Laboratoire Cobra

Ecole thématique du CNRS

Spectrométrie de masse à transformée de Fourier (FT- ICR et Orbitrap)

Trapped ion mobility mass spectrometry

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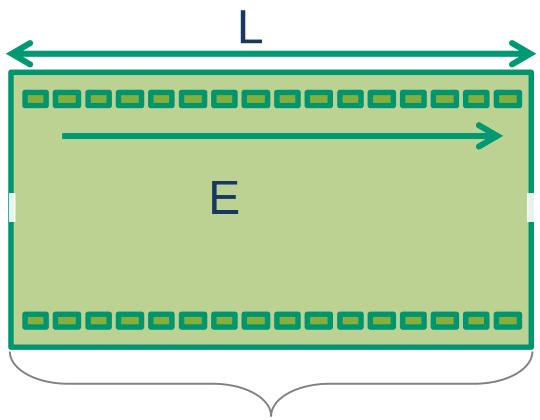
The promises of ion mobility mass spectrometry

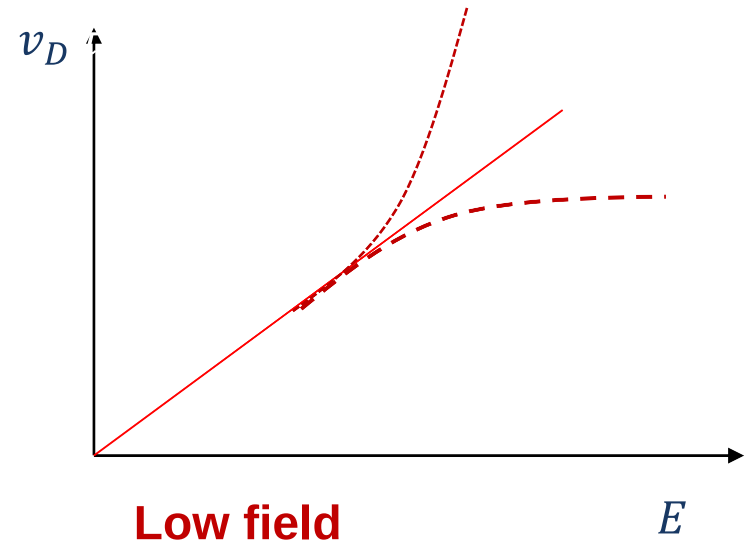
- ✓ High speed separation
- ✓ Gas phase separation
- ✓ Identification of ions
- ✓ Measurement of collision cross sections (CCS)
- ✓ Structure elucidation
- ✓ Ion molecule reaction

How can it be applied to FTMS ?

Fundamentals of ion mobility



He or N_2
(1 bar - 1 mbar)



$$v_D = KE$$

Ion mobility *K* *(cm²/V)* **Electric field** *E (V/cm)*

Gas number density *(part. m^{-3})*

$$N = \frac{n \times N_A}{V} = \frac{P}{kT}$$

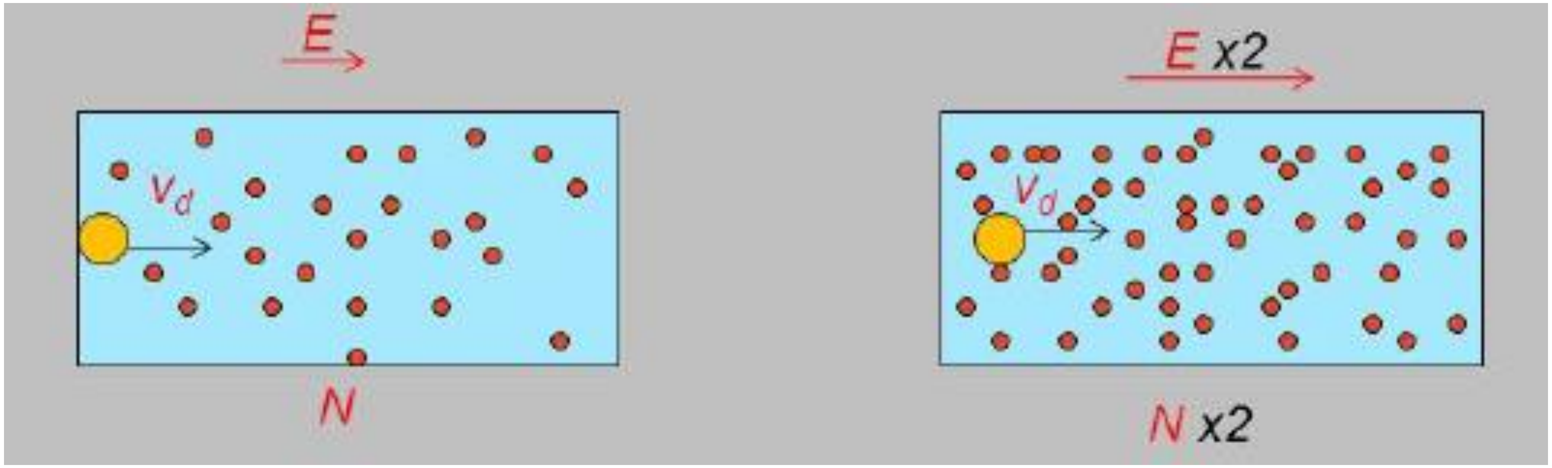
N_A Avogadro number
k = 1,38.10^{-23} J. K^{-1} Boltzman constant
n number of moles
V volume
P pressure
T temperature (Kelvin)

Reduced ion mobility K_0

$$K_0 = K\frac{N}{N_0} = K\frac{T_0}{T}\frac{P}{P_0}$$

N_0= 2,69.10^{25} m^{-3} Normal conditions (P_0 = 1 bar , T_0 = 273 K)

E/N (reduced field) is a key IMS scaling factor

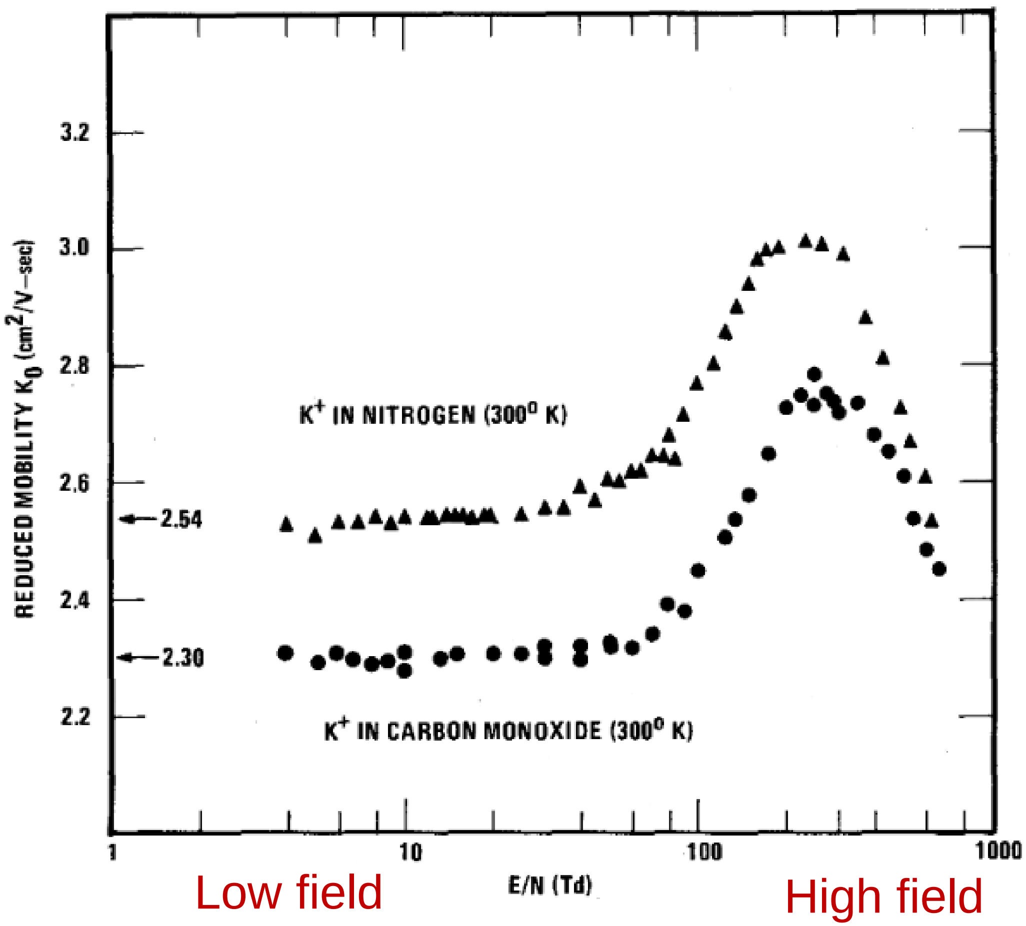


E / N in Townsend 1 Td = 10^{-17} V cm^2

K depends on E/N

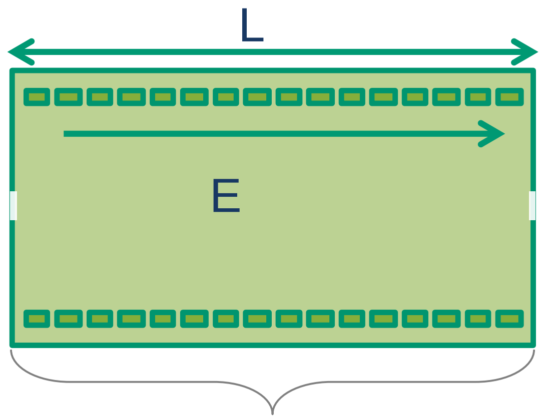
W. F Siems Short course ASMS 2013

E/N (reduced field) is a key IMS scaling factor



G. M. Thomson et al. *J. Chem. Phys.* **1973**, *58*, 2402.

Mason – Schamp equation



He ou N_2
(1 bar - 1 mbar)

Low field (E/N) :
Thermal equilibrium between ions and the gas molecules

Ion motion :
Random motion (heat energy) + small drift component (E)
Balance between acceleration (field) and deceleration (collisions)

$$v_D = KE$$

$$K = \frac{\sqrt{18\pi}}{16} \frac{e}{N\sqrt{kT}} \frac{z}{\sqrt{\mu}} \frac{1}{\Omega}$$

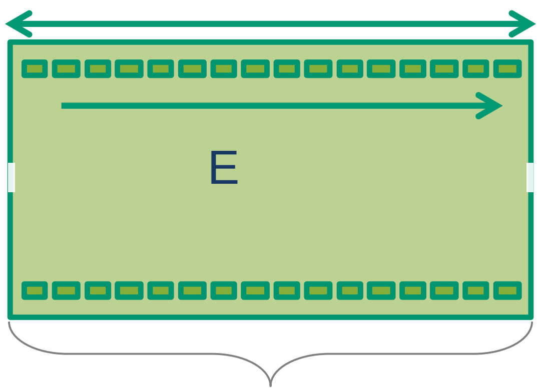
$$\mu = \frac{mM}{(m+M)}$$

e = 1,602. 10 $^{-19}$ C
k = 1,38.10^{-23} J. K^{-1} Boltzman constant
T temperature (Kelvin)
N buffer gas number density (m^{-3})
μ reduced mass (molecule and buffer gas) (kg)
z charge number
Ω Collision cross section

Revercomb,. Mason. *Anal. Chem.* **1975**, *47*, 970.

Ion mobility measurement

Uniform field drift tube ion mobility



He ou N_2
(1 bar - 1 mbar)

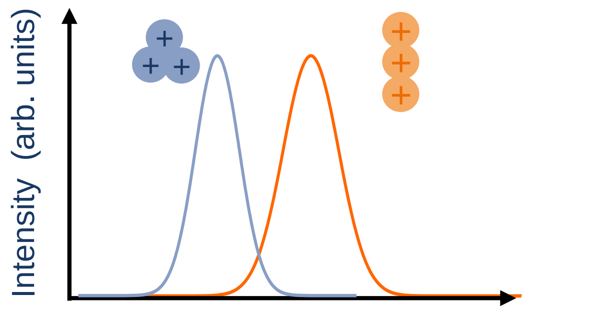
$$v_D = KE$$

Linear function t_D *vs* 1/V :

Slope L^2/K

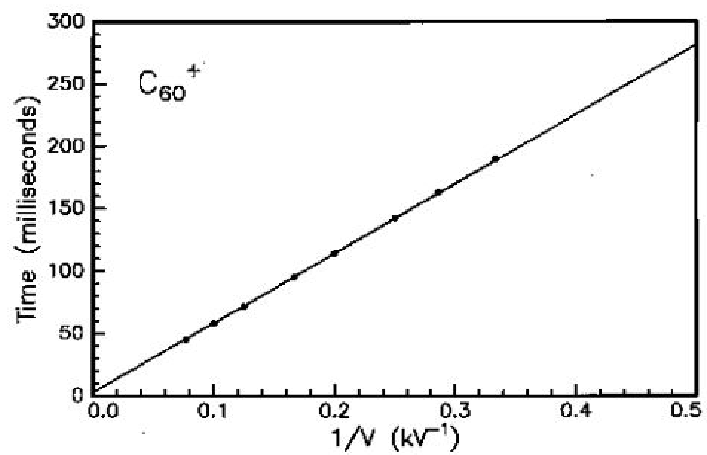
Extracted ion mobility spectrum (*m/z*)

Arrival time distribution (ATD)



t_D drift time (ms)

$$t_D = \frac{L}{KE} \qquad t_D = \frac{L^2}{K}\frac{1}{V}$$

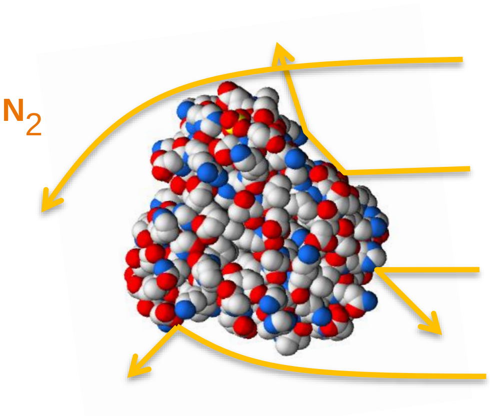


Dugourd P, Hudgins RR, Clemmer DE, Jarrold MF, *Review of Scientific Instruments*, **68**, 1122 (1997).

Collision cross section

$$K = \frac{\sqrt{18\pi}}{16}\frac{e}{N\sqrt{kT}}\frac{z}{\sqrt{\mu}}\frac{1}{\Omega} \qquad t_D = \frac{L}{KE} \qquad t_D \propto \frac{\sqrt{\mu}}{z}\Omega$$

Collision cross section (CCS) with He or N_2 : Ω_{He} ou Ω_{N_2}
area Å^2 accounting for the scattering process
in the drift tube: **ion conformation in the gas phase**



$$\Omega_{avg}^{(1,1)} = \frac{1}{4\pi^2}\int_0^{2\pi} d\theta \int_0^{\pi} d\varphi \sin\varphi \int_0^{2\pi} d\gamma \frac{\pi}{8}$$

average over all ion rotations

$$\times \left(\frac{\mu}{k_B T}\right)^3 \int_0^{\infty} dg\, e^{-\mu g^2/2k_B T} g^5$$

average over all impact velocities

$$\times \int_0^{\infty} db\, 2b(1 - \cos\chi(\theta,\varphi,\gamma,g,b))$$

momentum transfer

Mesleh *et al.* *J Phys. Chem.* **1996**, *100* (40), 16082–16086.

Types of ion mobility mass spectrometry

Low field (E/N)

Time dispersive

Bath gas (fixed)
- Uniform field drift tube (DTIMS)
  - Agilent, TOFWerk
- Travelling wave (TWIMS)
  - Waters

Mobility selective

Gas flow – ion confinement
- Trapped ion mobility (TIMS)
  - Bruker

Gas flow – spatial dispersion
- Differential mobility analyzer (DMA)
  - www.seadm.com

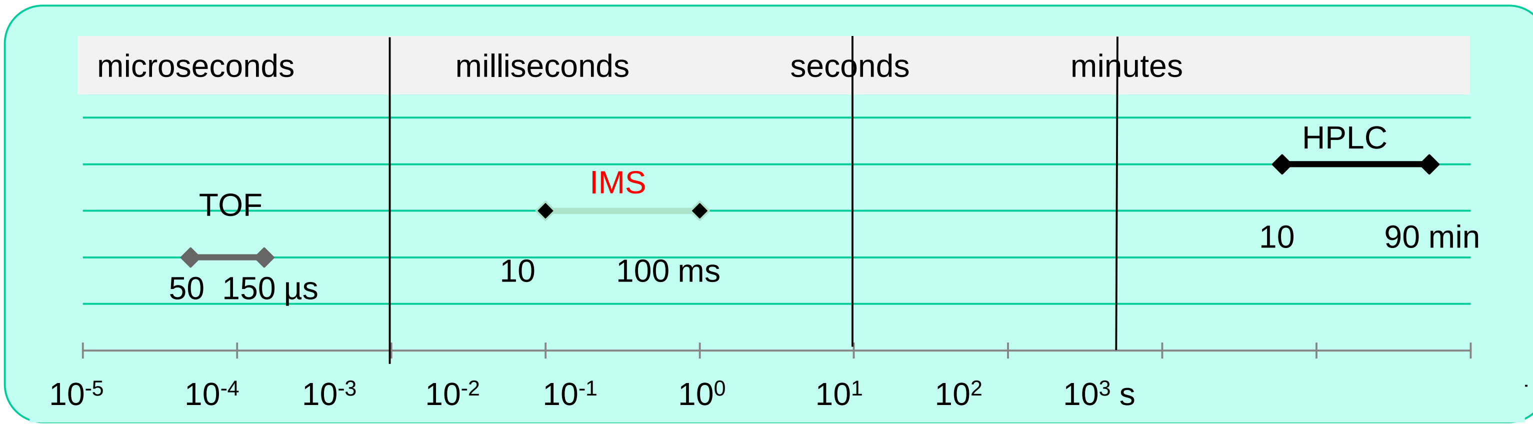
High field (E/N)

Field Asymmetric Waveform (FAIMS)

Differential mobility (DMS or DIMS)

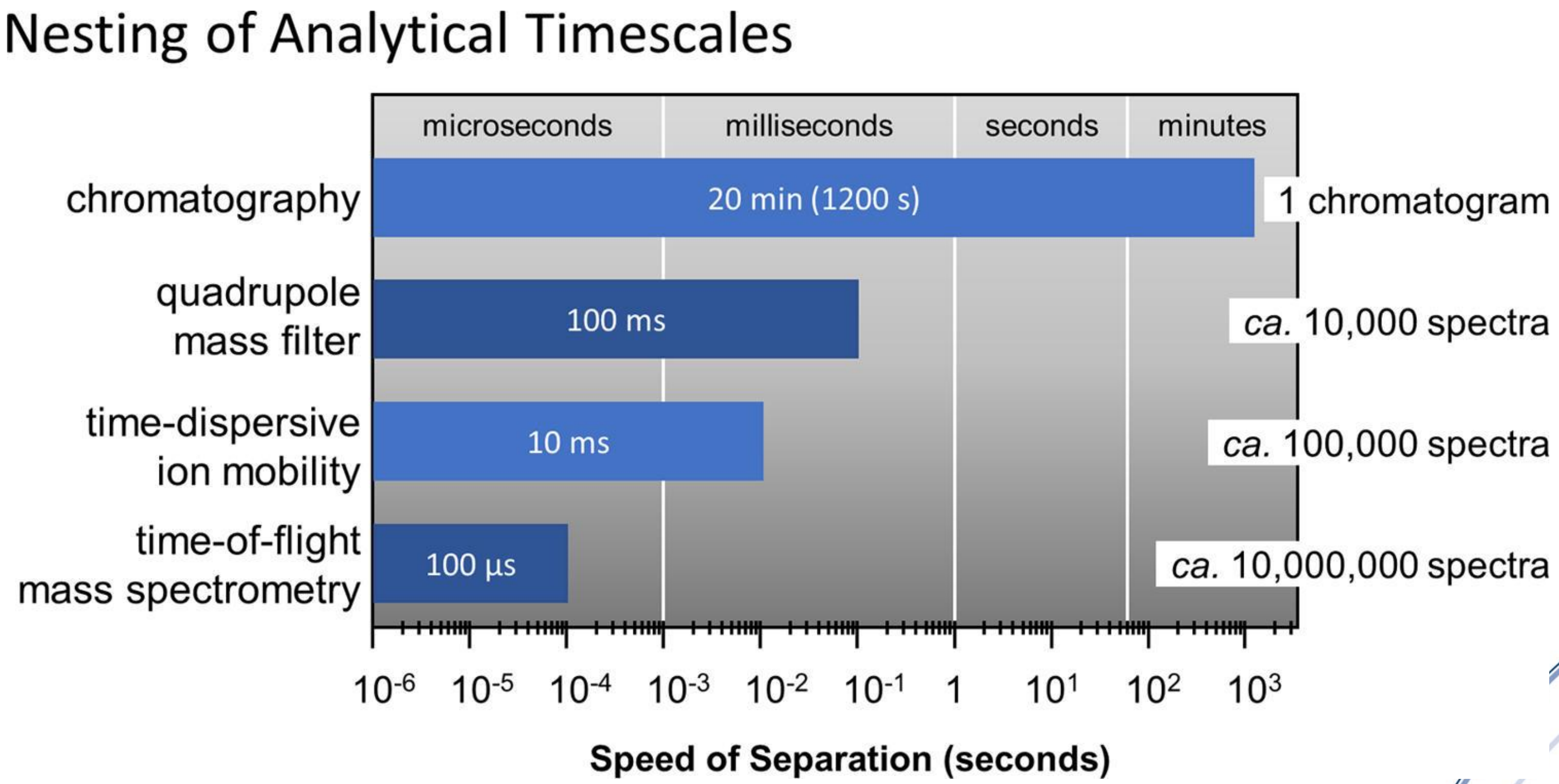
J. C. May et al. *Analytical Chemistry* **2015**, *87*, 1422.

Time ranges of analytical techniques



Time–dispersive ion mobility :
Not compatible with slower mass analyzers

Time ranges of analytical techniques



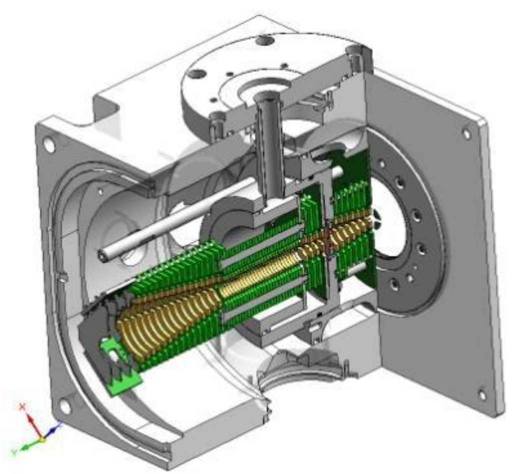
J. C. May et al. *Analytical Chemistry* **2015**, *87*, 1422.

Trapped ion mobility spectrometry

2010-2012

Development of the first TIMS prototype using a micro-q-TOF at Bruker Daltonics Inc., Billerica site

Francisco Fernandez-Lima
Melvin Park
Mark Ridgeway



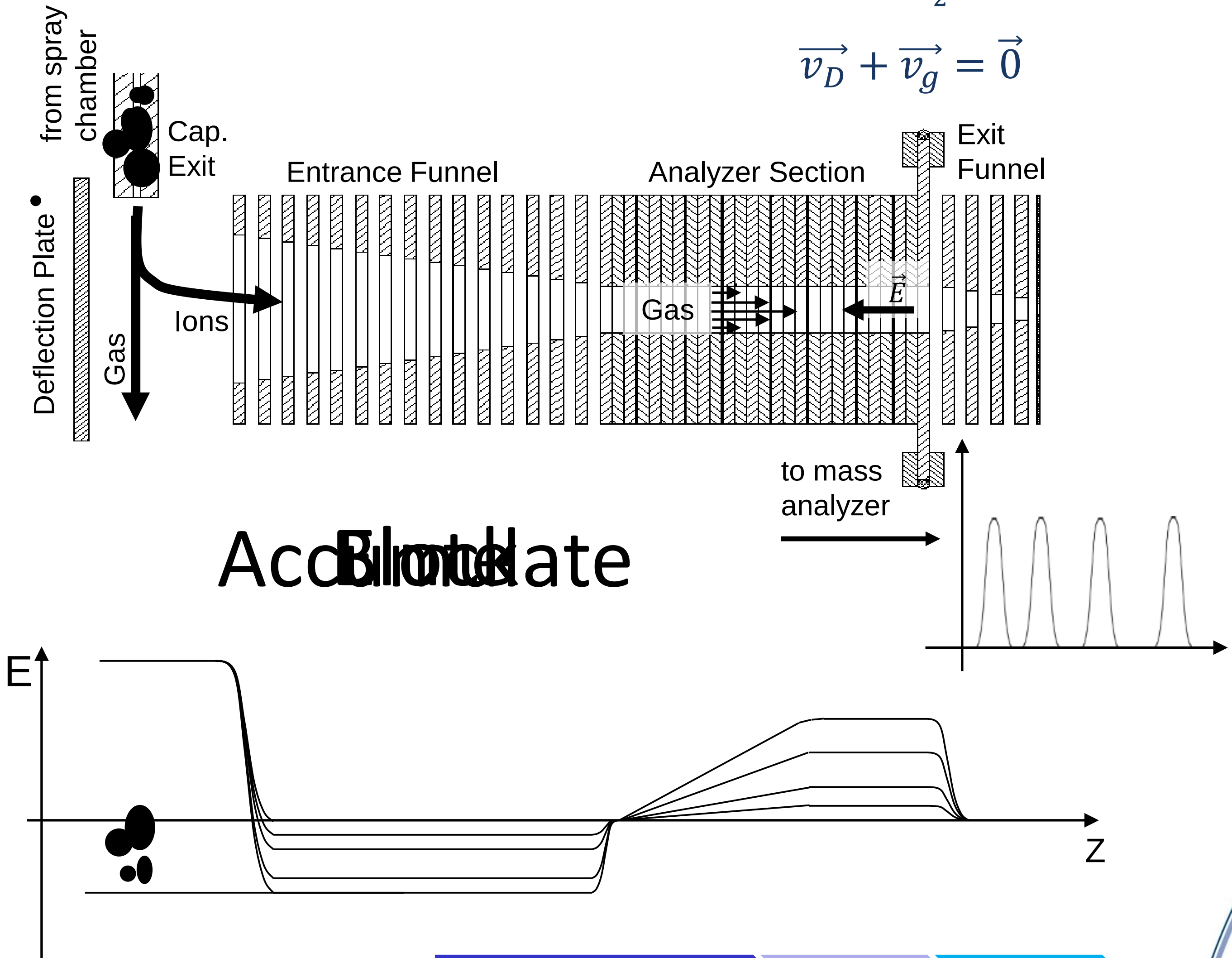
Adapted from a slide from the F. F.-L. group

Trapped ion mobility spectrometry

TIMS

Trapping: $\overrightarrow{v_D} + \overrightarrow{v_{N_2}} = \vec{0}$

$\overrightarrow{v_D} + \overrightarrow{v_g} = \vec{0}$

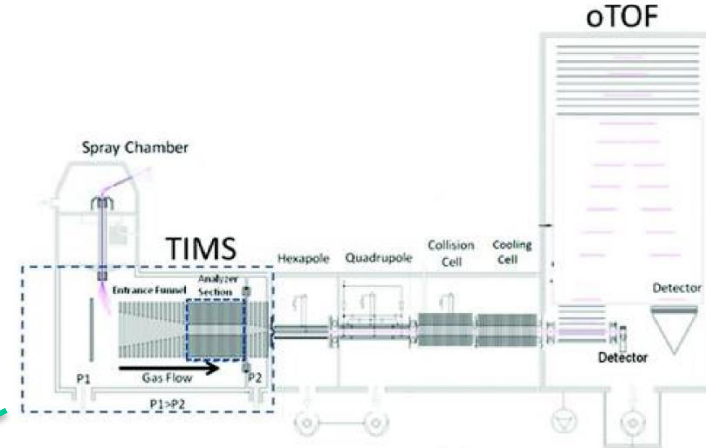


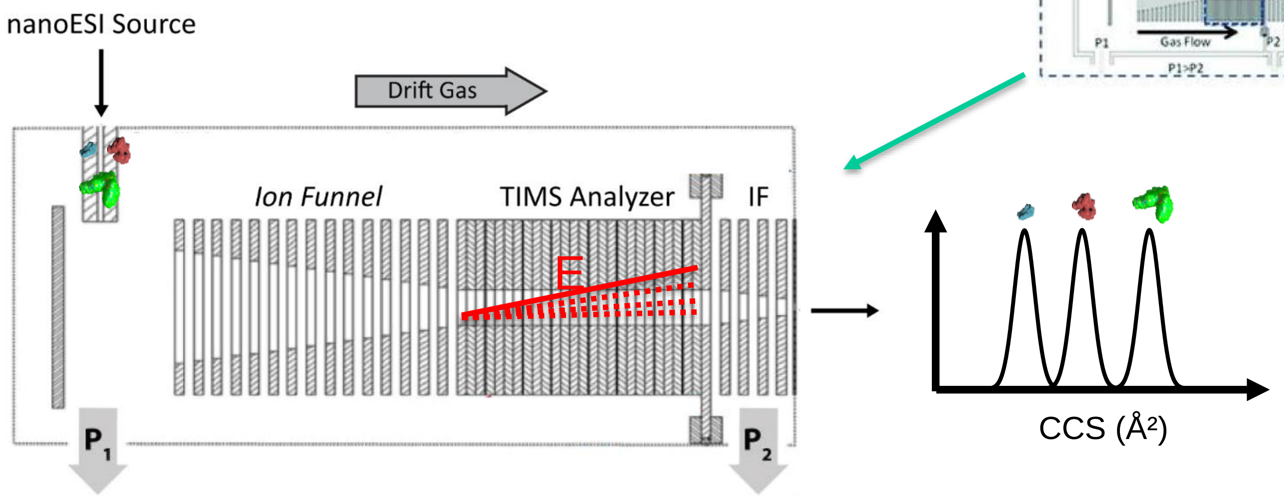
Accumulate → Trap → Elute

Adapted from a slide from Bruker (Y. Hébert)

Trapped ion mobility spectrometry

- Holding the ions stationary in a flowing buffer gas by an electric field gradient
- Collision Cross Section (CCS): conformation of ions in the gas phase





Unique to TIMS: higher CCS elute first.

Adapted from a slide from Bruker (Y. Hébert)

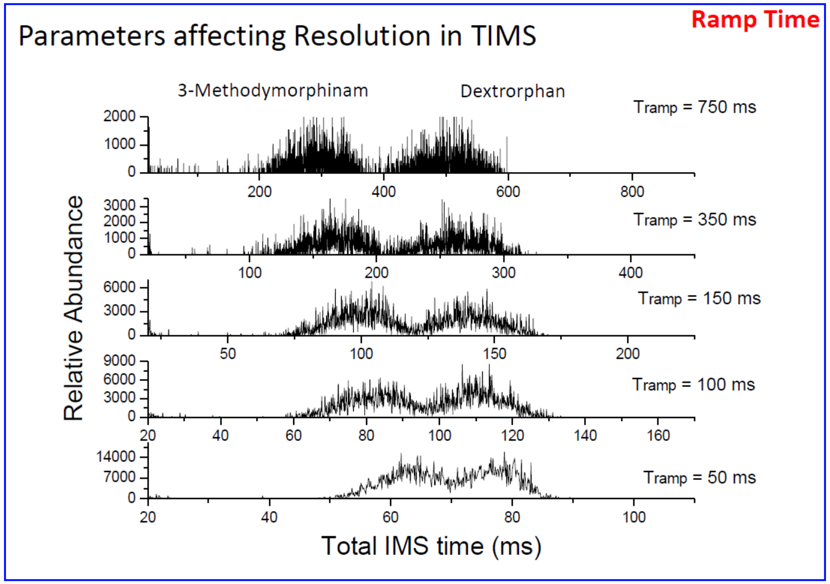
Adjustable ion mobility resolution

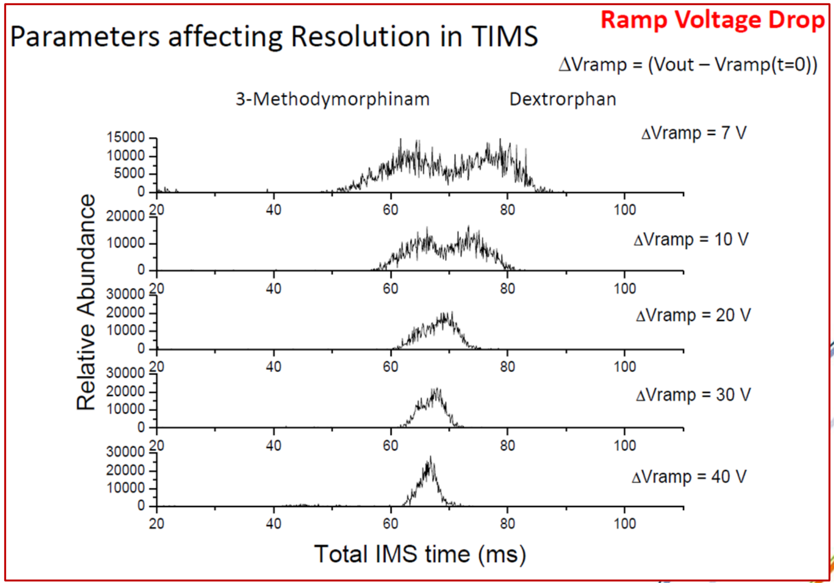
Resolution in drift tube ion mobility

$$R = \frac{t_d}{\Delta t_{FwHM}} = \sqrt{\frac{zeLE}{16 ln2\ kT}}$$

- Resolution in TIMS
  - Scan rate ($V.ms^{-1}$)
  - Velocity of gas (pressure difference)
  - TIMS trap time
  - TIMS ramp voltage

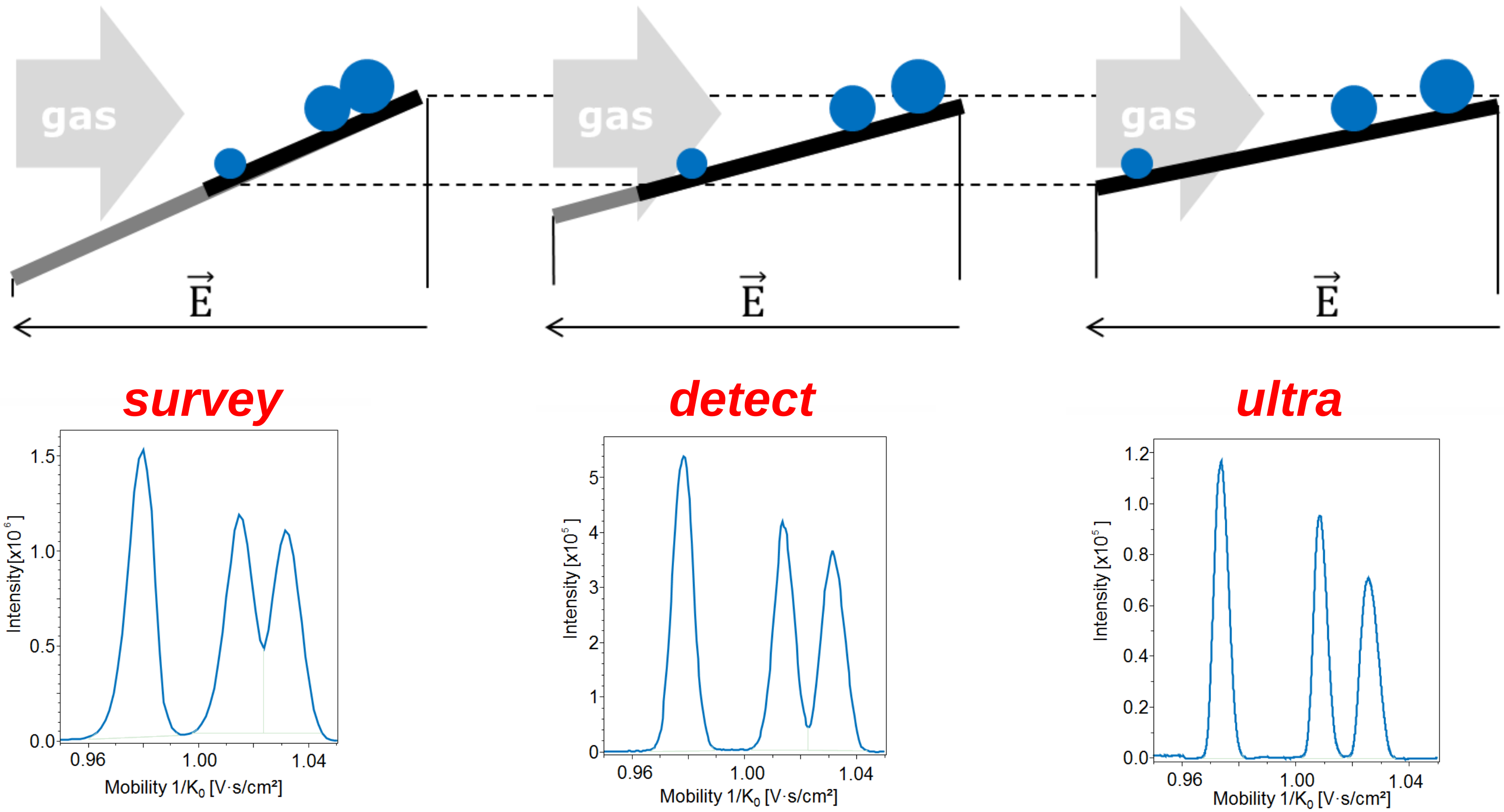
$$R = \sqrt{\frac{q\, v_g t_p E_e}{16\, ln2\, k_b\, T}}$$





* F. A. Fernandez-Lima, D. A. Kaplan, M. A. Park. Integration of Trapped Ion Mobility Spectrometry with Mass Spectrometry. Rev. Sci. Instrum. 82, 126106, 2011

Adjustable ion mobility resolution

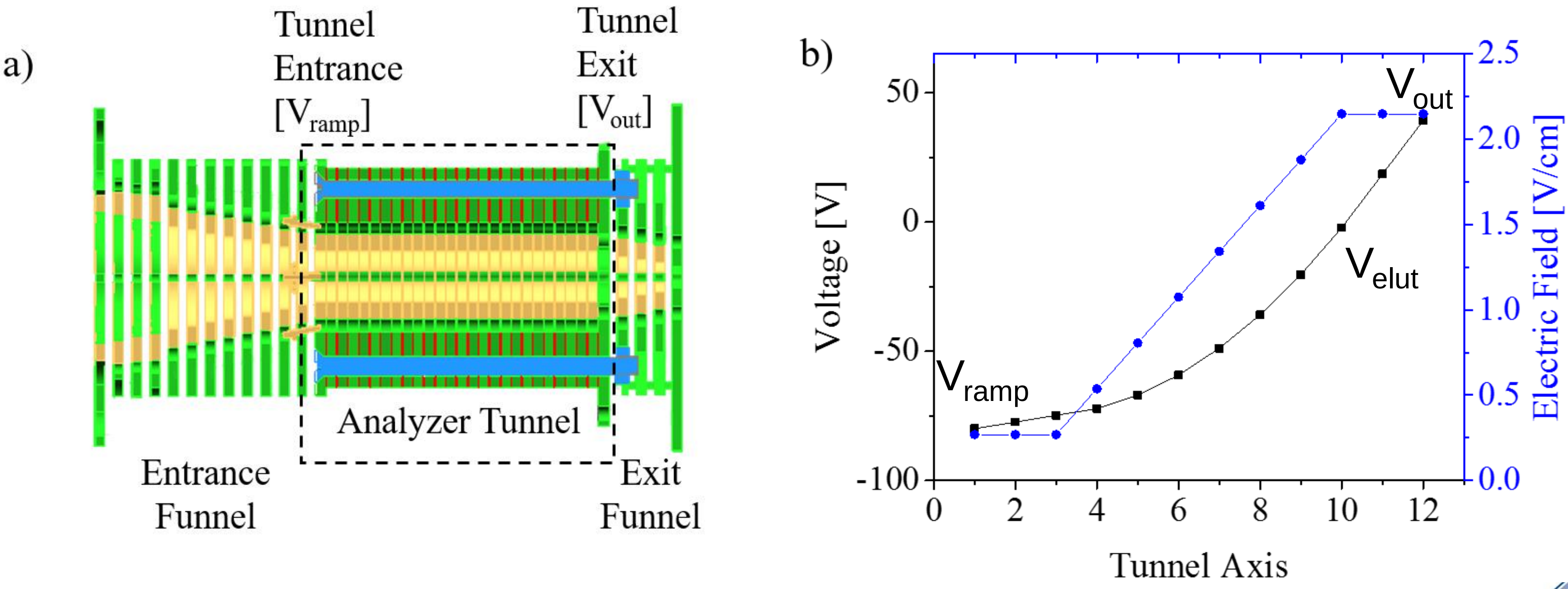


▶ **imeX™ Technology:** *patent pending*

Adapted from a slide from Bruker (Y. Hébert)

Trapped ion mobility spectrometry

Voltage and electric field

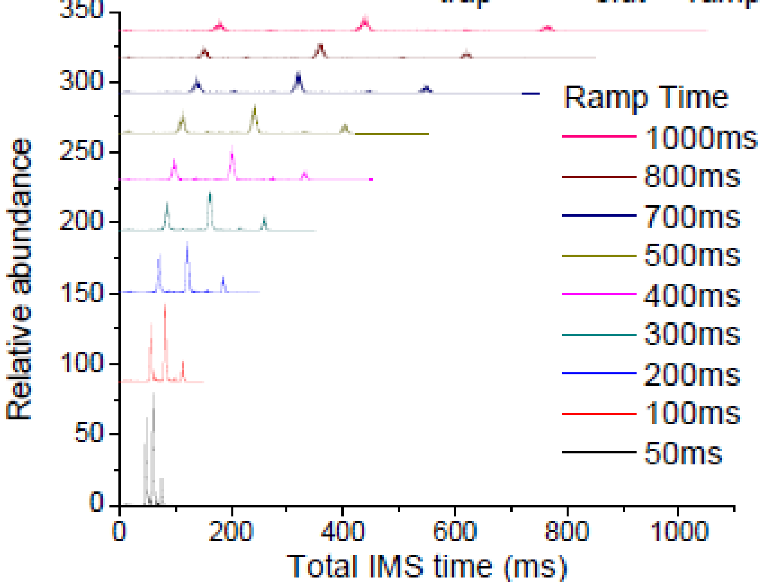


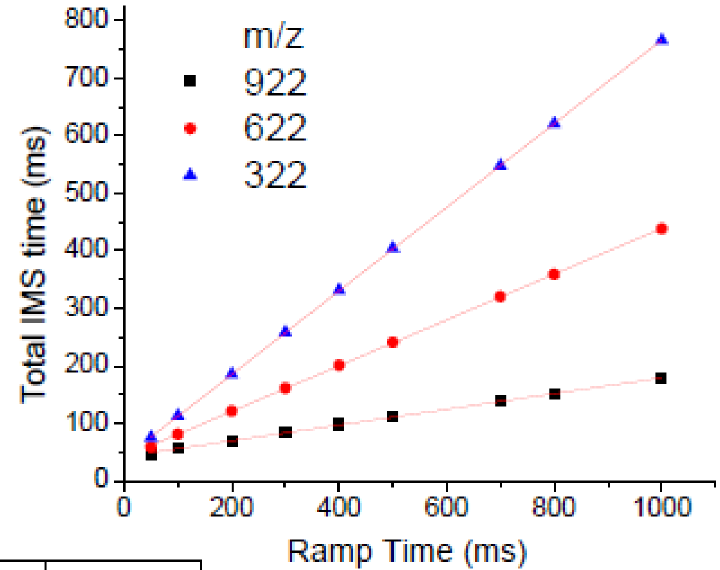
$E_z = - dV/dz$

P. Benigni, F. Fernandez-Lima," Oversampling SA-TIMS coupled to FT-ICR MS: Fundamentals and Applications". Anal .Chem. 2016.

Ion mobility K_0 and CCS measurement

$$\text{Total IMS time} = t_{trap} + (V_{elut}/V_{ramp})^{*}t_{ramp} + \text{ToF} = t_o + (V_{elut}/V_{ramp})^{*}t_{ramp}$$





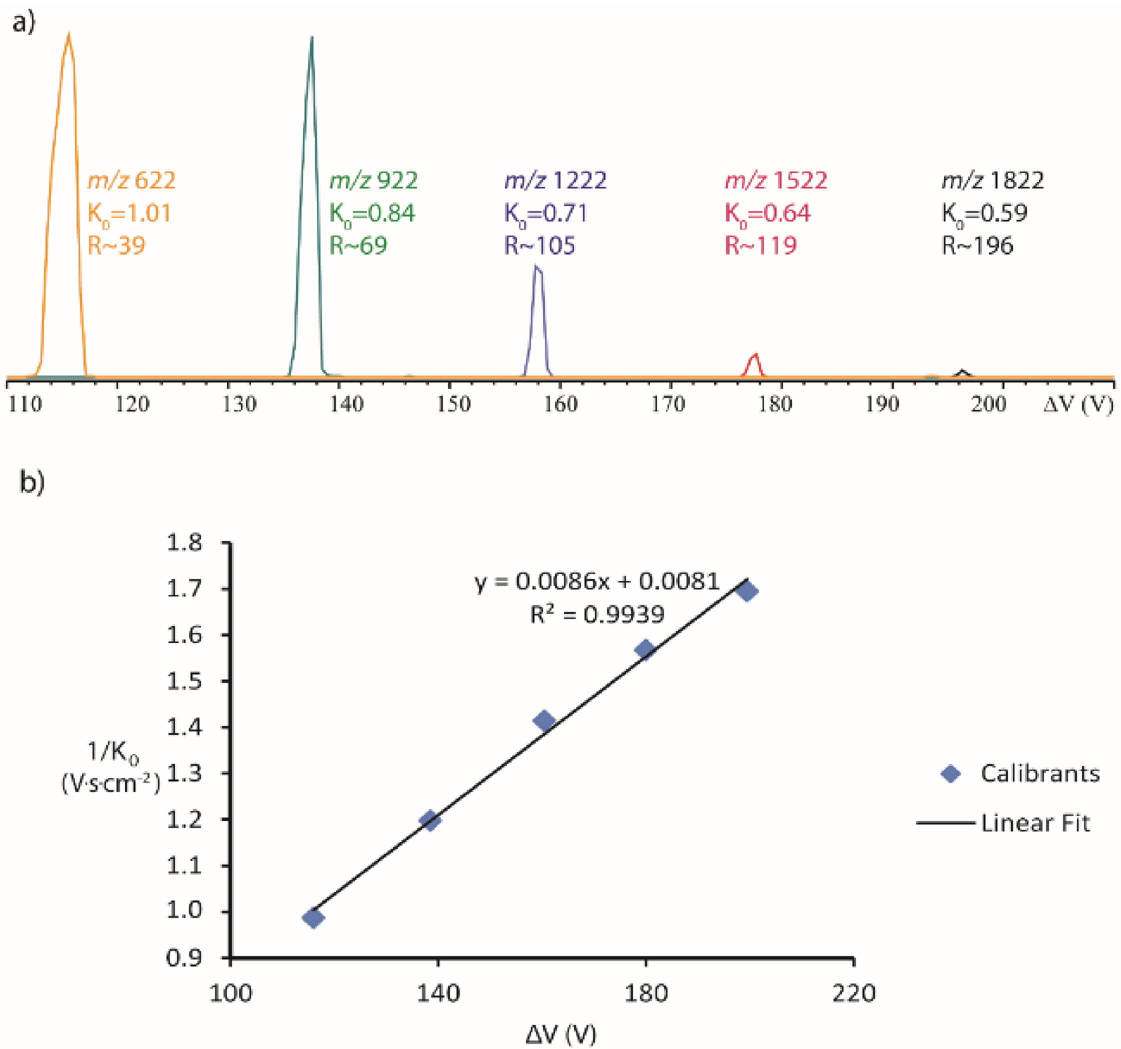
Molecular ion (m/z)	To (ms)	V_{elut}/V_{ramp}	V_{elut} (V)	Ko (cm²/Vs)	CCS (A²)
Tunemix (322)	40.21	0.725	43.50	1.3760	151
Tunemix (622)	41.66	0.397	23.82	1.0130	202
Tunemix (922)	42.63	0.136	8.16	0.8350	243

$$K_x = v_g / E_x$$

$$K_x = A * (1/(V_{out} - V_{elut}(x))$$

Adapted from a slide from the F. F.-L. group

Ion mobility K_0 and CCS measurement



$$KE_e = v_g = constant$$

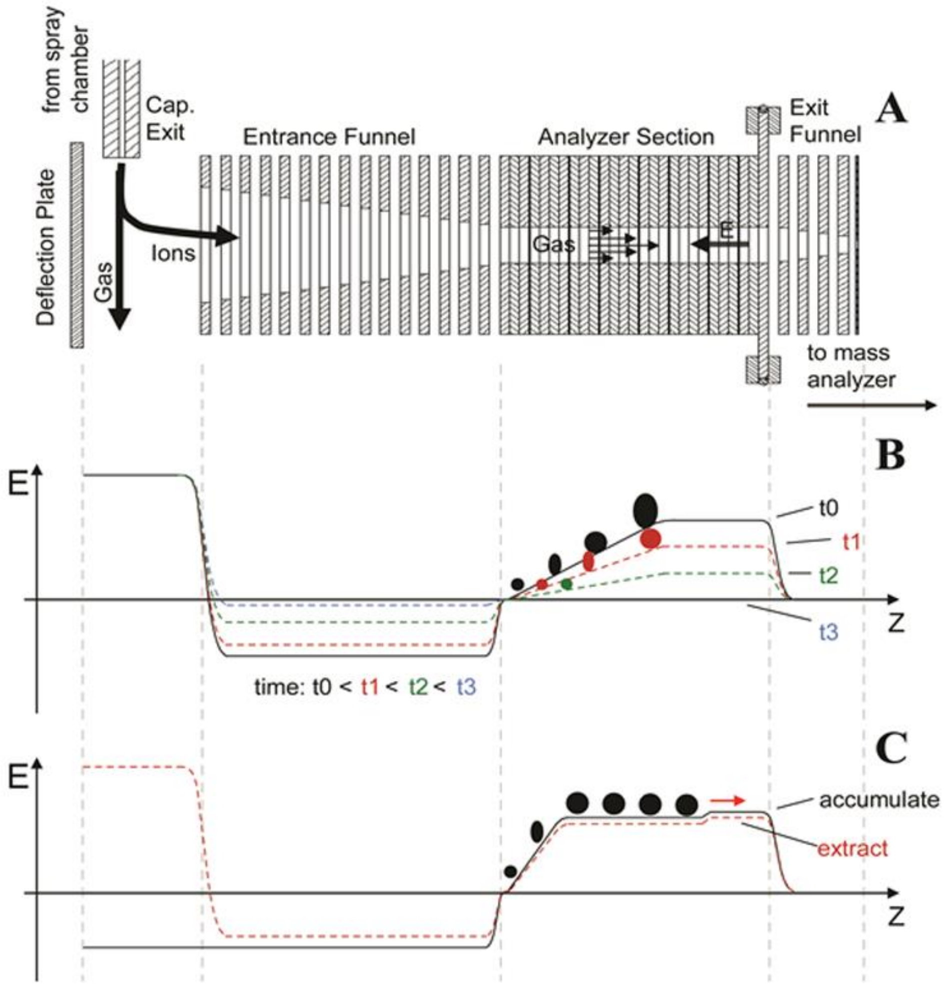
$$K_0 = K\frac{N}{N_0} = K\frac{T_0}{T}\frac{P}{P_0}$$

$$E_e = \frac{\Delta V}{\Delta z}$$

$$\frac{1}{K_0} \propto \Delta V$$

Y. Pu *et al.* Anal. Chem. 2016, 88, 3440.

Trapped ion mobility spectrometry : adding FTMS



Selected accumulation trapped ion mobility spectrometry

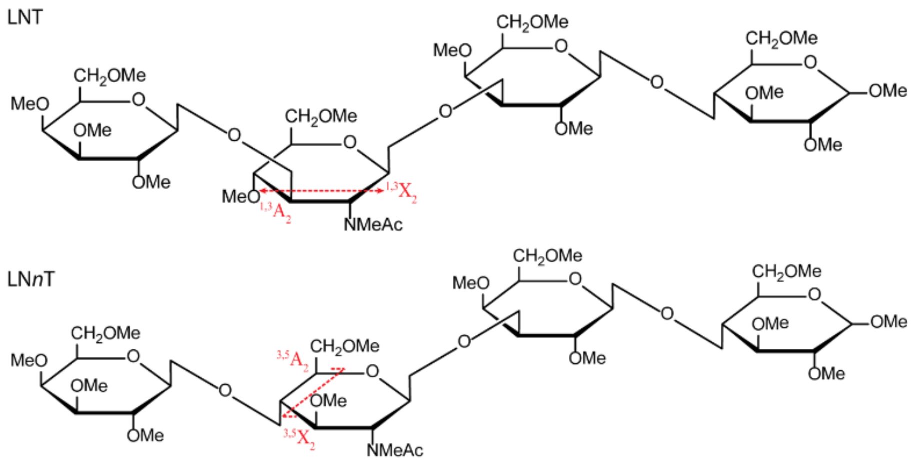
and Gated TIMS

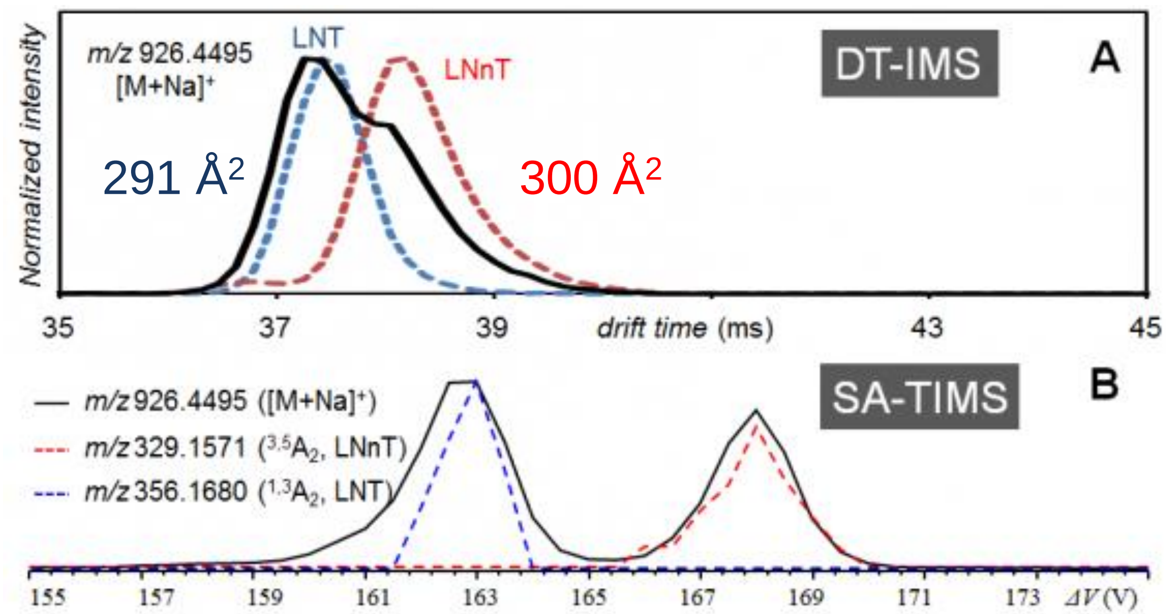
Long trapping time :

- ✓ higher *S/N* ratio per scan
- ✓ coupling to slower analysis methods, including FTICR

Ridgeway et al. IJIMS 2016 (19) 77-85

Trapped ion mobility spectrometry : adding FTMS

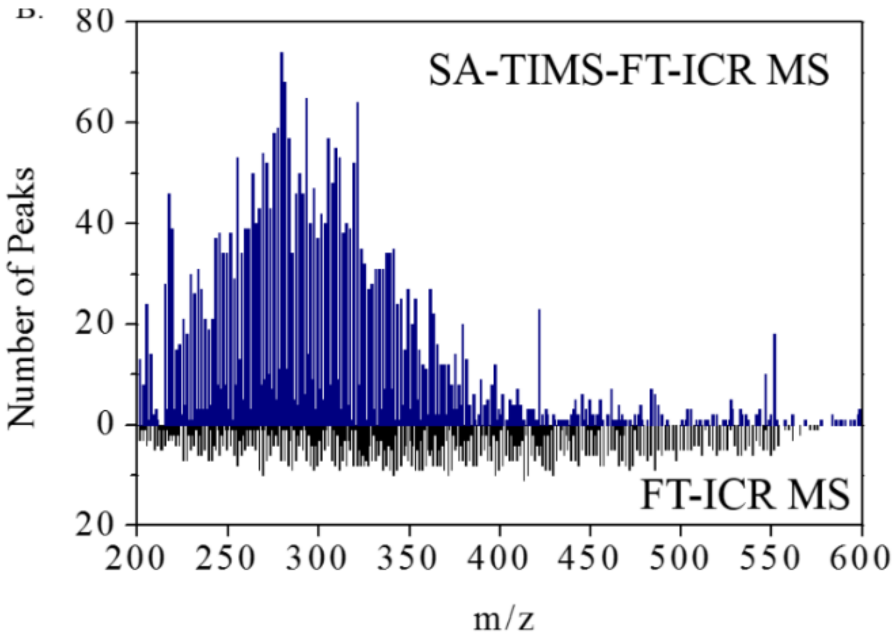




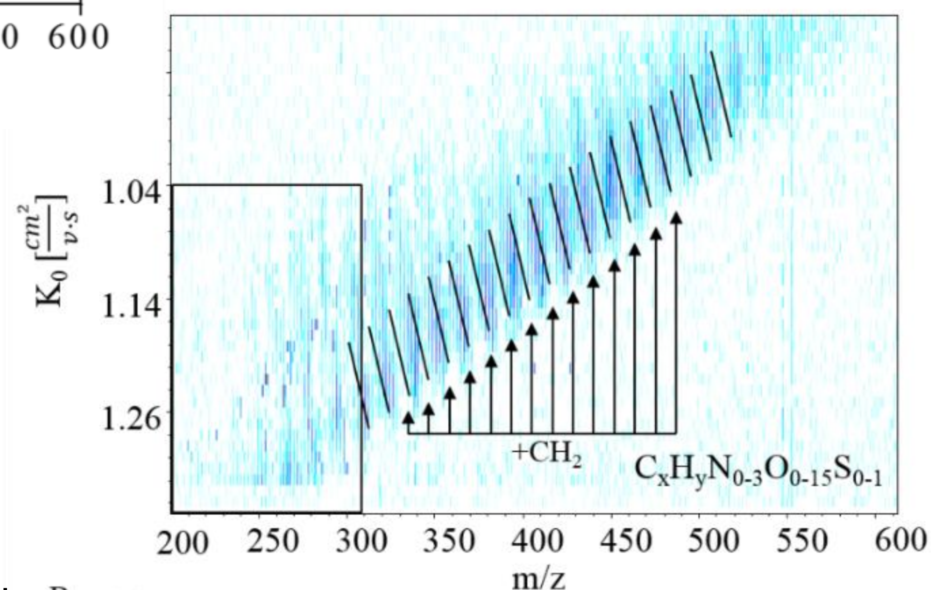
Y. Pu *et al.* Anal. Chem. 2016, 88, 3440.

Trapped ion mobility spectrometry : adding FTMS

SA-TIMS

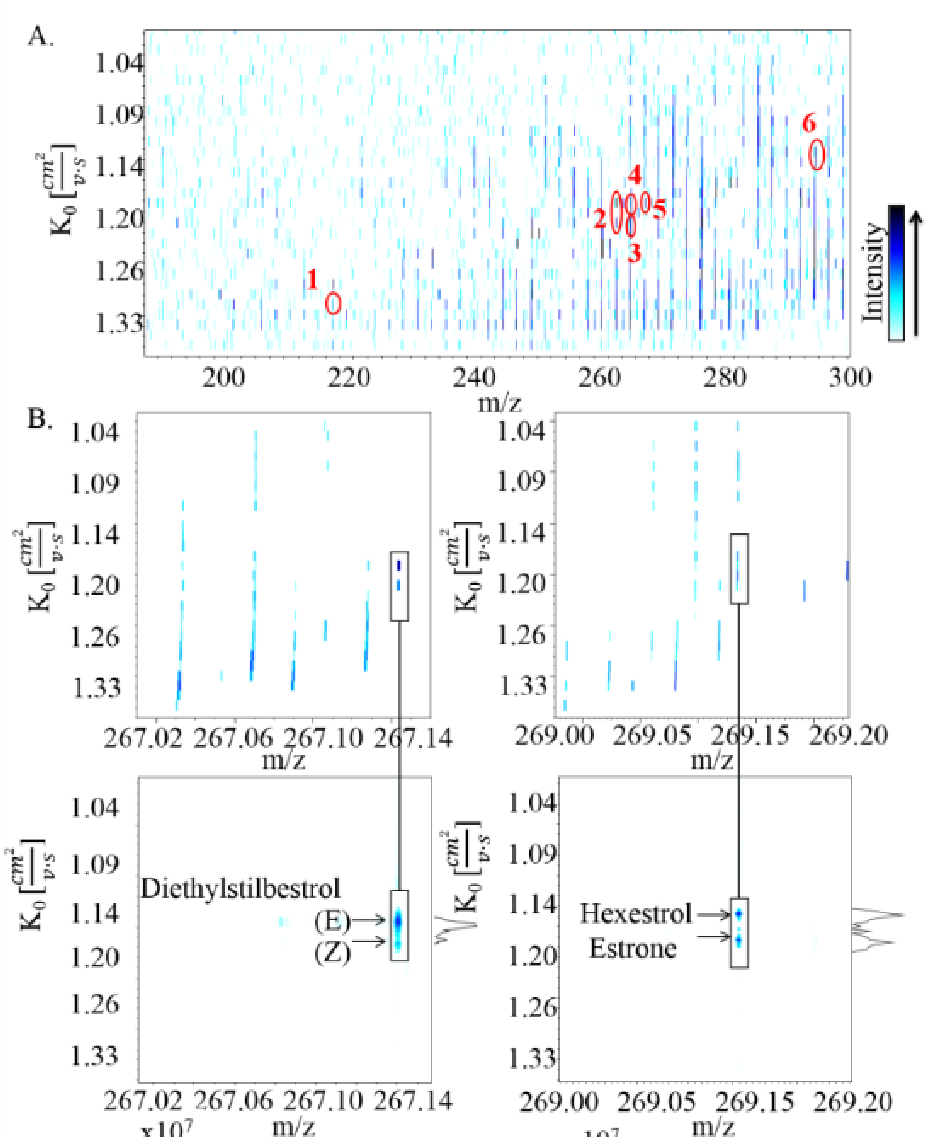


Suwannee River Fulvic Acid Standard II (SRFA) 20 µg/mL doped 5 ppb of
(1) bisphenol A
(2) diethylstilbestrol (Z and E)
(3) estrone
(4) hexestrol
(5) α-estradiol
(6) 17-α-ethynylestradiol



Benigni P et al. Anal. Chem. 2015, 87 (8), 4321–4325.

Trapped ion mobility spectrometry : adding FTMS



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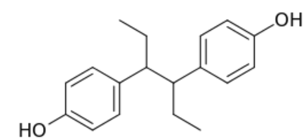
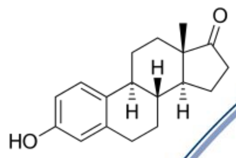




$C_{18}H_{22}O_2$

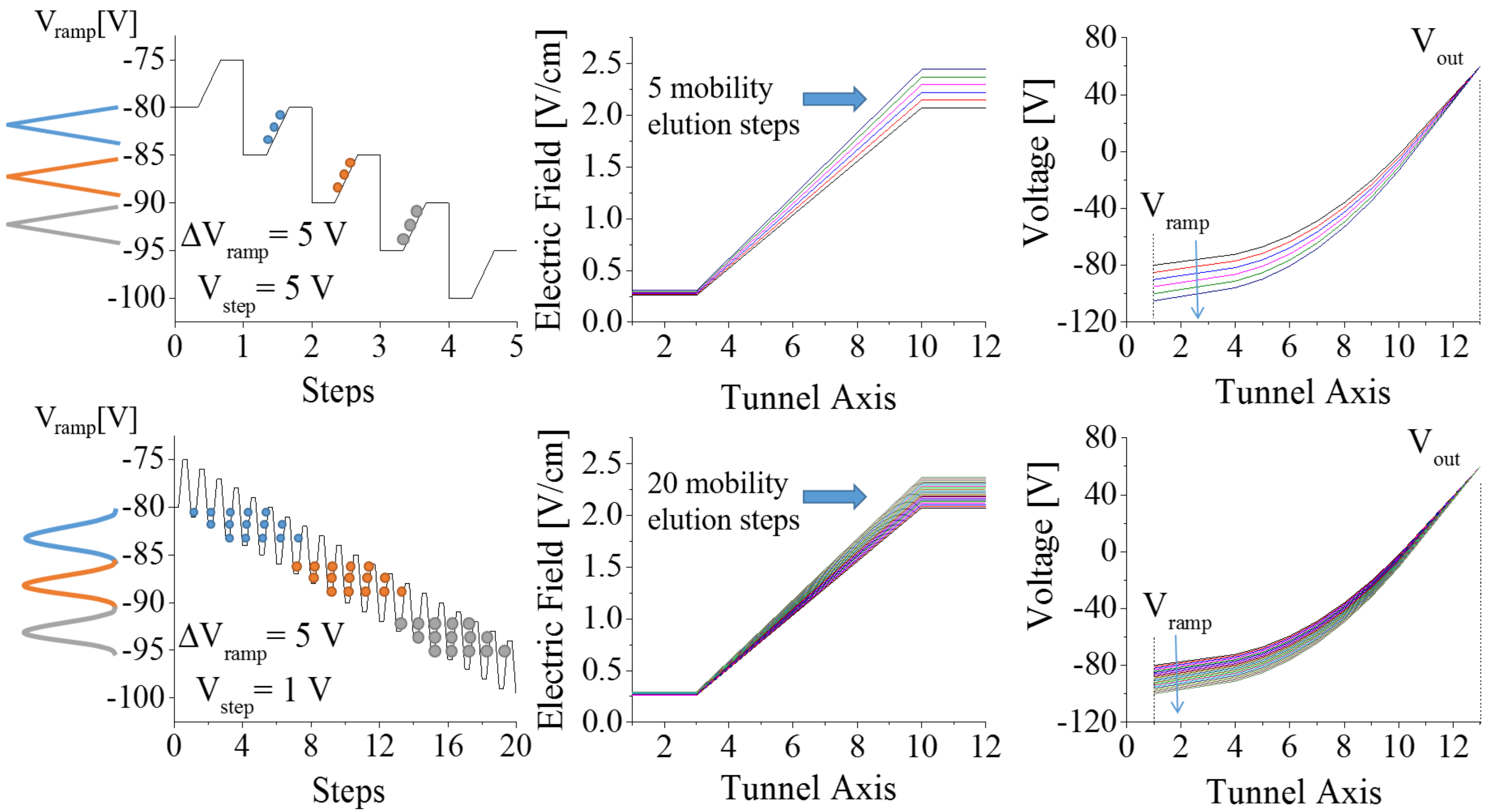
177 Å²

174 Å²

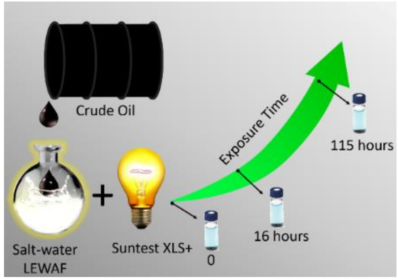
Benigni P et al. Anal. Chem. 2015, 87 (8), 4321–4325.

Trapped ion mobility spectrometry : adding FTMS

Oversampling SA-TIMS

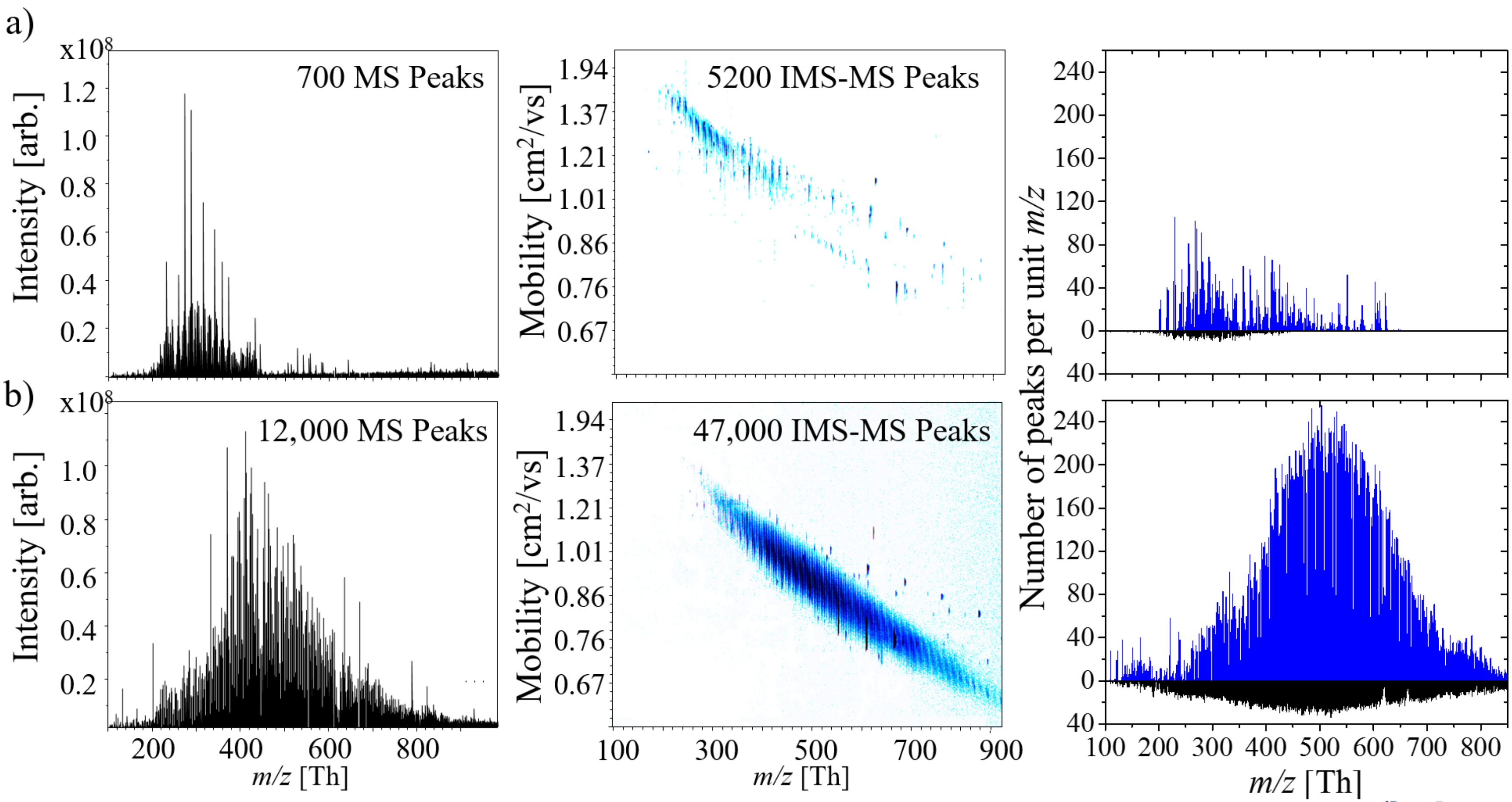


P. Benigni, F. Fernandez-Lima,” Oversampling SA-TIMS coupled to FT-ICR MS: Fundamentals and Applications”. Anal .Chem. 2016.



Trapped ion mobility spectrometry : adding FTMS

Oversampling SA-TIMS



P. Benigni, K. Sandoval, C. J. Thompson, M. E. Ridgeway, M. A. Park, P. Gardinali, F. Fernandez-Lima. "Analysis of photo-irradiated water accommodated fractions of crude oils using tandem TIMS and FT-ICR MS" Environ. Sci. Technol. 51 (11) (2017) 5978–5988

Summary

M. E. Ridgeway, M. Lubeck, J. Jordens, M. Mann, M. A. Park. Trapped ion mobility spectrometry: A short review. *International Journal of Mass Spectrometry* **2018**, *425*, 22.

TIMS is a very **flexible** ion mobility technique

Elution of ions : analytical field strength E decreased, E_e can be measured

Slow/rapid scans : high resolving power / high spectral rates,

Limited voltage range scans = limited mobility range scans

Variety of methods :

original “sequential analysis” TIMS,

selective accumulation TIMS, parallel accumulation TIMS, Gated TIMS,

Oversampling SA-TIMS adapted to FT-ICR

Many future evolutions possible !