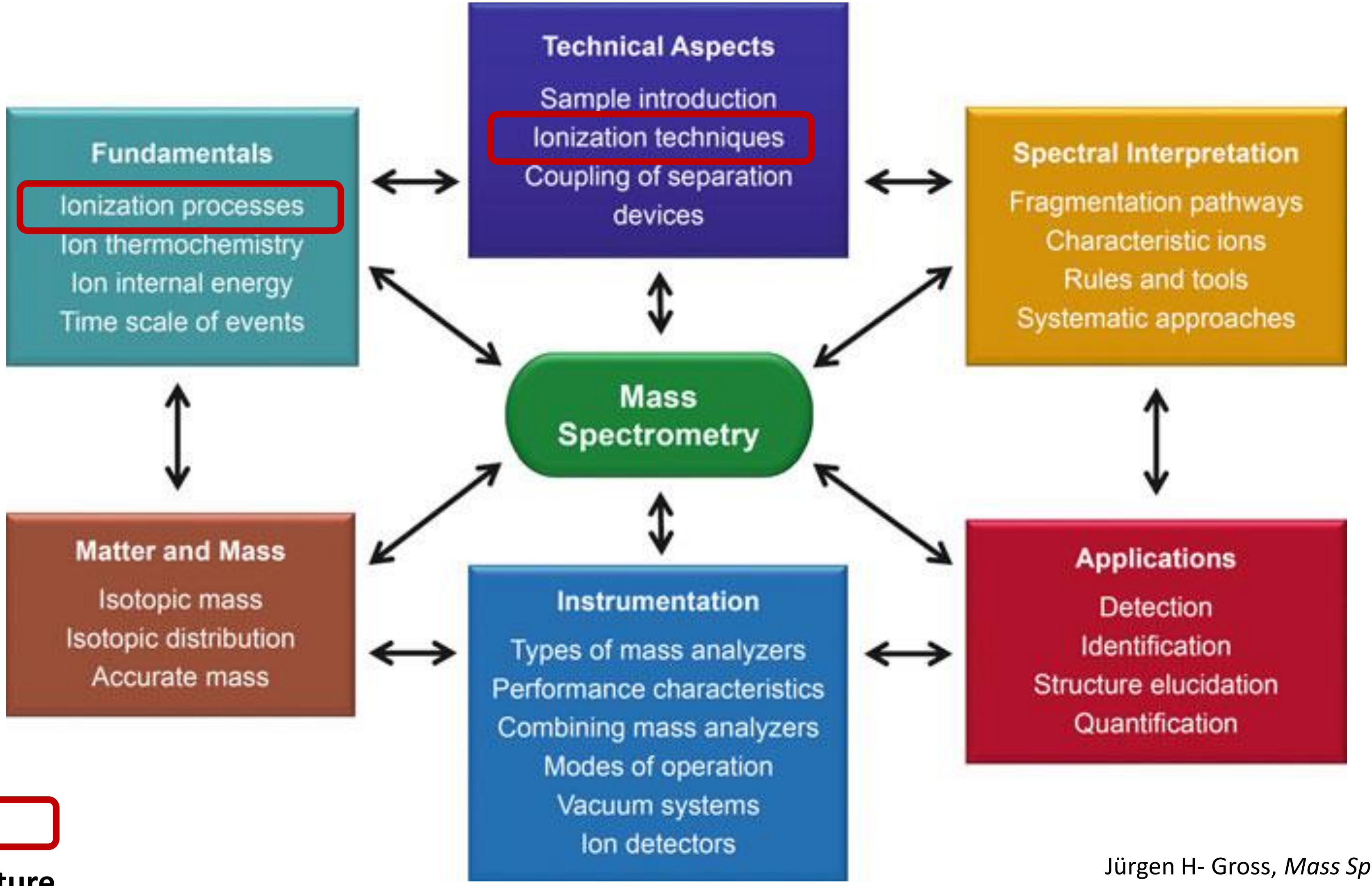
aliphatic and naphthenic saturated hydrocarbons

aromatic hydrocarbons and heteroatom-containing aromatic hydrocarbons

resins
(enriched in heteroatoms N,O,S, highly polar fraction)

asphaltenes
(enriched in heteroatoms N,O,S, and metals, highly polar and highly aromatic fraction)

The many Facets of Mass Spectrometry



Technical Aspects
Sample introduction
Ionization techniques
Coupling of separation devices

Fundamentals
Ionization processes
Ion thermochemistry
Ion internal energy
Time scale of events

Spectral Interpretation
Fragmentation pathways
Characteristic ions
Rules and tools
Systematic approaches

Mass Spectrometry

Matter and Mass
Isotopic mass
Isotopic distribution
Accurate mass

Instrumentation
Types of mass analyzers
Performance characteristics
Combining mass analyzers
Modes of operation
Vacuum systems
Ion detectors

Applications
Detection
Identification
Structure elucidation
Quantification

covered in this lecture

Jürgen H- Gross, *Mass Spectrometry – A Textbook*, **2017**, Spinger, ISBN *978-3-319-54398-7*

FT-ICR MS Instrumentation

Manufactures 2005…

Bruker Daltonics

Varian

Thermo

slide original from Peter O'Connor, adapted

FT-ICR MS Instrumentation

Manufactures today

Bruker Daltonics

solariX / solariXR

scimaX

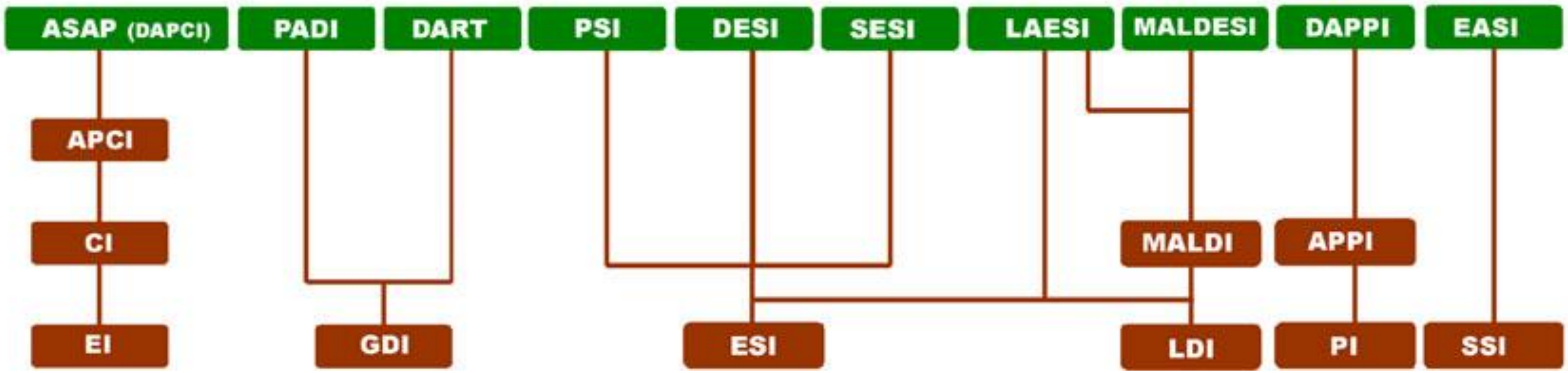
FT-ICR MS Instrumentation

Non-commercial Platforms

21 T FT-ICR MS system at Pacific Northwest National Laboratory – PNNL (Washington, USA)

21 T FT-ICR MS system at National High Magnetic Field Laboratory – MagLab (Florida, USA)

Creating Ions – Main Physicochemical Pathways



ASAP (DAPCI)
PADI
DART
PSI
DESI
SESI
LAESI
MALDESI
DAPPI
EASI

APCI
CI
MALDI
APPI

EI
GDI
ESI
LDI
PI
SSI

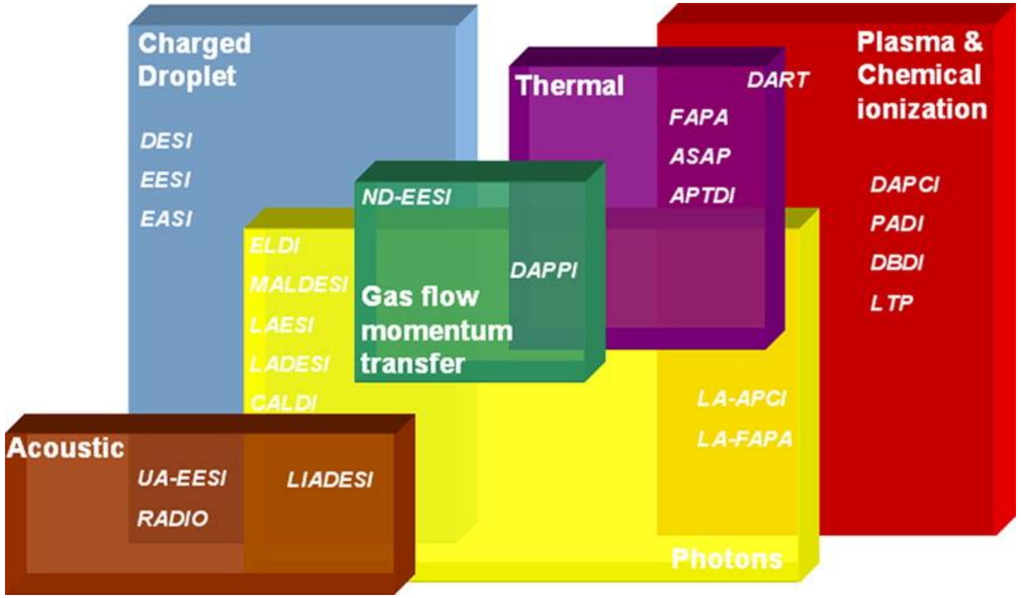
Simplified “ionization tree” – “root” technique given in brown and selected concepts based on them in green

Alberici et al., *Anal Bionanal Chem*, **2010**, 398:265–294

Creating Ions – Main Physicochemical Pathways

	Molecular Ionization		
Atomic Ionization	Sample Phase	Mode	Pressure[a]
Thermal ionization	Gas phase	Electron ionization	HV
Spark source		Chemical ionization (CI)	IV
Glow discharge		Photoionization (PI)	HV
Inductively coupled plasma		Field ionization	HV
Resonance ionization		Metastable atom bombardment	HV
	Solution phase	Thermospray	LV
		Atmospheric-pressure CI	AP
		Atmospheric-pressure PI	AP
		Electrospray	AP
	Solid phase	Plasma desorption	HV
		Field desorption	HV
		Secondary-ion MS	HV
		Fast atom bombardment	HV
		Matrix-assisted laser desorption	HV

[a] HV, high vacuum; IV, intermediate vacuum; LV, low vacuum; AP, atmospheric pressure.

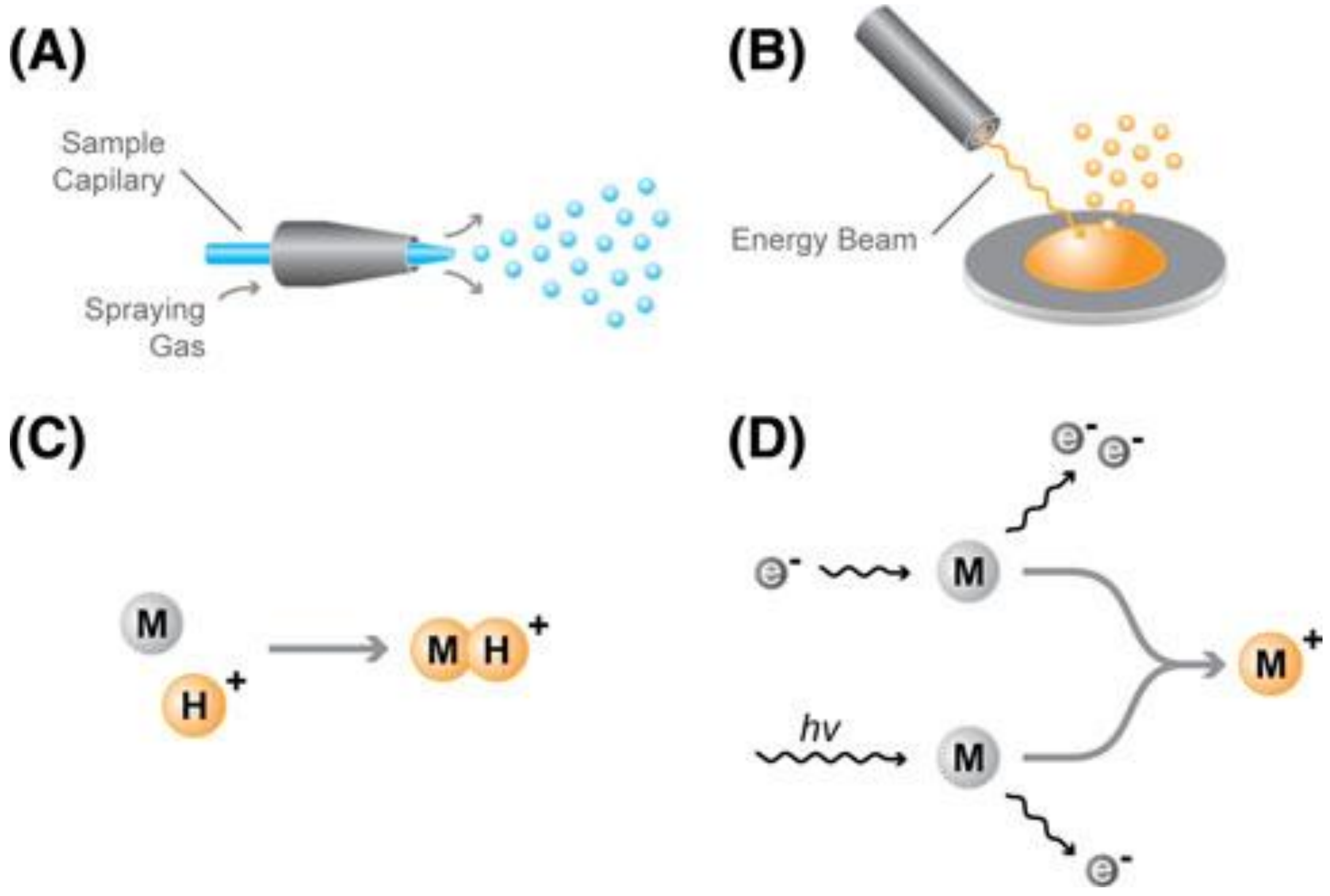


Structuring ionization concepts in MS
with main physicochemical background

Chen et al., *JASMS*, **209**, 1947-1963

Ionization Techniques

Basic Physical Concepts and Schemes for Ionization



A) Spray Ionization

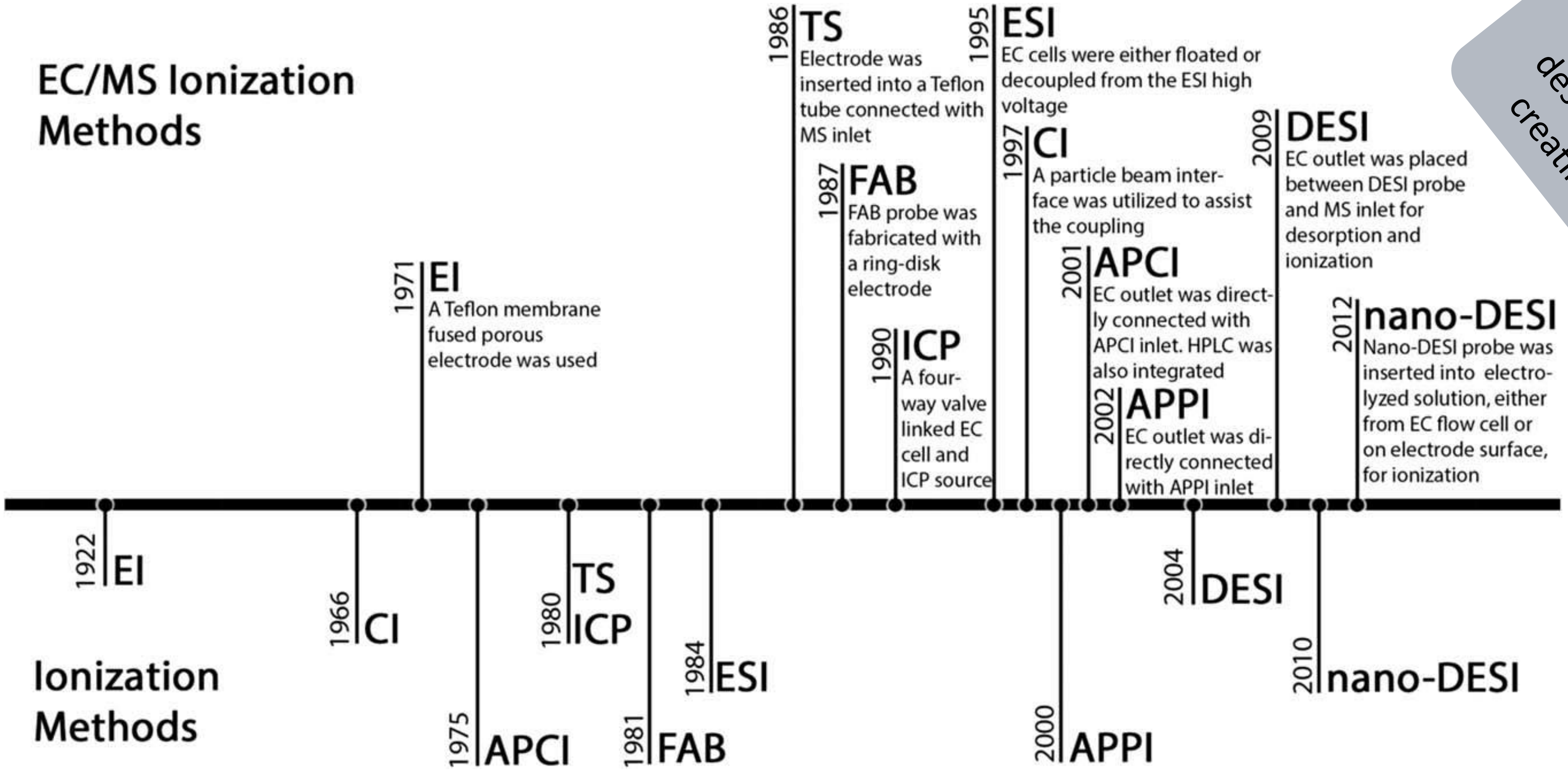
B) Desorption Ionization

C) Chemical Ionization

D) Electron/Photon Ionization

Pól et al., *Histochem Cell Biol*, **2010**, 134:423–443

Timeline and the Ambient Ionization Techniques “Zoo”



EC/MS Ionization Methods

1971 **EI** A Teflon membrane fused porous electrode was used

1986 **TS** Electrode was inserted into a Teflon tube connected with MS inlet

1987 **FAB** FAB probe was fabricated with a ring-disk electrode

1990 **ICP** A four-way valve linked EC cell and ICP source

1995 **ESI** EC cells were either floated or decoupled from the ESI high voltage

1997 **CI** A particle beam interface was utilized to assist the coupling

2001 **APCI** EC outlet was directly connected with APCI inlet. HPLC was also integrated

2002 **APPI** EC outlet was directly connected with APPI inlet

2009 **DESI** EC outlet was placed between DESI probe and MS inlet for desorption and ionization

2012 **nano-DESI** Nano-DESI probe was inserted into electrolyzed solution, either from EC flow cell or on electrode surface, for ionization

Ionization Methods

1922 **EI**

1966 **CI**

1975 **APCI**

1980 **TS** **ICP**

1981 **FAB**

1984 **ESI**

2000 **APPI**

2004 **DESI**

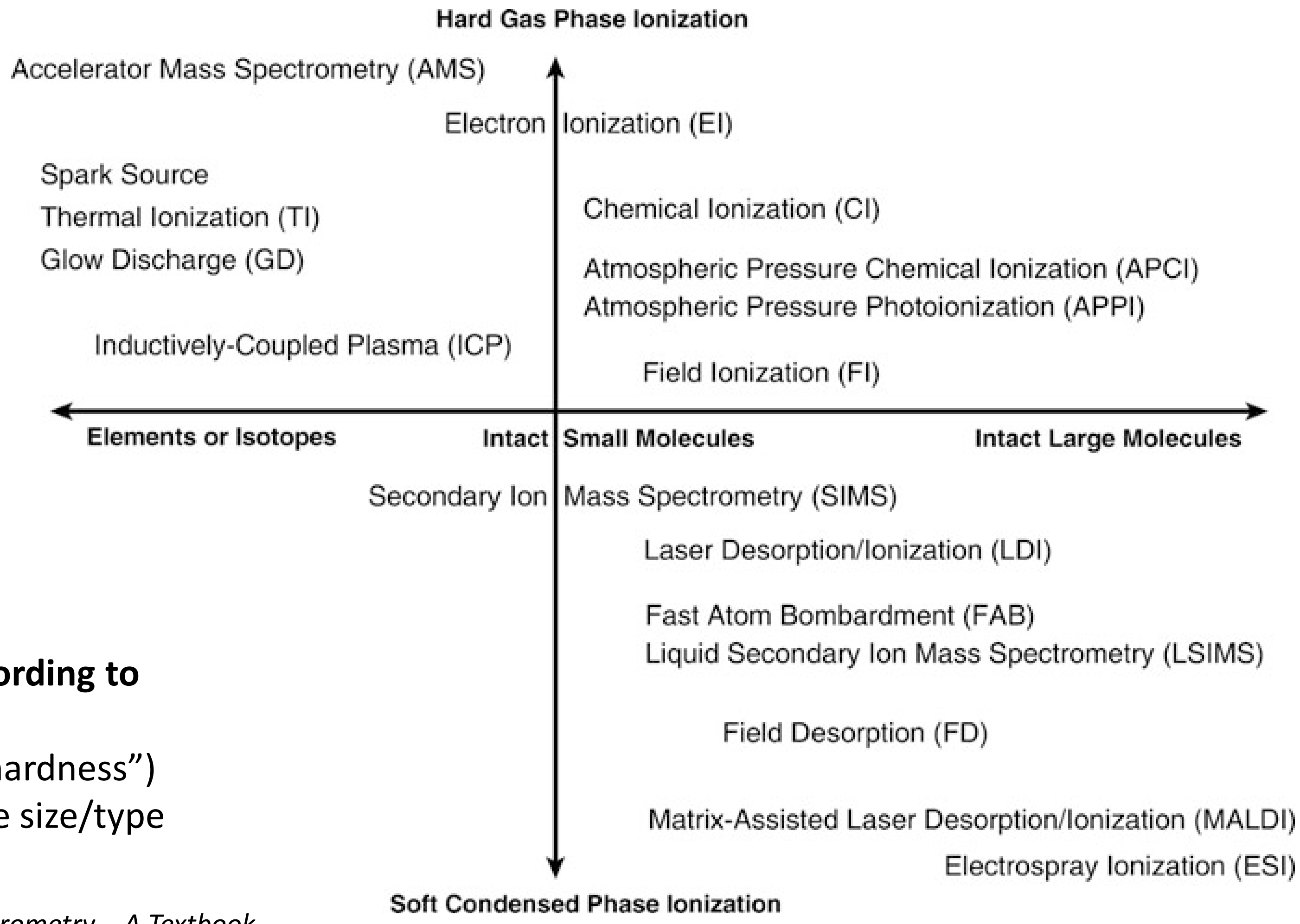
2010 **nano-DESI**

After ~2013 endless variations of desorption and spray techniques creating an abbreviation „zoo“

Liu et al., *The Analyst*, **2013**, 138, 5519

Ionization Techniques

Trying to get an overview of existing ionization concepts and schemes…

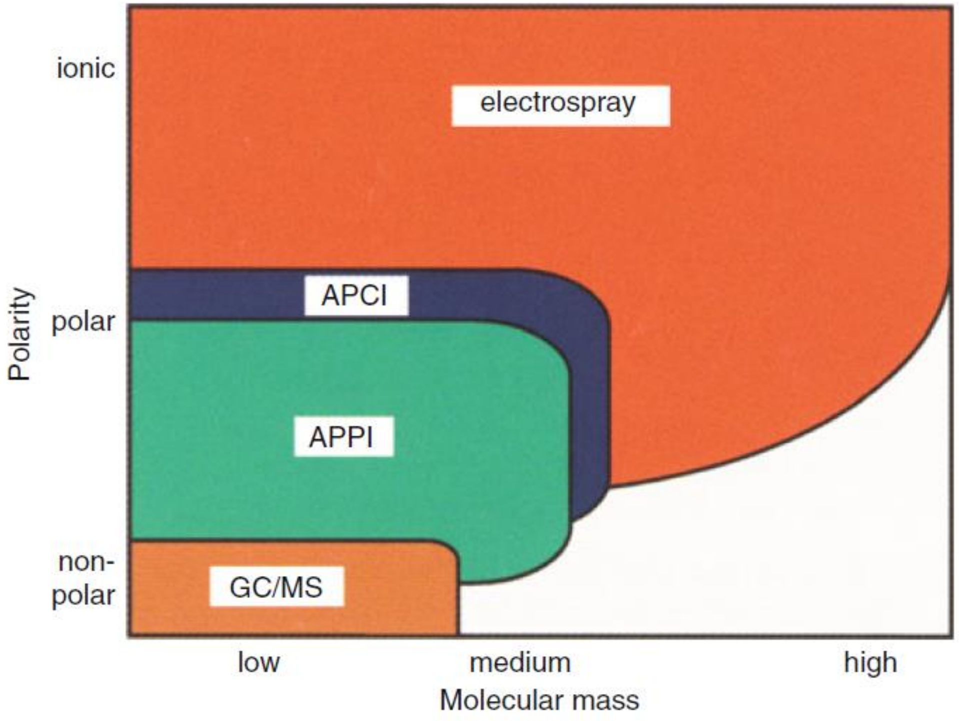


Structuring here according to

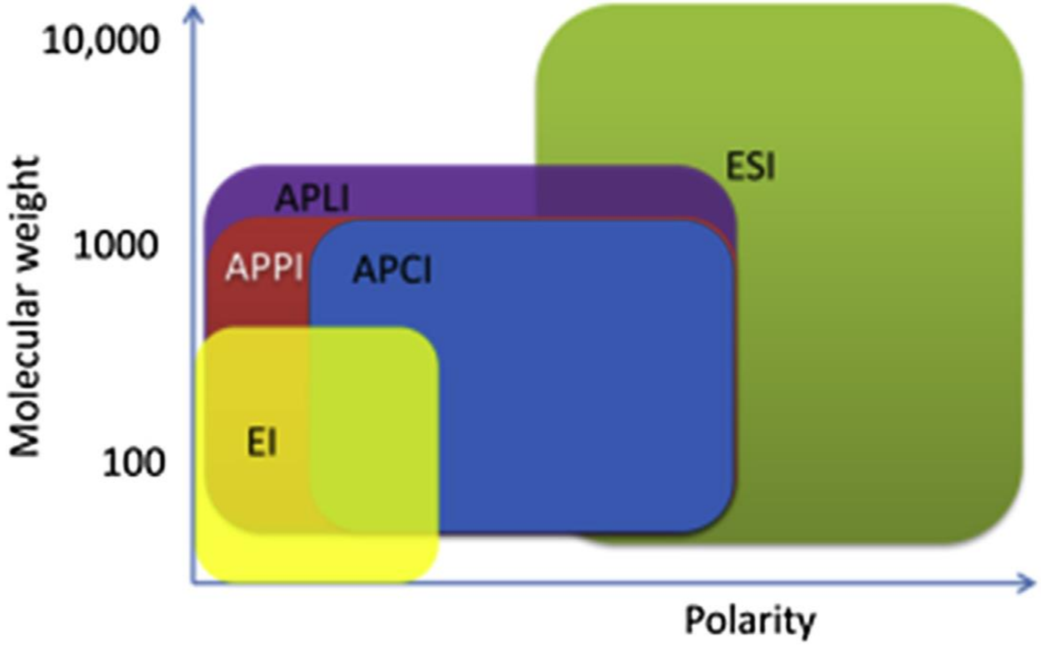
- energy uptake (“hardness”)
- molecular/analyte size/type

Jürgen H- Gross, *Mass Spectrometry – A Textbook*, **2017**, Spinger, ISBN *978-3-319-54398-7*

Selectivity of Ionization in Mass Spectrometry – “Analytical Glasses”

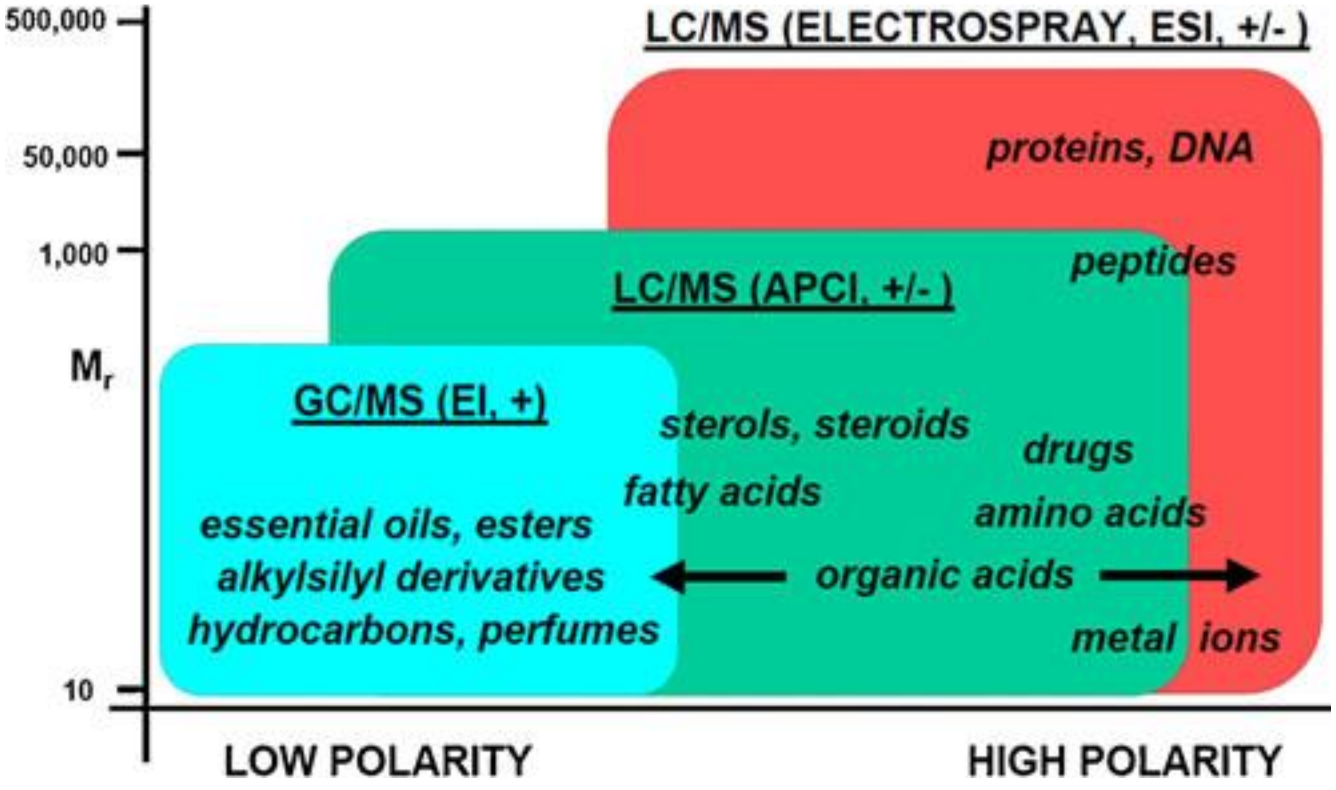


Cover of *Anal. Bioanal. Chem.*, **2004**, 378(4)



Li et al., *Analytica Chimica Acta*, **2015**, *43-61*

Selectivity of Ionization in Mass Spectrometry – "Analytical Glasses"



Halket et al., *J. Exp. Bot.*, **2005**, *56(410):219–243*

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Is this of relevance for the FT-ICR MS community?

Yes and No!

State-of-the-art FT-ICR MS comes with
- ESI/MALDI
- Optional: APPI, APCI, GC-APCI, nanoESI, DIP…

Electron and chemical ionization source

+ self-build and customized solutions

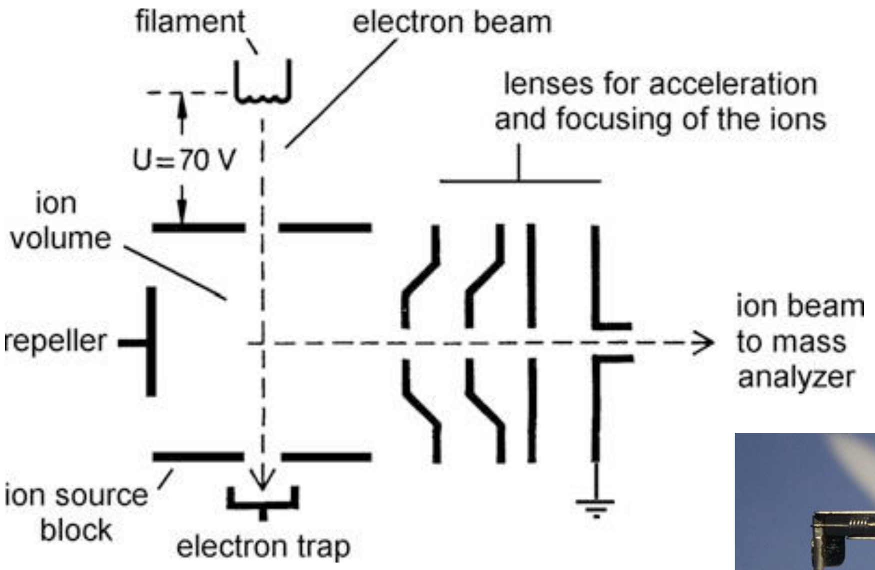
+ small specialized companies offering solutions

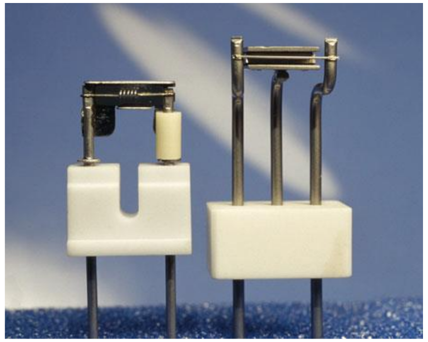
Electron (Impact) Ionization - EI

Basics and Technical Aspects

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

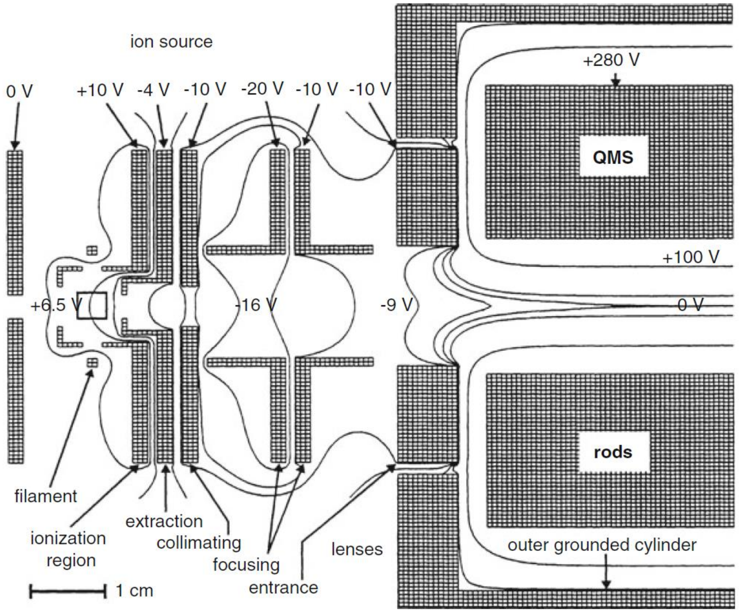
neutral hit by energetic electron – effective collision exceed ionization energy (IE) and ejection of an electron forming a radical cation





Principle layout of an EI source with photography of filaments

Schröder (1991), Massenspektrometrie – Begriffe und Definitionen, Heidelberg

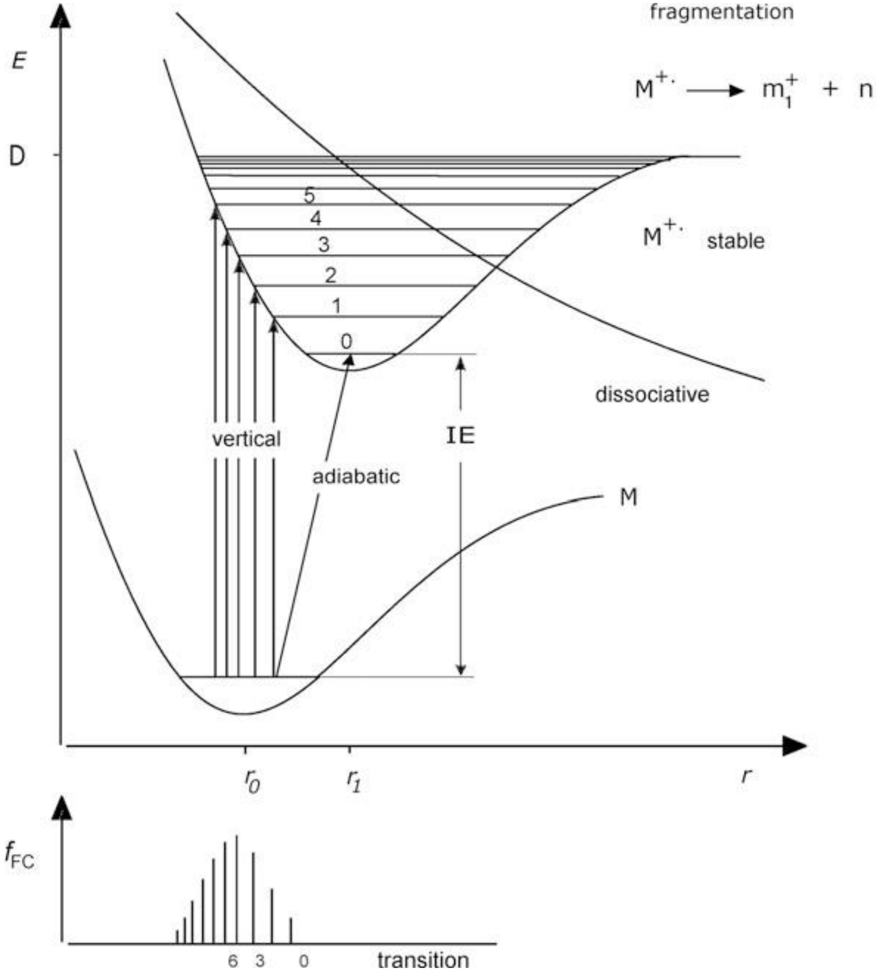


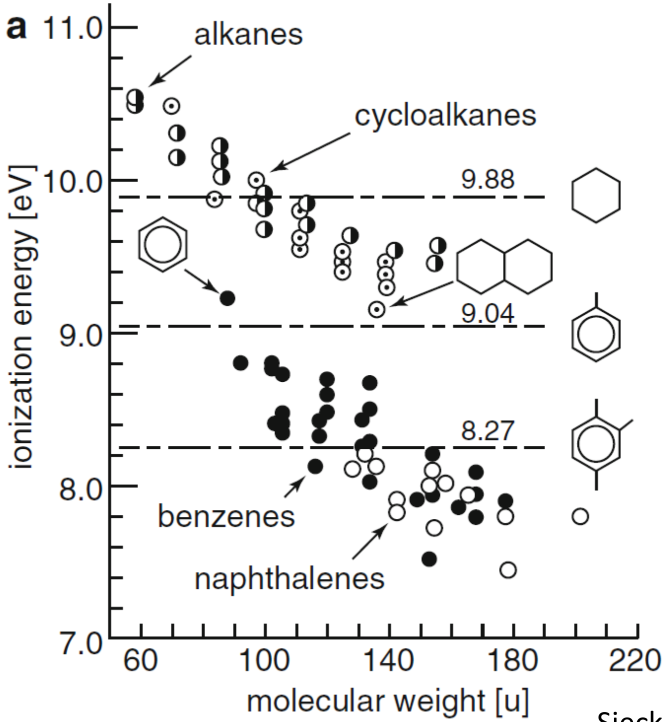
SIMION field simulation of a EI source of a quadrupole MS

Blaum et al., *Int J Mass Spectrom*, **1998**, 181:67-87

Electron (Impact) Ionization - EI

The concept of ionization energy (IE)

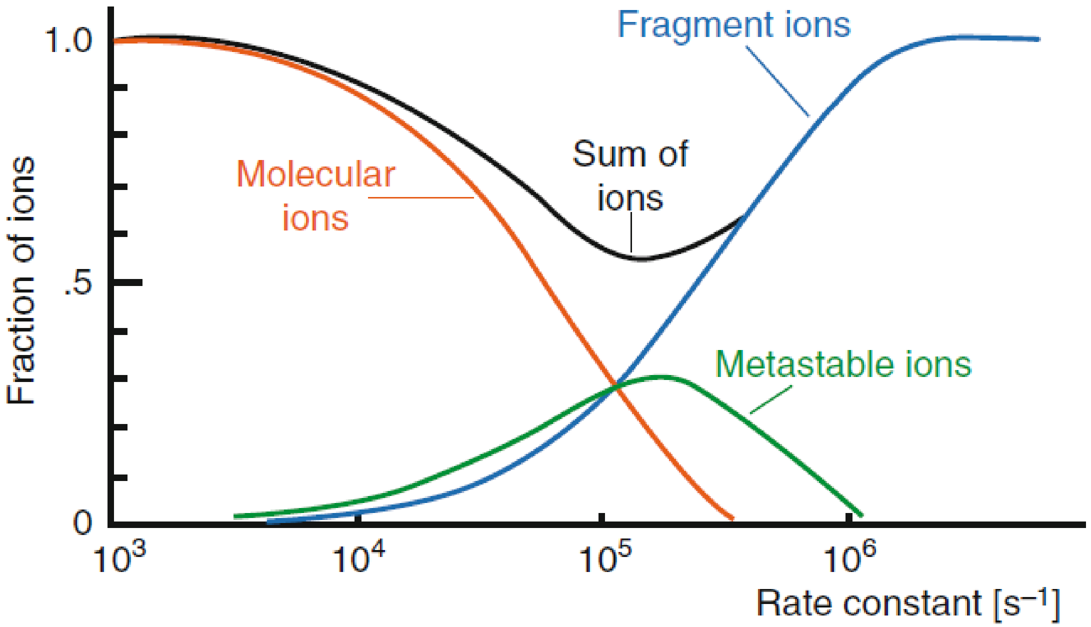




Sieck, *Anal Chem*, **1983**, 55:38-41

- fast process → vertical transition (Franck-Condon principle)
- e$^-$ from the highest occupied molecular orbital (HOMO) is removed (IE ~ negative energy of the HOMO (Koopman’s theorem)
- ionization energy of most organic molecules range from 7-15 eV

Stability of Ions – Stable, Metastable and Unstable Ions



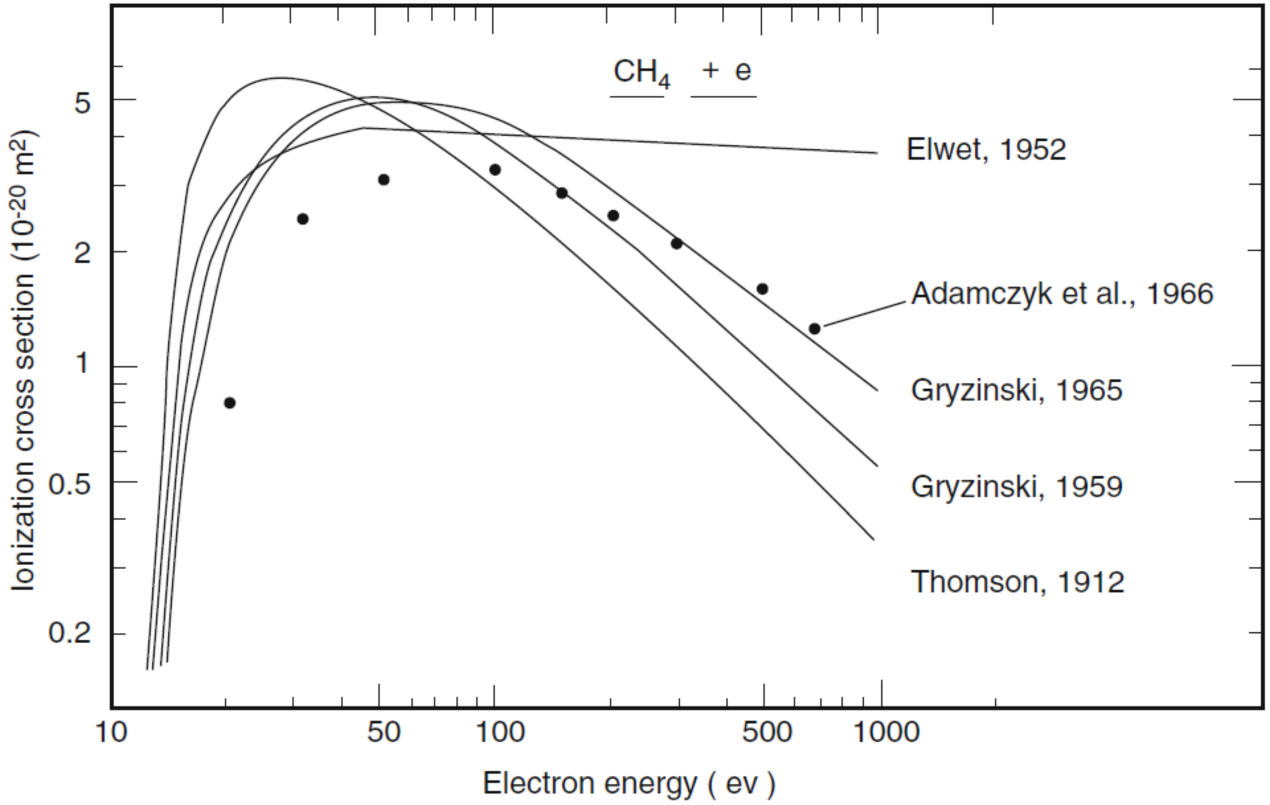
stable ions: $k < 10^5\ s^{-1}$
metastable ions: $10^5\ s^{-1} < k < 10^6\ s^{-1}$
unstable ions: $k > 10^6\ s^{-1}$

- needs to be considered for all ionization techniques
- in particular for mass storing devices in the mass spectrometric setup (ion traps or other ion accumulation)

“Do my ion arrive at the mass analyzer without further reactions and if not how does these reactions look like?”

Chupka, *J Chem Phys*, **1959**, 30:191-211

Ionization Cross Sections – a Measure for Ionization Efficiency

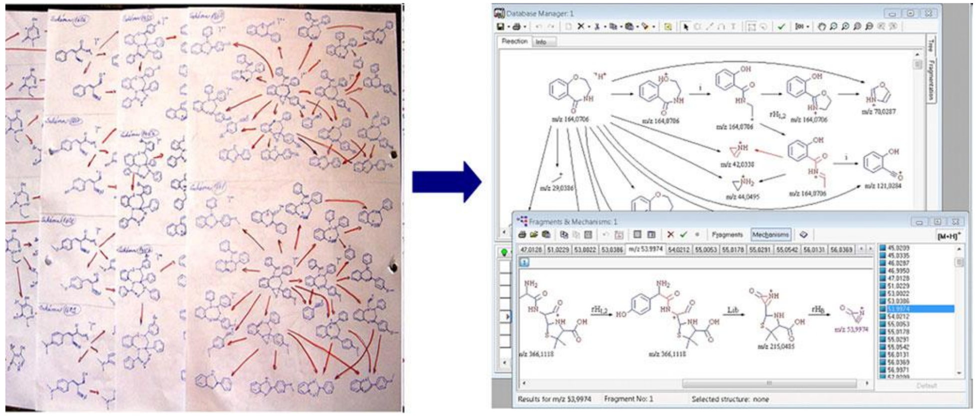


Märk, *Electron impact ionization. In: Futrell JH (ed) Gaseous Ion Chemistry and Mass Spectrometry.*, **1986**

- ionization cross section within on-order-of-magnitude
- universal + no matrix effects → quantification possible
- high ionization efficiency + highly reproducible

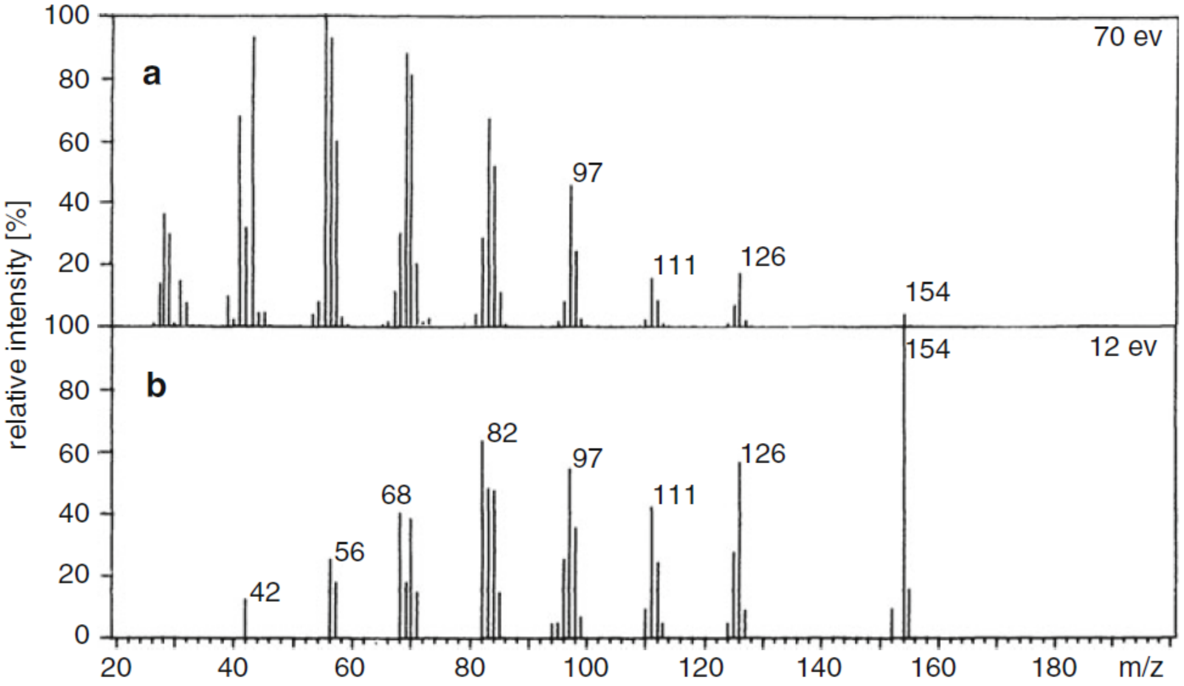
Problems and Limitations of EI

Fragmentation: Benefit and drawback at the same time



Highly complex fragmentation pattern are a problem for complex mixture analysis – particularly for comprehensive analysis of unknowns

Kind and Fiehn, *Bioanal Rev*, **2010**, 2:23-60

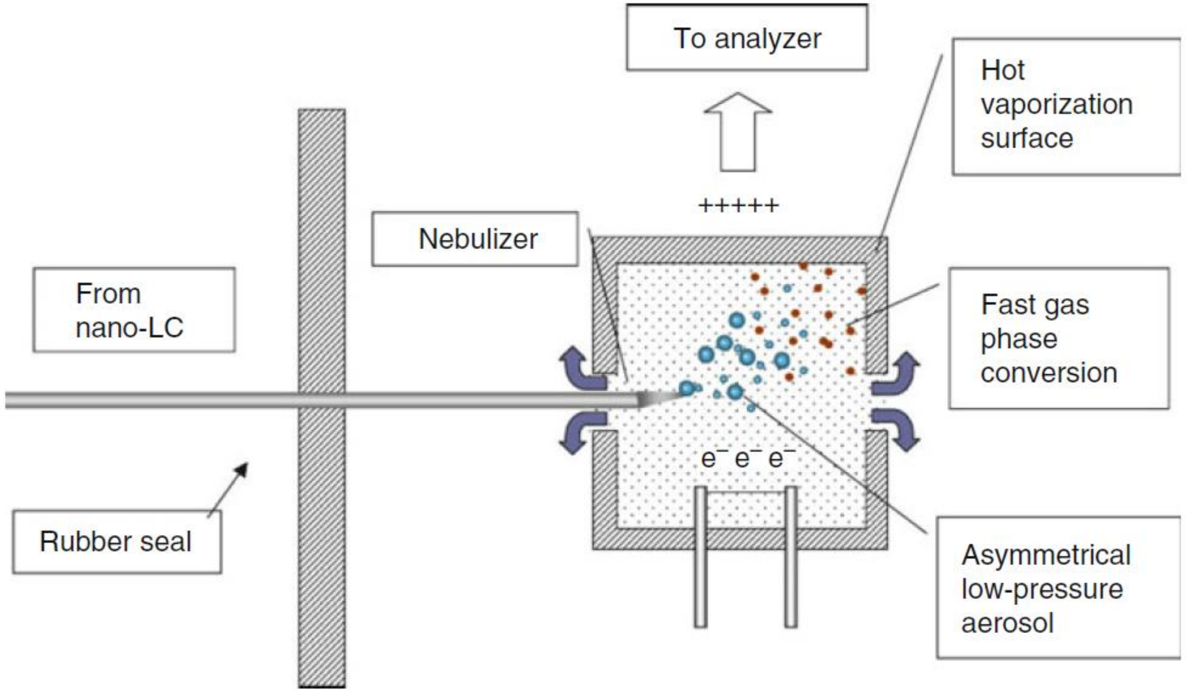


Comparison of the fragmentation pattern of Undecan-1-ol of EI at 70 and 12 eV (significant loss in sensitivity for low eV EI!)

Brophy et al. , *Org Mass Spectrom*, **1988**, 23:659-662

Electron (Impact) Ionization - EI

Problems and Limitations of EI – Coupling of LC to vacuum ionization

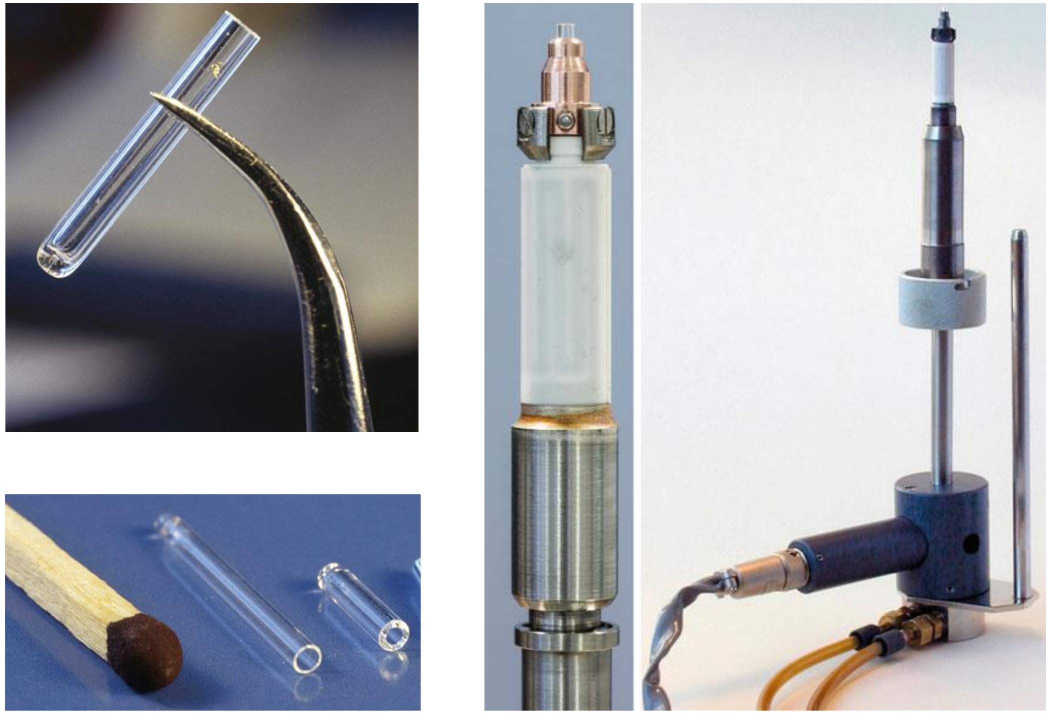


Nano-LC-EI interface with direct connection of LC effluent into the vacuum ionization chamber

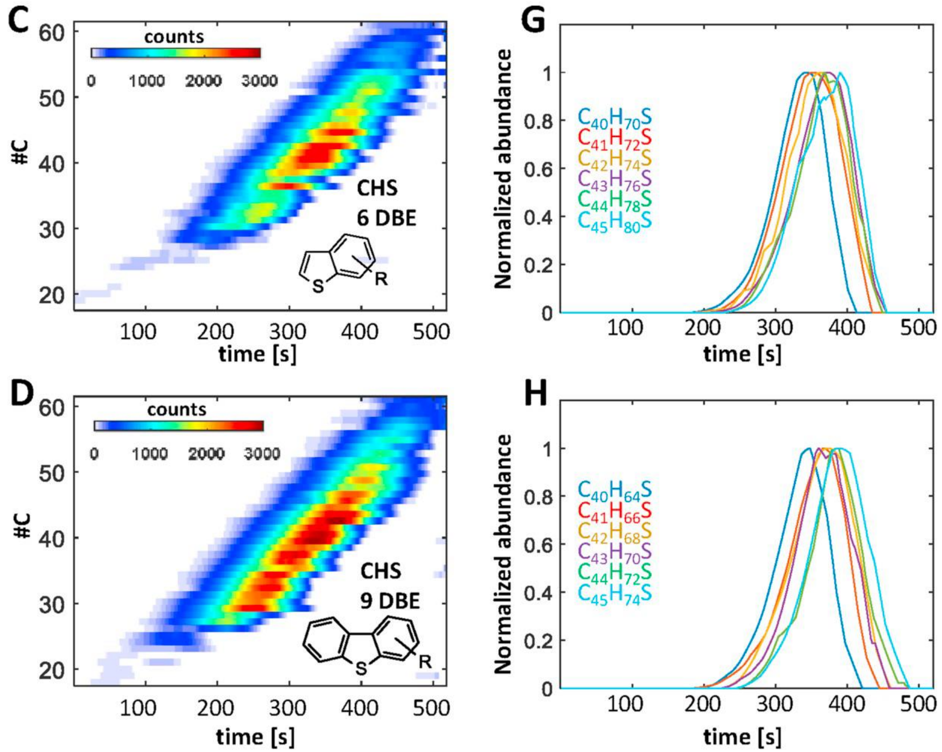
LC coupling to vacuum ionization technically difficult due to 1) challenge in maintaining the vacuum (high **pumping requirements**, potential discharge for pressure spikes, etc.), and 2) adiabatic expansion caused by the pressure drop leads to **freezing out** the solvent blocking the inlet capillary easily.

Käfer et al., *Talanta*, **2019**, 309-316

Direct Inlet Probe as Sample Introduction Technique



inlet technique for solid and high-viscous materials, a temperature program is applied to evaporate and consequently ionize the analytes in the ionization source

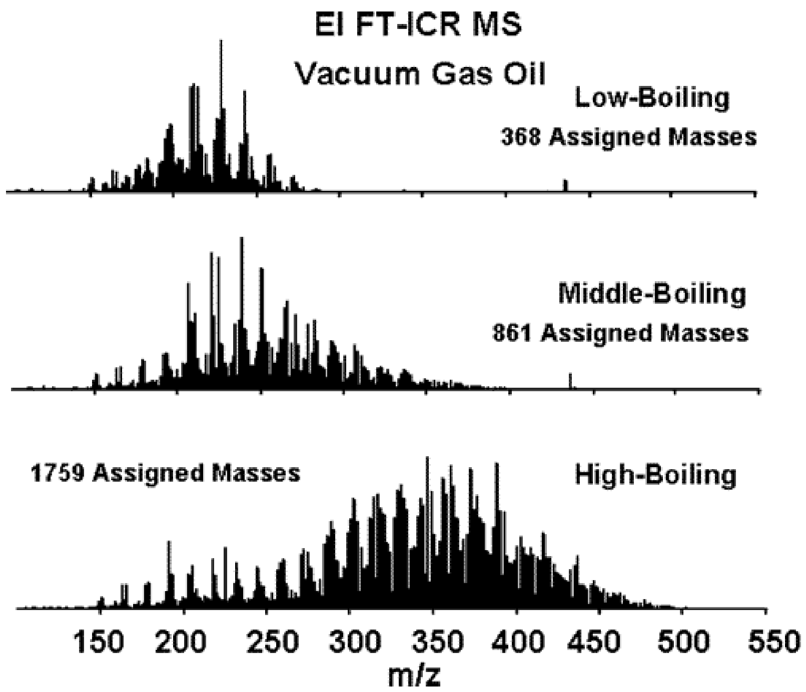


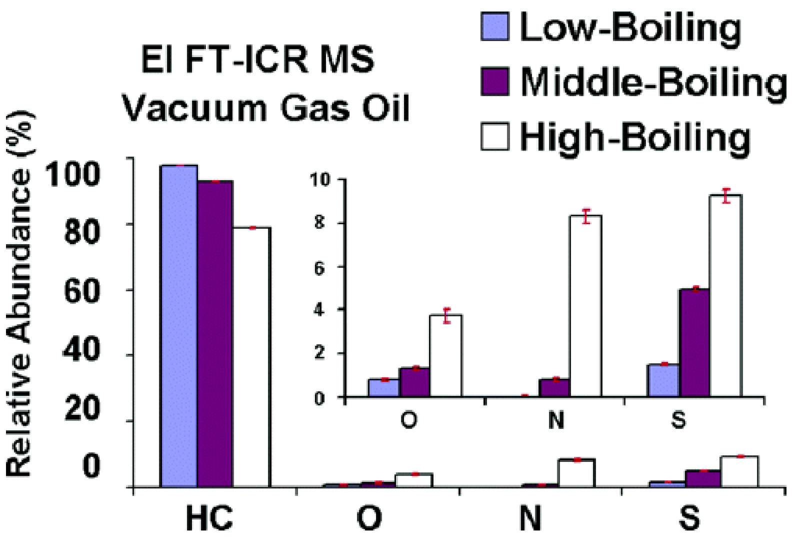
analysis of bitumen by DIP-EI high-resolution time-of-flight mass spectrometry

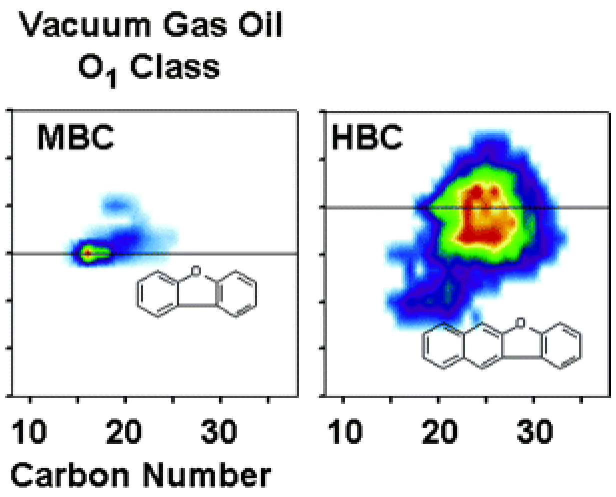
Käfer et al., *Talanta*, **2019**, 309-316

Electron (Impact) Ionization - EI

Application of EI in FT-ICR MS







EI FT-ICR MS of vacuum gas oil distillation fractions – aromatic constituents show less fragmentation and the molecular analysis advantageous for spectral analysis in complex mixtures (but limited)

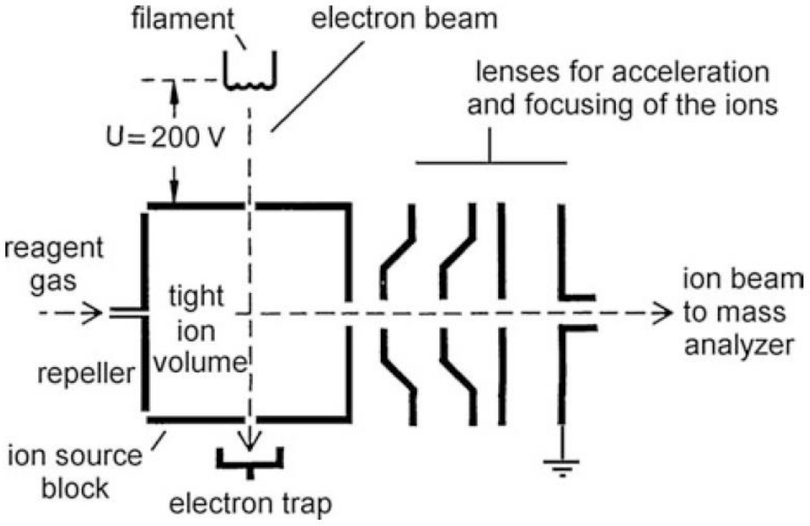
Fu et al., *Energy and Fuels*, **2006**, 661-667

but EI almost not featured anymore as a consequence of the drawbacks and manufacturer orientation

Chemical Ionization - CI

Brief Basics and Variations

- gaseous molecules react with ions → ion-molecule reactions (bimolecular processes)
- may involve transfer of an electron, proton, or other ions between the reactants
- low mbar vacuum in the source increasing dwell time and collisions
- formation of quasi-molecular ions, *e.g.*, $[M+H]^+$ and $[M-H]^+$



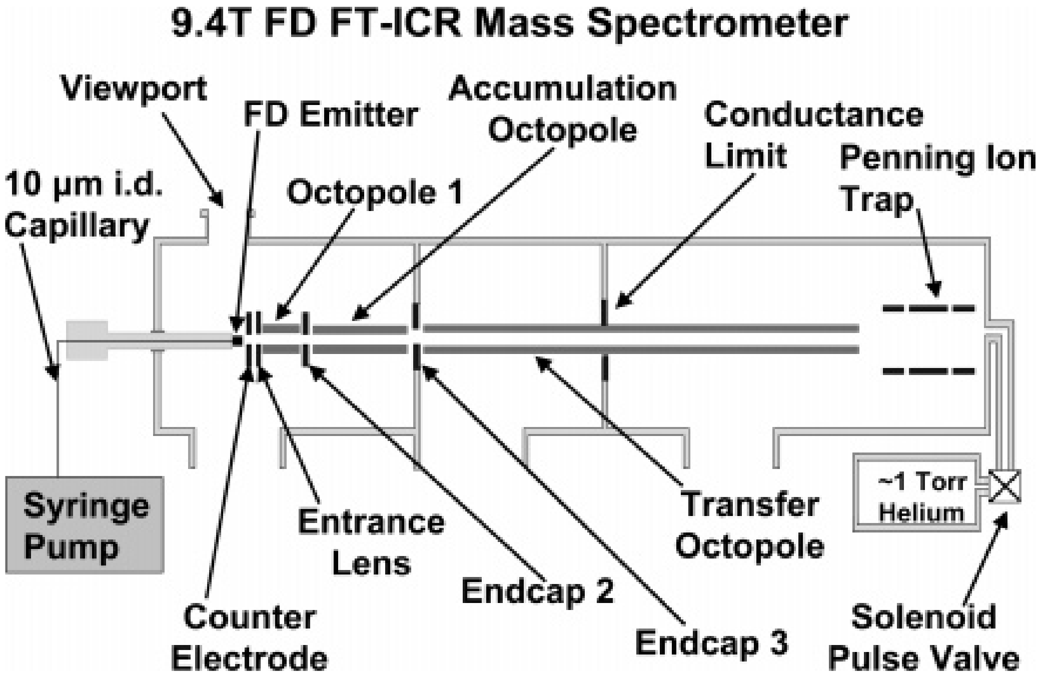
Layout of a chemical ionization source

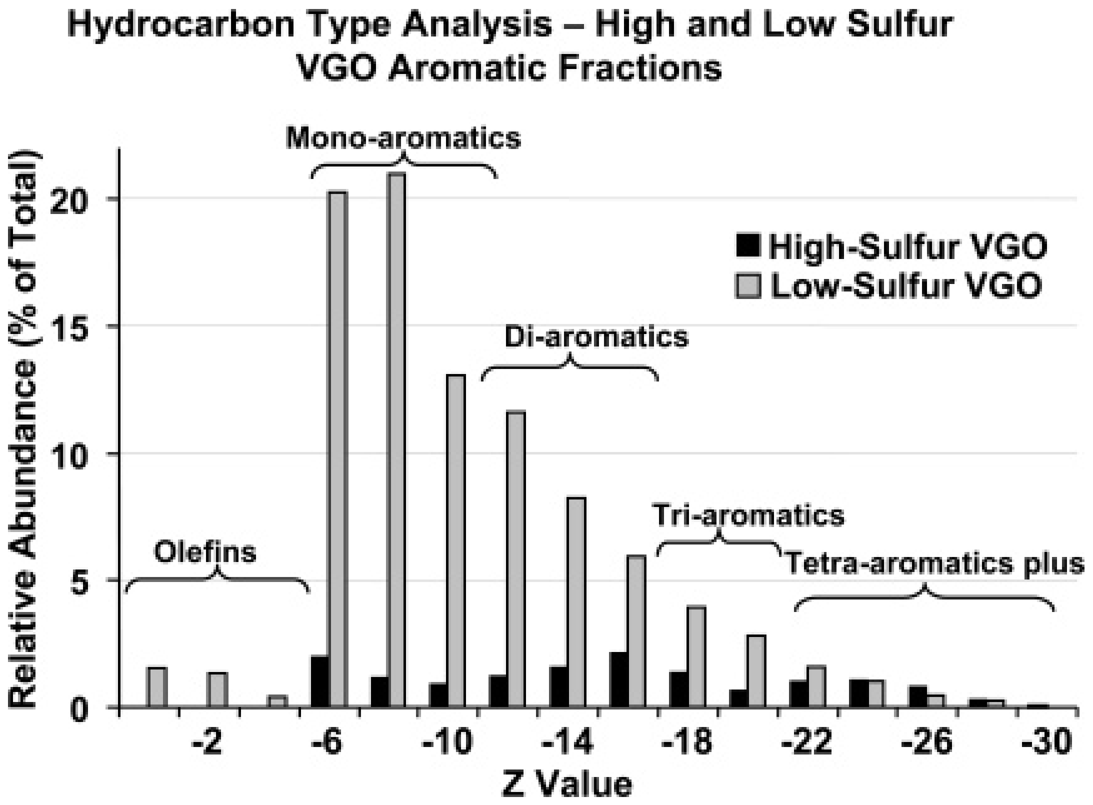
Schröder (1991), Massenspektrometrie – Begriffe und Definitionen, Heidelberg

Reagent gas	Reagent ions	Neutral from reagent ions	*PA* of neutral product [kJ mol^{-1}]	Analyte ions and relative analyte ion masses
H_2	H_3^+	H_2	424	$[M+H]^+$, $[M–H]^+$ [M+1], [M–1]
CH_4	CH_5^+ ($C_2H_5^+$ and $C_3H_5^+$)	CH_4	552	$[M+H]^+$, also $[M+C_2H_5]^+$ and $[M+C_3H_5]^+$ [M+1], [M+29], [M+41]
i-C_4H_{10}	t-$C_4H_9^+$	i-C_4H_8	820	$[M+H]^+$, also $[M+C_4H_9]^+$, (eventually $[M+C_3H_3]^+$, $[M+C_3H_5]^+$ and $[M+C_3H_7]^+$), [M+1], [M+57]
NH_3	NH_4^+	NH_3	854	$[M+H]^+$, $[M+NH_4]^+$, [M+1], [M+18]

Common positive chemical ionization reagent gases

Field Desorption (FD) Ionization FT-ICR MS Example Study

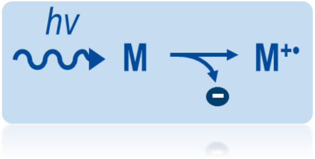




Schaub et al., *Energy and Fuels*, **2005**, 1566-1573

Ionization – Photoionization

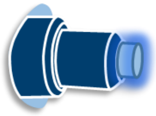
Soft ionization of analytes by photon irradiation



at atmospheric pressure

Most often divided in:

- **a**tmospheric **p**ressure **p**hoto **i**onization utilizing rare gas discharge lamps (APPI using Krypton lamps, 10/10.6 eV)
- **a**tmospheric **p**ressure **l**aser **i**onization (APLI, most often 248/266 nm)



APPI

NdYag-Laser (266nm)
2 x 4,66eV = 9,3eV

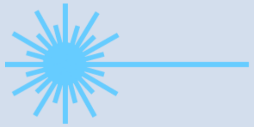
at reduced pressure / vacuum

Most often divided in:

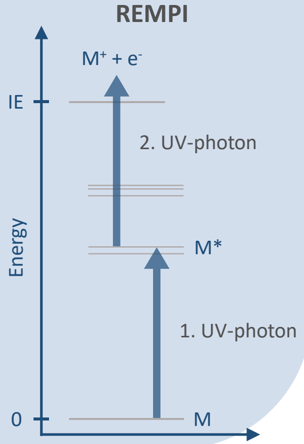
- **s**ingle-**p**hoton **i**onization (SPI) using VUV laser, synchrotron radiation or discharge lamps
- **r**esonance-**e**nhanced **m**ulti**p**hoton **i**onization (REMPI)

no matrix effects

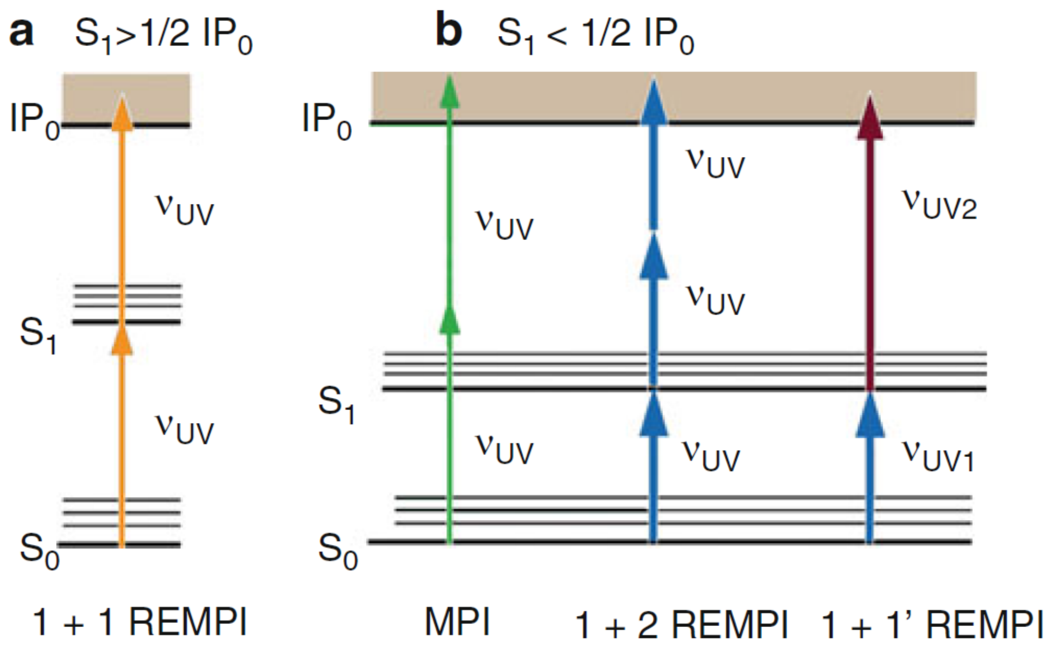
almost no fragmentation



F2-Laser (157nm)
7.9eV

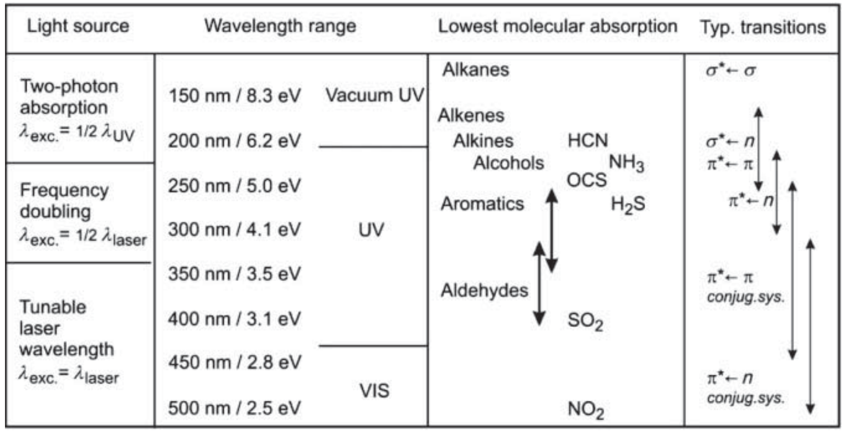


General Concept and Light Sources - REMPI

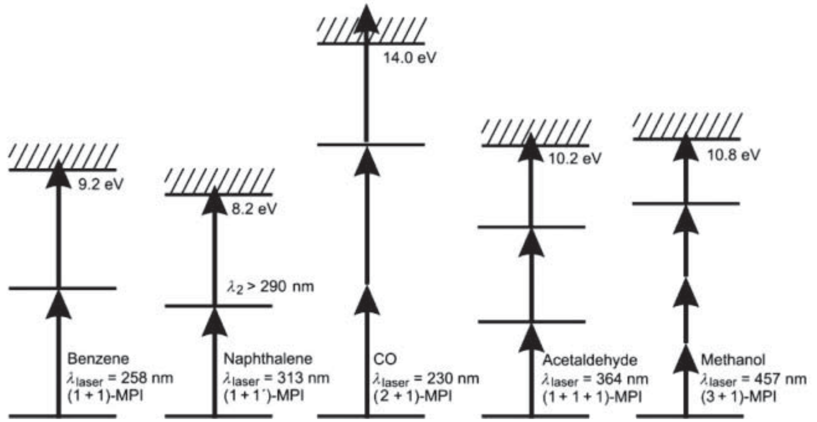


Multiphoton ionization schemes, a) Resonant 1+1 process, b) multicolor less frequently used multiphoton ionization schemes

Matsumoto et al., *Shinku*, **2007**, 50:241-245



Light source	Wavelength range		Lowest molecular absorption	Typ. transitions
			Alkanes	σ*← σ
Two-photon absorption $\lambda_{exc.}$= 1/2 λ_{UV}	150 nm / 8.3 eV 200 nm / 6.2 eV	Vacuum UV	Alkenes Alkines HCN Alcohols NH_3	σ*← n π*← π
Frequency doubling $\lambda_{exc.}$= 1/2 λ_{laser}	250 nm / 5.0 eV 300 nm / 4.1 eV	UV	OCS Aromatics H_2S	π*← n
Tunable laser wavelength $\lambda_{exc.}$= λ_{laser}	350 nm / 3.5 eV 400 nm / 3.1 eV		Aldehydes SO_2	π*← π conjug.sys.
	450 nm / 2.8 eV 500 nm / 2.5 eV	VIS	NO_2	π*← n conjug.sys.



Photoionization and Photo-Induced Processes in Mass Spectrometry, Ralf Zimmermann and Luke Hanley, 2021 WILEY-VCH GmbH

General Concept and Light Sources - REMPI

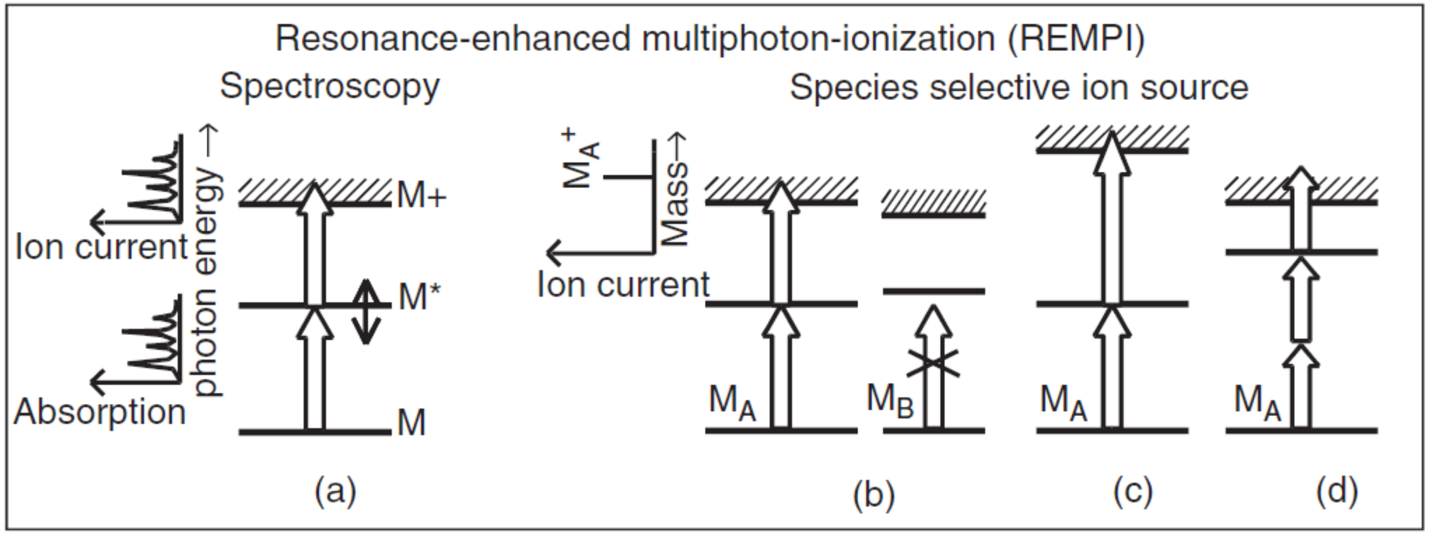
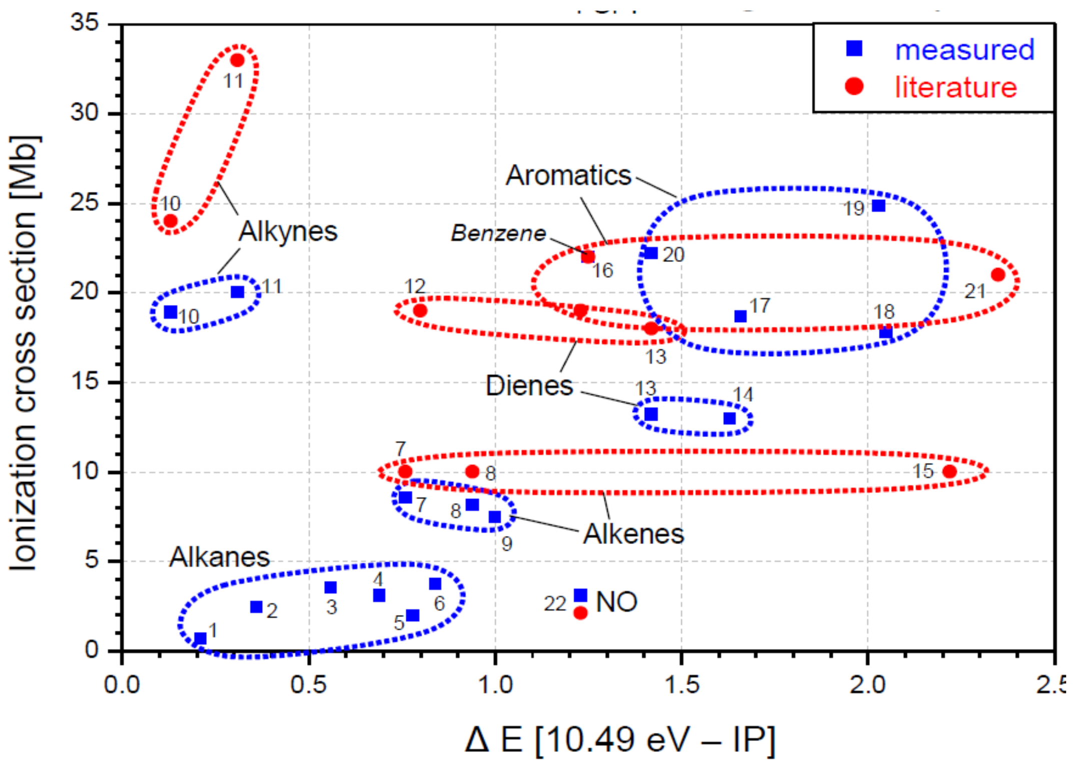


Figure 2.1 Schematic representation of the different possibilities of REMPI: (a) tuning the wavelength of the ionizing laser: the ion current (REMPI signal) reflects the gas-phase UV spectrum; (b) resonance-enhanced, two-photon ionization with photons of same energy (one-color REMPI) and illustration of selective ionization; (c) resonance-enhanced, two-photon ionization with photons of different energies (two-color REMPI); and (d) resonance-enhanced, three-photon ionization of higher order, here the example of (2 + 1)-REMPI.

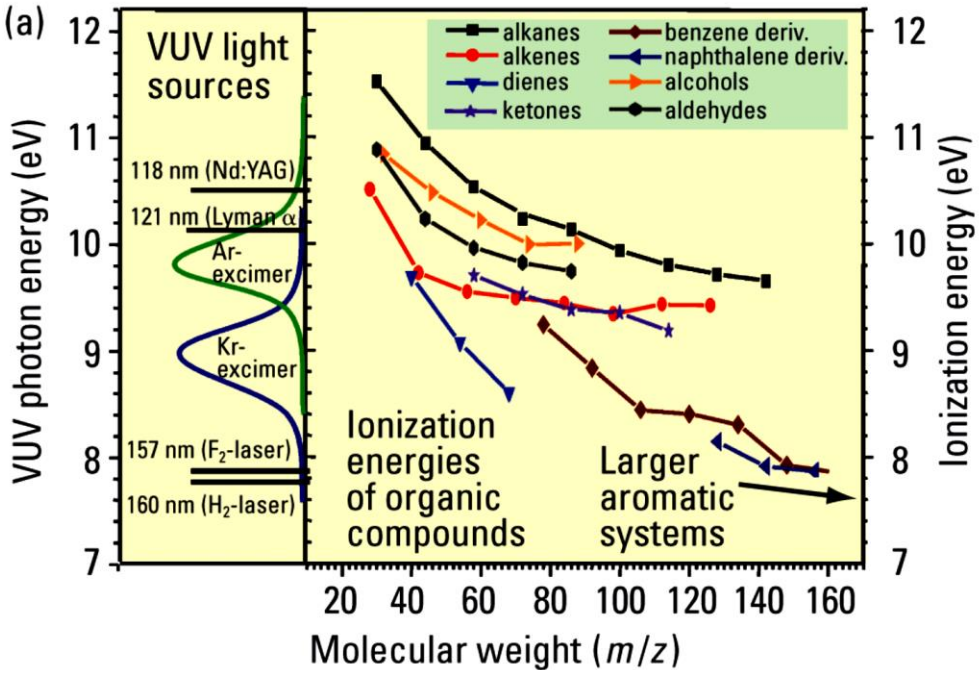
Photoionization and Photo-Induced Processes in Mass Spectrometry, Ralf Zimmermann and Luke Hanley, 2021 WILEY-VCH GmbH

Photoionization – PI

Ionization Cross Sections



Adam et al., *Anal Bioanal Chem*, **2007**



Hanley, L.; Zimmermann, R. *Analytical Chemistry* **2009**

- single photon ionization ion yield ~ concentration x VUV intensity x cross section
- variability of cross section in single photon ionization roughly one order of magnitude
- quantification feasible!

VUV Light Sources in Single Photon Ionization

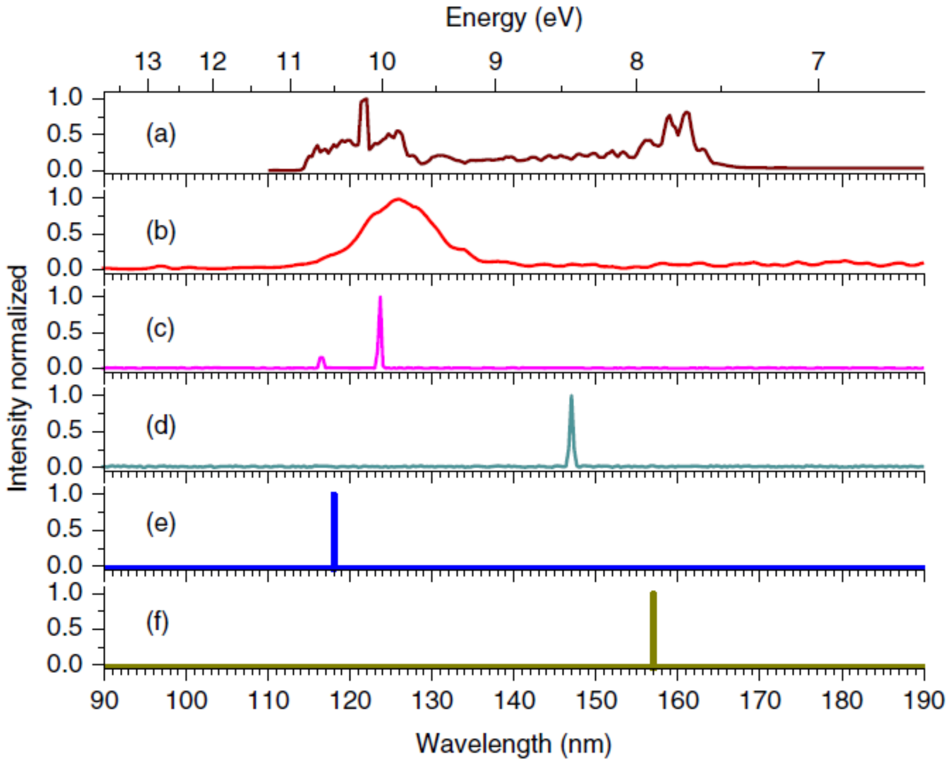


Figure 3.1 Measured emission spectra of different VUV light sources in the wavelength range between 90 and 190 nm, corresponding to photon energies from 6.5 to 13.75 eV (VUV spectrometer with low resolution monochromator): (a) D_2-Lamp (McPherson), (b) Ar-Electron beam-pumped lamp, (c) Kr-discharge lamp (PID), (d) Xe-discharge lamp (PID), (e) ninth harmonic frequency of the Nd:YAG laser line (sketched), and (f) F_2-Excimer laser line (sketched).

Photoionization and Photo-Induced Processes in Mass Spectrometry, Ralf Zimmermann and Luke Hanley, 2021 WILEY-VCH GmbH

Single Photon Ionization – Example and Cross Section Correction

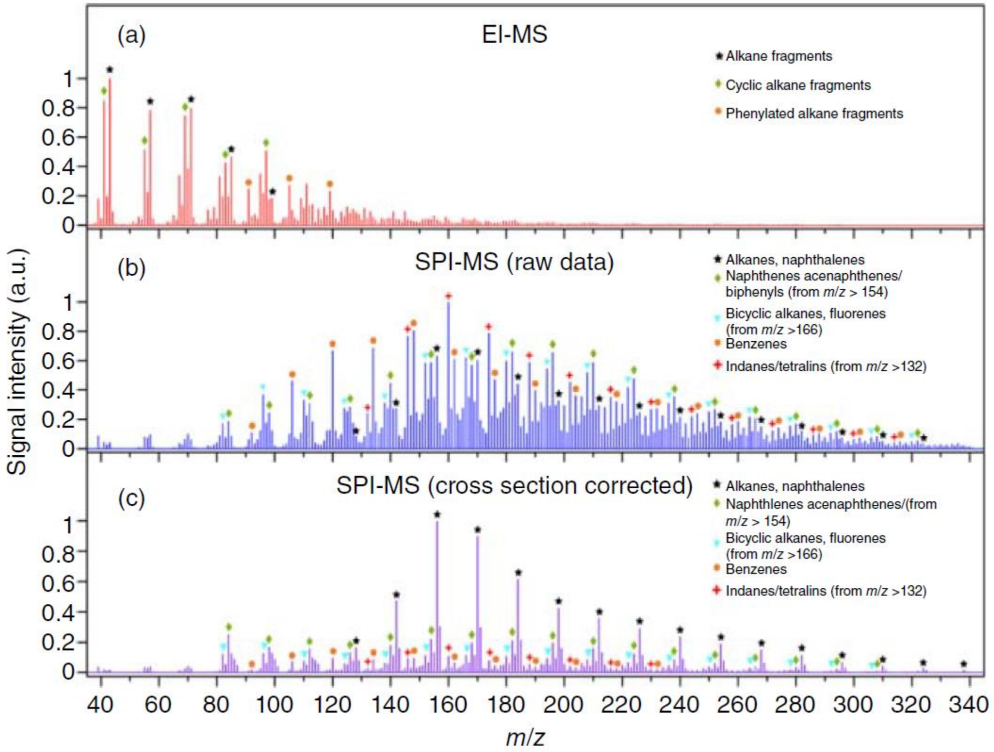


Figure 3.3 Three mass spectra of a mineral oil-type fuel (diesel fuel, fully vaporized). (a) 70 eV EI mass spectrum obtained by summing up over the total gas chromatographic run. (b) SPI mass spectrum (raw data) obtained by summing up over the total gas chromatographic run. (c) Cross section corrected SPI mass spectrum (averaged cross sections for compound classes) approximating the molar concentration profile of the mineral oil distillate sample. Source: Modified from Eschner et al. (2011b).

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Single Photon Ionization – Examples

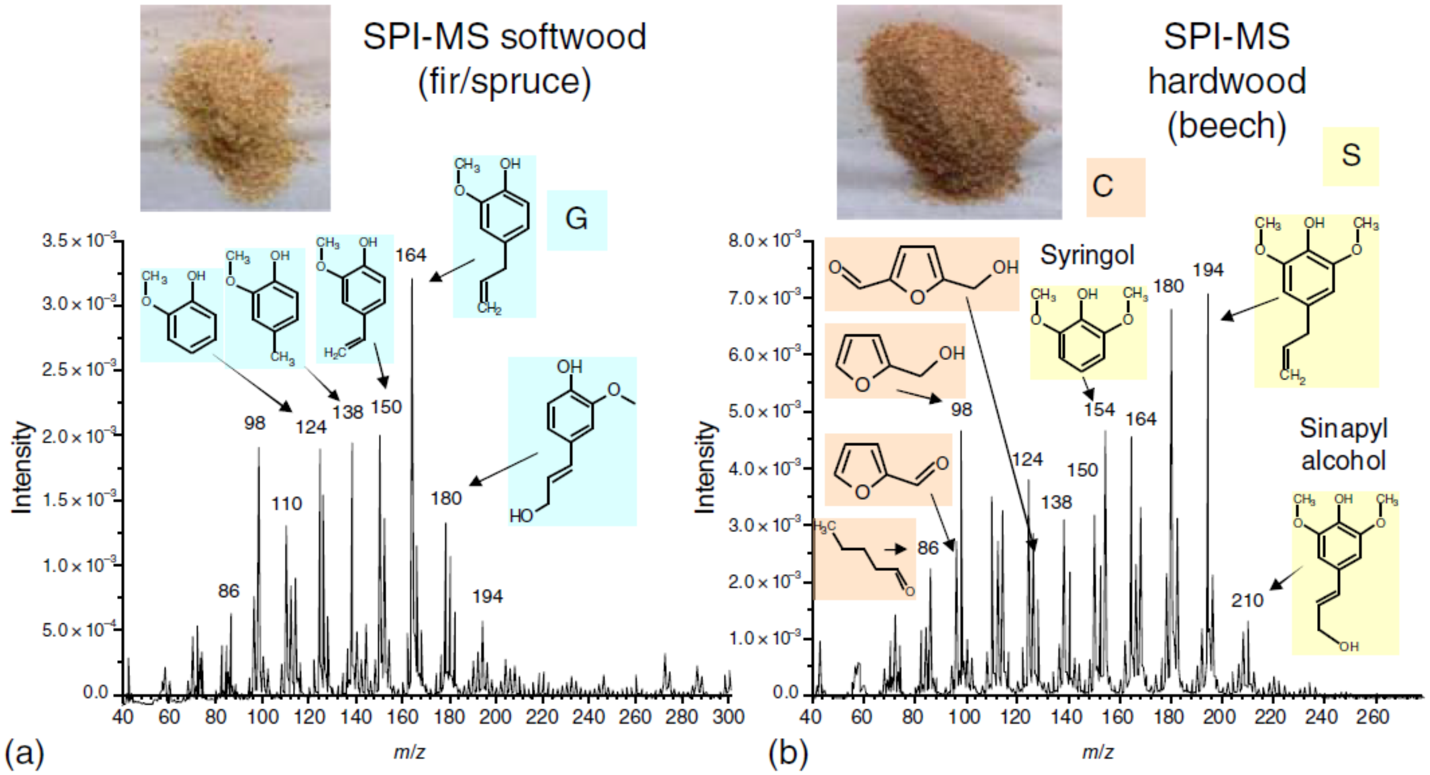


Figure 3.7 Emerging gas-phase products from wood pyrolysis recorded by real-time SPI-ToFMS depicting differences between softwood (a) and hardwood (b) via the respective patterns of phenolic and furanoic species. G stands for guaiacol derivatives, S for syringol derivatives, and C for cellulose decomposition products. See also: Fendt et al. (2012).

Photoionization and Photo-Induced Processes in Mass Spectrometry, Ralf Zimmermann and Luke Hanley, 2021 WILEY-VCH GmbH

Photoionization – PI

Single Photon Ionization – Examples

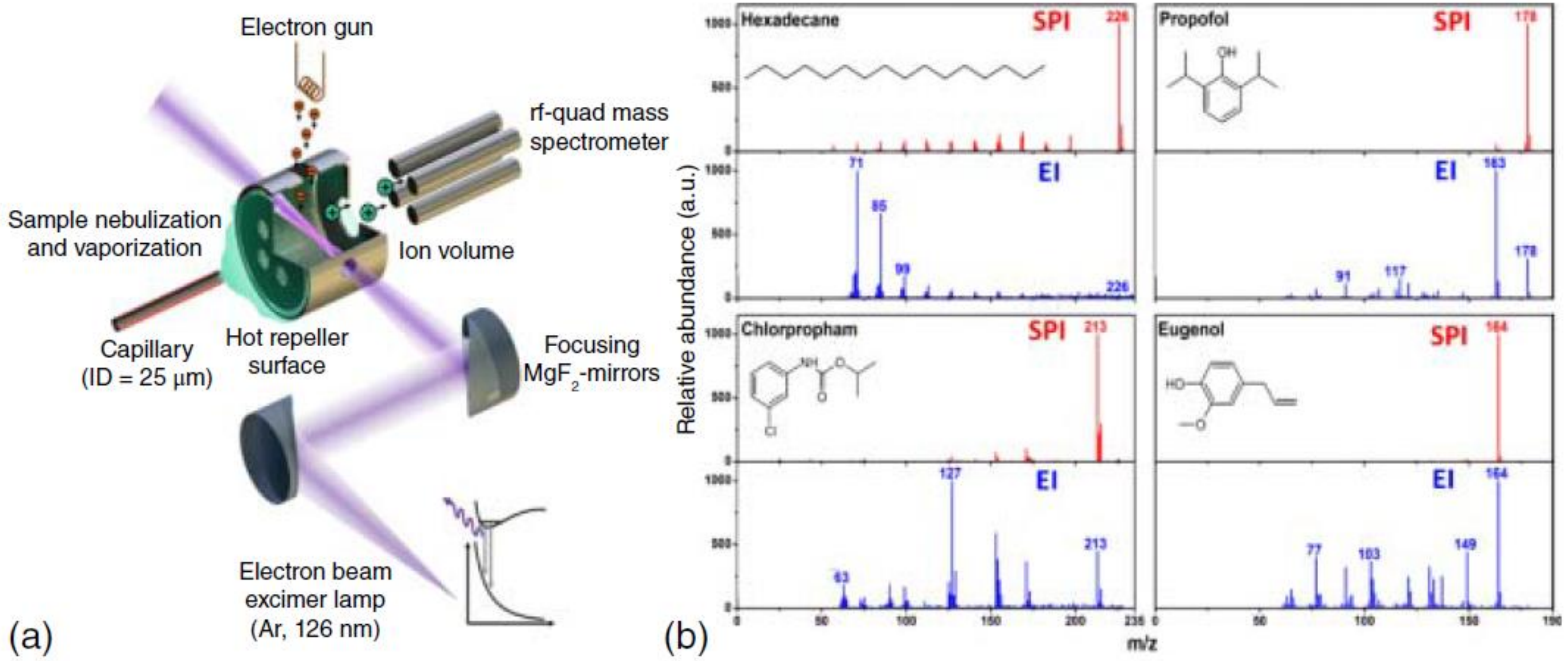
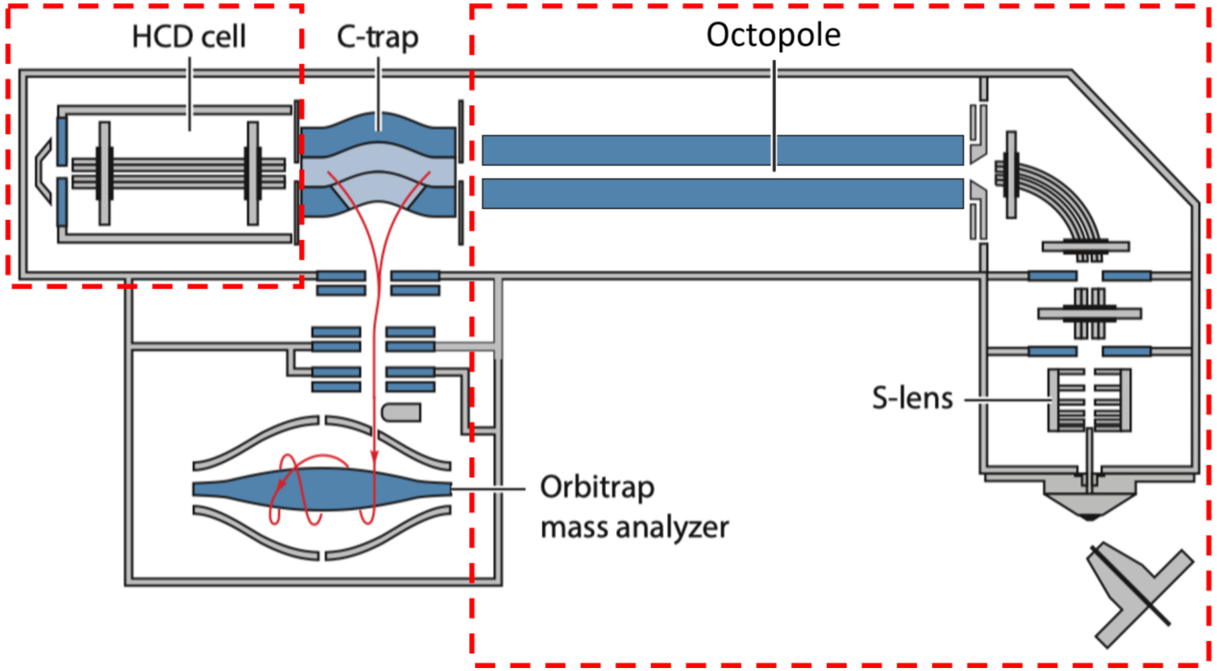


Figure 3.14 (a) Setup of a direct inlet for liquid samples with photoionization and electron ionization. (b) Corrected SPI (top) and EI (bottom) spectra and the respective NIST spectra (inset) for hexadecane, propofol, chlorpropham, and eugenol: the EI fragment mass spectra depict the fragmentation pattern in good agreement, whereas the SPI spectra are dominated by the molecular ions. Source: From Schepler et al. (2013).

Photoionization and Photo-Induced Processes in Mass Spectrometry, Ralf Zimmermann and Luke Hanley, 2021 WILEY-VCH GmbH

Vacuum Photoionization on an Orbitrap FTMS

Goal: Vacuum photoionization on an Orbitrap mass analyzer



Idea of the so-called "naked" Orbitrap

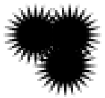
- removing the ion transmission optics and components for the atmospheric pressure inlet
- adaption of the vacuum system allowing direct sampling of the evolved gas mixture

→ compact and robust instrumentation for field usage at the emissions site maintaining high-resolving power and high mass accuracy

Schematic setup of the Orbitrap Exactive™ mass spectrometer used as a basis for the novel photoionization platform. Components in the dashed red boxes are removed. Adapted based on (1).

(1) Eliuk, S.; Makarov, A. *Annual review of analytical chemistry* **2015.** "Evolution of Orbitrap Mass Spectrometry Instrumentation", DOI: 10.1146/annurev-anchem-071114-040325.

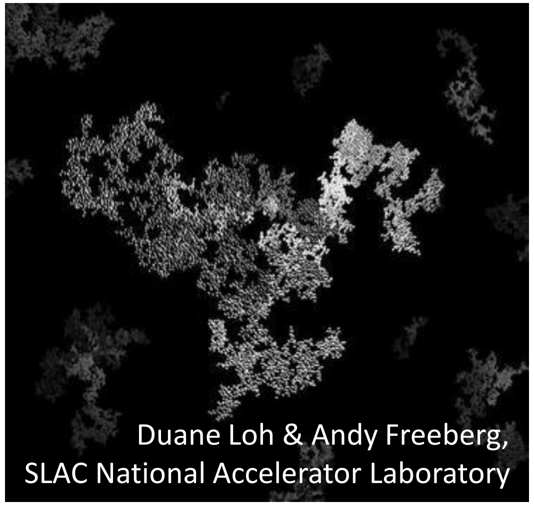
Particulate Matter and Carbonaceous Aerosols



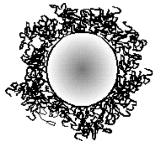
carbon cores

lung depos., inflamm.

Janssen et al. WHO, 2012, wedocs.unep.org/handle/20.500.11822/8699



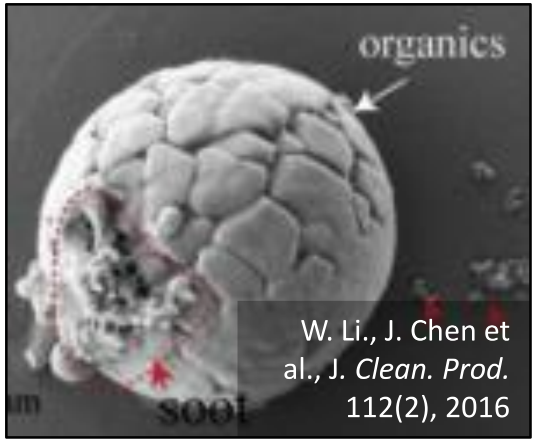
Duane Loh & Andy Freeberg, SLAC National Accelerator Laboratory



organic coatings

carcinogenic PAHs

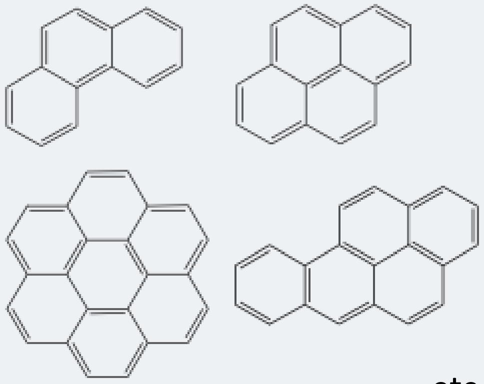
Kim, K.-H. et al. *Environ. Int.* **60**, 71-80, **2013**
Boström, C.-E. et al. *Environ. Health Perspect.* **110**, Suppl 3, 451-488, **2002**



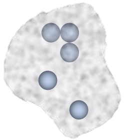
W. Li., J. Chen et al., J. *Clean. Prod.* 112(2), 2016

Polycyclic aromatic hydrocarbons (PAHs)

- formation in combustion processes
- absorption of UV-light
- some with carcinogenic, mutagenic, genotoxic potential



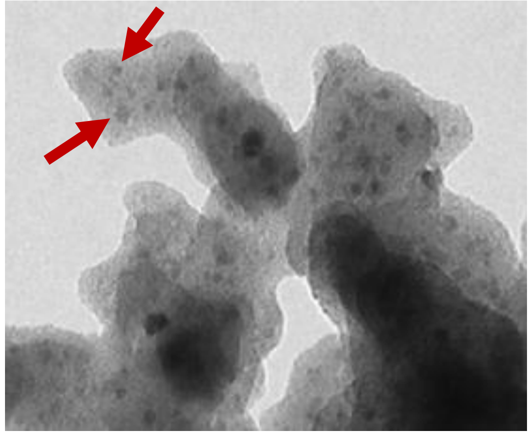
etc.



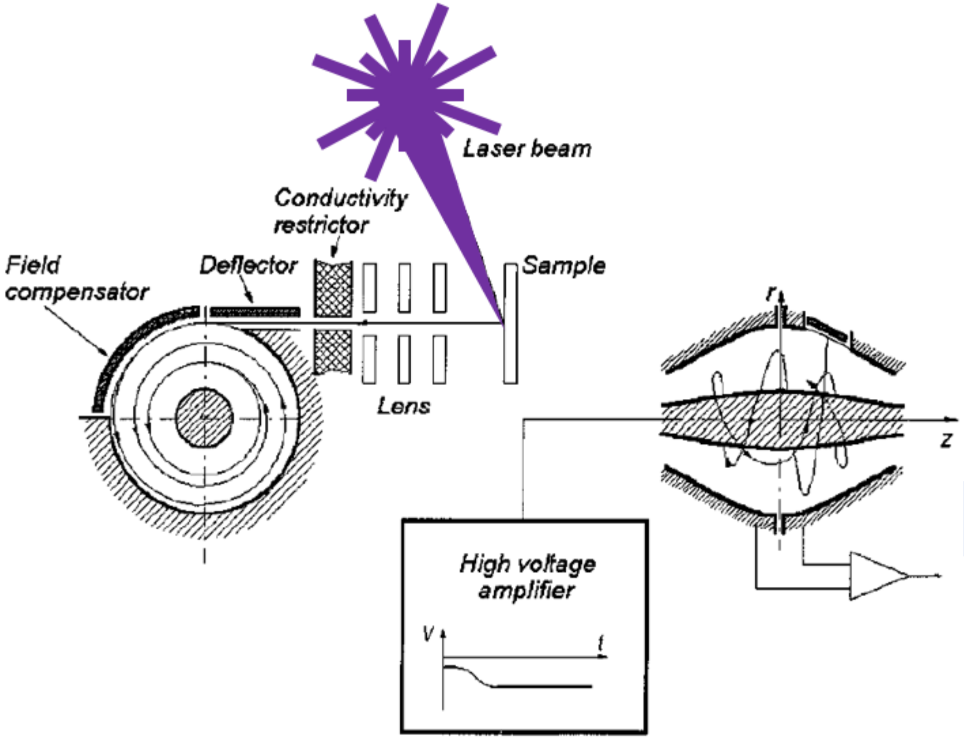
metal oxides

cardiov. desease

Fang, T. et al. *Environ. Sci. Technol.* **51**, 2611-2620, **2017**
Ye, D. et al. *Environ. Health Perspect.* **126**, 2, 27007, **2018**



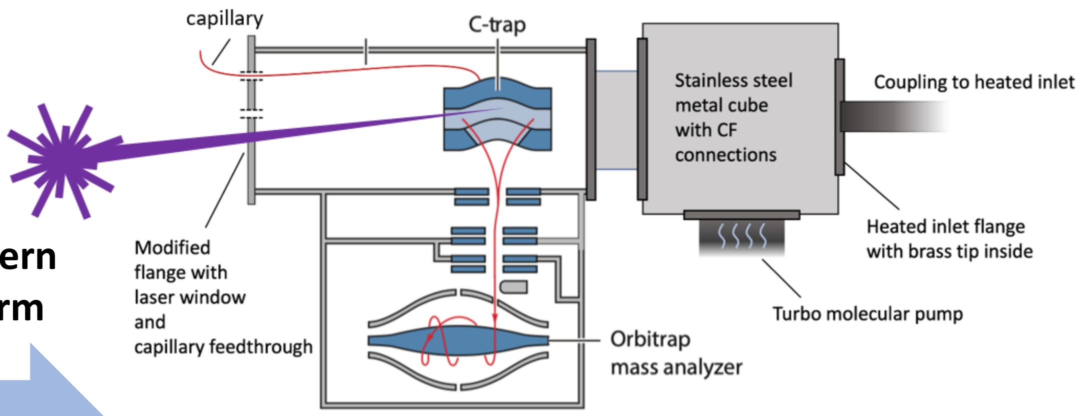
Vacuum laser ionization on an Orbitrap mass analyzer – A not very new idea…



Adapted based on Makarov, A. Analytical Chemistry 2000. "Electrostatic axially harmonic orbital trapping: a high-performance technique of mass analysis", DOI: 10.1021/ac991131p.

Transfer to modern Orbitrap platform

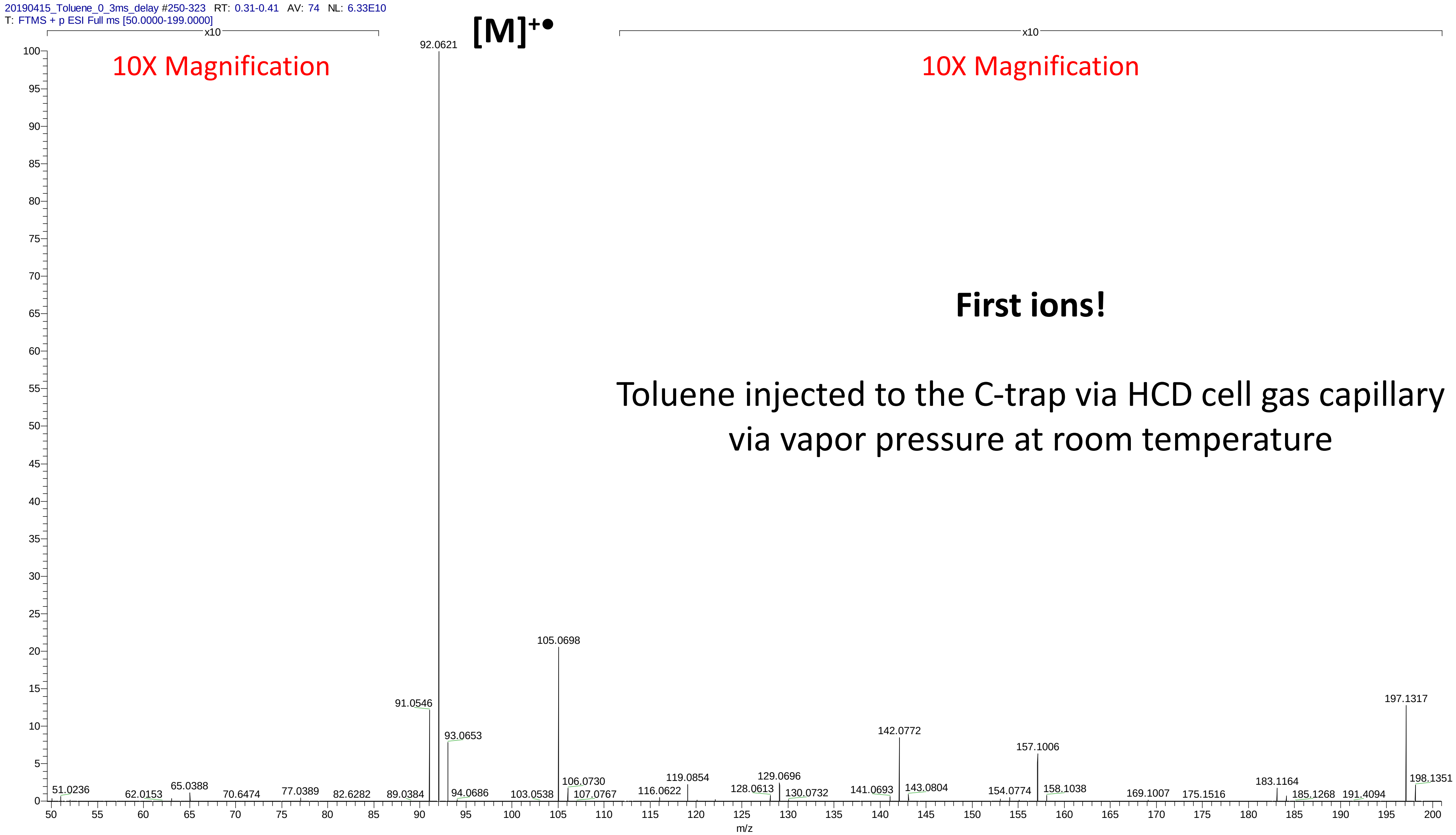
First theoretical conception



… **but** not realized in C-trap so far and various problems might occur due to

- restricted ionization volume and space
- difficult sample introduction
- vacuum requirements …

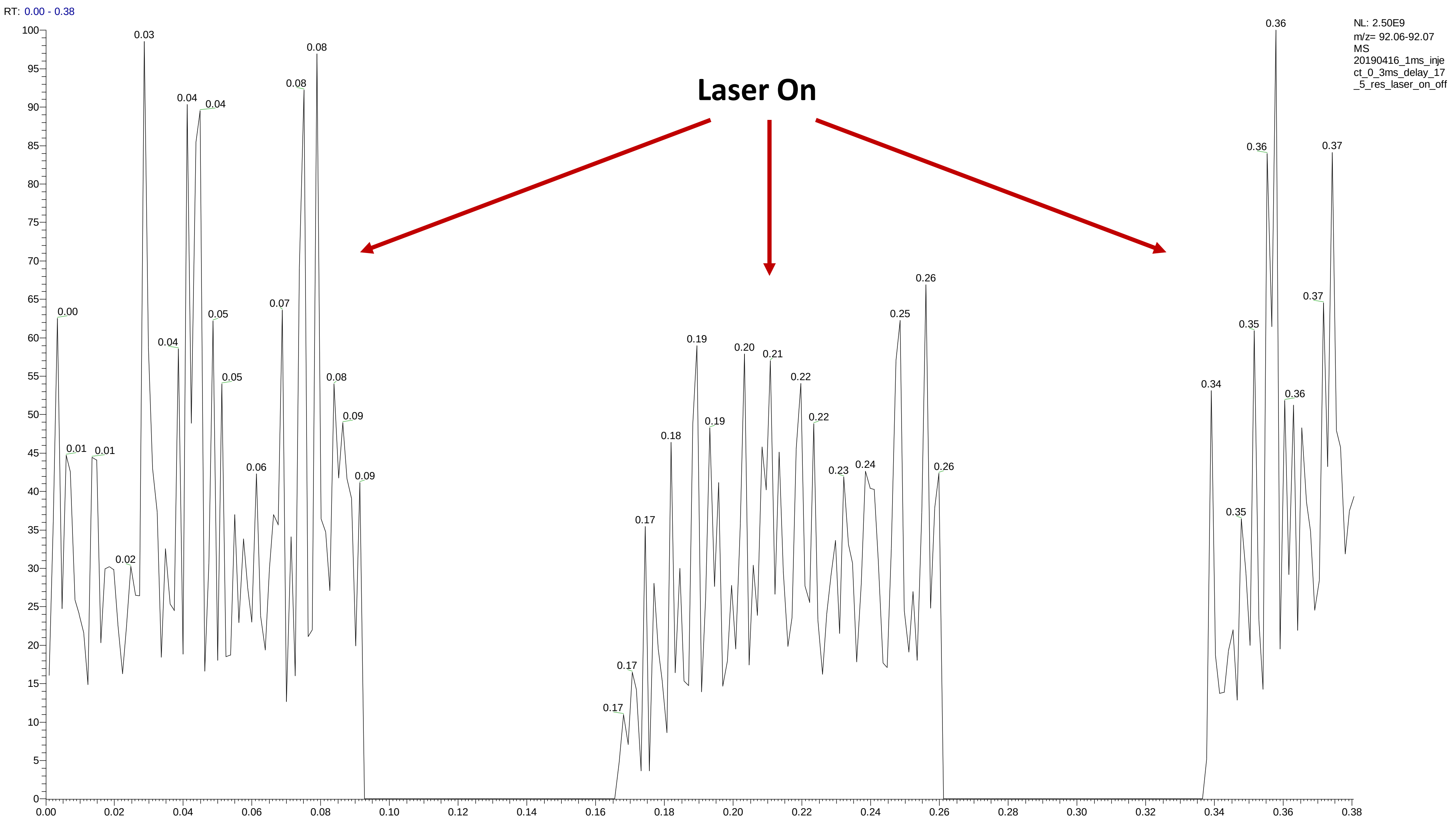
Vacuum Photoionization Orbitrap



First ions!

Toluene injected to the C-trap via HCD cell gas capillary via vapor pressure at room temperature

Vacuum Photoionization Orbitrap



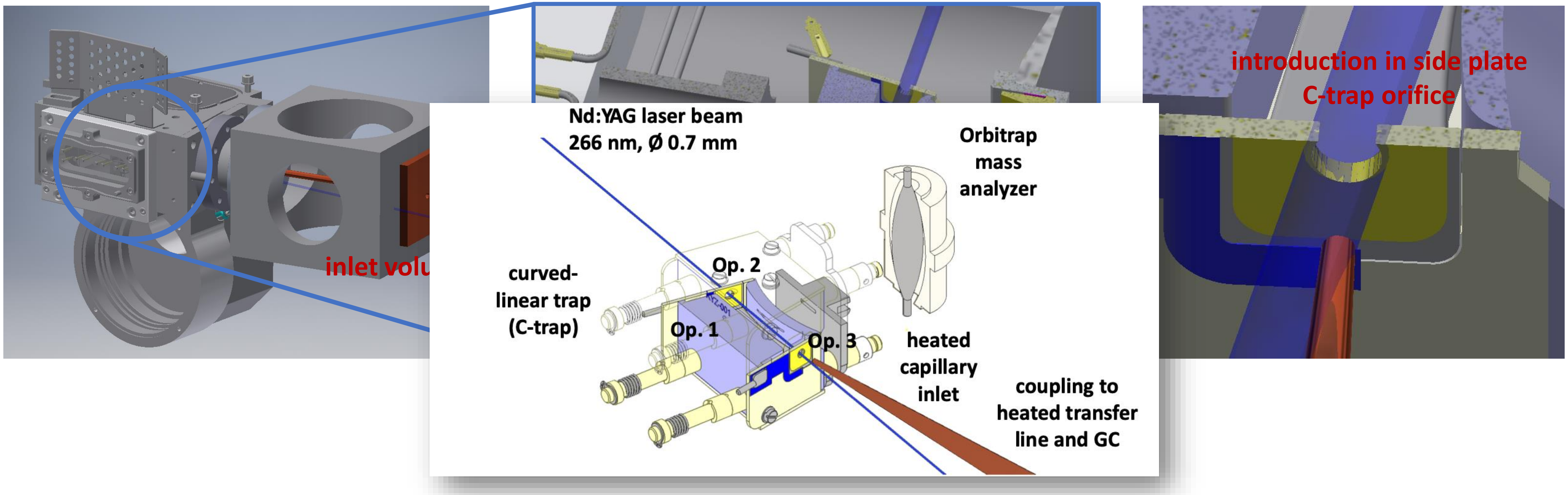
Laser On

Setting-up the Photoionization Prototype

Hardware changes and reconstruction

→ physical removement (before just electronic unplugging) of the components related to the atmospheric pressure inlet

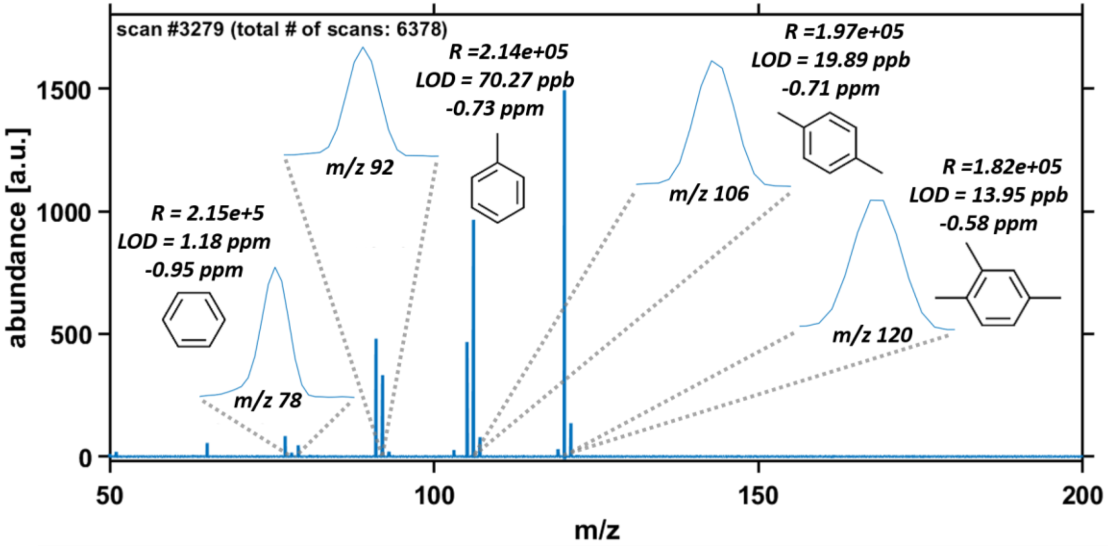
→ design of heated inlet system with introduction volume for additional turbo molecular pumping

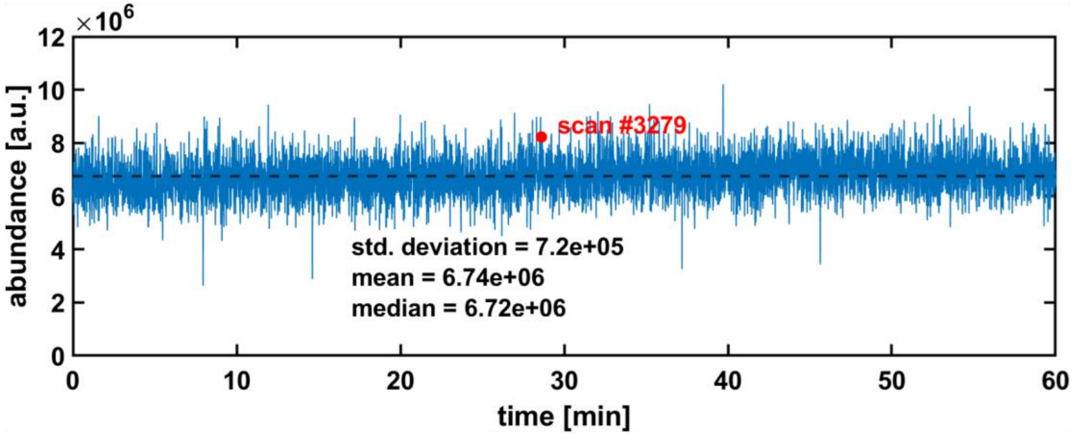


Testing and Evaluation of the Gas Inlet

Benzene, Toluene, p-Xylene and 1,2,4-trimethylbenzene (BTX)

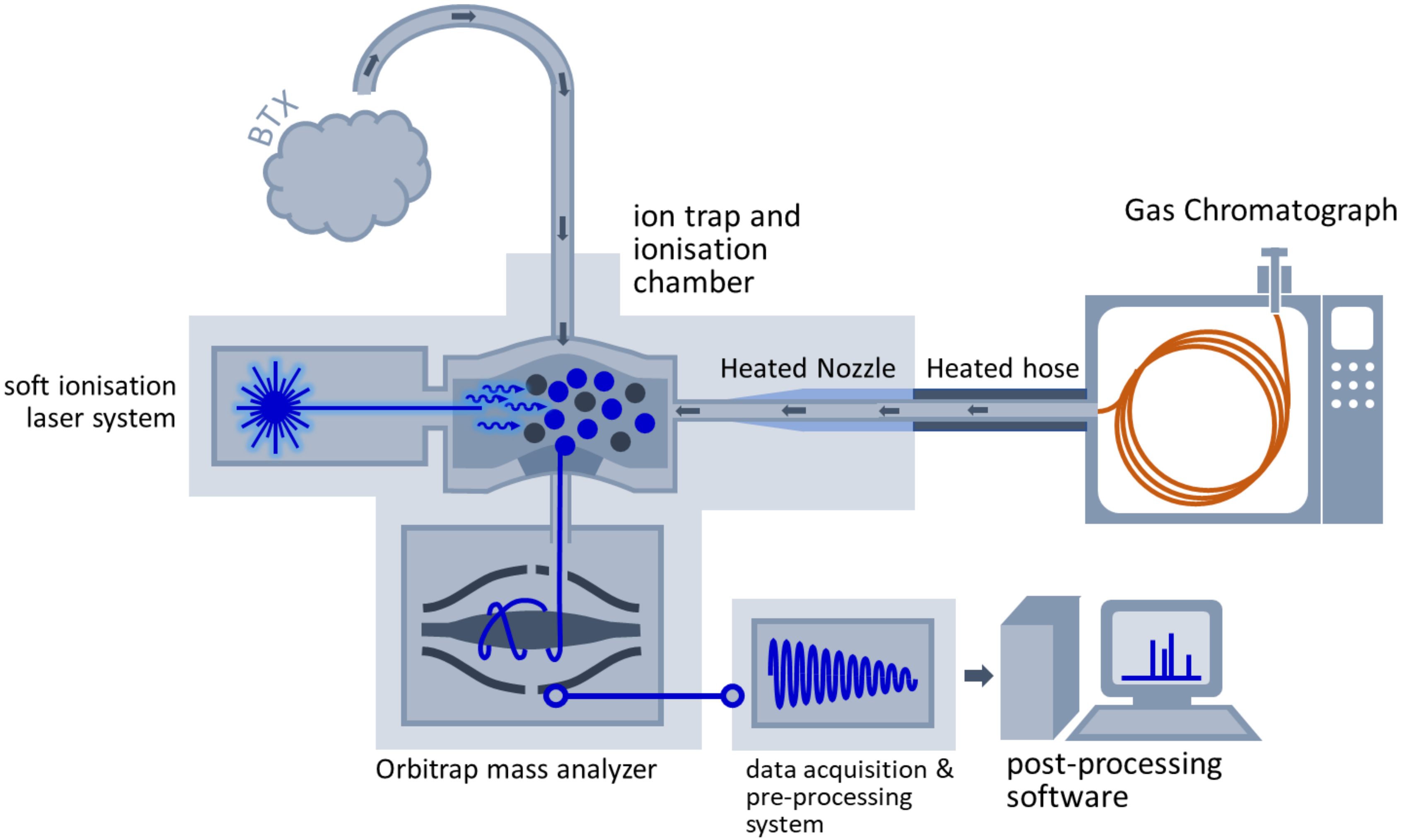
→ sensitivity, stability, mass accuracy and other figures of merit





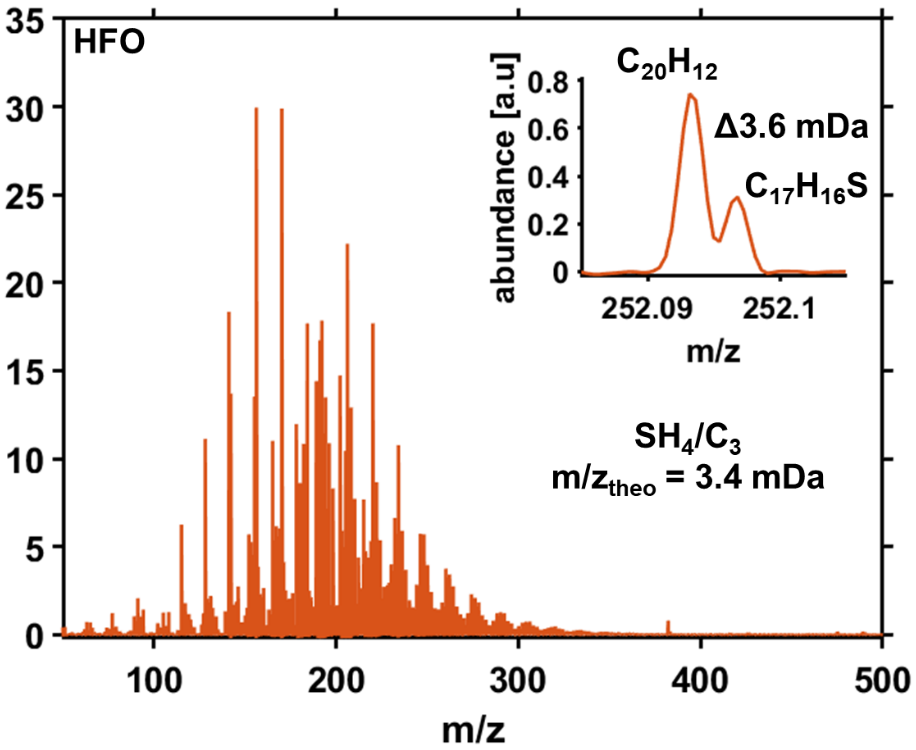
- high resolution and sub-ppm mass accuracy could be retained
- signal stability for hours (mainly effects due to laser energy drift)
- sensitivity in low ppm/ppb-range comparable to time-of-flight MS solutions

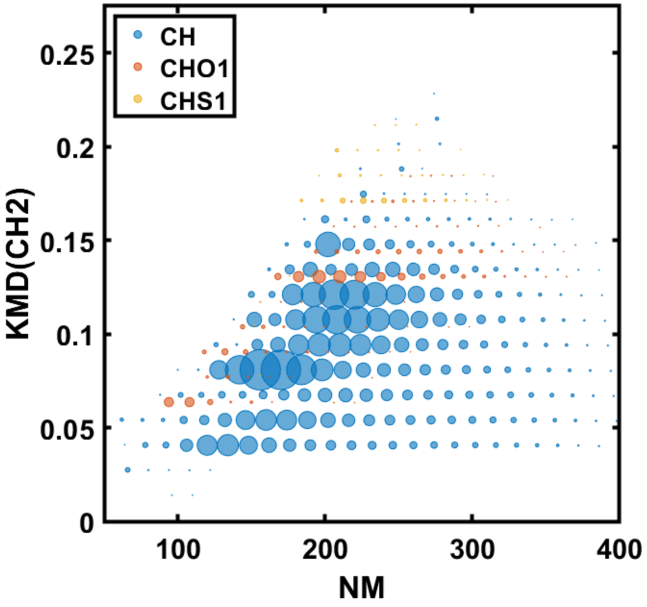
Evaluation of the platform with higher boiling point constituents



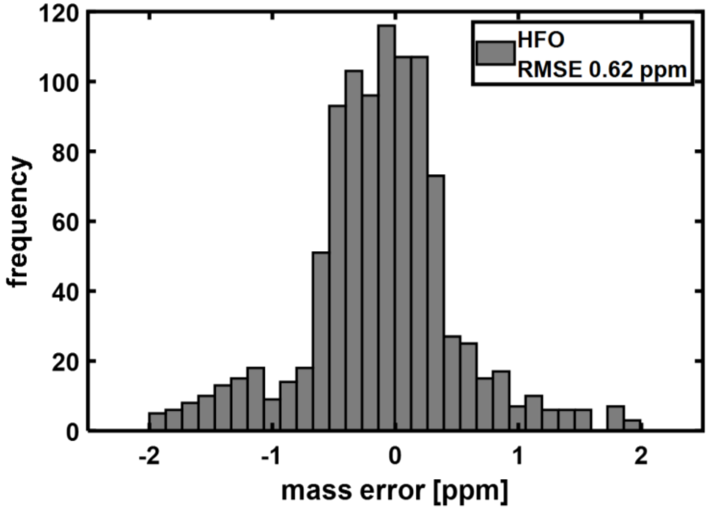
Petroleomics sample material introduced via gas chromatography hyphenation

Heavy fuel oil (HFO) as petrochemical feed fuel for ship diesel engines → precursor for aerosol emissions





Kendrick mass defect plot
Horizontal lines – alkylation



Attribution error histogram
with < 1 ppm RMSE

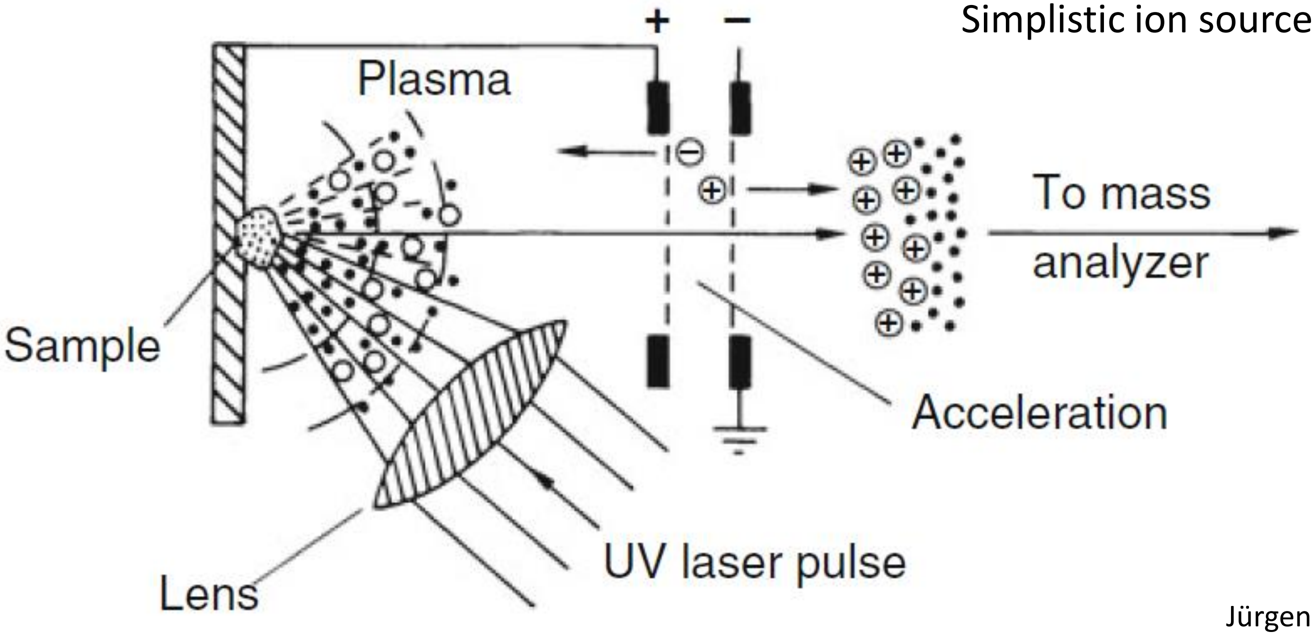
Analytical Chemistry, **2021**, 93, 27, 9418–9427
DOI: 10.1021/acs.analchem.0c04740

→ preserving the molecular complexity of alkylated PAHs
→ high mass resolving power and mass accuracy allows to separate isobaric interferences

Laser Desorption Ionization – LDI

Concept and Basics

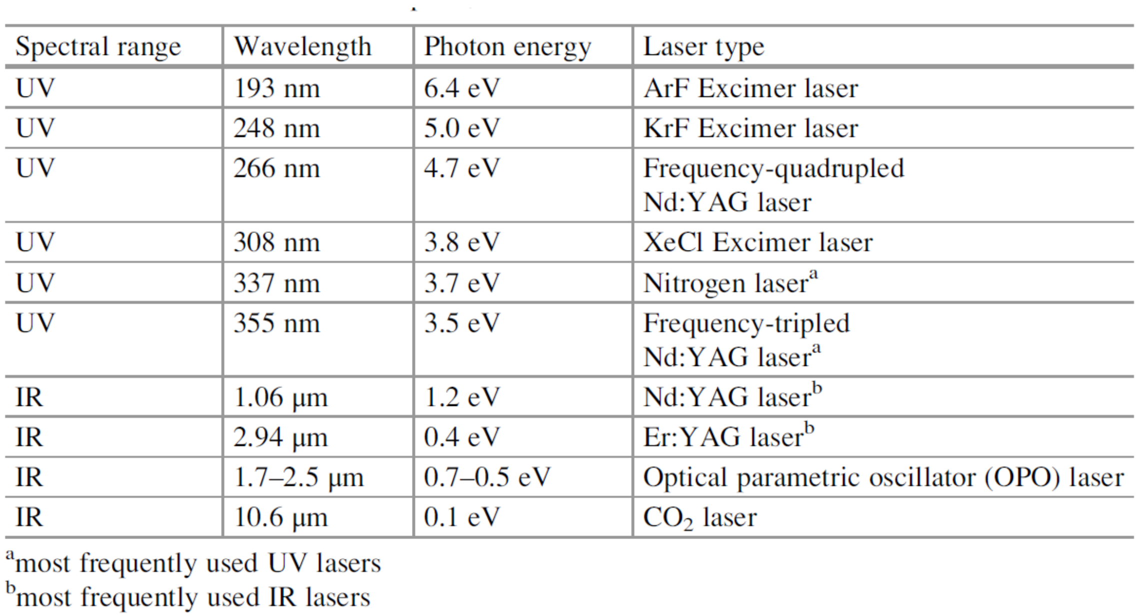
- pulsed laser light as a source of energy for desorption and ionization
- ion formation from thin solid layers
- matrix assistance as a key to soft desorption/ionization
- vacuum and atmospheric pressure sources for MALDI
- MALDI imaging techniques as one important application



Simplistic ion source for LDI design

Jürgen H- Gross, *Mass Spectrometry – A Textbook*, **2017**, Spinger, ISBN *978-3-319-54398-7*

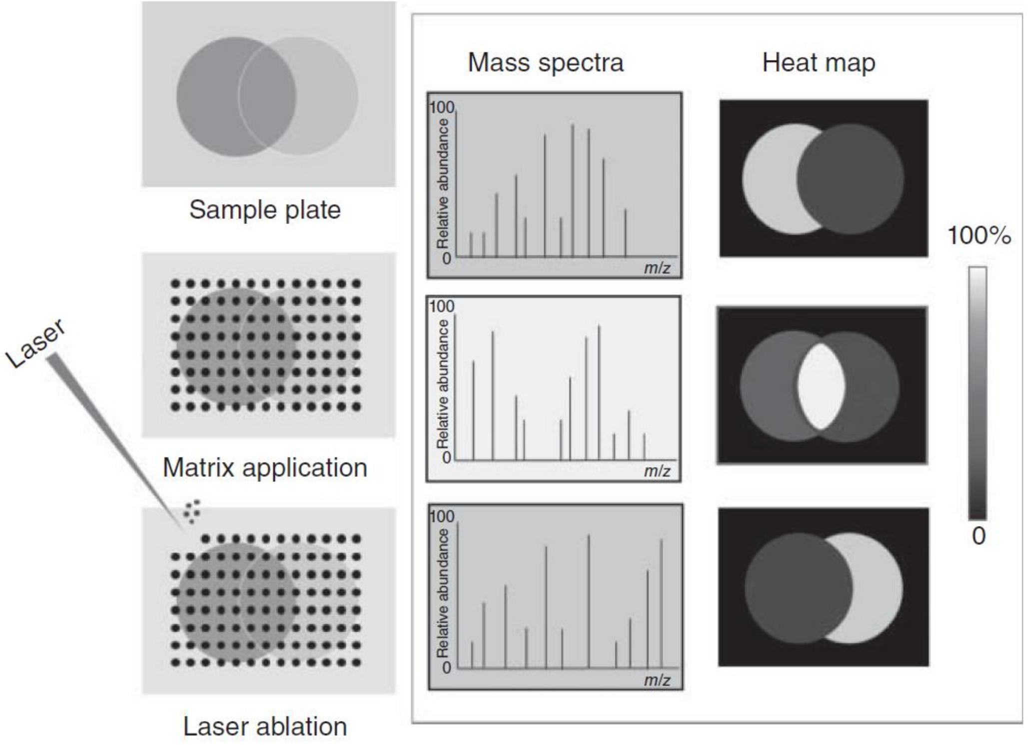
Laser Usage and Imaging Concept



Spectral range	Wavelength	Photon energy	Laser type
UV	193 nm	6.4 eV	ArF Excimer laser
UV	248 nm	5.0 eV	KrF Excimer laser
UV	266 nm	4.7 eV	Frequency-quadrupled Nd:YAG laser
UV	308 nm	3.8 eV	XeCl Excimer laser
UV	337 nm	3.7 eV	Nitrogen laser[a]
UV	355 nm	3.5 eV	Frequency-tripled Nd:YAG laser[a]
IR	1.06 µm	1.2 eV	Nd:YAG laser[b]
IR	2.94 µm	0.4 eV	Er:YAG laser[b]
IR	1.7–2.5 µm	0.7–0.5 eV	Optical parametric oscillator (OPO) laser
IR	10.6 µm	0.1 eV	CO_2 laser

[a] most frequently used UV lasers
[b] most frequently used IR lasers

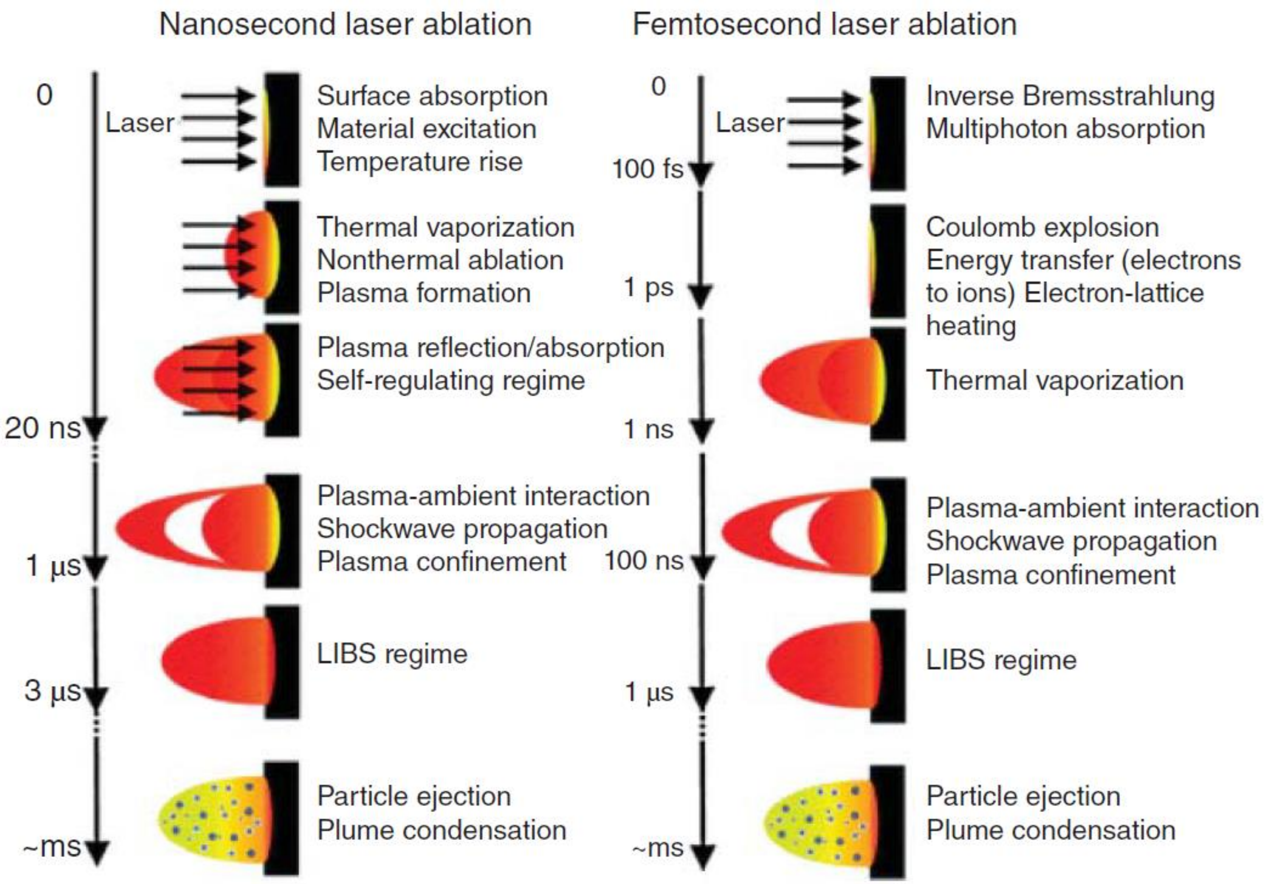
Common laser types for laser desorption ionization



General concept for (MA)LDI imaging creating three-dimensional information from the lateral distributed spectral data

Matsumoto et al., *Shinku*, **2007**, 50:241-245

Approximate timescales of nanosecond and femtosecond energy absorption and laser ablation (in atmosphere)

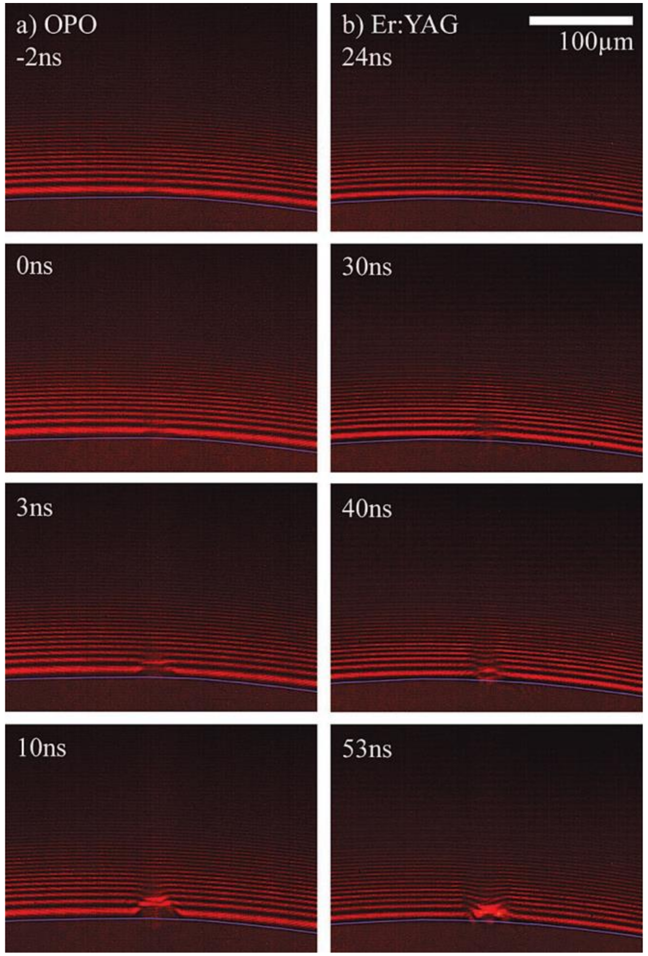


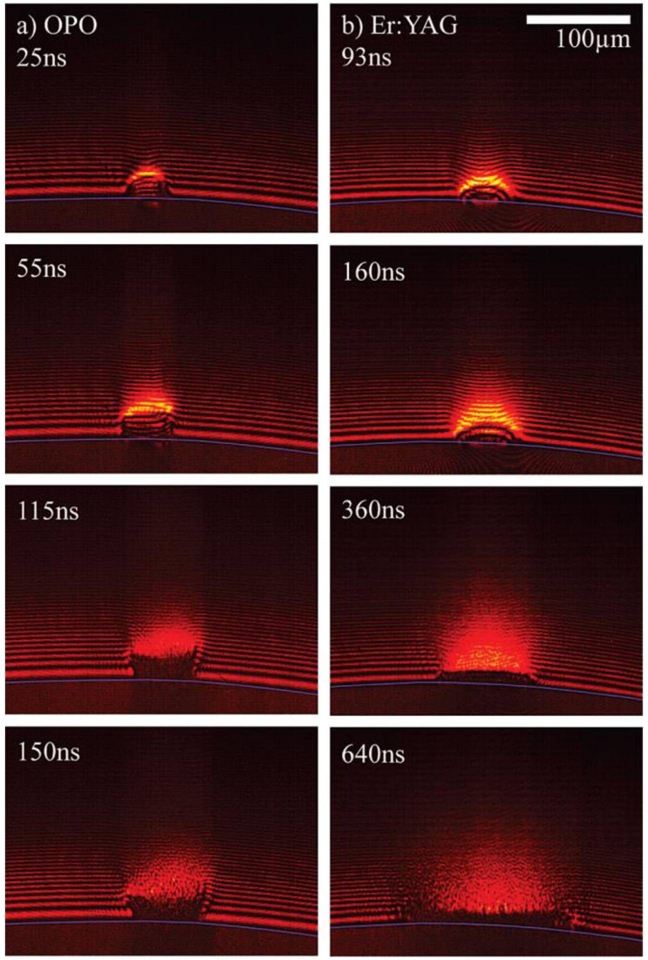
Photoionization and Photo-Induced Processes in Mass Spectrometry, Ralf Zimmermann and Luke Hanley, 2021 WILEY-VCH GmbH

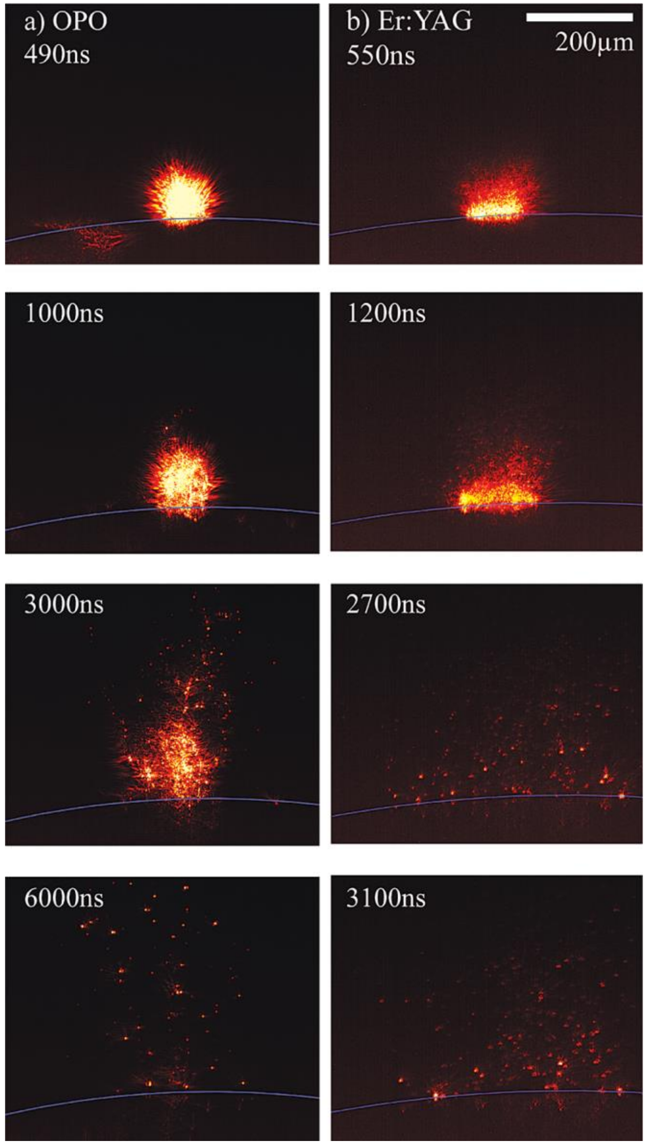
Harila et al., **2014**

Laser Desorption Ionization – LDI

Laser Ablation Process



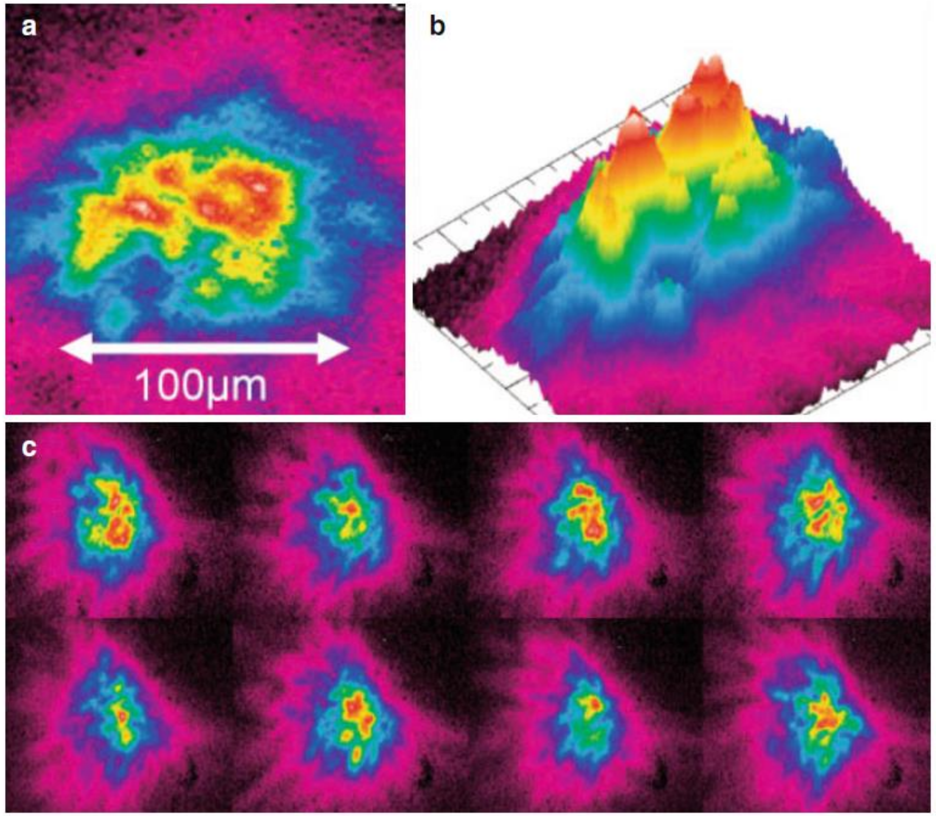




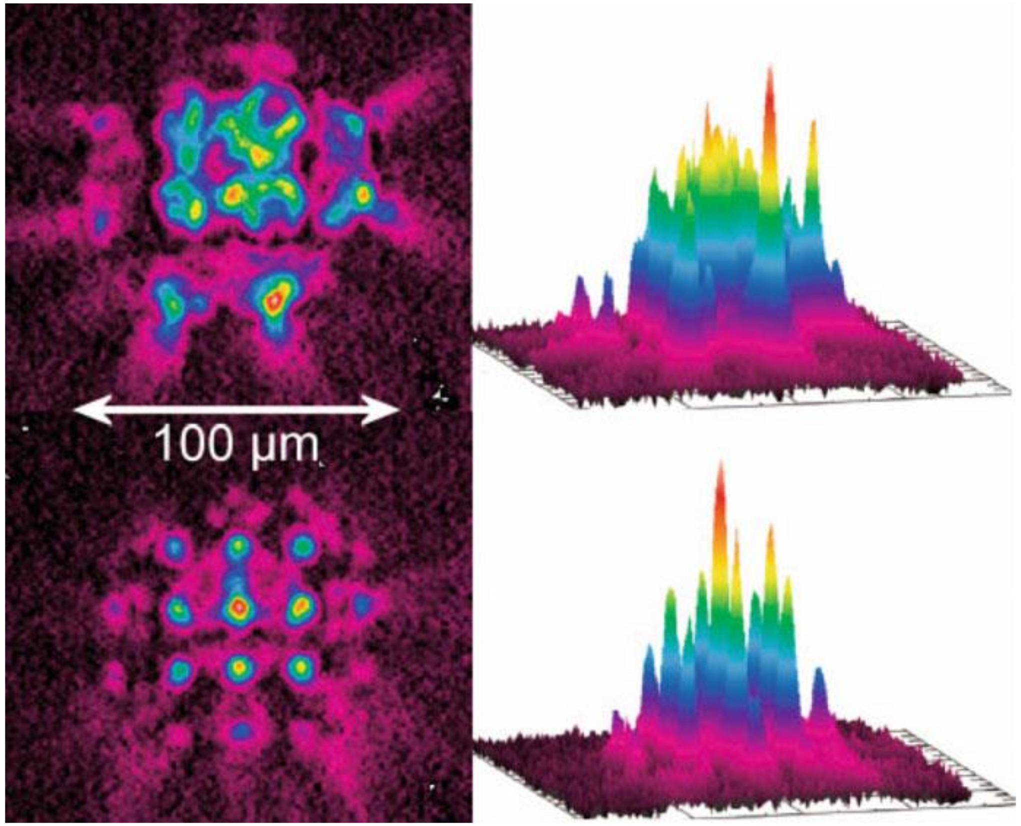
Leisner et al., *J. Phys. Chem. B*, **2005**, 11661-11666

Laser Desorption Ionization – LDI

Laser Profile and the Ablation Process



Nitrogen laser beam profile

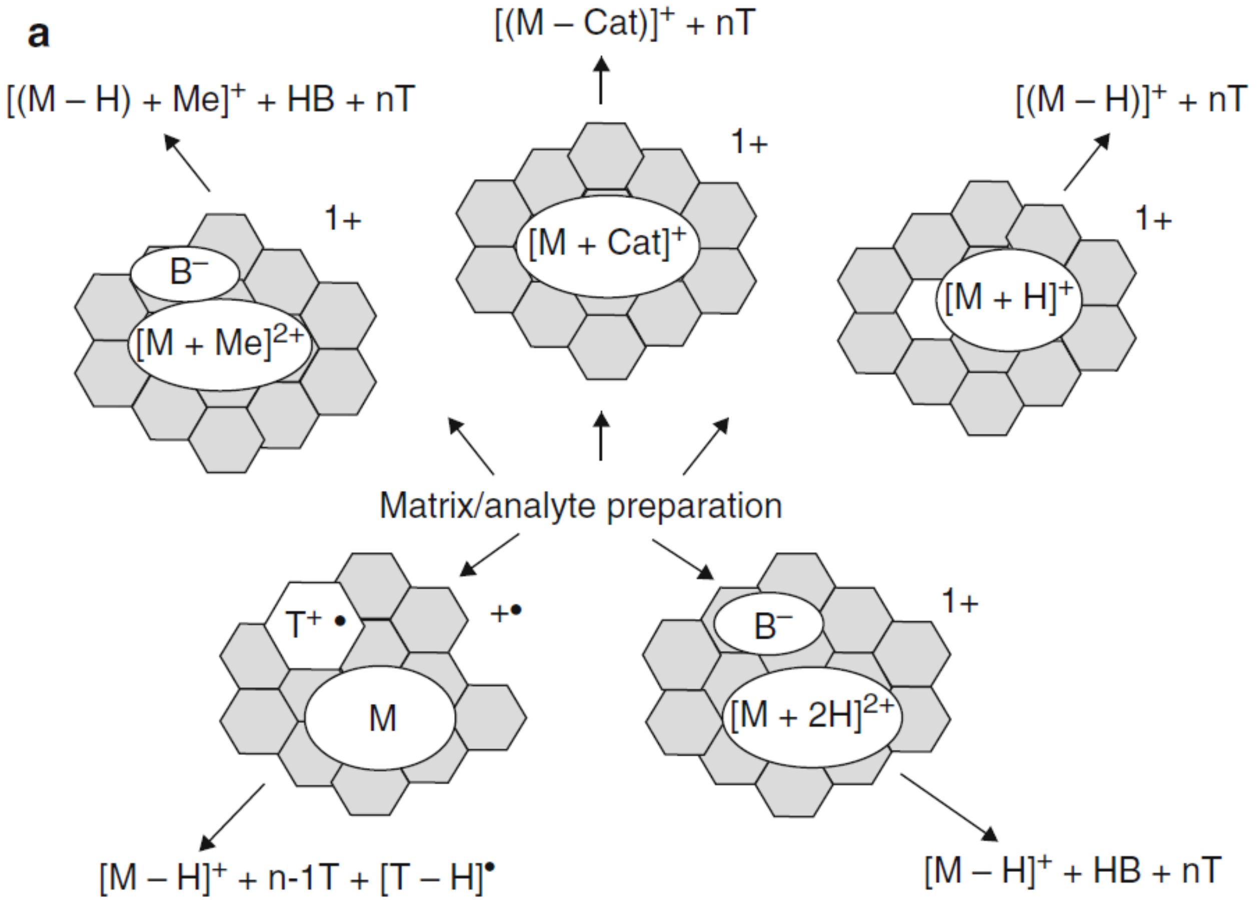


Nd:YAG Bruker Smartbeam laser beam profile

Nitrogen laser beam profile, the non-homogenous energy distribution has to be considered for imaging aspects

Holle et al., *J Mass Spec*, **2006**, 41:705–716

The Use of Matrices for Energy Uptake and Adapting Ionization Behavior

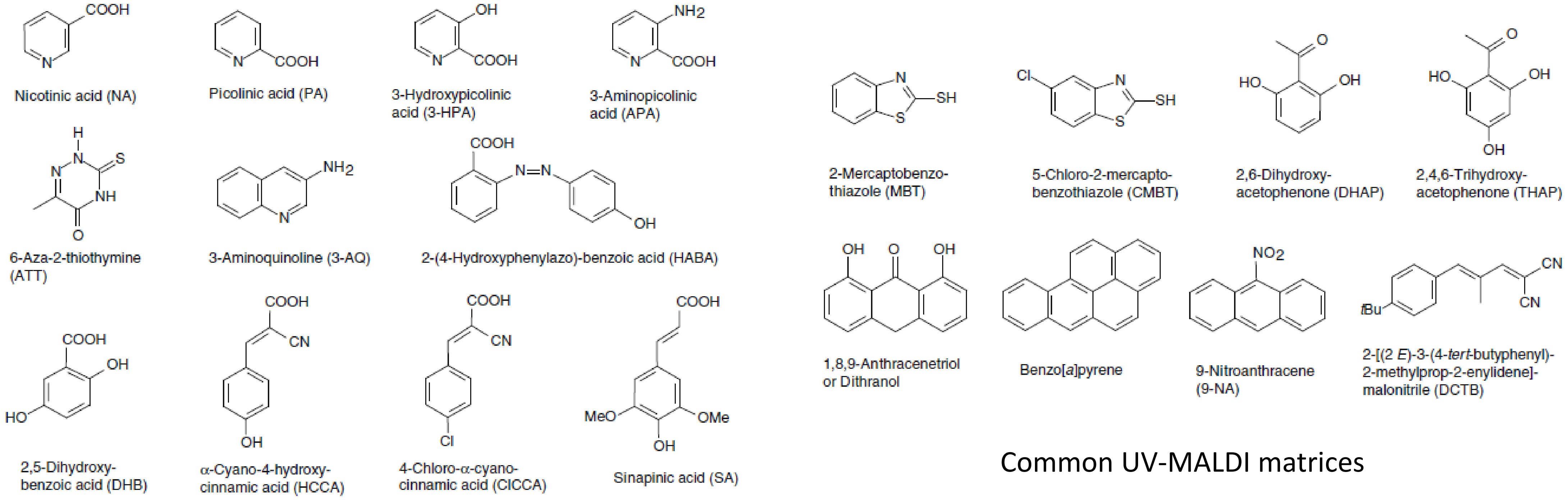


Pathways of formation of singly charged ions from sample–matrix preparations according to the lucky survivor model.

M: analyte molecule
T: matrix molecule
Cat: small cation
Me: metal^{2+}
B: base

Karas et al., *J Mass Spectrom*, **2000**, 35:1–12

The Use of Matrices for Energy Uptake and Adapting Ionization Behavior


Nicotinic acid (NA)

Picolinic acid (PA)

3-Hydroxypicolinic acid (3-HPA)

3-Aminopicolinic acid (APA)

6-Aza-2-thiothymine (ATT)

3-Aminoquinoline (3-AQ)

2-(4-Hydroxyphenylazo)-benzoic acid (HABA)

2,5-Dihydroxy-benzoic acid (DHB)

α-Cyano-4-hydroxy-cinnamic acid (HCCA)

4-Chloro-α-cyano-cinnamic acid (ClCCA)

Sinapinic acid (SA)

2-Mercaptobenzo-thiazole (MBT)

5-Chloro-2-mercapto-benzothiazole (CMBT)

2,6-Dihydroxy-acetophenone (DHAP)

2,4,6-Trihydroxy-acetophenone (THAP)

1,8,9-Anthracenetriol or Dithranol

Benzo[*a*]pyrene

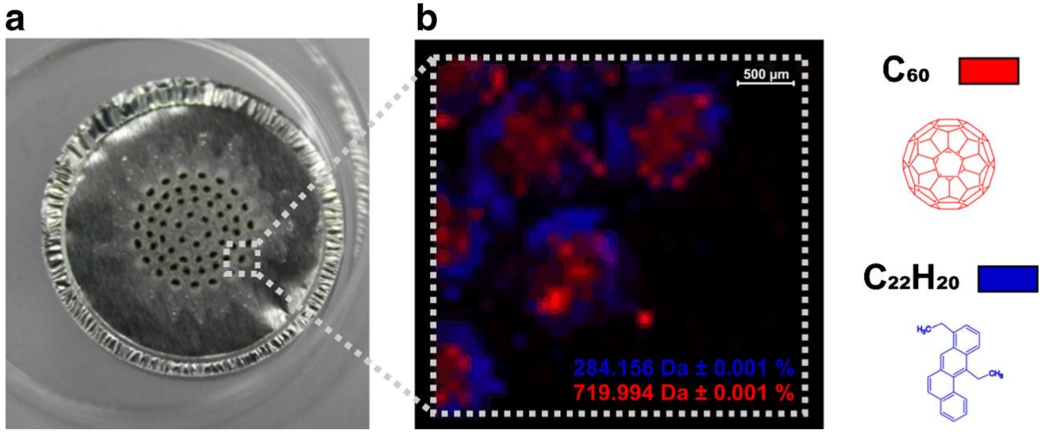
9-Nitroanthracene (9-NA)

2-[(2 *E*)-3-(4-*tert*-butyphenyl)-2-methylprop-2-enylidene]-malonitrile (DCTB)

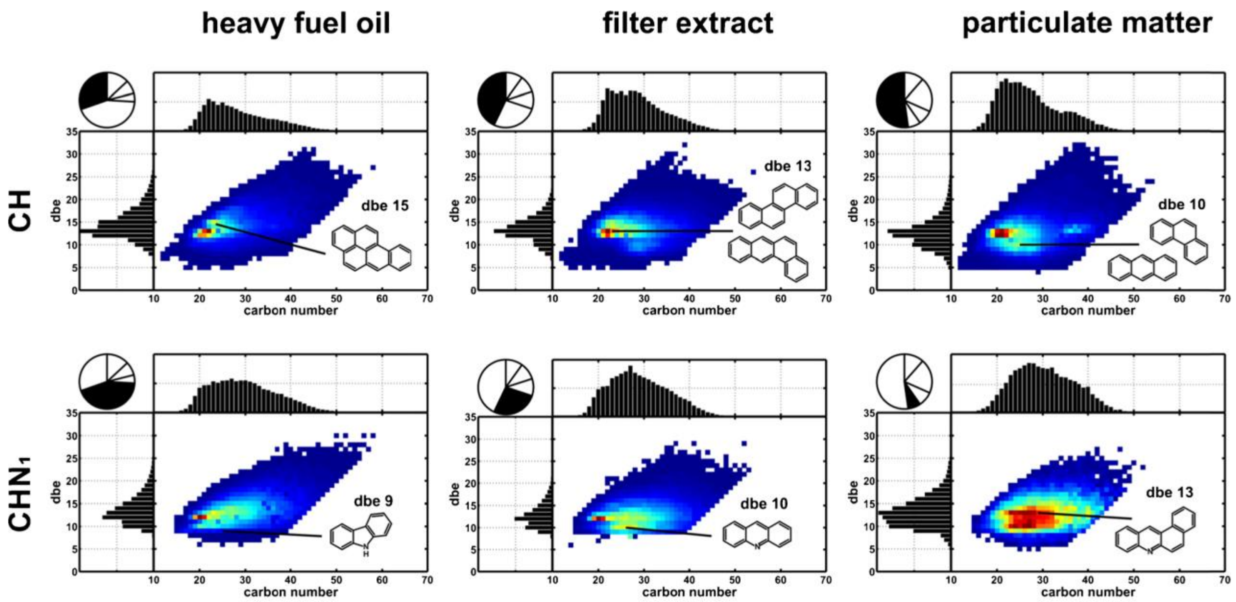
Common UV-MALDI matrices

Jürgen H- Gross, *Mass Spectrometry – A Textbook*, **2017**, Spinger, ISBN *978-3-319-54398-7*

Application – Ship Aerosol Emissions by LDI FT-ICR MS



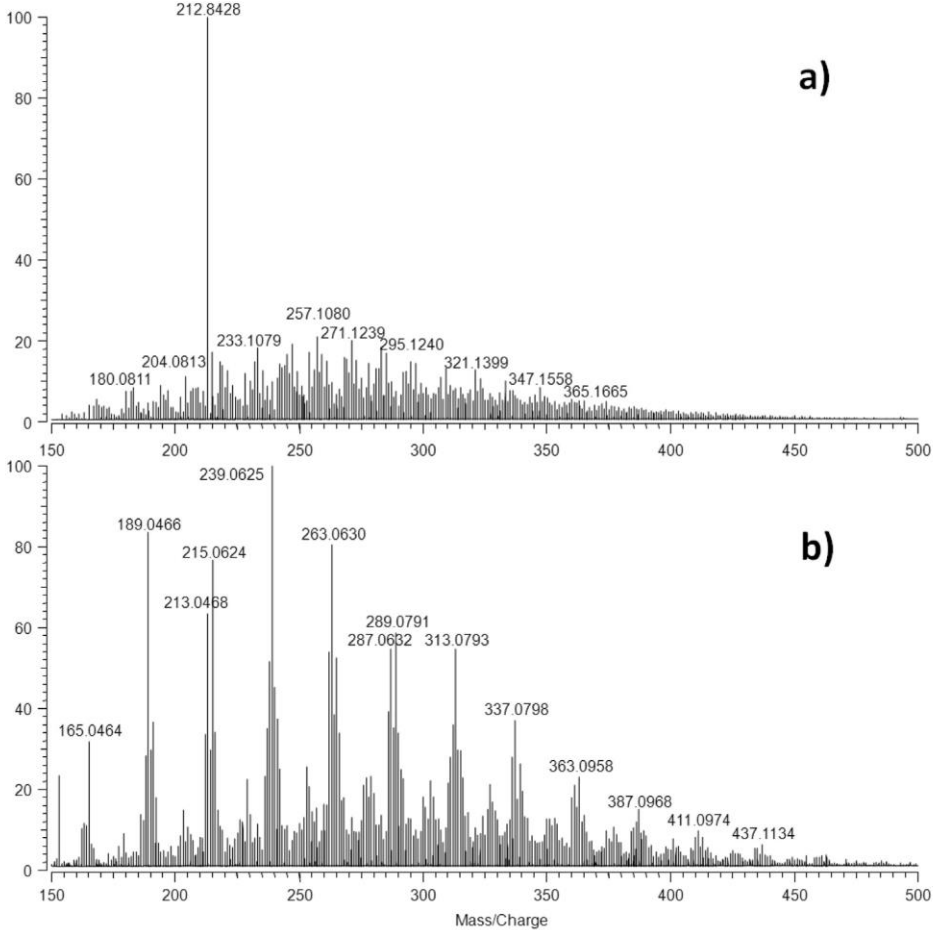
Imaging of the ship diesel aerosol particles by (GA)LDI FT-ICR MS, LDI parameters (spot size and energy) have to be carefully adjusted to prevent ionization artifacts



Cartographic visualization using carbon number versus double bond equivalent diagrams comparing the heavy fuel oil feed with aerosol emission, (+)LDI shows a high sensitivity towards Nitrogen-containing aromatics

Rüger et al., *Anal Bioanal Chem*, **2015**, 5923–5937

Application – Cigarette Smoke Analysis by LDI FT-ICR MS



Positive and negative LDI mass spectra of smoke aerosol after inhalation

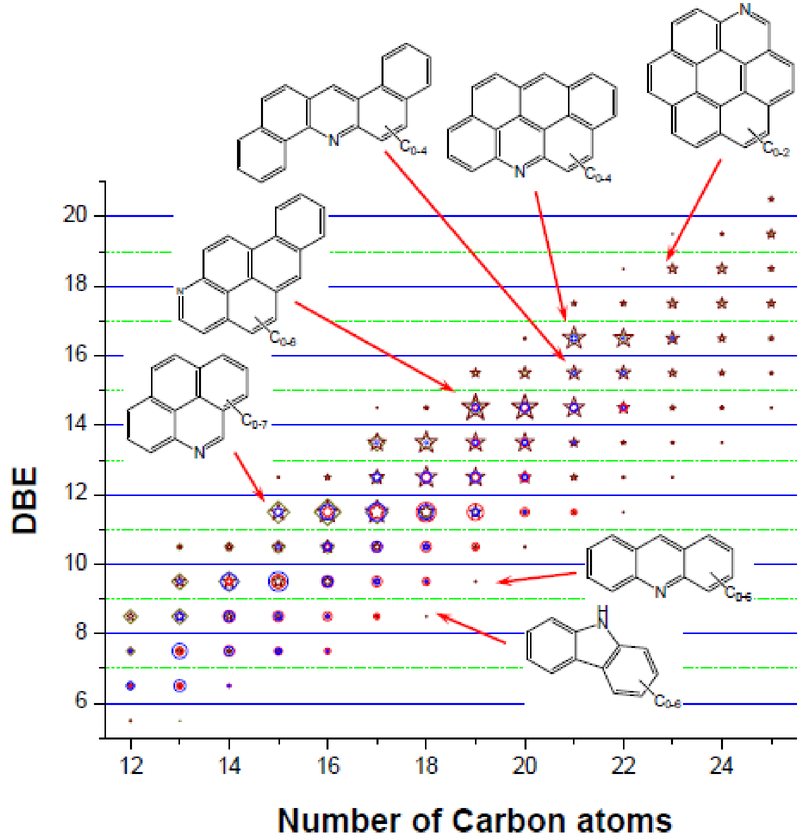
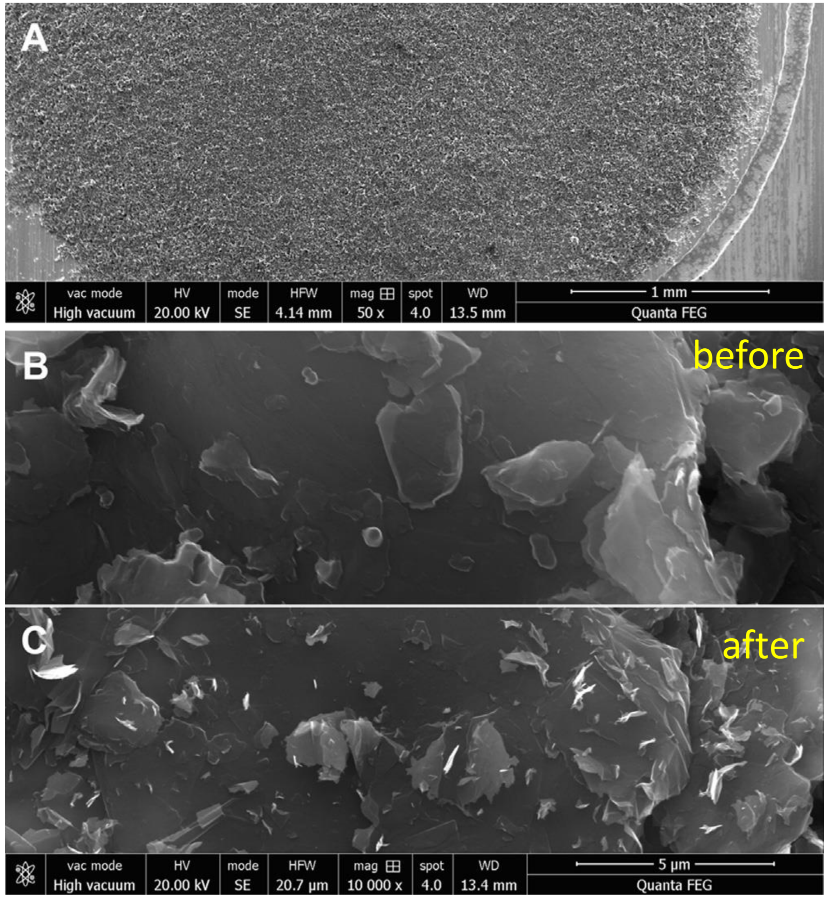
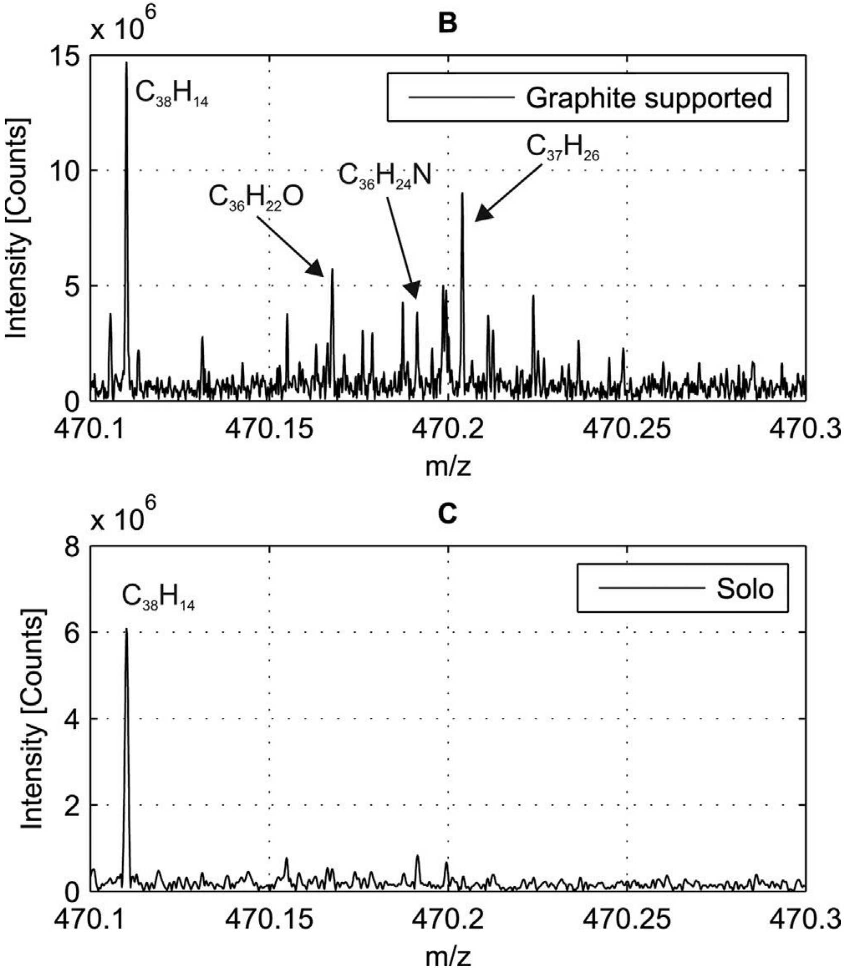


Fig. 8. Distribution of aza-arenes and alkyl-aza-arenes detected as $[M+H]^+$ in respect with the number of carbon and the double bound equivalent (DBE) in MSS ○, SSS ○ and, EXS for smoker F ☆ and smoker V ◇. The size of the symbol is associated to its relative abundance on the mass spectrum. For MSS and SSS, the relative abundance is multiple by a factor of 5.

Schramm et al., *Atmospheric Environment*, **2014**, 411-420

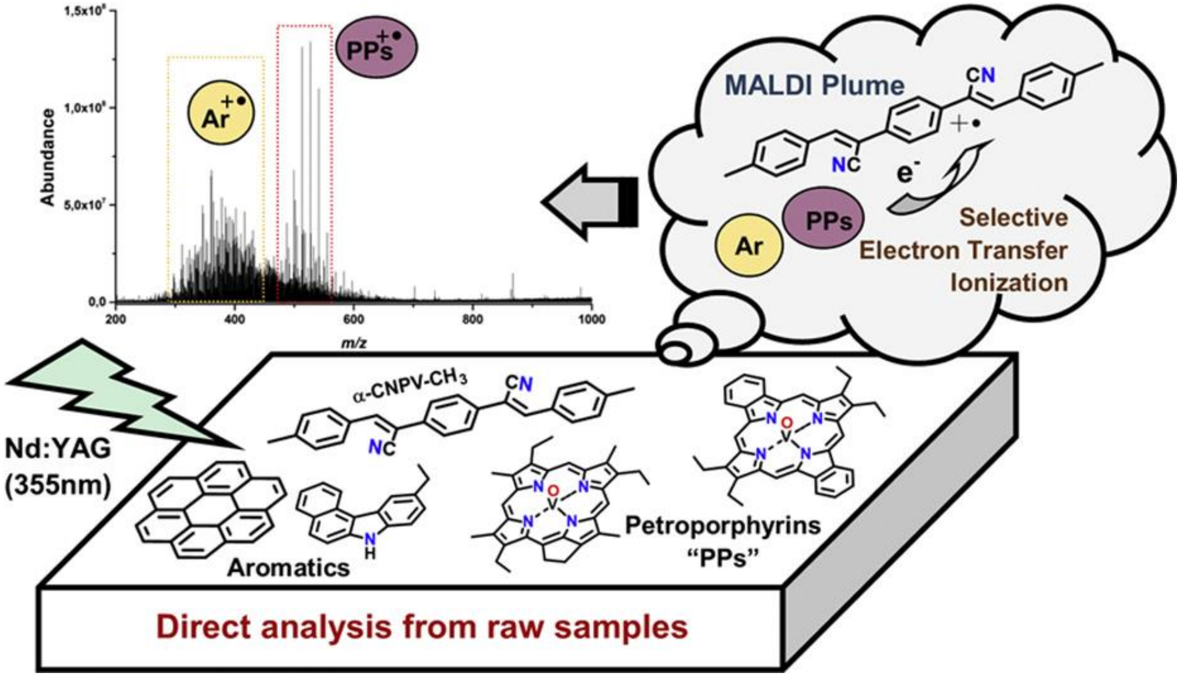
Application – Coal Analysis by GALDI FT-ICR MS

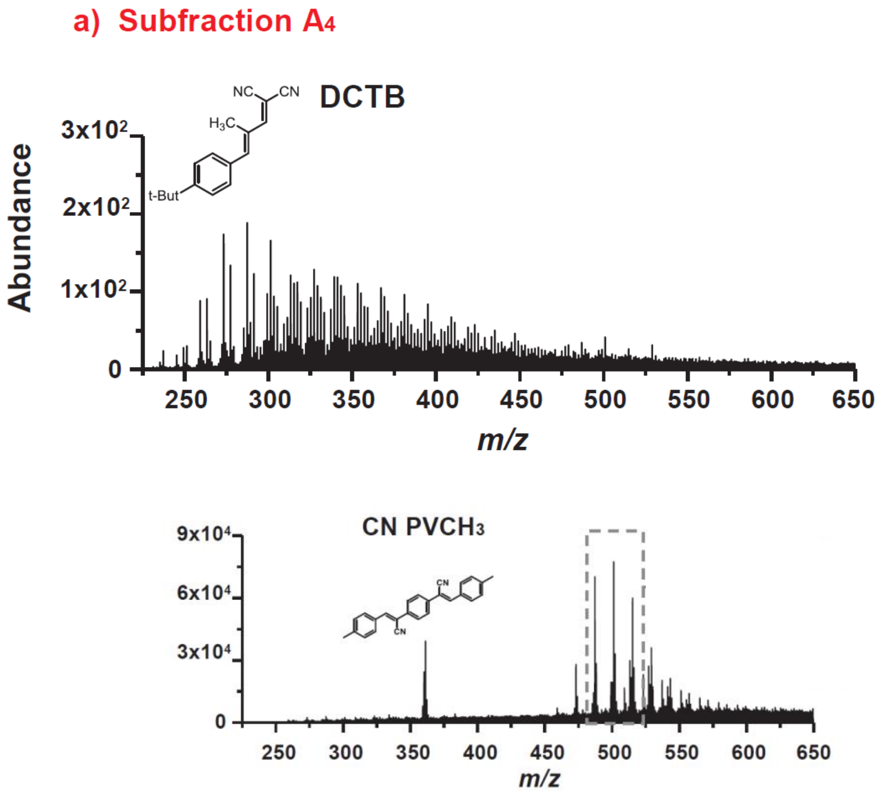




Rathsack et al., *Journal of Analytical and Applied Pyrolysis,* **2014**, 142–149

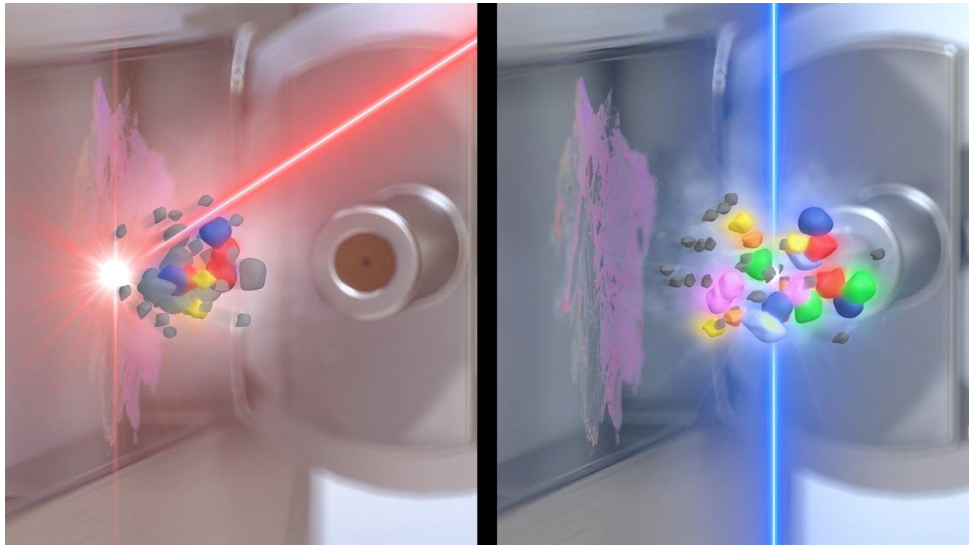
Application – Petroporpyhrin Analysis from Cruse Oils



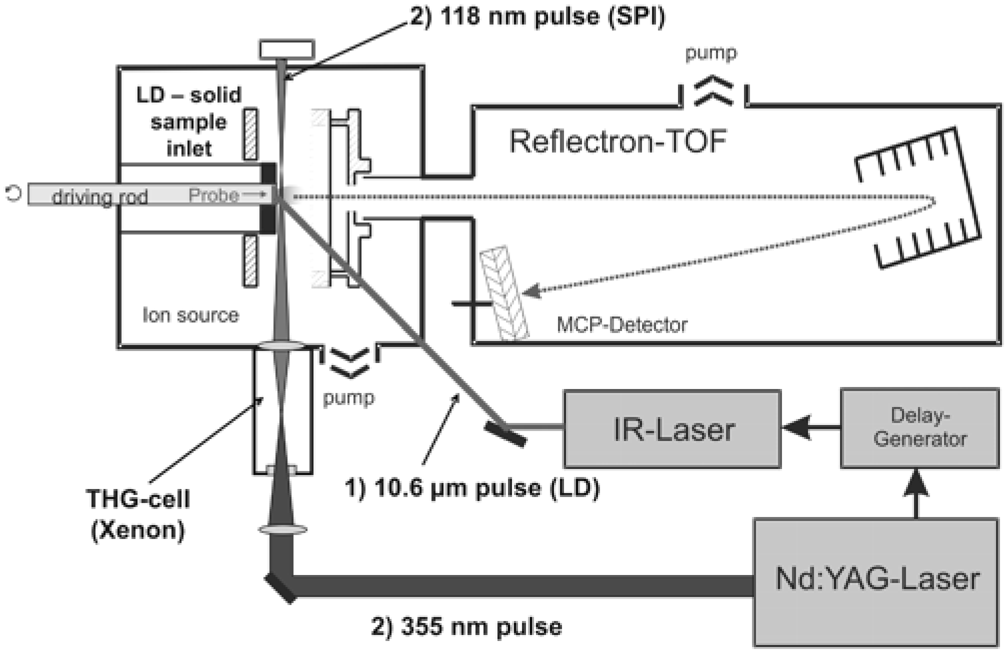


Giraldo-Dávila et al., *Fuel*, **2018**, 103-111

Outlook: Two-Step Laser Desorption Photo Ionization – the timsTOF flex



Two-Step Process: 1) Laser Desorption event creating an energetic plume, and 2) ionization of the plume analytes by a second UV laser.

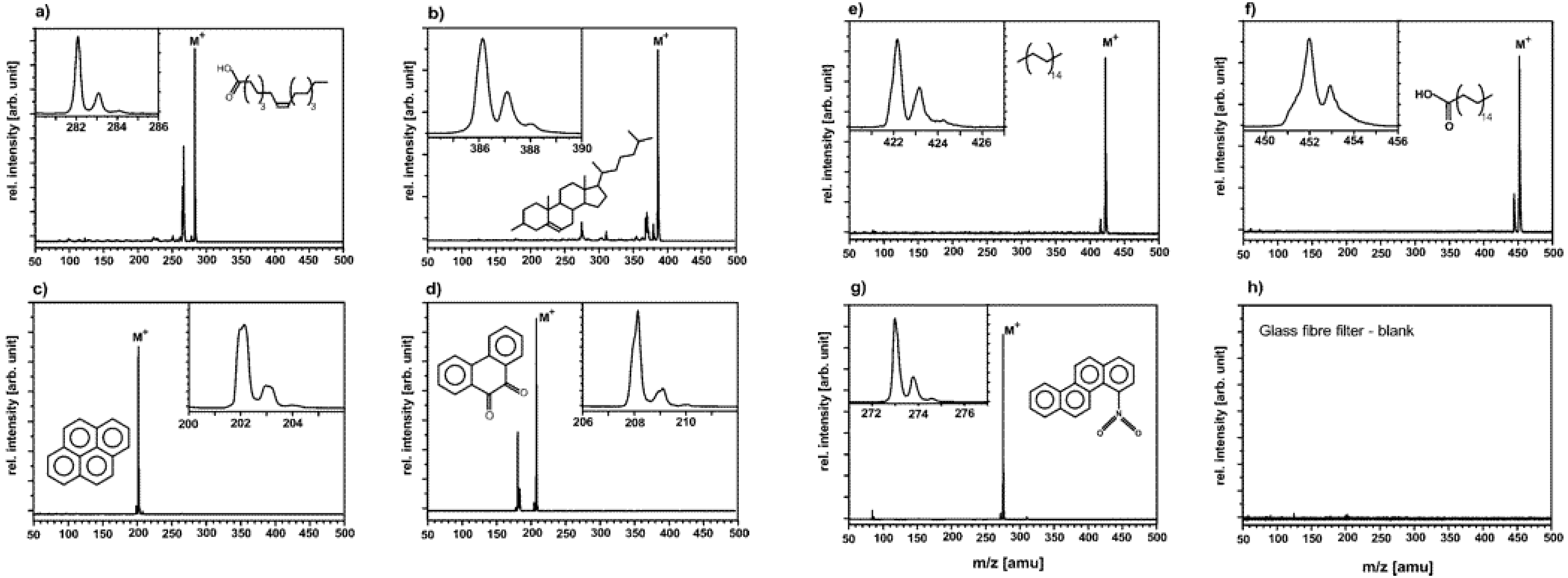


Two-Step Laser Desorption Ionization (L2MS) – actually a very old and heavily used technique on time-of-flight mass analyzers

Ferge et al., *Analytical Chemistry*, **2005**, 4528–4538

Commercialization might be realized in the next FT-ICR MS systems and become broadly available!

Outlook: Two-Step Laser Desorption Photo Ionization



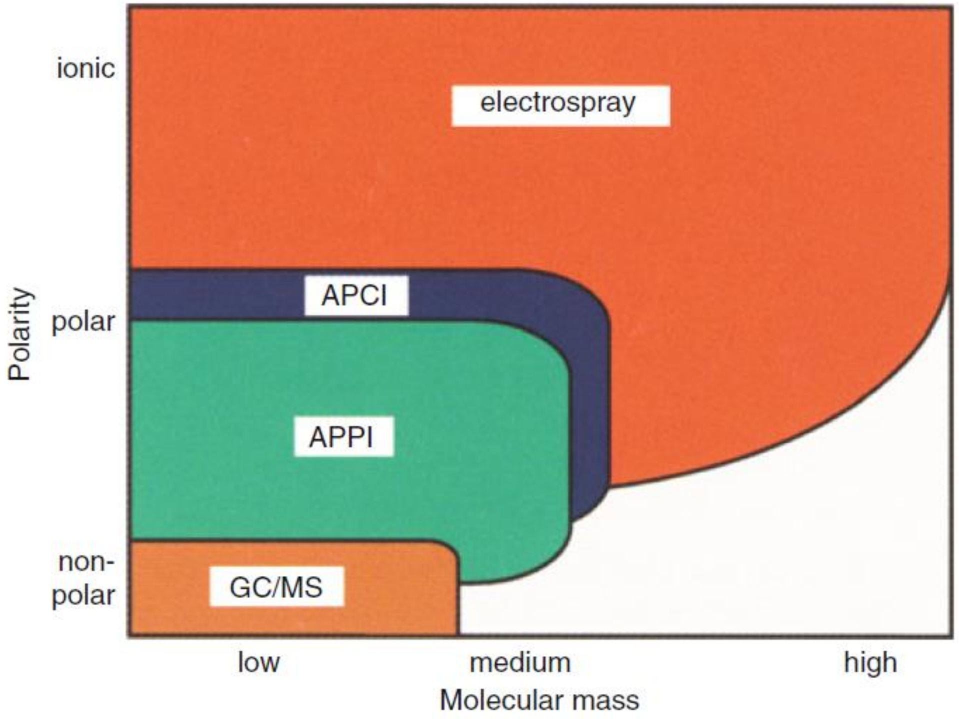
Infrared laser desorption with UV laser post ionization mass spectrometry for aerosol analysis

Ferge et al., *Analytical Chemistry*, **2005**, 4528–4538

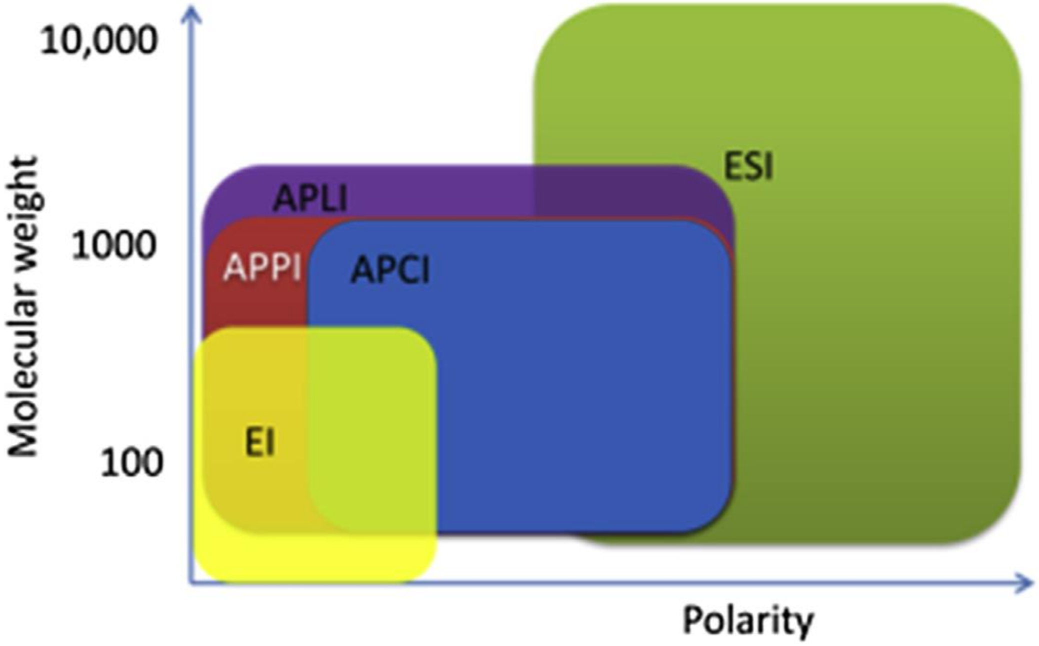
Outline

- **Introduction and Motivation**
    - Chemical Space, Selectivity of Ionization Techniques, Overview of Schemes and Concepts
- **Vacuum Ionization**
    - Electron Impact, Chemical Ionization and Photoionization
    - Laser Desorption Ionization and Allied Techniques
- **Atmospheric Pressure Ionization**
    - Electrospray Ionization, Atmospheric Pressure Chemical/Photo/Laser Ionization
    - Other Concepts and Combination, Applications
- **Summary**

Selectivity of Ionization in Mass Spectrometry – "Analytical Glasses"



Cover of *Anal. Bioanal. Chem.*, **2004**, 378(4)

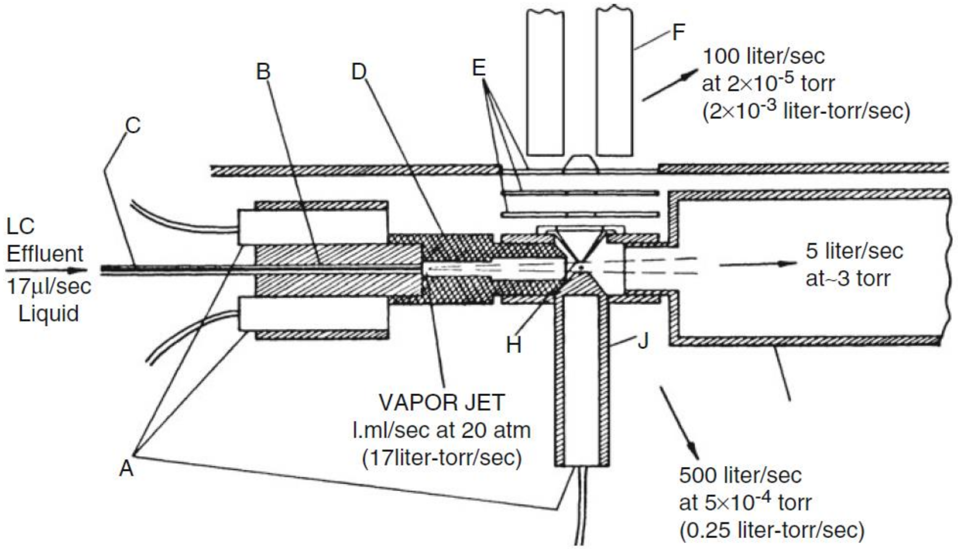


Li et al., *Analytica Chimica Acta*, **2015**, *43-61*

Electrospray Ionization – ESI

Brief History and Importance

- most prominent technique in the realm of atmospheric pressure ionization schemes
- “wings for molecular elephants” [1]
- ESI was <u>not</u> a straight-forward development – many predecessors
  - thermospray (solution + volatile buffer evaporated from heated capillary)
  - electrohydrodynamic ionization (spraying electrolyte solution with low volatility)
  - …



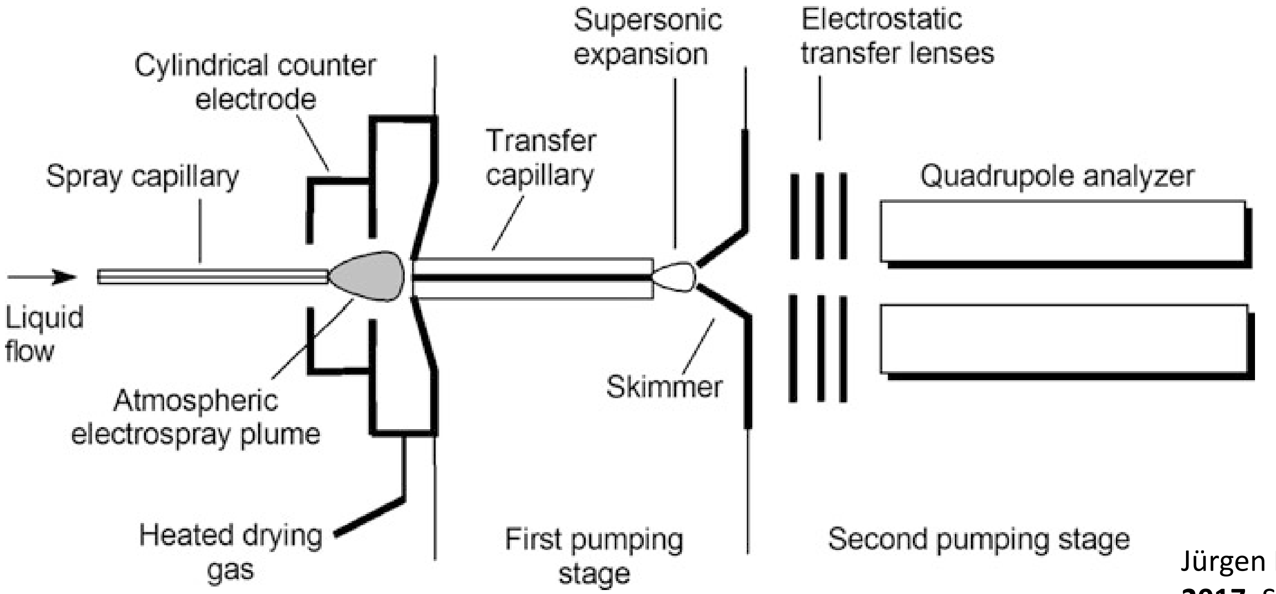
Thermospray interface.
A cartridge heater
B copper block brazed to stainless steel capillary
C capillary
D copper tube
E ion lenses
F quadrupole mass analyser
G line to rotary vane pump
H ion exit aperture
J source heater

Jürgen H- Gross, *Mass Spectrometry – A Textbook*, **2017**, Spinger, ISBN *978-3-319-54398-7*

Electrospray Ionization – ESI

Concept and Basics

- mist of µm-sized electrically charged droplets is generated from almost any standard solvent
- repetitive shrinking and droplet disintegration
- droplets would freeze on their transition from atmosphere to vacuum (adiabatic expansion) → heated counter gas stream or heated capillary (common to all ESI sources)
- contrast to vacuum ionization → differential pumping needed to remove the concomitant gas



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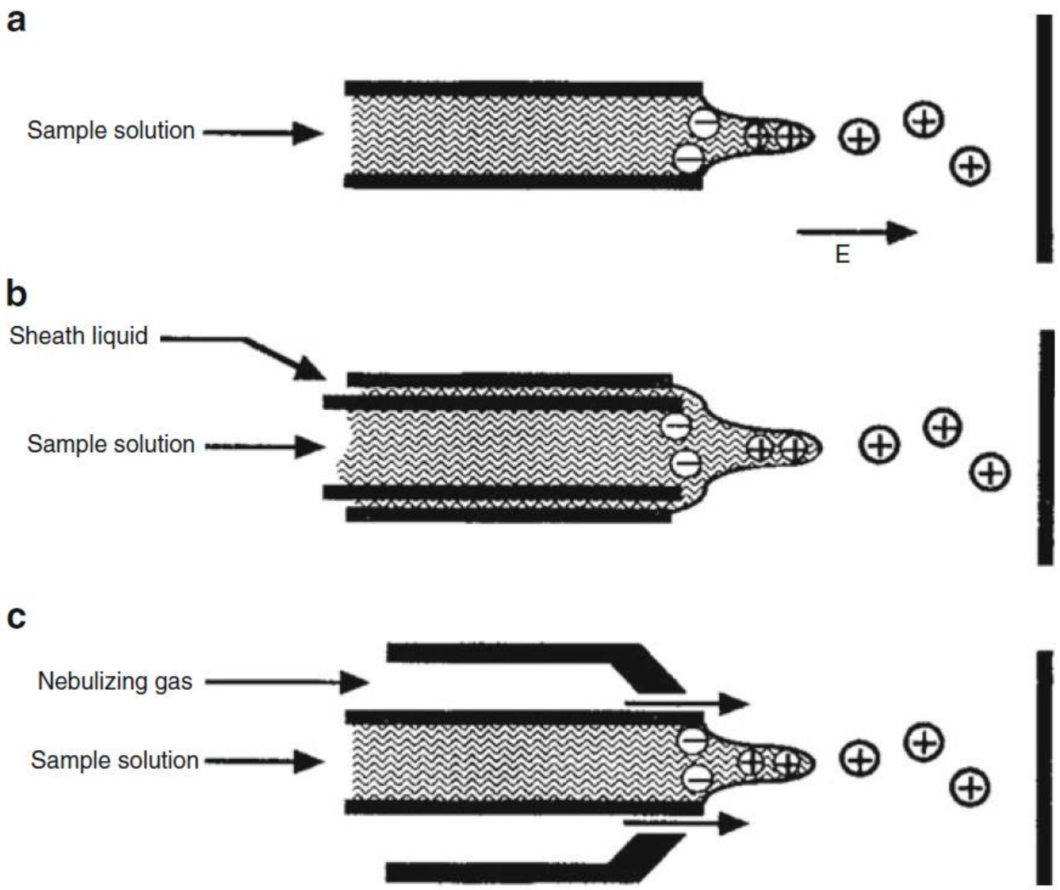
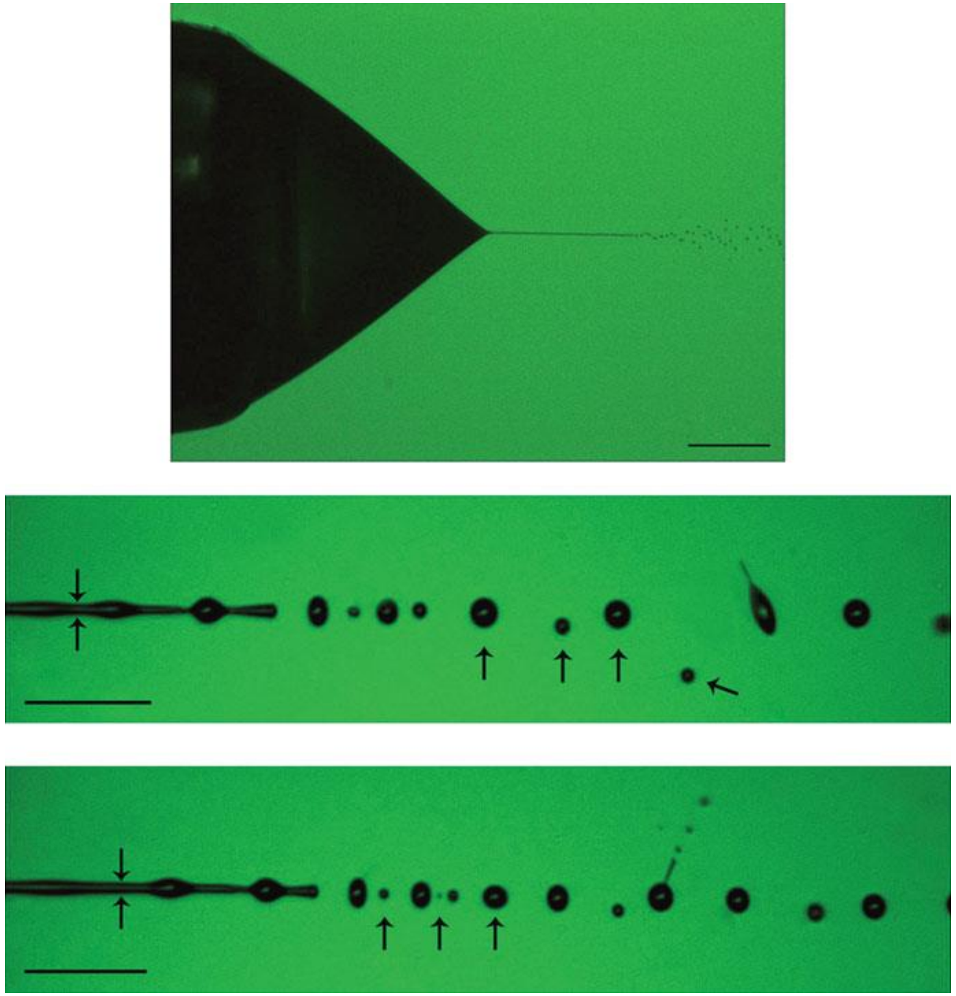
Electrospray Ionization – ESI

Concept and Basics





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Overview Ion Formation in Electrospray Ionization

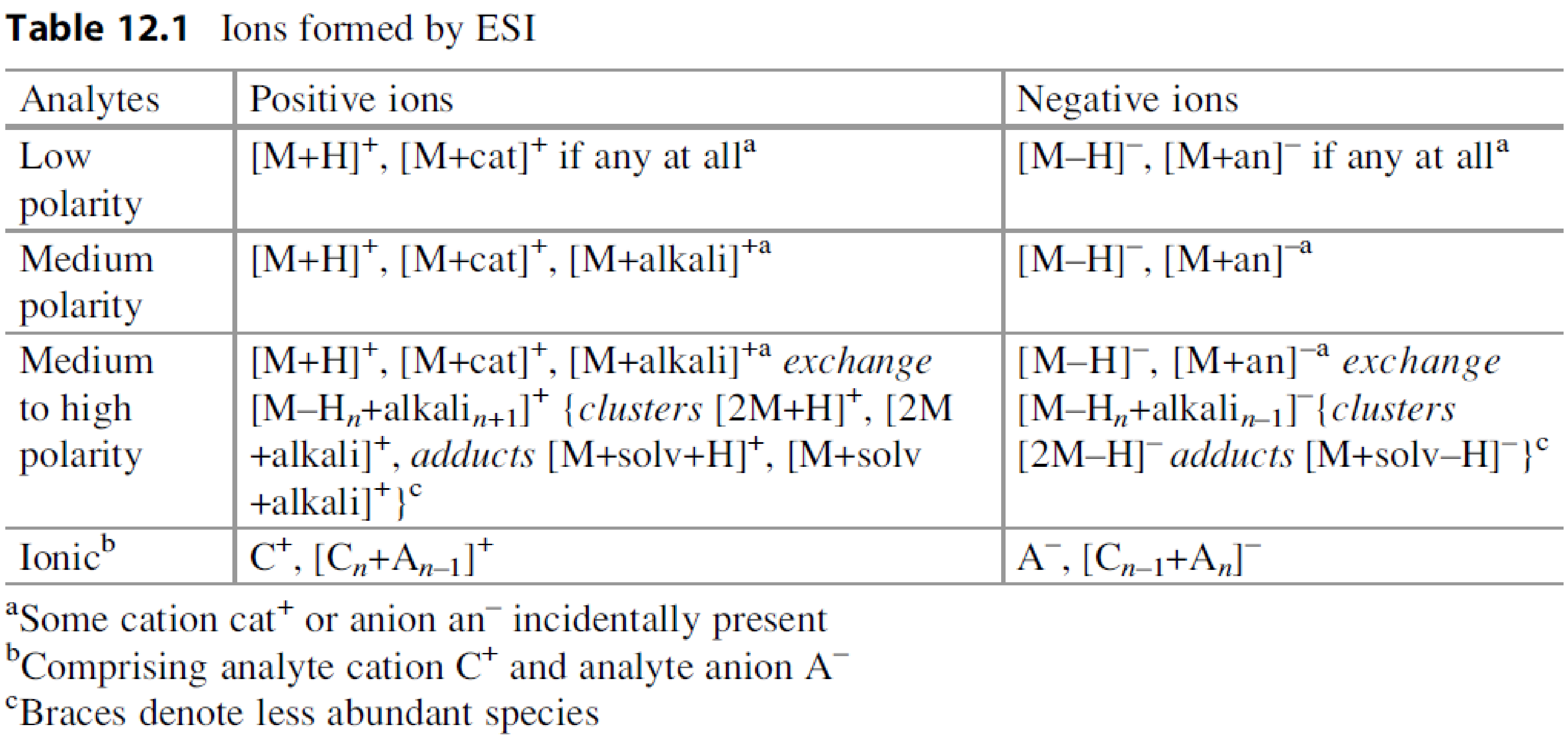

Table 12.1 Ions formed by ESI

Analytes	Positive ions	Negative ions
Low polarity	$[M+H]^+$, $[M+cat]^+$ if any at all[a]	$[M-H]^-$, $[M+an]^-$ if any at all[a]
Medium polarity	$[M+H]^+$, $[M+cat]^+$, $[M+alkali]^+$[a]	$[M-H]^-$, $[M+an]^-$[a]
Medium to high polarity	$[M+H]^+$, $[M+cat]^+$, $[M+alkali]^+$[a] *exchange* $[M-H_n+alkali_{n+1}]^+$ {*clusters* $[2M+H]^+$, $[2M+alkali]^+$, *adducts* $[M+solv+H]^+$, $[M+solv+alkali]^+$}[c]	$[M-H]^-$, $[M+an]^-$[a] *exchange* $[M-H_n+alkali_{n-1}]^-${*clusters* $[2M-H]^-$ *adducts* $[M+solv-H]^-$}[c]
Ionic[b]	C^+, $[C_n+A_{n-1}]^+$	A^-, $[C_{n-1}+A_n]^-$

[a] Some cation cat^+ or anion an^- incidentally present
[b] Comprising analyte cation C^+ and analyte anion A^-
[c] Braces denote less abundant species

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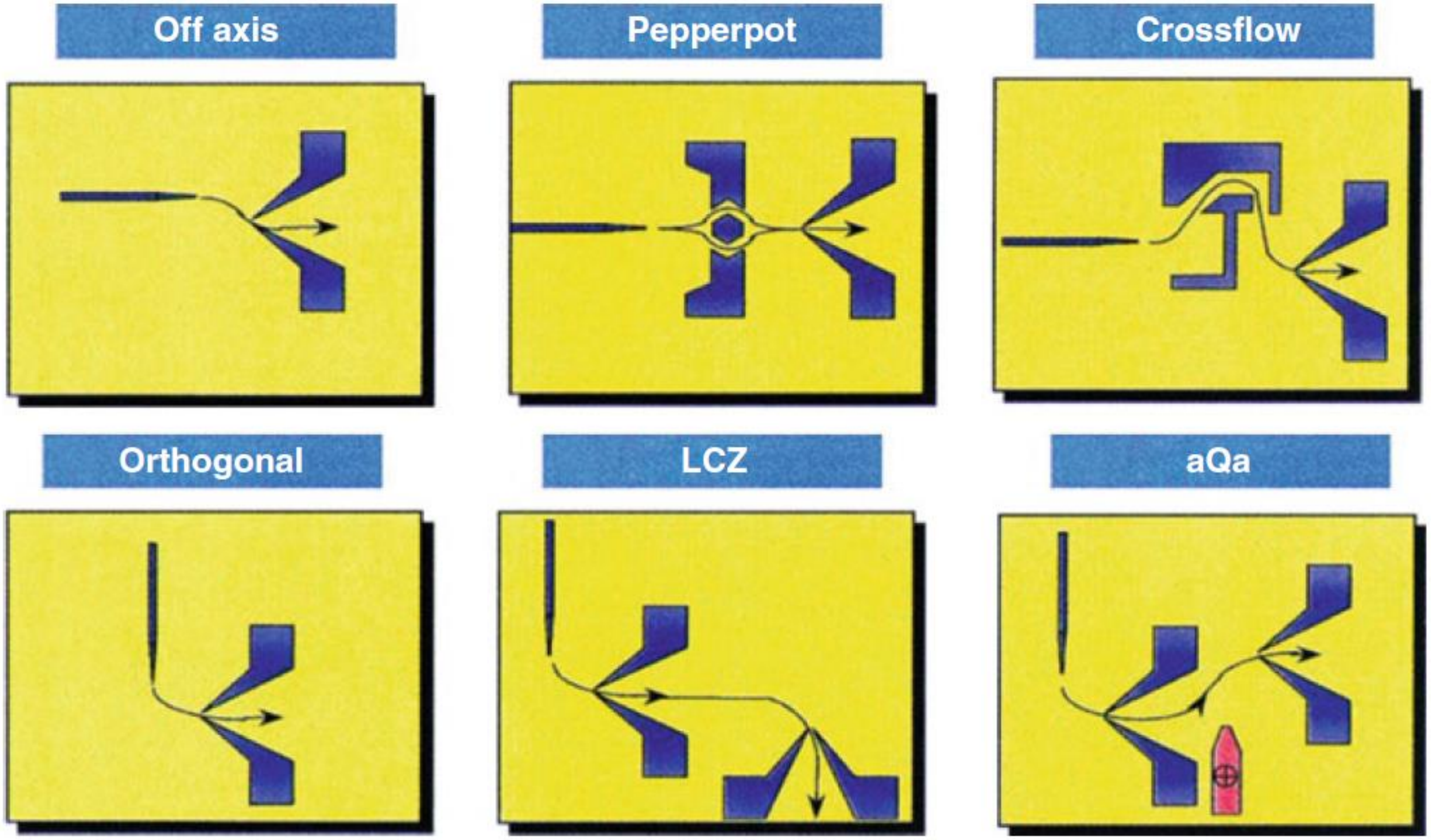
Electrospray Ionization – ESI

Geometry and Designs



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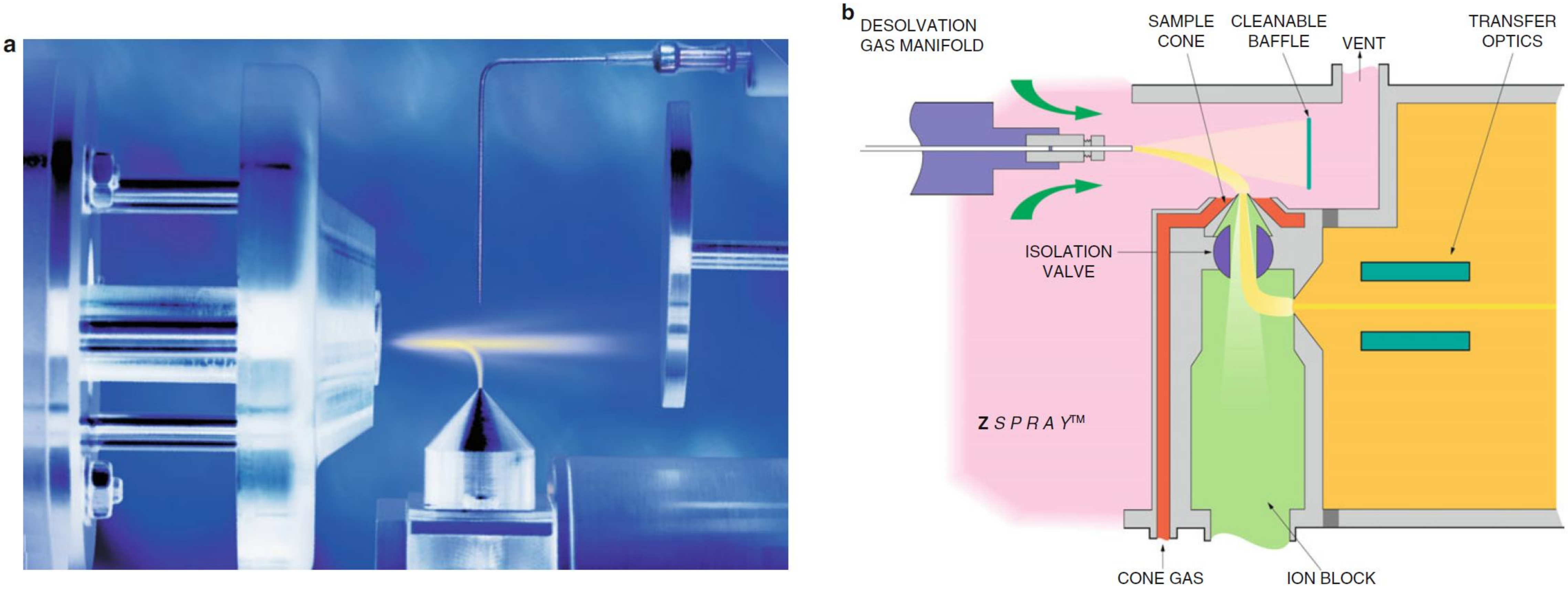
Electrospray Ionization – ESI

Geometry and Construction



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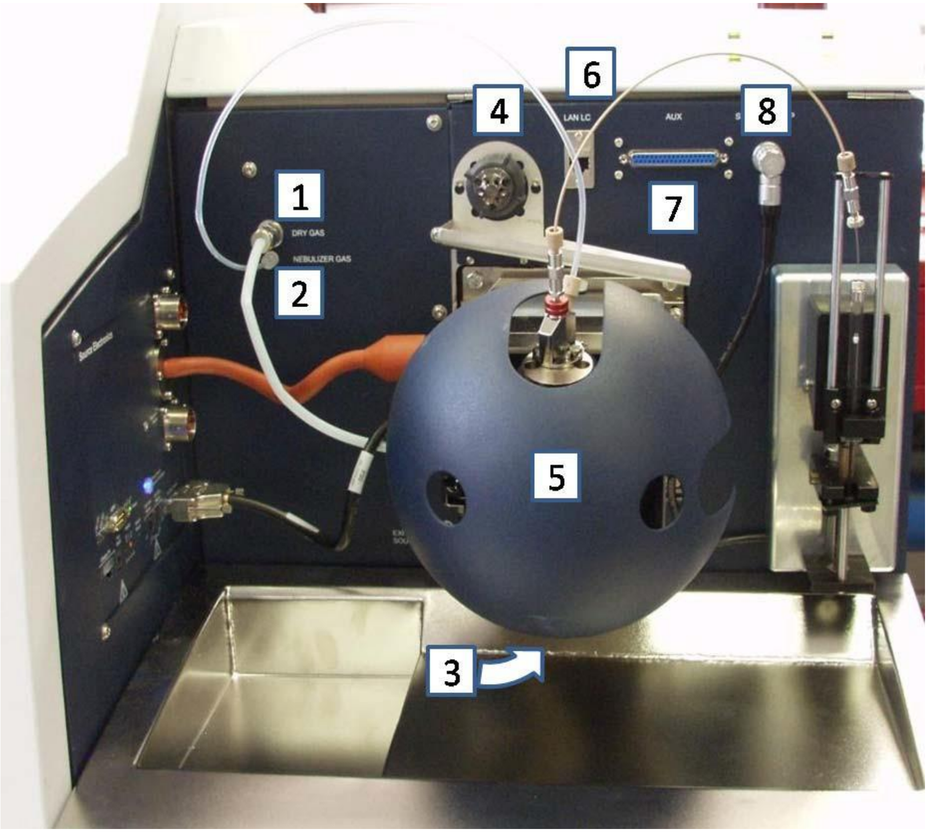
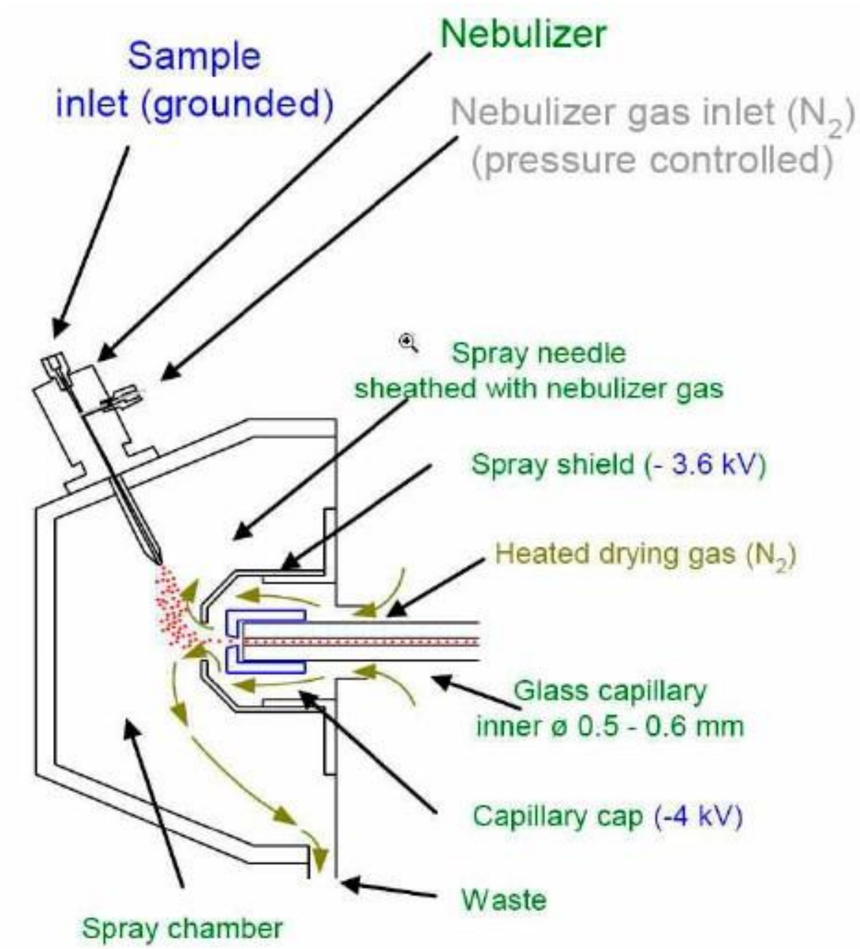
Electrospray Ionization – ESI

Common Bruker ESI source in FT-ICR MS



Bruker Daltonics ESI source at a solariX MRMS equipped with a Apollo II interface



Scheme of the Bruker ESI general construction

Bruker Daltonics Tutorial Material

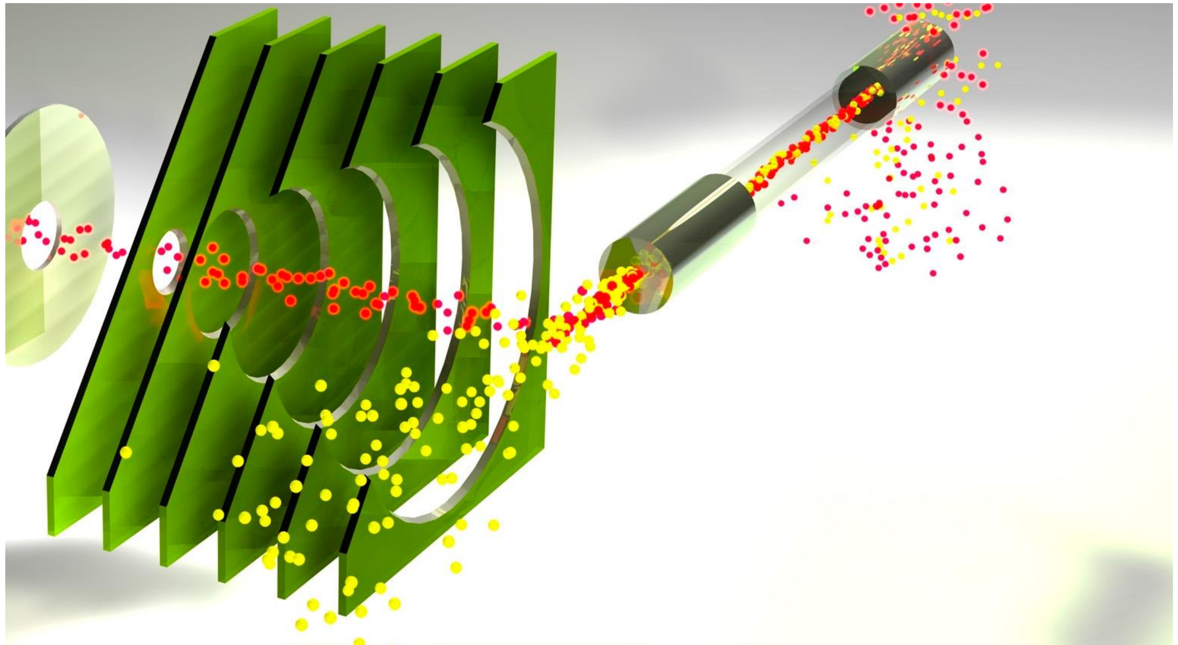
Common Bruker ESI source in FT-ICR MS - Atmospheric Pressure Interface

Bruker Apollo II API interface found at almost all Bruker FT-ICR MS

Electrospray Ionization – ESI

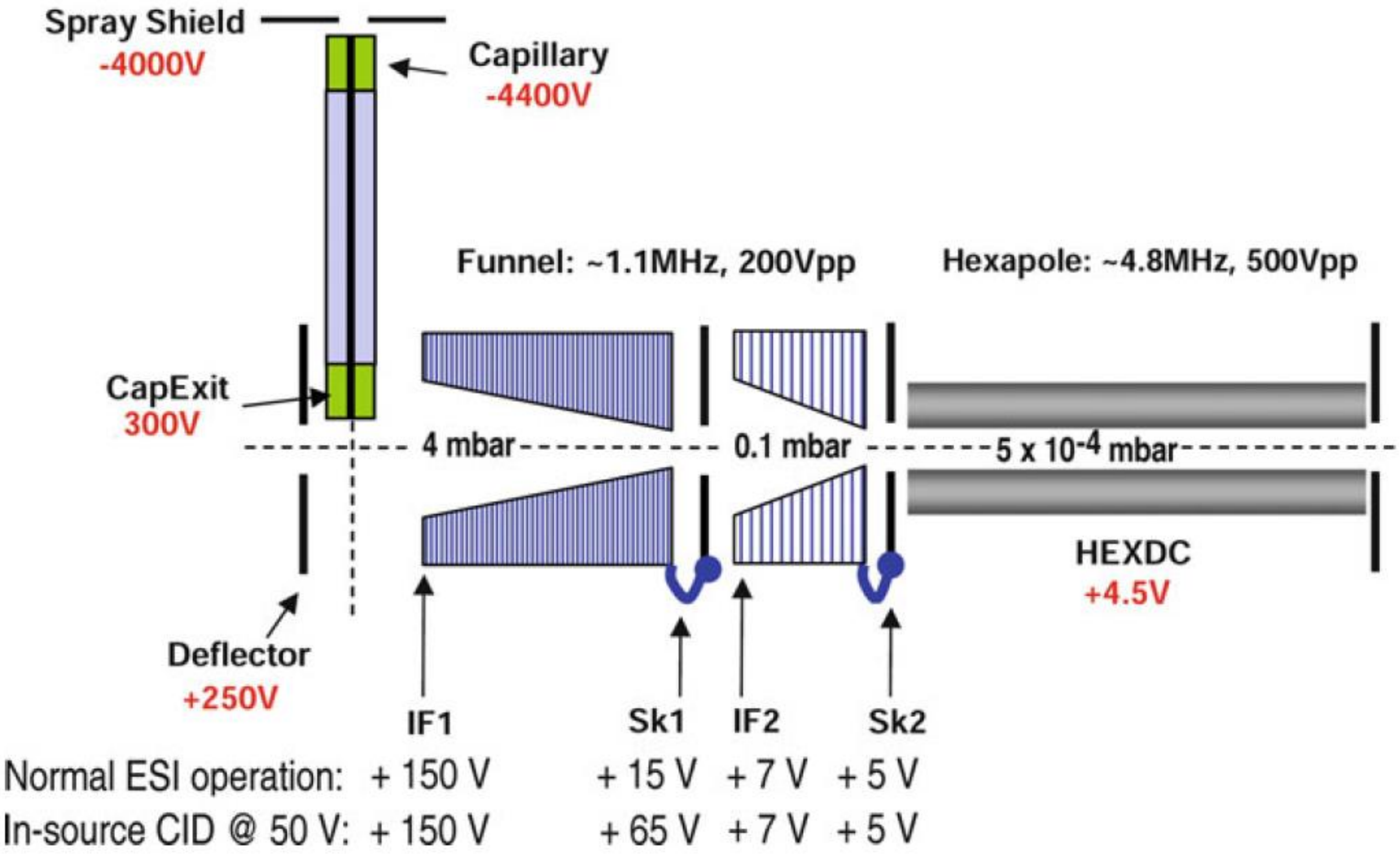
Collision Induced Dissociation in AP Ionization Interfaces – Do we want that?

- weekly bonded substituents can cleave of even at low collision energies
- Bruker Apollo II source common in FT-ICR MS features dual ion funnel setup
  - first funnel: 3-4 mbar, directly collecting the ions after supersonic expansion from AP to the vacuum
  - second funnel prior RF hexapol to guide/collect ions (~0.1 mbar)
- in-source CID (Bruker terminology!): shifting DC potential to have large drop from first to second funnel



Scheme of the atmospheric pressure interface: Glass-capillary inlet coupling atmospheric pressure to first vacuum stage ~mbar

Collision Induced Dissociation in AP Ionization Interfaces – Do we want that?



	IF1	Sk1	IF2	Sk2
Normal ESI operation:	+ 150 V	+ 15 V	+ 7 V	+ 5 V
In-source CID @ 50 V:	+ 150 V	+ 65 V	+ 7 V	+ 5 V

Bruker Daltonics Tutorial Material

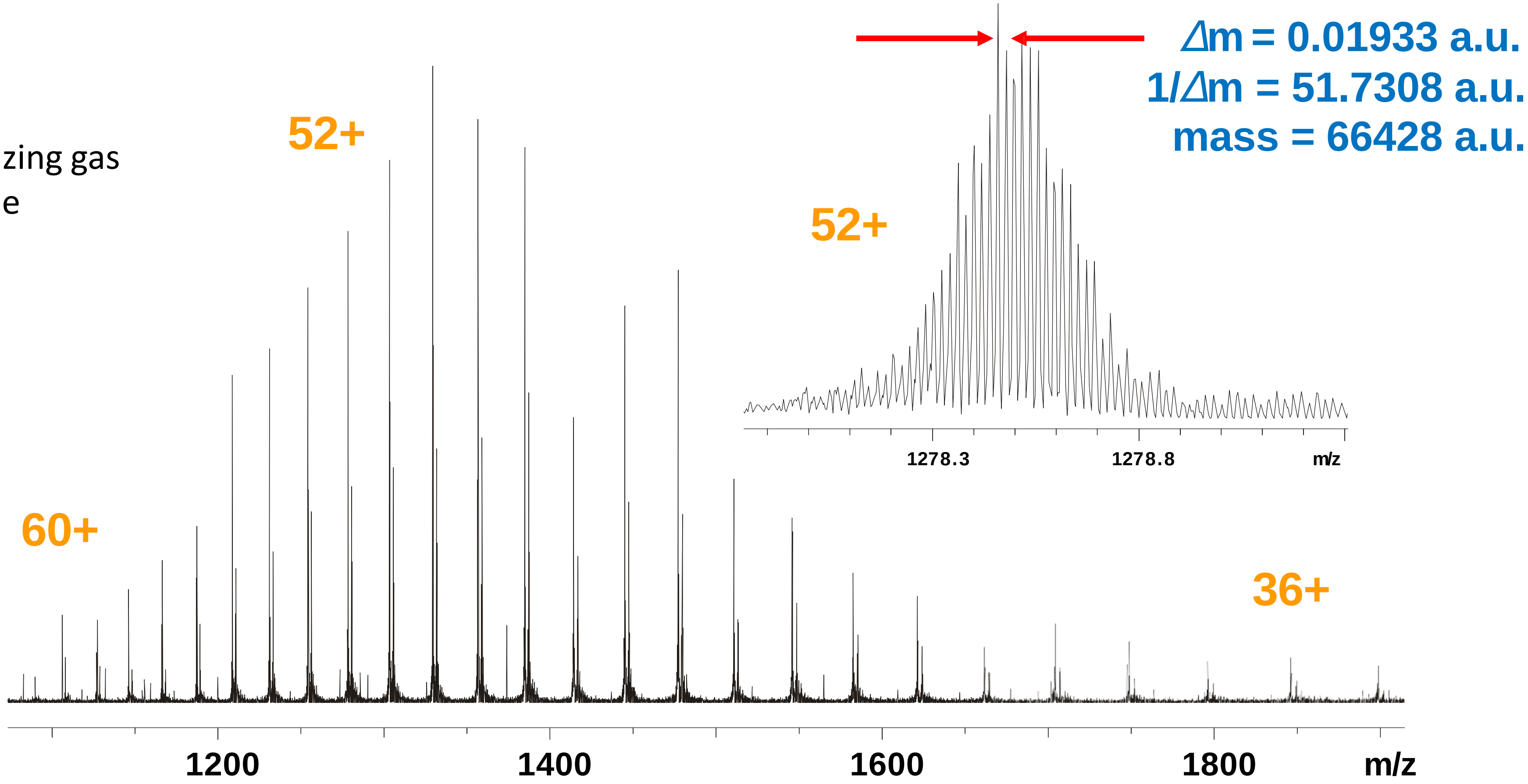
Electrospray Ionization – ESI

Charge State Distribution

Influencing parameters:

- pH of the sprayed solution,
- flow of sample solution,
- flow (or pressure) of nebulizing gas
- flow and temperature of the desolvation gas
- temperature of the heated desolvation capillary
- …

ESI: Broadband Spectrum of BSA (66kDa)



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Electrospray Ionization – ESI

Charge State Distribution and How to Influence it

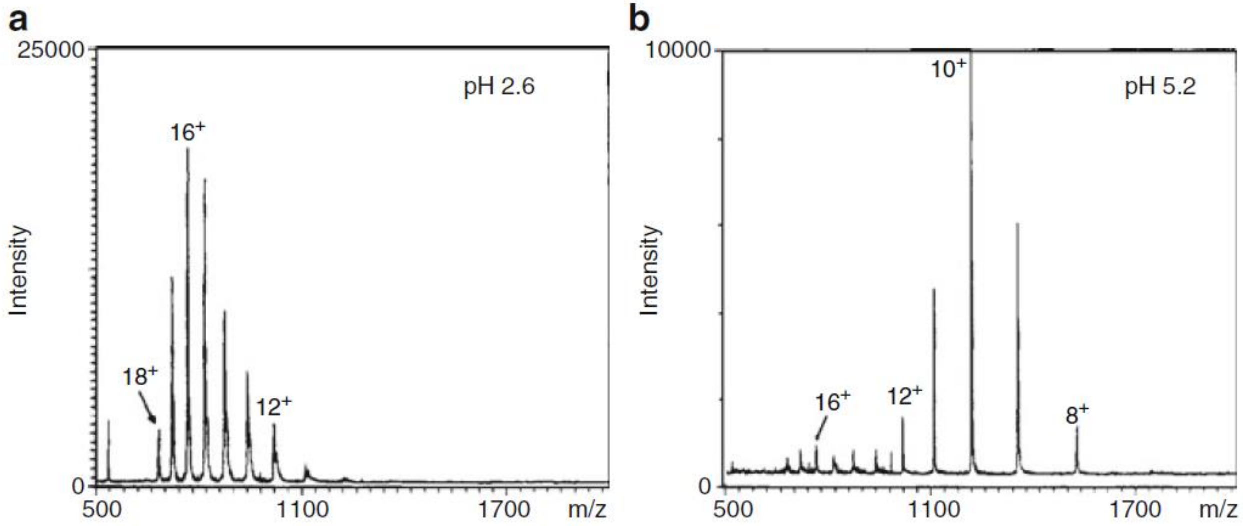
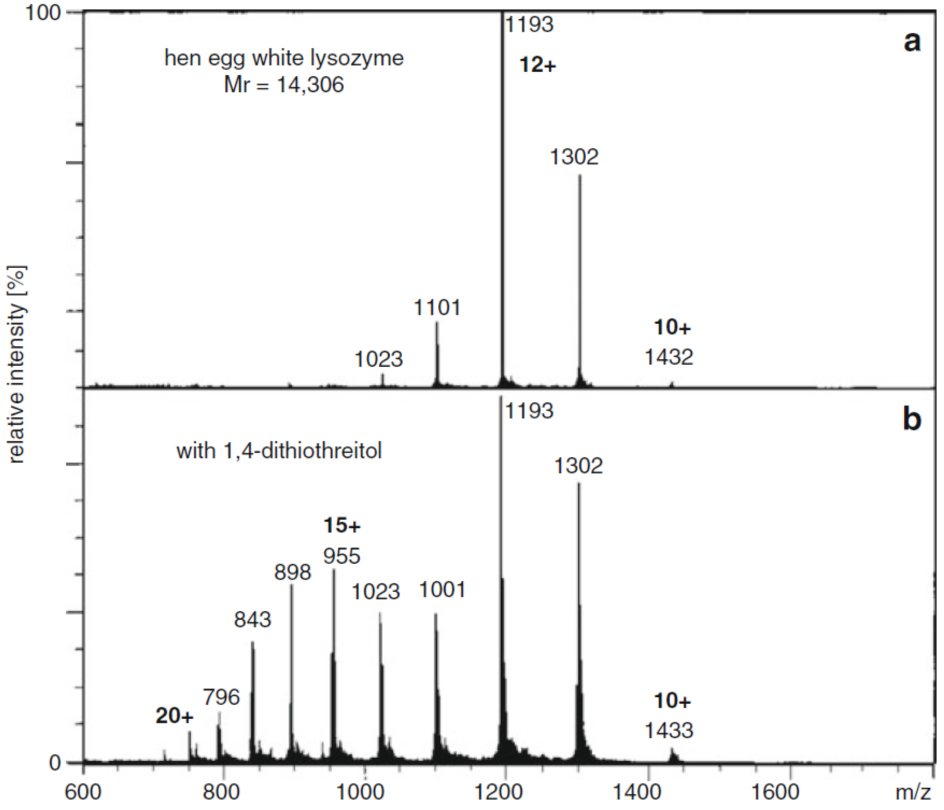


Fig. 12.21 Positive-ion ESI mass spectra of cytochrome c at different pH of the sprayed solution: (**a**) at pH 2.6, (**b**) at pH 5.2 (Adapted from Ref. [107] by permission. © American Chemical Society, 1990)



Charge state can be influenced by pH and reduction agent!

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Charge Deconvolution and the Benefit of Ultrahigh Resolving Power

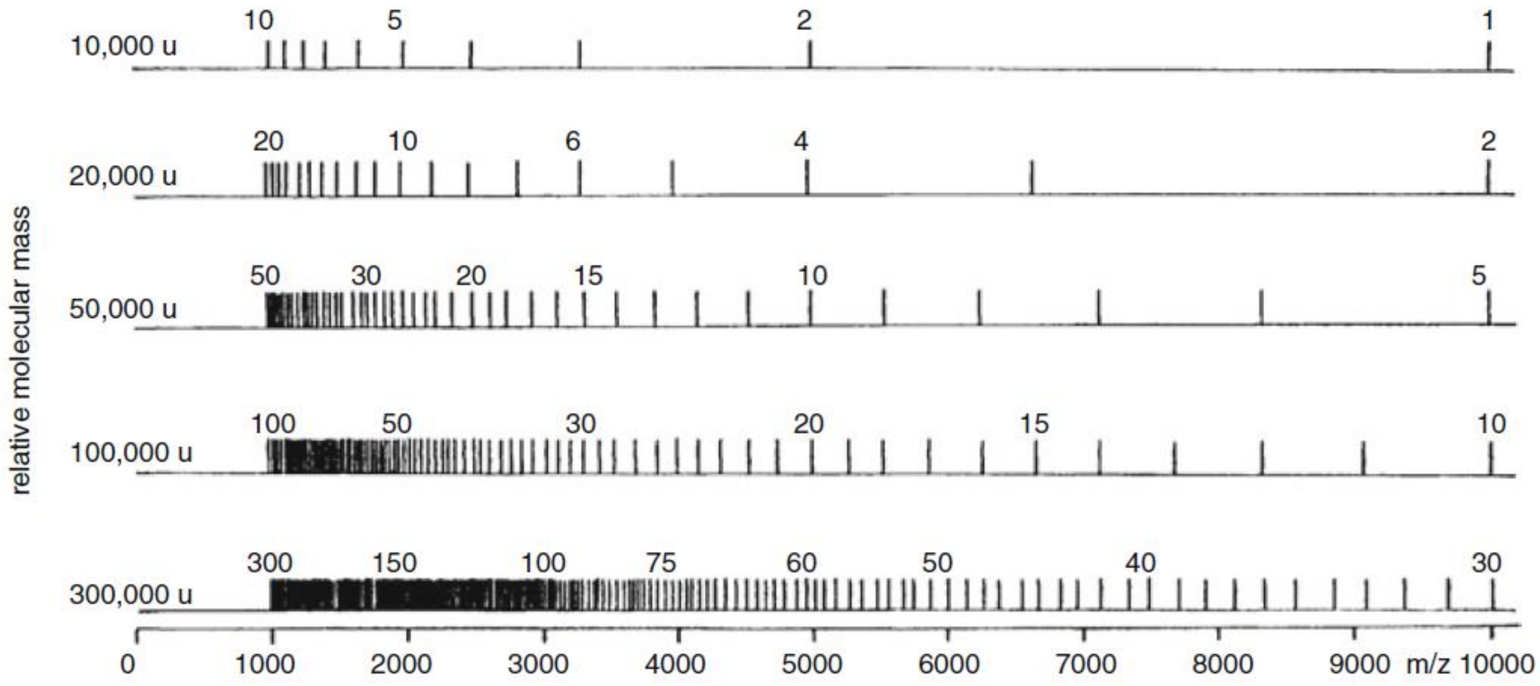

Fig. 12.24 Calculated *m*/*z* values for the different charge states of molecules of different molecular weight. Representative peaks are labeled with their corresponding charge state (Adapted from Ref. [116] by permission. © John Wiley & Sons, 1992)

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Charge Deconvolution and the Benefit of Ultrahigh Resolving Power

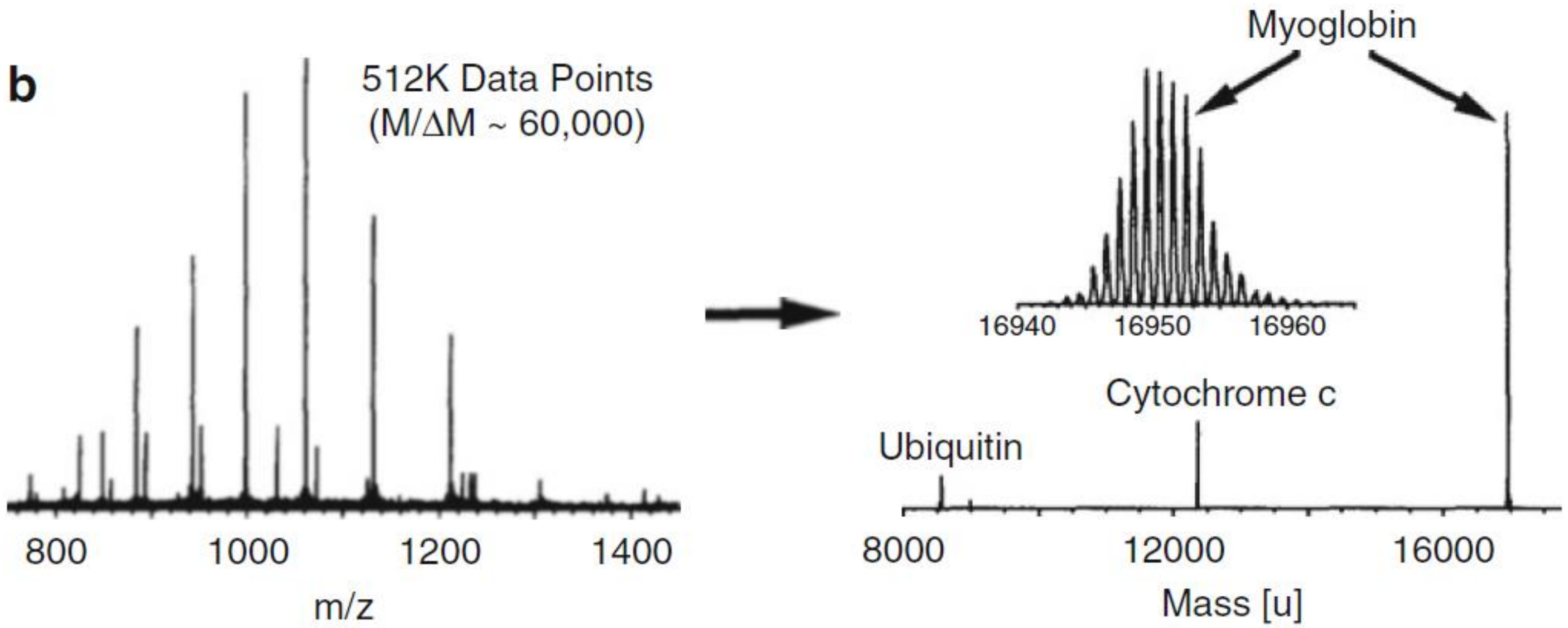

Fig. 12.27 Charge deconvolution of (**a**) LR and (**b**) HR positive-ion ESI spectra of an artificial protein mixture. The “zero-charge” peak of myoglobin is also shown in expanded view to reveal the delineation of the isotopic pattern (Adapted from Ref. [123] by permission. © Elsevier, 1998)

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Charge Deconvolution and the Benefit of Ultrahigh Resolving Power

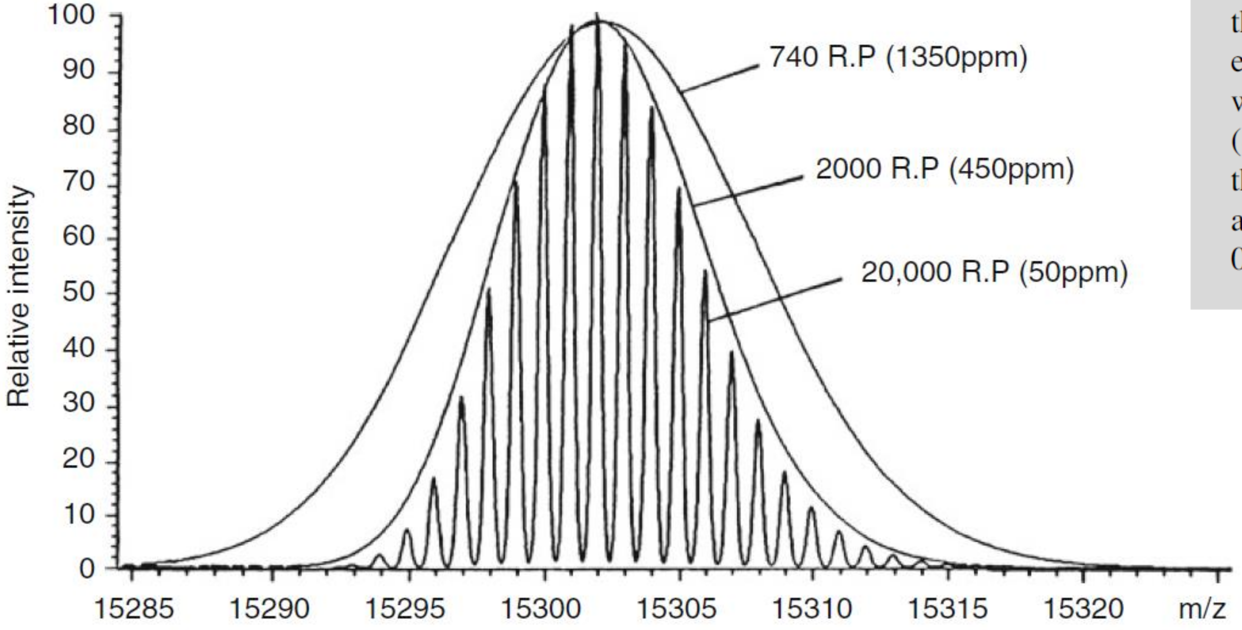

Fig. 12.28 Theoretical peak shape for a hypothetical singly charged protein ion of $M_r = 15{,}300$ u at different settings of resolution (Reproduced from Ref. [116] by permission. © John Wiley & Sons, 1992)

Rule for minimum resolving power: The mass resolving power to achieve full separation of isotopic peaks only depends on the molecular weight, M_r, of the analyte, but it is independent of the number of charges, z, of the ions. For example, the isotope peaks of the $[M+H]^+$ ion of thioredoxin (Fig. 12.1) would appear at m/z 11674 and be spaced at $\Delta(m/z) = 1$. Using $R = m/\Delta m$ (Sect. 3.4) we calculate the minimum value $R_{min} = 11674 / 1 = 11674$. For the $[M+8H]^{8+}$ ion of this protein ($z = 8$), the signals are centered at m/z 1459 and spaced at $\Delta(m/z) = 0.125$. Thus, we calculate $R_{min} = m/\Delta m = 1459 / 0.125 = 11674$. In brief, the numerical value of M_r directly reflects R_{min}.

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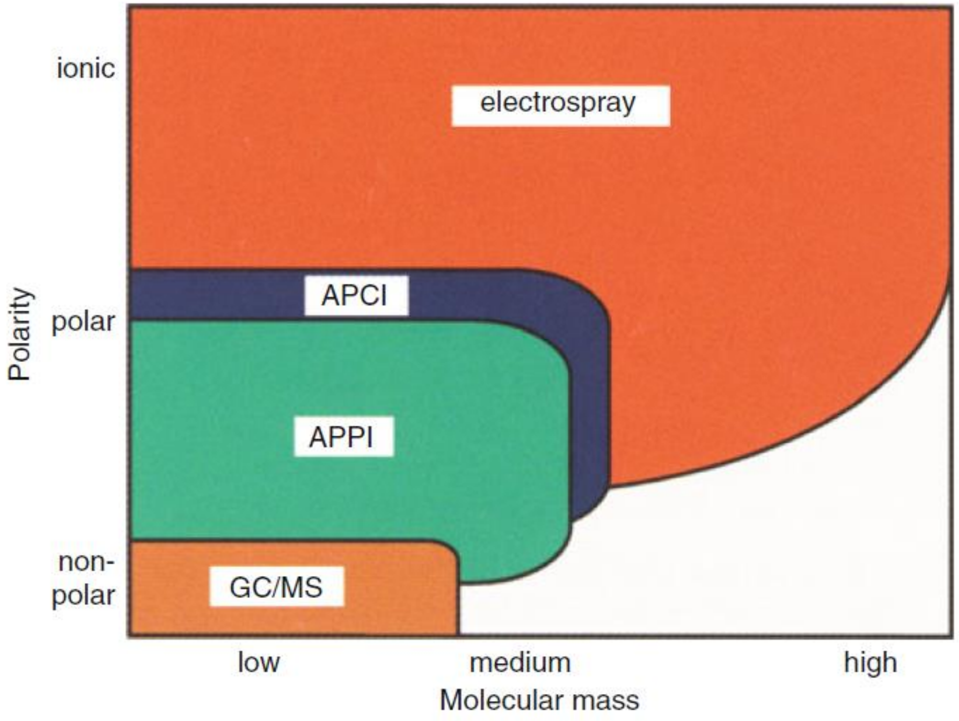
Selectivity of Ionization in Mass Spectrometry – "Analytical Glasses"



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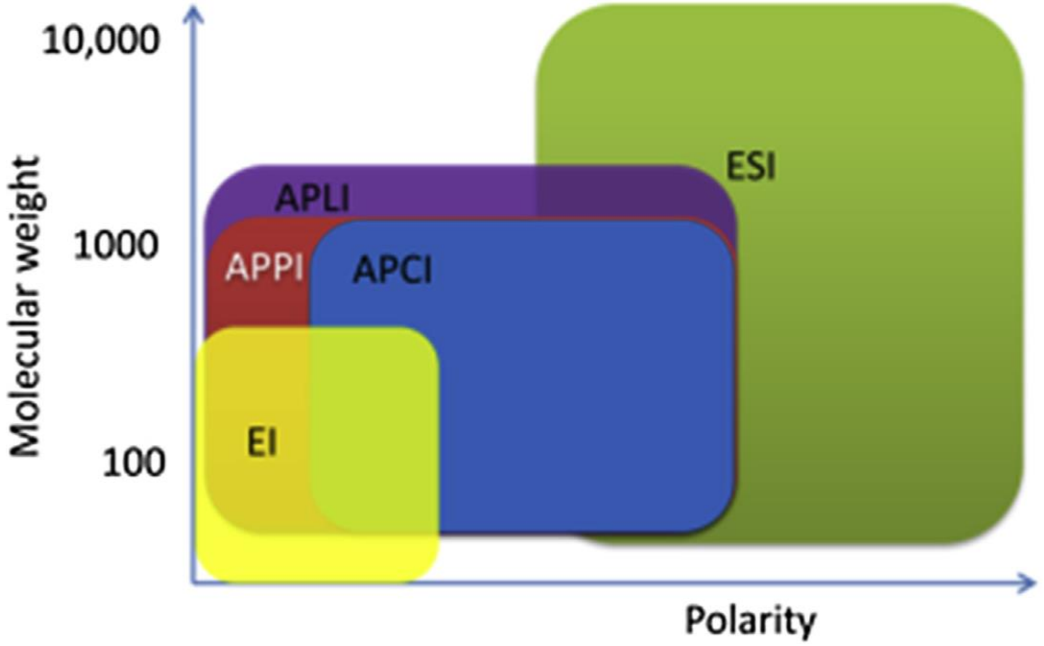


Li et al., *Analytica Chimica Acta*, **2015**, *43-61*

Historic Background – Atmospheric Pressure Ionization

- first technique combining solution liquid introduction with mass spectrometry
- diluted solution of the analyte is sprayed into a hot Nitrogen gas stream (~200 °C)
- vapor is guided into an ionization chamber containing a β emitter (^{63}Ni foil) followed by complex reaction cascade – finally leading to protonated water clusters acting as ionization reagent

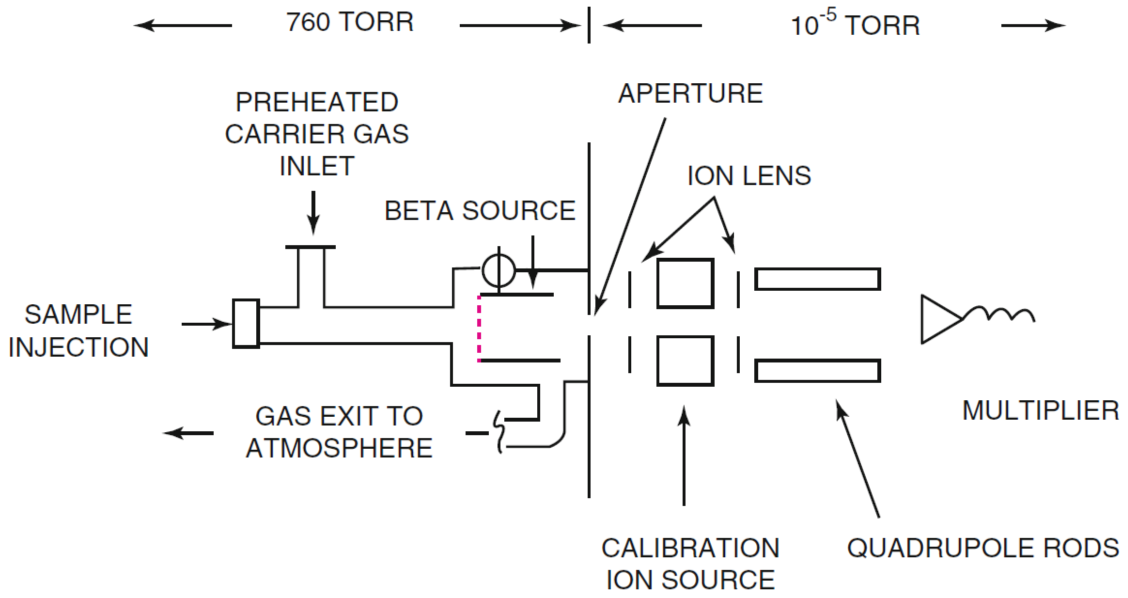
$$N_2 + e^- \rightarrow N_2^{+\bullet} + 2e^-$$

$$N_2^{+\bullet} + N_2 + N_{2(\mathrm{3rd\ body})} \rightarrow N_4^{+\bullet} + N_{2(\mathrm{3rd\ body})}$$

$$N_4^{+\bullet} + H_2O \rightarrow H_2O^{+\bullet} + 2N_2$$

$$H_2O^{+\bullet} + H_2O \rightarrow H_3O^+ + OH^\bullet$$

$$H_3O^+ + H_2O \rightarrow \left[(H_2O)_2 + H\right]^+$$



→ but radioactive source not suitable for common laboratories

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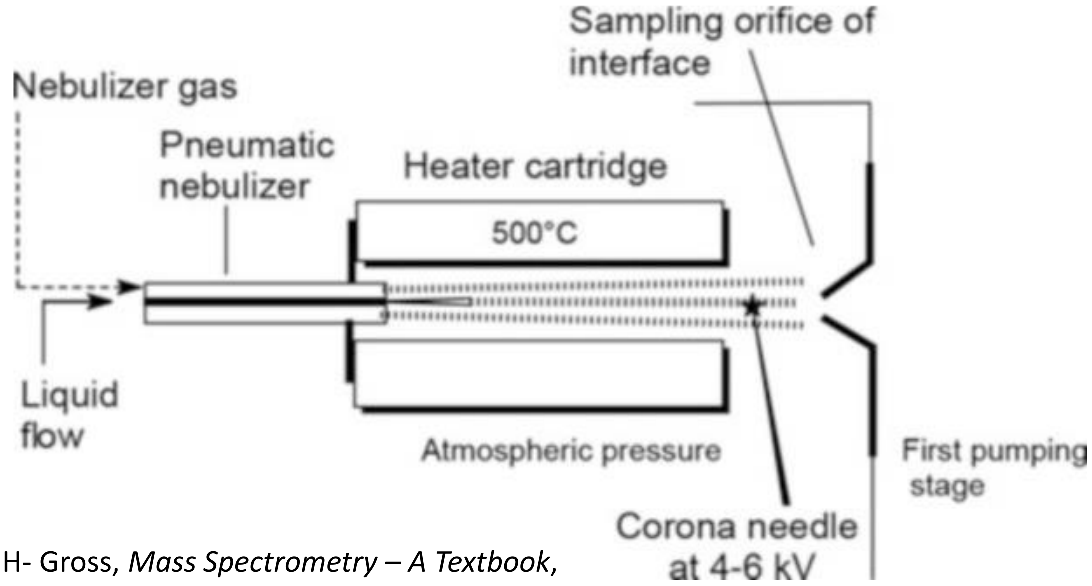
Atmosphere Pressure CI – APCI

Modern Version commonly named APCI

- introduced by Horning et al. by changing the β emitter to a corona discharge plasma
- reagent ion plasma is maintained by a current applied between the sharp tip of the corona needle and the counter electrode (spray inlet)
- basically atmospheric pressure analogous of classical vacuum chemical ionization but at atmospheric pressure higher number of collisions and probability of subsequent reactions



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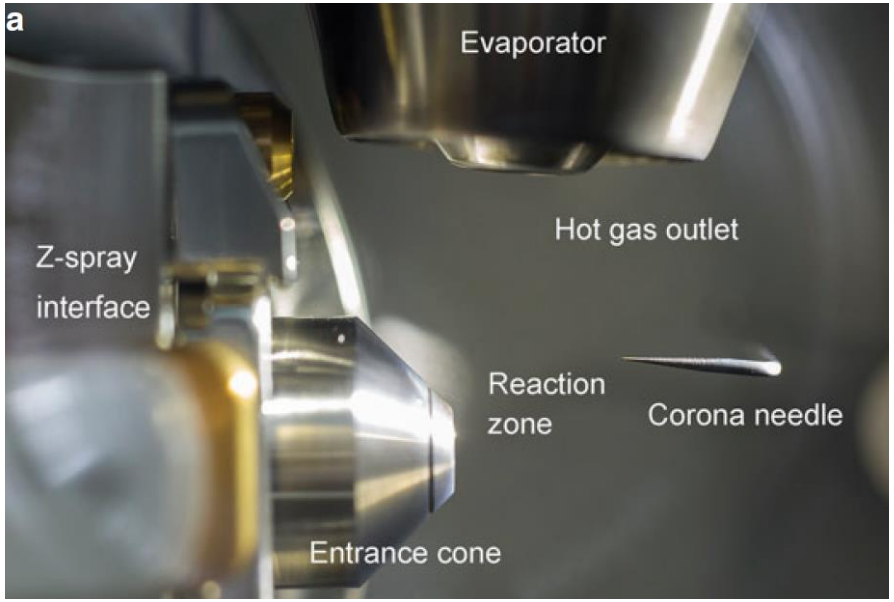

Ion Formation in Positive and Negative Polarity

- complex reaction cascade comparable the API scheme
- strongly influenced by water and oxygen concentration and dwell time in the reagent zone → ionization source parameter (flow rates of dry and nebulizer gas, source and gas temperatures, etc.) have a significant effect on the ionization conditions!

positive polarity

$$\text{corona discharge} + N_2 \rightarrow N_2^{+\bullet} + e^-$$

$$N_2^{+\bullet} + N_2 + N_{2(\text{3rd body})} \rightarrow N_4^{+\bullet} + N_{2(\text{3rd body})}$$

$$N_4^{+\bullet} + H_2O \rightarrow 2N_2 + H_2O^{+\bullet}$$

$$H_2O^{+\bullet} + H_2O \rightarrow H_3O^+ + OH^\bullet$$

$$H_3O^+ + nH_2O \rightarrow \left[(H_2O)_n + H\right]^+$$

$$M + \left[(H_2O)_n + H\right]^+ \rightarrow [M + H]^+ + nH_2O$$

negative polarity

$$O_2 + e^- \rightarrow O_2^{-\bullet}$$

$$O_2^{-\bullet} + M \rightarrow [M + O_2]^{-\bullet}$$

$$M^{-\bullet} + O_2 \rightarrow [M + O_2]^{-\bullet}$$

$$[M + O_2]^{-\bullet} \rightarrow M^{-\bullet} + O_2$$

$$[M + O_2]^{-\bullet} \rightarrow [M - H]^- + HOO^\bullet$$

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Atmosphere Pressure CI – APCI

Nebulizer temperature commonly >350 °C – does this cause problems?

Yes and No!

- very labile molecules might degrade and fragment **but** the majority of organic molecules is softly ionized (even “softer” compared to classical vacuum CI)

Why?

- temperature of the aerosol droplet stays low as the energy is taken to evaporate the solvent
- at the end of the vaporization process only 150-200 °C
  - 150-200 °C ~ 0.1-02. eV but bond braking starts commonly > 2 eV
- thermal cooling – Millions of collisions per Second at atmospheric pressure dissipating the excess energy efficiently

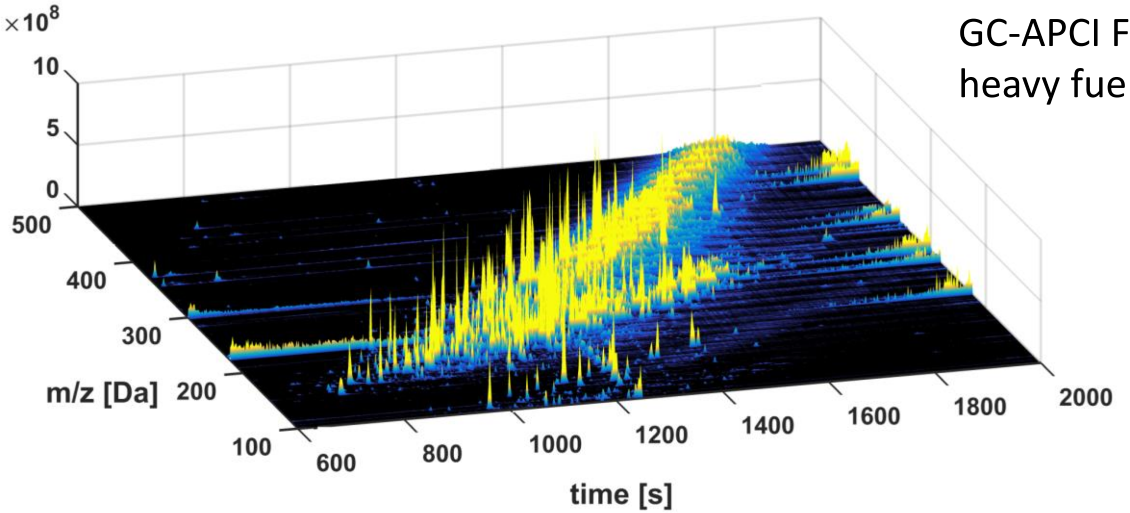
Atmosphere Pressure CI – APCI

Problems and Disadvantages

- frequent formation of ionization artifacts (adducts and additional reaction pathways)
  - ammonium adducts in pos. mode (mostly delivered by the sample, *e.g.*, buffer solution)
  - halogenide adducts in negative mode or less common CO_3^-, NO_2^-, or OH^-
  - oxidation (strongly depending on oxygen and water concentration)
  - …

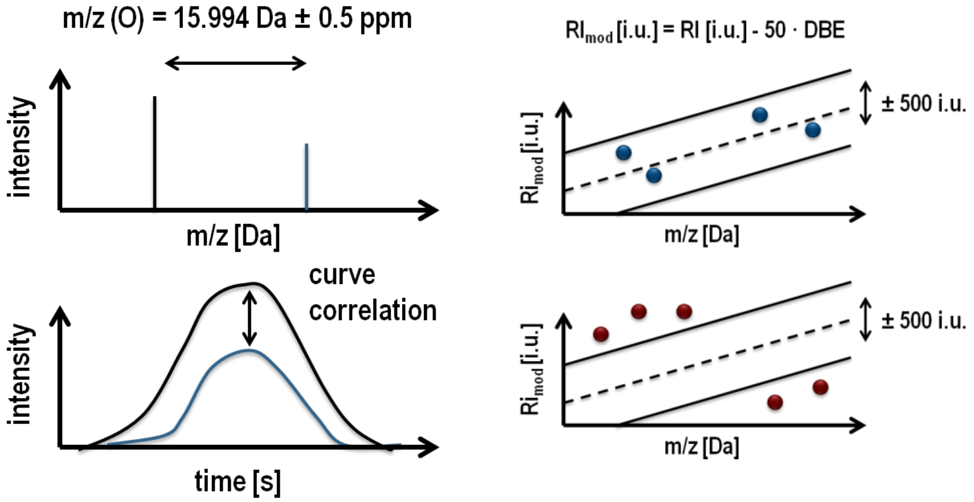
$$M + [NH_4]^+ \rightarrow [M + NH_4]^+$$

$$M + Hal^- \rightarrow [M + Hal]^-$$



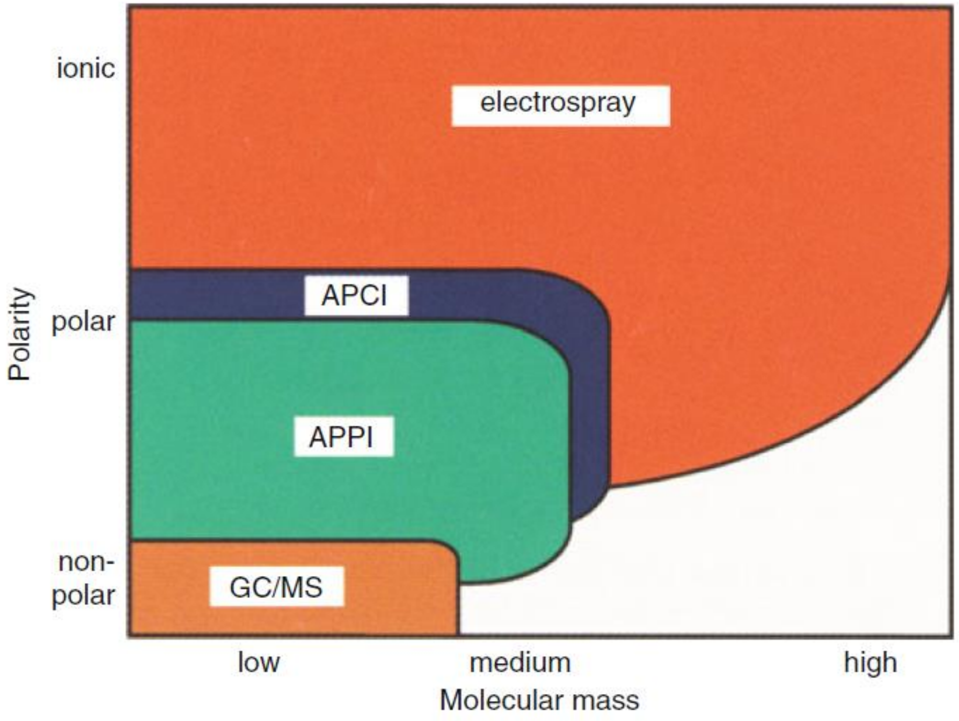
GC-APCI FT-ICR MS of heavy fuel oil

Artifact correction concepts



Schwemer et al., *Analytical Chemistry*, **2015**, 11957–11961
Rüger et al., *EJMS*, **2017**, 28–39

Selectivity of Ionization in Mass Spectrometry – "Analytical Glasses"



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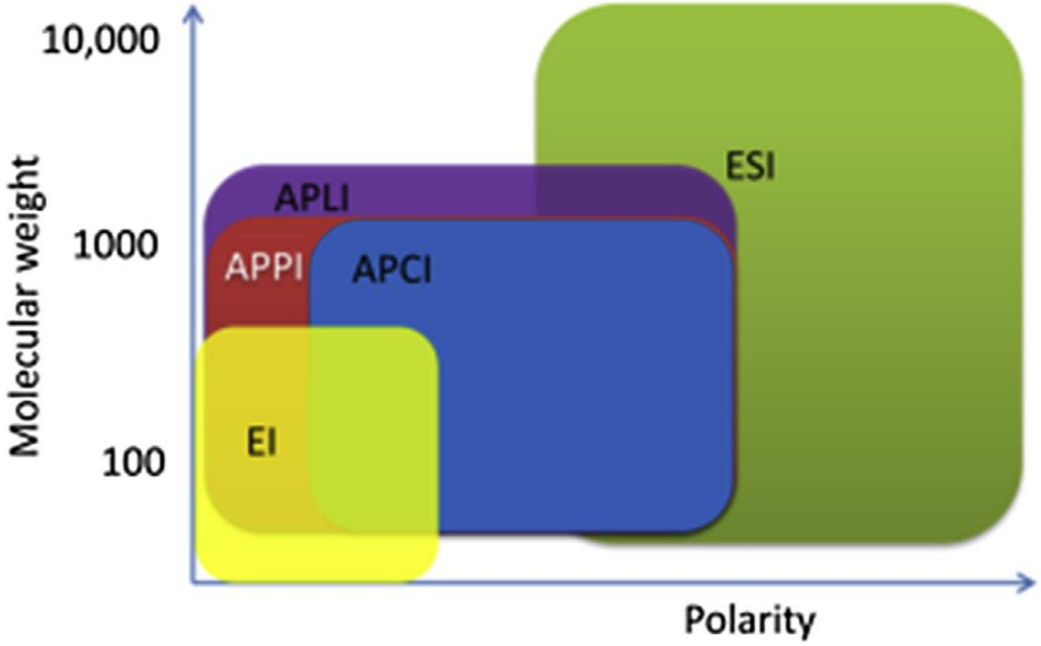
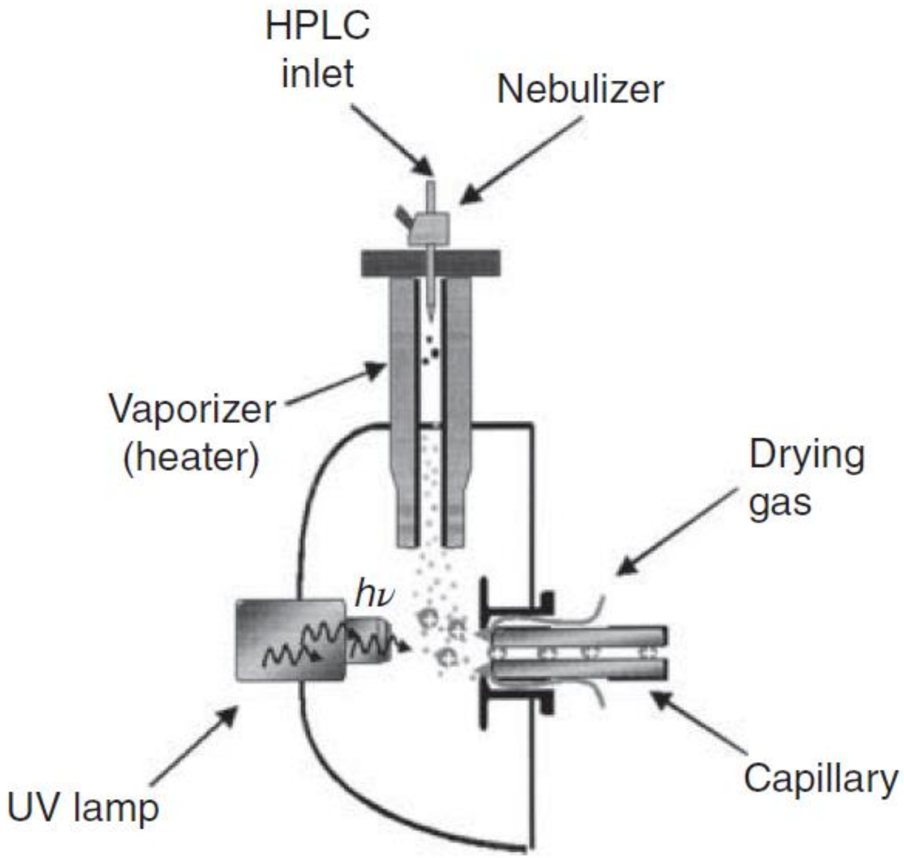


Li et al., *Analytica Chimica Acta*, **2015**, *43-61*

Atmospheric Pressure PI – APPI

Basics and Geometry



$M + h\nu \rightarrow M^{+\cdot} + e^{-}$, if IE (M) < 10 eV (1)

$S + h\nu \rightarrow S^{+\cdot} + e^{-}$, if IE (S) < 10 eV (2)

$D\text{ (dopant)} + h\nu \rightarrow D^{+\cdot} + e^{-}$ (3)

$D^{+\cdot} + M \rightarrow M^{+\cdot} + D$, if IE (M) < IE (D) (4)

$D^{+\cdot} + nH_2O \rightarrow [D^{+\cdot}(H_2O)_n]$ (5)

$D^{+\cdot} + nS \rightarrow [D^{+\cdot}(S)_n]$ (6)

$[D^{+\cdot}(H_2O)_n] \rightarrow [(H_2O)_n{+}H]^{+} + [D{-}H]^{\cdot}$ (7)

$[D^{+\cdot}(H_2O)_n] \rightarrow (H_2O)_n^{+} + D^{\cdot}$ (8)

$[(H_2O)_n{+}H]^{+} + M \rightarrow [M{+}(H_2O)_n{+}H]^{+} + H_2O$ (9)

$[(H_2O)_n{+}H]^{+} + M \rightarrow [M{+}(H_2O)_n{+}H]^{+}$ (10)

$[M{+}(H_2O)_n{+}H^{+}] \rightarrow [M{+}H]^{+} + nH_2O$ (11)

Scheme 8.1 Ionization reactions in APPI (Kauppila et al. 2002; Syage 2004; Klee et al. 2013).

Photoionization and Photo-Induced Processes in Mass Spectrometry, Ralf Zimmermann and Luke Hanley, 2021 WILEY-VCH GmbH

Adjusting the Ionization Properties – The Use of Dopants

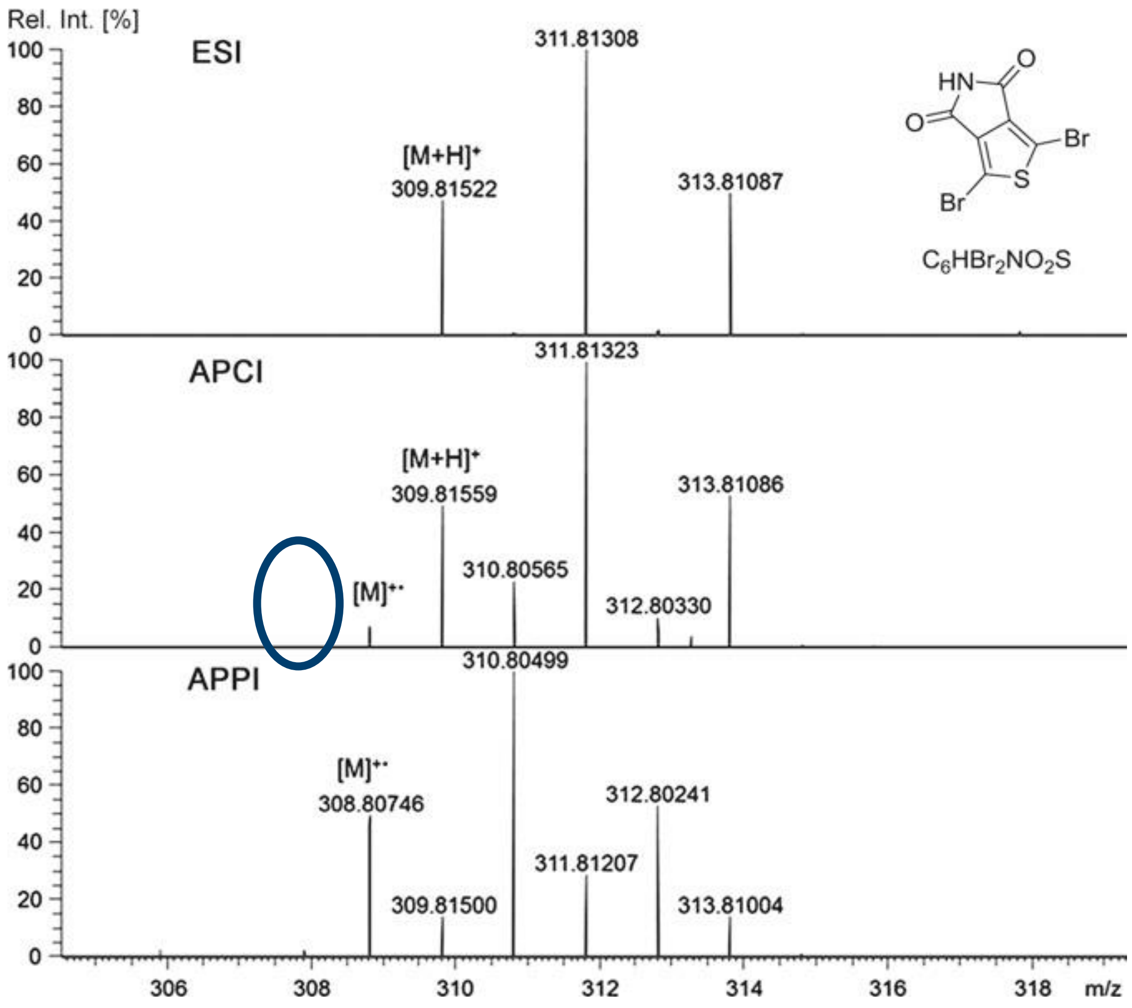


Table 8.1 Properties of the most typical dopants.

Dopant	IE (eV)	PA (kJ/mol)
Toluene	8.83	784.0
Anisole	8.20	839.6
Chlorobenzene	9.07	753.1
Acetone	9.70	812.0

IE = ionization energy, PA = proton affinity
Source: From Linstrom and Mallard (2015).

Jürgen H- Gross, *Mass Spectrometry – A Textbook*, **2017**, Spinger, ISBN *978-3-319-54398-7*

GC-APPI Interface Designs

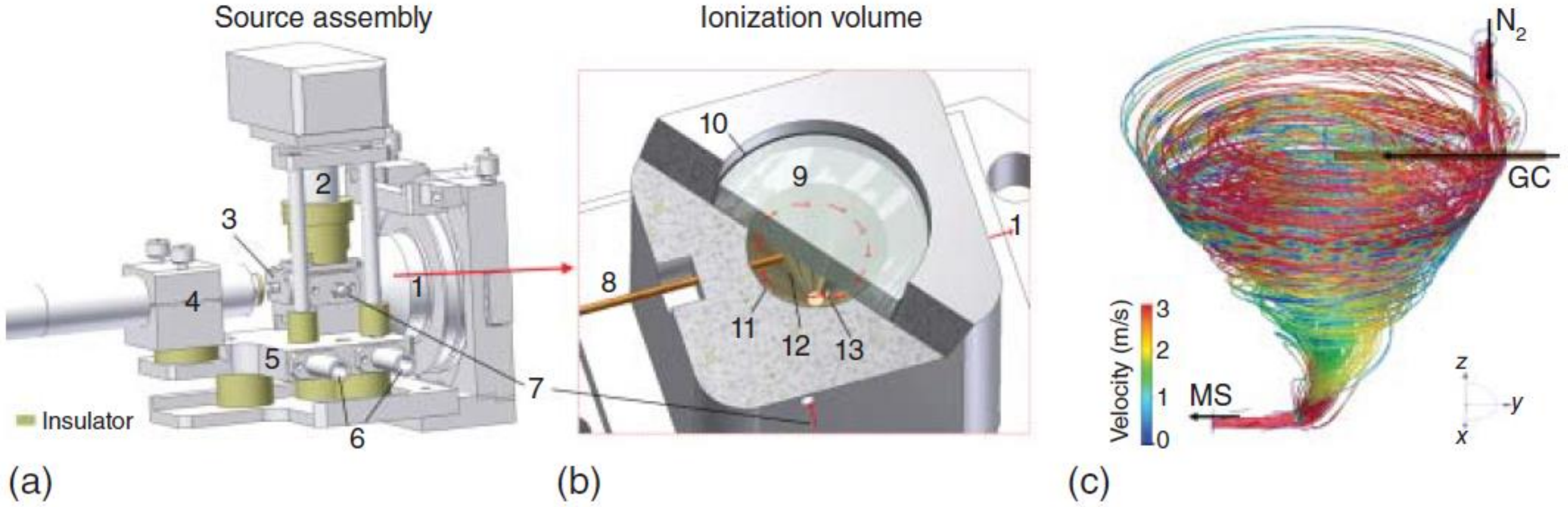


Figure 8.5 Schematic of the GC-APPI-Orbitrap interface by Kersten et al. (a) 1. MS, 2. VUV lamp, 3. GC column adapter, 4. GC transfer line assembly, 5. heater table, 6. heater cartridges, 7. makeup gas adapter, 8. GC column, 9. MgF_2 window; (b) 10. sealing with cement and inorganic coating, 11. makeup gas inlet, 12. conical ionization volume, 13. exit to MS, (c) massless particle trace simulation of the makeup gas inside the conical ionization volume. Source: Kersten et al. (2016). Copyright 2016, Reprinted with permission of Springer Nature.

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in Mass Spectrometry, Ralf Zimmermann and
Luke Hanley, 2021 WILEY-VCH GmbH

Desorption-APPI Interface Designs

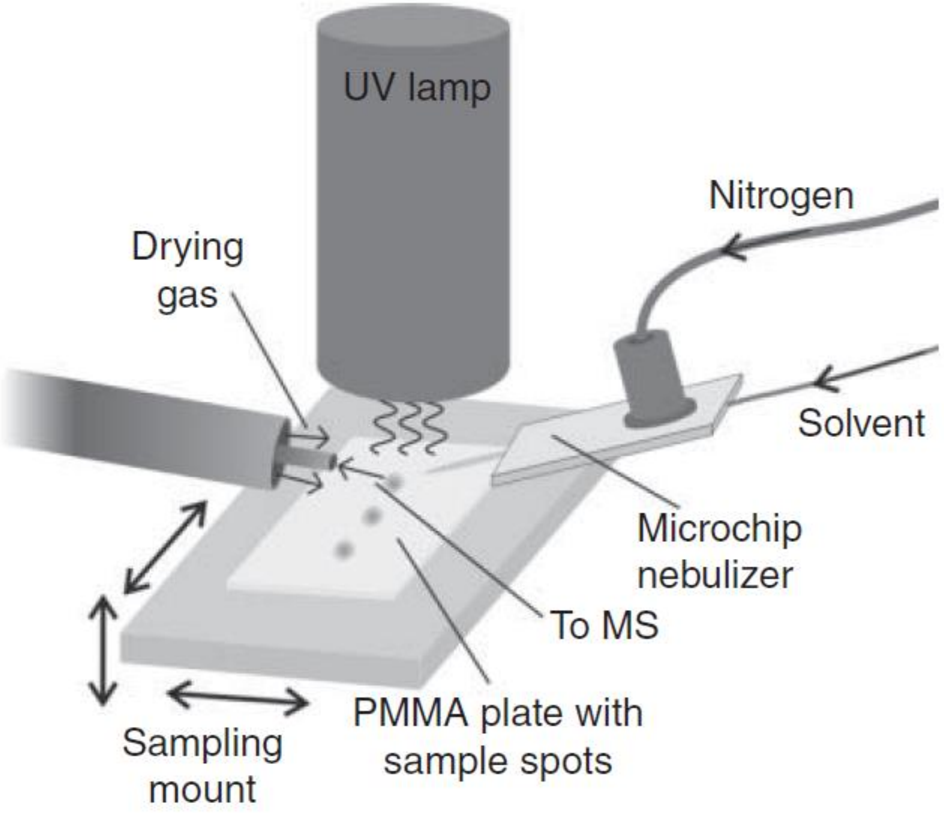

Figure 8.7 Schematic of the desorption atmospheric pressure ionization (DAPPI) source. Source: Haapala et al. (2007b). Copyright 2007, Reprinted with permission of American Chemical Society.

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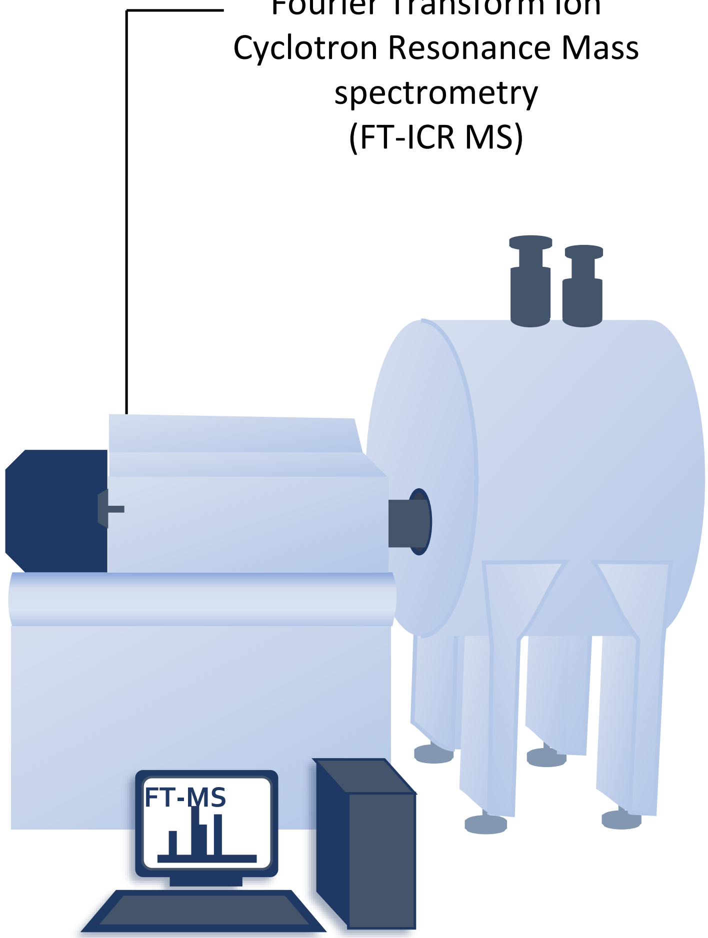
Mass Spectrometric Platform – FT-ICR MS

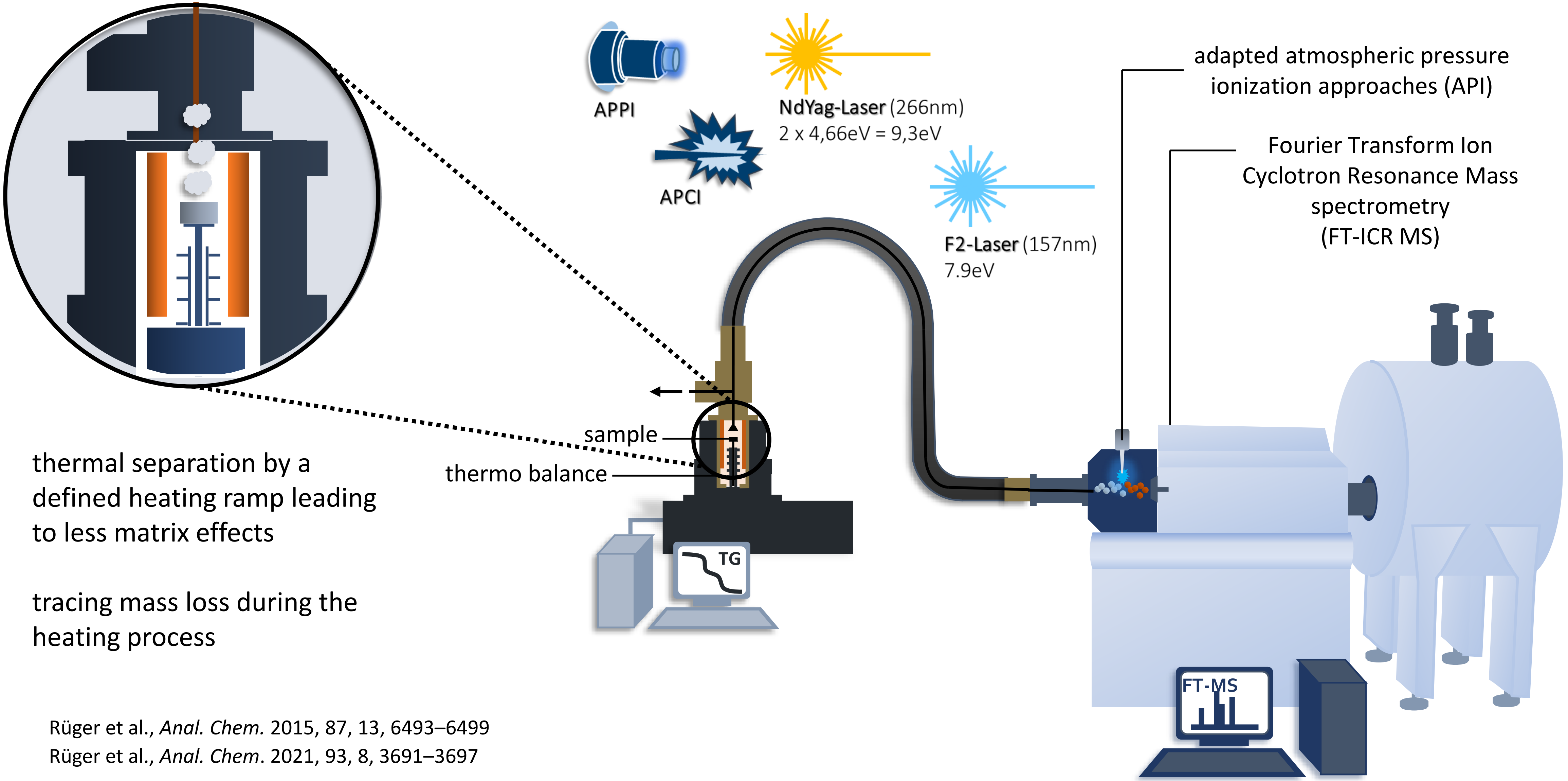


Fourier Transform Ion
Cyclotron Resonance Mass
spectrometry
(FT-ICR MS)

Limitations:
especially for high complex mixtures, ion suppression is a critical issue

→ **reduction of matrix effects by prior separation or novel ionization schemes**

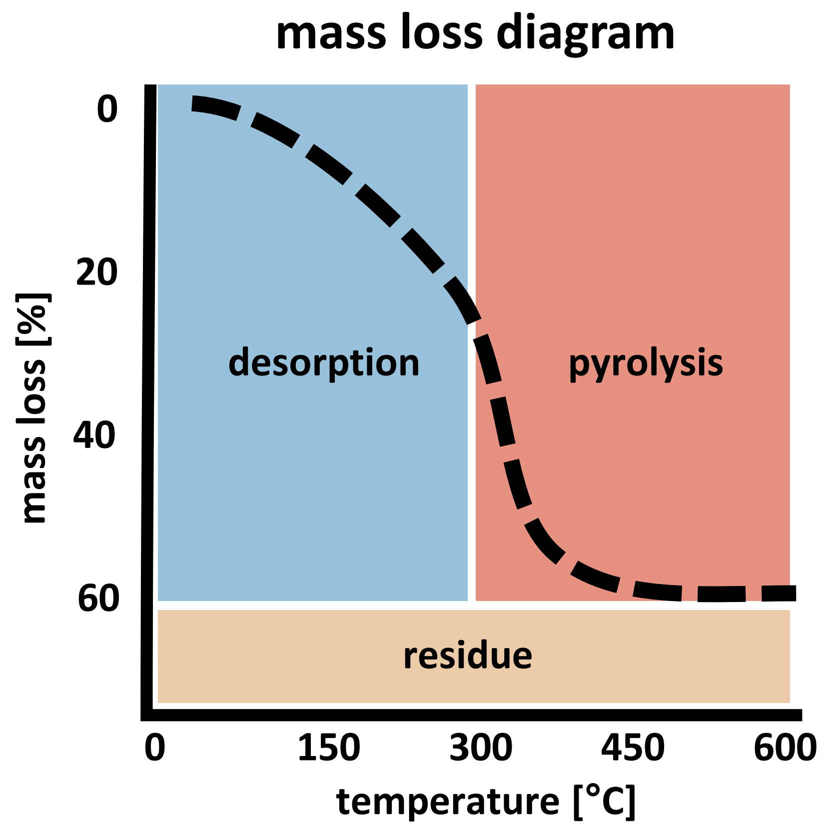
Mass Spectrometric Platform – FT-ICR MS

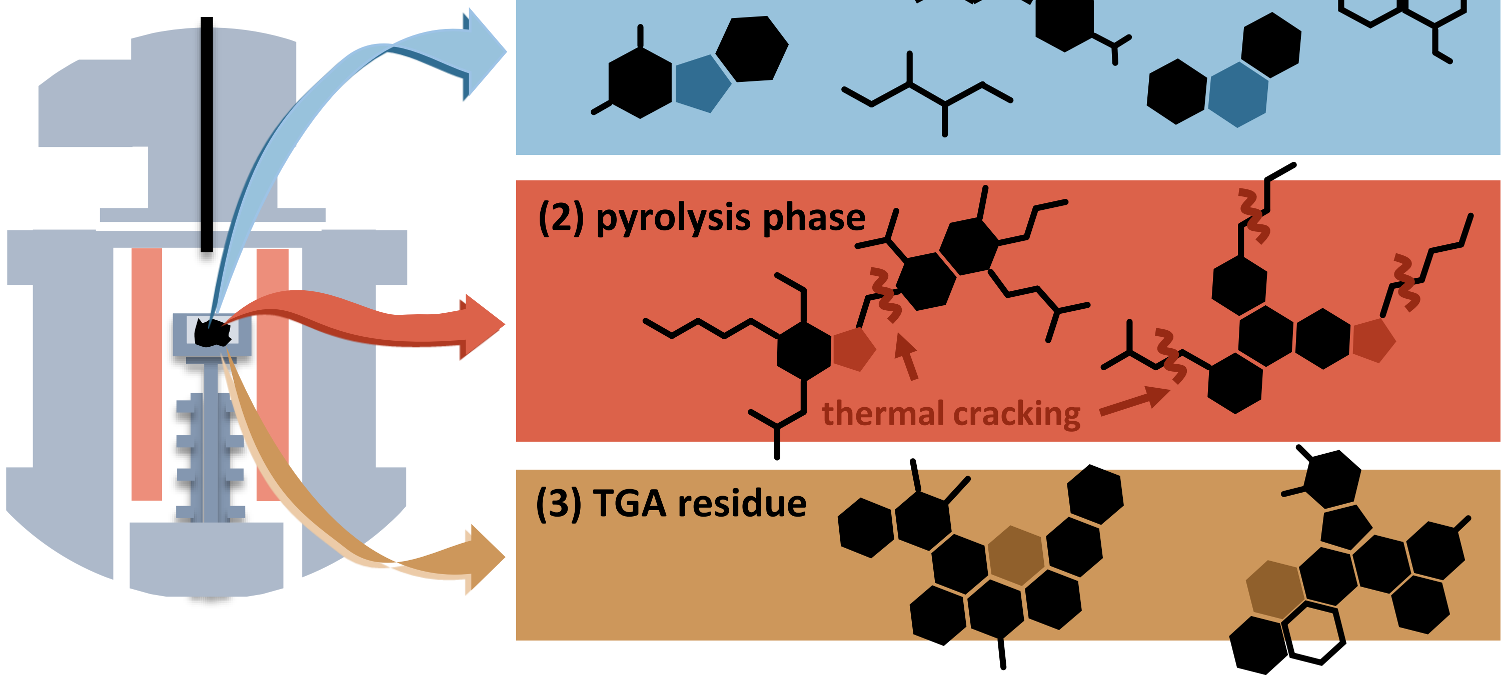


- thermal separation by a defined heating ramp leading to less matrix effects
- tracing mass loss during the heating process

Rüger et al., *Anal. Chem.* 2015, 87, 13, 6493–6499
Rüger et al., *Anal. Chem*. 2021, 93, 8, 3691–3697

Thermogravimetric Processes



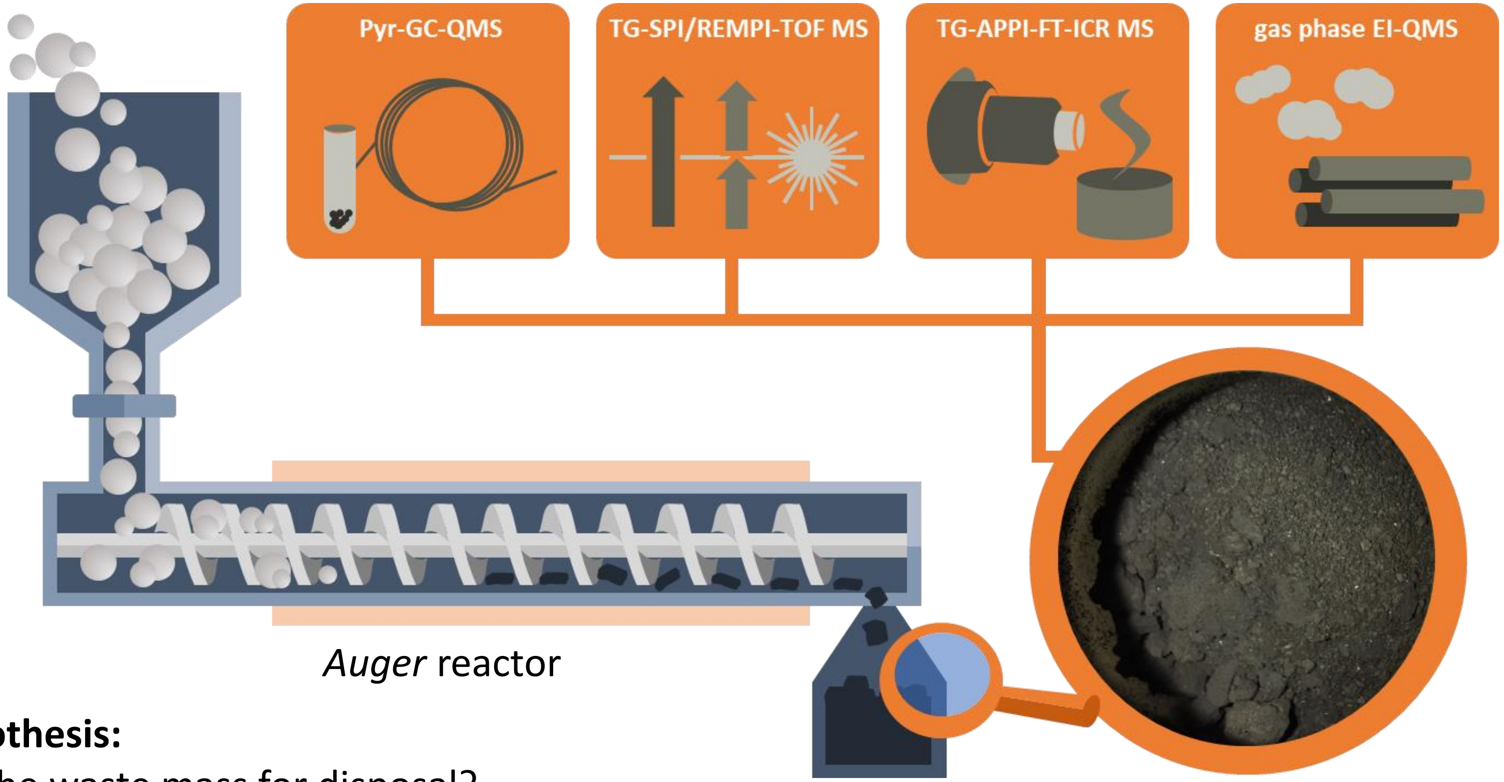


Three processes occur during the thermogravimetric heating process:

(1) Desorption: mostly evaporation of intact compounds
(2) Pyrolysis: thermal decomposition of high molecular weight species (starting at 300-350 °C)
(3) Residue: coke formation of high aromatic compounds and highly stable aggregates

Plastic Pyrolysis Coke

Chemical description of plastic pyrolysis coke residues for improved recycling



Auger reactor

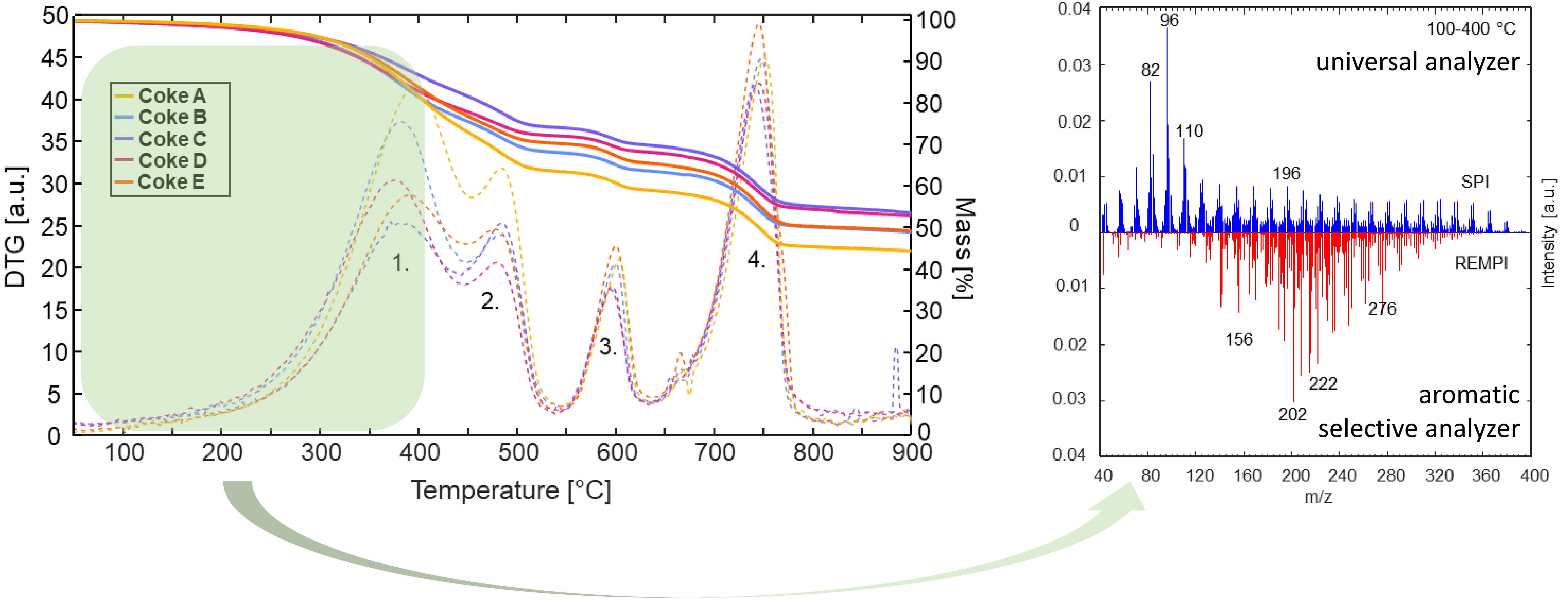
Main research hypothesis:

- Can we reduce the waste mass for disposal?
- Can we examine the quality and purity/toxicity of the coke?
- Are valuable chemicals be accessible based on a second pyrolysis step?
- Is there a potential for usage of the residue in material science?

TotalEnergies

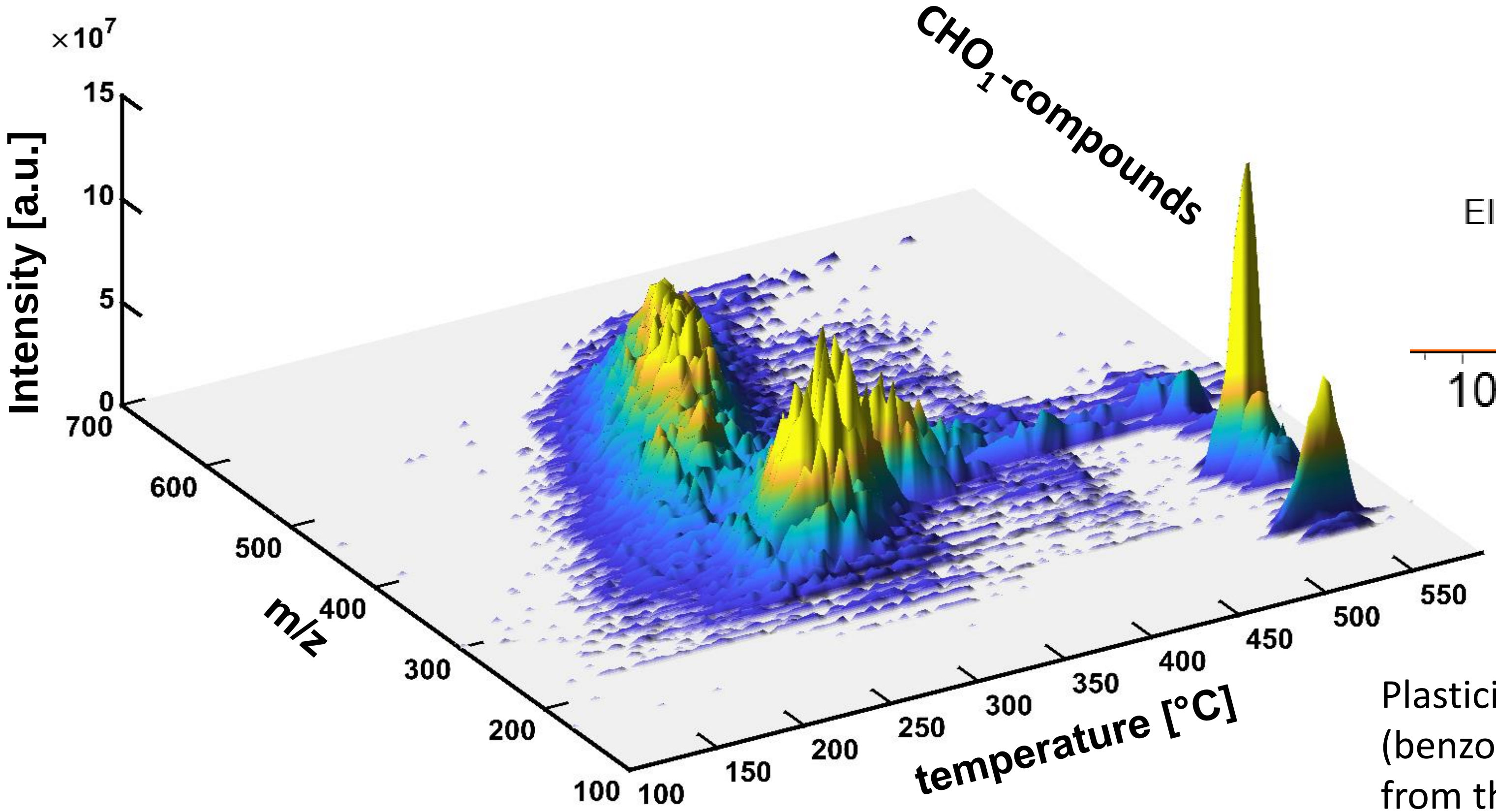
Plastic Pyrolysis Coke

Unique thermogravimetric behavior with several distinct mass loss events

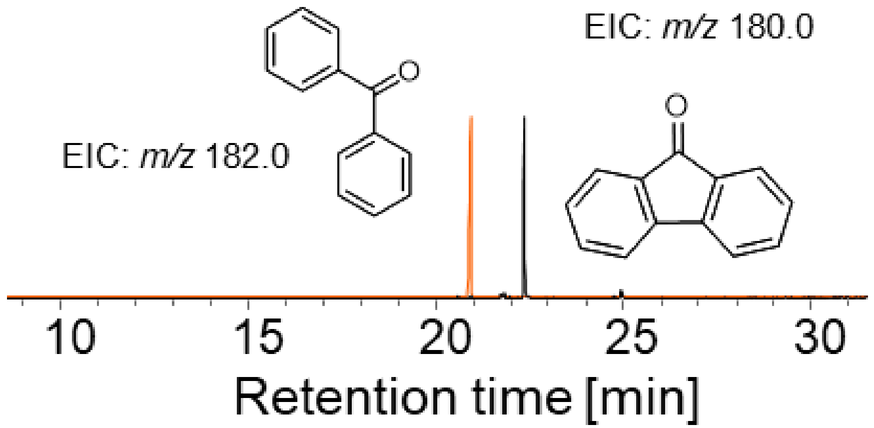


Plastic pyrolysis - coke

Polymer additives and plasticizers cause unique pyrolysis chemistry



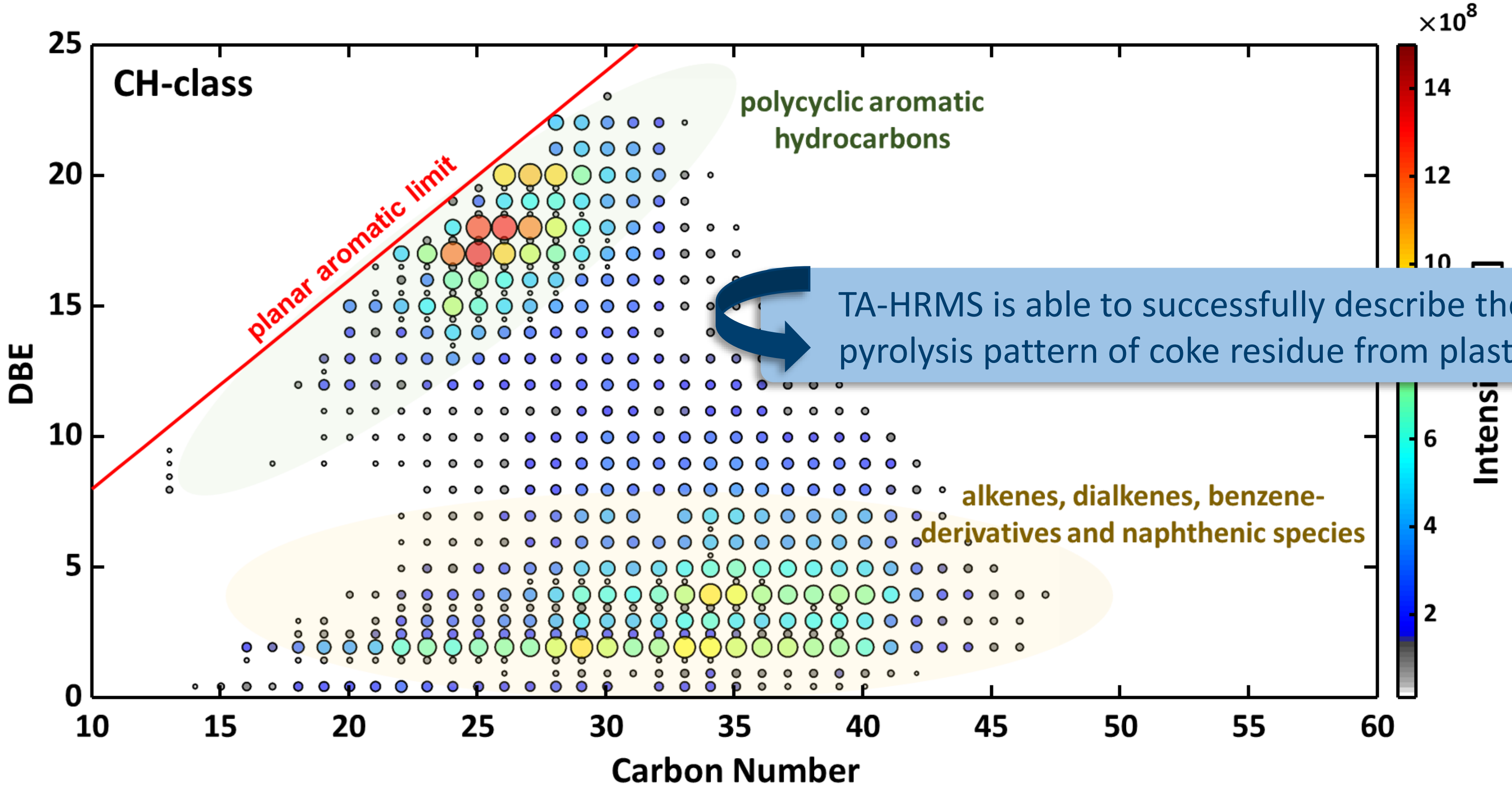
Survey view of the thermal analysis high-resolution mass spectrometric data



Plasticizer derivatives, such as UV-stabilizers (benzophenones) released at elevated temperatures from the char network (strongly bound and/or integrated in the macromolecular structure.

Plastic pyrolysis - coke

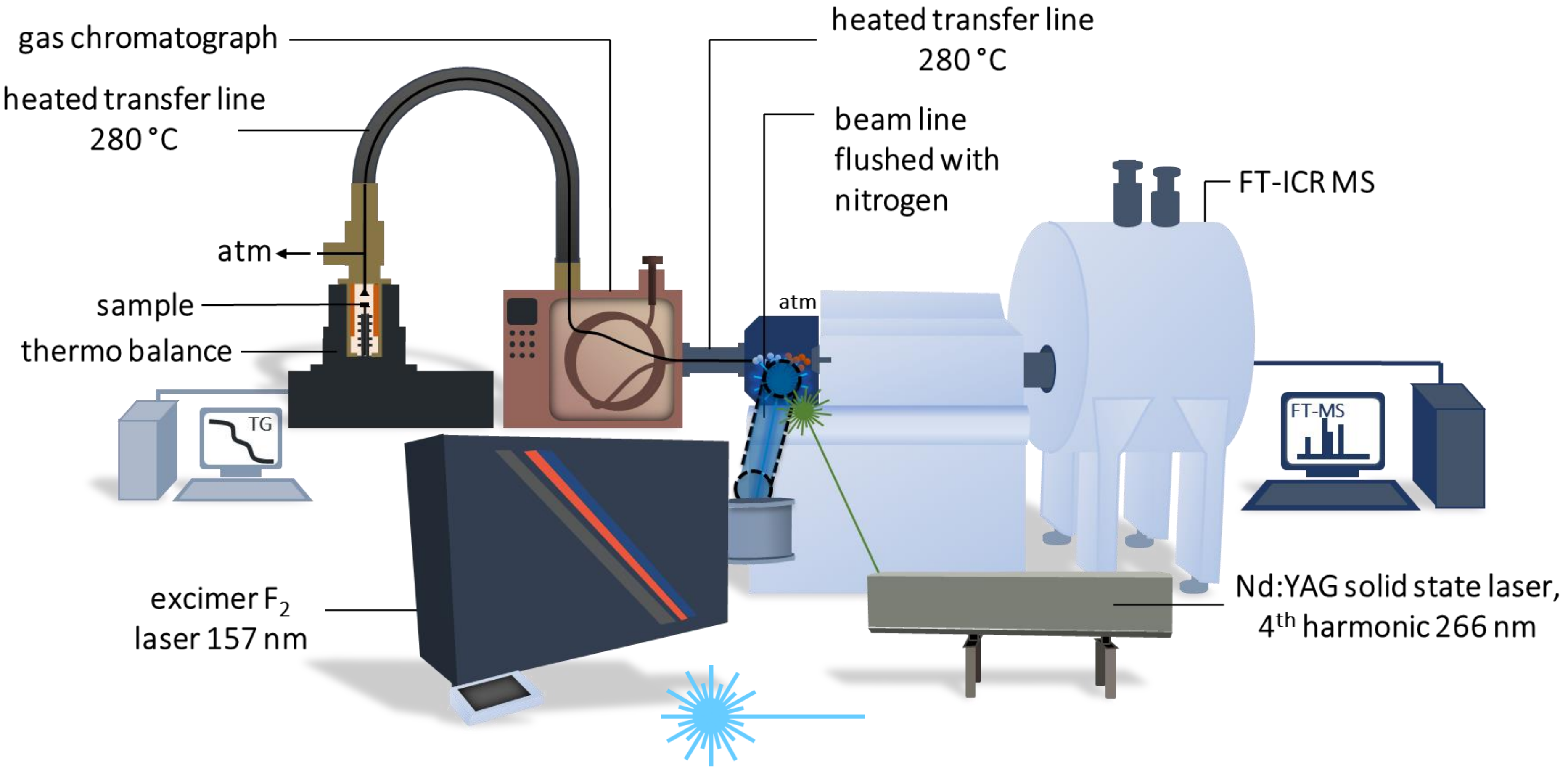
Island/Archipelago-type structural motives with low heteroatom count



TA-HRMS is able to successfully describe the complex pyrolysis pattern of coke residue from plastic recycling

Comprehensive Chemical Description of Pyrolysis Chars from Low-Density Polyethylene by Thermal Analysis Hyphenated to Different Mass Spectrometric Approaches, Friederici et al., *Energy and Fuels*, 2021, DOI 10.1021/acs.energyfuels.1c01994

Novel Concepts for APLI – Deploying < 200 nm radiation for ionization

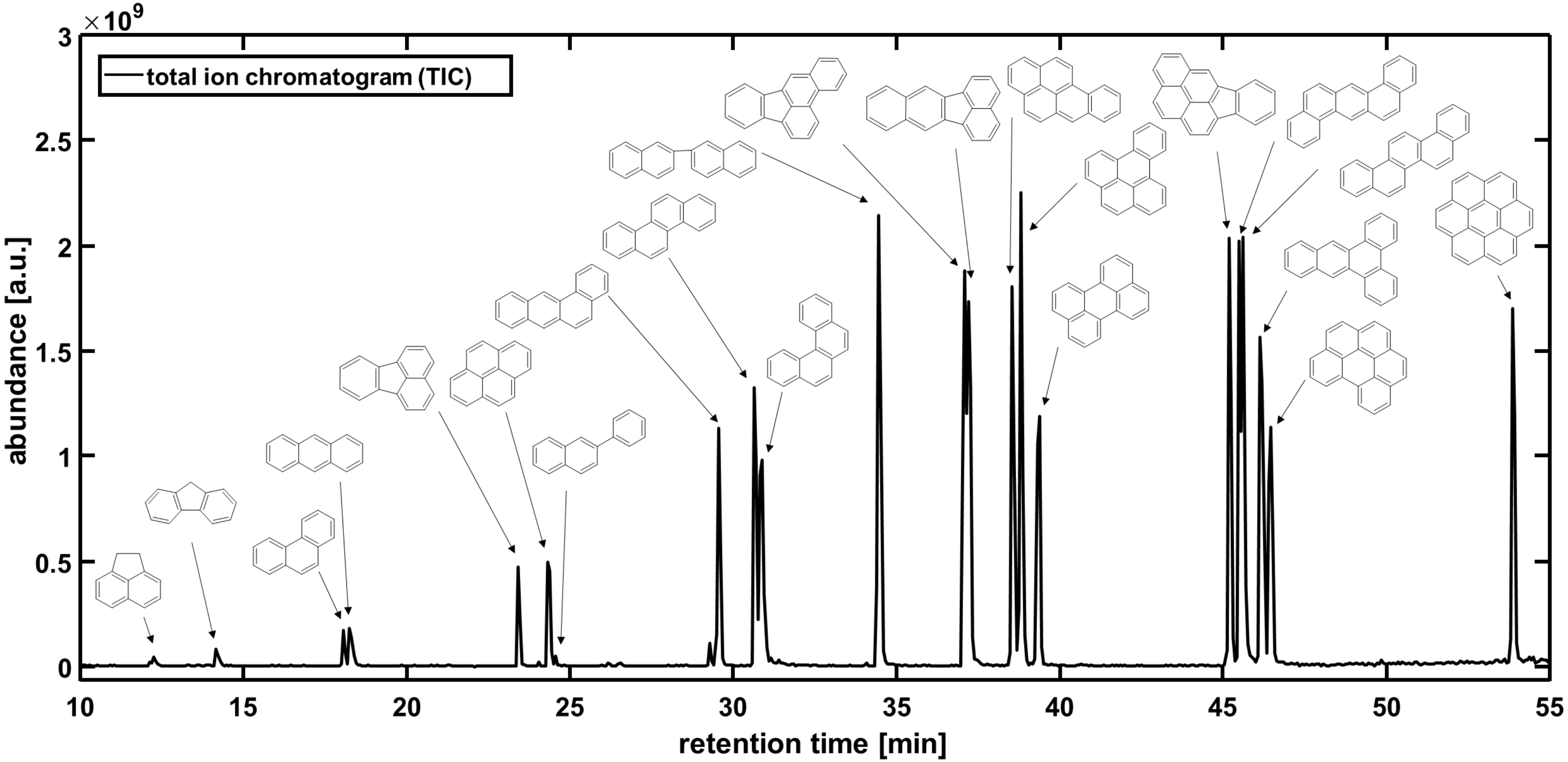


F2-Laser (157nm)
7.9eV

Rüger et al., *Analytical Chemistry* 2021, 93, 8, 3691–3697

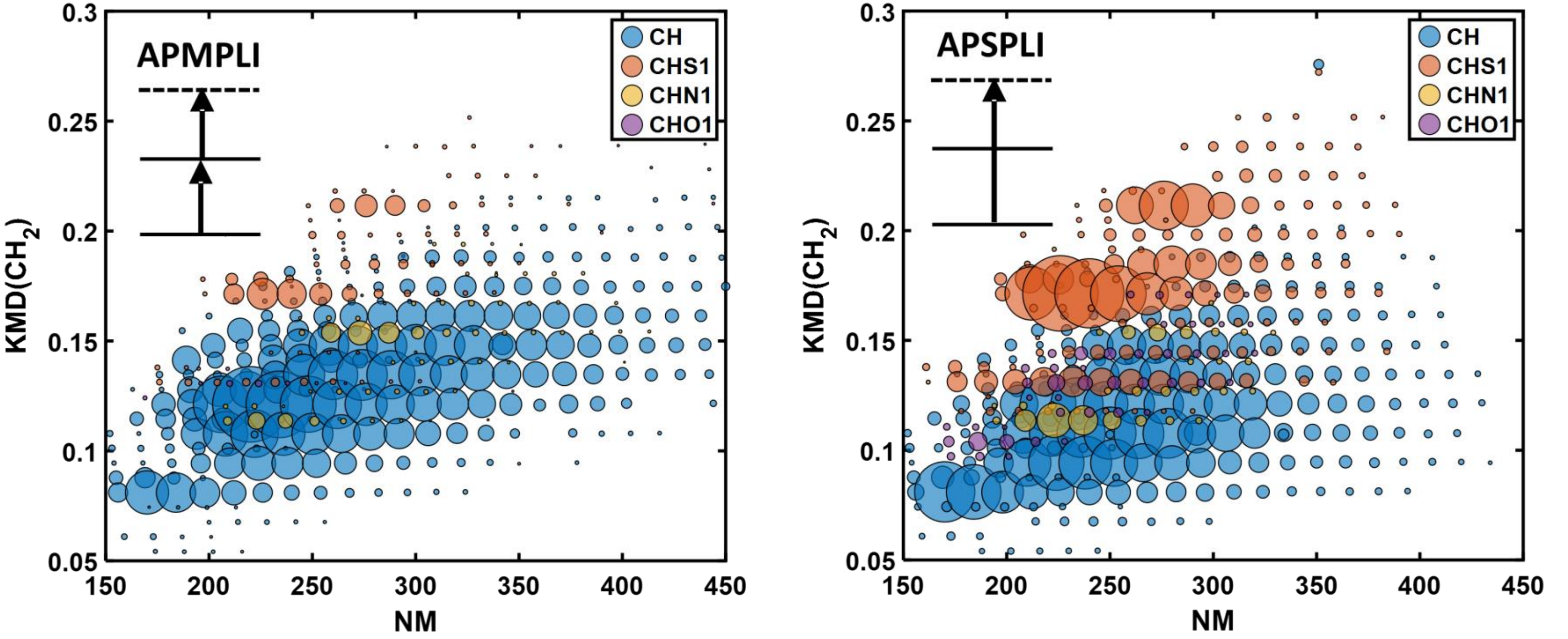
Atmospheric Pressure Laser Ionization (APLI)

Gas chromatographic investigation of PAH mixtures



Rüger et al., *Analytical Chemistry* 2021, 93, 8, 3691–3697

Application towards complex mixtures – additional chemical space addressed



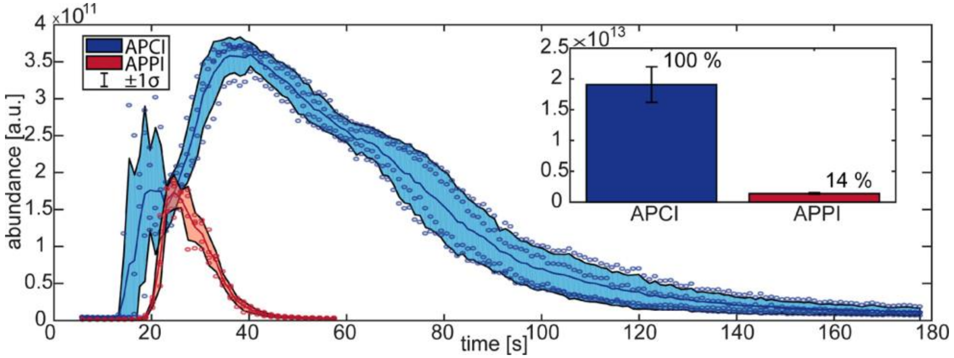
APLI at 157 nm allows to target a broader chemical space compared to APLI at 266 nm – sensitive detection of heteroatom containing aromatics

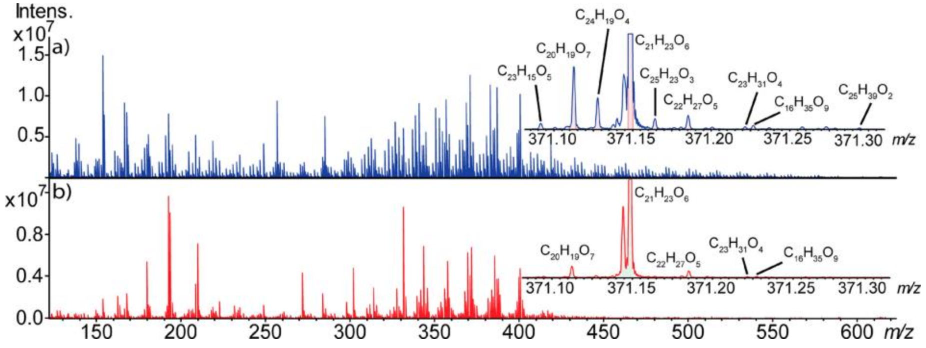
Rüger et al., *Analytical Chemistry* 2021, 93, 8, 3691–3697

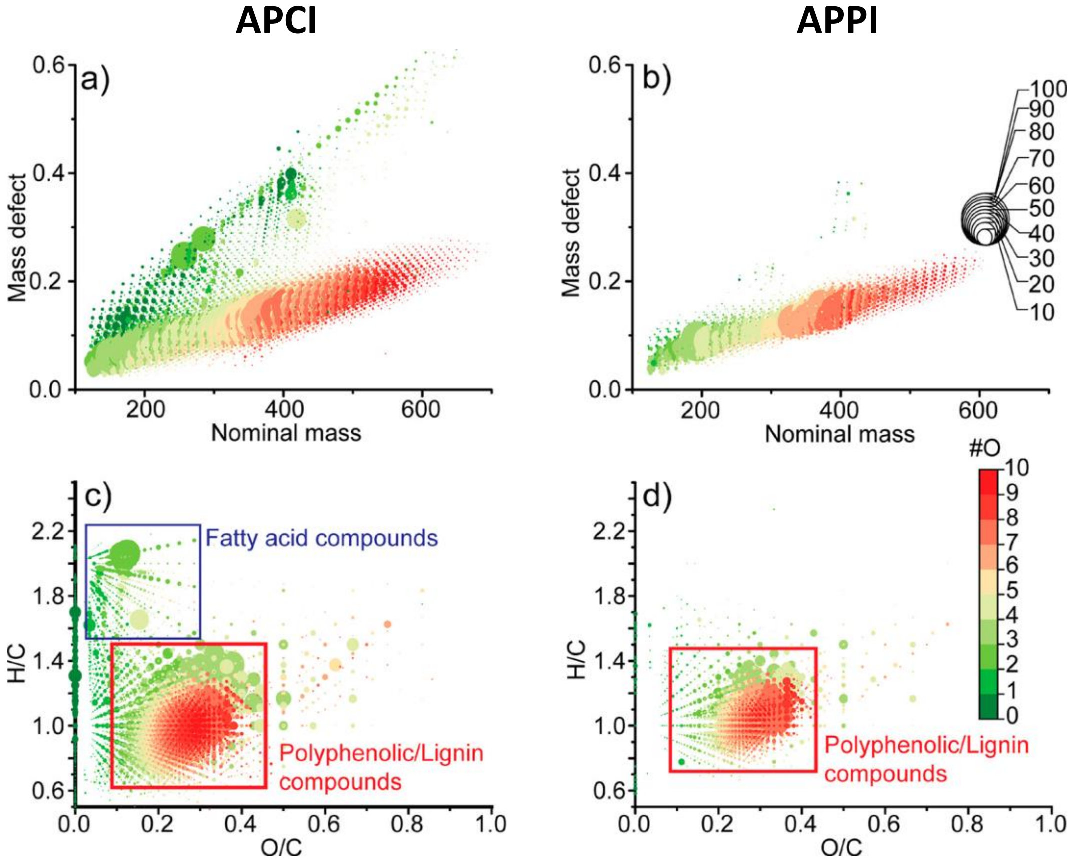
Customized photoionization concepts allow for novel analytical approaches with unique capabilities

Selected Comparison Studies of Ionization Techniques

Direct insertion probe APCI (blue) and APPI (red) analysis of lignocellulosic biomass



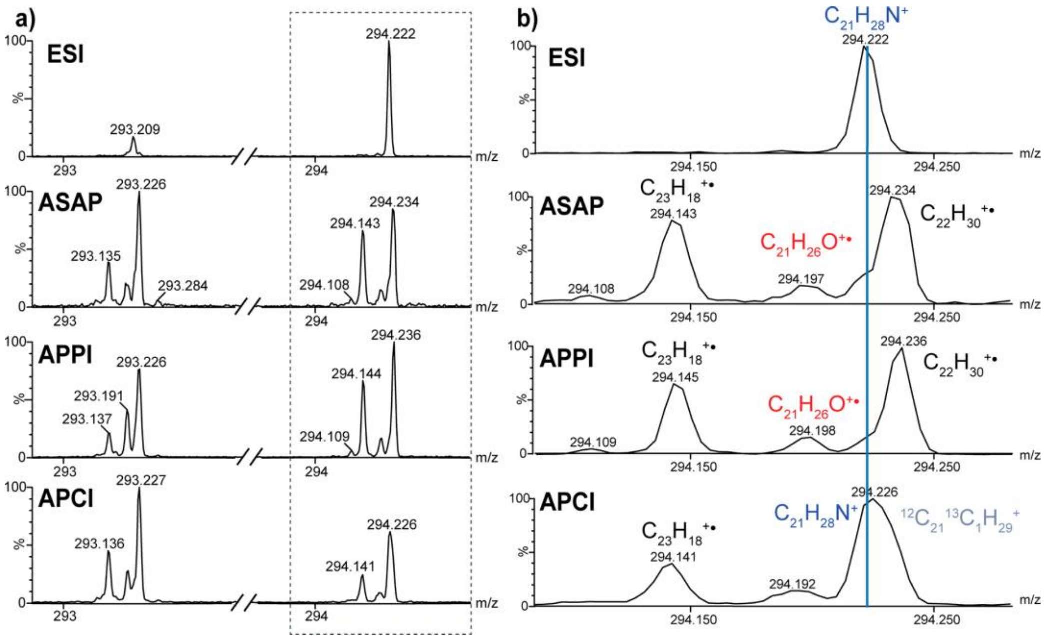


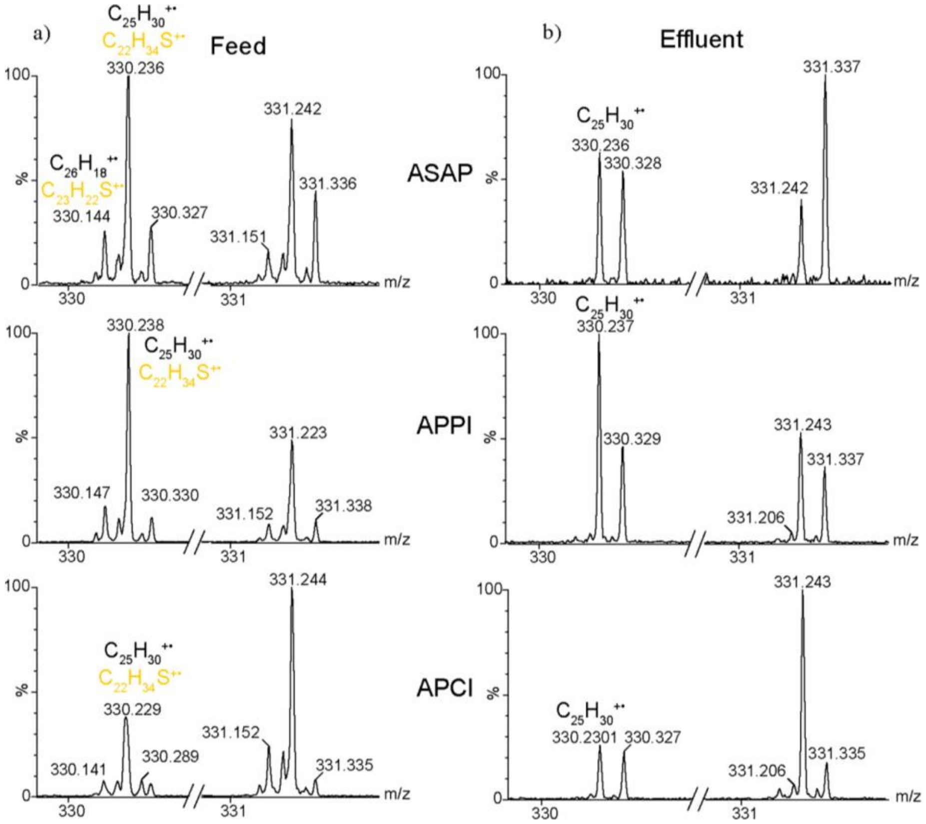


Castilla et al., *JASMS*, **2020**, 822-831

Selected Comparison Studies of Ionization Techniques

Heavy petroleum fractions analyzed by high-resolution time of flight mass spectrometry (HR-TOF)

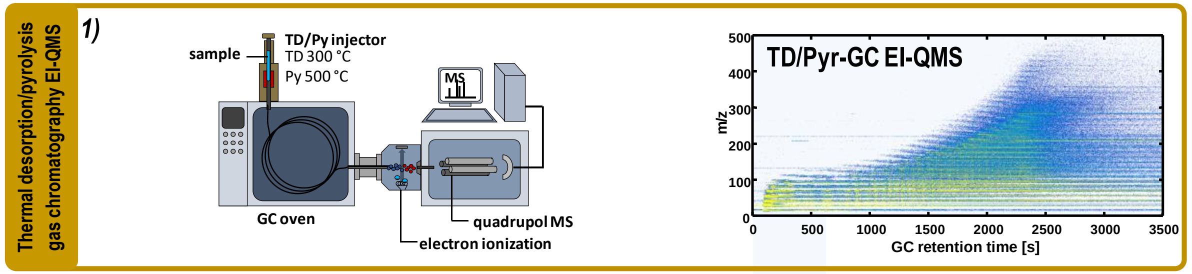




HR-TOF cannot resolved the isobaric complexity but the different selectivity of ionization is nicely visible, *e.g.*, CH-species absent in ESI spectra

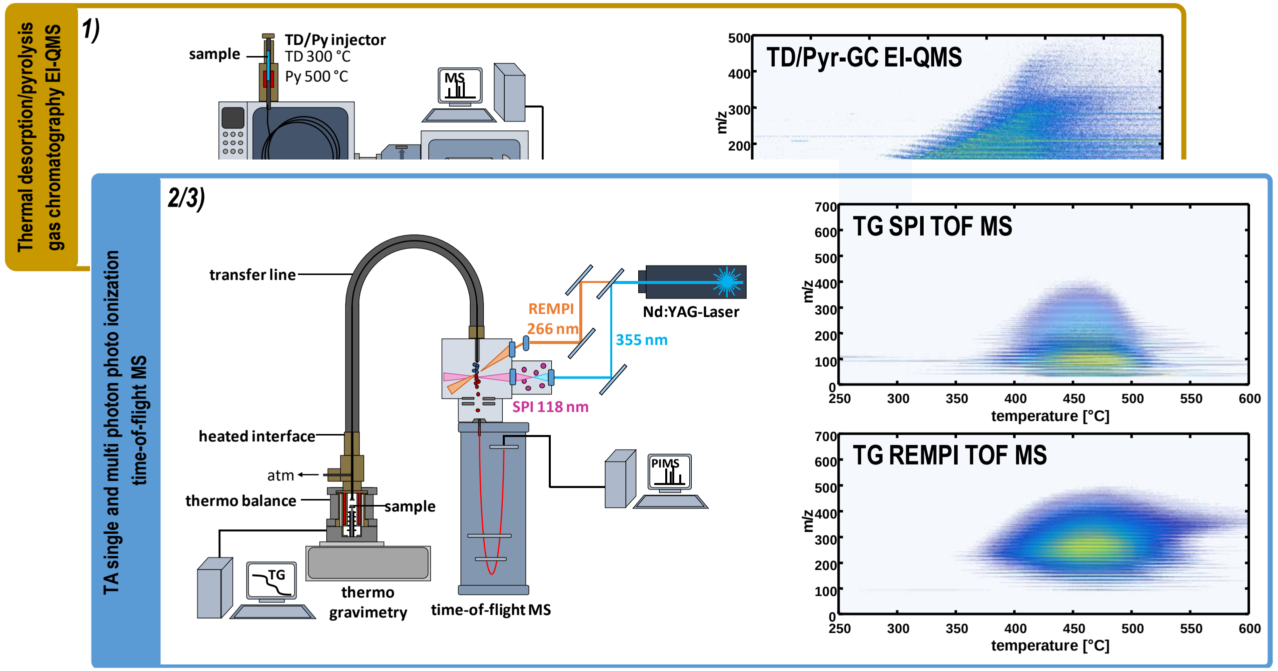
Farenc et al., *Energy and Fuels*, **2016**, 8896-8903

Asphaltenes – Study on the Combination of Information retrieved from Different Ionization Techniques



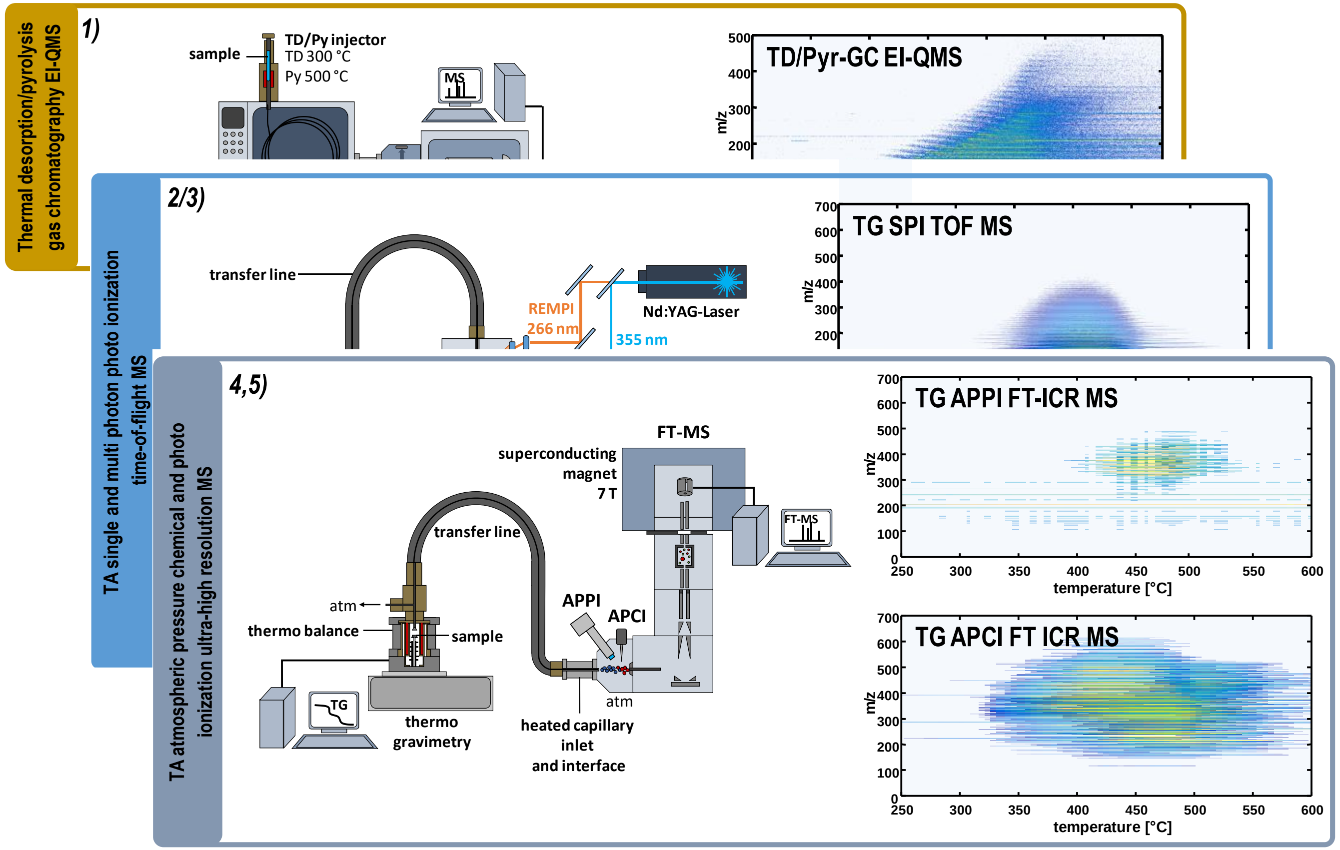
Rüger et al., *Energy and Fuels*, **2016**, 2699-2711

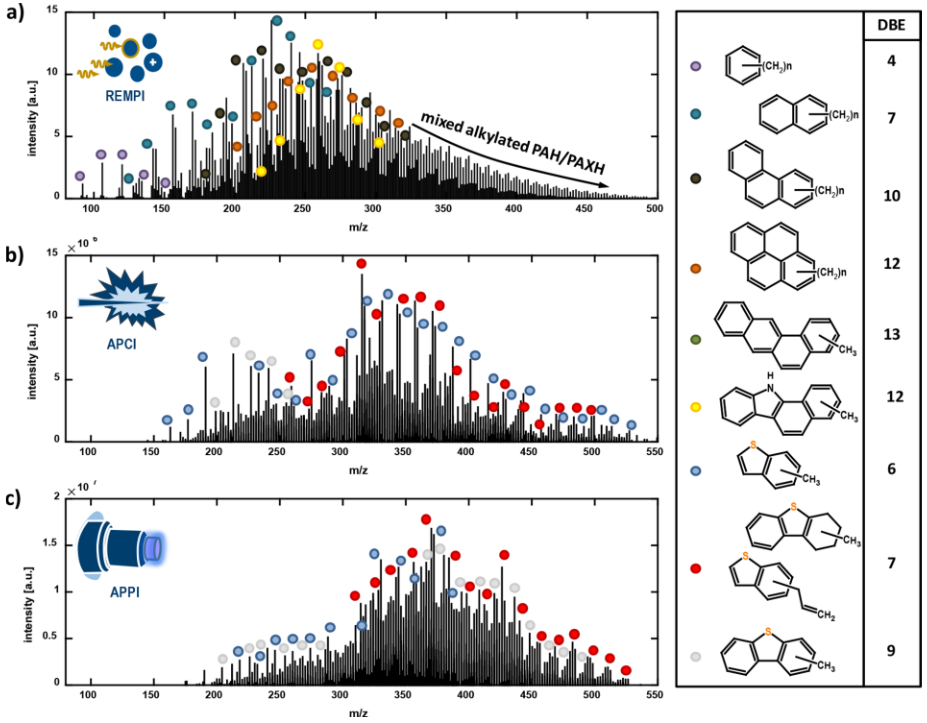
Asphaltenes – Study on the Combination of Information retrieved from Different Ionization Techniques



Rüger et al., *Energy and Fuels*, **2016**, 2699-2711

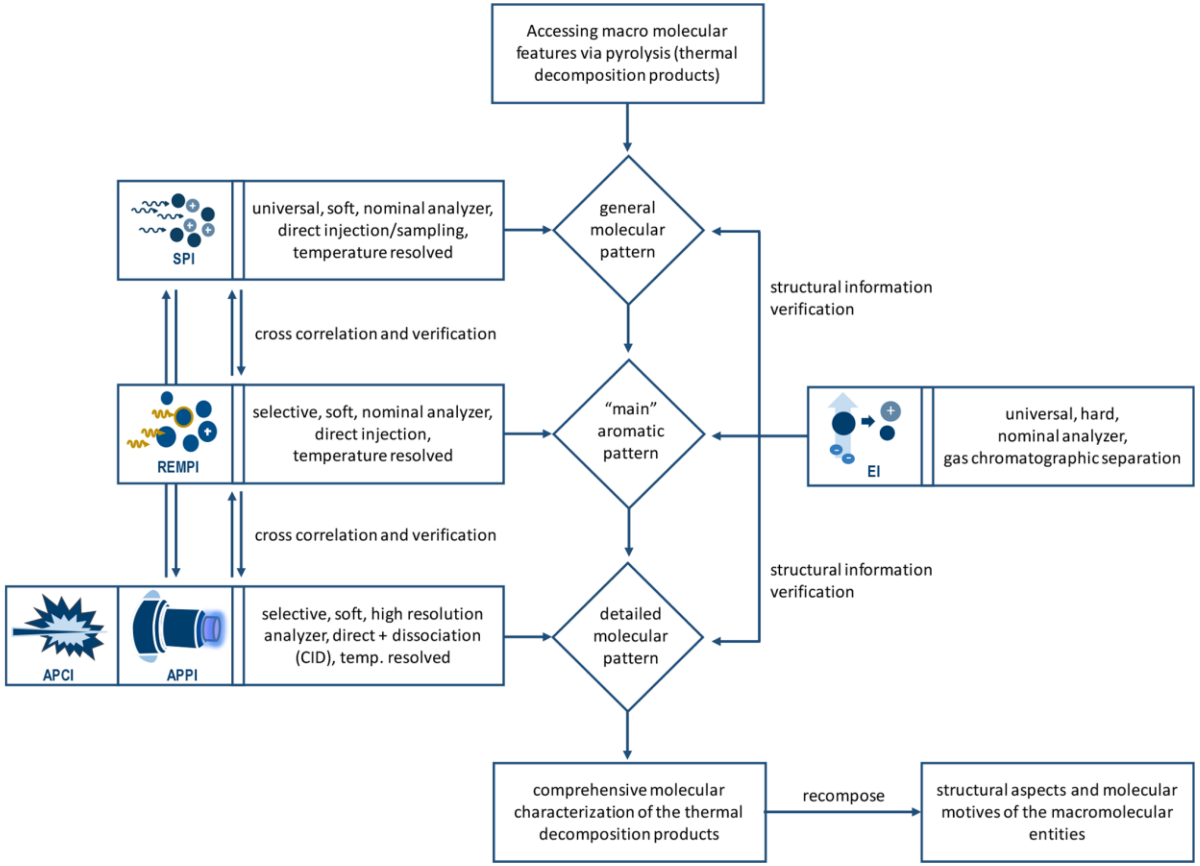
Asphaltenes – Study on the Combination of Information retrieved from Different Ionization Techniques





Rüger et al., *Energy and Fuels*, **2016**, 2699-2711

Asphaltenes – Study on the Combination of Information retrieved from Different Ionization Techniques



Accessing macro molecular features via pyrolysis (thermal decomposition products)

SPI: universal, soft, nominal analyzer, direct injection/sampling, temperature resolved → general molecular pattern

cross correlation and verification

REMPI: selective, soft, nominal analyzer, direct injection, temperature resolved → "main" aromatic pattern

EI: universal, hard, nominal analyzer, gas chromatographic separation

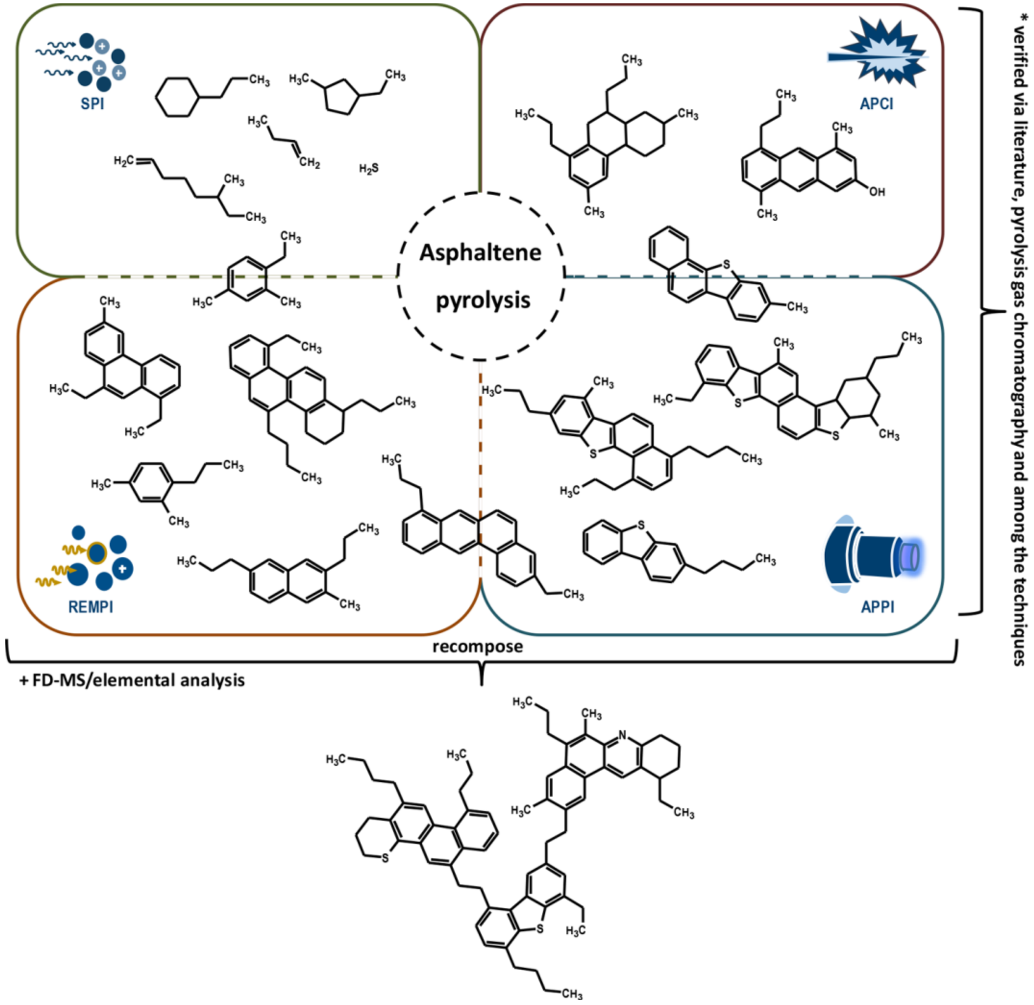
cross correlation and verification

APCI, APPI: selective, soft, high resolution analyzer, direct + dissociation (CID), temp. resolved → detailed molecular pattern

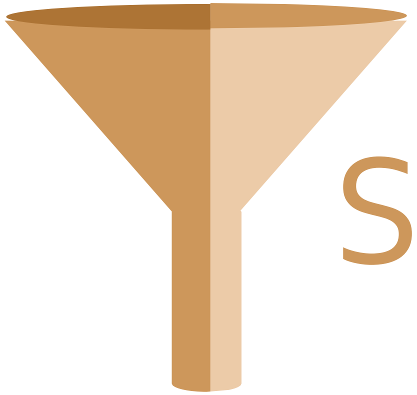
structural information verification

structural information verification

comprehensive molecular characterization of the thermal decomposition products → recompose → structural aspects and molecular motives of the macromolecular entities

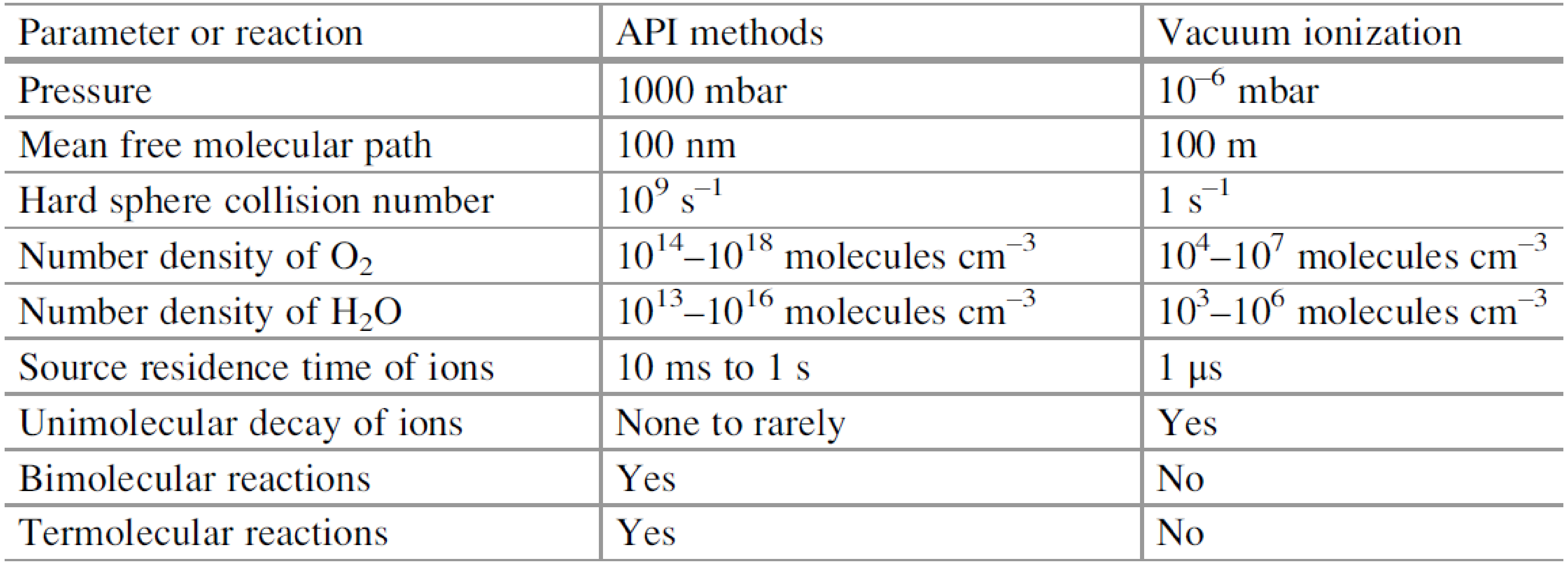


Rüger et al., *Energy and Fuels*, **2016**, 2699-2711



Summary

Atmospheric pressure versus vacuum ionization

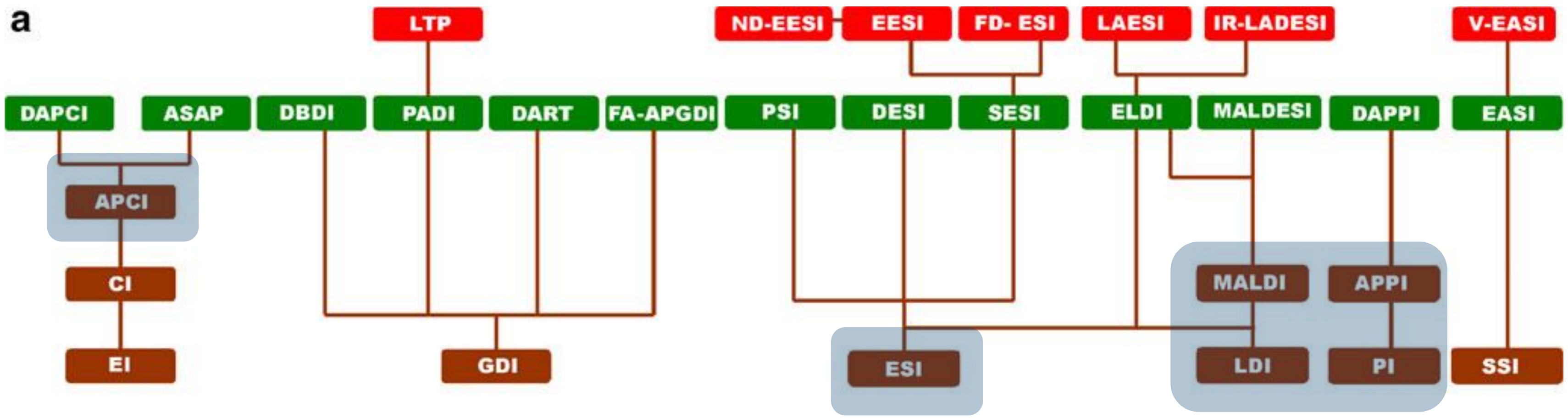


Parameter or reaction	API methods	Vacuum ionization
Pressure	1000 mbar	10^{-6} mbar
Mean free molecular path	100 nm	100 m
Hard sphere collision number	10^9 s^{-1}	1 s^{-1}
Number density of O_2	10^{14}–10^{18} molecules cm^{-3}	10^4–10^7 molecules cm^{-3}
Number density of H_2O	10^{13}–10^{16} molecules cm^{-3}	10^3–10^6 molecules cm^{-3}
Source residence time of ions	10 ms to 1 s	1 µs
Unimolecular decay of ions	None to rarely	Yes
Bimolecular reactions	Yes	No
Termolecular reactions	Yes	No

Typical conditions and occurrence of elementary processes in atmospheric pressure ionization and vacuum ionization techniques

Jürgen H- Gross, *Mass Spectrometry – A Textbook*, **2017**, Spinger, ISBN *978-3-319-54398-7*

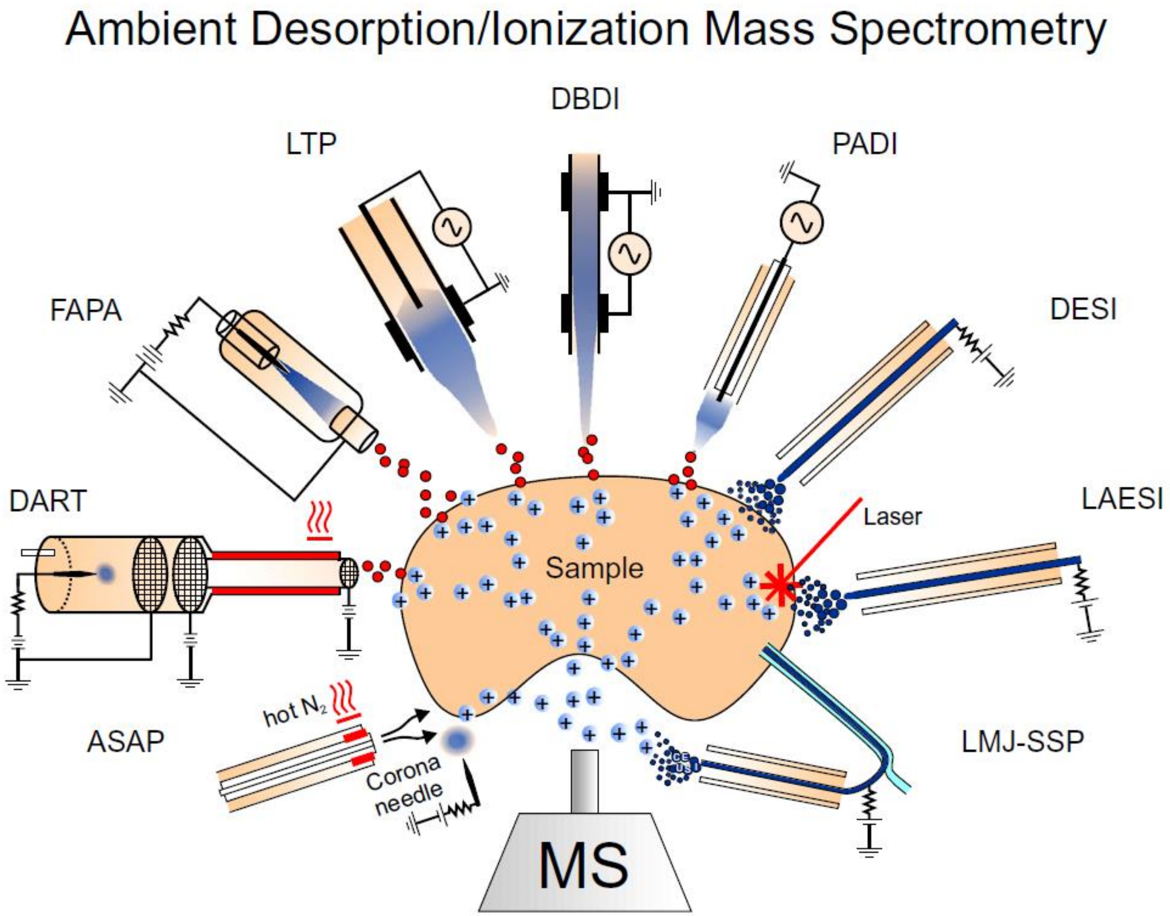
Ionization Concepts Frequently Found in Applied FT-ICR MS Studies



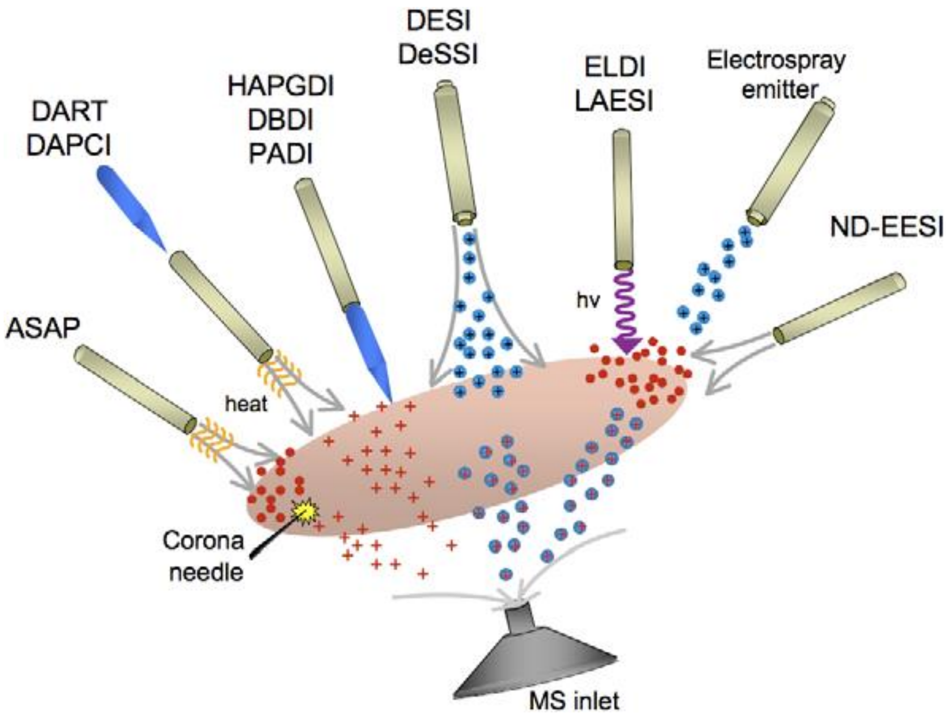
but many other research grade or customized solutions available, *e.g.*, laser ionization concepts, numerous variations of desorption/spray solutions

Alberici et al., *Anal Bionanal Chem*, **2010**, 398:265–294

Ionization Concepts Found in Applied FT-ICR MS Studies



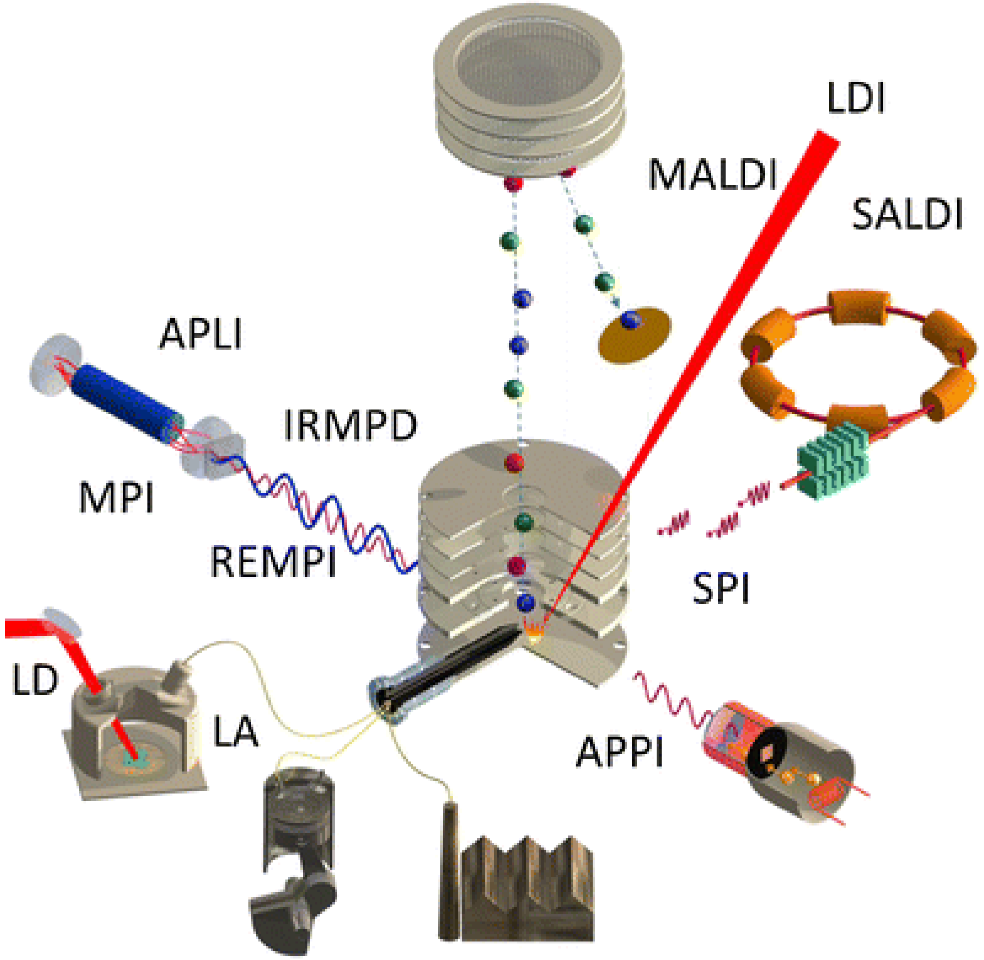
Shelley et al., *Anal Bioanal Chem*, **2018**, 410:4061–4076



Venter et al., *Trends in Analytical Chemistry,* Vol. 27, No. 4, **2008**

Summary

The Potential of Light Based Ionization Techniques



Zimmermann et al., *Anal Bioanal Chem*, **2013**, 6901–6905

Take Home Messages

Summary

- **choosing the right ionization scheme** for the given research questions is an early and highly important step
- EI, FD/FI and SPI as only true universal ionization techniques but FT-ICR MS dominated by atmospheric pressure ionization concepts and laser desorption ionization
- common atmospheric pressure techniques are not universal and strongly favor certain chemical functionalities
    - **selectivity** has always taken into account analyzing complex mixtures → What can I “see” in theory?
    - ionization might suffer from strong charge competition – **matrix effects** → What can I “see” in my real-world complex sample?
    - **sample preparation** and ionization **parameters** have significant effect on spectral pattern and behavior

      → Am I doing everything “correctly” for my given problem?
- **hyphenation techniques** (gas/liquid chromatography, thermal analysis) for pre-separation overcoming some API limitations (ion mobility occurs after ionization process and does not help with ionization aspects!)
- **combination** of the information from several **ionization schemes** can be beneficial for complex mixtures analysis

Acknowledgment

Thank you for the kind attention!

christopher.rueger@uni-rostock.de

Questions and Discussion!?