

Fourier Transform Ion Cyclotron resonance mass spectrometry. The fundamentals

Christian ROLANDO

Miniaturization for Synthesis, Analysis & Protéomics USR 3290

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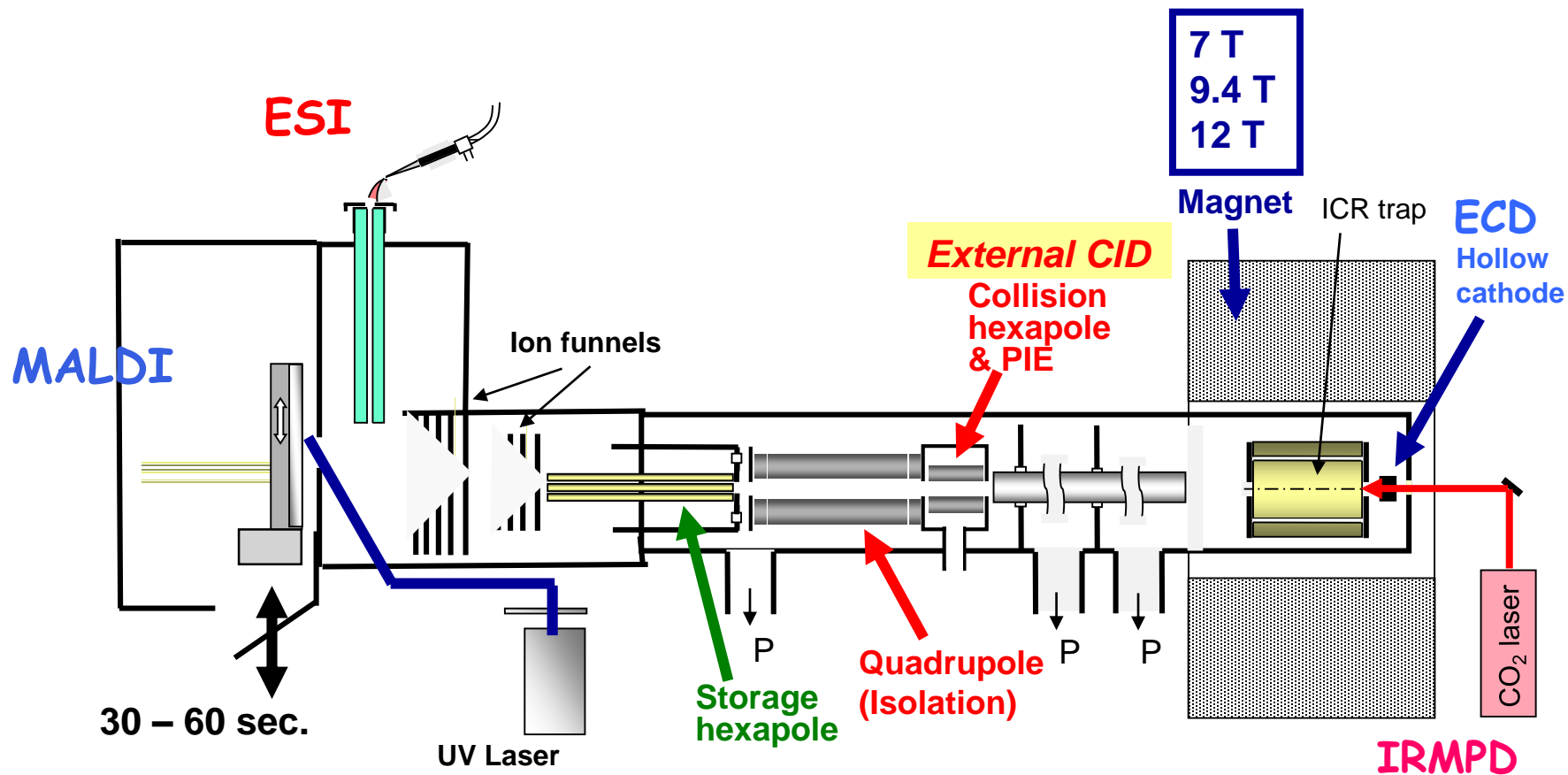
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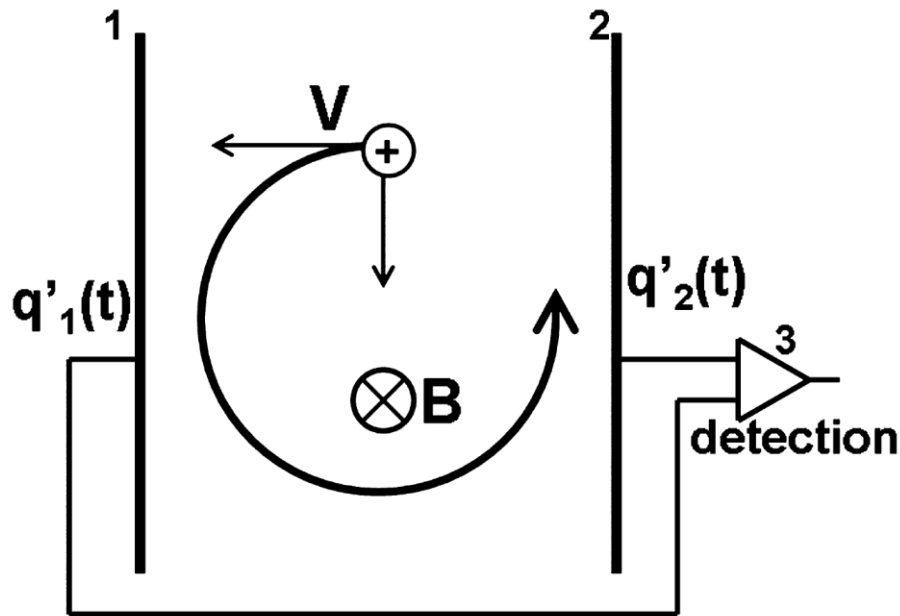
Carlos Afonso, Spectrométrie de masse FT-ICR : Aspects instrumentaux. Guillaume Van der Rest, Manipulation des ions dans une cellule FT-ICR & Méthodes d'activation électronique , Ecole thématique FT-MS (FT-ICR et Orbitrap): Fondements, mise en œuvre et applications à l'analyse de mélanges complexes, Avril 2014, Dammarie Les Lys, <http://www.fticr.org/article168.html>

A schematic drawing of an high field FTICR MS

Schematic drawing of a Bruker Apex FTICR MS



Single charged particle in a homogeneous magnetic field



The principle of the ICR signal measurement. 1, 2: detection electrodes; $q_{01}(t)$ $q_{02}(t)$: induced image charges; and 3: preamplifier.

$$m \frac{dv}{dt} = qE + qv \wedge B$$

$$\frac{mv_{xy}^2}{r} = qv_{xy}B_0$$

$$v_{xy} = \sqrt{v_x^2 + v_y^2}$$

$$\omega = \frac{v_{xy}}{r}$$

The fundamental equation

$$\omega = \frac{qB_0}{m}$$

$$\nu = \frac{qB_0}{2\pi m}$$

$$\nu = \frac{1.53 \times 10^7 B_0}{m/z}$$

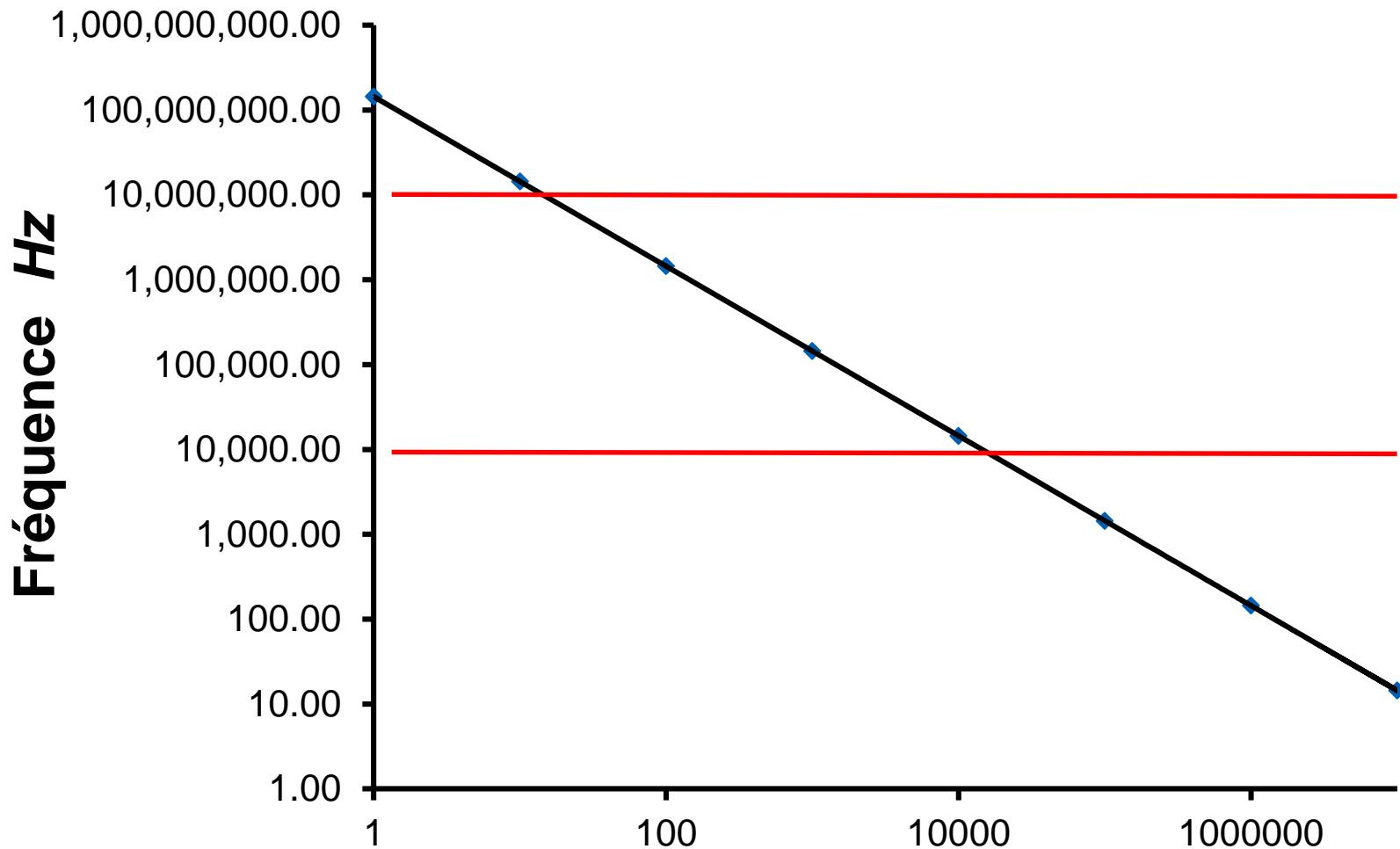
Resolution (low pressure limit)

$$\frac{m}{\Delta m} = - \frac{qB_0}{m} \cdot \frac{1}{\Delta\omega}$$

$$\Delta\omega \cong \frac{1}{T_{\text{Observation}}}$$

$$\frac{m}{\Delta m} \cong \frac{qB_0 T_{\text{Observation}}}{m}$$

The fundamental equation



$B = 9.4$ Tesla

Radius of an ion at thermic equilibrium

$$\frac{mv_{xy}^2}{r} = qv_{xy}B_0$$

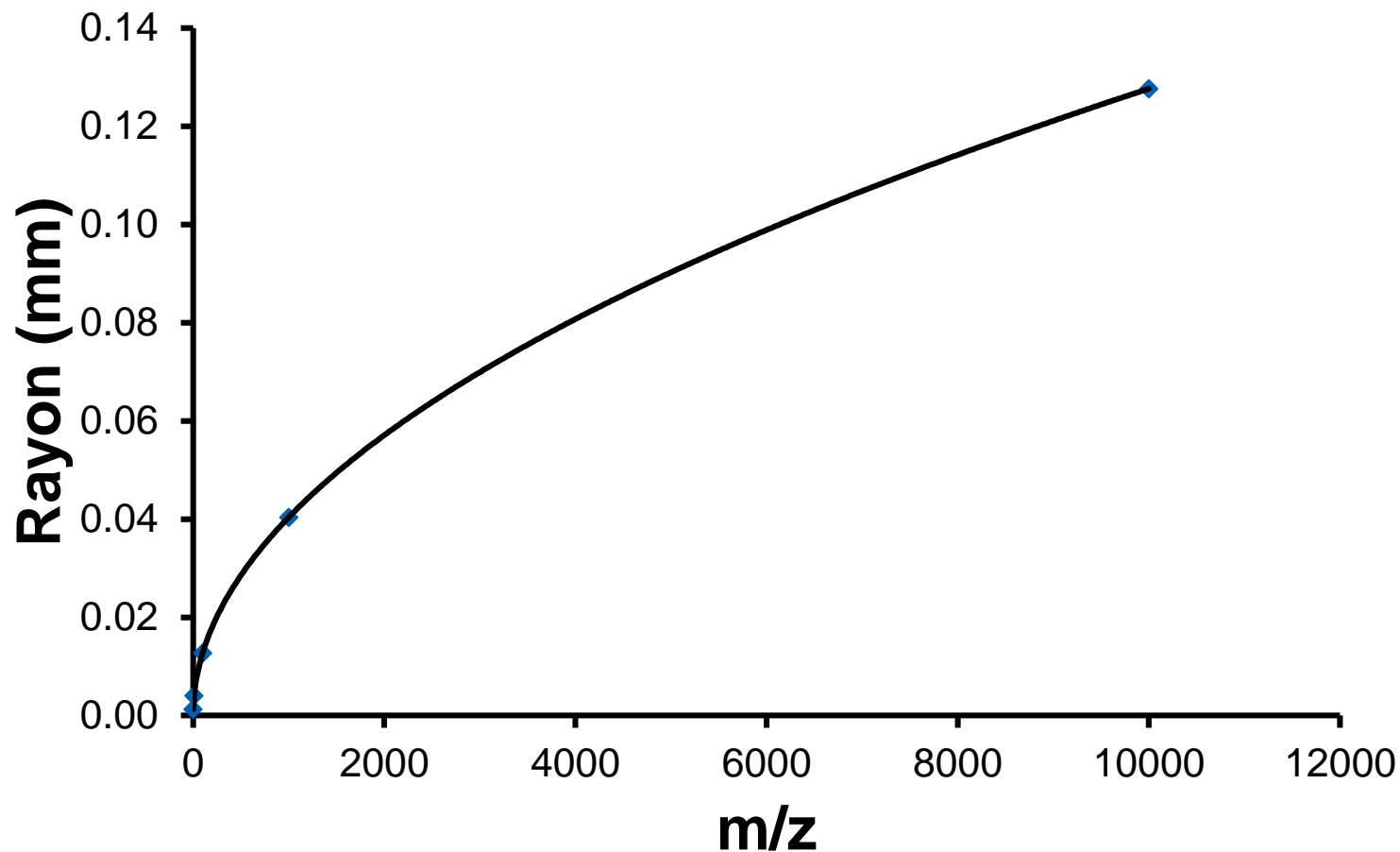
$$r = \frac{mv_{xy}}{qB_0}$$

$$\frac{m\langle v_{xy}^2 \rangle}{2} \cong kT$$

$$r = \frac{1}{qB_0} \sqrt{\frac{mkT}{2}}$$

$$r = \frac{1.336 \times 10^{-6}}{zB_0} \sqrt{mT}$$

Radius of an ion at thermic equilibrium



$B = 9.4$ Tesla

Distance traveled by an ion as a function of time

$$v = \frac{qB_0}{2\pi m}$$

$$m / z = 1000$$

$$B = 9.4 \text{ T}$$

$$r = 10 \text{ mm}$$

$$T = 1 \text{ s}$$

$$d = 2\pi \times r \times v \times T$$

Distance traveled = 10 km

Mean free path of an ion in a buffer gas

Mean free path inside the FT-ICR cell. Buffer gas N₂

| Name | Cytochrome c | Ubiquitin | Angiotensin I | Met-Arg-Phe-Ala |
|---|--------------|-----------|---------------|-----------------|
| Mass (amu) | 12 369 | 8 570 | 1 296 | 523 |
| Charge | 15 | 10 | 3 | 1 |
| CCS (Å ²) | 2579 | 1732 | 474 | 160 |
| Mean free path at 10 ⁻¹⁰ Torr (km) | 12 | 18 | 66 | 194 |

$$\text{Mean free path} \cong \frac{kT}{\sqrt{2\pi} \times p \times d_m \times d_M}$$

Kinetic energy of an ion in function of its diameter

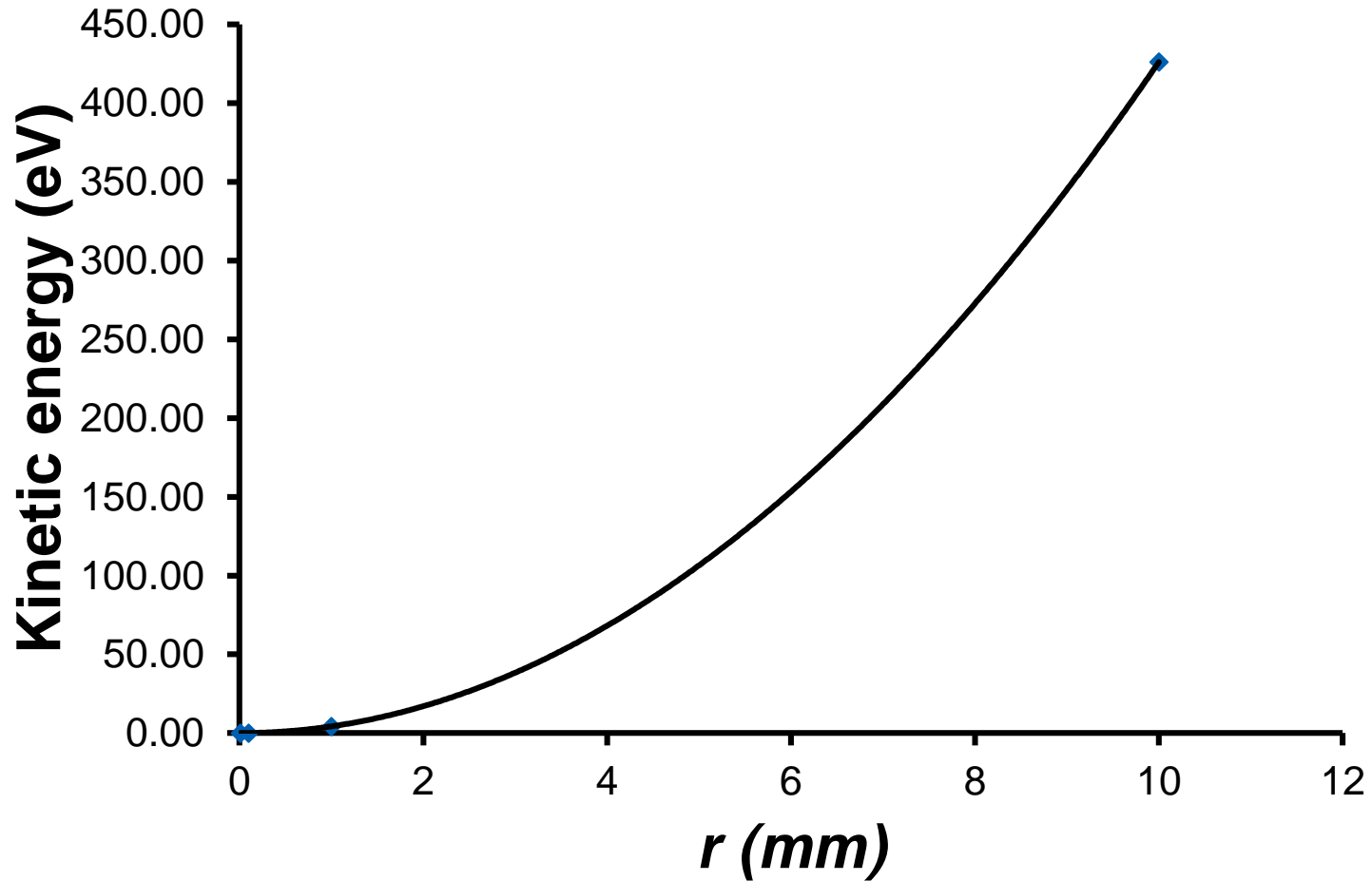
$$\frac{mv_{xy}^2}{r} = qv_{xy}B_0$$

$$v_{xy} = \frac{qB_0r}{m}$$

Kinetic energy

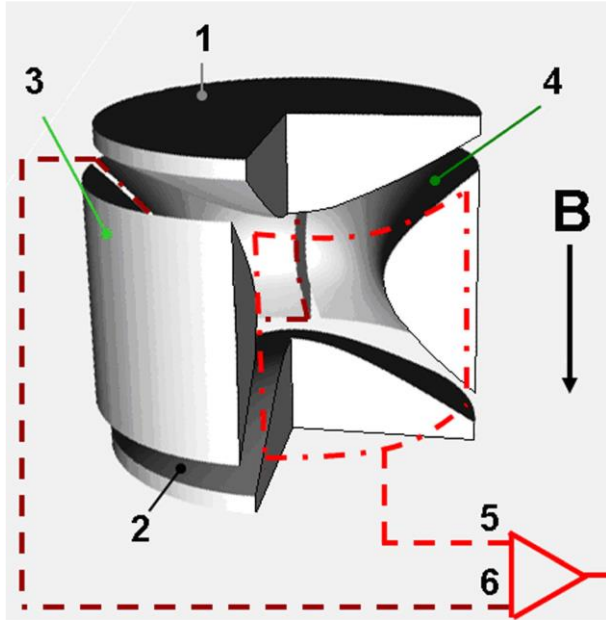
$$\frac{mv_{xy}^2}{2} = \frac{q^2 \times B_0^2 \times r^2}{2m}$$

Kinetic energy versus orbit radius



$B = 9.4$ Tesla, $m/z = 100$

Single ion in a Penning trap: the ideal case (1/6)



Hyperbolic ICR cell.

1, 2: trapping electrodes;
3, 4: excitation electrodes;
5, 6: detection electrodes

$$\Phi(x, y, z) = -\frac{V_{Trap}}{2} \times \left[1 + \frac{4}{a^2} (x^2 + y^2 - 2z^2) \right]$$

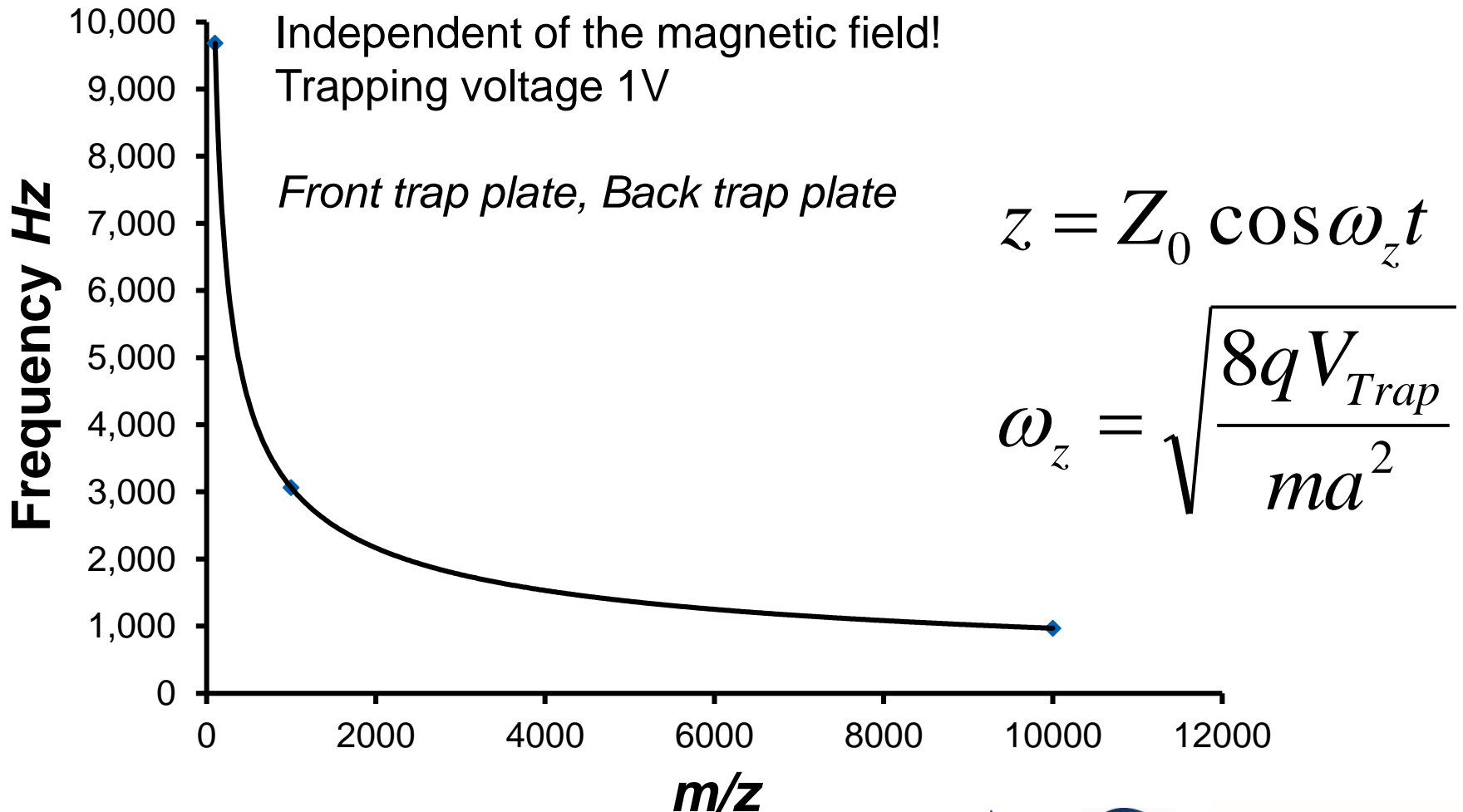
a characteristic dimension of the trap

$$m \frac{d^2 x}{dt^2} = qB \frac{dy}{dt} - 4 \frac{qV_{Trap}}{a^2} x$$

$$m \frac{d^2 y}{dt^2} = -qB \frac{dx}{dt} + 4 \frac{qV_{Trap}}{a^2} y$$

$$m \frac{d^2 z}{dt^2} = 8 \frac{qV_{Trap}}{a^2} z$$

Single ion in a Penning trap: the ideal case (2/6)



Single ion in a Penning trap: the ideal case (3/6)

$$m \left(\frac{d^2 x}{dt^2} + i \frac{d^2 y}{dt^2} \right) = -iqB \left(\frac{dx}{dt} + i \frac{dy}{dt} \right) - 4 \frac{qV_{Trap}}{a^2} x$$

$$x + iy = A_+ e^{i\varpi_+ t} + A_- e^{i\varpi_- t}$$

$$\varpi_{\pm} = \frac{qB \pm \sqrt{q^2 B^2 - \frac{16qV_{Trap}m}{a^2}}}{2m}$$

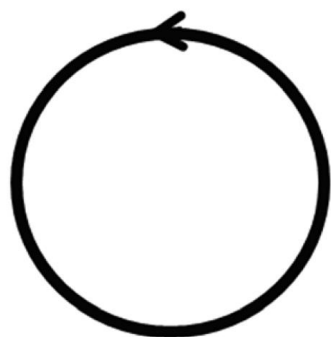
$$\varpi_{\pm} = \frac{\varpi_{Cyclotron}}{2} \pm \sqrt{\left(\frac{\varpi_{Cyclotron}}{2} \right)^2 - \frac{\varpi_Z^2}{2}} \quad \text{note that } \varpi_+ + \varpi_- = \varpi_{Cyclotron}$$

if $\varpi_{cyclotron} \gg \varpi_Z$

$$\varpi_+ = \varpi_{Cyclotron} \left(1 - \left(\frac{\varpi_Z}{\sqrt{2}\varpi_{Cyclotron}} \right)^2 \right) \quad \text{and} \quad \varpi_- = \varpi_{Magnetron} = \varpi_{Cyclotron} \left(\frac{\varpi_Z}{\sqrt{2}\varpi_{Cyclotron}} \right)^2$$

Single ion in a Penning trap: the ideal case (4/6)

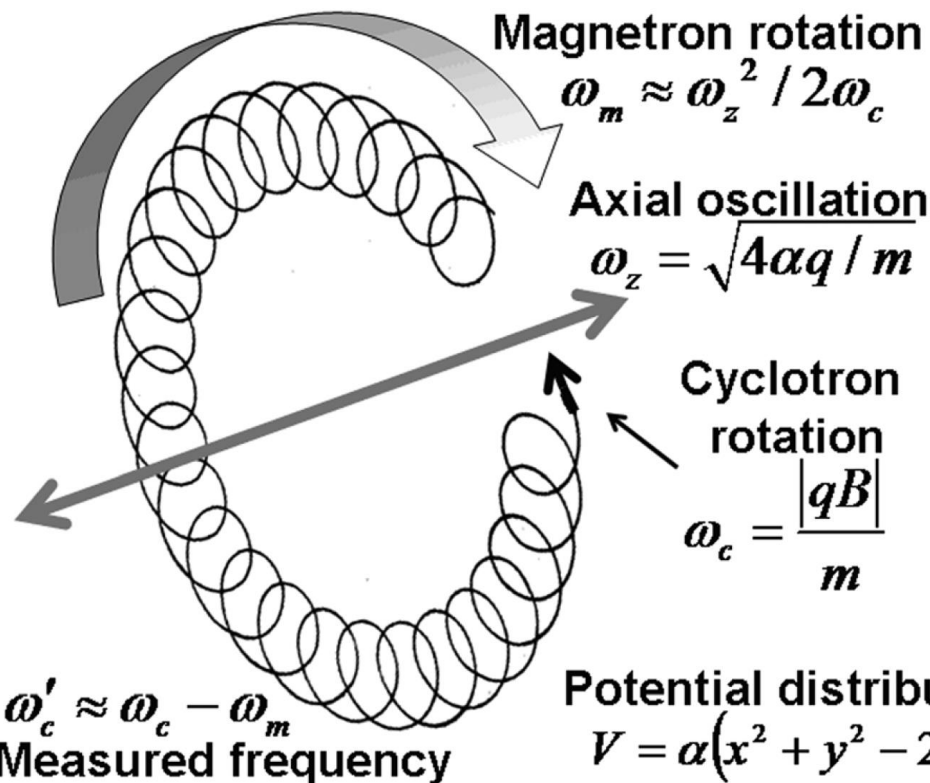
a Ion motion in electric field free space



Cyclotron rotation

$$\omega_c = \frac{|qB|}{m}$$

b Ion motion in an electrostatic trap



Magnetron rotation

$$\omega_m \approx \omega_z^2 / 2\omega_c$$

Axial oscillation

$$\omega_z = \sqrt{4\alpha q / m}$$

Cyclotron rotation

$$\omega_c = \frac{|qB|}{m}$$

Potential distribution:

$$V = \alpha(x^2 + y^2 - 2z^2)$$

Single ion in a Penning trap: the ideal case (5/6)

$$\omega_{\pm} = \frac{qB \pm \sqrt{q^2 B^2 - \frac{16qV_{Trap}m}{a^2}}}{2m}$$

$$q^2 B^2 - \frac{16qV_{Trap}m}{a^2} > 0 \Rightarrow \frac{m}{q} < \frac{B^2 a^2}{16V_{Trap}}$$

Upper mass limit: $B = 9.4$ T, Trapping voltage 1 V, $a = 2.5$ cm $\Rightarrow 10^5$ Da

Single ion in a Penning trap: the ideal case (6/6)

$$x + iy = A_+ e^{i\varpi_+ t} + A_- e^{i\varpi_- t}$$

$$x = A_+ \cos \varpi_+ t + A_- \cos \varpi_- t$$

$$y = A_+ \sin \varpi_+ t + A_- \sin \varpi_- t$$

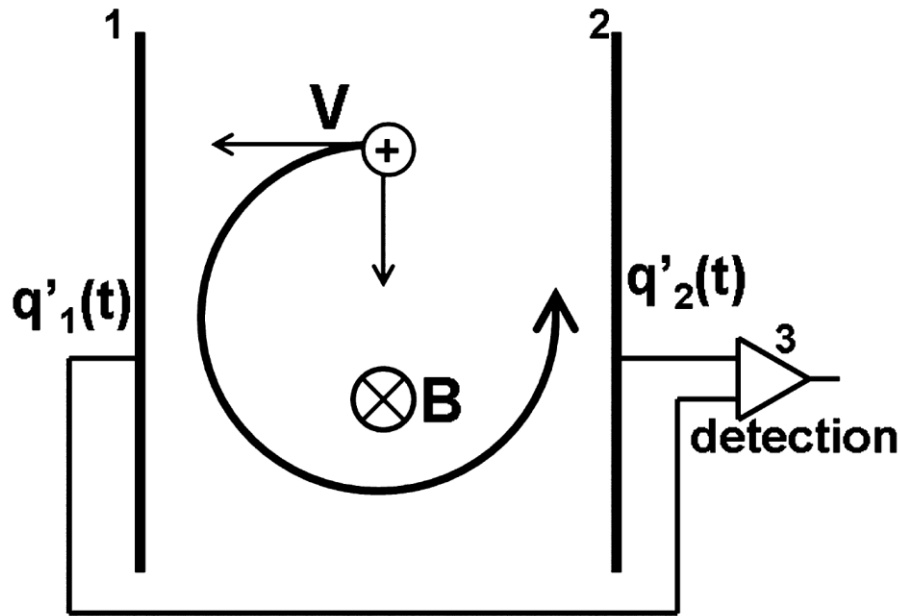
$$x_0 = A_+ + A_-$$

$$\frac{dy_0}{dt} = A_+ \varpi_+ + A_- \varpi_-$$

$$A_+ = \frac{\frac{dy_0}{dt} - x_0 \varpi_-}{\varpi_+ - \varpi_-}$$

$$A_- = \frac{x_0 \varpi_+ - \frac{dy_0}{dt}}{\varpi_+ - \varpi_-}$$

Signal induced in a planar capacitor



The principle of the ICR signal measurement. 1, 2: detection electrodes; $q_{01}(t)$ $q_{02}(t)$: induced image charges; and 3: preamplifier.

$$\Delta Q = -2 \frac{qy}{d}$$

$$i = \frac{d}{dt} \Delta Q$$

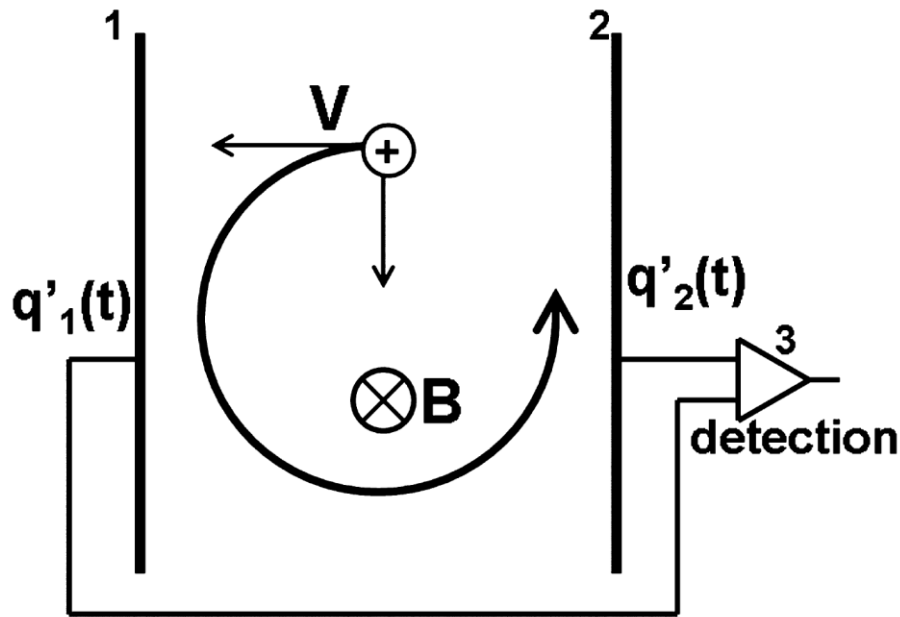
$$i = -\frac{2q}{d} \times \frac{dy}{dt}$$

$$i = -\frac{2qR\omega_{\text{Cyclotron}}}{d} \cos \omega_{\text{Cyclotron}} t$$

i proportional to B via ω

i proportional to R/d

Ion excitation



The principle of the ICR signal measurement. 1, 2: detection electrodes; $q_{01}(t)$ $q_{02}(t)$: induced image charges; and 3: preamplifier.

$$\Delta Q = -2 \frac{qy}{d}$$

$$i = \frac{d}{dt} \Delta Q$$

$$i = -\frac{2q}{d} \times \frac{dy}{dt}$$

$$i = -\frac{2qR\omega_{\text{Cyclotron}}}{d} \cos \omega_{\text{Cyclotron}} t$$

i proportional to B via ω

i is independent of m

i proportional to R/d

Coherent excitation of an ion

$$E = \frac{2V(\omega)}{d}$$

$$A(t) = qE \cdot v_{xy}$$

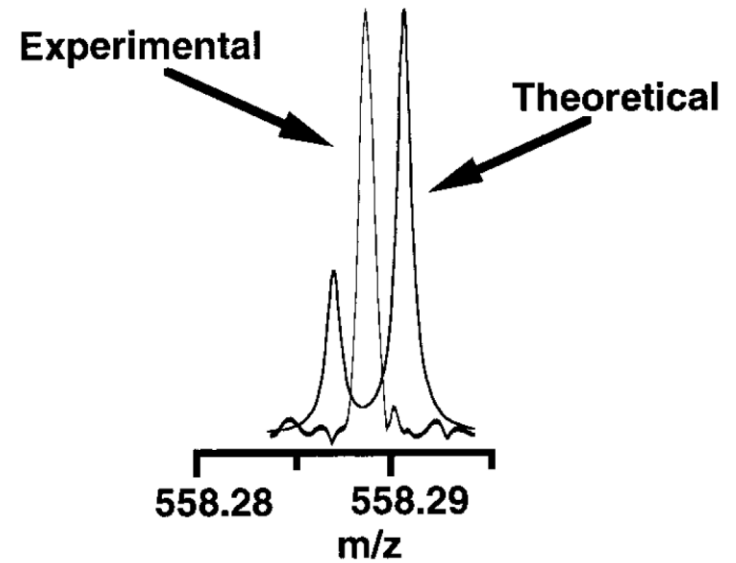
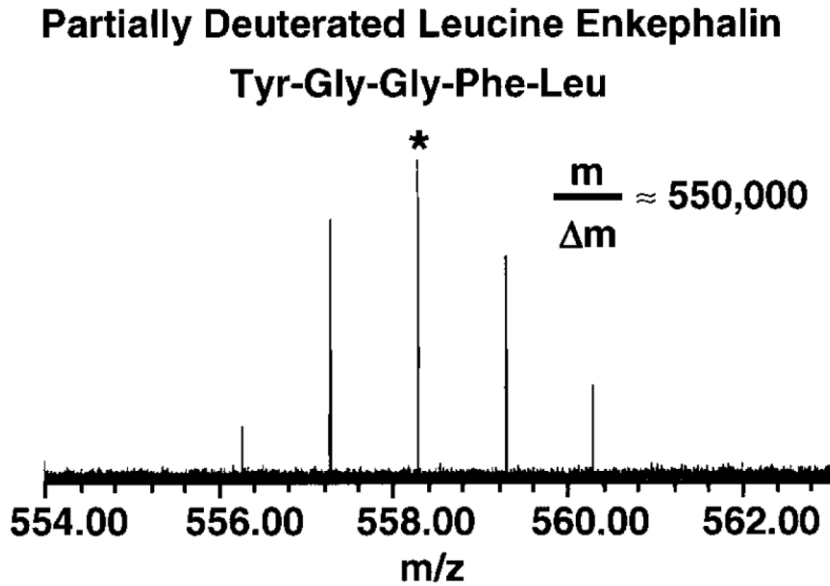
$$\frac{mv_{xy}^2}{2} = \int_0^{T_{excitation}} A(t) dt$$

The radius is independent of the mass

But not the energy, nor the distance traveled,
nor the phase ...

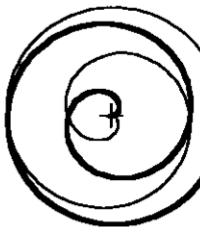
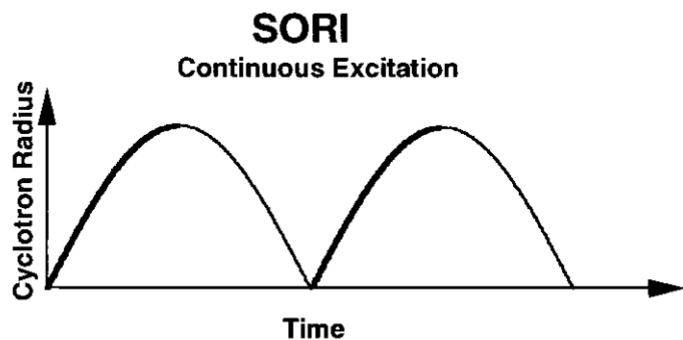
$$r = \frac{ET_{excitation}}{2B_0}$$

Peak coalescence

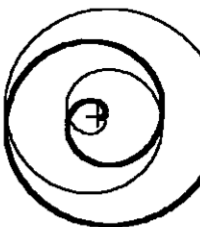
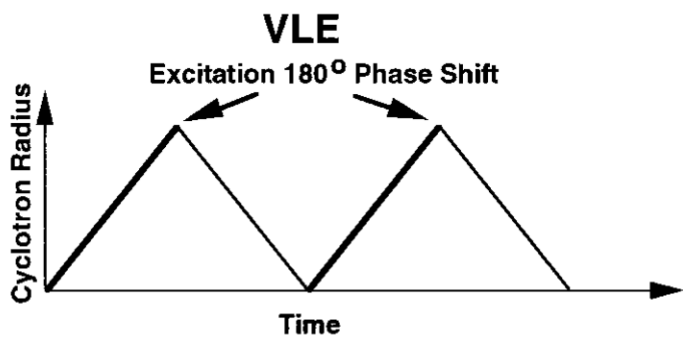


$$\frac{m}{\Delta m} < \approx \frac{B^2 R}{m(n_1 q_1 + n_2 q_2)}$$

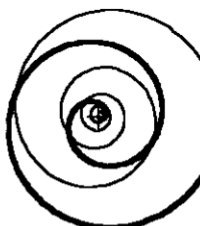
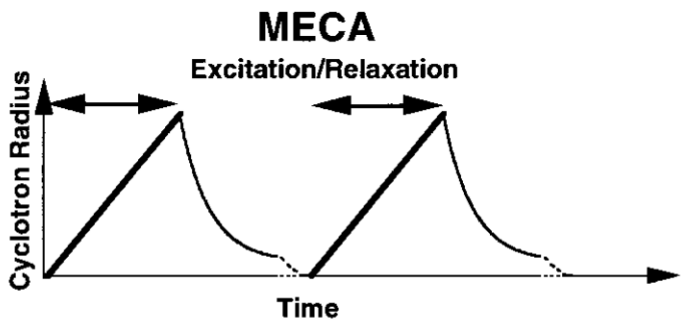
Ion excitation for in-cell CAD



Time evolution of ion cyclotron radius (left) and ion *motion* based on repeated single-frequency dipolar excitation for collision induced dissociation (CID).



In sustained off-resonance irradiation (**SORI**) ions of a selected m/z ratio are alternately excited and de-excited due to the difference between the excitation frequency and the ion cyclotron frequency.



In **very low energy (VLE) CID** ions are alternately excited and de-excited by resonant excitation whose phase alternates bimodally between 0 and π .

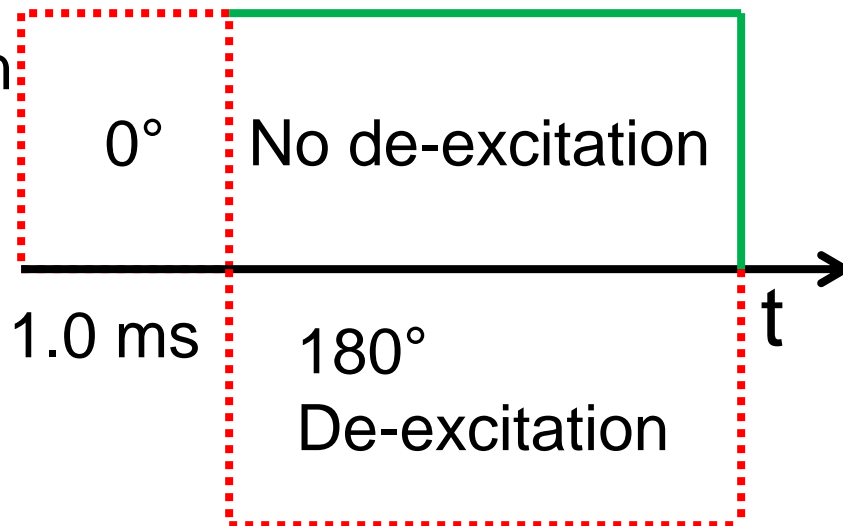
In multiple excitation for collisional activation (MECA) ions are resonantly excited and then allowed to relax by collisions.

Original ICR excitation reversibility proof

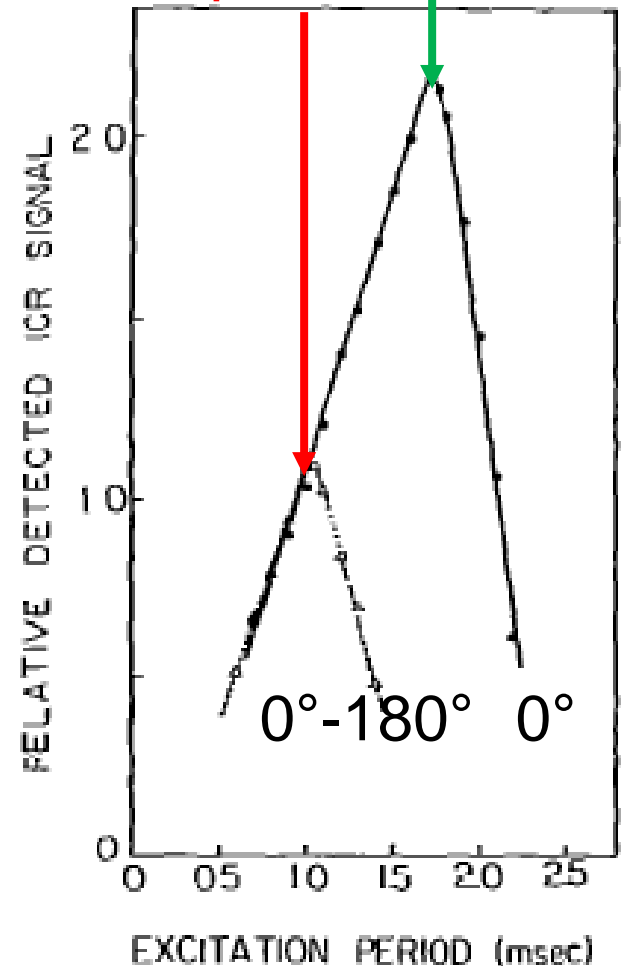
Coherently excited ions:

- Excitation voltage ***in phase with*** ion motion: ions excited to higher radius
- Excitation voltage ***in phase opposition with*** ion motion: ions de-excited to center of ICR cell.

Excitation
voltage
phase



R ions > R of ICR cell
180° pulse



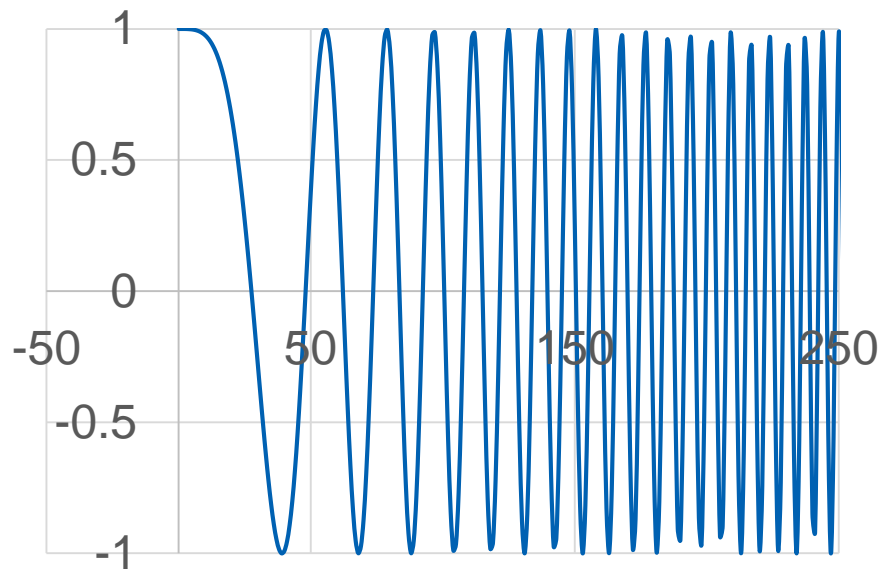
Uncoherent excitation of an ion

$$E = \frac{2V(\omega_{Excitation})}{d}$$

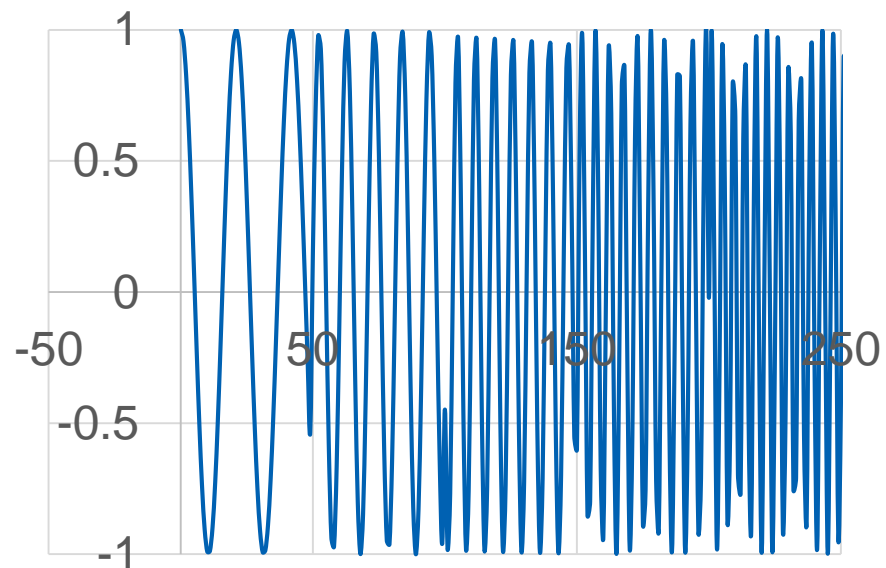
$$A(t) = qE \cdot v_{xy}(\omega_{Cyclotron})$$

$$\frac{mv_{xy}^2}{2} \cong \int_0^{T_{excitation}} \sin(\omega_{Excitation}t + \varphi) \sin(\omega_{Cyclotron}t) dt$$

Chirp excitation



Continuous chirp



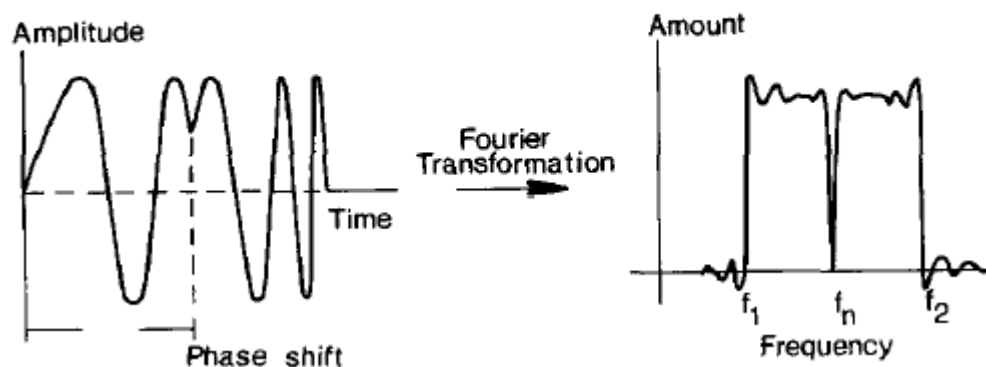
Chirp by block
Bruker

This scheme is weird see the next slide for explanation.

The phase must be continuous

Isolation by Notch Ejection Method

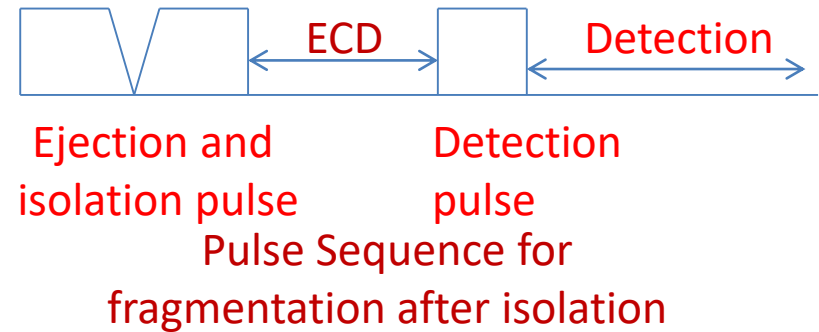
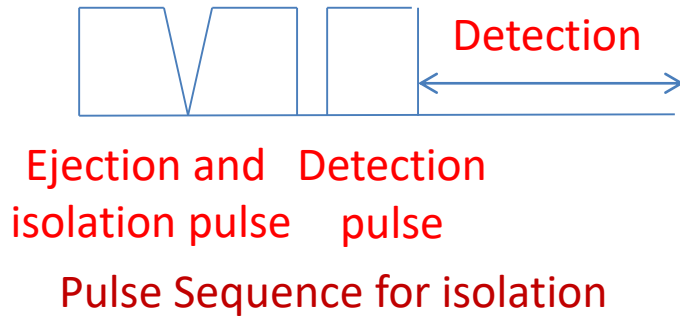
In this method,



- Phase inverted, introducing a notch centered on the frequency of interest, f_n .
- Ion to be selected remains in the centre, all others are ejected.

Experimental Technique

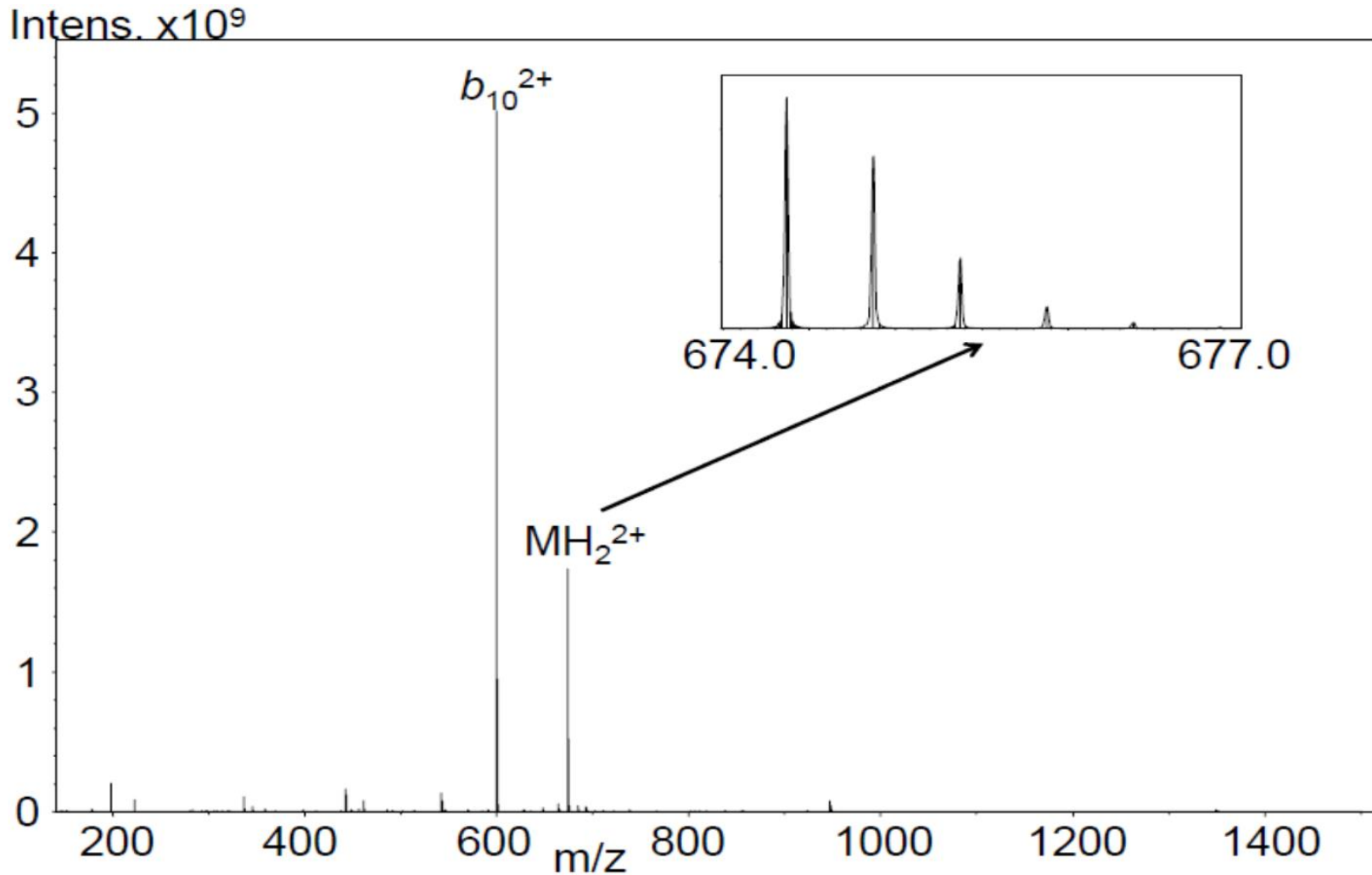
- Experiments performed on Bruker Daltonics 9.4 T ApexQE FT-ICR mass spectrometer.
- Sample: 1pm/ μl of substance P (MW 1347.63) in 50:50 $\text{H}_2\text{O}:\text{MeOH}$ + 0.1% formic acid



- Power level is an attenuation in dB
Power of all pulses = 25 dB
- Pulse lengths are in μs per frequency increment of 62.5 Hz
Ejection Pulse=300 μs , Detection Pulse= 100 μs
- Excitation pulse \rightarrow ion radius increased \rightarrow ion detectable
Longer pulse length \rightarrow ion ejected
Shorter pulse length \rightarrow ion detected
- For fragmentation by Electron Capture Dissociation
ECD heater at 1.7A , Electron beam pulse duration 0.03 s

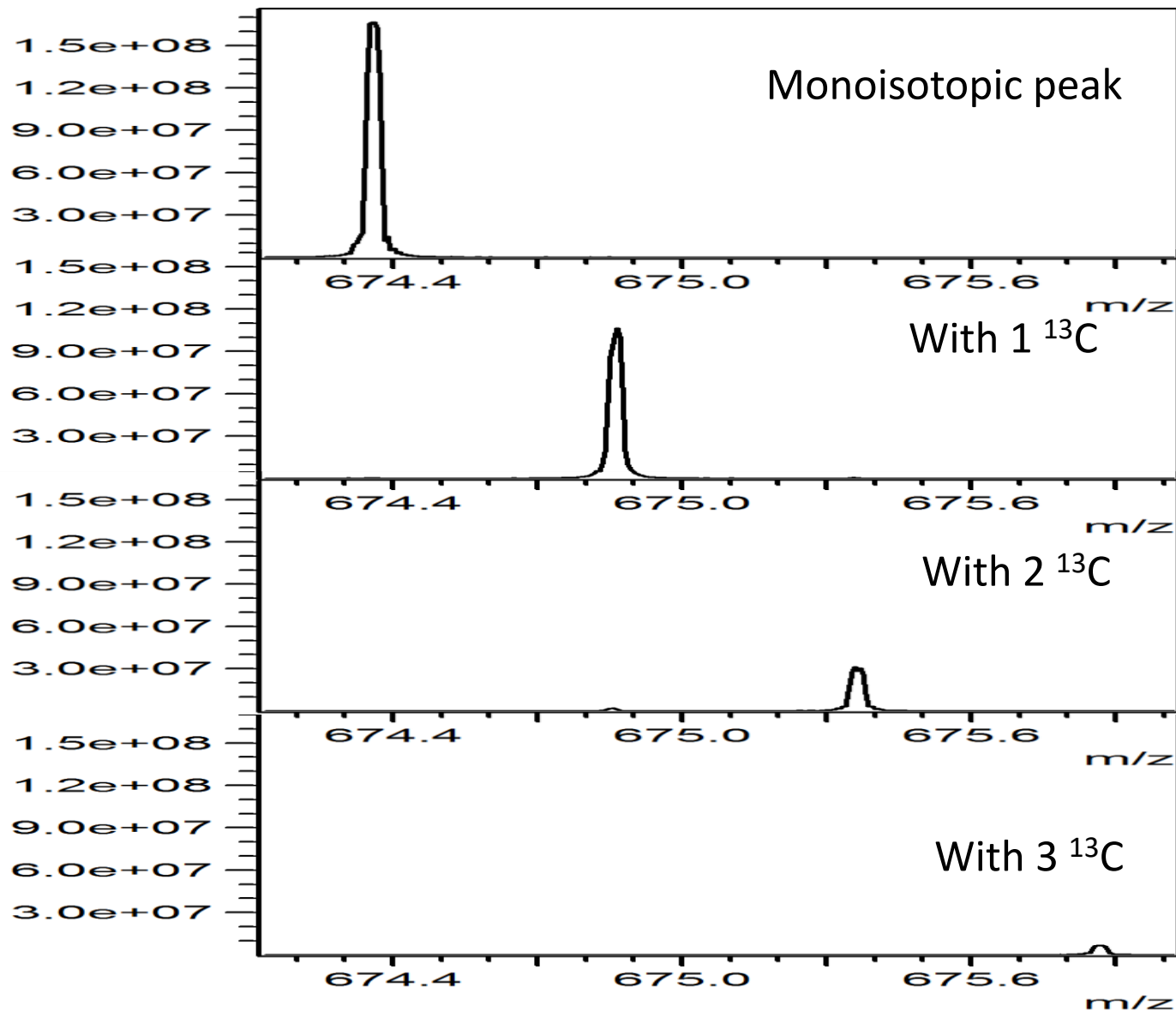
Results with this Method

Mass spectrum of **substance P**



Isolation of isotopes of MH_2^{2+} up to three ^{13}C isotope

Intens.



Calibration laws

TABLE 1. Proposed calibration procedures

| | |
|--|------------------------------------|
| $f = \frac{a}{m}$ | basic law of ions in a B field |
| $f^2 = \frac{a}{m^2} + \frac{b}{m}$ | (Beauchamp-Armstrong et al., 1969) |
| $f^2 = \frac{a}{m^2} + \frac{b}{m} + c$ | (Ledford et al., 1980) |
| $f_{sideband} = \frac{a}{m}$ | (Allemann et al., 1981) |
| $f = \frac{a}{m} + c$ | (Francl et al., 1983) |
| $\left(\frac{M}{Z}\right) = \frac{a}{f_{obsd}} + \frac{b}{f_{obsd}^2}$ | (Ledford et al., 1984b) |
| $f_{estimated} = f_{measured} + c(I_{calibrant} - I_{analyte})$ | |
| $\frac{m}{z} = \frac{A}{f_{estimated}} + \frac{B}{f_{estimated}^2} + \frac{C}{f_{estimated}^3}$ | (Easterling et al., 1999) |
| $M = \left(\frac{kB}{f_n + \Delta f}\right)n - n(M_c)$ | (Bruce et al., 2000) |
| $\left(\frac{M}{Z}\right)_i = \frac{a}{f_{obsd}} + \frac{b}{f_{obsd}^2} + \frac{CI_i}{f_{obsd}^2}$ | (Masselon et al., 2002) |
| $\frac{m}{z} = \frac{A}{v} + \frac{B}{v^2} + \frac{C}{v^3} + \frac{BC}{Av^4}$ | (Wang et al., 1988) |

Calibration (Bruker)

2 parameters

$$f = \frac{ML1}{m} - ML2$$

$$m = \frac{ML1}{f + ML2}$$

3 parameters

$$f = \frac{ML1}{m} + \frac{ML3}{m^2} - ML2$$

$$m^2 f = mML1 + ML3 - m^2 ML2$$

$$m^2 (f + ML2) - mML1 - ML3 = 0$$

$$\delta = ML1^2 + 4(f + ML2)ML3$$

$$m = \frac{ML1 + \sqrt{\delta}}{2(f + ML2)}$$

Broad band digital acquisition

The **Nyquist-Shannon** theorem states that the **sampling frequency** of a signal must be equal to or greater than **twice the maximum frequency** contained in this signal, in order to convert this signal from an analog form to a digital form without loss or aliasing

$$V_{\text{Nyquist-Shannon}} = \frac{qB_0}{2\pi m_{\text{Start}}}$$

$$V_{\text{Sampling}} \cong \frac{1}{m_{\text{Start}}}$$

$$\Delta t_{\text{Sampling}} \cong m_{\text{Start}}$$

Acquisition from 8 k ($2^{13} = 8\,192$) words to 8 M ($2^{23} = 8\,386\,608$) words or above

From ions to spectrum

Broad band acquisition

$$acquisition\ time = v_{sampling} \times memory_size$$

$$acquisition\ time \cong m_{Start} \times memory_size$$

$$\frac{m}{\Delta m} \cong \frac{qB_0 T_{Acquisition}}{m}$$

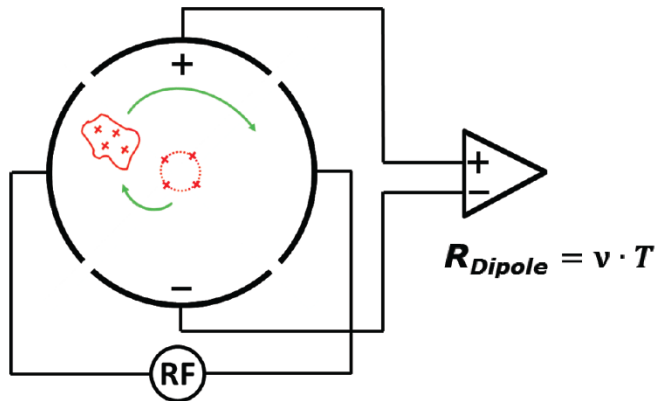
$$\frac{m}{\Delta m} \cong \frac{1}{m} \times m_{Start} \times memory_size$$

Dependence of parameters according to the magnetic field

| | | |
|---|--|----------|
| 1 | Frequency at a given mass | B^{-1} |
| 2 | Resolution | B |
| 3 | Acquisition time at a given resolution | B^{-1} |
| 4 | Kinetic energy for a given radius | B^2 |
| 5 | Highest mass | B^2 |
| 6 | Number of trapped ions | B^2 |

Quadrupolar detection

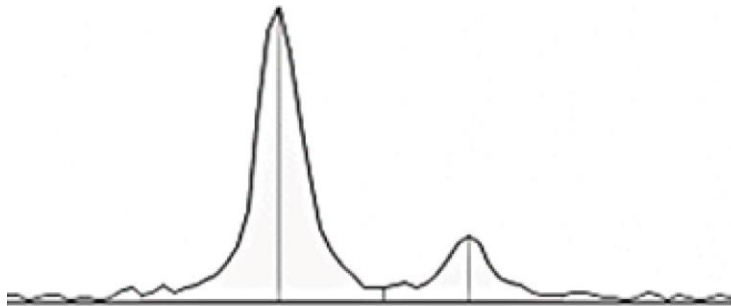
Standard 1ω Dipole Detection



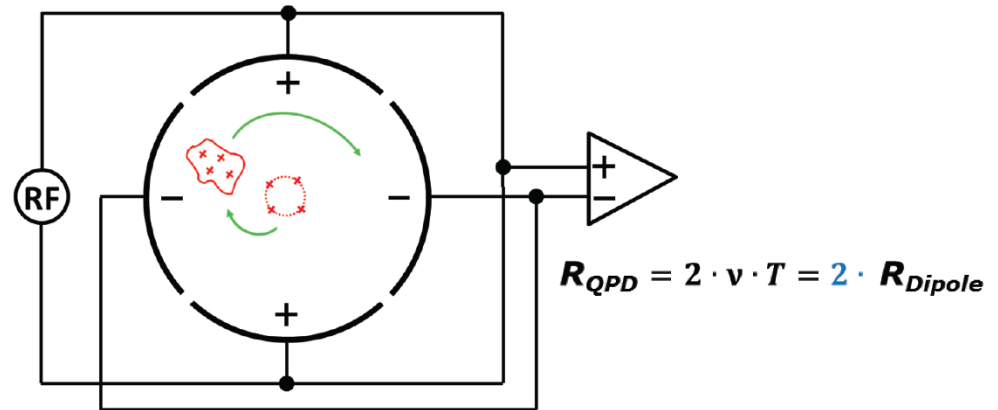
Direct detection of the cyclotron frequency ω_+

Direct detection of the cyclotron frequency

$$R_{DD} = \nu \cdot T$$



2ω Quadrupolar Detection (QPD)

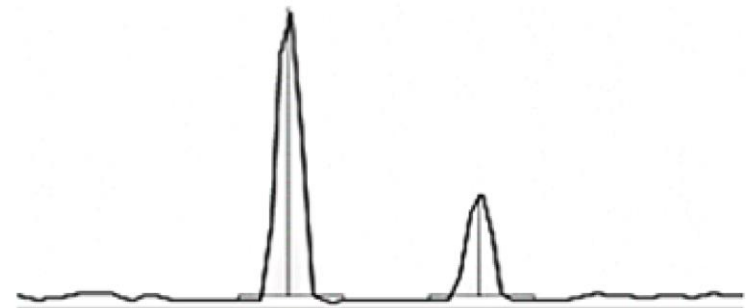


QUADRUPOLE-DETECTION FT-ICR MASS SPECTROMETRY*
L. SCHWEIKHARD, M. LINDINGER and H.-J. KLUGE published 1990

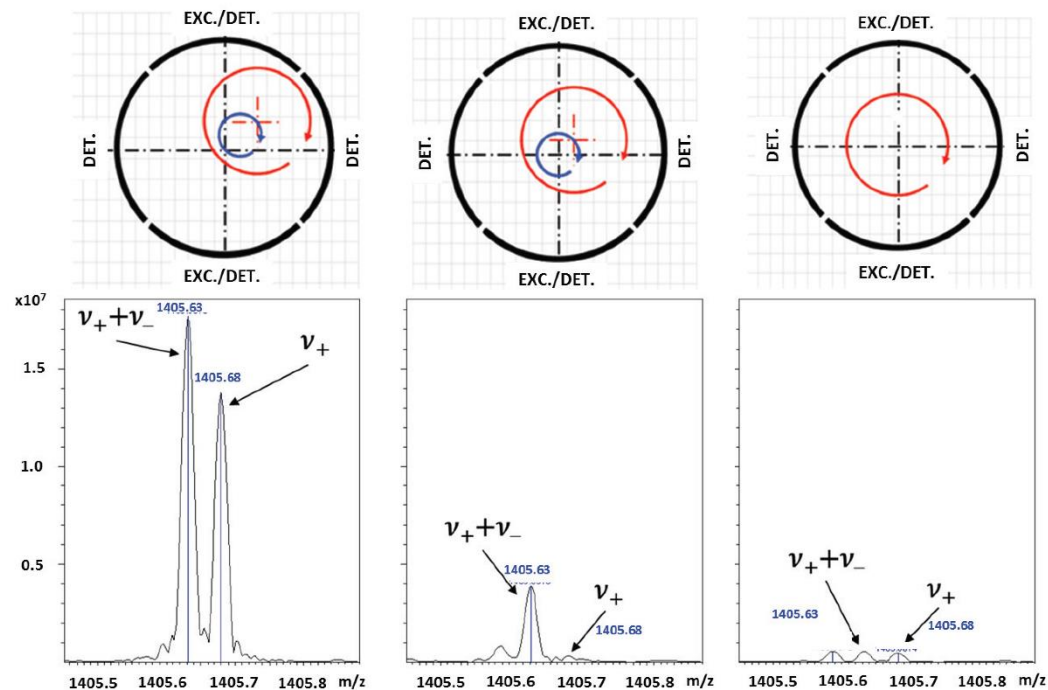
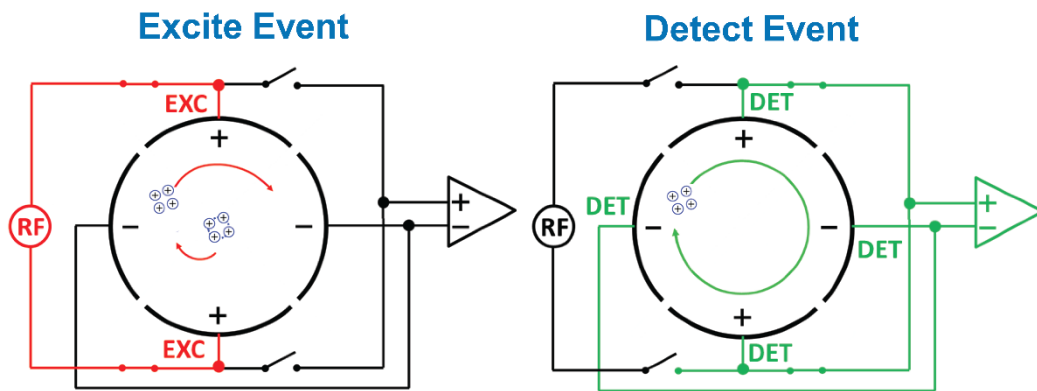
Direct detection of the **double** cyclotron frequency $2\omega_+$

Direct detection of the double cyclotron frequency

$$R_{QPD} = 2 \cdot \nu \cdot T = 2 \cdot R_{DD}$$

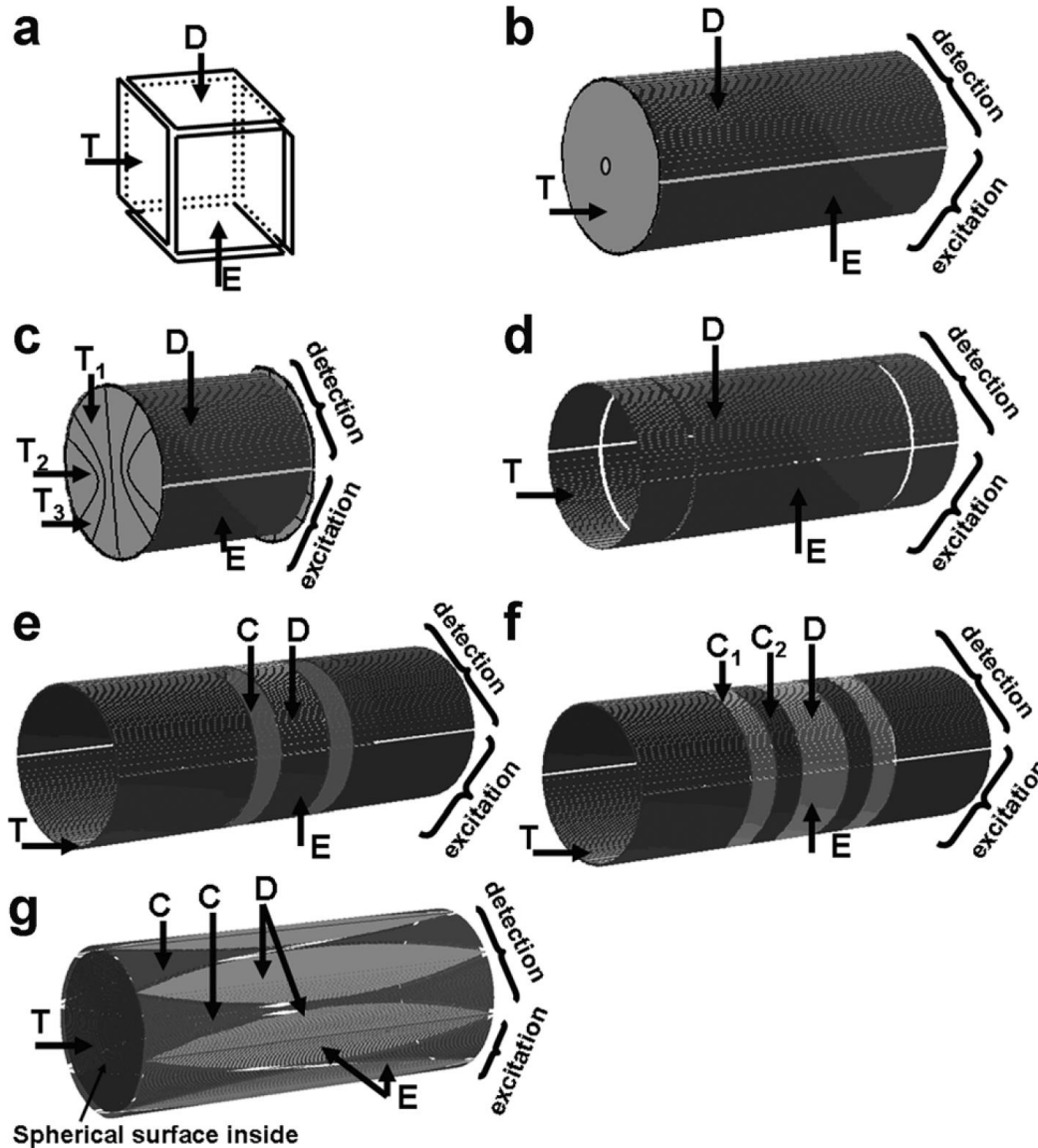


Quadrupolar detection



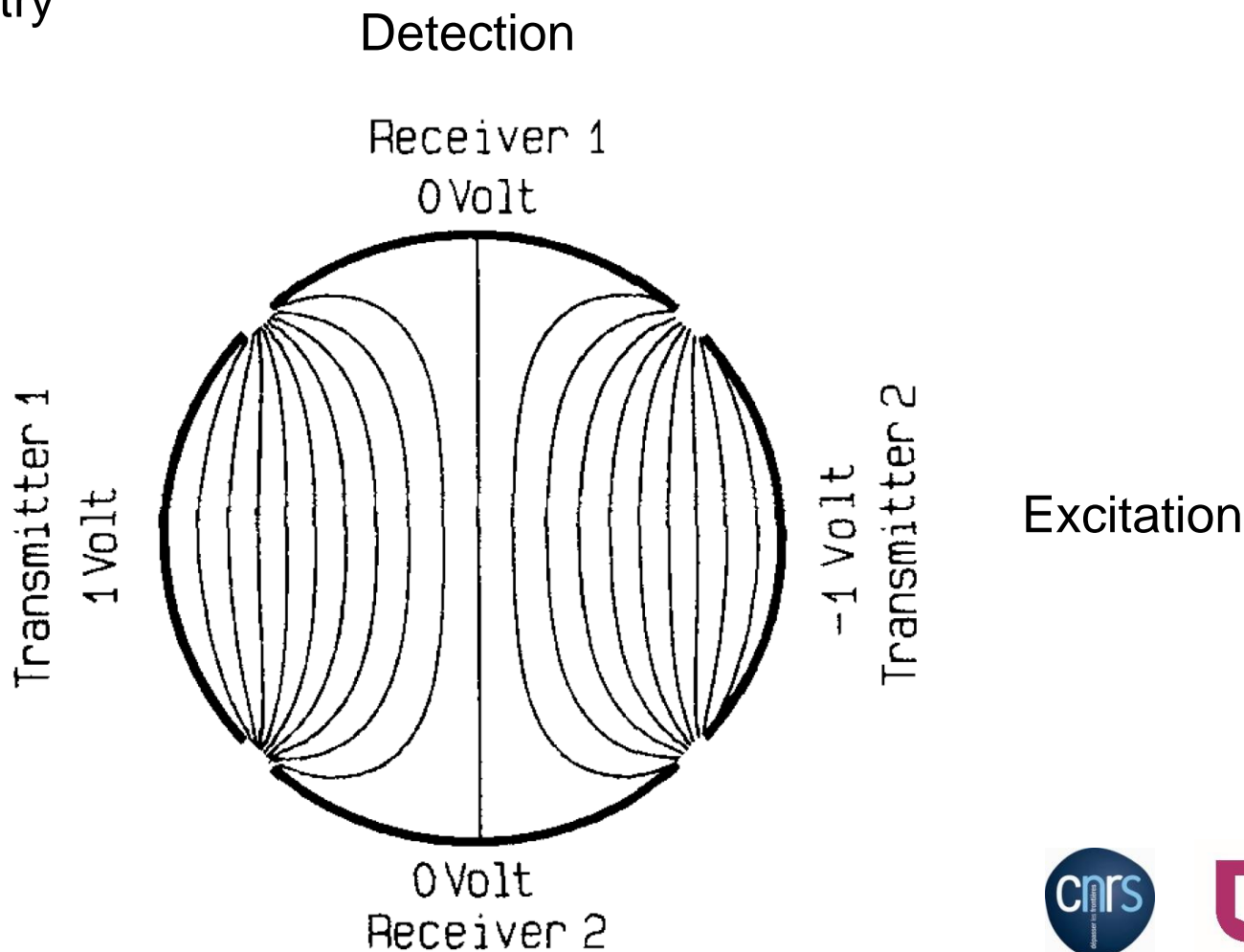
Uncorrected → dc Shimming → Gated Deflection

The cell zoology



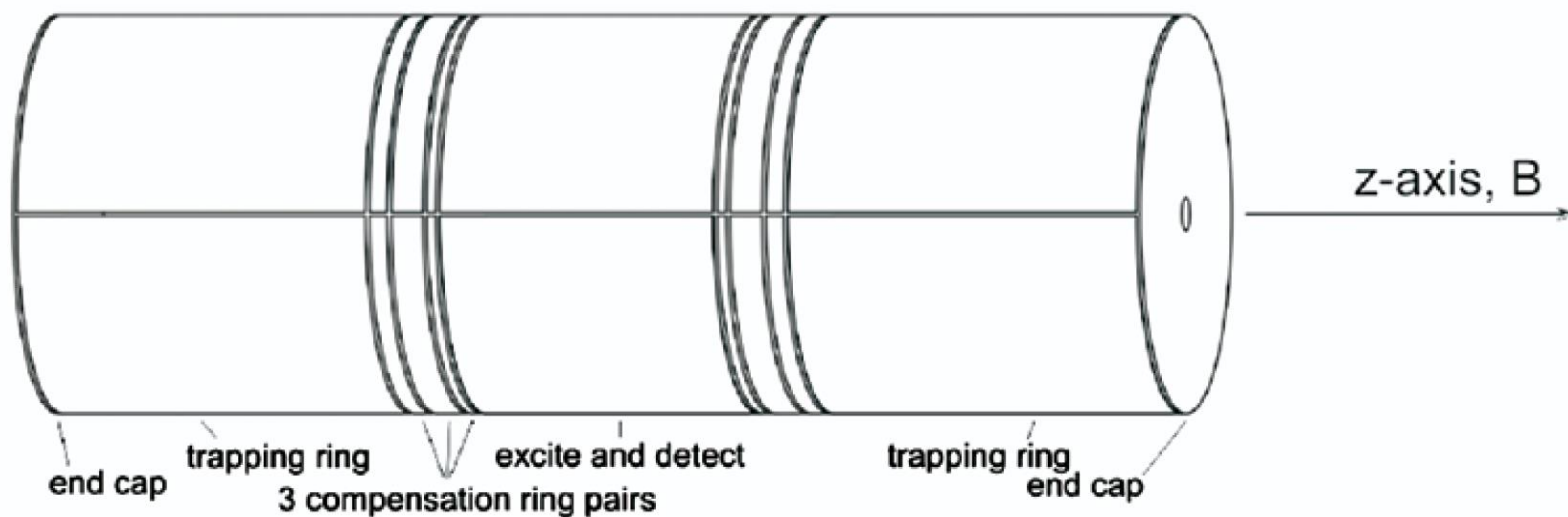
Infinity cell

The 'Infinity Cell': a New Trapped-ion Cell With Radiofrequency Covered Trapping Electrodes for Fourier Transform Ion Cyclotron Resonance Mass Spectrometry



Compensated cells

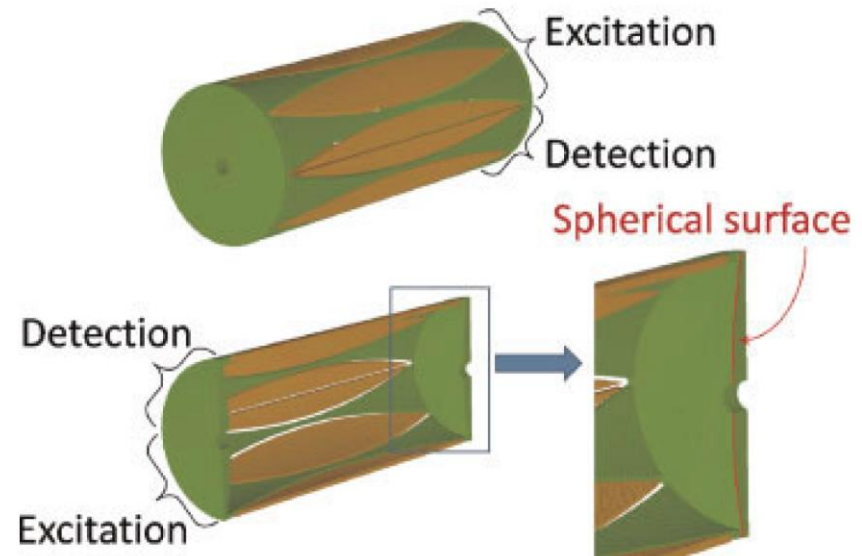
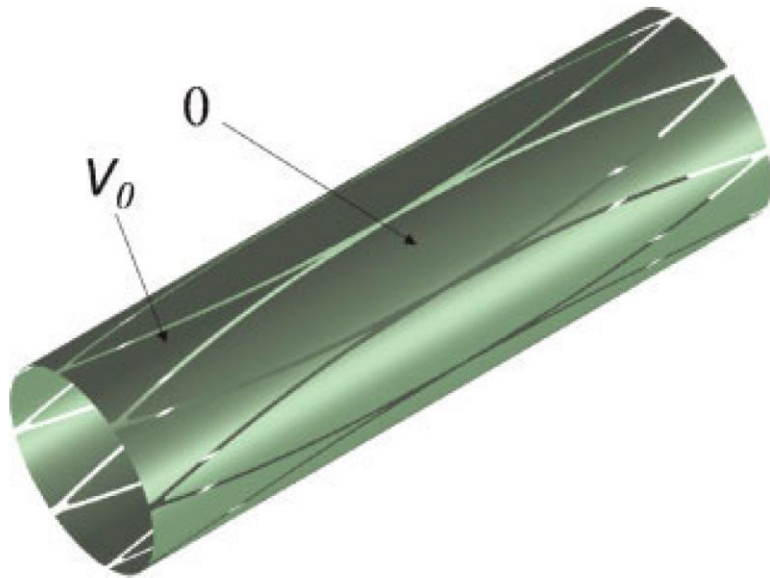
An Electrically Compensated Trap Designed to Eighth Order for FT-ICR Mass Spectrometry



Harmonized cell (Paracell®)

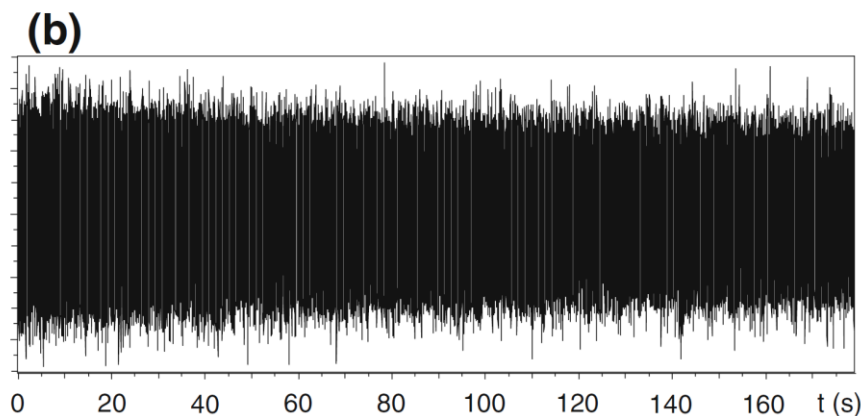
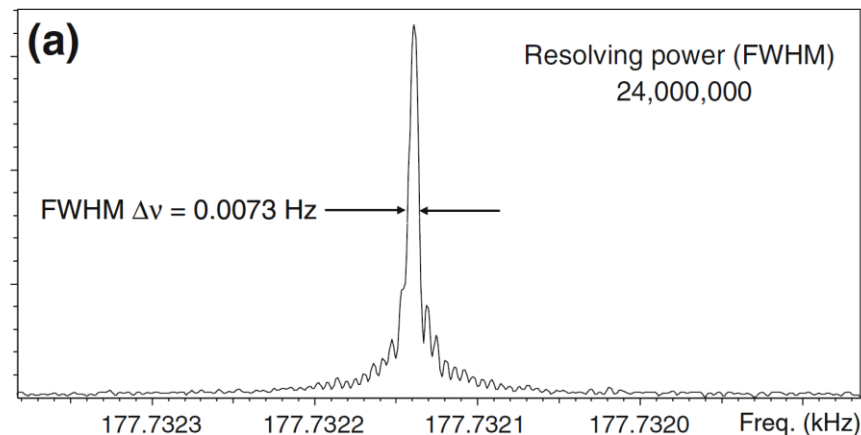
The method extends the region of harmonicity potentially to the entire cell volume. It is based on subdividing cell cylindrical surface into segments with shapes producing quadratic dependence on axial coordinate of an **averaged (along cyclotron orbit) electric potential** at any radius of cyclotron motion.

$$\Phi(x, y, z) = -\frac{V_{Trap}}{2} \times \left[1 + \frac{4}{a^2} (x^2 + y^2 - 2z^2) \right]$$

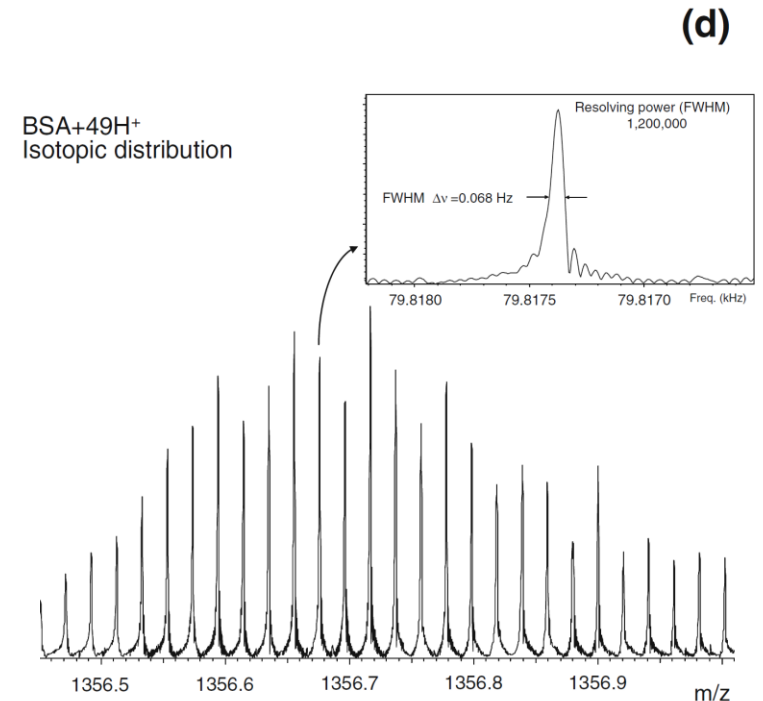
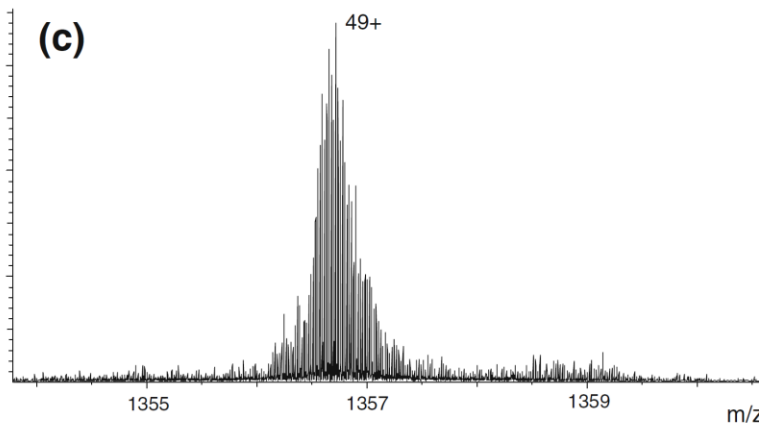
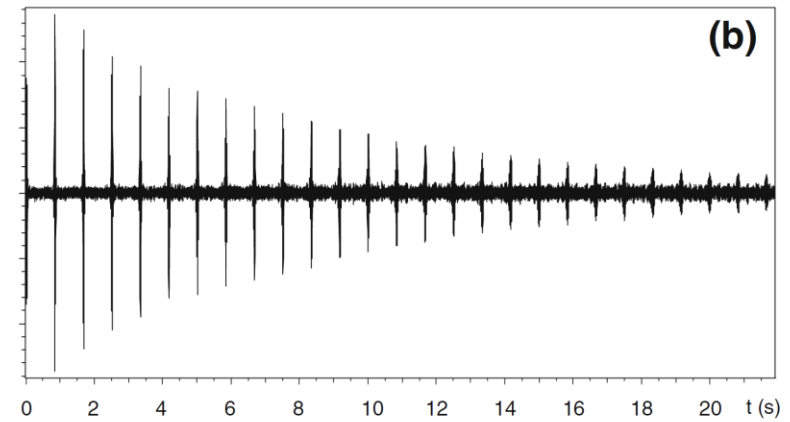
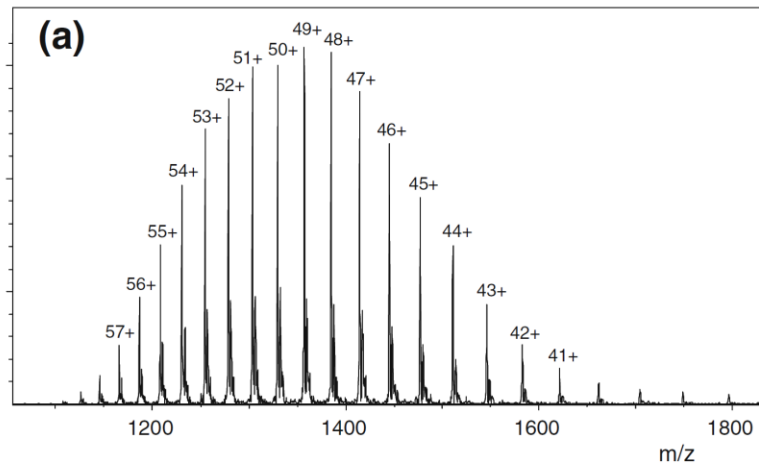


Harmonized cell (Paracell®)

- (a) Frequency spectrum (not calibrated) of the mono isotopic peak of singly charged, protonated reserpine (m/z 609.28066) with a resolving power of 24,000,000, resulting from magnitude FFT calculation without apodization.
- (b) Time domain spectrum of reserpine, detected over 3 min

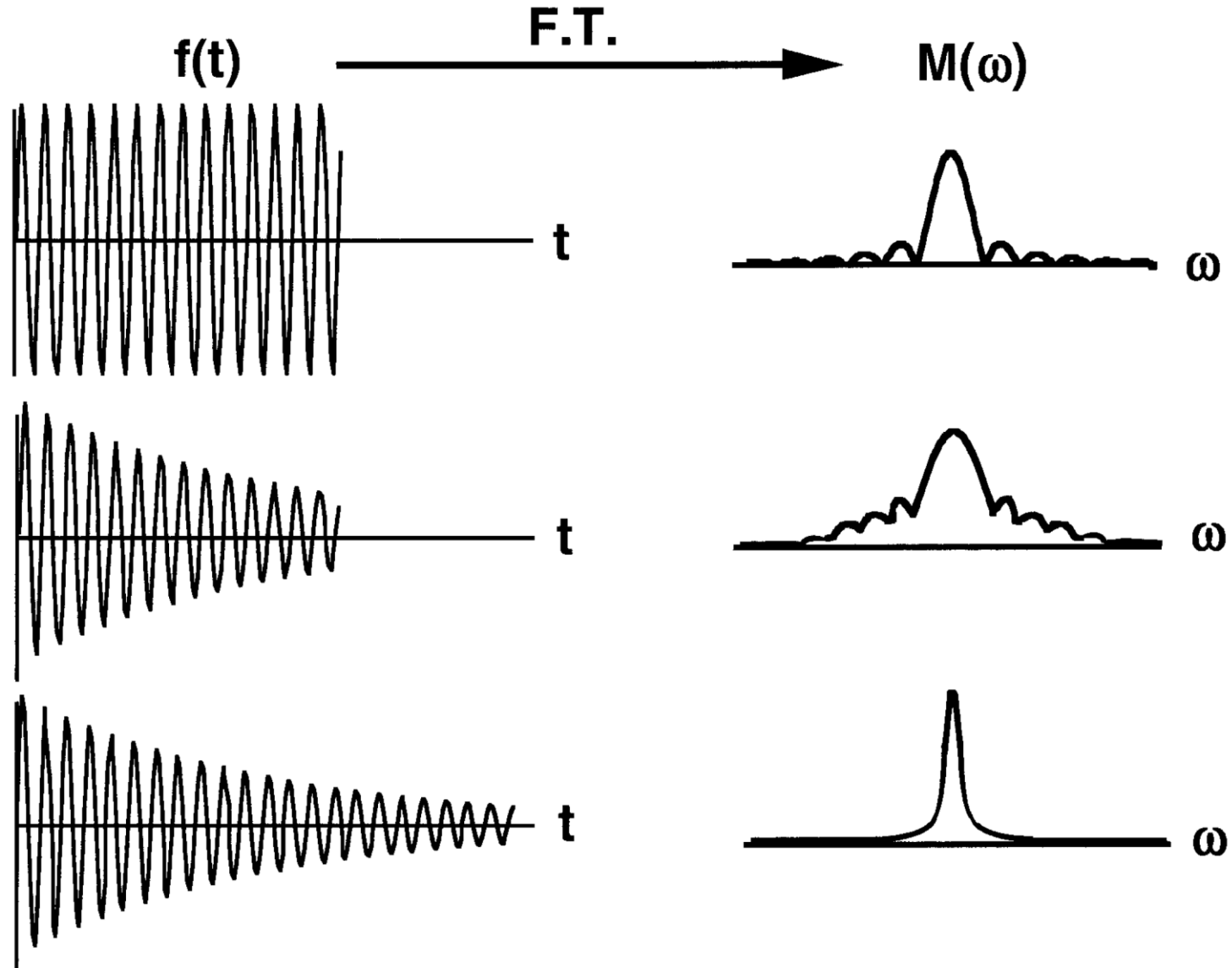


Harmonized cell (Paracell®)

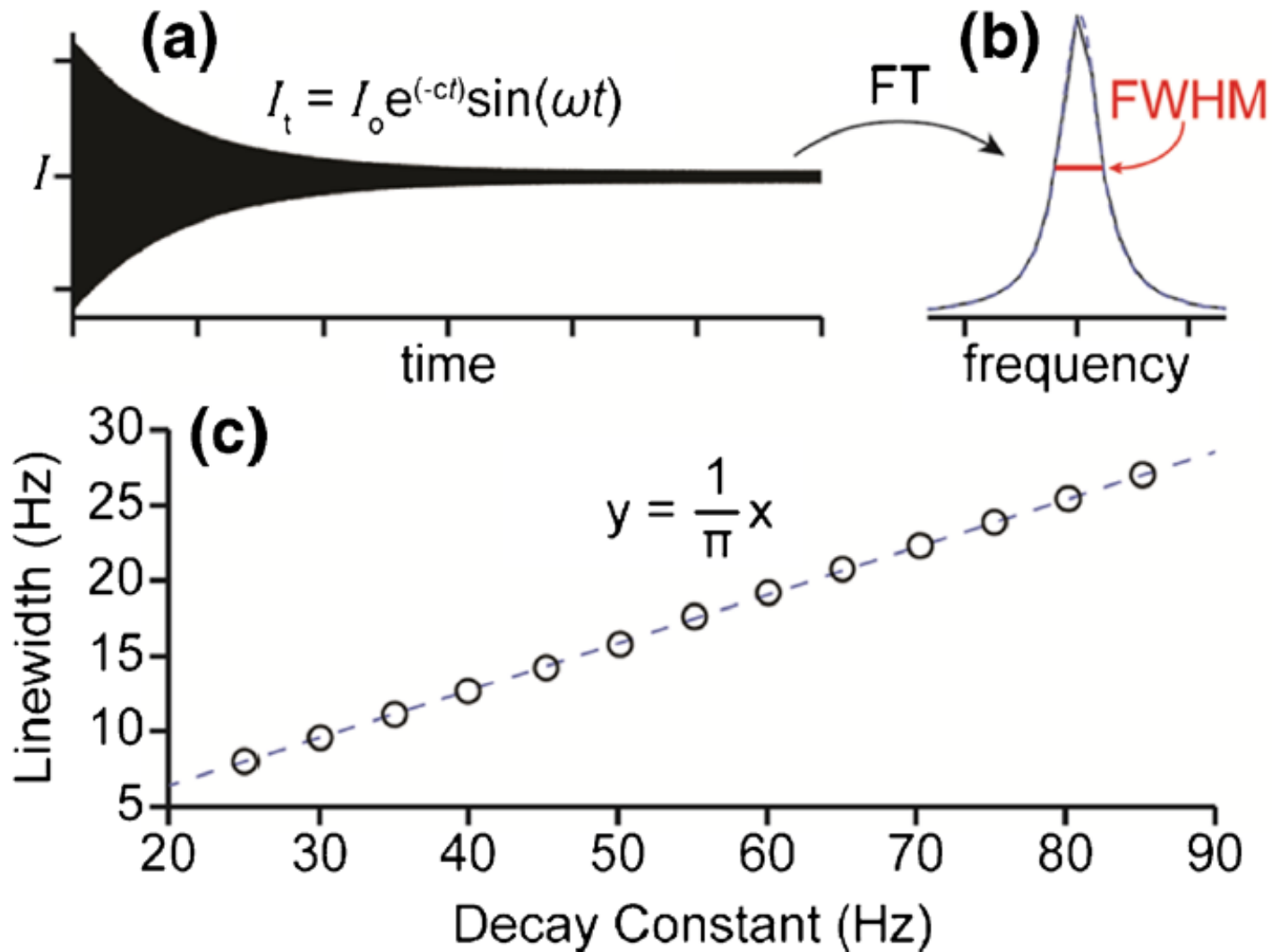


- (a) Broadband mass spectrum of bovine serum albumin (BSA) showing the distribution of charge states ranging from 37+ up to 60+.
- (b) Time domain spectrum of the isolated charge state 49+ (BSA with 49 protons) detected over 22 s.
- (c) Mass spectrum of the isolated charge state isotopic distribution of 49+ of BSA achieved by magnitude FFT calculation from the transient (b).
- (d) Zoom in of the mass spectrum (c), demonstrating a resolving power of 1,200,000

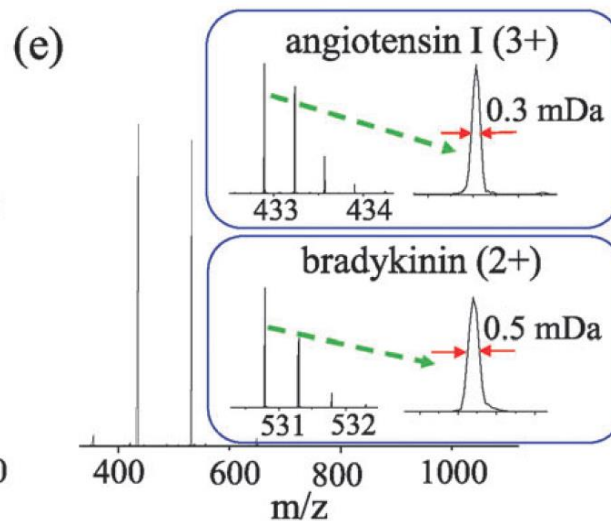
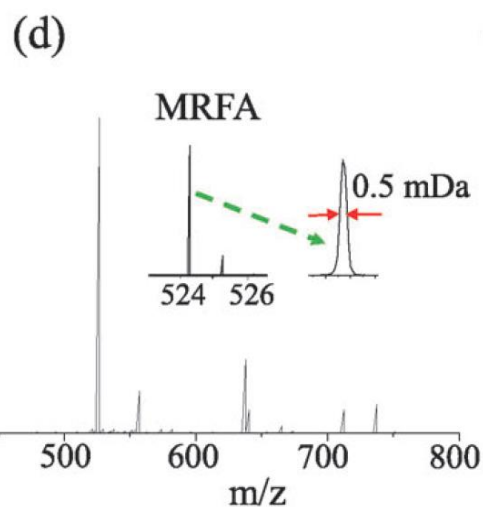
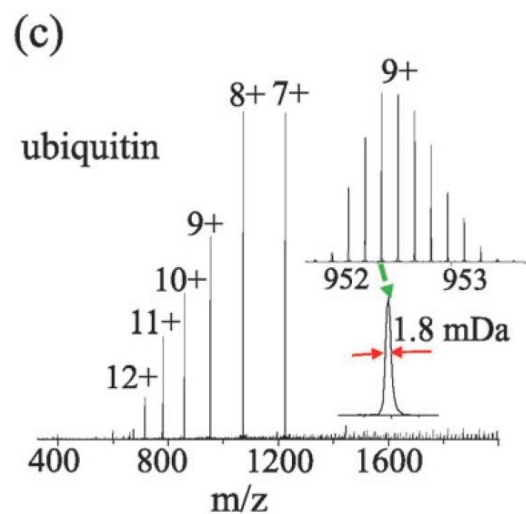
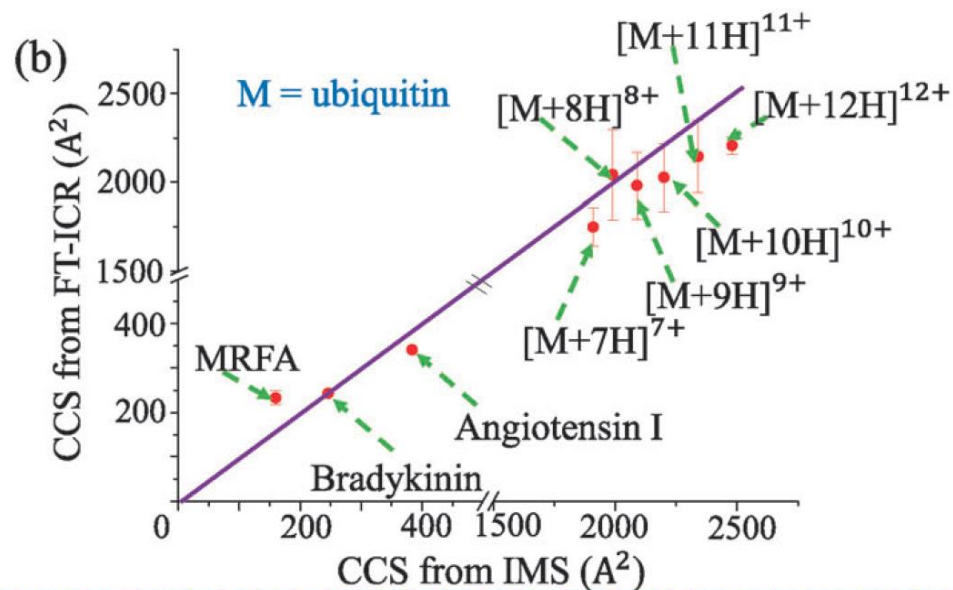
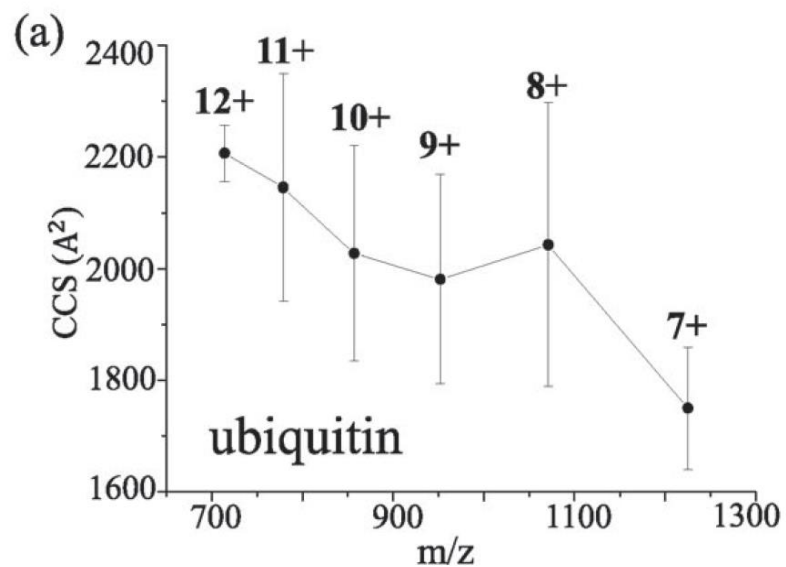
Different pressure regime



Radius of an ion at thermic equilibrium



Ion mobility in the ICR cell



The Bruker pulse programming language

```
#=====
You may create your own program. Here a 2D sequence
#=====
```

```
# EXCITATION_KEY:
EXCITATION.lines = 12
#Not all the p_x and pl_y values are working; do not change the names
EXCITATION.1 = " 10u pl1:f1 ; set attenuation for encoding sequence (FCU-1)"
EXCITATION.2 = "EXC_SWEC1, (p10 ph3 fq1):f1 ; Excitation pulse P1 sweep"
EXCITATION.3 = " lo to EXC_SWEC1 times l31 ; L[31] steps in sweep"
#EXCITATION.4 = "d26 ; Encoding period 2D delay with increment delay"
EXCITATION.4 = "vd ; Encoding period 2D delay with vd list"
EXCITATION.5 = "EXC_SWEC2, (p10 ph3 fq1):f1 ; Encoding pulse P2 sweep"
EXCITATION.6 = " lo to EXC_SWEC2 times l31 ; L[31] steps in sweep"
EXCITATION.7 = " d13 setnmr3|12 ; trigger IRMPD laser pulse (XGPP_OUT[2])"
EXCITATION.8 = " 10u setnmr3^12"
EXCITATION.9 = " 10u pl3:f1 ; set attenuation for observe pulse (FCU-1)"
EXCITATION.10 = "EXC_SWO, (p3 ph3 fq1):f1 ; Observe pulse P3 sweep"
EXCITATION.11 = " lo to EXC_SWO times l31 ; L[31] steps in sweep"
#EXCITATION.12 = " 0.1u id26 ; fixed increment to next encoding delay t1 of value id26"
EXCITATION.12 = " 0.1u ivd ; increment to next encoding delay t1 in VD_2D list"

# PHASE_PROGRAM_DEFS_KEY:
#phase value angle degree 0 0; 1 90; 2 180
PHASE_PROGRAM_DEFS.lines = 4
PHASE_PROGRAM_DEFS.1 = " ph1= 0 0 2 2 ; normal phase program for compensating physical differential entries inverion"
PHASE_PROGRAM_DEFS.2 = " ph2= 0 1 2 3 ; phase program: 0 1 2 3 (all other RF)"
PHASE_PROGRAM_DEFS.3 = " ph3= 0 0 2 2 ; phase program: 0 0 2 2 (all other RF)"
PHASE_PROGRAM_DEFS.4 = " ph4= 2 2 2 2 ; phase program: 2 2 2 2 (all other RF)"
```

European network EU_FT-ICR_MS

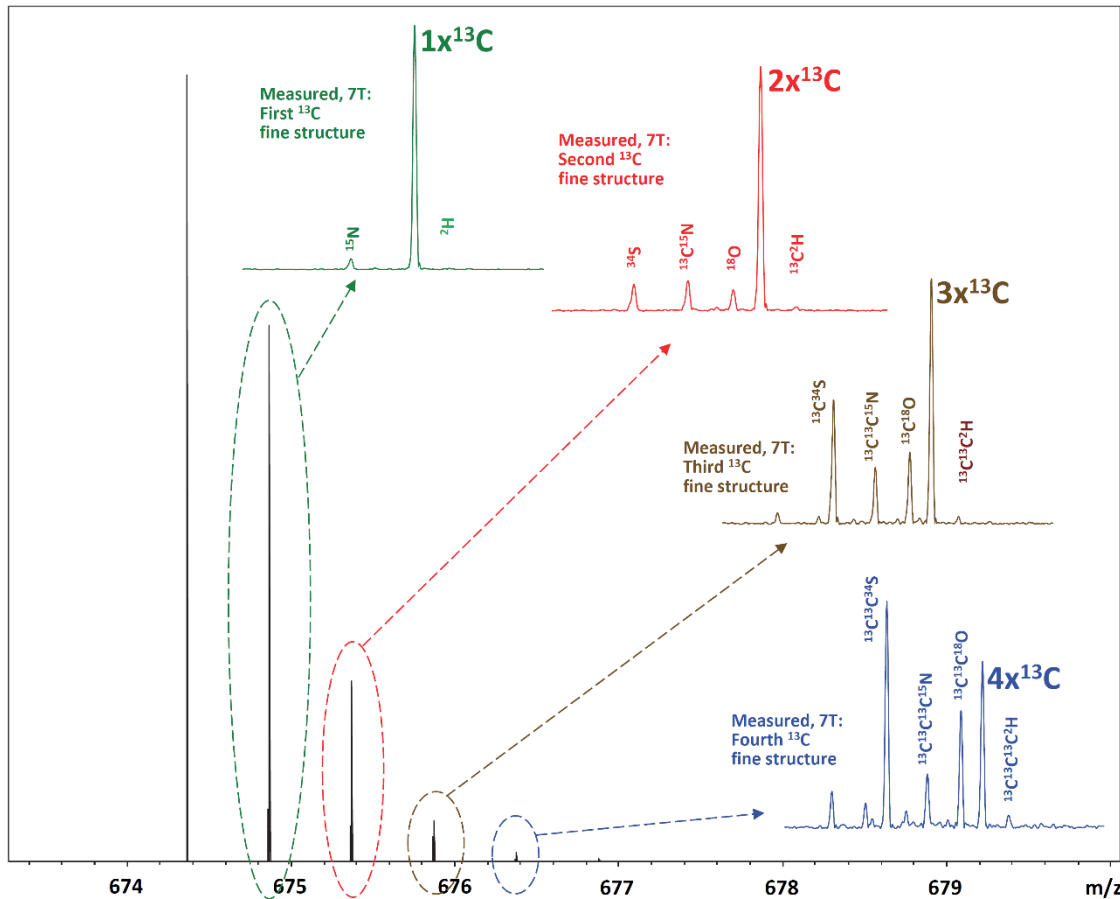
An Horizon 2020 INFRA for Starting Communities network



www.eu-fticr.eu



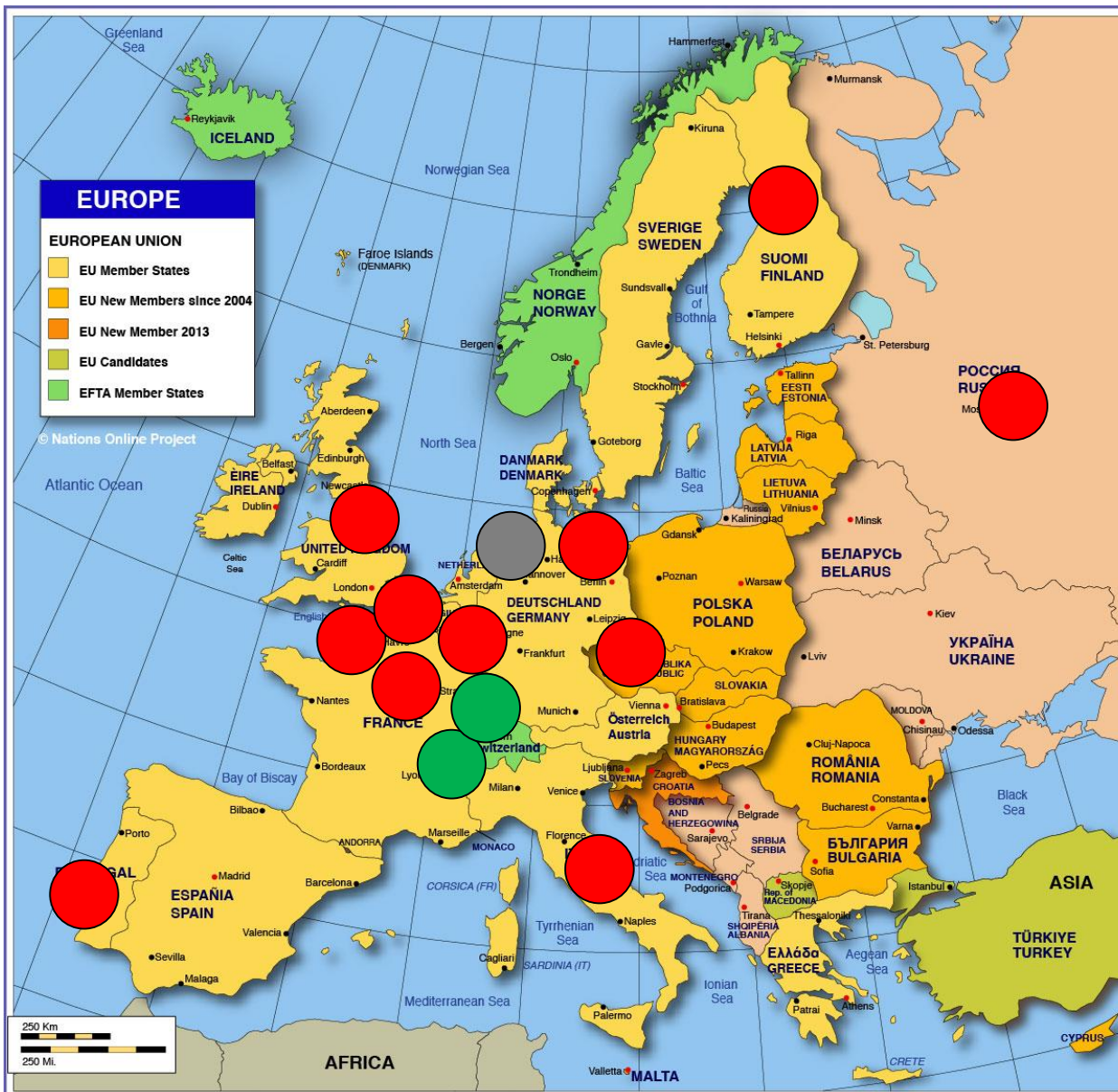
Why a FT-ICR MS centers network?



15 Tesla FT-ICR MS at the Czech Academy of Science, Institute of Microbiology (Prague) funded in part with EU ERDF funds (highest commercial magnetic field).

- **The most resolving mass spectrometer ($\times 10$ versus the best other MS)**
- **Ubiquitous use in different scientific fields**
- Cost between 1.5 and 3 million euros
- But requires a skilled team

The EU_FT-ICR_MS network



11 academic FT-ICR MS center (3 in France) from 9 countries

2 companies (2 in France)

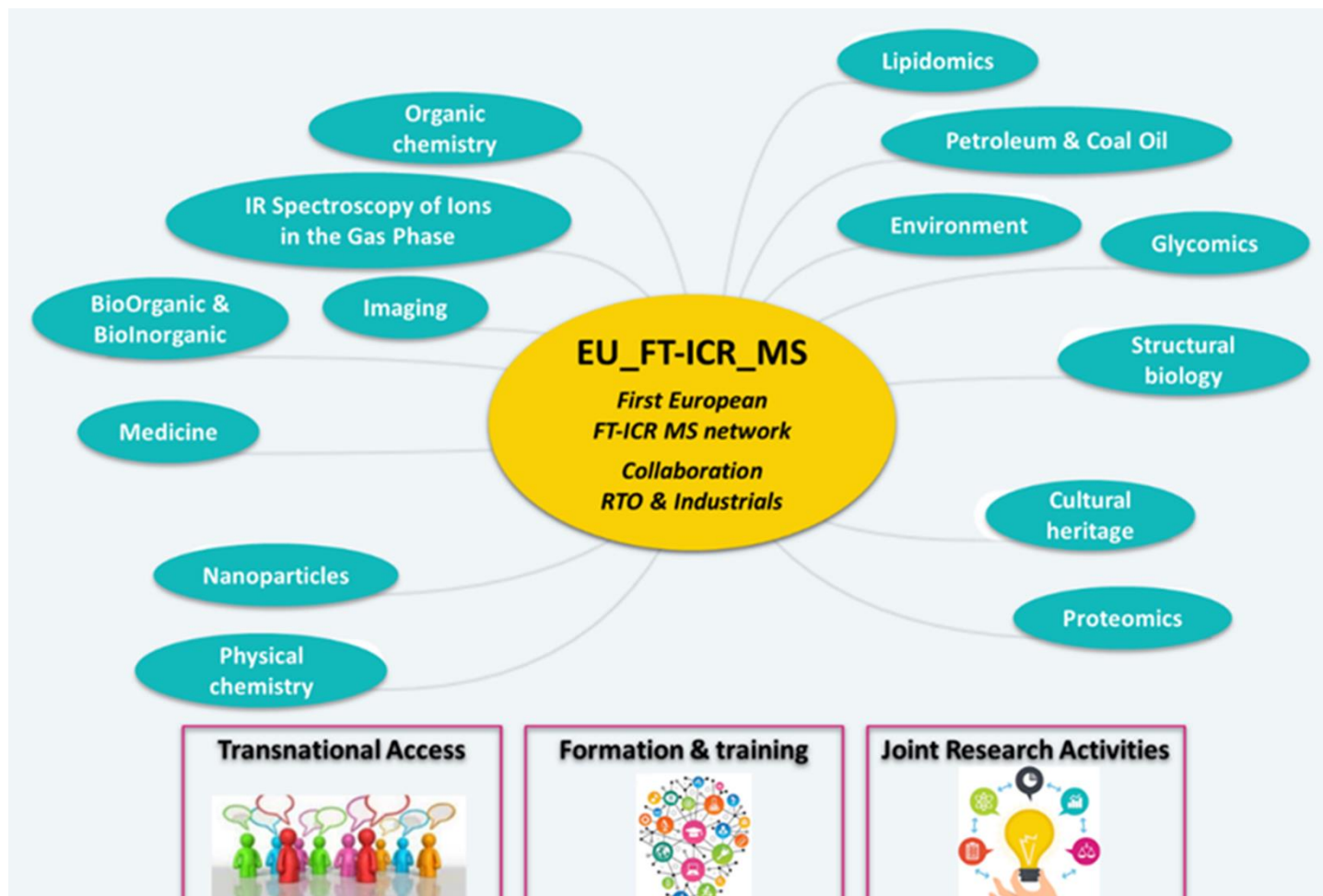
**Bruker Daltonik
CAS4CADE (SME)
Absiskey**

5 millions euros (4 years)

A funding equal between partners (not a two circles model)

Started January 1st 2018, 0 hour

The site specificities and the different workpackages



And the very important WP **Open Data and e-Infrastructure**



EU_FT-ICR_MS first actions

Transnational access

Apply on the web site.

Experiments, travels and accommodation paid by EU. One restriction: you should apply in a center from a different country than your own country of origin

First Short course

Atmospheric pressure ionization techniques for high resolution mass spectrometry of complex samples

5-7 March 2018, University of Rostock

First summer school

19-24 August 2018, University of East Finland (Joensuu)

Booth or sessions at EFTMS 2018 meeting, 23-27 April, Munich and **IMSC conference** (International Mass Spectrometry Conference), 26-31 August, Florence

First Short Course of the EU FT-ICR MS network

**atmospheric pressure ionization
techniques for high resolution
mass spectrometry of complex
samples**

When?

5-7 March 2018

Where?

University of Rostock
Research building LL&M
Albert-Einstein-Strasse 25
18059 Rostock



Universität
Rostock



Traditio et Innovatio

Overview of the program



Tutorial Lectures
Basics of FT-ICR MS
using atmospheric
pressure ionization



Instrument demos



Hands-On Exercises
Electrospray
ionization (ESI) and
Atmospheric
pressure chemical
ionization (APCI)



Data analysis
Comparison of
ionization features
of ESI, APCI and
GC- APCI/
Atmospheric
pressure photo
ionization (APPI)
samples;
In parallel: running
GC – APCI/APPI
measurements



You want to learn more about high
resolution mass spectrometry and
atmospheric pressure ionisation
techniques?

Registration:

please send an E-Mail using the application
form to

martin.sklorz@uni-rostock.de

We will response as fast as possible and
inform you about acceptance.
The application form is available as a
download on our website.

www.zimmermann.chemie.uni-rostock.de/forschung/advanced-mass-spectrometry/hochaufloesende-massenspektrometrie/eu-ft-icr-ms/

NO CONFERENCE FEES !

Each participant (limited seats) will
receive support for travelling and
accommodation.

REGISTER SOON!

Acknowledgements

