22èmes rencontres du club jeune SFSM - 20 au 24 mars 2017 - Trélon

Ambient Sampling/Ionization Mass Spectrometry

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INSTITUT DES SCIENCES ANALYTIQUES

Lyon 1

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Overview

I- Introduction

II- ElectroSpray Ionization-based ambient ionization techniques
- II-1) Direct Desorption : DESI, EASI
- II-2) Sampling and Transferring through a gas stream: ND-EESI, FD-ESI
- II-3) Laser Desorption/ablation : ELDI, MALDESI, LAESI, LIAD-ESI
- II-4) Thermal Desorption : ESA-Py, TPD/ESI

III- Atmospheric Pressure Chemical Ionization-based ambient ionization techniques
- III-1) Direct Desorption : DAPCI, DCBI, DBDI, LTP, FAPA
- III-2) Laser Desorption/ablation : LD-APCI, IR-LAMICI, LA-FAPA
- III-3) Thermal Desorption : DART, ASAP

IV- Atmospheric Pressure Photo-Ionization-based ambient ionization techniques : DAPPI

V- Comparaison of techniques

VI- Conclusions

I- Introduction

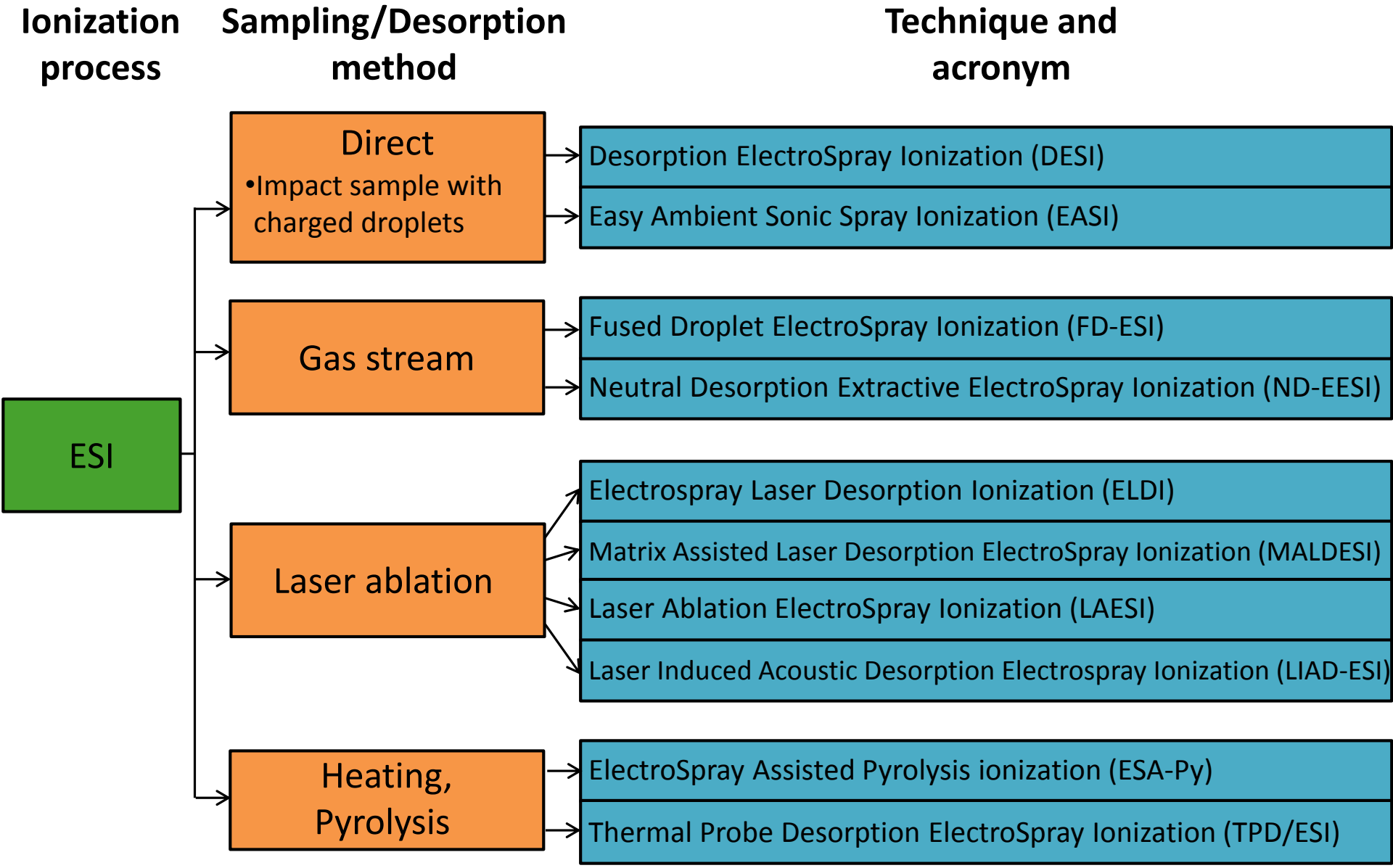
- Ambient ionization mass spectrometry allows the rapid analysis of samples or objects in their native state in the open environment with no or little prior preparation.

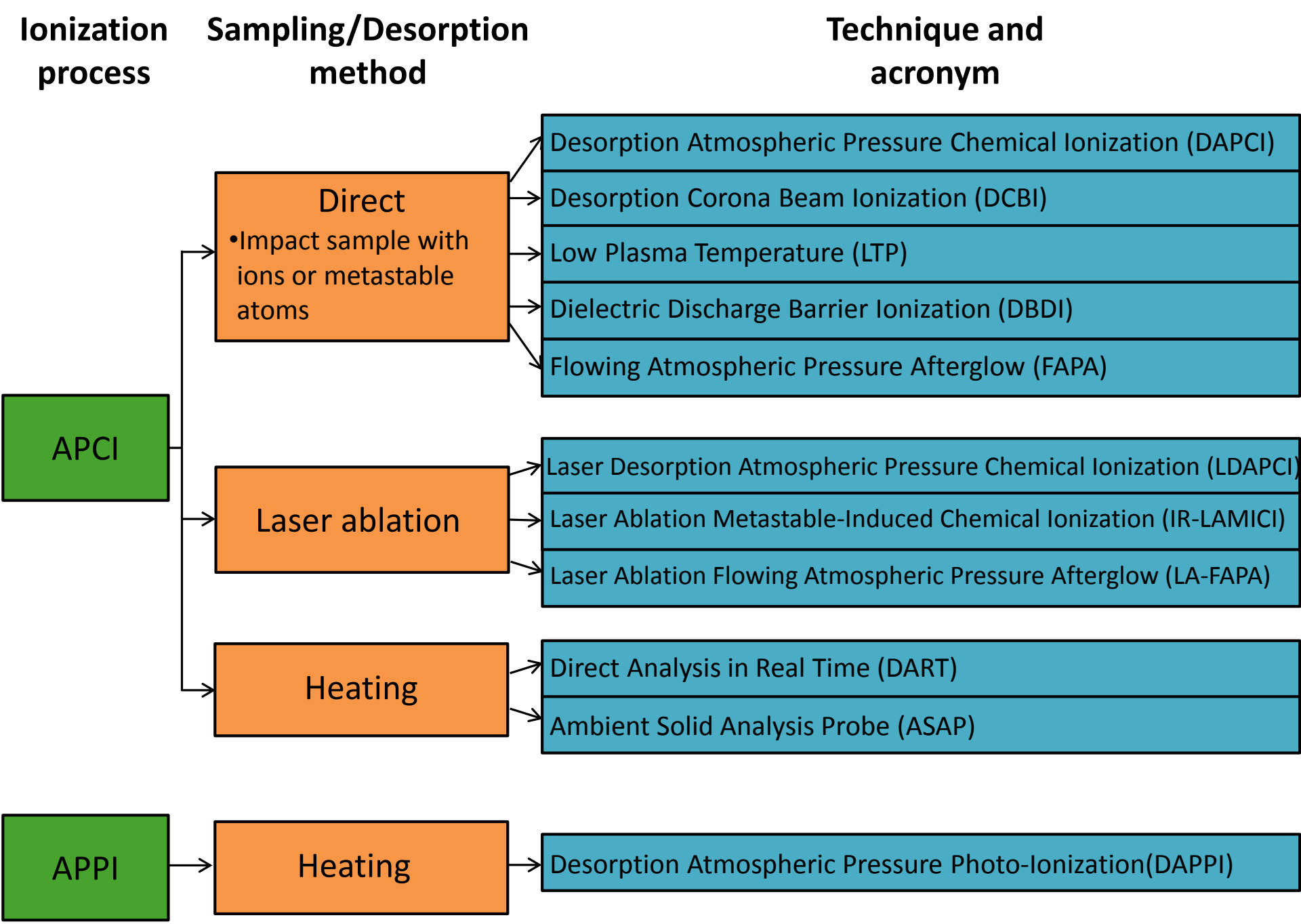
- Ambient ionization techniques combine a **desorption process** of the analytes, with their **ionization**. Electrospray, atmospheric pressure chemical ionization and photo-ionization are the most used techniques for the ionization in ambient MS.

- These techniques allow the analysis of a wide range of substances (polar/non-volatile and non-polar/volatile) from various surfaces and matrices.
Broad application areas, both qualitative and quantitative in nature, including pharmaceutical analysis, process chemistry, biological imaging, in vivo analysis, proteomics, metobolomics, forensics and explosives detection.

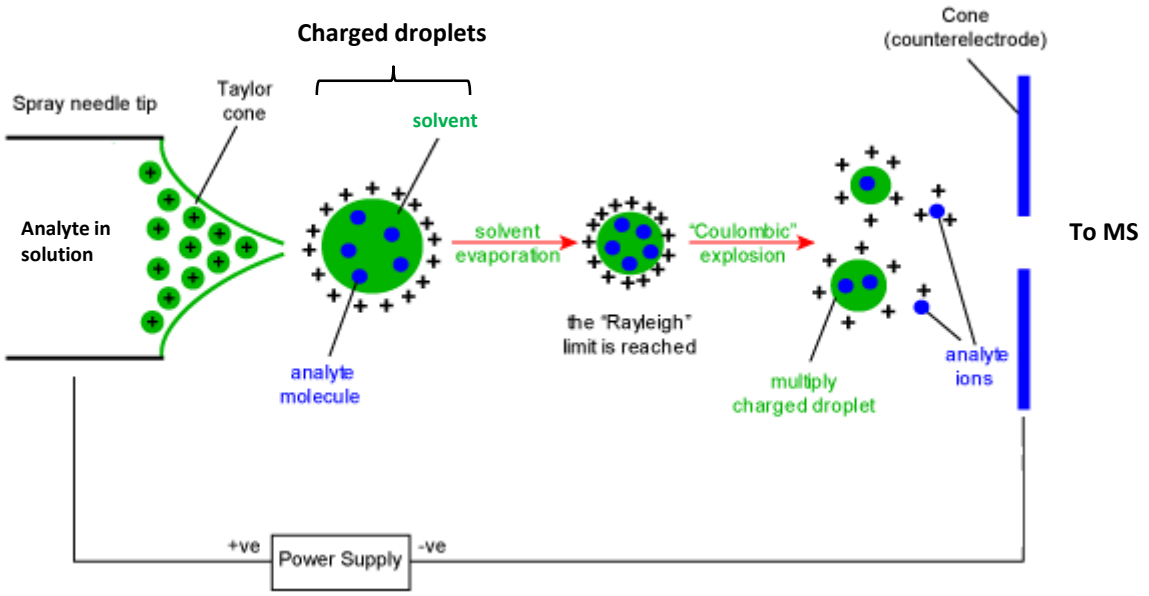
I- Introduction

-Since the early 2000's, many ambient ionization techniques have been developed (~ 30 ambient ionization sources are reported in the literature) due to the large number of possible combinations of desorption and ionization processes, giving rise to the proliferation of many acronyms always more complicated.


Ionization process
Sampling/Desorption method
Technique and acronym
ESI
Direct
•Impact sample with charged droplets
Desorption ElectroSpray Ionization (DESI)
Easy Ambient Sonic Spray Ionization (EASI)
Gas stream
Fused Droplet ElectroSpray Ionization (FD-ESI)
Neutral Desorption Extractive ElectroSpray Ionization (ND-EESI)
Laser ablation
Electrospray Laser Desorption Ionization (ELDI)
Matrix Assisted Laser Desorption ElectroSpray Ionization (MALDESI)
Laser Ablation ElectroSpray Ionization (LAESI)
Laser Induced Acoustic Desorption Electrospray Ionization (LIAD-ESI)
Heating, Pyrolysis
ElectroSpray Assisted Pyrolysis ionization (ESA-Py)
Thermal Probe Desorption ElectroSpray Ionization (TPD/ESI)


Ionization process
Sampling/Desorption method
Technique and acronym
APCI
APPI
Direct
•Impact sample with ions or metastable atoms
Laser ablation
Heating
Heating
Desorption Atmospheric Pressure Chemical Ionization (DAPCI)
Desorption Corona Beam Ionization (DCBI)
Low Plasma Temperature (LTP)
Dielectric Discharge Barrier Ionization (DBDI)
Flowing Atmospheric Pressure Afterglow (FAPA)
Laser Desorption Atmospheric Pressure Chemical Ionization (LDAPCI)
Laser Ablation Metastable-Induced Chemical Ionization (IR-LAMICI)
Laser Ablation Flowing Atmospheric Pressure Afterglow (LA-FAPA)
Direct Analysis in Real Time (DART)
Ambient Solid Analysis Probe (ASAP)
Desorption Atmospheric Pressure Photo-Ionization(DAPPI)

II- ESI-based ambient ionization techniques



In ambient ionization techniques using this mode of ionization, the **solvent charged droplets** formed by ESI allow the **post-ionization** of the desorbed analytes.

- Direct desorption/ionization
- Two-step ionization: desorption/sampling first and then contact with the ESI plume

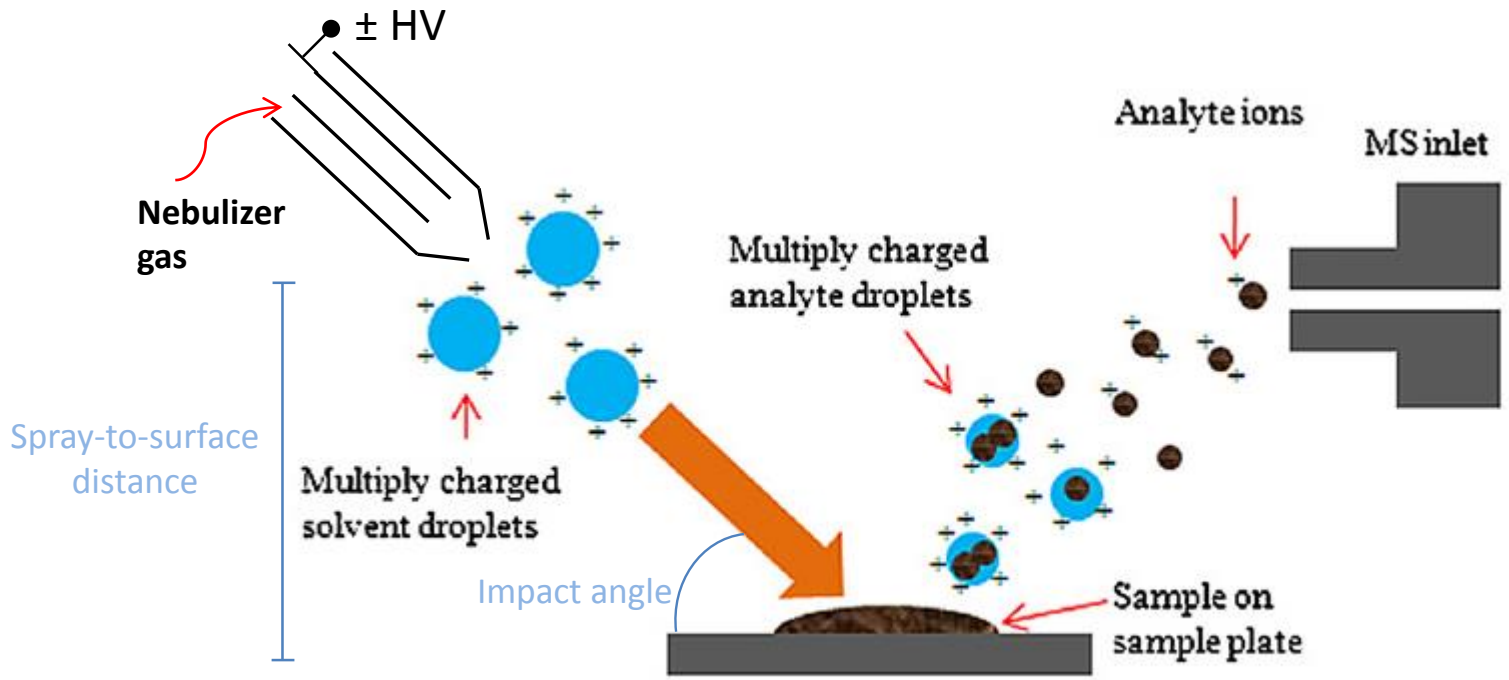
Samples can be gaseous, liquid or solid. The use of ESI for the post-ionization produces singly and multiply charged ions, which allows analysis of small species as well as biological macromolecules.

II-1) Direct Desorption

Analytes are directly desorbed from the surface of the sample by the ionization agent

Desorption ElectroSpray Ionization (DESI)

Science 2004, 306, 471–473

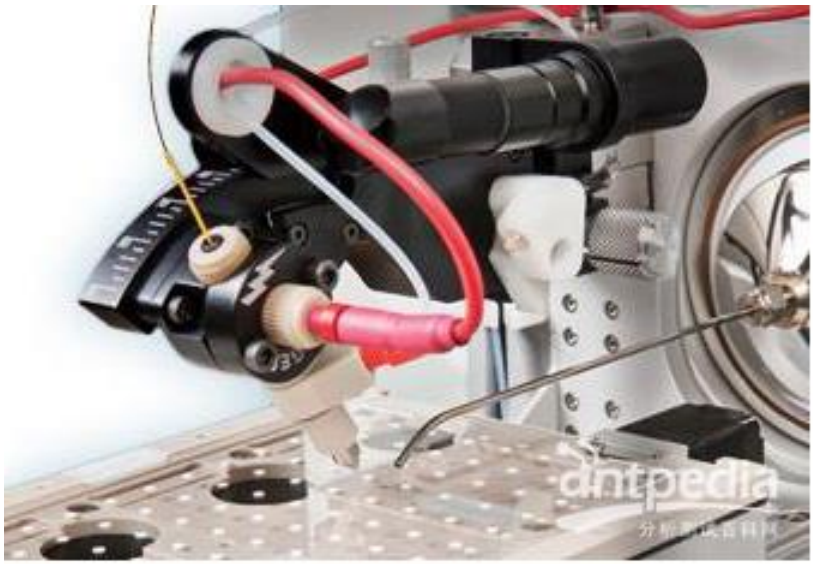


- Electrospray dissolves/extracts analytes on the surface: « droplet pick-up ».
- Secondary droplets are transported into inlet.
- Classical evaporation/fission of analyte droplets.

II-1) Direct Desorption

Desorption ElectroSpray Ionization (DESI)

- Instrumentation and operating parameters:



Parameter	Range of settings	
Solvent flow rate	3–5 µl.min^{-1}	Spot size
Nebulizer gas pressure	8–12 bar	
Spray voltage	2–6 kV	
Spray-to-surface distance	1–5 mm	
Spray-to-surface angle	30–70°	
Surface-to-MS inlet	1–3 mm	
Temperature of desolvation capillary	200–300°C	

Surface = glass, PTFE, PMMA, TLC paper… → importance of the wettability

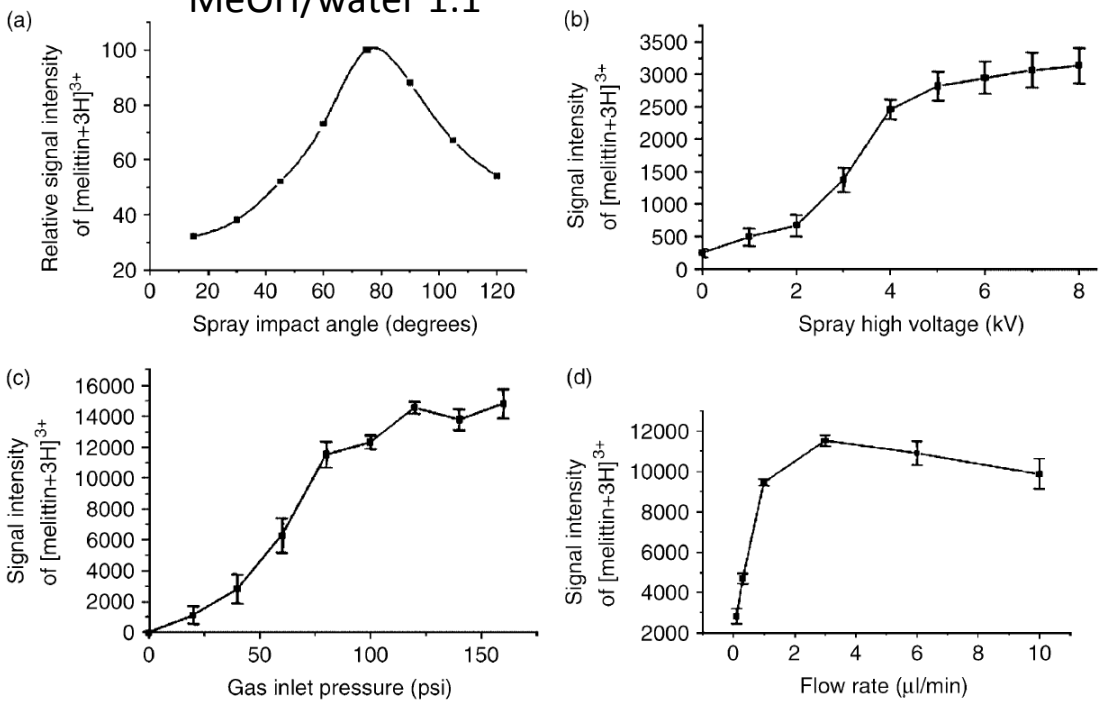
Solvent composition = organic solvent (EtOH, MeOH, ACN)/water ± acid or base; in some cases $CHCl_3$/MeOH or ACN; + surfactant or specific reagent in ReactiveDESI → needs to desolve analytes, spray stability issues

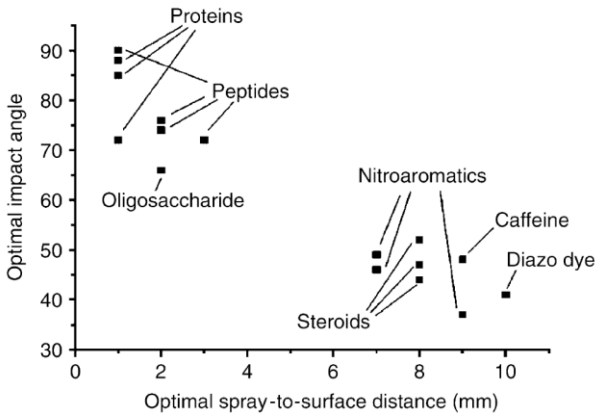
II-1) Direct Desorption

Desorption ElectroSpray Ionization (DESI)

- Instrumentation and operating parameters:

MeOH/water 1:1





J. Mass. Spectrom. 2005, 40, 1261–1275

Spray size	~ 1.24 mm	~ 1.38 mm	~ 1.59 mm	~ 2.01 mm
				
Gas Pressure:	150 psi	150 psi	200 psi	150 psi
Spray-to-surface distance:	5 mm	5 mm	5 mm	3 mm
H_2O :	20 %	50 %	50 %	20 %

Spot size ↗ : signal ↗
but spatial resolution ↘

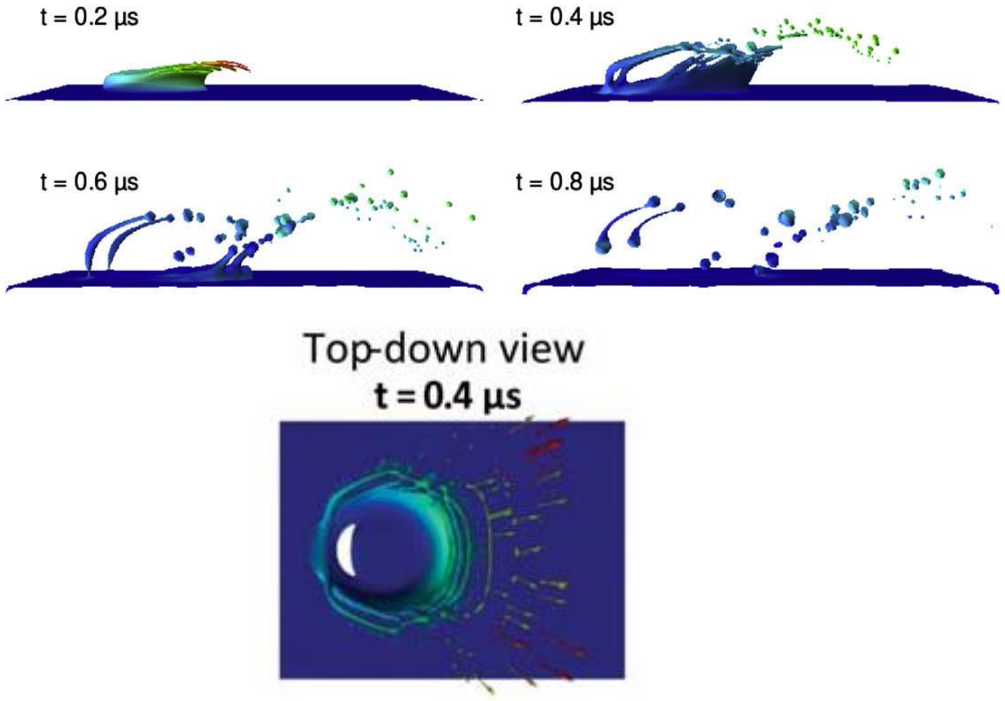
II-1) Direct Desorption

Desorption ElectroSpray Ionization (DESI)

- Characterization:

Chemical Physics Letters 2008, 464, 1–8

Multiphase computational fluid dynamics simulations



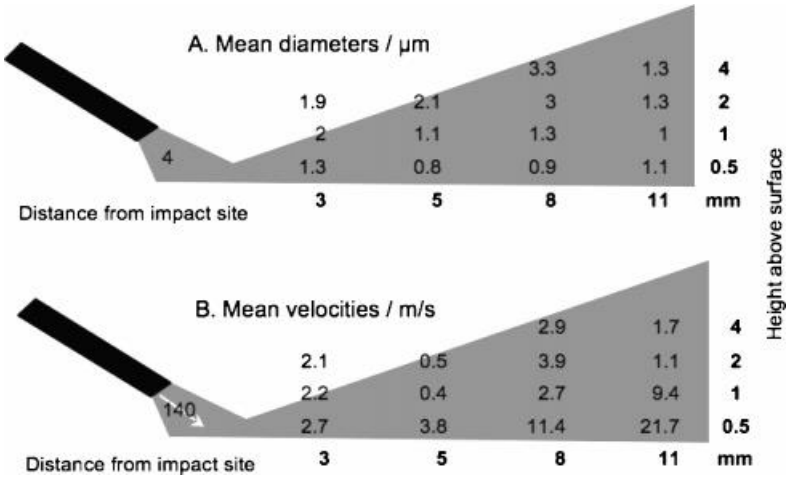
→ Surface-to-MS inlet angle important = 10-20°

Anal. Chem. 1999, 71, 4111-4113

Phase Doppler Anemometry

MeOH/water 1:1

PTFE surface



Primary droplets size: 4 µm
Primary droplets velocity: 140 m/s

Secondary droplets size: ~ 1 µm
Secondary droplets velocity: 2 - 20 m/s

II-1) Direct Desorption

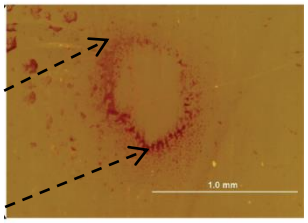
Desorption ElectroSpray Ionization (DESI)

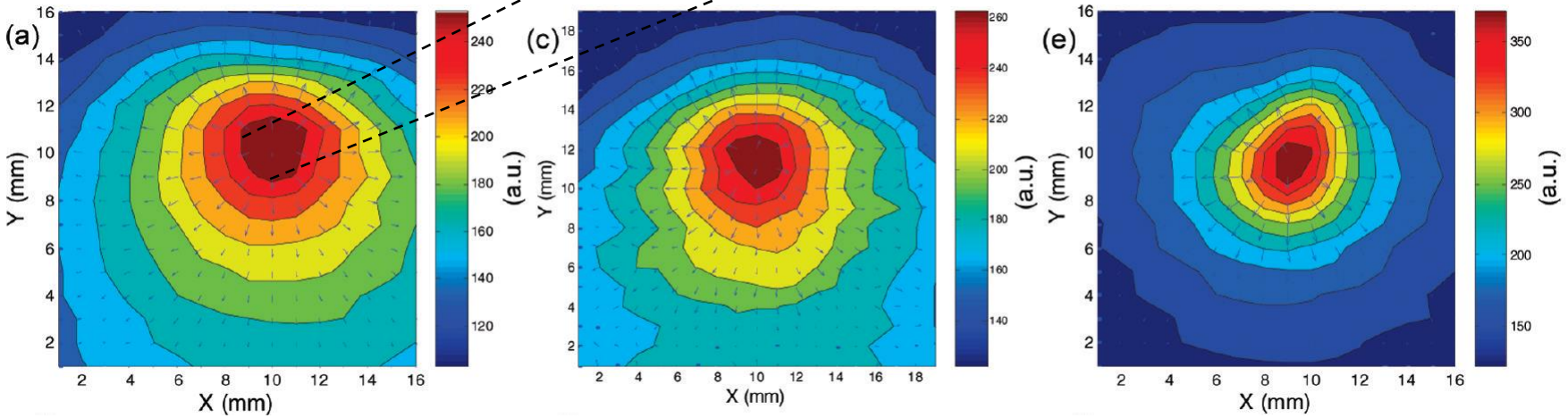
- Characterization: *J. Phys. Chem. C, 2010, 114, 5331-5337*

Static charge detection measurements

MeOH/water 1:1

PTFE surface





(a) 55° spray angle, 130 psi sheath gas pressure, and 2 μL/min flow rate;
(c) 30° spray angle, 100 psi sheath gas pressure, and 2 μL/min flow rate;
(e) 55° spray angle, 100 psi sheath gas pressure, and 1 μL/min flow rate

→Highest charge density located in the small desorption area (~1mm²)

II-1) Direct Desorption

Desorption ElectroSpray Ionization (DESI)

- Mechanisms of ion formation:

- For large molecules : mostly droplet «pick-up»

→ Large charged solvent droplets making contact with the surface, dissolving the analyte and then producing ions through ESI like mechanisms (fission/evaporation)

$$[M + mS + nH]^{n+}_{(l)} \rightarrow [M + mS + nH]^{n+}_{(g)} \rightarrow [M + nH]^{n+}_{(g)}$$

Solvated ion in liquid phase — Solvated ion in gas phase — Ion in gas phase

- For low molecular weight molecules: Droplet «pick-up» can occur but other mechanisms are proposed:

→ Direct charge transfer between the ionized solvent and the solid analyte at the surface which is removed through static repulsion or sputtering into the gas phase

$$S^+_{(aq)} + A_{(s)} \rightarrow S_{(aq)} + A^+_{(s)} \rightarrow A^+_{(g)}$$

→ Neutral volatization i.e. volatile analyte molecules leaving the surface, interacting with the spray itself, being ionized via charge transfer

$$S^+_{(g)} + A_{(g)} \rightarrow S_{(g)} + A^+_{(g)}$$

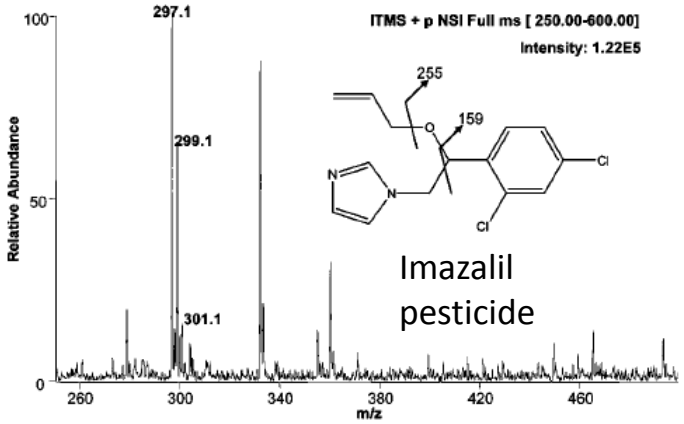
II-1) Direct Desorption

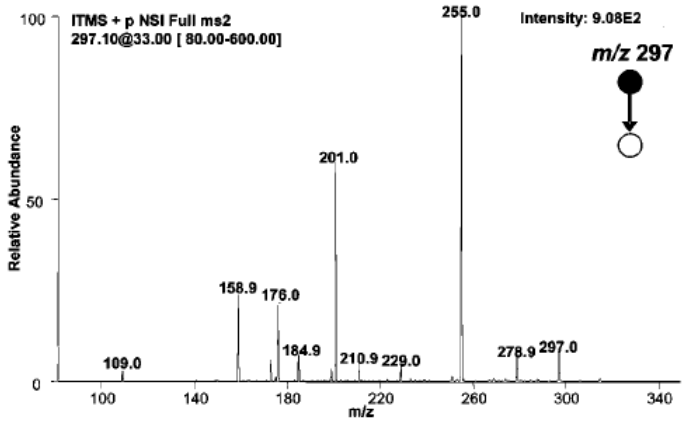
Desorption ElectroSpray Ionization (DESI)

- Applications:

Testing in food industry

Anal. Chem. 2009, 81, 820–829

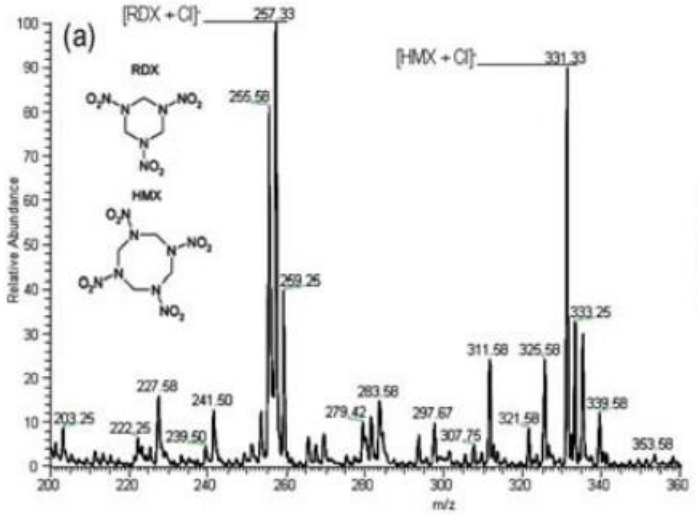




DESI-MS(/MS) on lemon peel

Homeland security

Analyst, 2010, 135, 1953–1960



DESI negative ion MS of a transfer wipe used to concentrate 33.3 ng of explosives spotted over a 10 cm^2 area onto a rough plastic surface

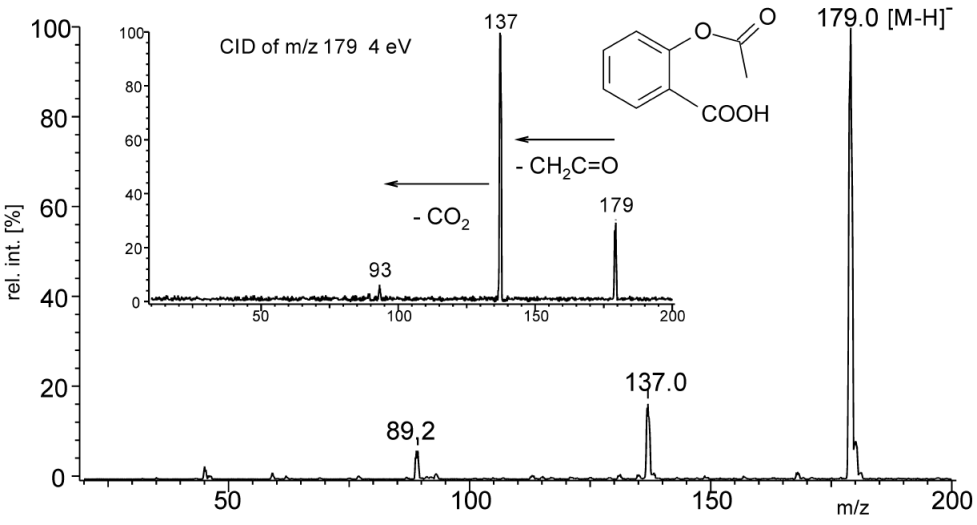
II-1) Direct Desorption

Desorption ElectroSpray Ionization (DESI)

- Applications:

Pharmaceutical industry

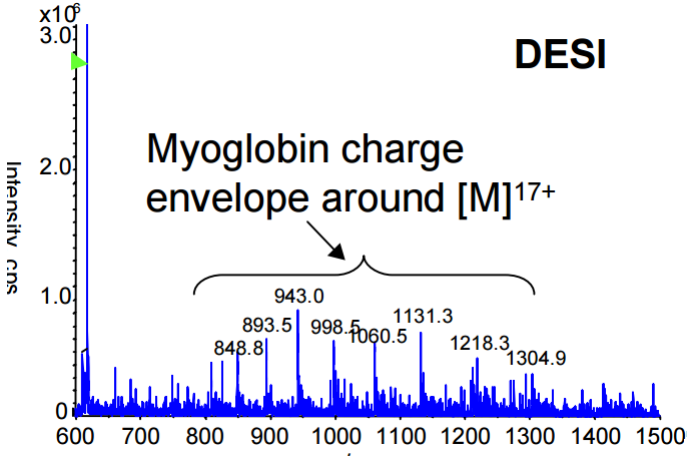
Anal. Chem. 2005; 77, 6915



Negative DESI-MS(/MS) on Aspirin tablet

Proteomics

Anal Chem. 2011, 86, 9603–9611



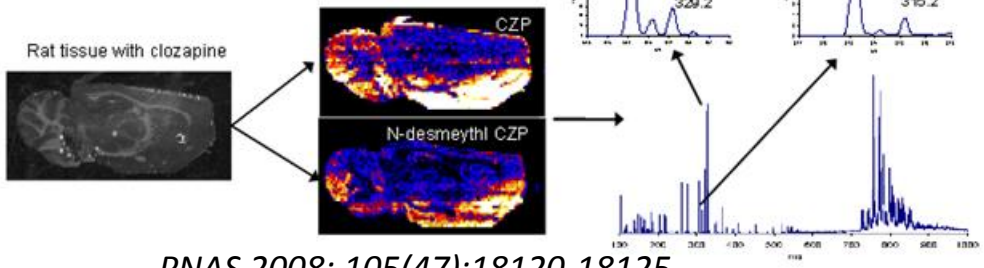
Positive DESI MS of myoglogin spotted onto a glass plate

II-1) Direct Desorption

Desorption ElectroSpray Ionization (DESI)

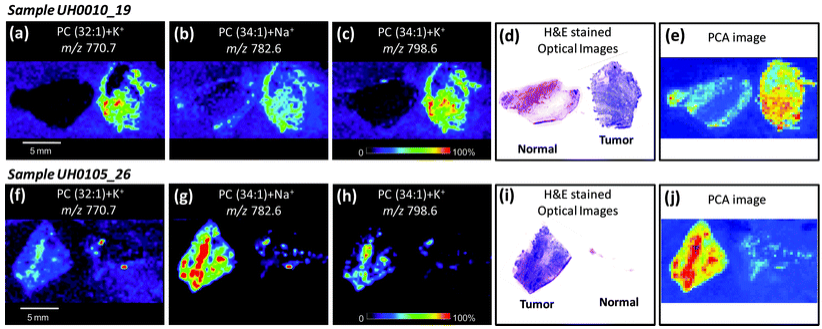
- Imaging: spatial resolution 100 µm

Drug mapping



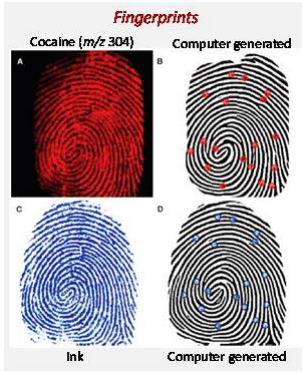
PNAS 2008; 105(47):18120-18125

Tumor Diagnosis



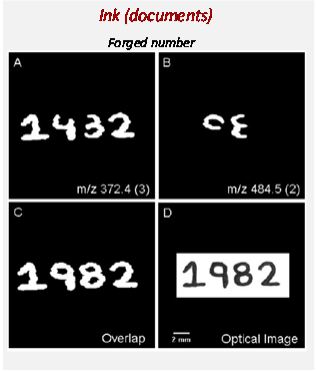
Chemistry-A Eur. J. 2010; 17(10), 2897- 2902

Chemical fingerprint



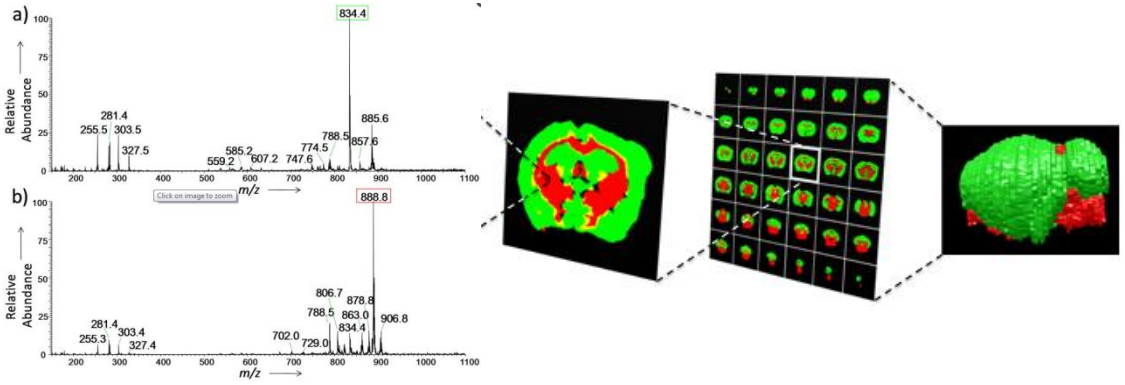
Science, 2008 , 321, 805 -805

Analysis of inks



Analyst 2007;132(5):461-467

3D molecular images



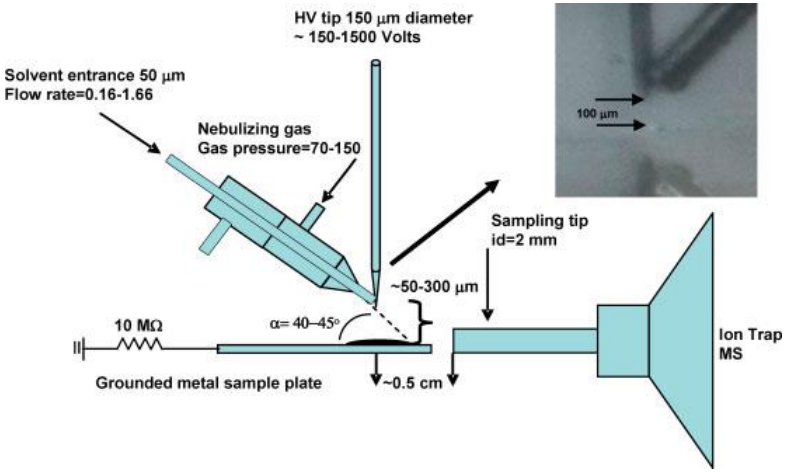
Angew Chem Int Ed Engl. 2010 ; 49(5): 873–876

II-1) Direct Desorption

Techniques closely related to DESI

Electrode-Assisted DESI (EADESI)

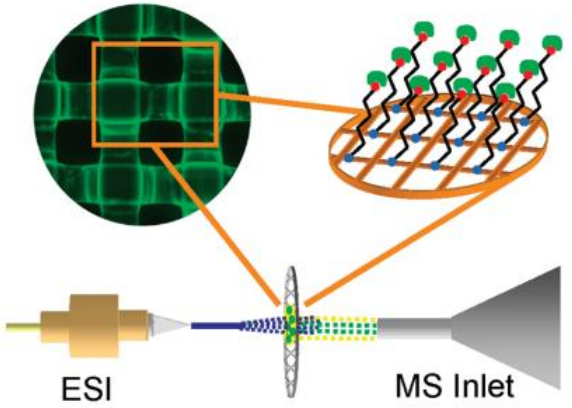
J. Mass. Spectrom. 2010, 45, 1203–1211



Sharp-edge tip subjected to a high applied voltage

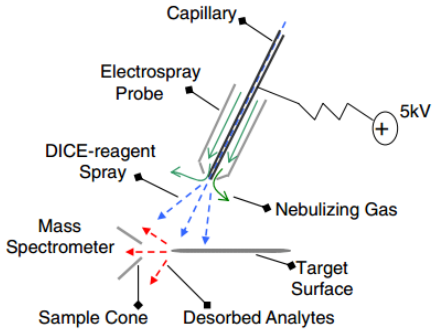
Transmission mode DESI (TM-DESI)

Anal. Chem. 2010, 82, 16–18



Passing ESI plume through a sample pre-deposited on a mesh substrate

Desorption Ionization by Charge Exchange (DICE)



J Am Soc Mass Spectrom 2010, 21, 1554 –1560

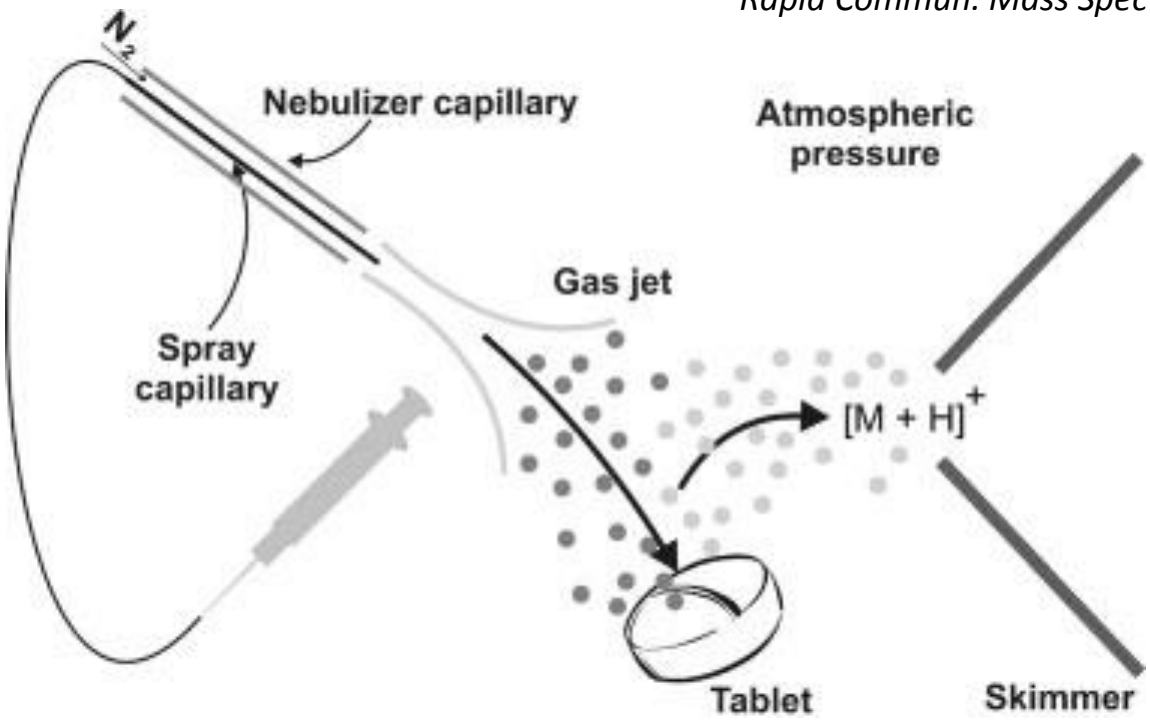
Use toluene as solvent for the spray to ionize low polarity analytes by charge exchange

II-1) Direct Desorption

Easy Ambient Sonic spray Ionization (EASI)

previously referred to Desorption Sonic Spray Ionization (DeSSI)

Rapid Commun. Mass Spectrom. 2006, 20, 2901–2905



- Neutral (super)sonic spray impinges on surface.
- Spray dissolves analytes.
- Secondary droplets are transported into inlet.
- Ionization via non-statistical charge distribution.

II-1) Direct Desorption

Easy Ambient Sonic spray Ionization (EASI)

- Instrumentation and operating parameters:

Nebulizer gas pressure = 200 psi (~15 bar)
Solvent mixture = MeOH/water 1:1 + 0.1 % formic acid
No heating and voltage are required

- Mechanisms of ion formation:

* High-velocity sprayer forms small droplets.
* Ionization occurs due to statistical imbalanced distribution between cations and anions in the spray.
* Then, desorption and ionization of the analytes from the surface follow similar mechanisms as DESI.

→ No electrochemical or oxidation processes, low charge density of droplets

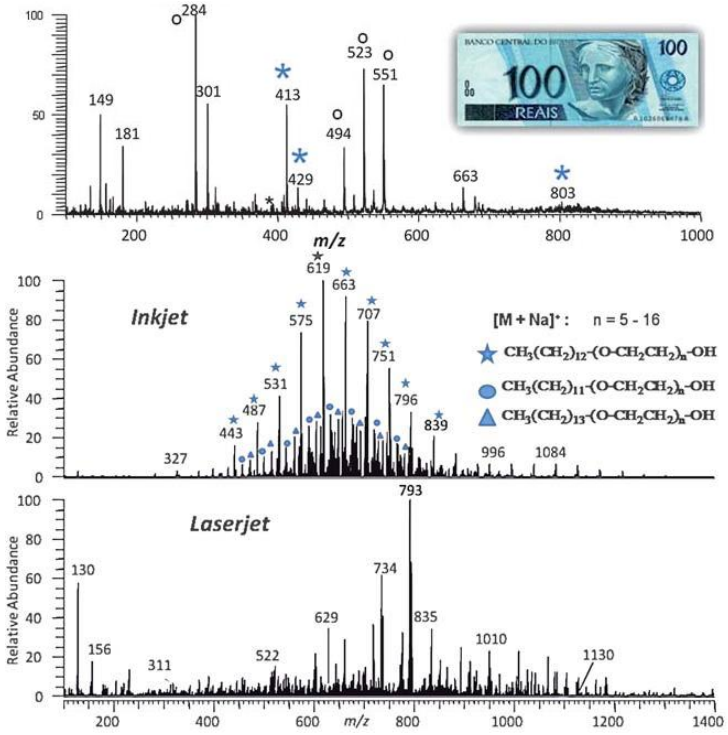
II-1) Direct Desorption

Easy Ambient Sonic spray Ionization (EASI)

- Applications:

Forensic

Analyst, 2010, 135, 2533–2539

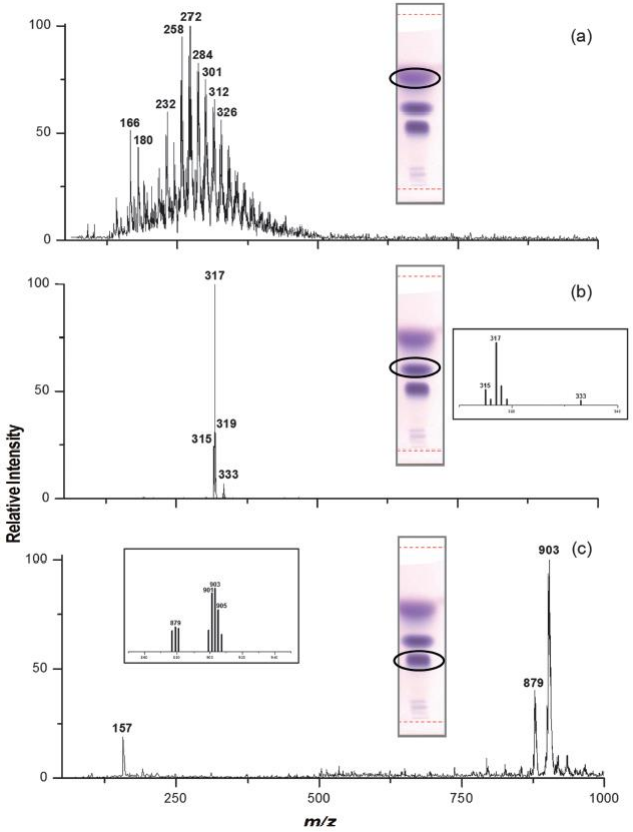


EASI(+) MS spectra of (a) authentic Brazilian R$ banknote and counterfeit banknotes made by using (b) inkjet and (c) laserjet printers

Biodiesels analysis

Analyst, 2009, 134, 1652–1657

Coupled with TLC separation

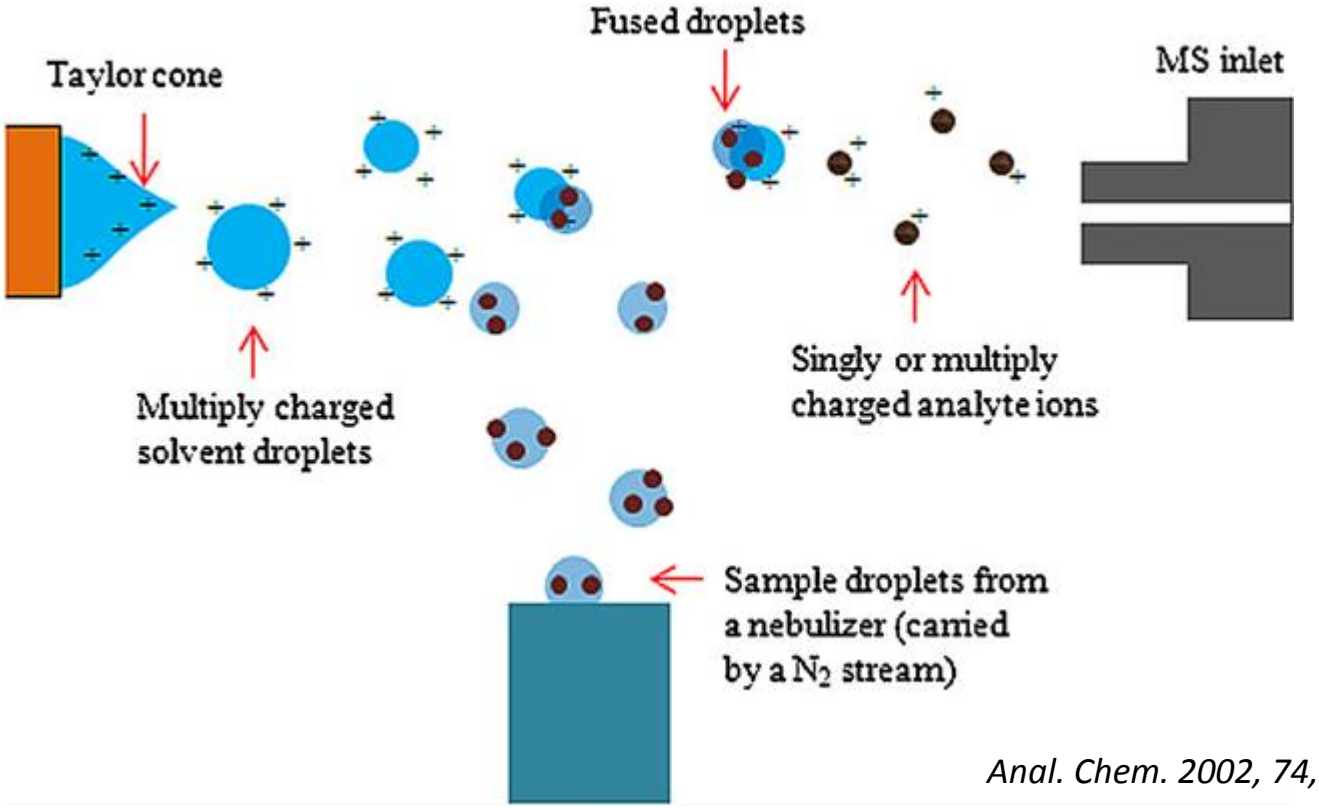


On-spot HPTLC-EASI-MS of: (a) petrodiesel; (b) soybean biodiesel; and (c) soybean oil

II-2) Sampling/Transferring through a gas stream

Gas is used to transport the analytes and put them in contact with the charged droplets

Fused Droplet ElectroSpray Ionization (FD-ESI)



Anal. Chem. 2002, 74, 2465-2469

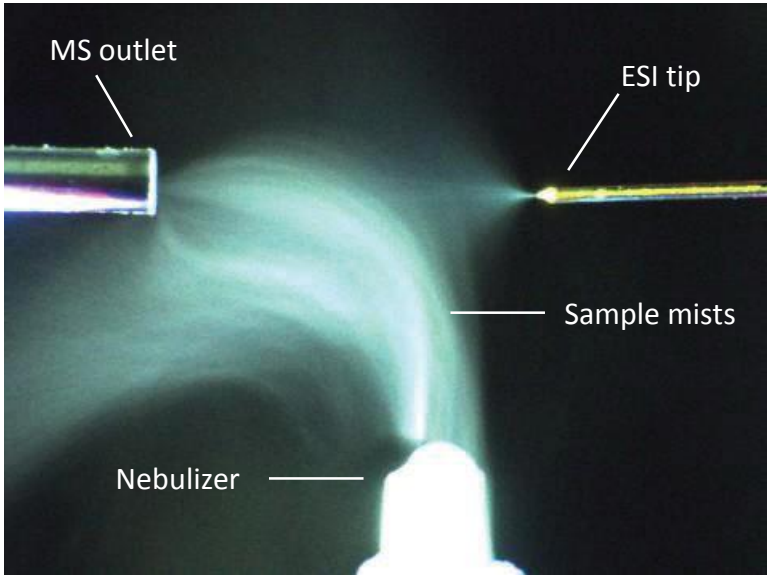
- Analyte droplets generated from a nebulizer.
- Analyte droplets are delivered in N_2 gas stream to the ESI plume .
- Analyte droplets fusing with the charged solvent droplets.

II-2) Sampling/Transferring through a gas stream

Fused Droplet ElectroSpray Ionization (FD-ESI)

- Characteristics:

  For liquid samples
  Ultrasonic, pneumatic or piezoelectric nebulizer (~1µm neutral droplets)
  Analyte solution in « native » conditions
  ESI solvent mixture adapted to the analyte polarity (mainly MeOH)



- Mechanisms of ion formation:

  * Fusion of analyte droplets with ESI droplet.
  * Analytes are selectively extracted into the charged droplets.
    → Low salts solubility in MeOH → FD-ESI has a higher salt tolerance than ESI
  * Charge transfer between the analytes and the charged solvent.
  * Then, classical evaporation/fission of analyte droplets.

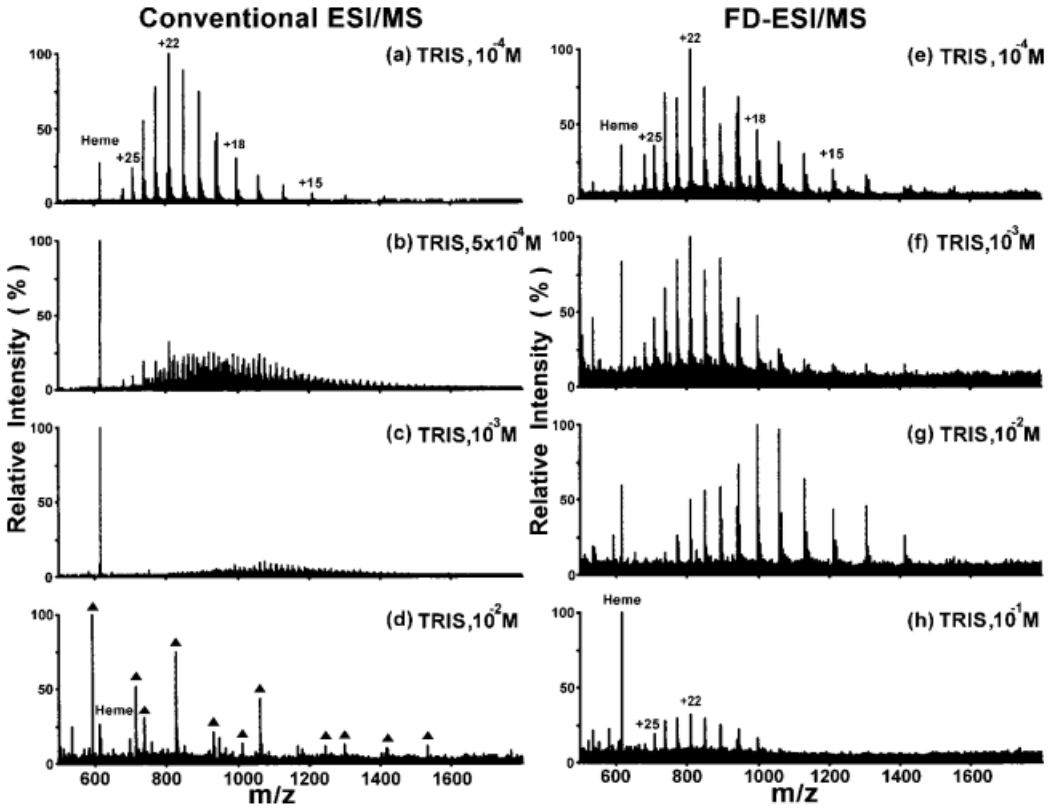
II-2) Sampling/Transferring through a gas stream

Fused Droplet ElectroSpray Ionization (FD-ESI)

- Application:

Proteomics

J. Proteome Res., 2005, 4 (2), pp 606–612



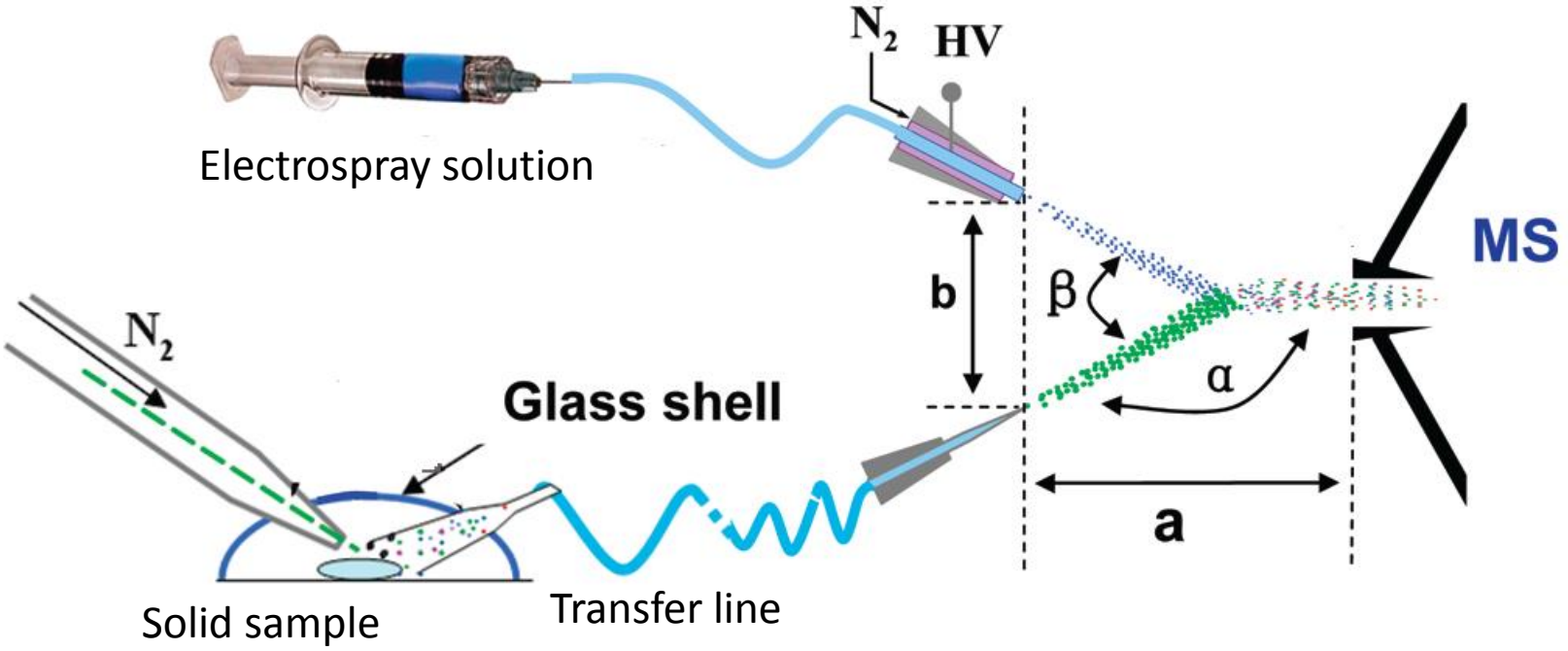
Conventional ESI (left side, a-d) and FD-ESI (right side, e-h) mass spectra of myoglobin/TRIS solutions.

→ No interference from salts using FD-ESI

II-2) Sampling/Transferring through a gas stream

Neutral Desorption Extractive ElectroSpray Ionization (ND-EESI)

J. Mass Spectrom. 2007; 42: 1123–1135



- Analyte desorption by N_2 stream.
- Desorbed neutrals are transported to the ESI plume.
- Analytes merge with the charged droplets for post-ionization by charge transfer.

II-2) Sampling/Transferring through a gas stream

Neutral Desorption Extractive ElectroSpray Ionization (ND-EESI)

- Characteristics:

  For solid samples

  Unheated gas stream (20°C)

  Gas flow of 200 mL/min

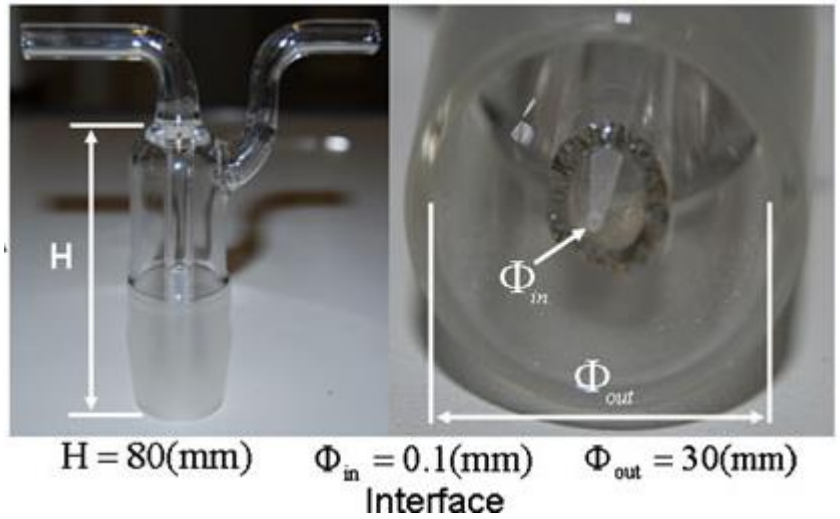
  Gas-to-surface angle = 30-90°

  Glass enclosure to cover the sample

  Transfer line length up to 10 m

  Classical ESI solvent mixture; + specific reagent for ion/molecule reactions

  Angle between the ESI plume and the neutral analyte plume β = 50-60°



- Mechanisms of ion formation:

  Sames mechanisms as FD-ESI;

  Difficulty to desorb large molecules with an unheated gas stream: limit < *m/z* 500

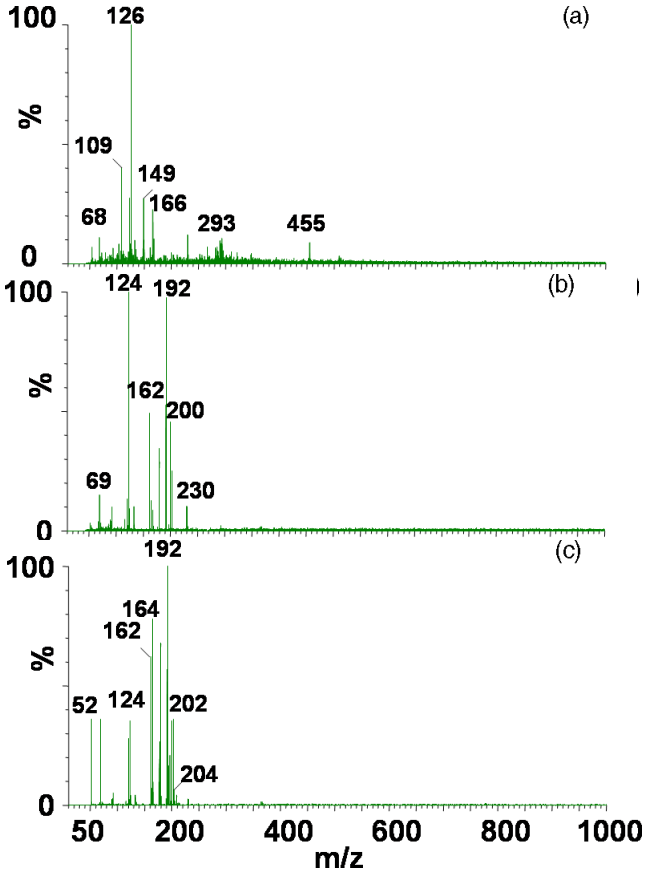
II-2) Sampling/Transferring through a gas stream

Neutral Desorption Extractive ElectroSpray Ionization (ND-EESI)

- Applications:

Food

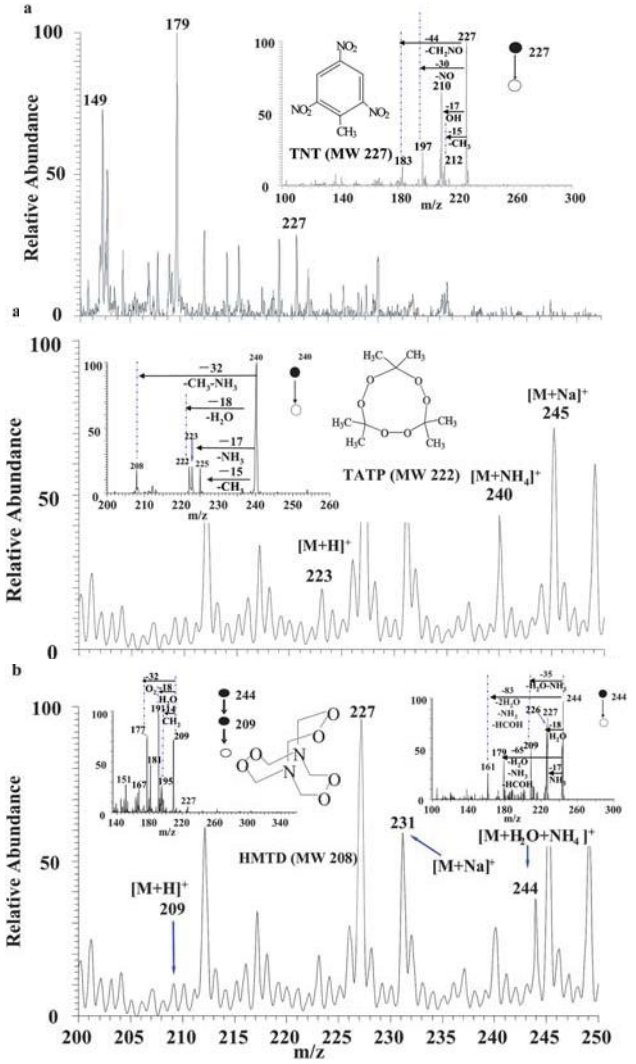
J. Mass Spectrom. 2007; 42: 1123–1135



ND-EESI spectra of frozen beef samples: (a) without exposure to room temperature; (b) after exposure to room temperature for 1 day; (c) after exposure to room temperature for 2 days.

Homeland Security

Analyst, 2010, 135, 779–788



LOD 5pg

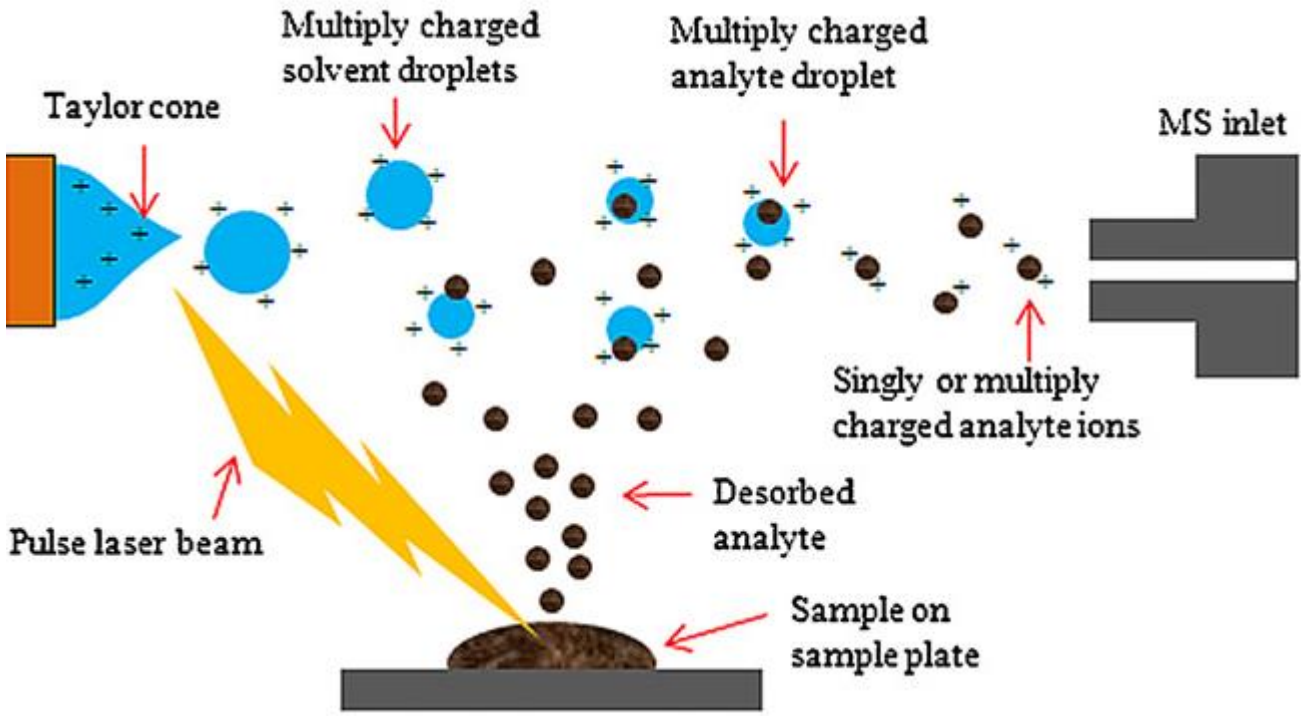
ND-EESI spectra of explosives on human skin

II-3) Laser Desorption/ablation

Analytes are desorbed from the surface by a laser pulse

Electrospray Laser Desorption Ionization (ELDI)

Rapid Commun. Mass Spectrom. 2005; 19: 3701–3704



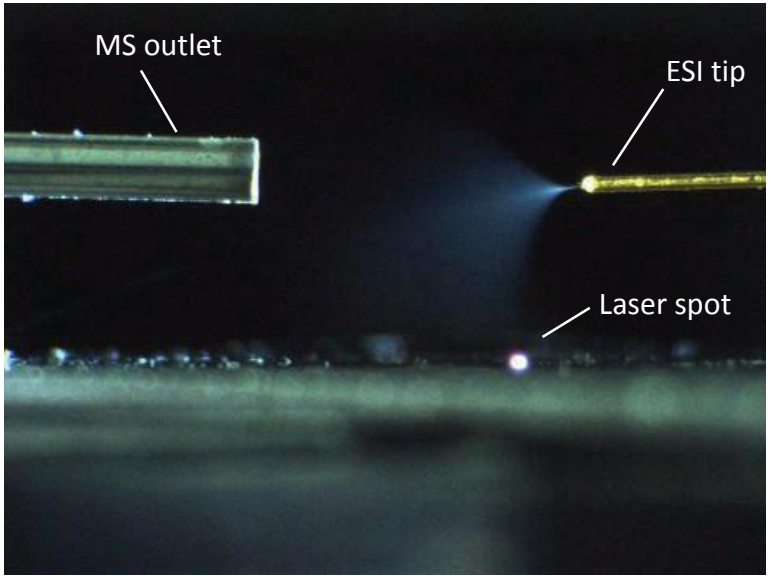
- Laser desorbs/ablates neutrals from sample surface.
- Neutral plume is entrained by the ESI droplets cloud.
- Analytes are desolved in the droplets and ionized through ESI mechanisms.

II-3) Laser Desorption/ablation

Electrospray Laser Desorption Ionization (ELDI)

- Characteristics:

  UV wavelength (Nd:YAG 266 nm or N_2 337 nm) for nanosecond duration @ 10 Hz
  Pulse energy = 150-300 µJ
  Incident laser beam angle to the surface = 45°
  Surface = glass, PTFE, paper, TLC paper
  ESI solvent adapted to the analyte polarity
  For small organic molecules and large biomolecules



- Mechanisms of ion formation:

  * Absorption of the laser energy by the analytes.
  * Excitation and sublimation of the analytes.
  * Formation of gaseous plasma plume of neutral analytes.
  * Dissolution of the analytes in the ESI droplets.
  * Ionization via charge transfer, then, classical evaporation/fission of analyte droplets.

II-3) Laser Desorption/ablation

Techniques closely related to ELDI

Laser Ablation ElectroSpray Ionization (LAESI)

Mid-IR wavelength (2.94 µm) for 5 ms duration @ 100 Hz
Pulse energy = 100 µJ
Incident laser beam angle to the surface = 90°

InfraRed Laser Desorption ElectroSpray Ionization (IR-LDESI)

IR wavelength (10.6 µm) for 5 ms duration @ 5 kHz
Pulse energy = 100 µJ
Incident laser beam angle to the surface = 90°

Matrix-Assisted Laser Desorption ElectroSpray Ionization (MALDESI)

Mid-IR wavelength (2.94 µm) or UV (349 nm) for 5 ms duration @ 100 Hz
Pulse energy = 100 µJ
Incident laser beam angle to the surface = 90°
Use of matrix for desorption

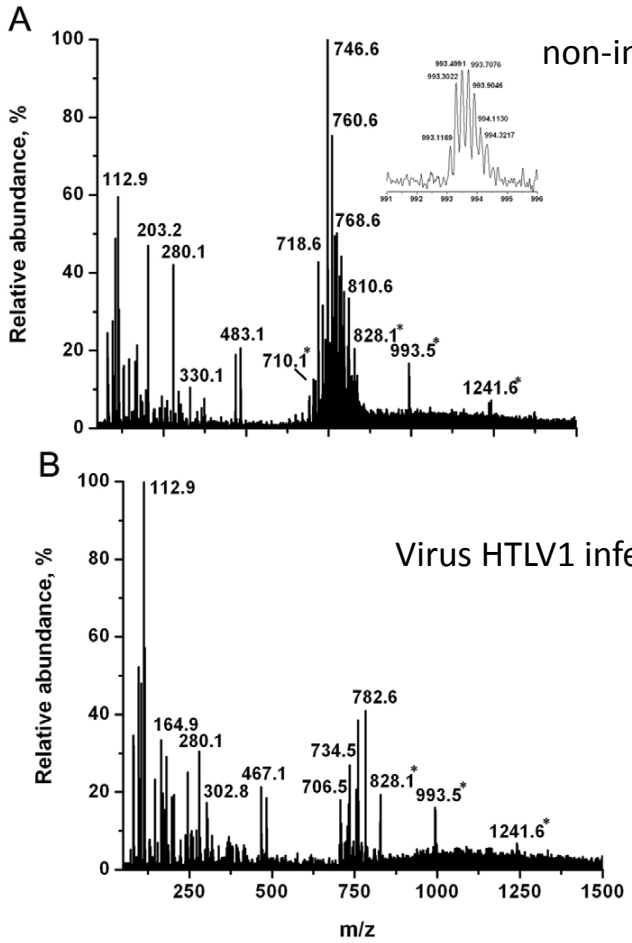
II-3) Laser Desorption/ablation

Electrospray Laser Desorption Ionization (ELDI) and others….

- Applications:

Metabolomics

PLoS One 2010, 5, e12590−e12604

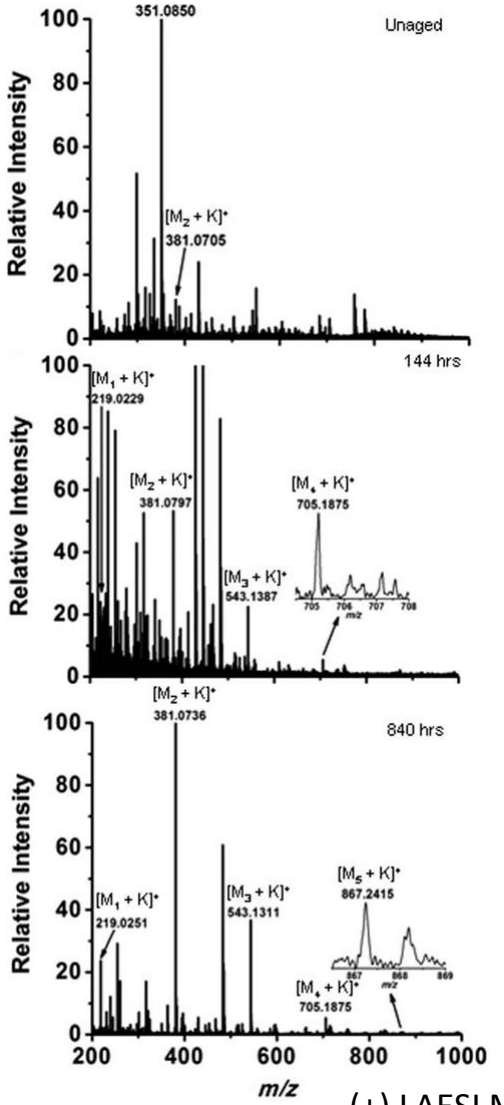


(+) LAESI MS spectra of T-lymphocytes

Q-ToF

Forensics

Analyst, 2010, 135, 2434–2444



cellulose degradation

(+) LAESI MS on paper

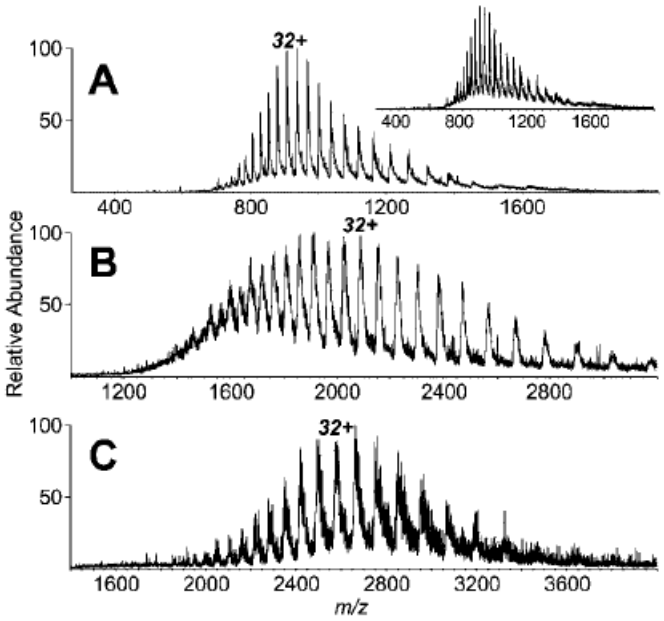
II-3) Laser Desorption/ablation

Electrospray Laser Desorption Ionization (ELDI) and others….

- Applications:

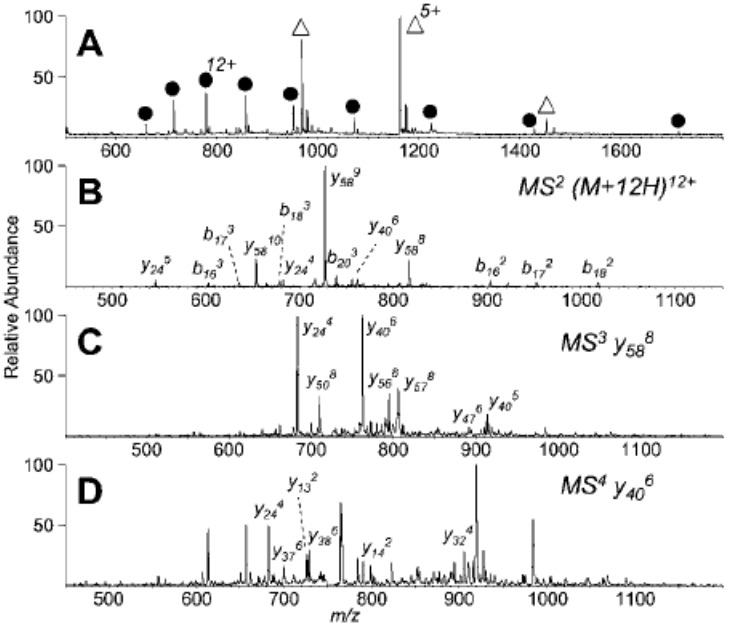
Proteomics

Analyst, 2010, 135, 767–772



ELDI-MS spectra (A) 1 mL of 200 mM bovine carbonic anhydrase, (B) 1 mL of 500 mM bovine serum albumin, and (C) 1 mL of 500 mM transferrin applied on-target. 1.06 µm; solvent mixture: ACN/water 1:1 + 0.2 % FA

Top-down analysis



ELDI-MS and MS^n of bovine ubiquitin. (A) IR-ELDI-MS. (B) MS^2 analysis of the 12+ ubiquitin ion (*m/z* 714). (C) MS^3 of y_{58}^8 ion (*m/z* 817). (D) MS^4 analysis of y_{40}^6 ion (*m/z* 761)

LTQ-Orbitrap

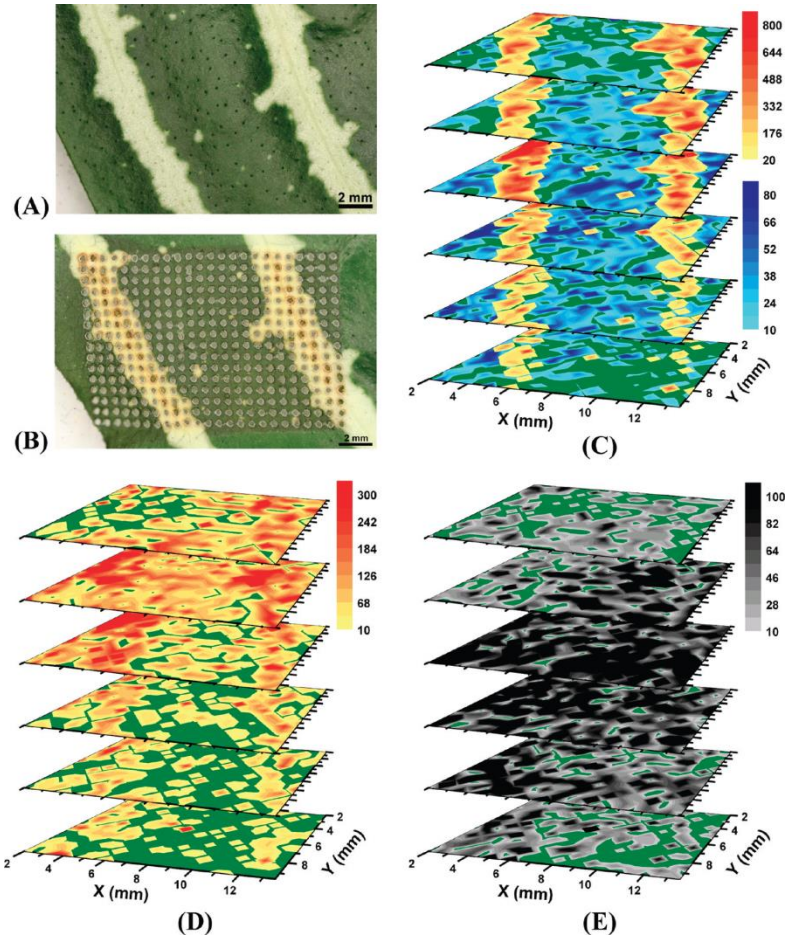
II-3) Laser Desorption/ablation

Electrospray Laser Desorption Ionization (ELDI) and others….

- Imaging – spatial resolution = 100 µm:

Plant slice

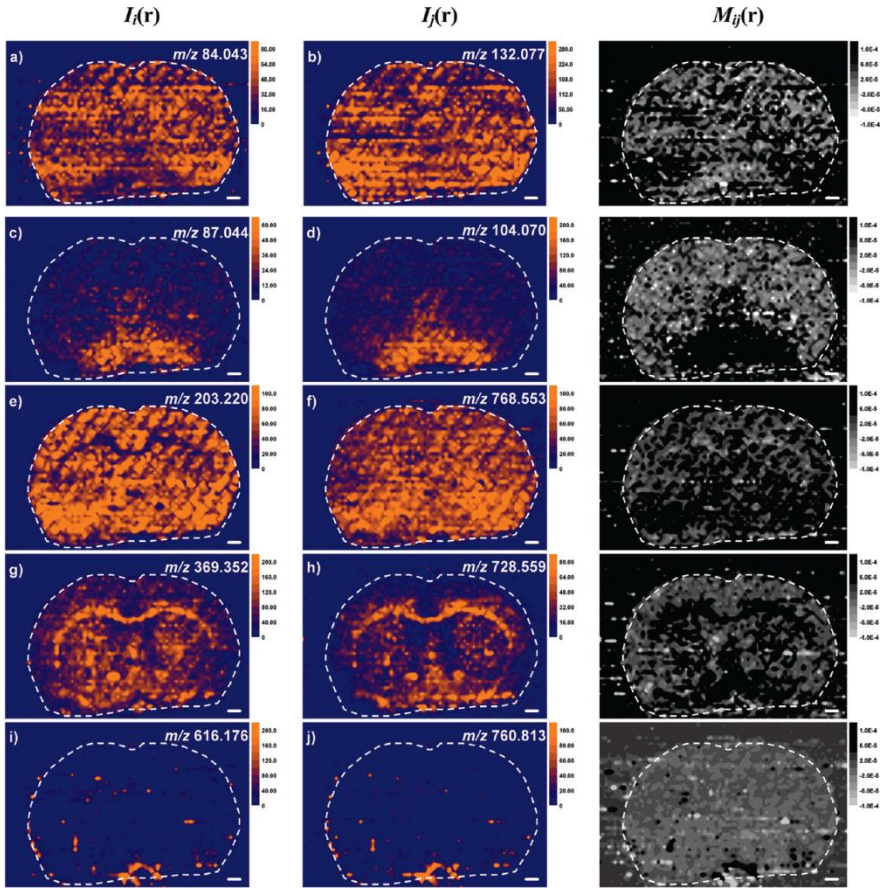
Anal. Chem. 2009, 81, 6668–6675



Metabolites in relation to *A. squarrosa* leave tissue architecture captured by LAESI 3D imaging MS

Biological sample

Anal. Chem. 2010, 82, 982–988

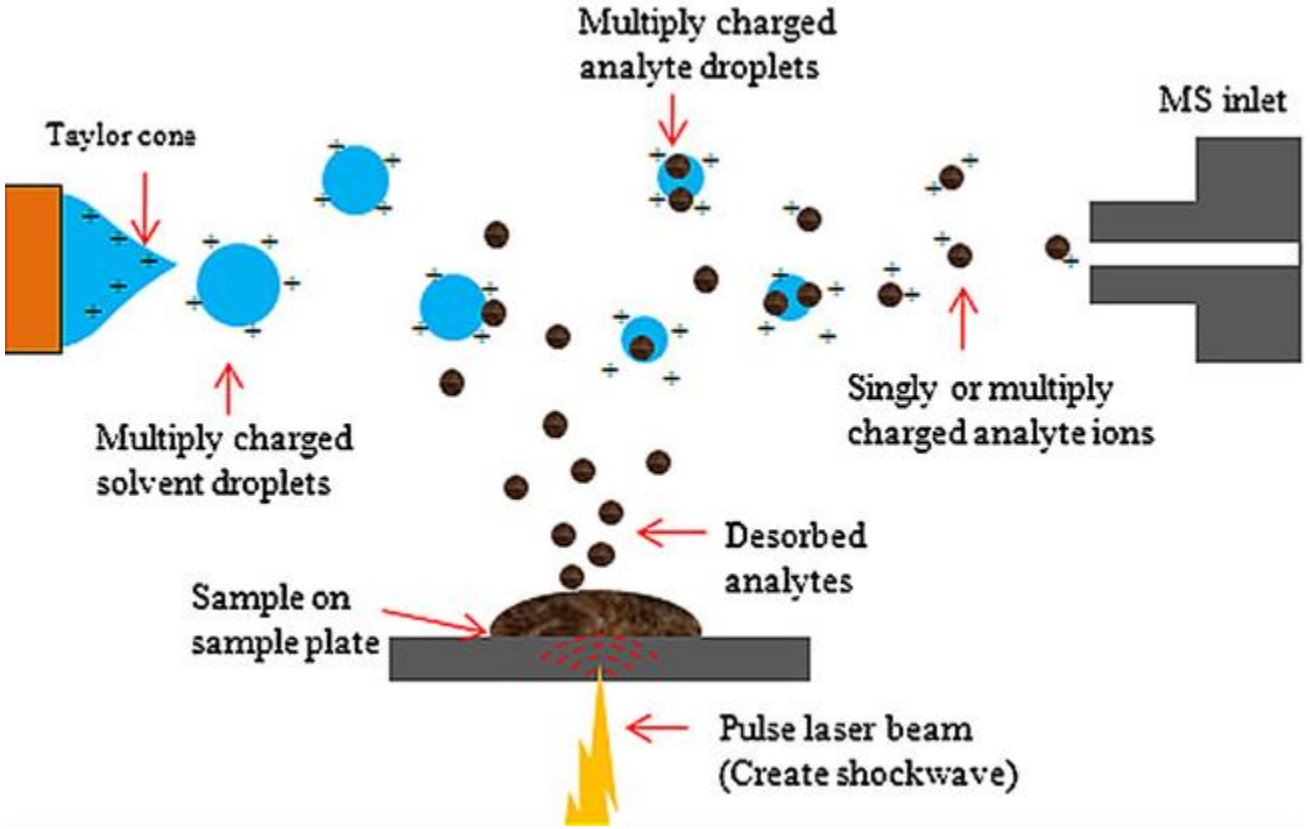


LAESI MS imaging of rat brain: (a) ethanolamine (b) creatine; (c) *γ*-butyrolactone (d) *γ*-aminobutyric acid; (e) spermine (f) PC(35:4); (g) cholesterol-H2O (h) plasmalogens PC(O-33:3); and (i) heme (j) R chain of hemoglobin.

II-3) Laser Desorption/ablation

Laser-Induced Acoustic Desorption ESI (LIAD-ESI)

Anal. Chem., 2009, 81, 868–874



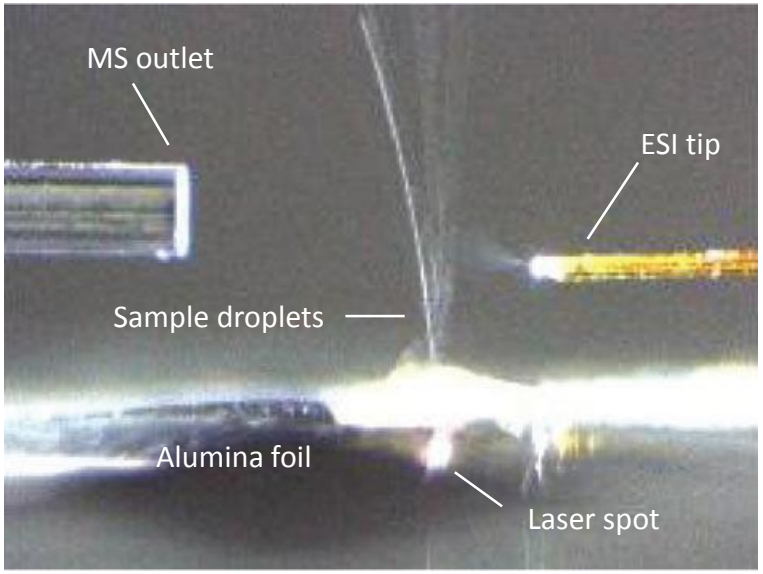
- Analytes are desorbed or aerosolized by laser-induced acoustic wave through special substrate.
- Neutral plume is entrained by the ESI droplets cloud.
- Analytes are desolved in the droplets and ionized through ESI mechanisms.

II-3) Laser Desorption/ablation

Laser-Induced Acoustic Desorption ESI (LIAD-ESI)

- Characteristics:

Nd:YAG 532 nm or 10.64 µm laser for nanosecond duration @ 10 Hz
Pulse energy = 100 mJ
Laser beam backside (45°)
Surface = titanium or aluminum foil (10-15 µm thick)
ESI solvent adapted to the analyte polarity



- Mechanisms of ion formation:

* Absorption of laser energy by the thin foil produces mechanical tension and generate an acoustic pulse, that propagates toward the other side and desorbs analytes.
* Fusion of analyte droplets with ESI droplet.
* Charge transfer between the analytes and the charged solvent.
* Then, classical evaporation/fission of analyte droplets.

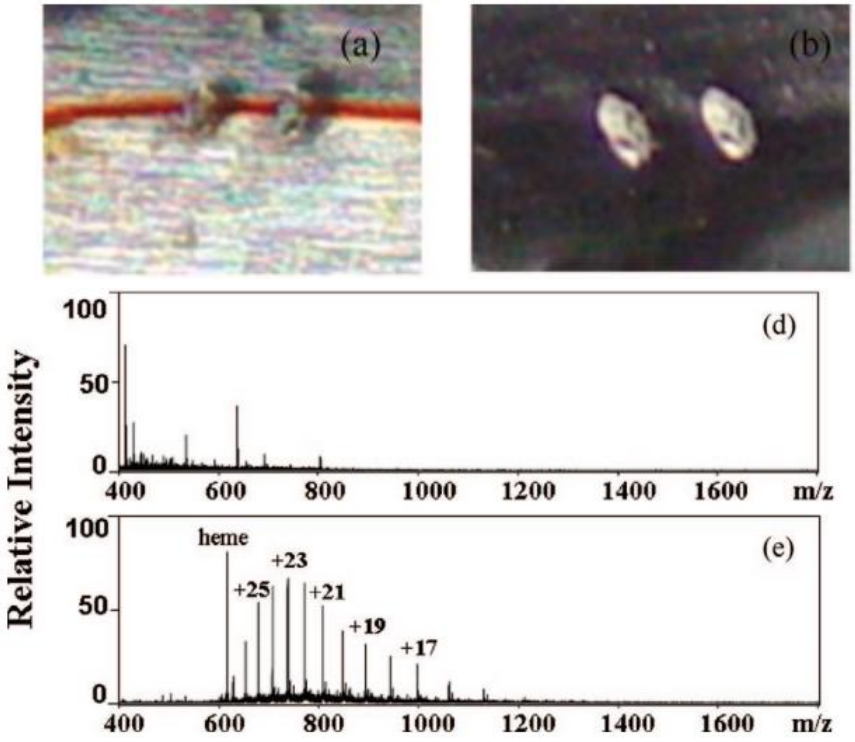
II-3) Laser Desorption/ablation

Laser-Induced Acoustic Desorption ESI (LIAD-ESI)

- Applications:

Proteomics

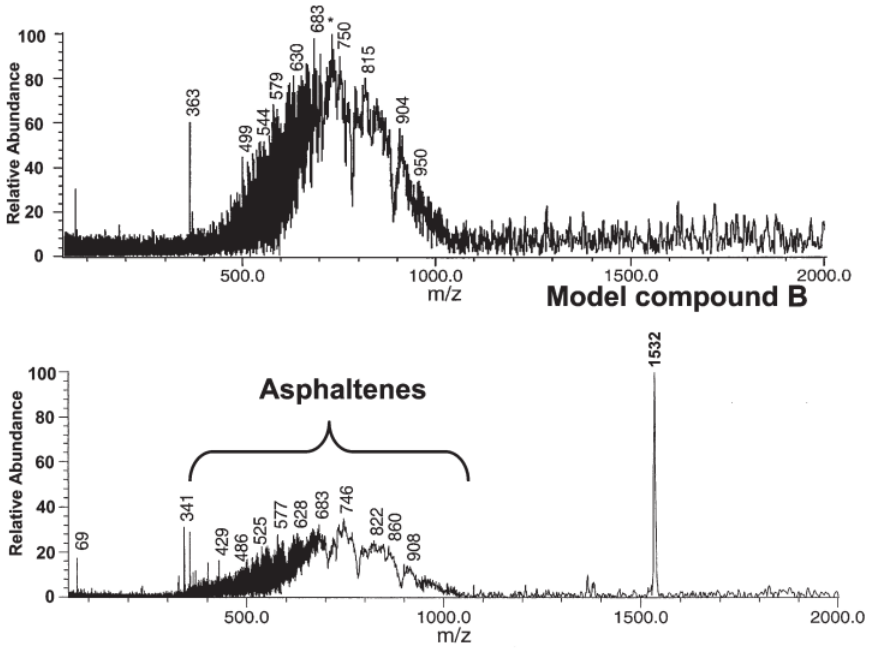
Anal. Chem. 2009, 81, 868–874



Photographs of the (a) front and (b) rear sides of an aluminum foil, revealing the path of desorption of a dry myoglobin solution line after irradiation of the rear side of the foil using an IR laser.
(d and e) Positive-ion LIAD-ESI mass spectra of the background and myoglobin

Fuel analysis

Energy Fuels 2009, 23, 5564–5570



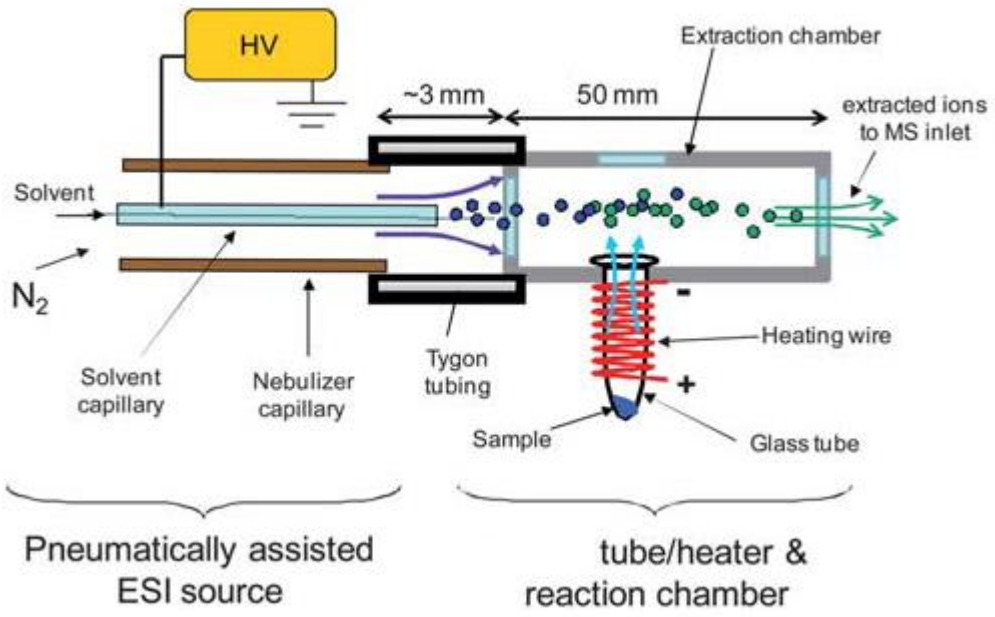
Top: LIAD-ESI (60 eV, 18 mJ, 30 laser pulses) mass spectrum of an asphaltene sample.
Bottom: asphaltene sample spiked with model compound B (MW 1532)

II-4) Thermal Desorption

Analytes are desorbed from the surface by heating or pyrolysis

ElectroSpray-Assisted Pyrolysis Ionization (ESA-Py)

Anal. Chem. 2005, 77, 7744-7749



- Analytes are desorbed by pyrolysis/heating.
- Desorbed gaseous analytes are in contact with the charged droplets in the extraction chamber.
- Charge transfer with the charged solvent.

II-4) Thermal Desorption

ElectroSpray-Assisted Pyrolysis Ionization (ESA-Py)

- Characteristics:

  Pyrolysis up to 940°C
  Other classical temperature = 350°C
  For volatile thermally stable analytes
  ESI solvent adapted to the analyte polarity

- Mechanisms of ion formation:

  * Analytes are put into the gas phase by thermal desorption.
    → Possible thermal decomposition products
  * Analytes are in contact with the charged droplets in the reaction chamber.
  * Charge transfer between the analytes and the charged solvent.
  * Then, classical evaporation/fission of analyte droplets.

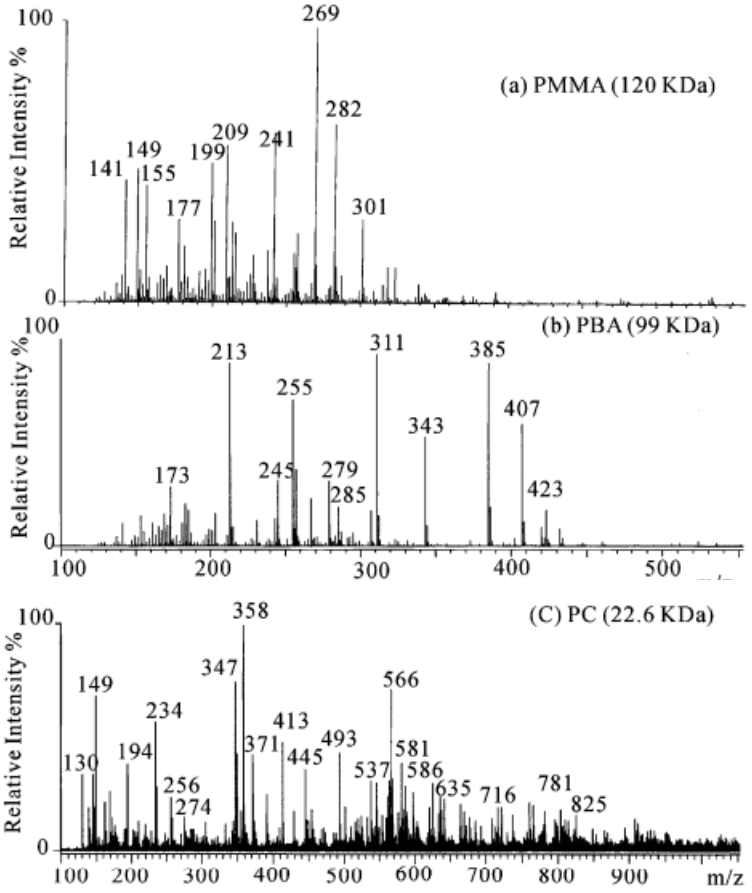
II-4) Thermal Desorption

ElectroSpray-Assisted Pyrolysis Ionization (ESA-Py)

- Applications:

Polymer analysis

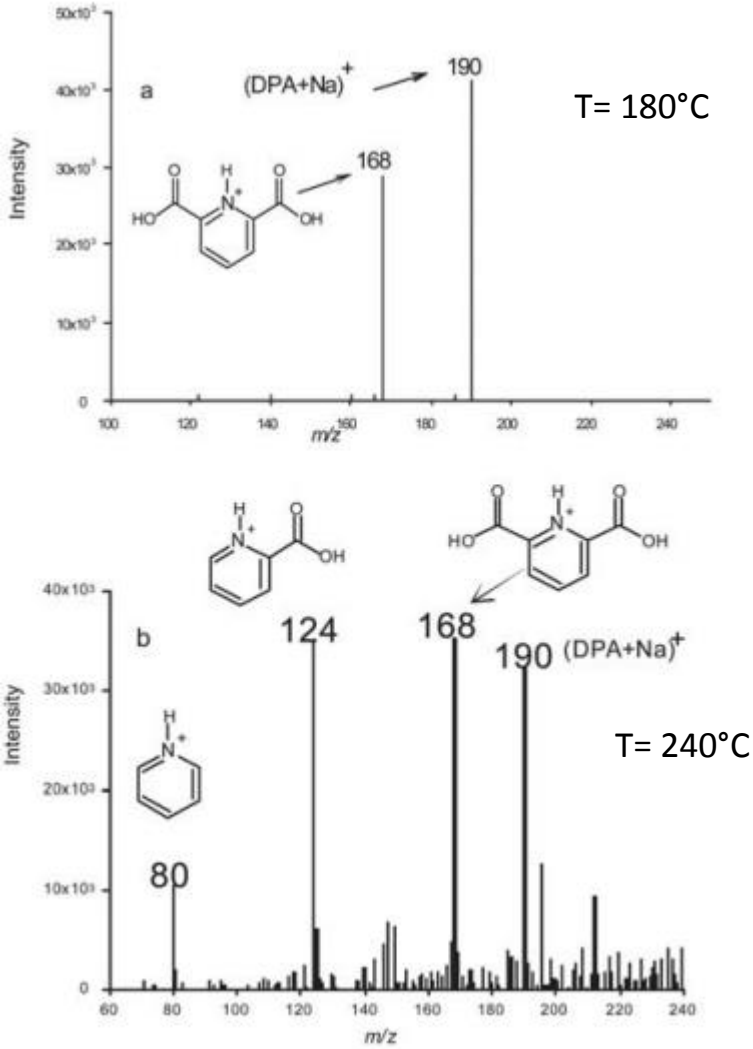
Anal. Chem. 2005, 77, 7744-7749



Positive-ion ESA-Py MS spectra of polymers
T= 590°C

Homeland security

Analyst, 2010, 135, 797–803

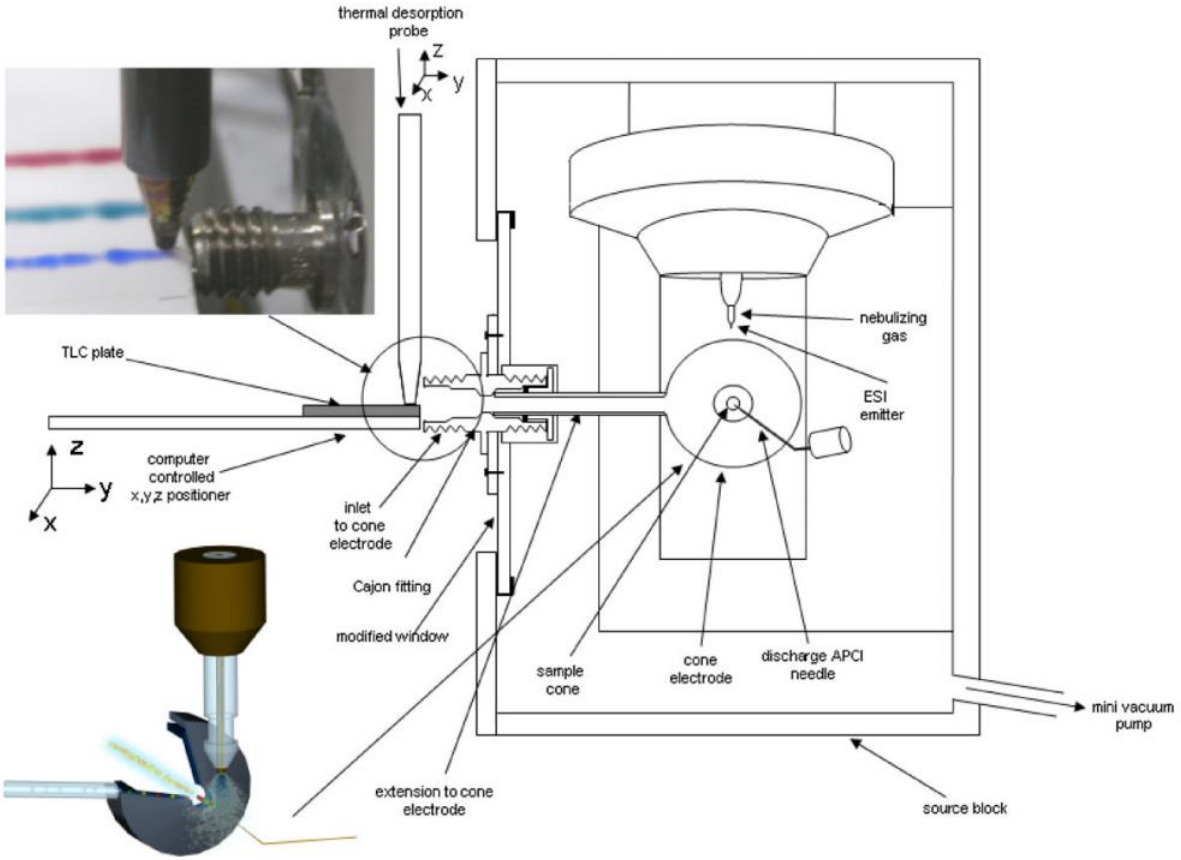


ESA-Py MS of *Bacillus* spores

II-4) Thermal Desorption

Thermal Probe Desorption ElectroSpray Ionization (TPD-ESI)

Rapid Commun. Mass Spectrom. 2010; 24 : 1721–1729



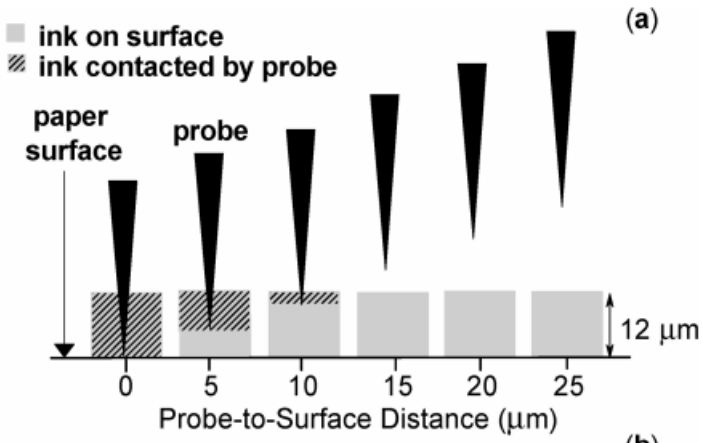
- Thermal probe desorbes the analytes from the surface.
- Desorbed gasous analytes are in contact with the charged droplets in a special cone electrode.
- Charge transfer between the analytes and the charged solvent.

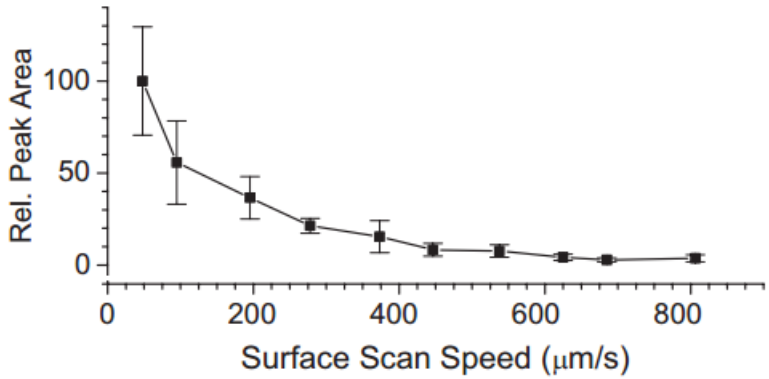
II-4) Thermal Desorption

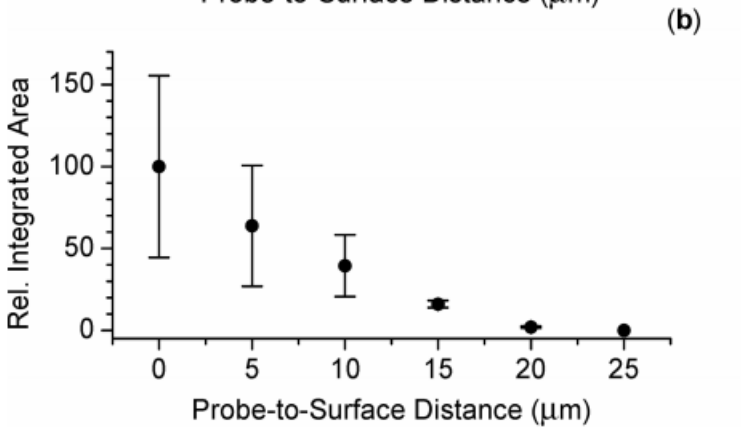
Thermal Probe Desorption ElectroSpray Ionization (TPD-ESI)

- Characteristics:

  Classical temperature = 350°C
  Probe tips diameter of 50 µm
  Surface = Glass slide, TLC paper
  Probe-to-surface distance ~ 5 µm
  Classical ESI solvents adapted to the analytes
  Imaging capability







- Mechanisms of ion formation:
  Similar to ESA-Py

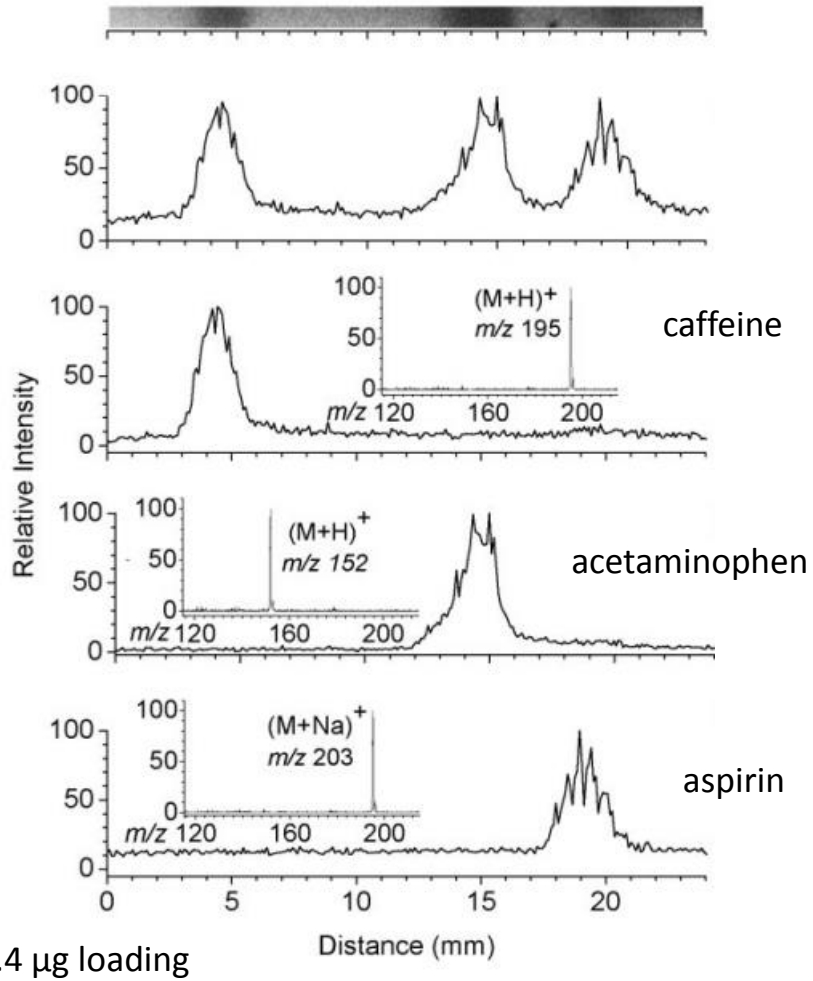
II-4) Thermal Desorption

Thermal Probe Desorption ElectroSpray Ionization (TPD-ESI)

- Applications:

Analysis on TLC plate

Rapid Commun. Mass Spectrom. 2010; 24: 1721–1729

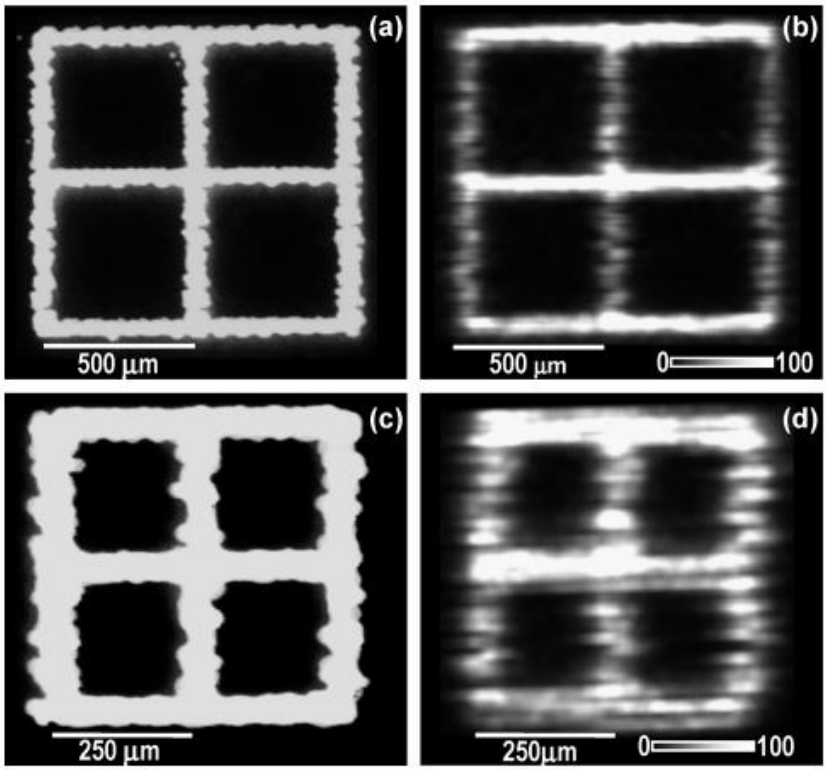


1.4 µg loading

T= 350°C , scan speed 700 µm/s

Imaging of printed inks

Anal. Chem. 2011, 83, 598–603



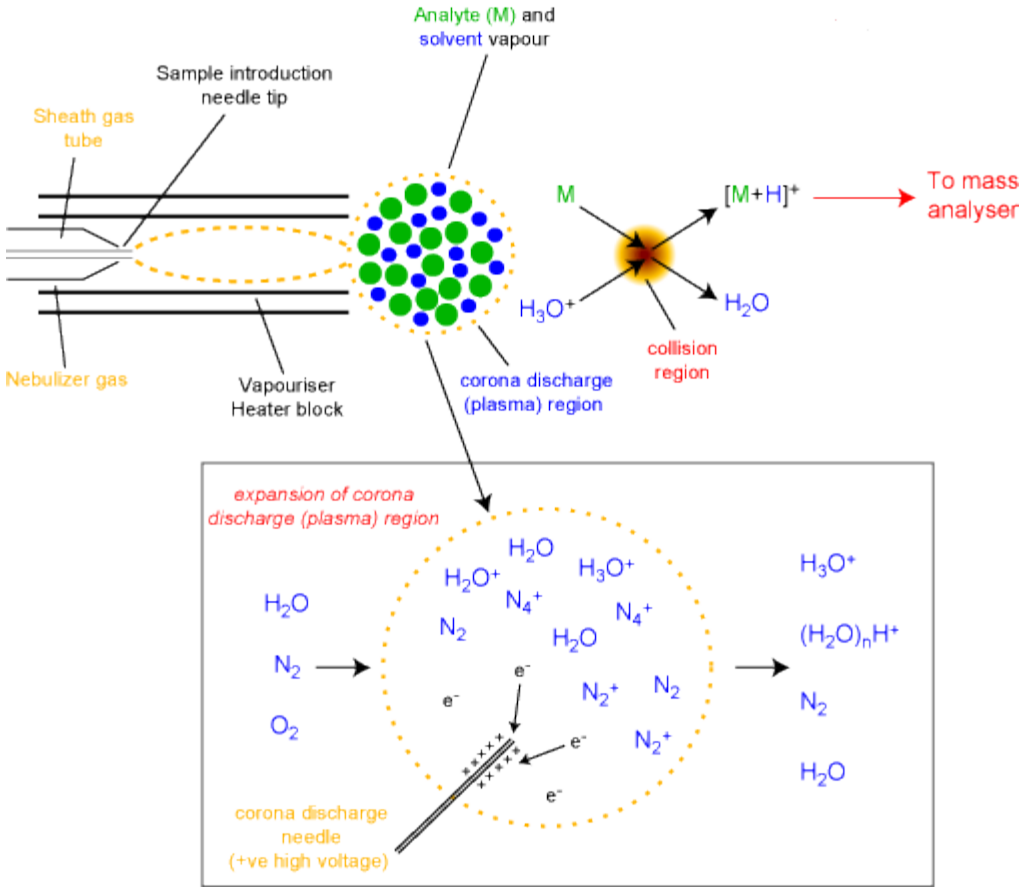
Optical images

Interpolated TPD-ESI MS chemical images (*m/z* 387)

T= 350°C , scan speed 100 µm/s

→ Spatial resolution 50 µm

III- APCI-based ambient ionization techniques



In ambient ionization techniques using this mode, the **charged species** formed by the APCI allow the **post-ionization** of the desorbed analytes (direct or in two steps).
Different methods are used to generate this plasma as a corona discharge, dielectric barrier discharge or glow-to-arc discharge.
Samples can be gaseous, liquid or solid. Widely used for the analysis of volatile and low polar compounds.

III- APCI-based ambient ionization techniques

Ionization of analyte molecules (M) by reactants (R)

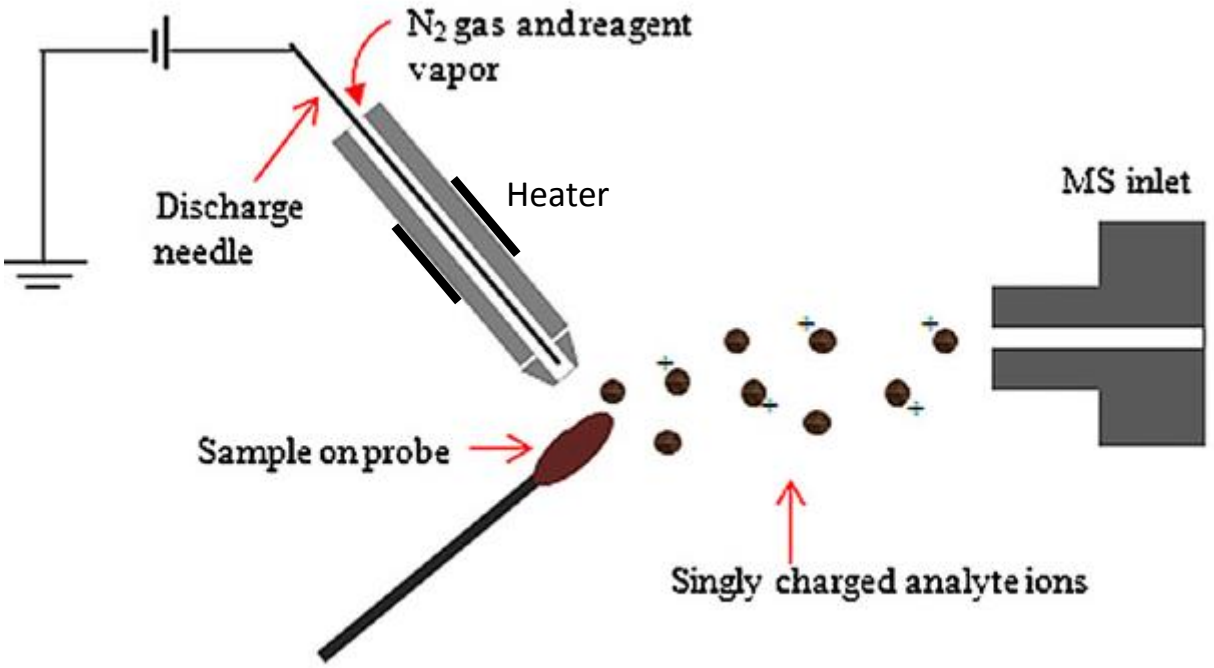
Ionization mechanism	Reaction pathway
Proton transfer	$M+[(H_2O)_n+H]^+ \rightarrow [M+H]^+ + nH_2O$
Charge transfer	$M+R^+ \rightarrow M^+ + R$ $R^+ = N_2^+, NO^+, O_2^+$ $M+R^- \rightarrow M^- + R$ $R^- = O_2^-$ (from $O_2 + e^- \rightarrow O_2^-$), OH^-
Penning ionization	$M+R^* \rightarrow M^{+\bullet} + R + e^-$ $R^* = He^*, N_2^*$
Electron attachment	$M+e^- \rightarrow M^{-\bullet}$
Ion attachment	$M+R^- \rightarrow [M+R]^-$ / $M+R^+ \rightarrow [M+R]^+$ $R^- = NO_2^-, NO_3^-$ / $R^+ = NH_4^+$
Proton/hydride abstraction	$M+R^-/R^+ \rightarrow [M-H]^-/[M-H]^+ + RH$ $R^- = OH^-$; $R^+ = NO^{+\bullet}$

III-1) Direct Desorption

Analytes are directly desorbed from the surface by the reagent species

Desorption Atmospheric Pressure Chemical Ionization (DAPCI)

Rapid Commun. Mass Spectrom. 2006; 20: 3130–3138



- Corona discharge is established between 2 electrodes.
- Reactive plasma desorbs analytes from the surface.
- Desorbed analytes are carried by the gas.
- Analytes ions are formed via ion/molecule reactions with plasma species.

III-1) Direct Desorption

Desorption Atmospheric Pressure Chemical Ionization (DAPCI)

- Characteristics:

Heated N_2 nebulizer gas (0.15~0.2 MPa, 250~450 mL/min)
Reagent solution = water, MeOH, ACN
Corona discharge voltage = ±4.5 kV
Discharge needle-to-surface distance = 2-3 mm
Discharge needle-to-surface angle = 30-45°
Surface = glass, PTFE, foodstuffs, skin…

- Mechanisms of ion formation:

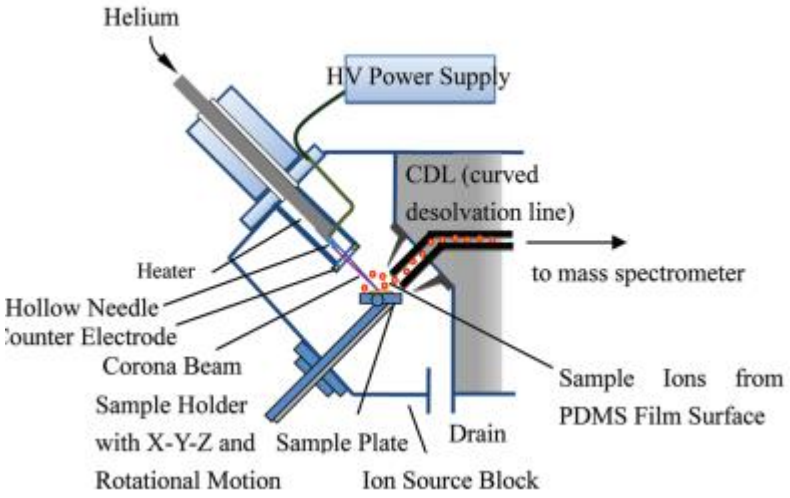
* Gas phase solvent vapors are ionized by corona discharge ionization.
* Reagent species (electrons, protons, metastable atoms, solvent ions = H_3O^+, N_2^+, OH^-, CN^-, CH_2CN^-) impact the surface.
* Analytes are desorbed by charge buildup on the surface : « chemical sputtering ».
* Charge or proton transfers with reagent species allow ionization of the desorbed analytes. Formation of singly charged analyte ions and complexes.

III-1) Direct Desorption

Technique related to DAPCI

Desorption Corona Discharge ionization (DCBI)

Analyst, 2010, 135, 688–695



No solvent needed

He reactive gas → ions and metastable He atoms

Low current (10-40 µA)

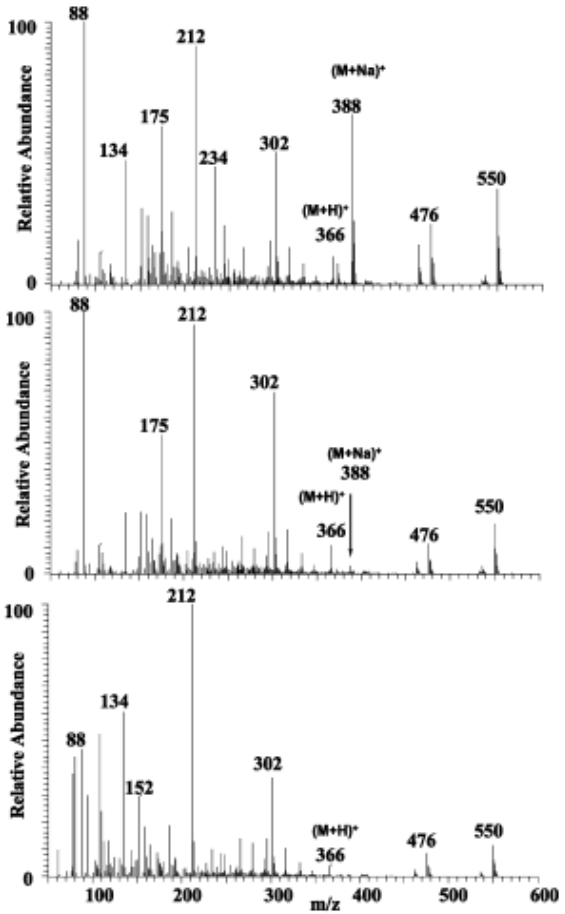
III-1) Direct Desorption

Desorption Atmospheric Pressure Chemical Ionization (DAPCI)

- Applications:

Pharmaceutical

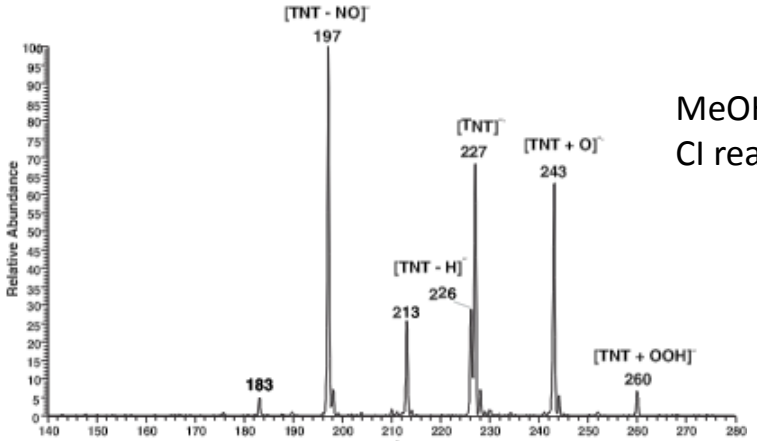
Anal. Chem. 2010, 82, 8060–8070



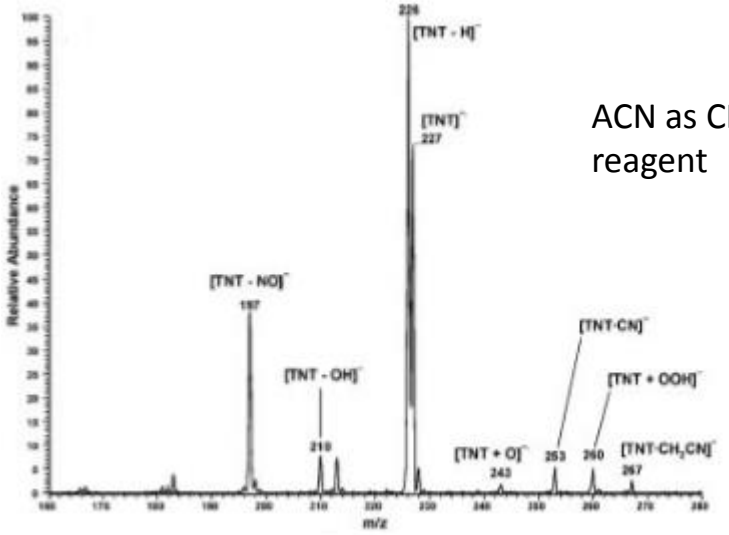
DAPCI(+) MS spectra of amoxicillin capsules from different origins

Homeland Security

Rapid Commun. Mass Spectrom. 2006; 20: 3130–3138



MeOH as CI reagent



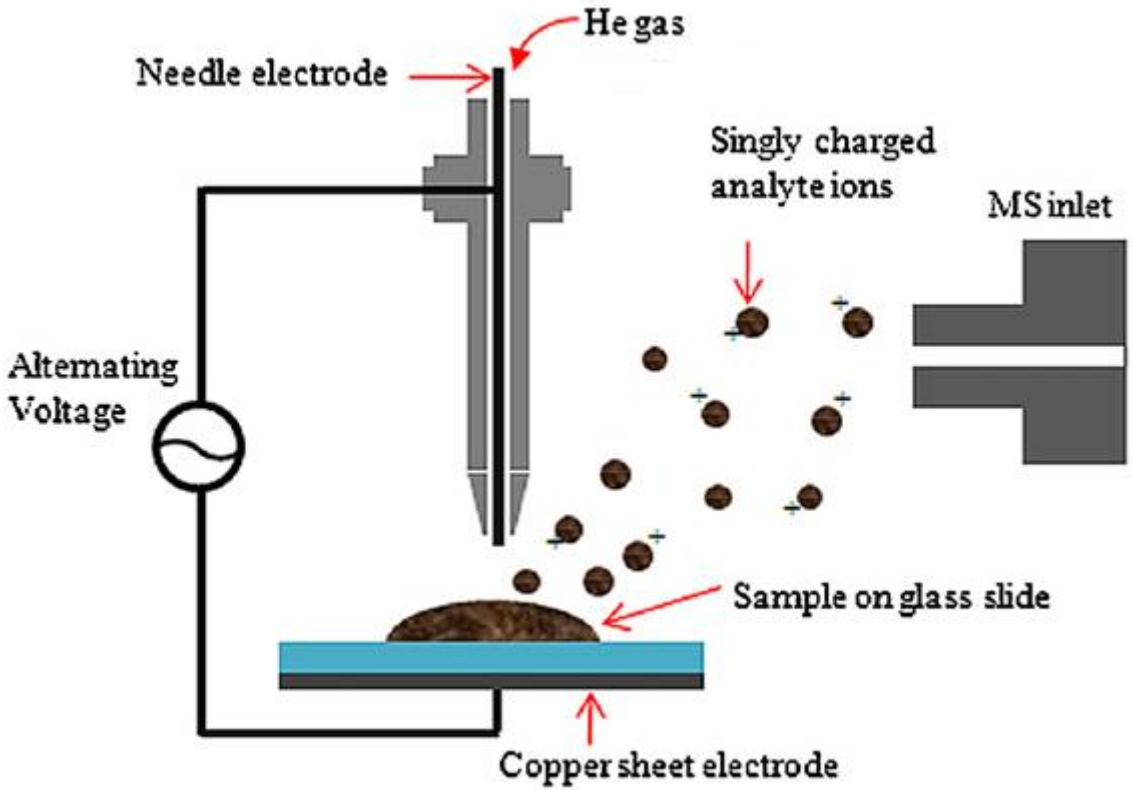
ACN as CI reagent

DAPCI(-) MS spectra TNT on cotton applicator

III-1) Direct Desorption

Dielectric Barrier Discharge Ionization (DBDI)

J Am Soc Mass Spectrom 2007, 18, 1859–1862



- Dielectric barrier discharge between the needle electrode and the sheet electrode generates plasma species.
- Reactive plasma desorbs analytes from the surface.
- Analyte ions are mainly formed via electron transfer with metastable atoms.

III-1) Direct Desorption

Dielectric Barrier Discharge Ionization (DBDI)

- Characteristics:

He gas (<0.2 L/min)
Alternative voltage of 3.5-4.5 kV @ 20 kHz
Copper sheet as counter electrode
Glass slide that served as both the discharge barrier and the sample plate
Discharge needle-to-surface distance = 5-10 mm

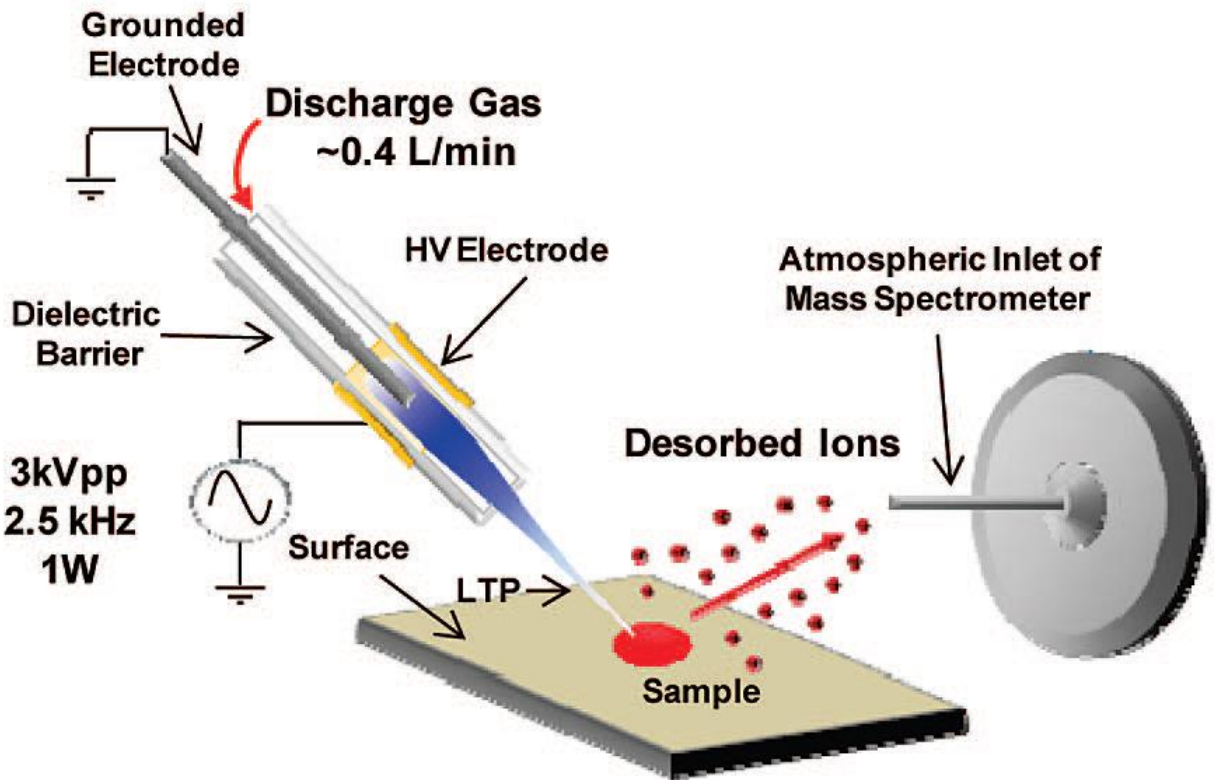
- Mechanisms of ion formation:

* Plasma is formed by dielectric barrier discharge.
* Reagent species (electrons, protons, metastable atoms, gas reagents) impact the surface.
* Analytes are desorbed by charge buildup on the surface : « chemical sputtering ».
* Ion/molecules reactions allow ionization of the desorbed analytes. Penning ionization by the bombardment of metastable gas may occur.

III-1) Direct Desorption

Low-Temperature Plasma (LTP)

Anal. Chem. 2008, 80, 9097–9104



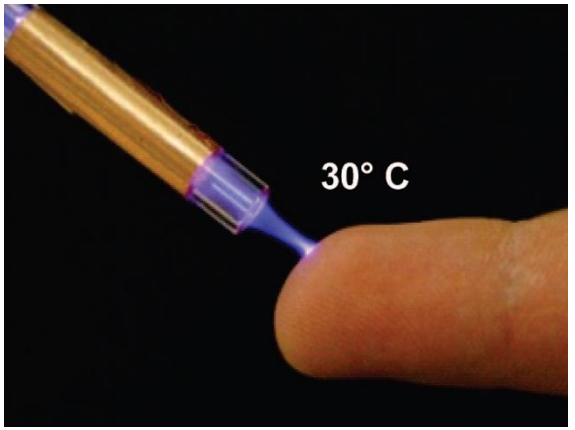
- Dielectric barrier discharge to create a low-temperature plasma.
- The counter electrode is placed within the probe.
- Direct interaction of the plasma with the sample.
- Analytes are ionized through proton or charge transfers.

III-1) Direct Desorption

Low-Temperature Plasma (LTP)

- Characteristics:

Glass tube (o.d. 6.35 mm and i.d. 3.75 mm) with an internal grounded electrode (stainless steel; d. 1.57 mm)
Outer electrode (copper tape) surrounding the outside
He, Ar, N_2, air gas (<0.4 L/min)
Alternative voltage of 2.5-5 kV @ 2-5 kHz
Probe-to-sample surface distance: 1 mm to 2 cm



- Mechanisms of ion formation:

Similar to DBDI (wide range of ionization processes)
Formation of $[M+H]^+$, $[M+H+(H_2O)_n]^+$, $[M+NO_2]^-$, $[M]^-$, $[M-NO_2]^-$

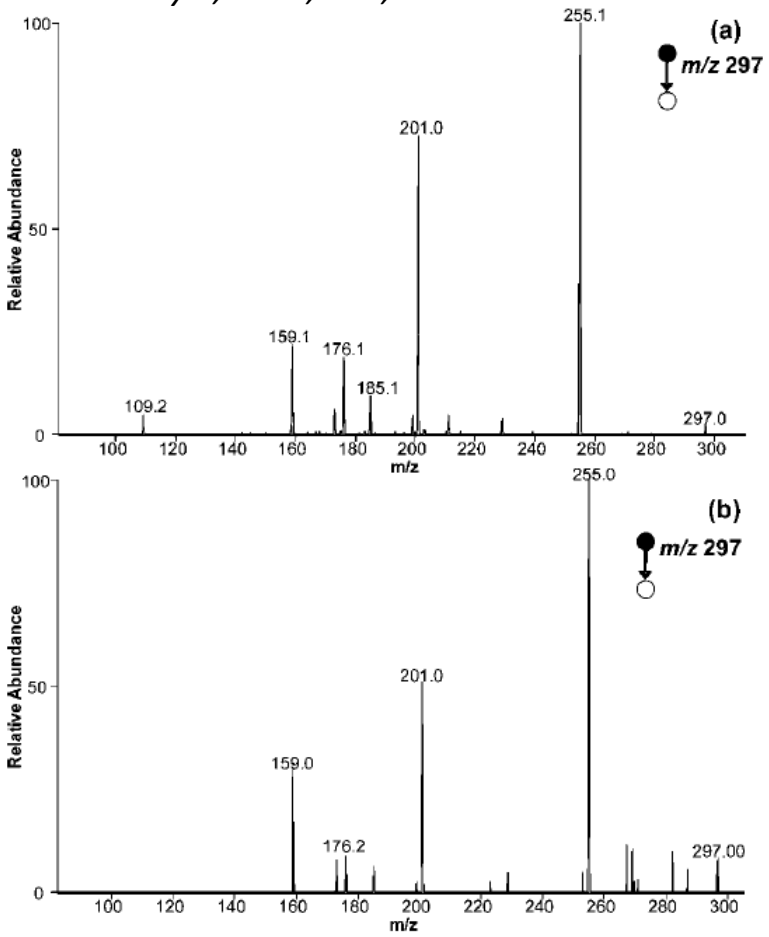
III-1) Direct Desorption

Low-Temperature Plasma (LTP)

- Applications:

Food Analysis

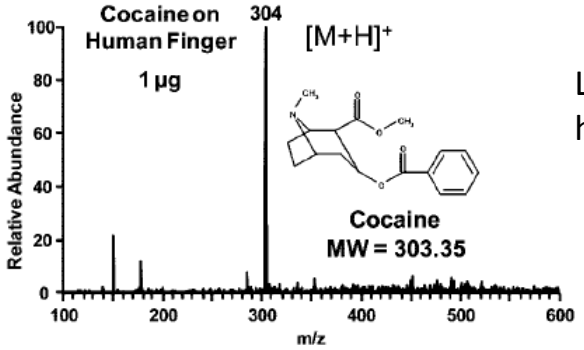
Analyst, 2010, 135, 971–979



LTP MS/MS spectra of fungicide imazalil on market-purchased (a) orange and (b) lemon peel.

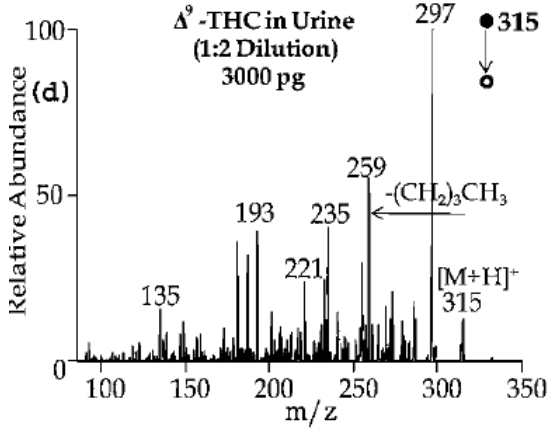
Drug abuse analysis

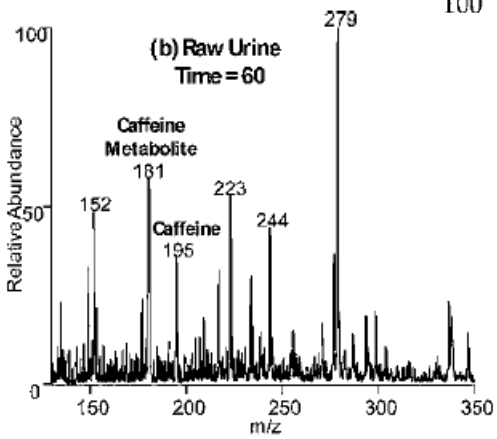
Analyst, 2010, 135, 927–933



LTP MS spectrum of humain skin

LTP MS/MS spectrum of THC (*m/z* 315) spiked in urine



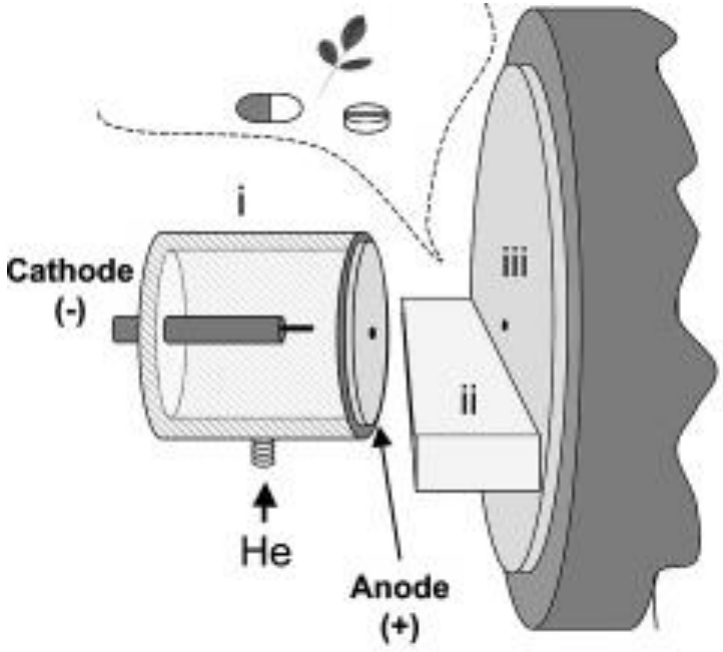


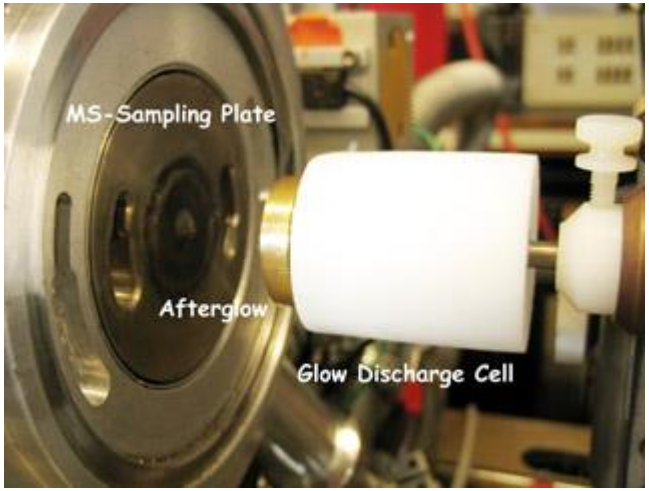
LTP MS spectrum after intake of a caffeinated (*m/z* 195) soft drink

III-1) Direct Desorption

Flowing Atmospheric Pressure Afterglow (FAPA)

Anal. Chem. 2008, 80, 2646-2653





- Glow-to-arc discharge generates metastable atoms.
- Gas stream is heated in discharge.
- Analytes ions are formed via proton transfer or charge exchange with metastable atoms.

III-1) Direct Desorption

Flowing Atmospheric Pressure Afterglow (FAPA)

- Characteristics:

Two electrodes (a cathode : 1.5 mm diameter tungsten pin mounted into a 5 mm diameter steel rod, and an anode: 10 mm diameter, 2 mm thick brass disk with a 1 mm diameter orifice in its center) tightly mounted in a discharge chamber
The body of the cell (T) is Teflon and has a suitable entrance orifice for the discharge gas (He, <0.4 L/min)
Direct current (DC) of 10-100 V

- Mechanisms of ion formation:

* Glow-to-arc discharge allows ionization of the flowing gas.
* Heating of the gas stream through Joule heating within the electrical discharge.
* Reagent plasma species impact the surface.
* Analytes are desorbed by charge buildup on the surface.
* Ion/molecules reactions allow ionization of the desorbed analytes (mainly proton transfer).

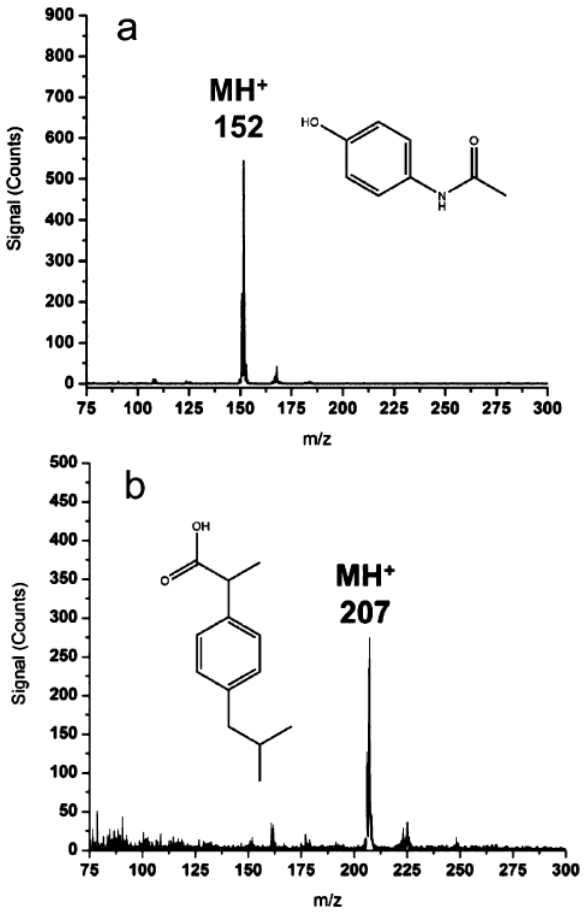
III-1) Direct Desorption

Flowing Atmospheric Pressure Afterglow (FAPA)

- Applications:

Pharmaceutical

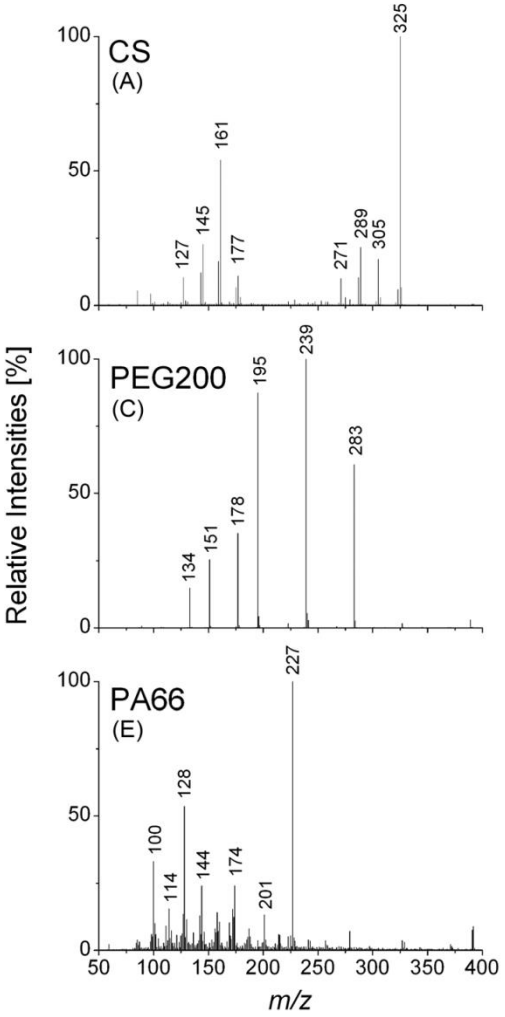
Anal. Chem. 2008, 80, 2654-2663



FAPA(+) MS spectra of (a) Tylenol tablet (acetaminophen), (b) Ibuprofen tablet

Polymer Analysis

Rapid Commun. Mass Spectrom. 2006; 20: 3130–3138



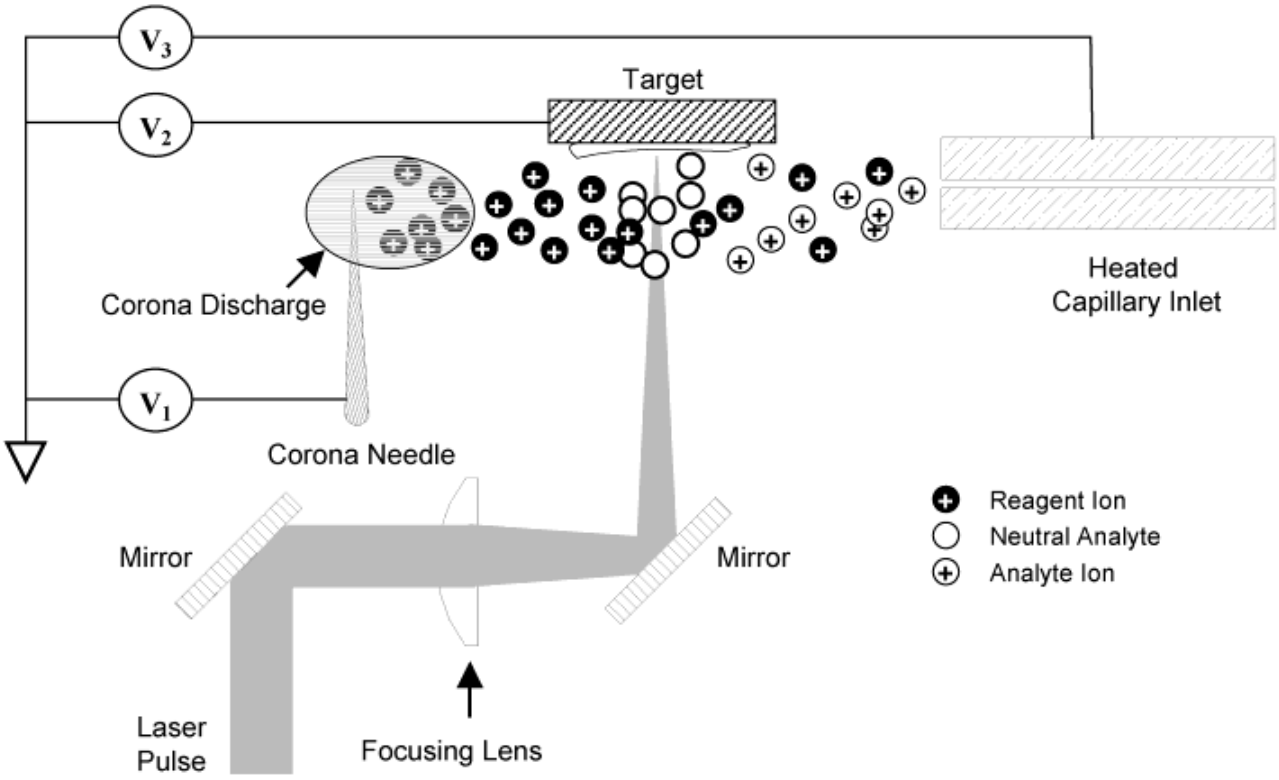
FAPA MS spectra of solid polymers

III-2) Laser Desorption/ablation

Analytes are desorbed from the surface by a laser pulse

Laser Desorption Atmospheric Pressure Chemical Ionization (LDAPCI

Anal. Chem. 2002, 74, 5600-5605



- Laser desorbs/ablates neutrals from sample surface.
- Corona discharge generates charged species.
- Reagent ions stream merges with neutral plume, reacting with analytes through ion/molecule reactions.

III-2) Laser Desorption/ablation

Laser Desorption Atmospheric Pressure Chemical Ionization (LDAPCI)

- Characteristics:

IR wavelength (CO_2 10.6 µm)
Incident laser beam angle to the surface = 90°
Spot diameter ~ 0.5 mm
Sample on stainless steel surface held at an offset potential of 2 kV.
The corona needle positioned ~3 cm from the inlet of the heated capillary
Corona discharge potential of +8.1 kV

- Mechanisms of ion formation:

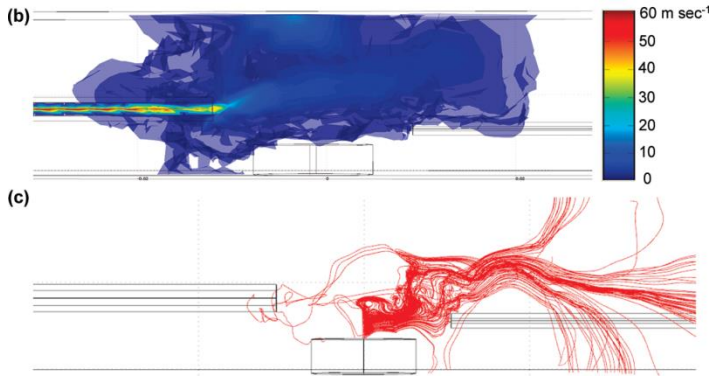
* Absorption of the laser energy by the analytes.
* Excitation and sublimation of the analytes.
* Formation of gaseous plume of neutral analytes.
* Neutral analytes react with plasma reagent species
* Formation of singly charged analyte ions and complexes.

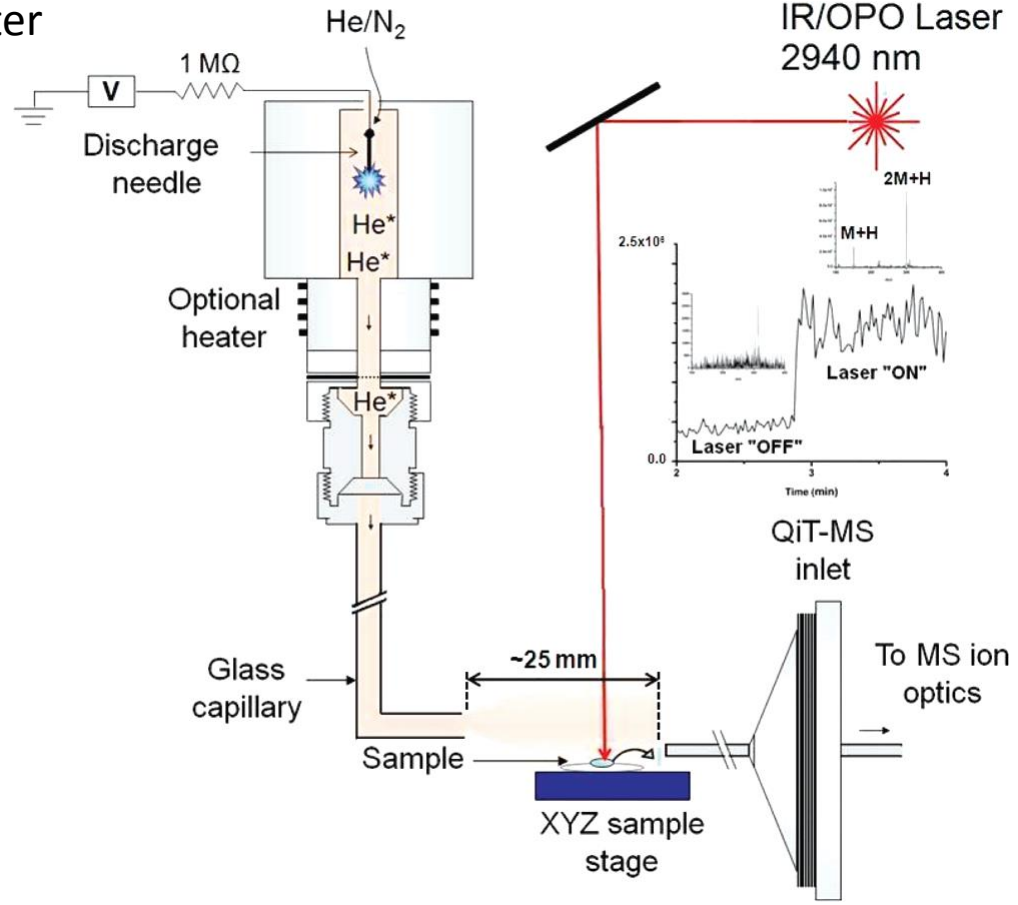
III-2) Laser Desorption/ablation

Techniques related to LD-APCI

InfraRed Laser Ablation Metastable-Induced Chemical Ionization (IR-LAMICI)

IR wavelength (2.94 µm) OPO Nd:YAG laser for 4 ns duration @ 20 Hz
Pulse energy = 2 mJ
Incident laser beam angle to the surface = 90°
Circular focal spots of ~300 μm diameter
He or N_2 gas
Glow discharge of ~10 V
Production of metastables





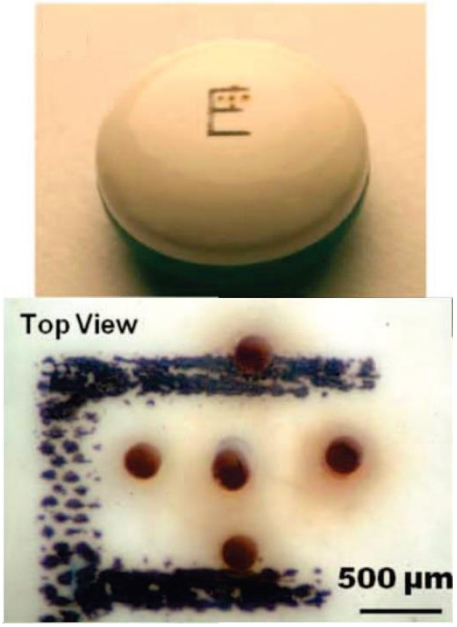
Anal. Chem. 2010, 82, 2178–2181

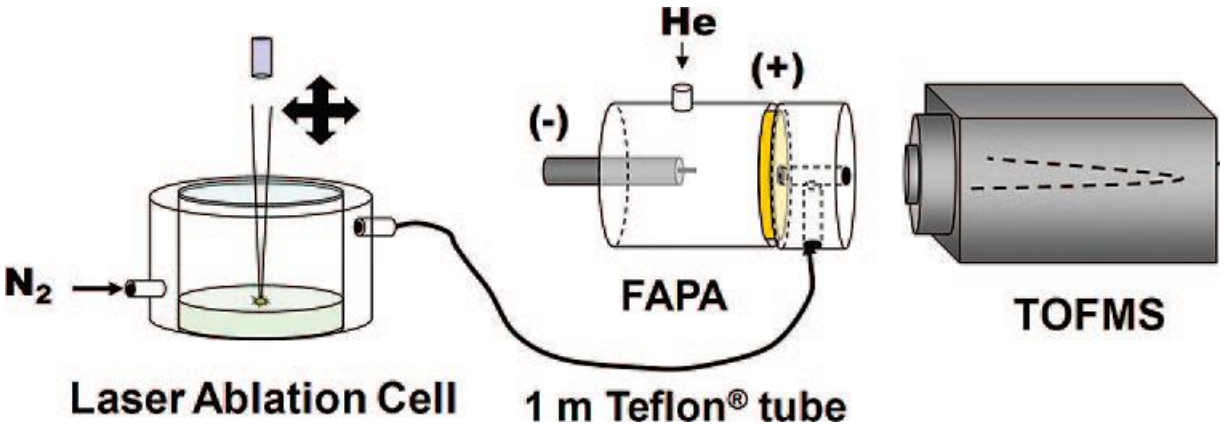
III-2) Laser Desorption/ablation

Techniques related to LD-APCI

Laser Ablation Flowing Atmospheric Pressure Afterglow (LA-FAPA)

UV 266 nm Nd:YAG laser operating at 20 Hz
Laser spot sizes between 10 and 300 μm in diameter.
Aerosol generated by the ablation event carried in a stream of N_2 at 0.3 L/min
1 m Teflon transfer tube to the FAPA chamber
Afterglow discharge. Direct current (DC) of 10-50 V





Anal. Chem. 2008, 80, 8308–8313

III-2) Laser Desorption/ablation

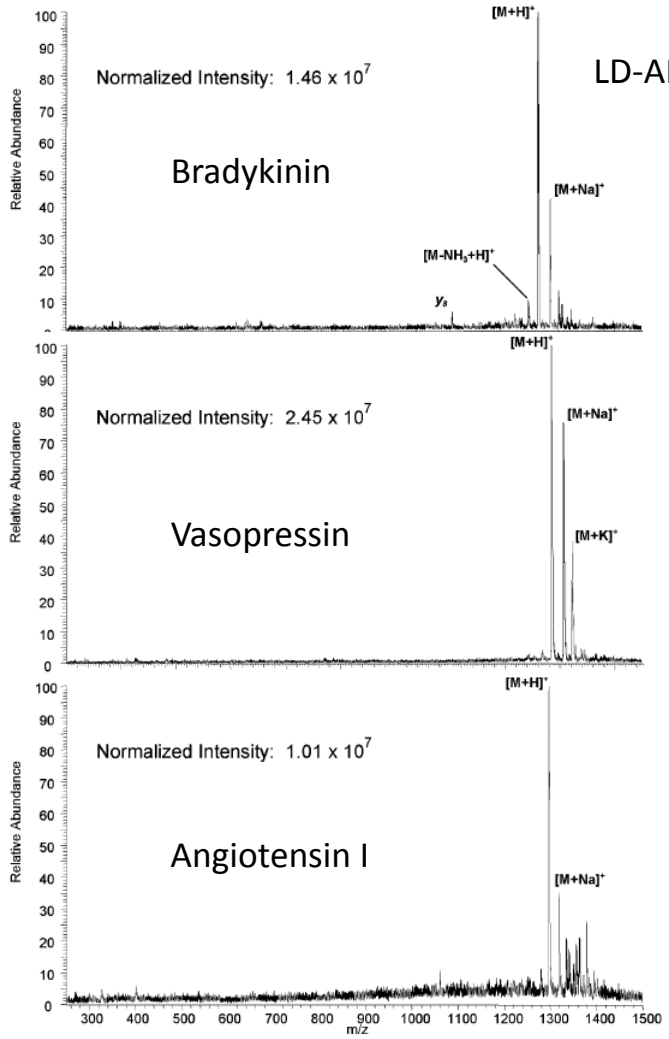
LD-APCI, IR-LAMICI and LD-FAPA

- Applications:

Peptideomics

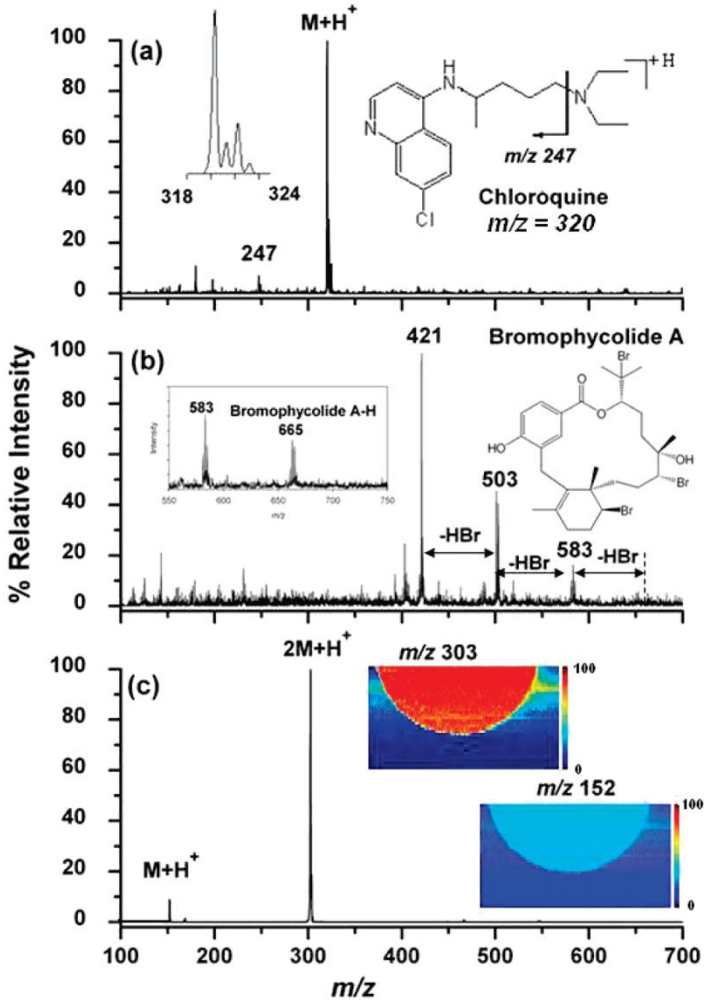
Anal. Chem. 2002, 74, 5600-5605

LD-APCI MS



Pharmaceutic

Anal. Chem. 2010, 82, 2178–2181



IR-LAMICI MS spectra of (a) a counterfeit artesunate antimalarial drug tablet; (b) a red macroalga, *Callophycus serratus*, and (c) a Tylenol tablet (325 mg of acetaminophen).

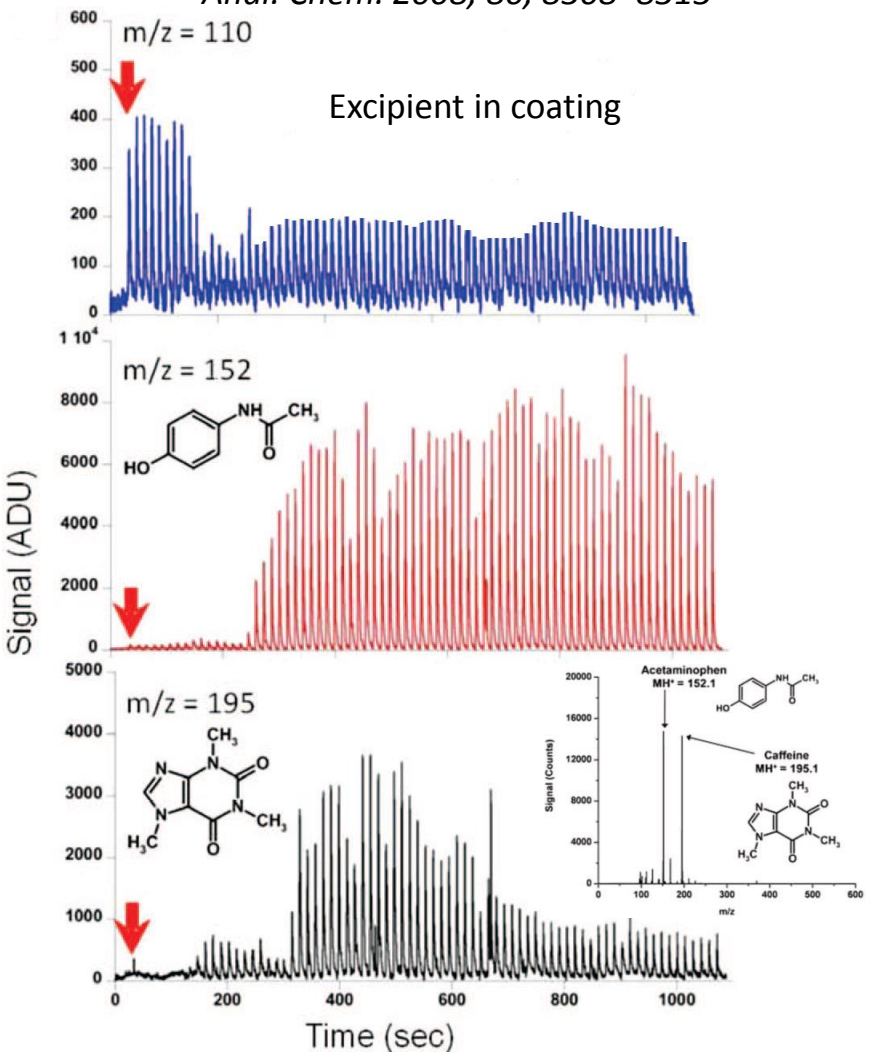
III-2) Laser Desorption/ablation

LD-APCI, IR-LAMICI and LD-FAPA

- Applications:

Pharmaceutical

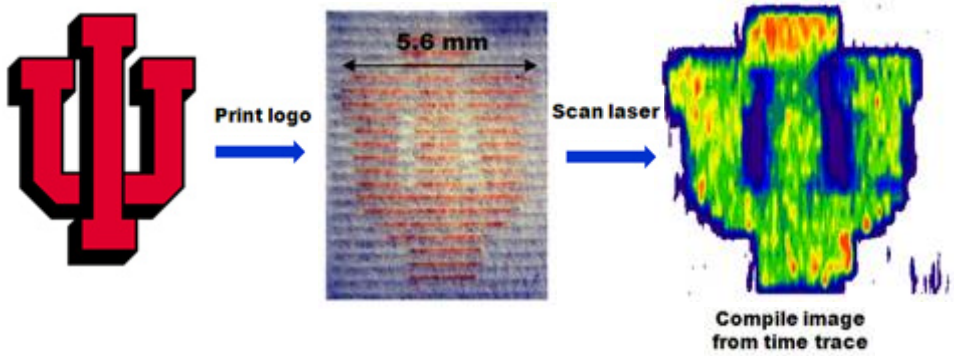
Anal. Chem. 2008, 80, 8308–8313



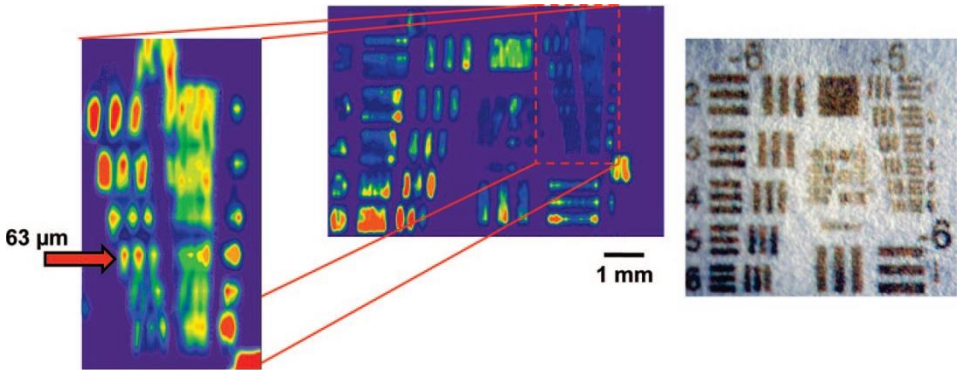
LA-FAPA depth profiling of an Excedrin tablet

Imaging analysis

Anal. Chem. 2008, 80, 8308–8313



LA-FAPA MS imaging of Indiana University logo printed on paper with caffeine-doped ink.



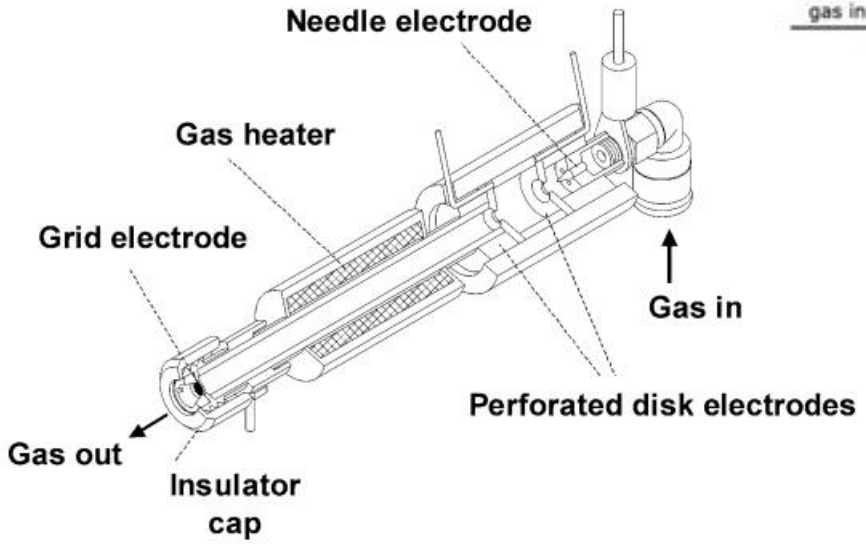
IR-LAMICI chemical images of the 1951 USAF resolution target (shown on right) printed with caffeine at 1200 dpi onto paper. Vertical and horizontal resolution are 178 and 63 µm.

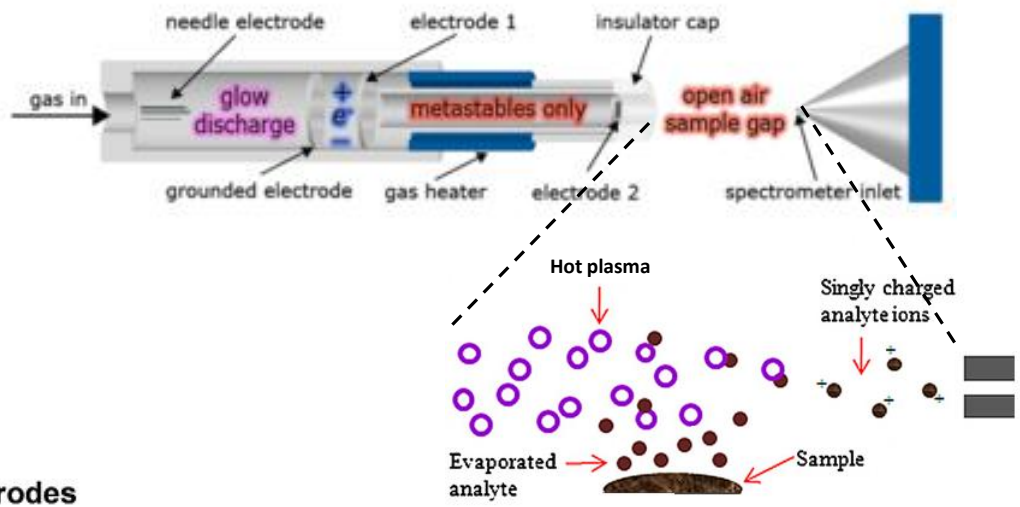
III-3) Thermal Desorption

Analytes are desorbed from the surface by heating or pyrolysis

Direct Analysis in Real Time (DART)

Anal. Chem., 2005, 77, 2297–2302



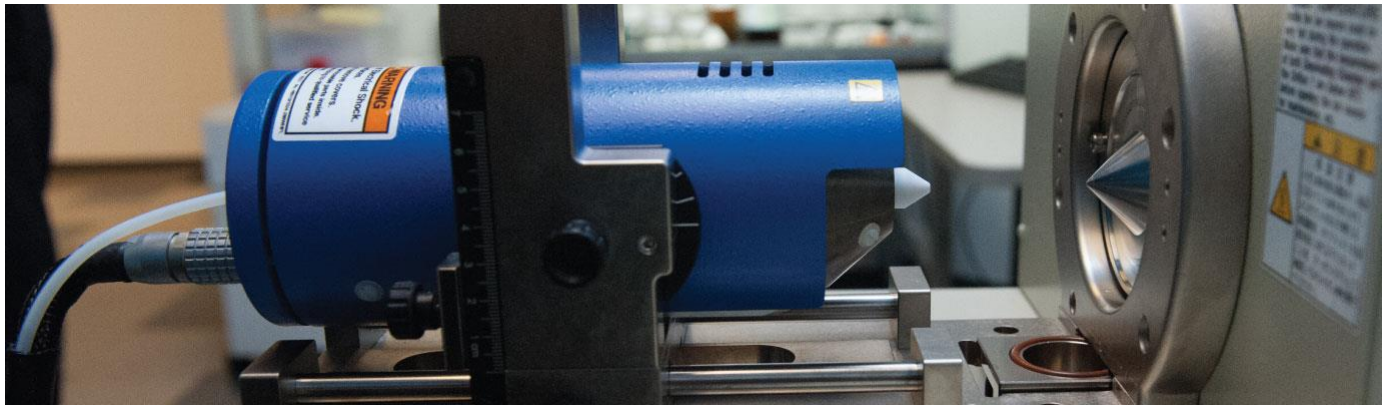


- Corona discharge generates plasma species. Ions from the plasma are removed; only metastable atoms are kept.
- Resistively heated gas stream thermally desorbs analytes.
- Analytes are ionized directly by metastables or via undirect ion/molecule reactions.

III-3) Thermal Desorption

Direct Analysis in Real Time (DART)

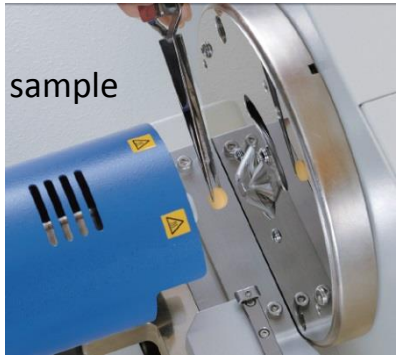
- Instrumentation and operating parameters:



He or N_2 nebulizer gas (~ 1L/min)
Corona discharge voltage = ± 1 to 5 kV
The potential of the second electrode (to remove ions) typical ± 100 V to ± 250 V
Gas temperature up to 250 °C
Typical DART/Sample/Orifice distance is 5 to 25 mm
Sample placed in «transmission» or «glancing» geometry

Liquid sample

Solid sample



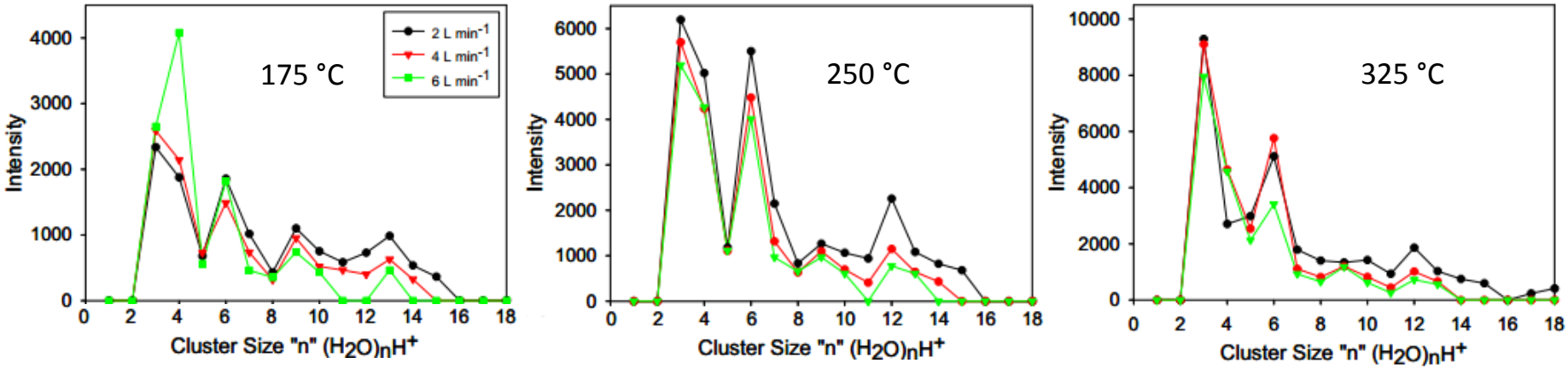
Powder

III-3) Thermal Desorption

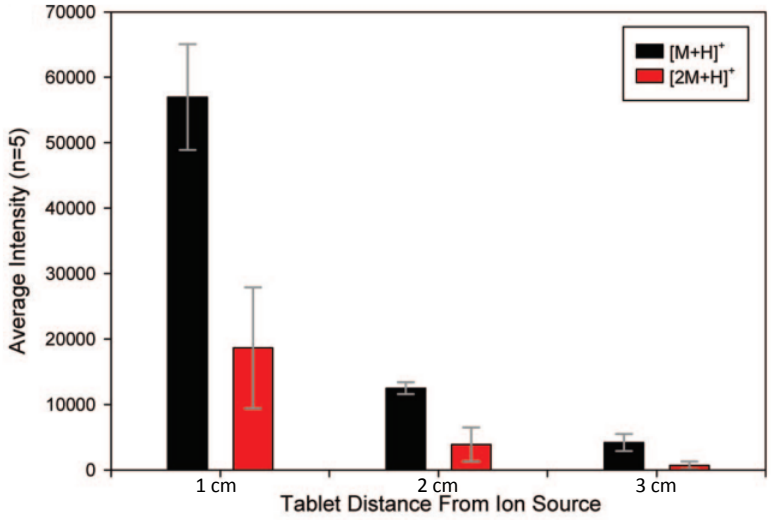
Direct Analysis in Real Time (DART)

- Characterization:

J Am Soc Mass Spectrom 2010, 21, 855– 863



Influence of DART temperature and discharge gas flow rate



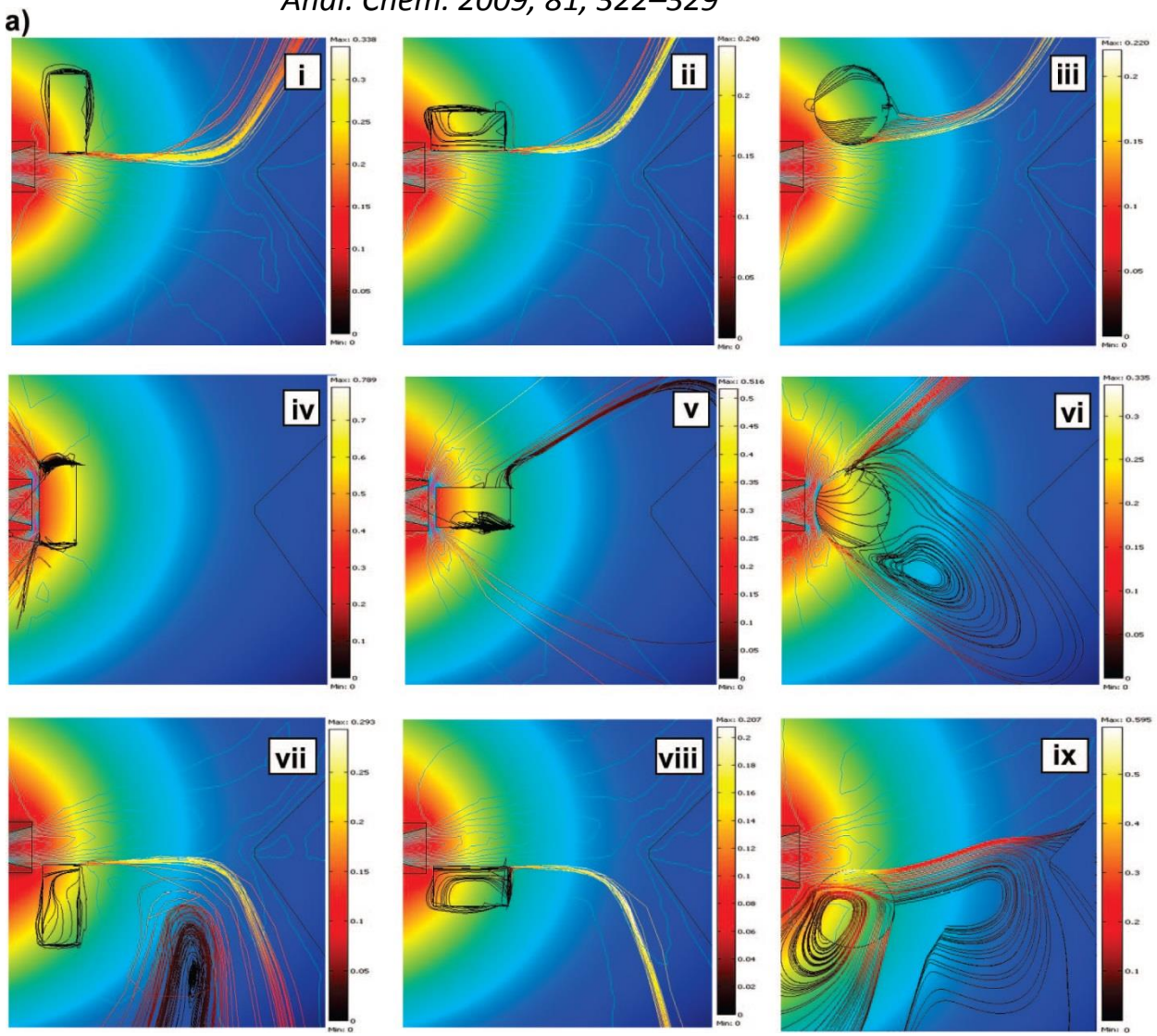
Distance-dependent sensitivity of a Tylenol tablet on both the acetaminophen protonated molecule and dimer

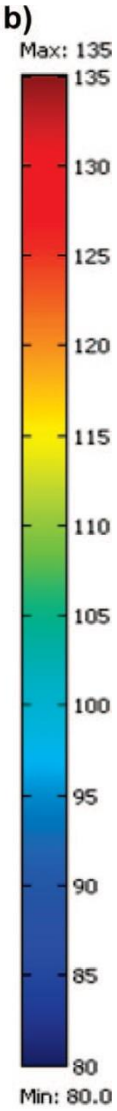
III-3) Thermal Desorption

Direct Analysis in Real Time (DART)

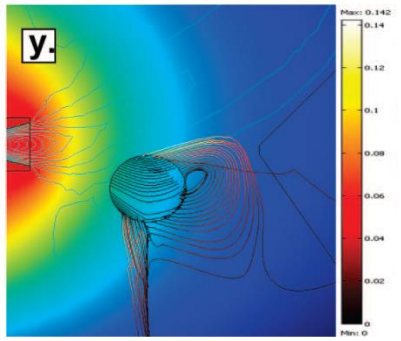
- Characterization:

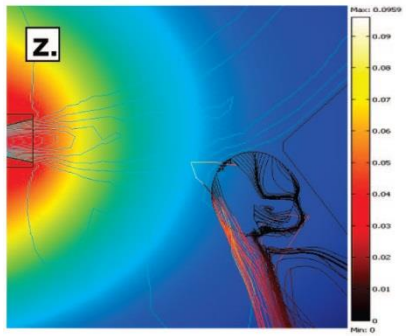
Anal. Chem. 2009, 81, 322–329





Particle desorption and transport by heated gas





III-3) Thermal Desorption

Direct Analysis in Real Time (DART)

- Mechanisms of ion formation:

i) Penning ionization: $M + R^{*} \rightarrow M^{+\bullet} + R + e^{-}$

ii) When He is used, positive ion formation involves formation of ionized water clusters followed by proton transfer reactions:

$$He^{*}_{(g)} + nH_2O_{(g)} \rightarrow He_{(g)} + (H_2O)_{n-1}H^{+}_{(g)} + OH^{-}_{(g)}$$

$$(H_2O)_m H^{+}_{(g)} + M_{(s/g)} \rightarrow MH^{+}_{(g)} + nH_2O_{(g)}$$

iii) Charge exchange reactions with oxygen molecular ions:

positive mode $O^{+\bullet}_{2(g)} + M_{(g)} \rightarrow M^{+\bullet}_{(g)} + O_{2(g)}$

negative mode $e^{-} + O_{2(g)} \rightarrow O^{-}_{2(g)}$

$$O^{-}_{2(g)} + M_{(g)} \rightarrow M^{-}_{(g)} + O_{2(g)}$$

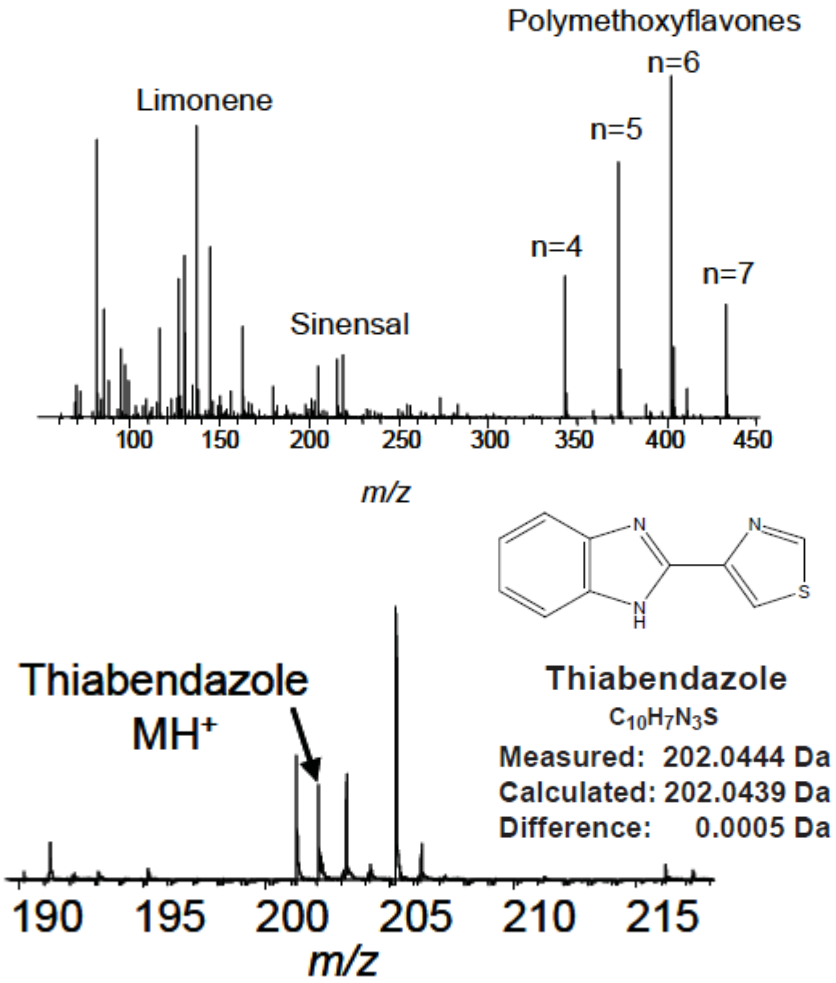
III-3) Thermal Desorption

Direct Analysis in Real Time (DART)

- Applications:

Food Analysis

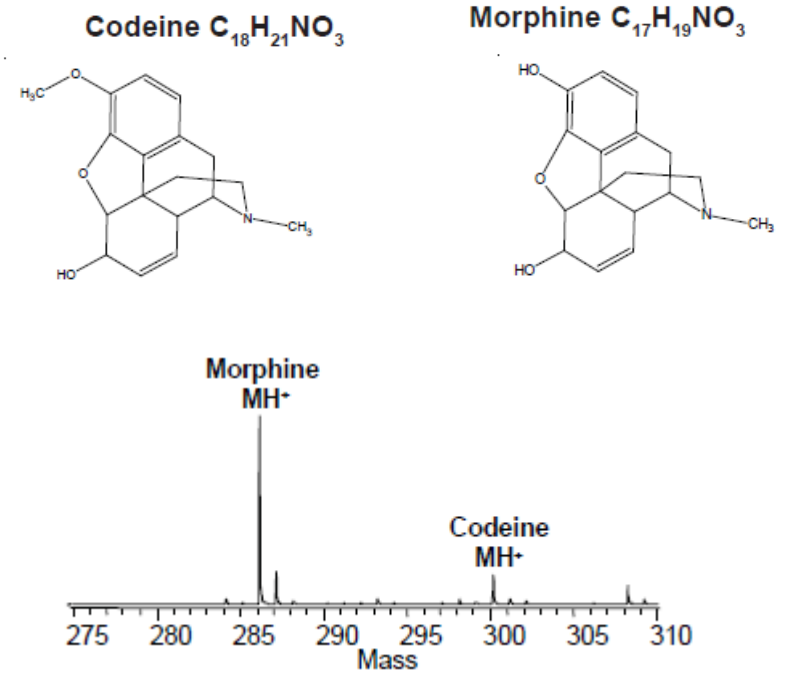
Rapid Commun. Mass Spectrom. 2011, 25, 127–139



DART MS spectra of orange peel

Food Analysis

J Forensic Sci. 2008, 96, 29-38



DART MS spectrum of poppy seed showing traces of opiate

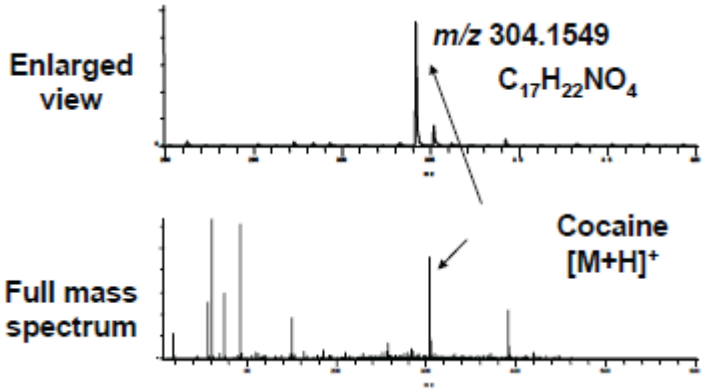
III-3) Thermal Desorption

Direct Analysis in Real Time (DART)

- Applications:

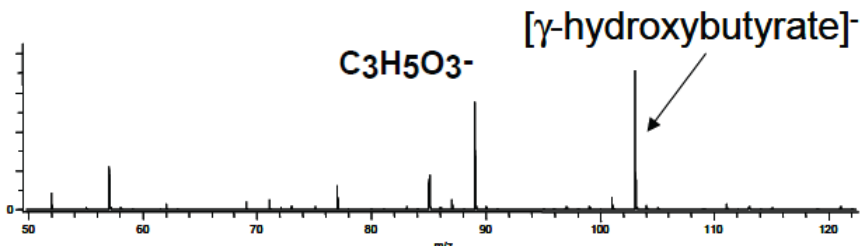
Forensics

J Am Soc Mass Spectrom 2009, 20, 891– 899



DART MS spectrum of 1$ bill

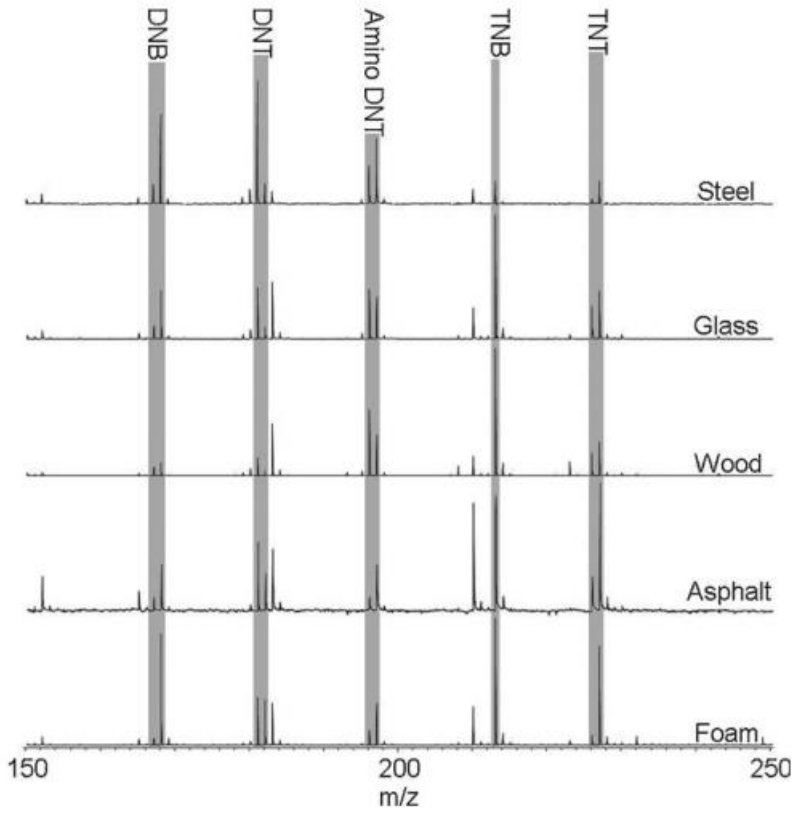
J Forensic Sci. 2009, 54, 370-375



DART(-) MS spectrum of GHB spiked in Ocean Spray Cranberry Juice

Homeland Security

Propellants Explos. Pyrotech. 2010, 35, 446 – 451



DART MS spectra of explosives on different surfaces

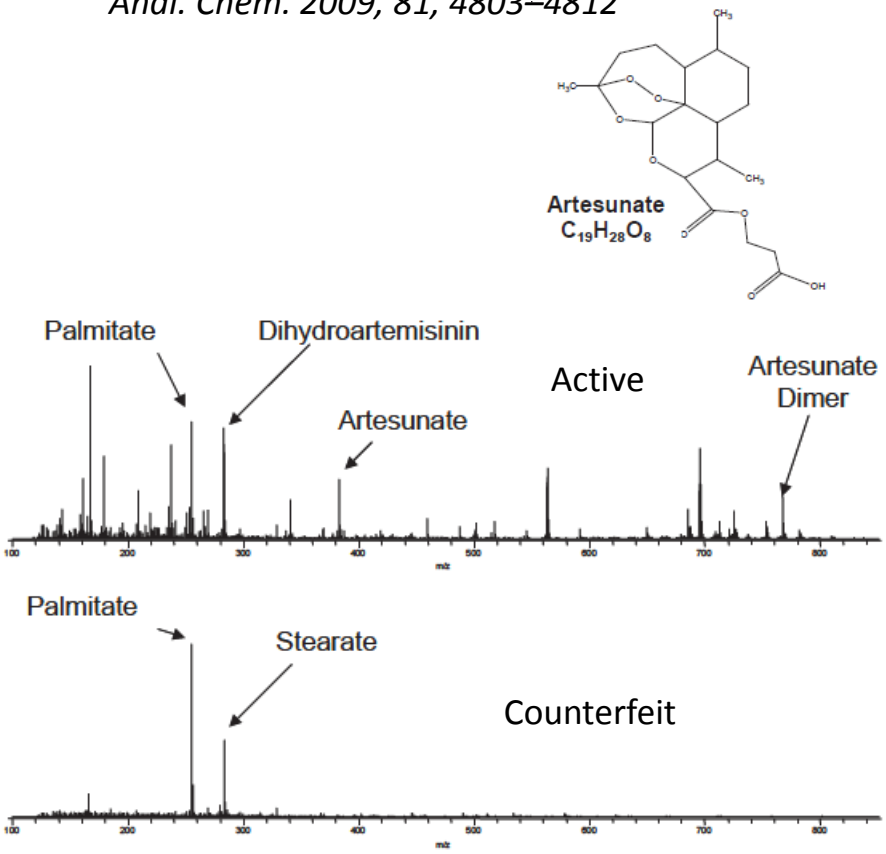
III-3) Thermal Desorption

Direct Analysis in Real Time (DART)

- Applications:

Pharmaceutical

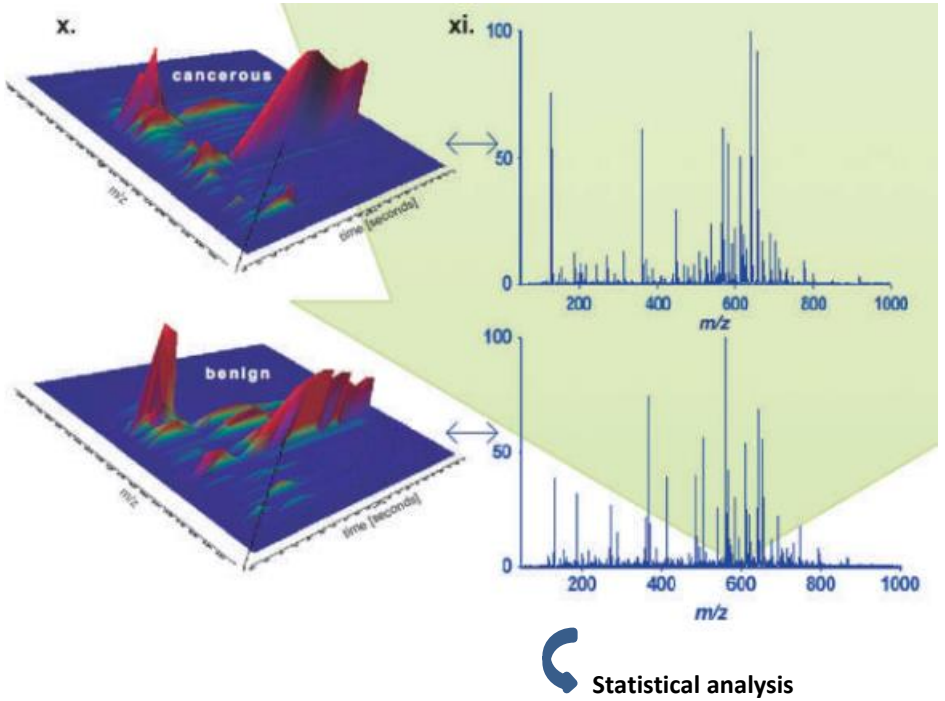
Anal. Chem. 2009, 81, 4803–4812



DART(-) MS spectra of anti-malarial drugs “Guilin B” pills

Metabolomic

Cancer Epidemiol. Biomarkers Prev. 2010, 19, 2262–2271

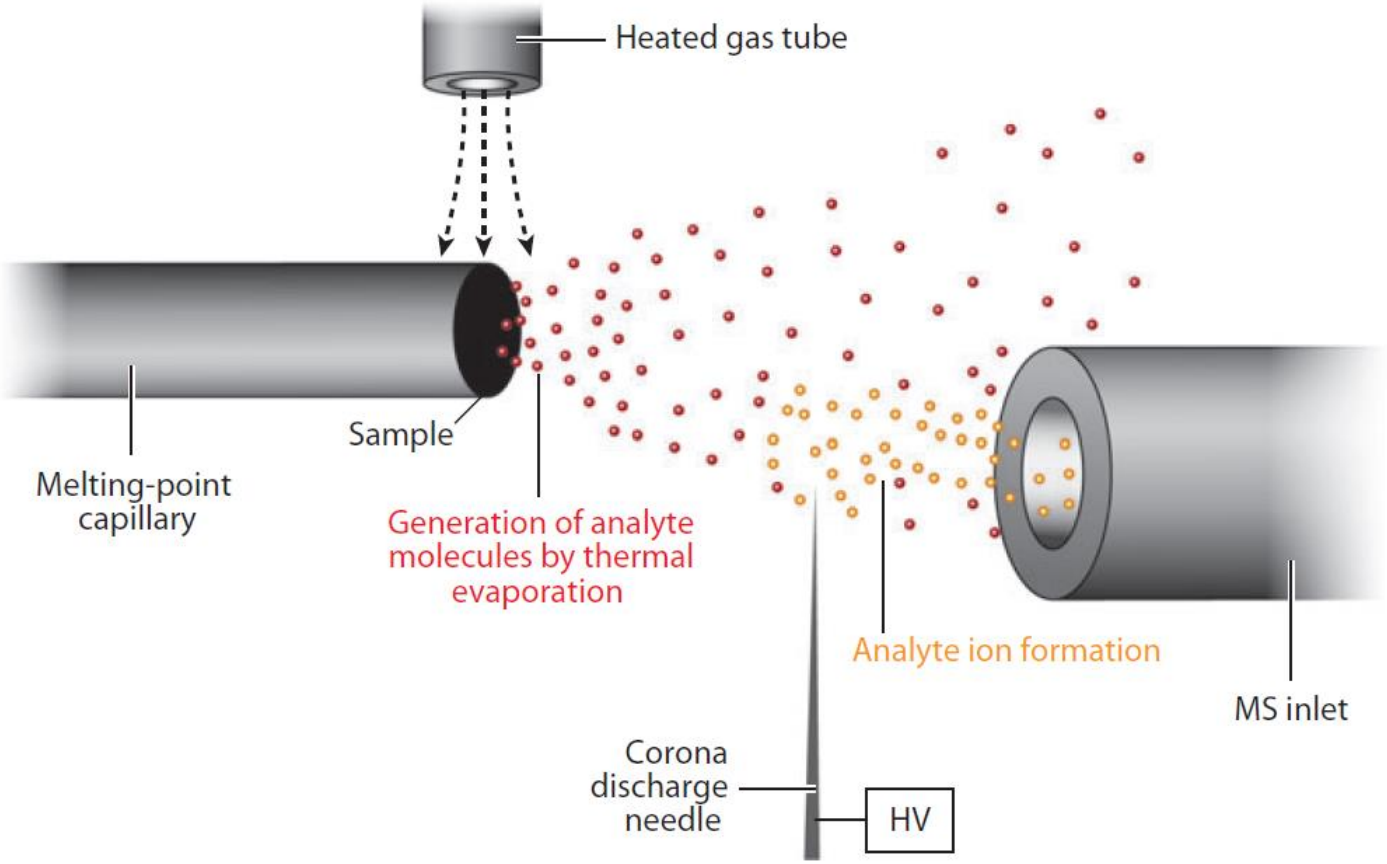


DART MS spectra of serum from women with ovarian cancer or healthy women

III-3) Thermal Desorption

Atmospheric Pressure Solids Analysis Probe (ASAP)

Anal. Chem. 2005, 77, 7826-7831



- Analytes are evaporated from the capillary surface by a heated gas.
- Stream of hot gas directs desorbed analytes to the MS inlet.
- Analytes are ionized by corona discharge by applying HV on a needle.

III-3) Thermal Desorption

Atmospheric Pressure Solids Analysis Probe (ASAP)

- Characteristics:

Classical APCI source used without solvent
Hole to plug the melting-point capillary with sample on it
N_2 gas flow rate : 0.4 L/min
Gas temperature ~ 300-400°C
Corona discharge of ± 3-6 kV

- Mechanisms of ion formation:

* Analytes are put into the gas phase by thermal desorption.
* Corona discharge on the N2 gas stream containing analytes allows ionization of the analytes molecules.
* Processes similar to APCI.

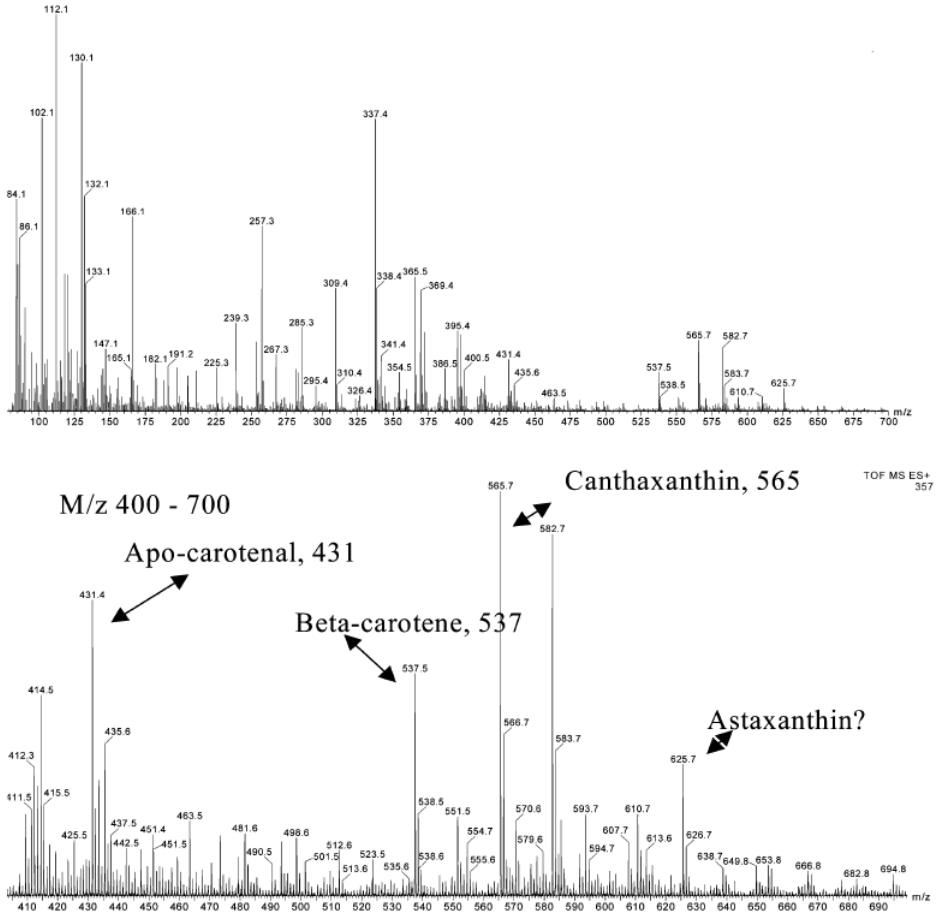
III-3) Thermal Desorption

Atmospheric Pressure Solids Analysis Probe (ASAP)

- Applications:

Food Analysis

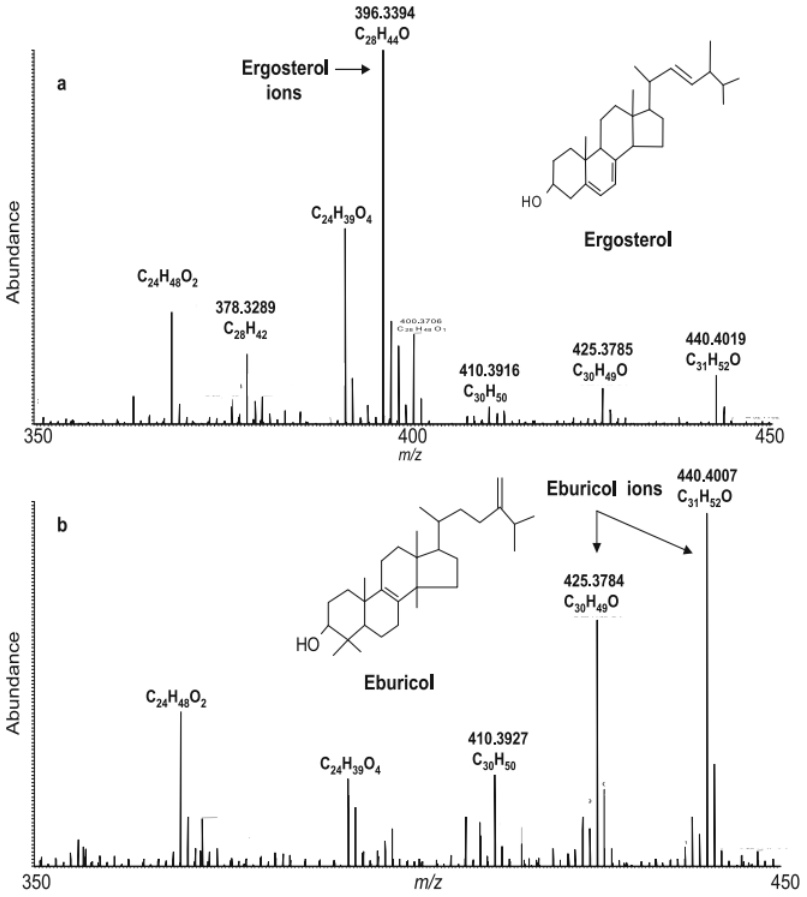
Anal. Chem. 2005, 77, 7826-7831



ASAP MS spectra of fresh spinach leaf

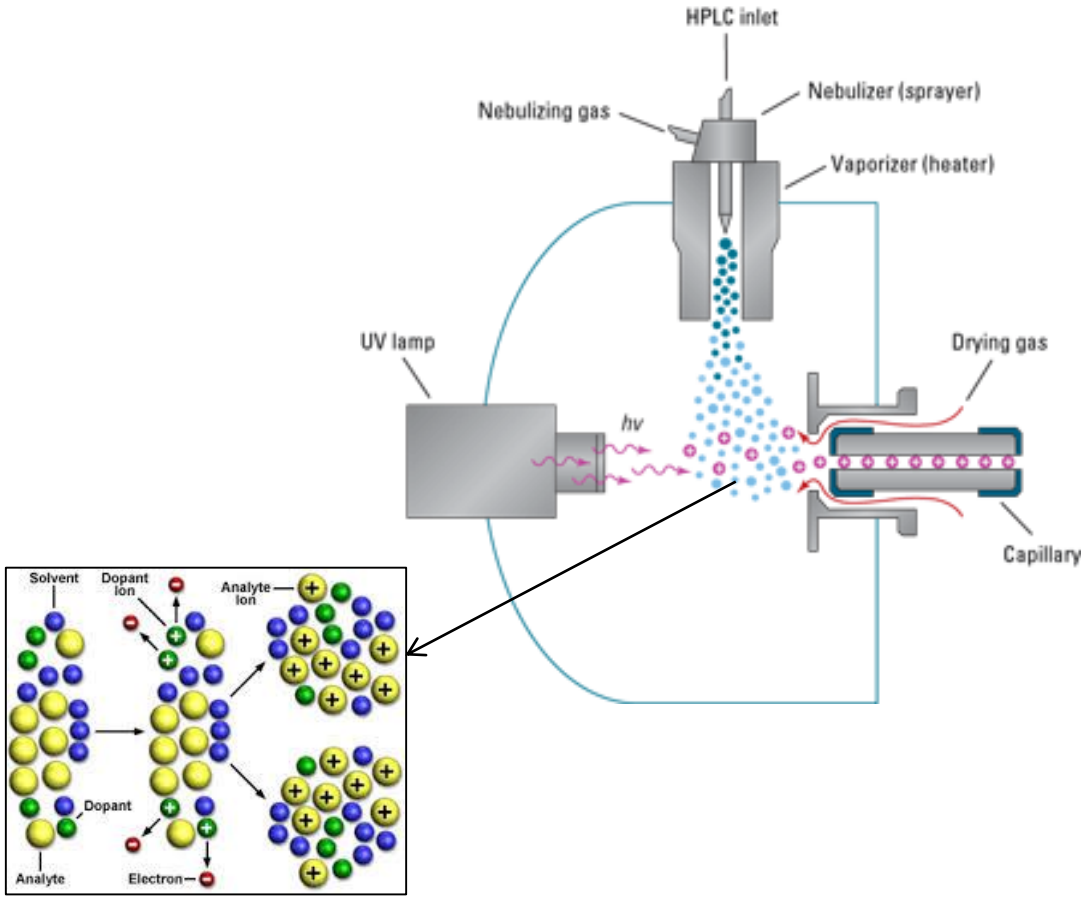
Cell analysis

J Am Soc Mass Spectrom 2007, 18, 1274 –1278



ASAP MS spectra of (a) untreated fungal cells (b) cells treated with the triazole inhibitor of C14-demethylase (4 M) added during growth.

IV- APPI-based ambient ionization techniques

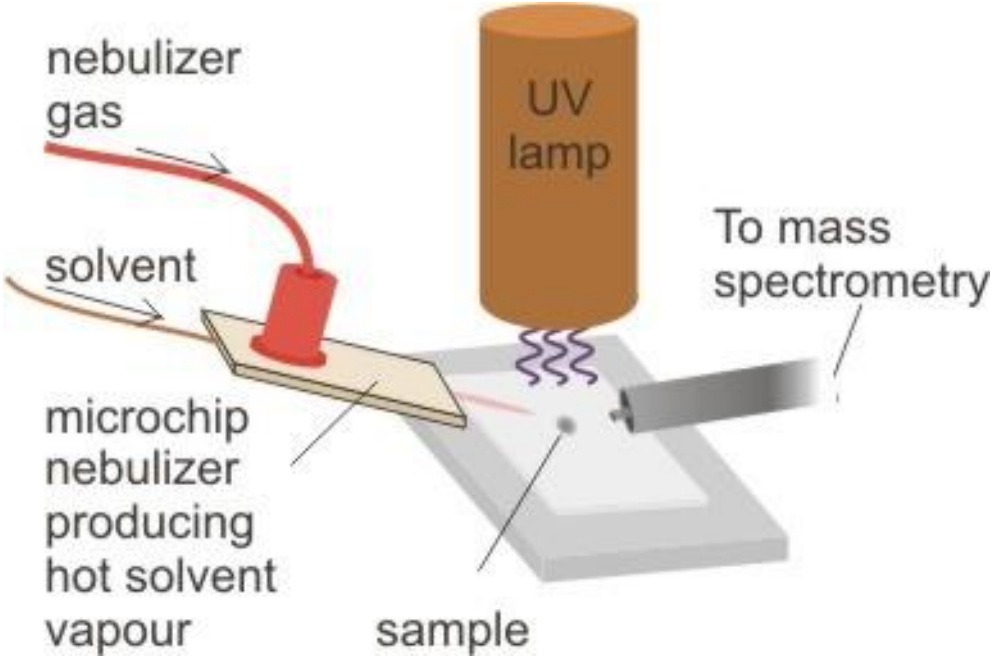


In ambient ionization techniques using this mode of ionization, **UV light** allows the **post-ionization** of the desorbed analytes (APPI processes).
Direct analysis of volatile sample species with a wide range of polarities from surface.

IV- 1) Thermal/chemical desorption

Desorption Atmospheric Pressure Photolonization (DAPPI)

Anal. Chem. 2007, 79, 7867-7872



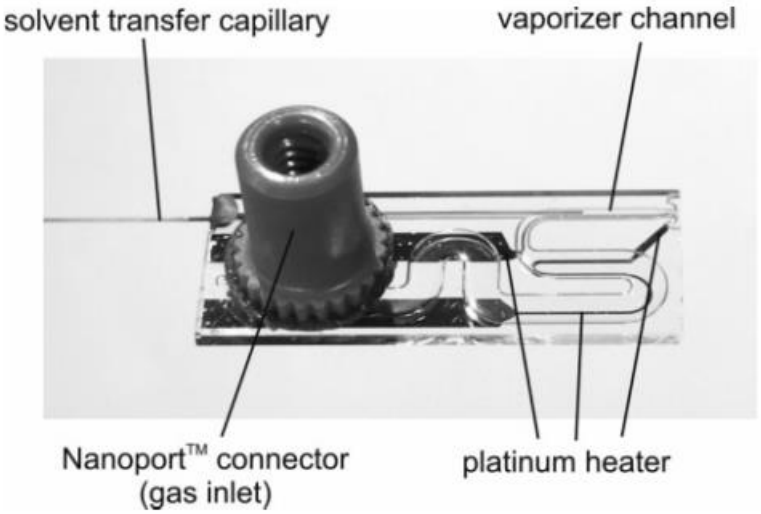
- Heated nebulizer gas evaporates solvent.
- Neutral hot vapor solvent jet impinges on the surface.
- Analytes are extracted from the surface by thermal desorption.
- Gas phase neutral analytes ionize directly by photon absorption or react with ionized solvent species.

IV- 1) Thermal/chemical desorption

Desorption Atmospheric Pressure Photolonization (DAPPI)

- Characteristics:

A nebulizer µchip for heated solvent/gas mixture. 50 µm diameter vaporizer channel
Microchip nebulizer is at an angle of ~45° and ~10 mm above the sampling surface



Solvent flow rate : 10 µL/min
Solvent mixture: adapted to the analyte polarity (± dopant : toluene or acetone)
N_2 nebulizer gas temperature ~ 150-300°C, and gas flow rate 180 mL/min
UV krypton lamp (10 eV) placed at 90° and ~10 mm above the sampling surface

IV- 1) Thermal/chemical desorption

Desorption Atmospheric Pressure Photolonization (DAPPI)

- Mechanisms of ion formation:

* Analytes are thermally desorbed by the hot solvent vapor jet.
* Photon absorption by the analyte molecule, leading to electron ejection, forming a molecular radical cation $M^{\bullet+}$

$$M + h\nu \rightarrow M^{\bullet+} + e^{-}$$

* Subsequent reaction of abstraction of a hydrogen atom from the abundant solvent to form the stable $[M+H]^{+}$ cation.

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

* Dopant (D) is first photo-ionized and then $D^{\bullet+}$ ionizes analytes via proton or electron transfers.

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

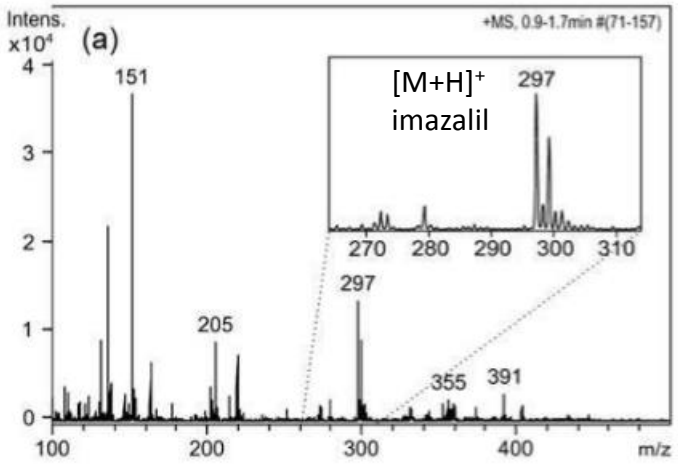
IV- 1) Thermal/chemical desorption

Desorption Atmospheric Pressure Photolonization (DAPPI)

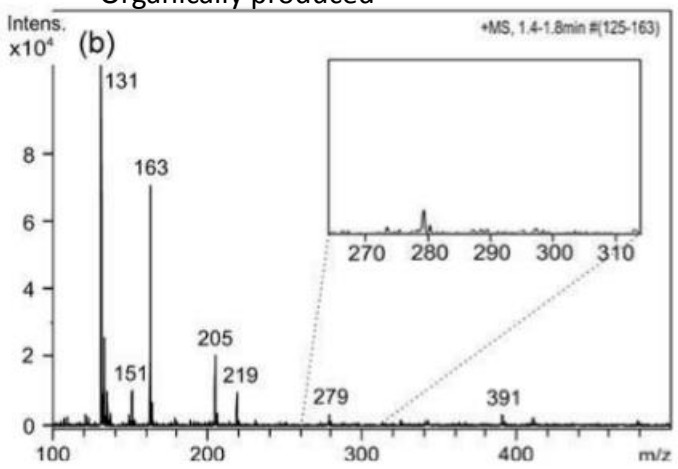
- Applications:

Food Analysis

Rapid Commun. Mass Spectrom. 2010; 1343–1350



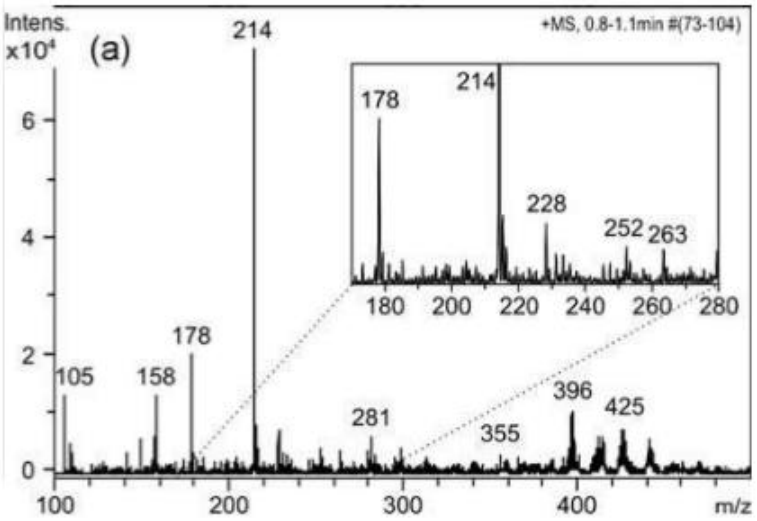
Organically produced



DAPPI MS spectra of orange peel with acetone dopant

Environmental Analysis

Rapid Commun. Mass Spectrom. 2010; 1343–1350



DAPPI MS spectra of soil spiked with PAHs peel with toluene dopant → $M^{\cdot+}$ species

LOD 100 pg

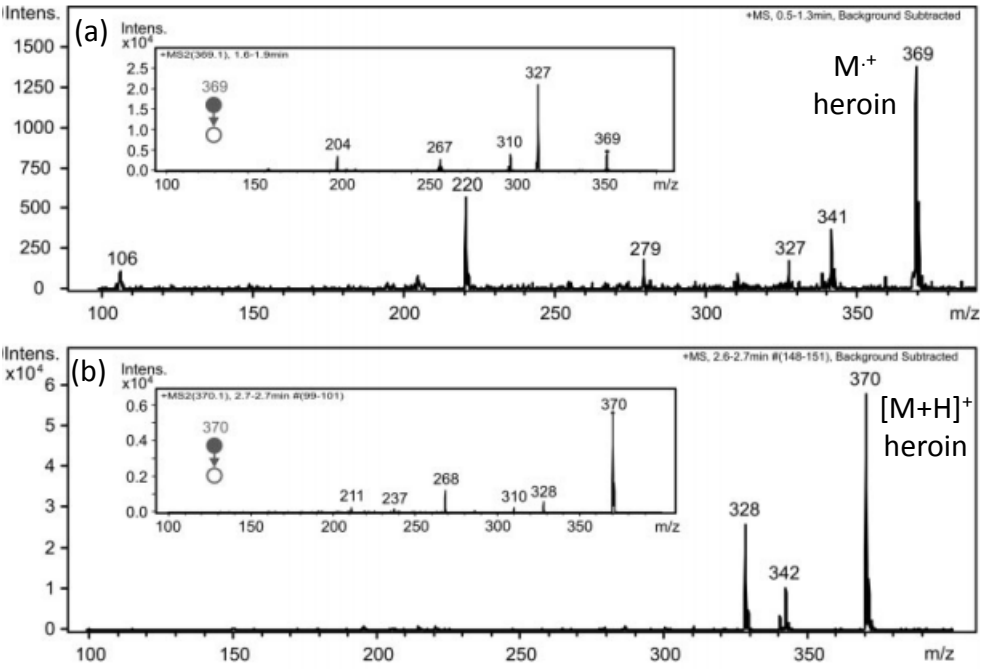
IV- 1) Thermal/chemical desorption

Desorption Atmospheric Pressure Photolonization (DAPPI)

- Applications:

Forensics

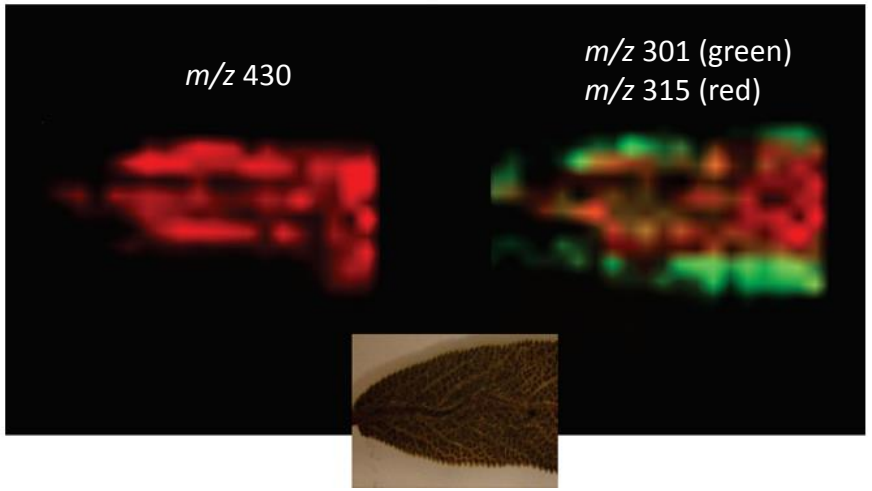
Rapid Commun. Mass Spectrom. 2009; 1401–1404



DAPPI MS spectra of illegal drugs with (a) toluene and (b) acetone dopant

Imaging

Anal. Chem. 2009, 81, 8479–8487



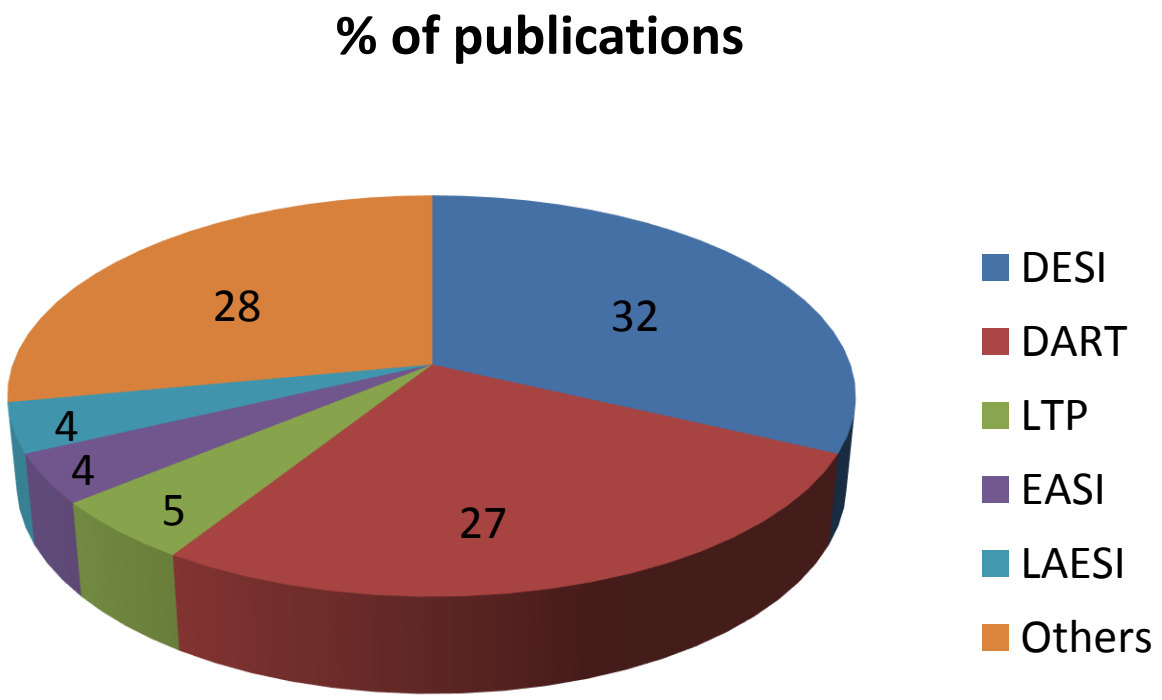
DAPPI MS chemical images of phyto-compounds in sage leaf

Spatial resolution 1 mm

V- Comparison of techniques

Technique	Surface sampling process	Ionization process	Highest mass	Analyte polarity	Sample state	Detection limit/Sample	Dynamic range
ASAP	Thermal	APCI	700 Da	Polar, non-polar	Solid, liquid	N/A	N/A
DAPCI	Direct	APCI	600 Da	Polar	Solid, liquid	1 $ng.cm^{-2}$/TATP	10^3
DAPPI	Thermal	APPI	600 Da	Polar, non-polar	Solid	56-670 fmol/Verapamil	N/A
DART	Thermal	APCI	~ 1kDa	Polar, non-polar	Solid, liquid, gas	7 fmol/Ethylpalmitate	10^3
DBDI	Direct	APCI	400 Da	Polar, non-polar	Solid, liquid	3.5 pmol/Alanine	10^2
DCBI	Direct	APCI	600 Da	Polar, non-polar	Solid, liquid	10 pg/Atrazine	10^3
DESI	Direct	ESI	66 kDa	Polar	Solid, liquid	100 pg/PETN	10^5
EADESI	Direct	ESI	24 kDa	Polar	Solid, liquid	10 pmol/Maltoheptaose	N/A
EASI	Direct	ESI	1 kDa	Polar	Solid, liquid	0.01 ppm/Nicotine	10^3
ELDI	Laser	ESI	66 kDa	Polar	Solid, liquid	30 fmol/Cytochrome C	10^4
ESA-Py	Thermal	ESI	1.5 MDa	Polar	Solid, liquid	1 ppm/dimethylated PDA	N/A
FAPA	Direct	APCI	38 kDa	Polar, non-polar	Solid, liquid	60 fmol/Acetophenone	N/A
FD-ESI	Gas stream	ESI	17 kDa	Polar	Liquid, gas	N/A	N/A
IR-LAMICI	Laser	APCI	665 Da	Polar, non-polar	Solid, liquid	30 pg/Acetaminophen	N/A
LAESI	Laser	ESI	66 kDa	Polar	Solid, liquid	8 fmol/Verapamil	10^4
LD-APCI	Laser	APCI	1.5 kDa	Polar, non-polar	Solid, liquid	N/A	N/A
LIAD-ESI	Laser	ESI	66 kDa	Polar	Solid, liquid	N/A	N/A
LTP	Direct	APCI	500 Da	Polar, non-polar	Solid, liquid, gas	500 fg/TNT	10^4
MALDESI	Laser	ESI	20 kDa	Polar	Solid, liquid	13 fmol/Angiotensin I	N/A
ND-EESI	Gas stream	ESI	1 kDa	Polar	liquid, gas	N/A	N/A
TPD-ESI	Thermal	ESI	379 Da	Polar	Solid, liquid	0.1 nmol/TNT	N/A

V- Comparison of techniques

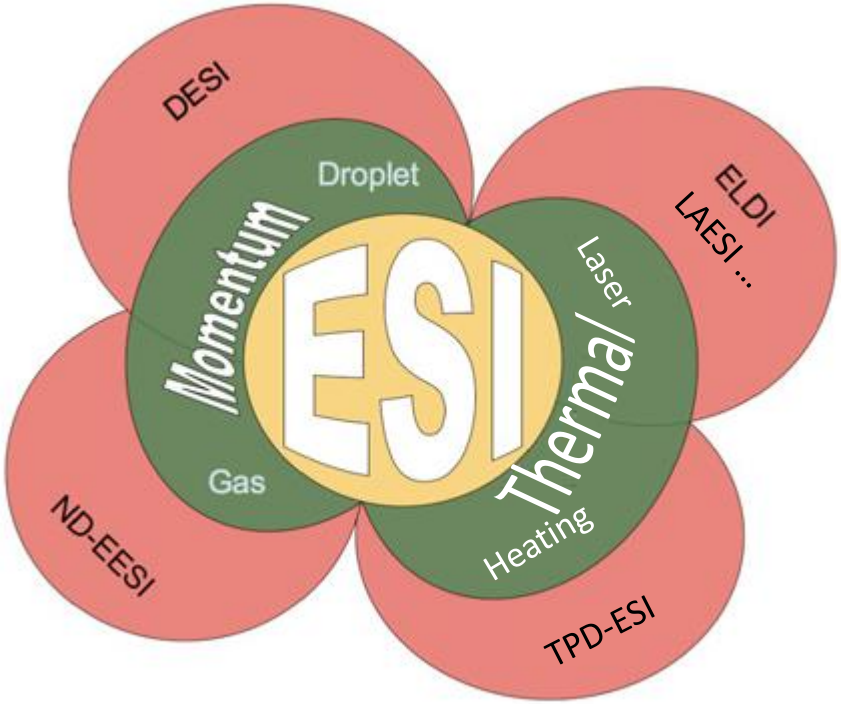


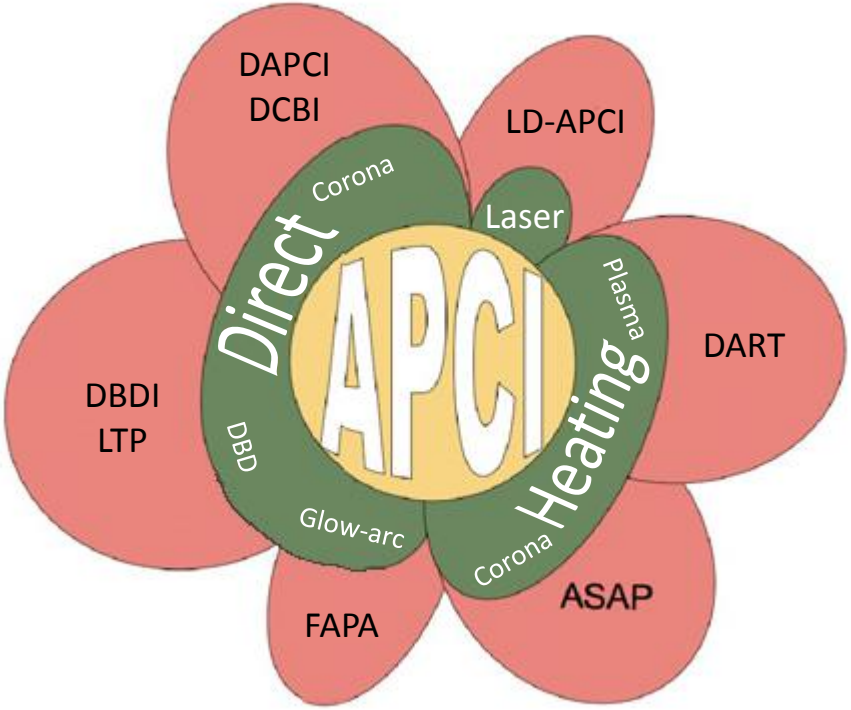
2009-2016

VI- Conclusions

- Ambient ionization MS techniques make use of well-established ionization principles such as ESI, chemical ionization or photo-ionization but in an open air which allows unique experiments to be performed with no or little sample preparation.

- These techniques employ various methods for the sampling of solids, liquids and gas through desorption (thermal evaporation, laser ablation , pneumatic nebulization or direct impinging on the surface with charged and metastable species).





VI- Conclusions

- There is a considerable overlap between various ambient ionization techniques because most of them combine a limited number of sample-introduction, desorption and ionization processes; nomenclature is confusing. Unifying naming may be in place for future work.

- Ambient ionization has already been an important part of modern MS, but much remains to be learned about the fundamental mechanisms.

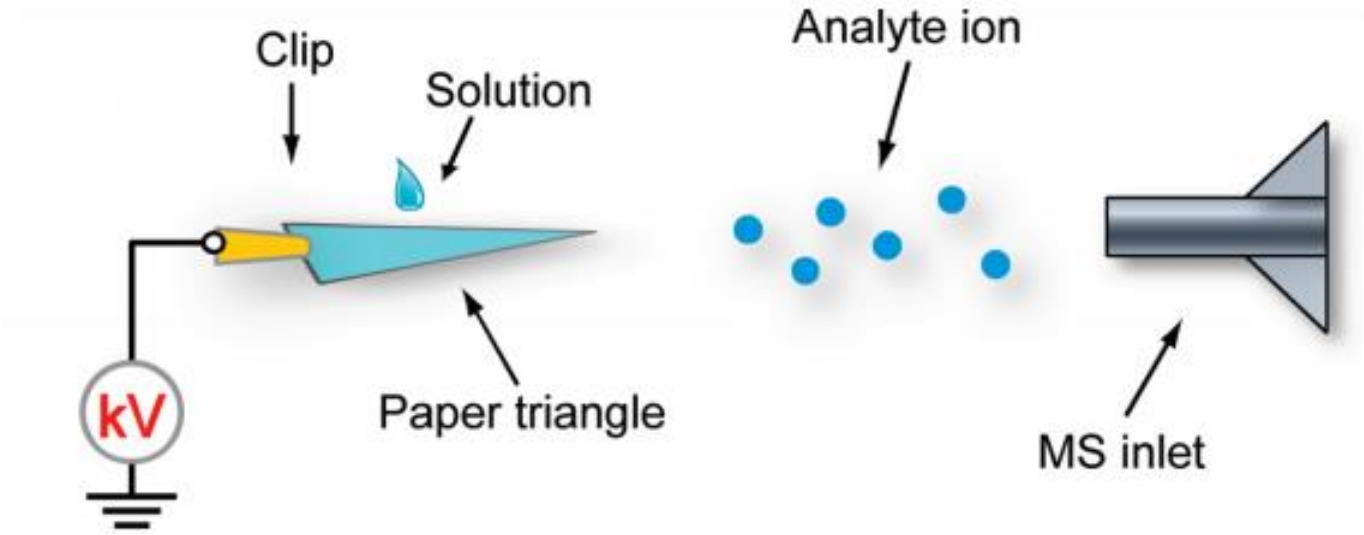
Reviews:

Mass Spectrometry Reviews, 2015, 34, 449–473
Analytical Chemistry 2011, 83, 4508–4538
Analytica Chimica Acta 2011, 702, 1– 15
Analyst, 2010, 135, 669–681
Annual Review of Analytical Chemistry 2010. 3:43–65
Trends in Analytical Chemistry 2008, Vol. 27, 284-289

….. Direct Ionization

Paper Spray Ionization (PSI)

Anal. Chem. 2010, 82, 2463–2471



- Analytes spotted or wiped on triangle shaped substrate.
- Substrate connected to a high voltage and wetted with solvent.
- Electrospray plume containing the analytes is formed at the tip of the substrate.

….. Direct Ionization

Paper Spray Ionization (PSI)

- Characteristics:

Substrate triangular shape: 10 mm long, 5 mm wide at base)
High voltage ± 4.5-5 kV
Solvent mixture: usually MeOH/water 1:1 but can be adapted to the analyte polarity
Substrate: filter papers, glass microfiber filter paper, chromatography paper, tissue, leaves…
Substrate at ~1 mm in front of the MS inlet

- Mechanisms of ion formation:

* Analytes are dissolved by the solvent.
* ESI droplets containing the analytes are formed from Coulombic forces as charge is accumulated at the tip of the substrate.
* Then, evaporation/fission of doplets similar to ESI.

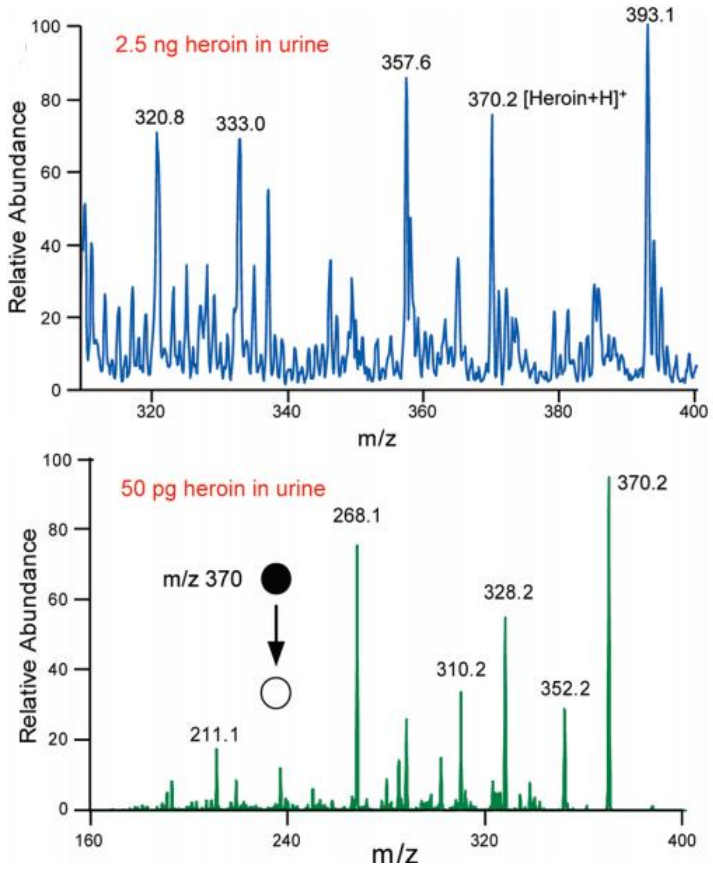
….. Direct Ionization

Paper Spray Ionization (PSI)

- Applications:

Drug analysis

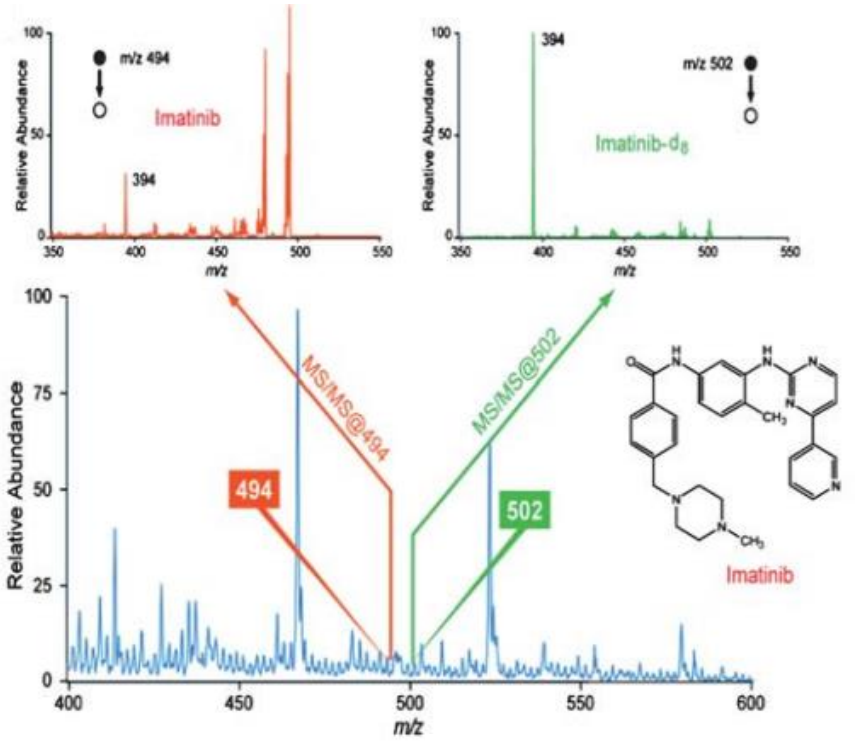
Anal. Chem. 2010, 82, 2463–2471



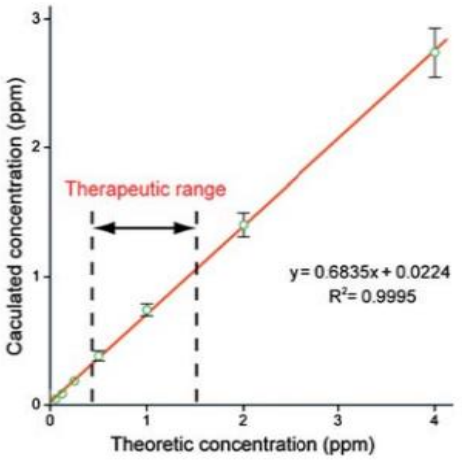
Paper Spray MS(/MS) spectra of dried urine with heroin spotted on filter paper. 10 µL of MeOH/water 1:1
LOD 125 ng/mL

Dried blood spot Analysis

Faraday Discuss., 2011, 149, 247–267



PaperSpray MS(/MS) spectra of imatinib and imatinib d8 in blood.



Calibration curve for imatinib in blood

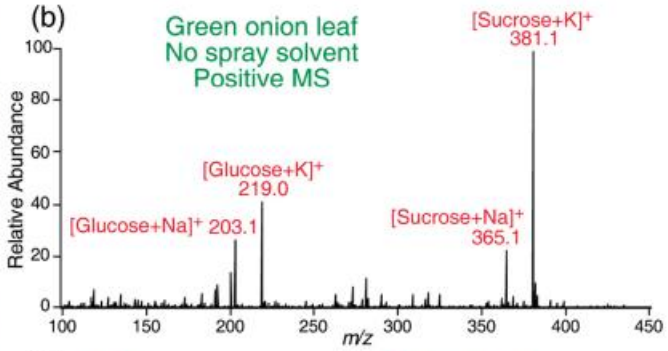
….. Direct Ionization

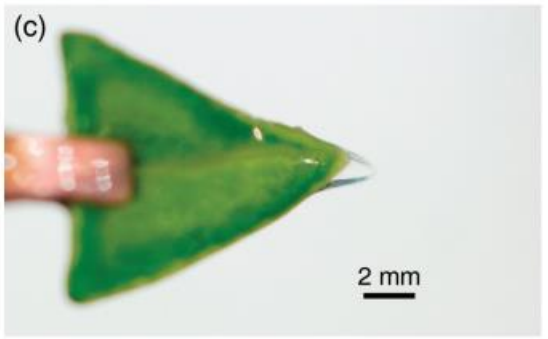
Paper Spray Ionization (PSI)

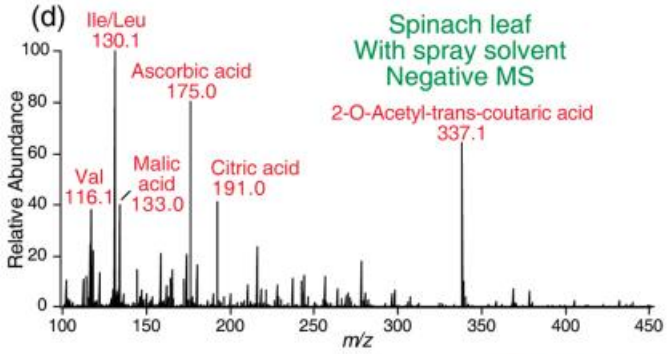
- Applications:

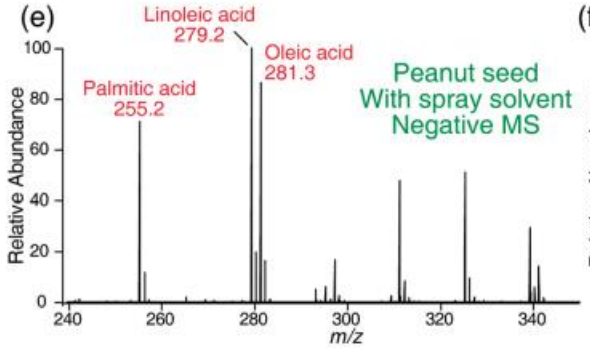
Leaves Analysis

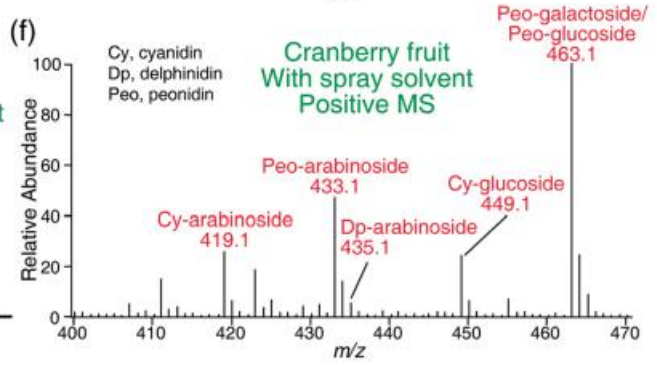
Anal. Chem. 2011, 83, 7608–7613

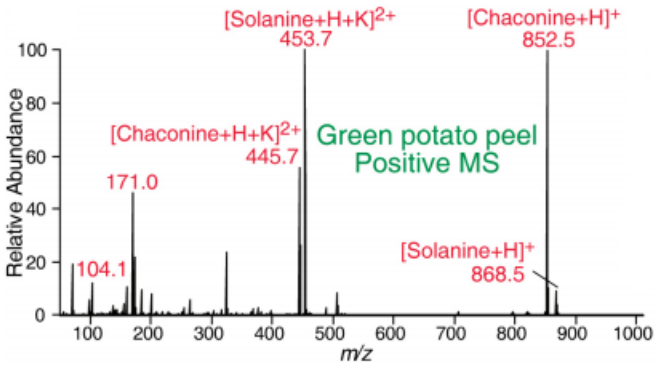


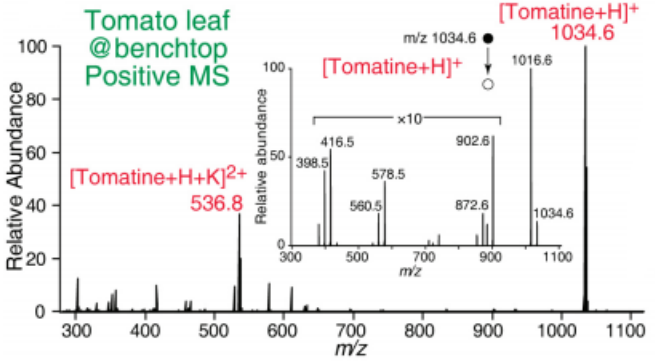










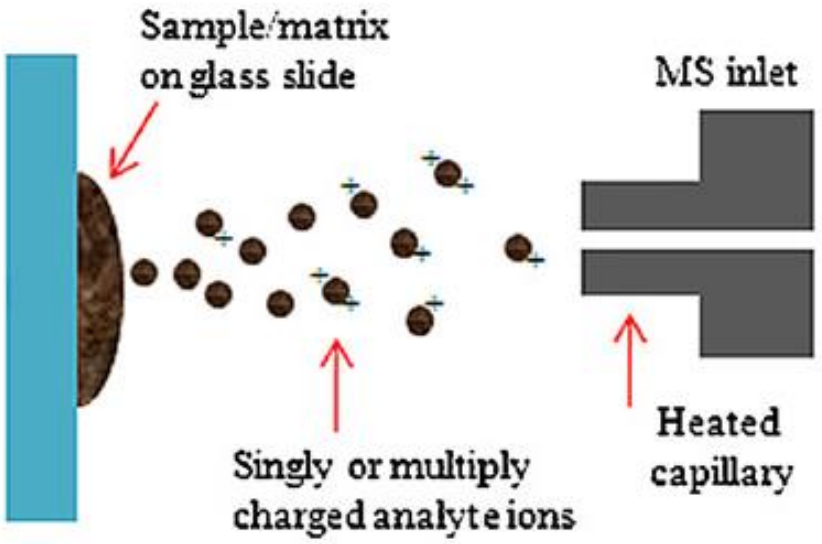


Leaf spray MS spectra

….. Direct Ionization

Matrix-Assisted Ionization (MAI)

Anal. Chem. 2010, 82, 9164–9168



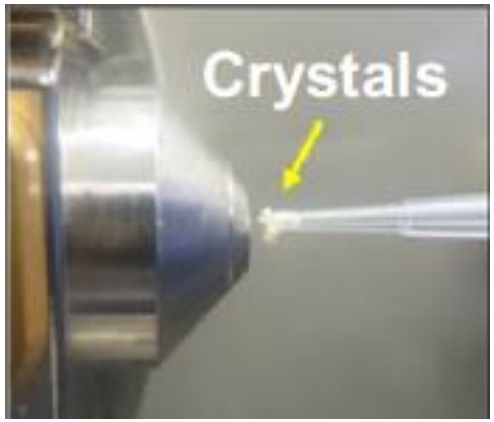
- Analytes and matricx on a surface.
- Differencial pressure between the atmosphere and the MS interface allows the evaporation analyte/matrix cluster.
- Multiply charged analytes ions are produced in the transfer capillary via collisions and charge transfer from the matrix.

….. Direct Ionization

Matrix-Assisted Ionization (MAI)

- Characteristics:

No need of laser or voltage
Analyte in solvent is mixed with the matrix and let dry (for recrystallyzation)
Matrices: MALDI Matrices (2,5-DHB dithranol CHCA 2,5-DHAP), multi-Substituted Nitro Compounds, Cyano Compounds, Linear and Non-Aromatic Compounds, Acetophenones, Alcohols, Heterocyclic and Anhydride Compounds, Heterocyclic and Anhydride Compounds….
Mixture put in front of the MS inlet
Transfer capillary temperature ~450 °C



Int. J. Mass Spectrom. 2015, 377, 532–545

- Mechanisms of ion formation:

* Analytes/matrix droplets are desorbed from the surface by the vaccum of the MS.
* Ionization of analytes occurs in the heated tranfer capillary due to statistical charging and rapid evaporation of the matrix.
* Coulombic explosion of charged analytes droplets allows formation of multiply charged analyte ions.

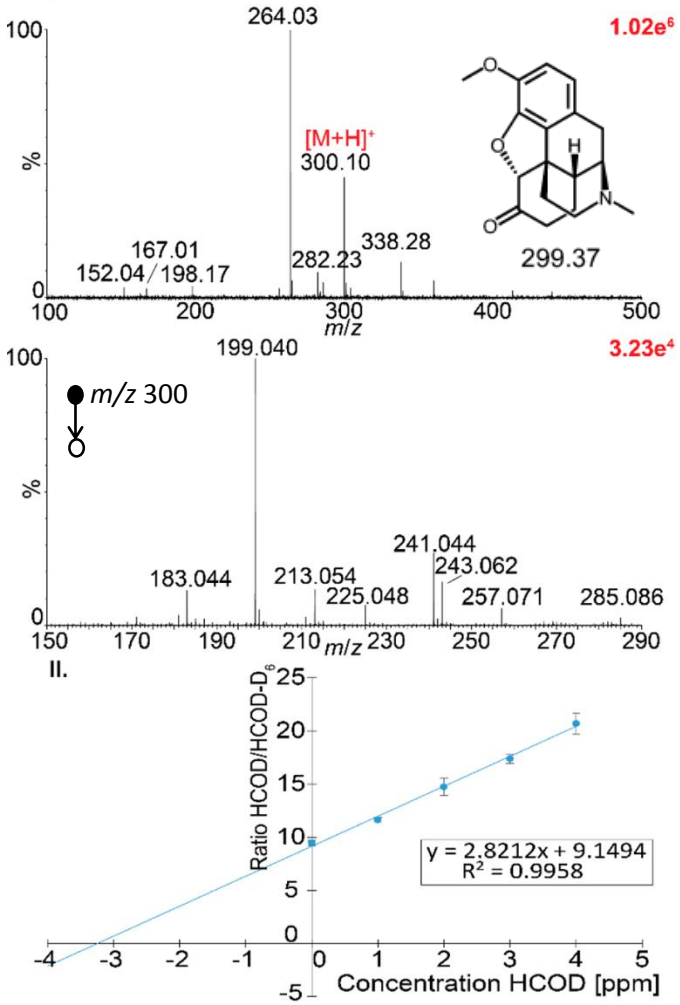
….. Direct Ionization

Matrix-Assisted Ionization (MAI)

- Applications:

Drug Analysis

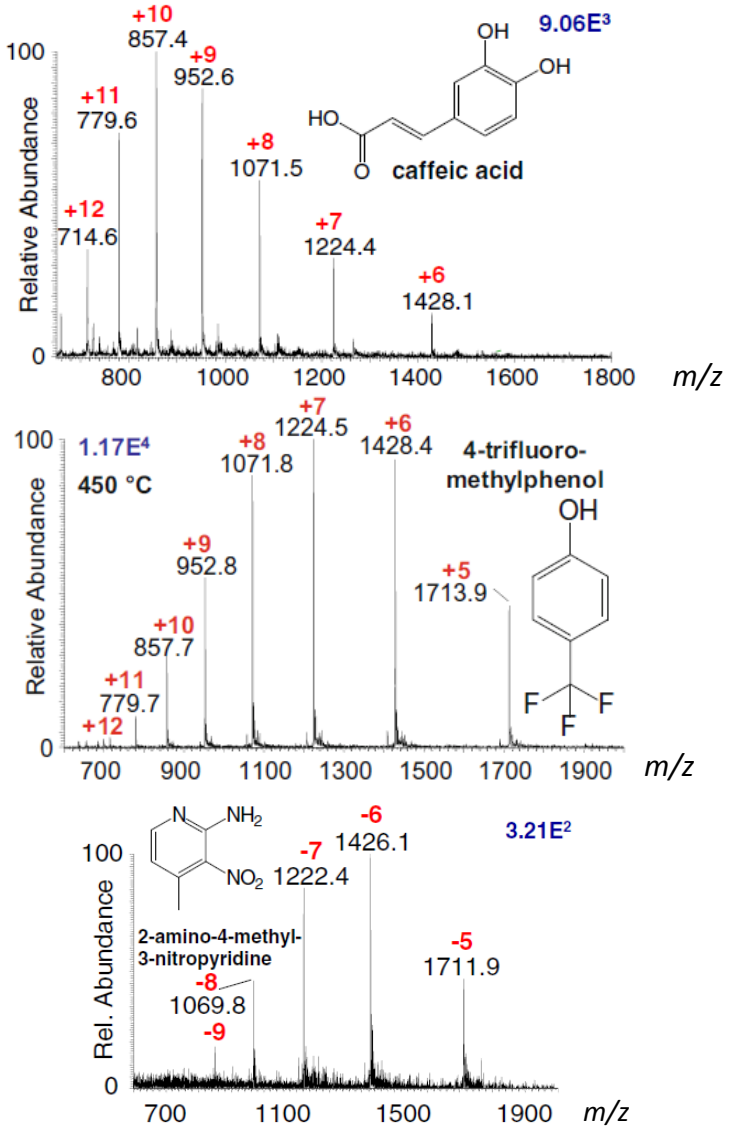
Anal. Chem. 2015, 87, 8301−8306



MAI MS(/MS) spectra of hydrocodone in urine.

Proteomics

J. Am. Soc. Mass Spectrom. 2012, 23, 1625-1643



MAI MS spectra of Ubiquitin

….. what’s next ?