Fourier Transform Ion Cyclotron Resonance Mass Spectrometry: Data Acquisition

Peter B. O'Connor

Critical Literature:

Qi, Y.; O'Connor, P. B., Data processing in Fourier transform ion cyclotron resonance mass spectrometry. *Mass Spectrometry Reviews* ***2014,*** *33, 333-352.*

Amster, I. J. Fourier Transform Mass Spectrometry *J. Mass Spectrom.* **1996**, *31*, 1325-1337.

Zhang, L. K.; Rempel, D.; Pramanik, B. N.; Gross, M. L. Accurate mass measurements by Fourier transform mass spectrometry *Mass Spectrom. Rev.* **2005**, *24*, 286-309.

Marshall, A. G.; Hendrickson, C. L.; Jackson, G. S. Fourier Transform Ion Cyclotron Resonance Mass Spectrometry - A Primer *Mass Spectrom. Rev.* **1998**, *17*, 1-35.

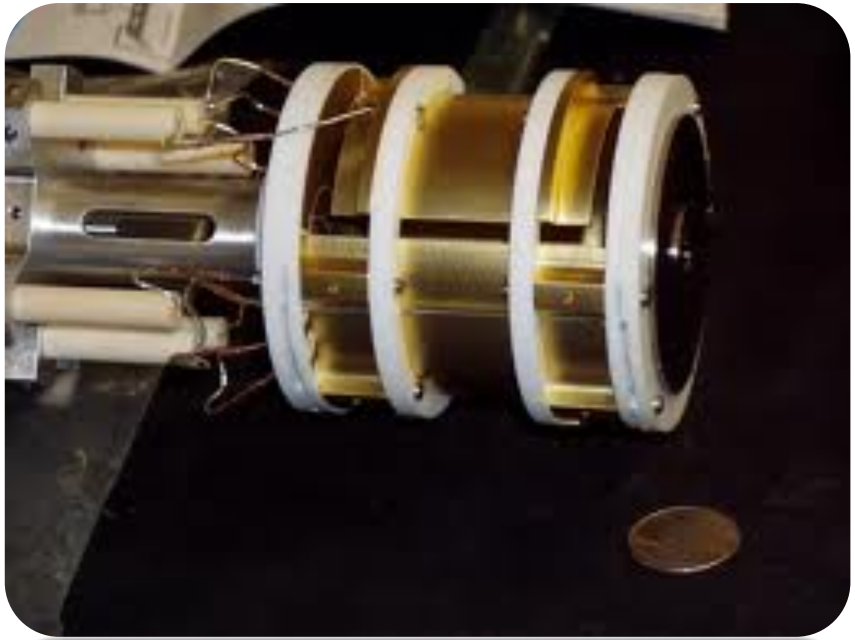
Special thanks to:

Mike Easterling (Bruker) and Jon Amster (Univ. Georgia) for slides.

Outline

- The Ion Cyclotron Resonance Cell
- Excite and detect
- Cyclotron Equations and calibration
- Fourier Transform
- Nyquist
- Zerofilling
- Apodization and Peakshapes
- Heterodyne Detection
- Phasing

ICR Cell



Caravatti, P.; Allemann, M., RF Shim by Trap Segmentation. *Org. Mass Spectrom.* ***1991, 26, 514-518.***

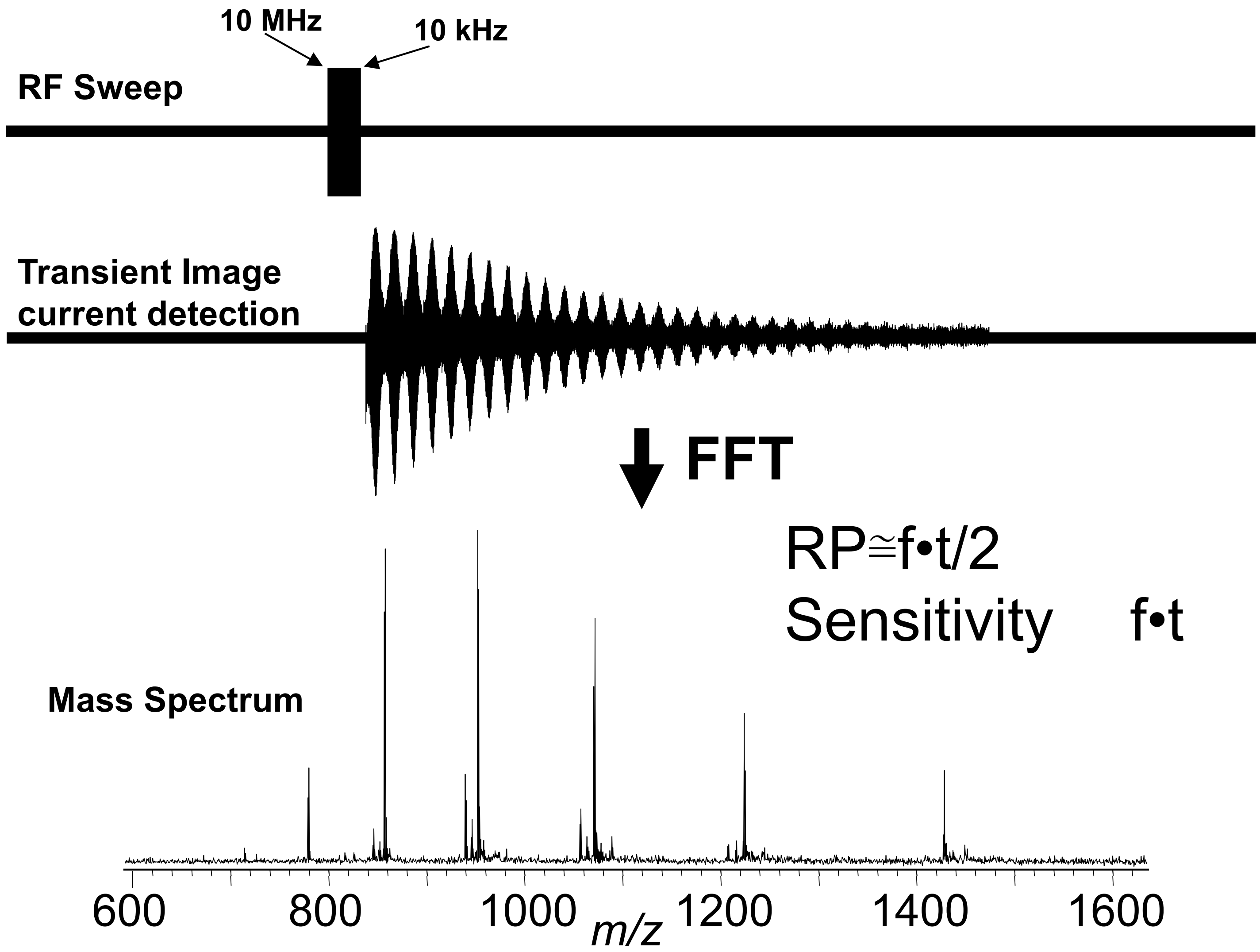


Figure 6. The principle of FT-ICR-MS.

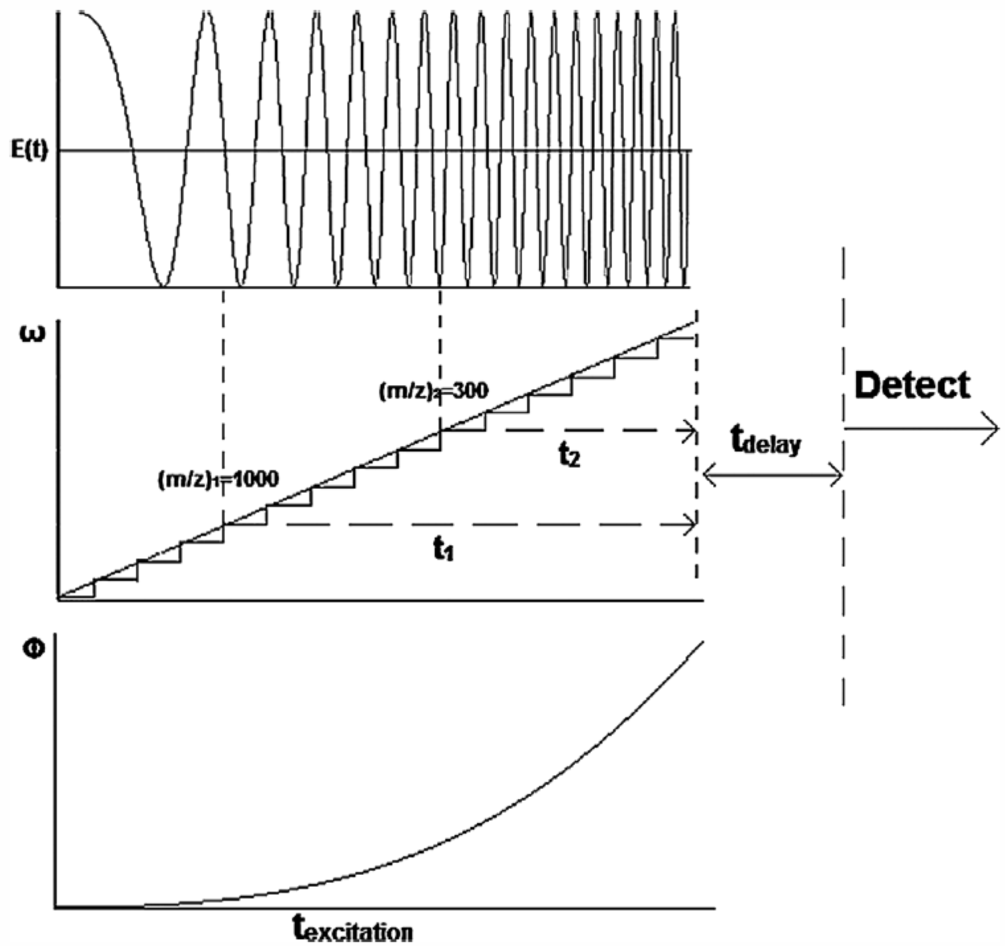


FIGURE 4. Top: Time-domain profiles of the RF chirp for ion excitation. Middle: Frequency for a linear polarized (upper line) or stepwise (lower line) frequency sweep. Bottom: Quadratic phase accumulation for the stepwise frequency sweep. Reprinted from Qi et al. (2011a), with permission from Springer, copyright 2011.

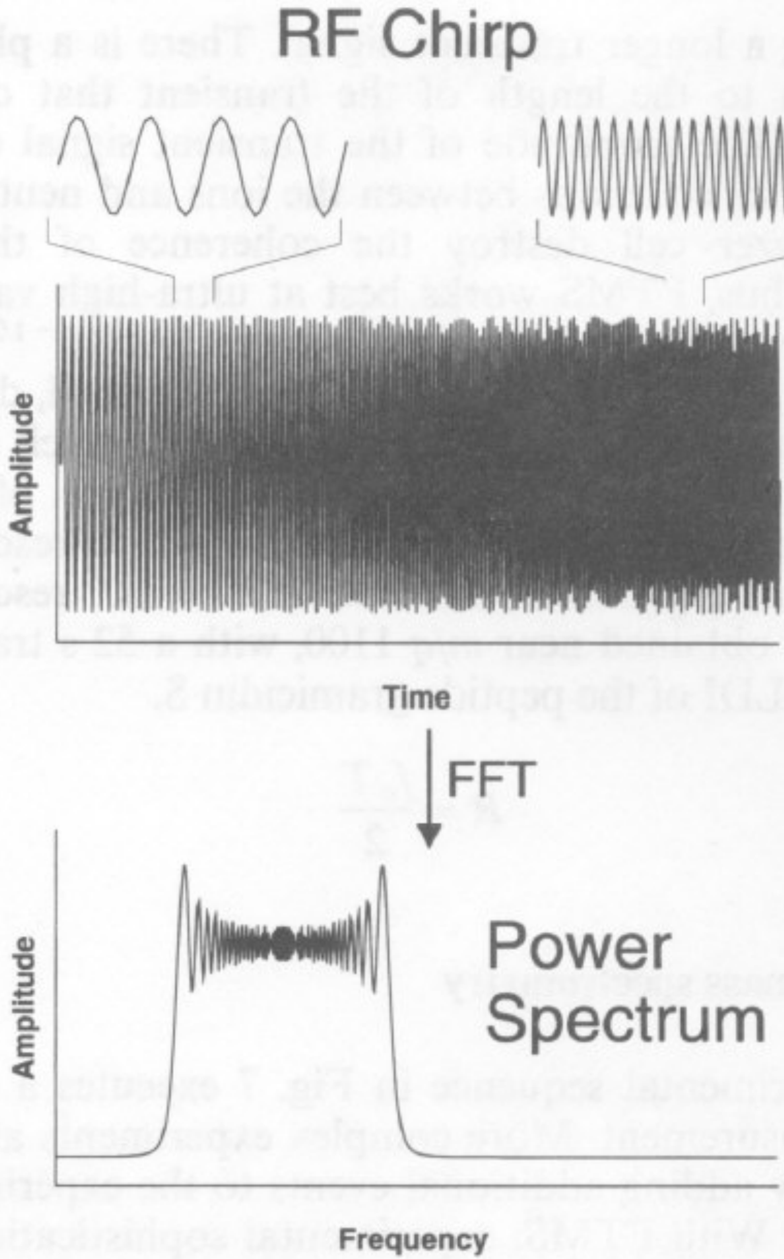


Figure 13. A r.f. chirp and its power spectrum. Power is observed to be unevenly distributed across the spectrum and drops off slowly outside the region of excitation.

Excitation

The standard excitation mode.

$$\boxed{r = \frac{\beta_{\mathrm{dipolar}} V_{p-p} T_{\mathrm{excite}}}{2dB_0}} \quad \text{(S.I. units)}$$

$$\boxed{r = \frac{\beta_{\mathrm{dipolar}} V_{p-p} \sqrt{\dfrac{1}{\text{Sweep Rate}}}}{2dB_0}}$$

SWIFT

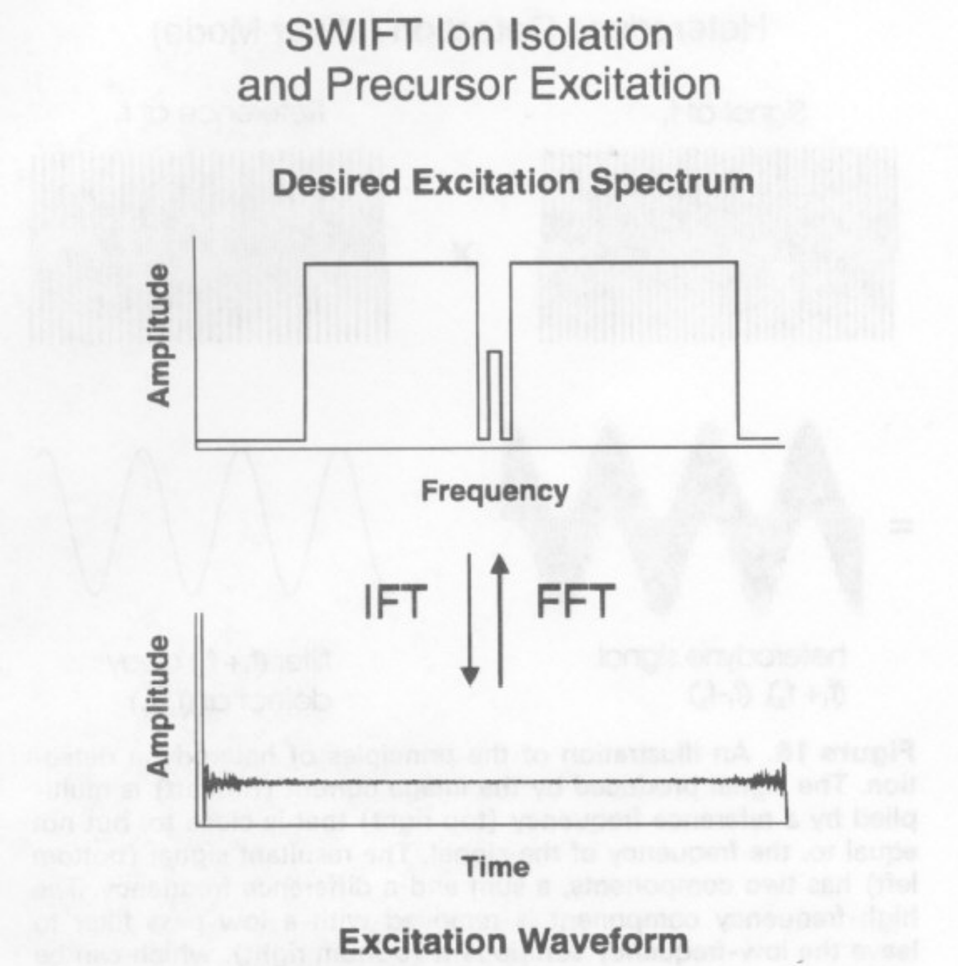
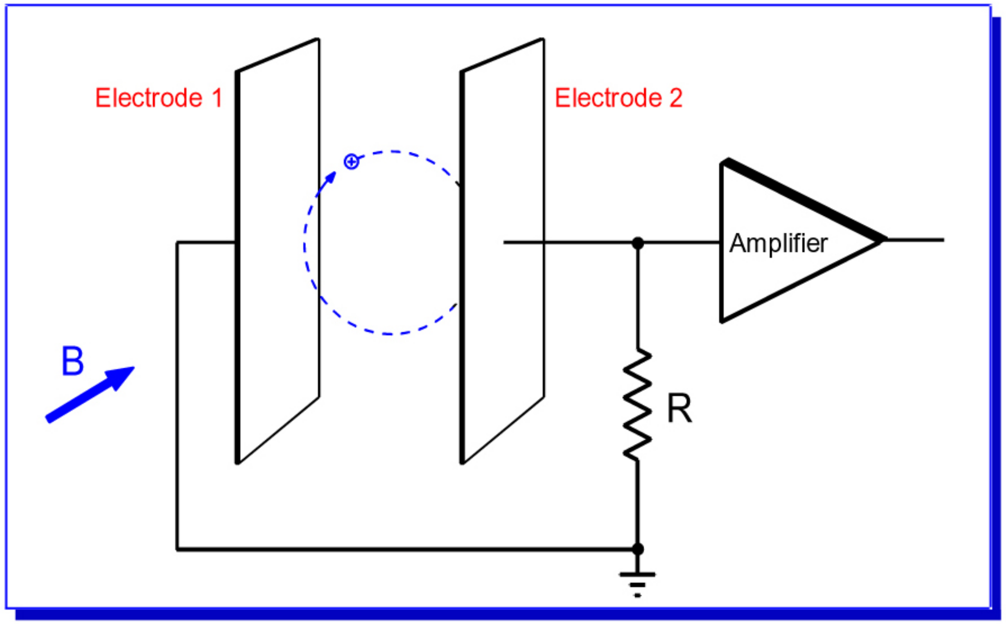


Figure 14. An illustration of the principles of SWIFT excitation. A frequency spectrum is defined at the top. Its corresponding Fourier transform, the SWIFT waveform, is shown at the bottom. Excitation with the SWIFT waveform will apply power as specified in the frequency spectrum.

Chen, L.; Wang, T. C. L.; Ricca, T. L.; Marshall, A. G., *Anal. Chem.* ***1987, 59, 449-454.***
Marshall, A. G.; Wang, T.-C. L.; Ricca, T. L., ***1985, 107, 7893-7897.***

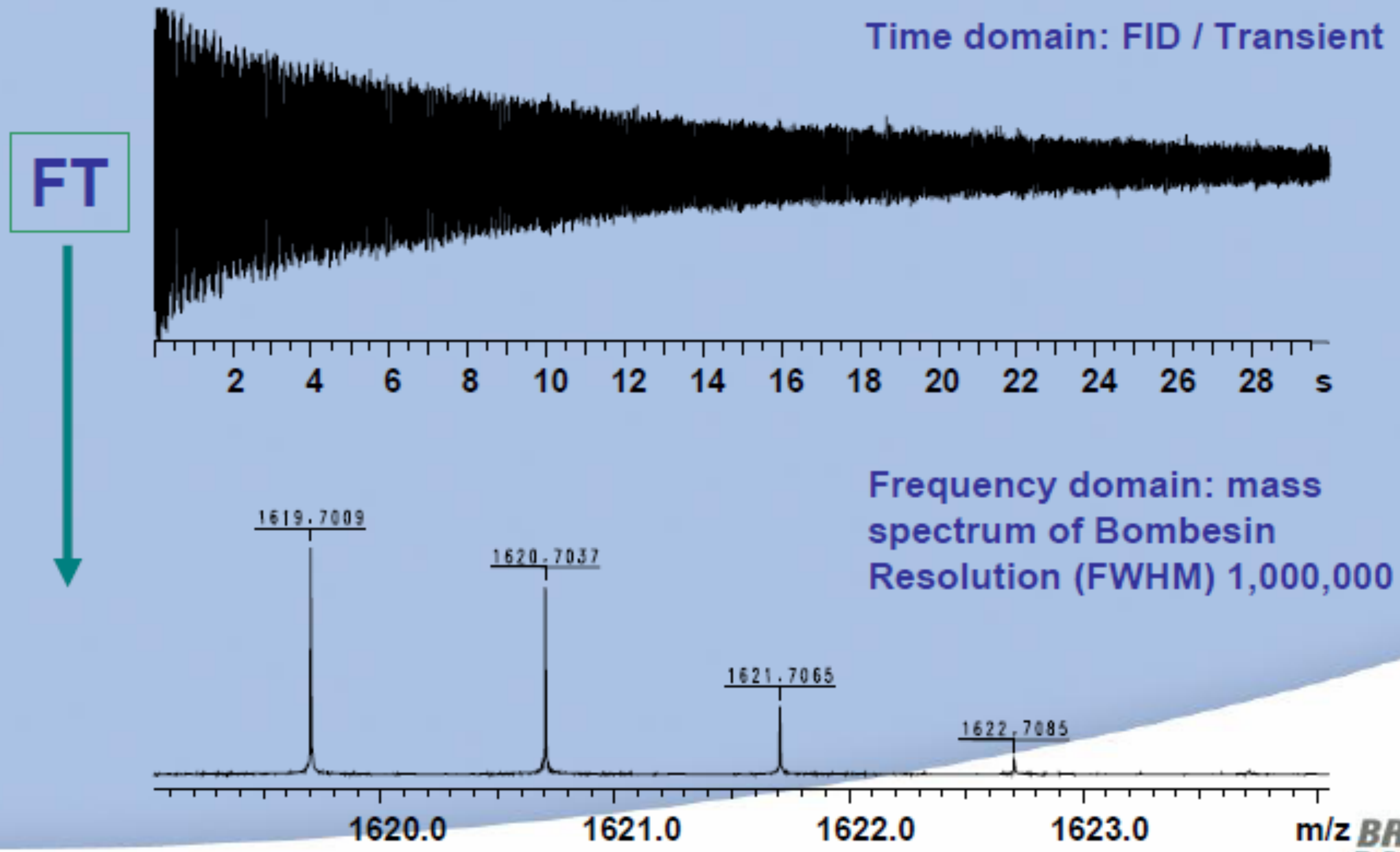
FTMS Ion Detection Method

- Image Current Detection



WARWICK

Fourier Transform of the Transient Signal



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Definition of the Fourier Transform

- This integral transforms the time-domain function h(t) to the frequency domain H(f) function

$$H(f) = \int_{-\infty}^{\infty} h(t) e^{-j2\pi f t} dt$$

Note that $e^{-j2\pi f t}$ is a complex exponential function where:

$j^2 = -1$
t = time
f = frequency
$\pi = 3.14159$

Discrete Fourier Transform (DFT)

$$H(f) = \int_{-\infty}^{\infty} h(t) e^{-j2\pi ft} dt$$

(analog)

$$\Downarrow$$

$$H(k) = \frac{1}{N} \sum_{n=0}^{N-1} h(n) e^{-j2\pi k \frac{n}{N}}$$

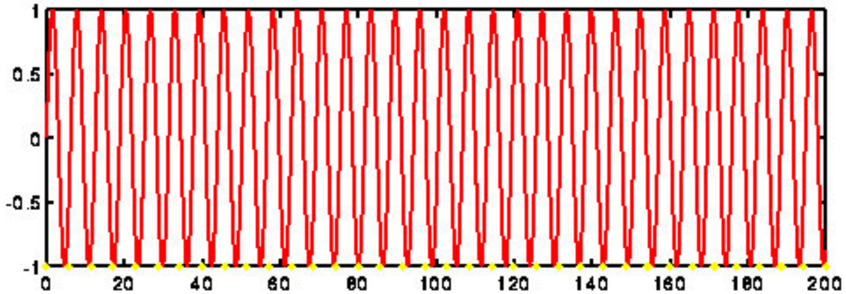
(digital)

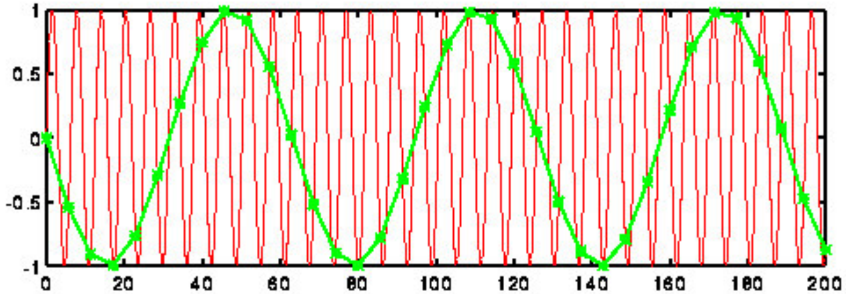
Nyquist

$$0 \le f \le \frac{1}{2\Delta}$$

f = frequencies observable

Δ = sampling period = 1/acquisition rate





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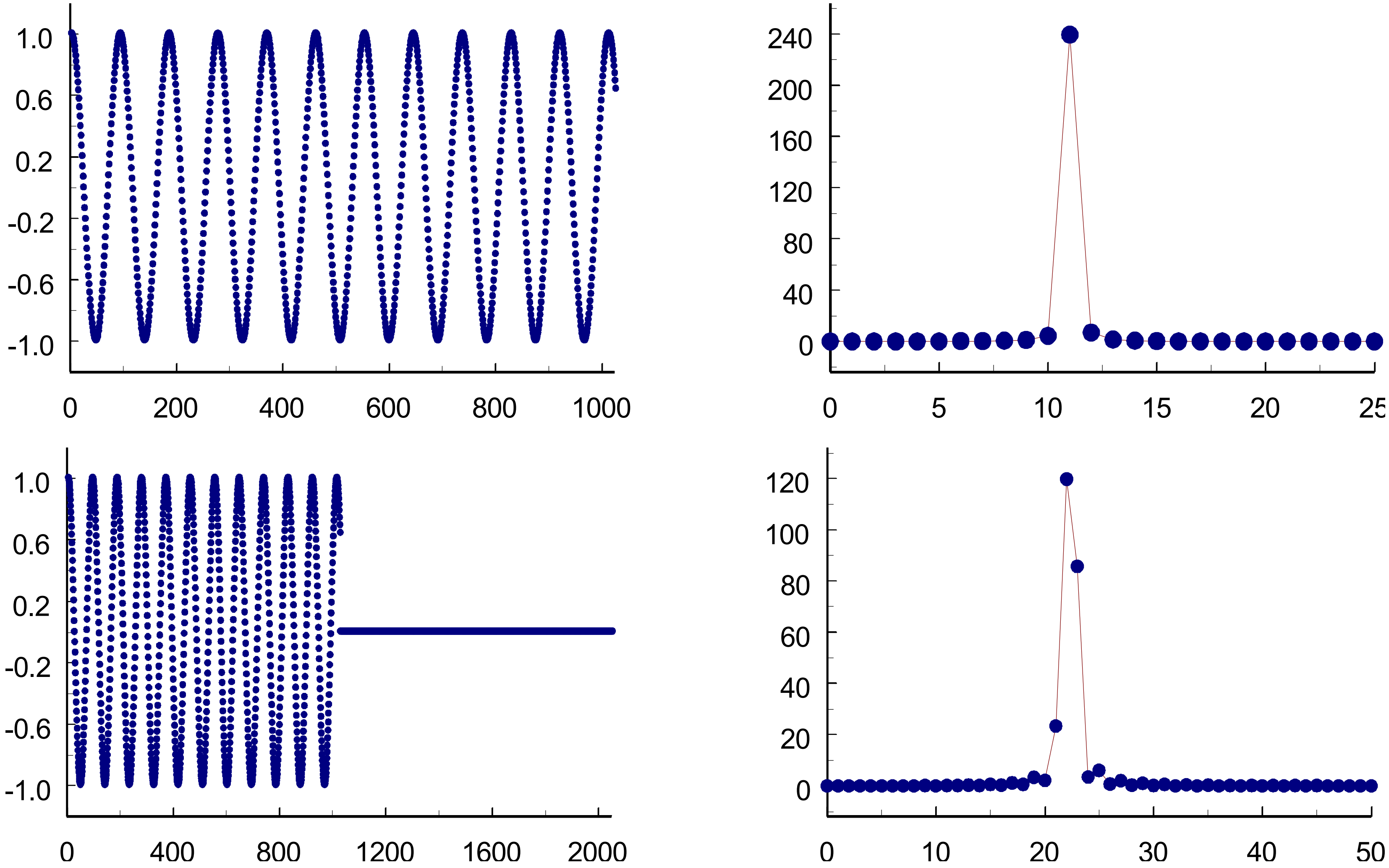
Zero-Filling Provides Better Peak Definition

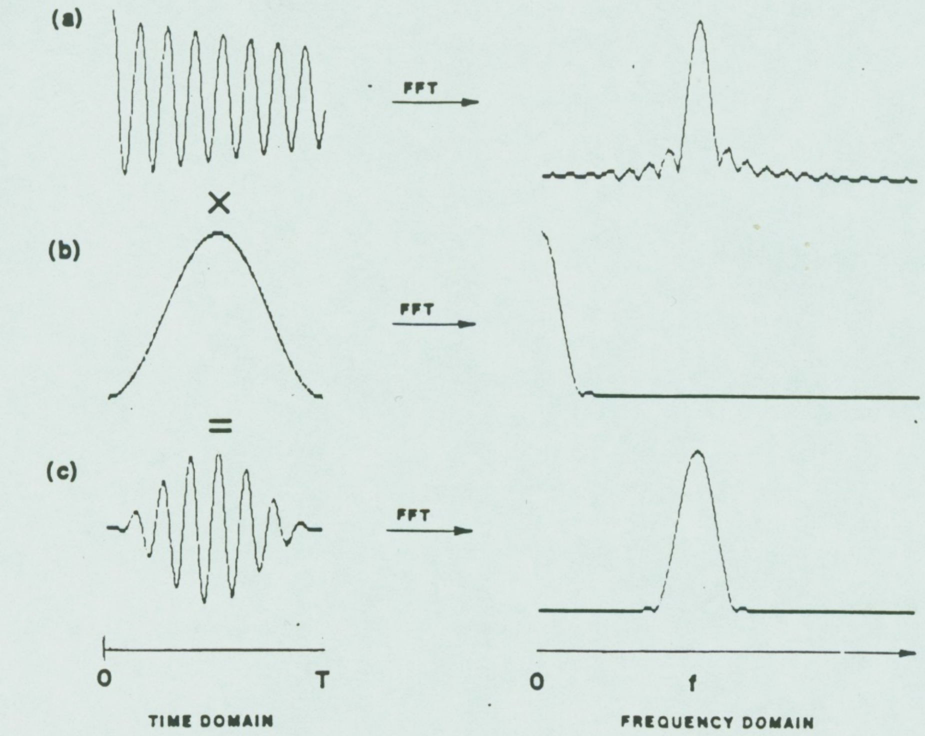


Qi, Y.; O'Connor, P. B., Data processing in Fourier transform ion cyclotron resonance mass spectrometry. *Mass Spectrometry Reviews* ***2014, 33 (5), 333-352.***

Mass Resolution in FTMS

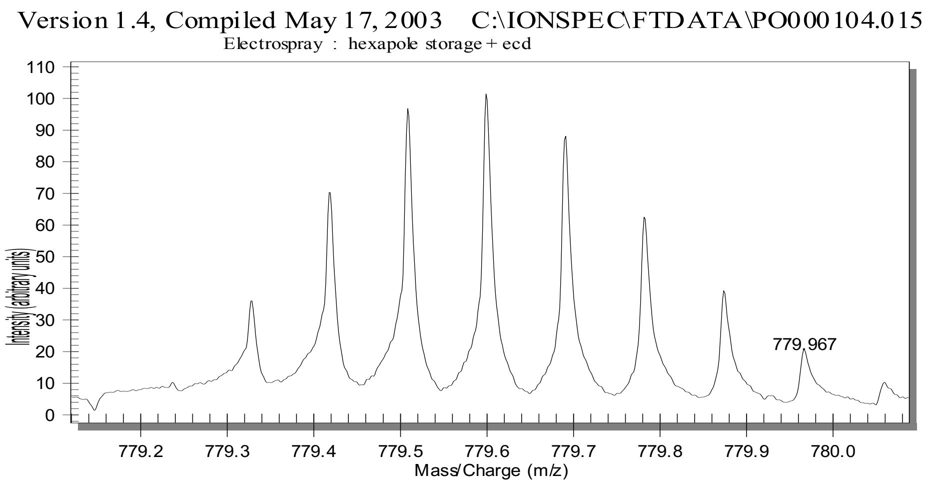
Effect of Windowing (Apodization)

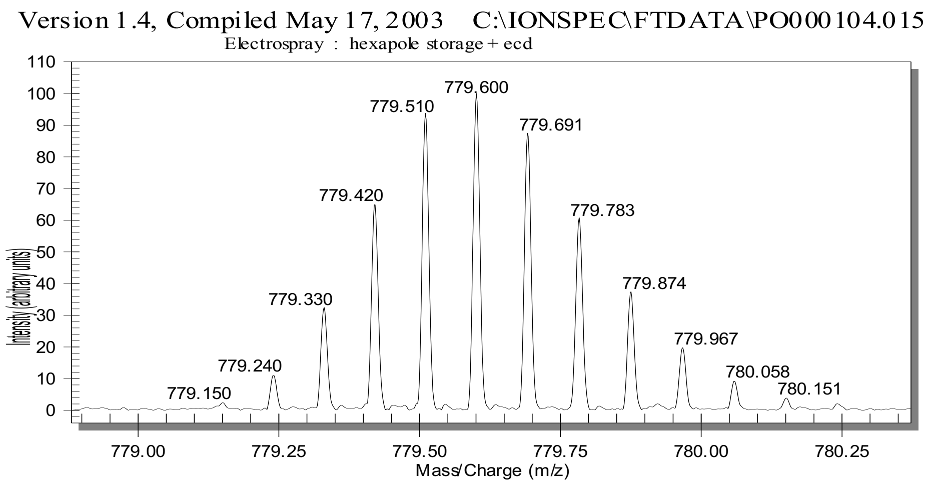
- Abrupt truncation of the time-domain signal causes auxiliary wiggles on both sides of the main peak.
- These artifacts are called Gibbs oscillations and are removed by multiplying the signal by an *apodization function*.
- Popular apodization functions are the Hanning Window function and the Blackman-Harris Window function.



(a) When a time-domain signal is observed for a finite time, the resulting frequency spectrum exhibits side lobes.
(b) The Hanning window function is multiplied times the time-domain signal
(c) FFT of the tapered transient signal shows suppressed side lobes

Apodization = Peak Shape Distortion





FTMS Lineshapes

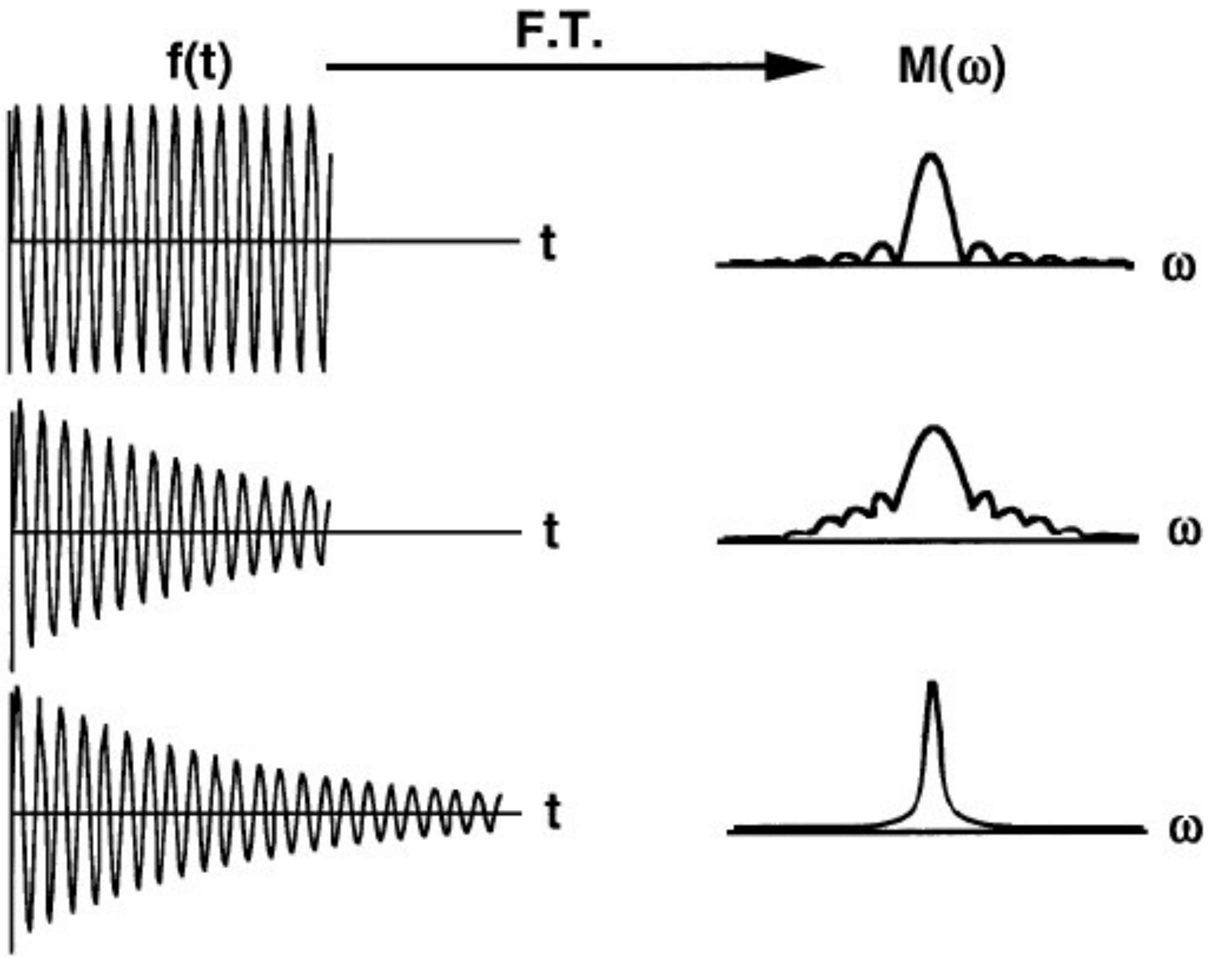


FIGURE 10. Simulated time-domain ICR signals (left) and frequency-domain magnitude spectra (right) for low-pressure, $\tau \gg T_{acq'n}$ (top), intermediate-pressure, $\tau \approx T_{acq'n}$ (middle), and high-pressure, $\tau \ll T_{acq'n}$ (bottom) limits.

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Heterodyne Detection

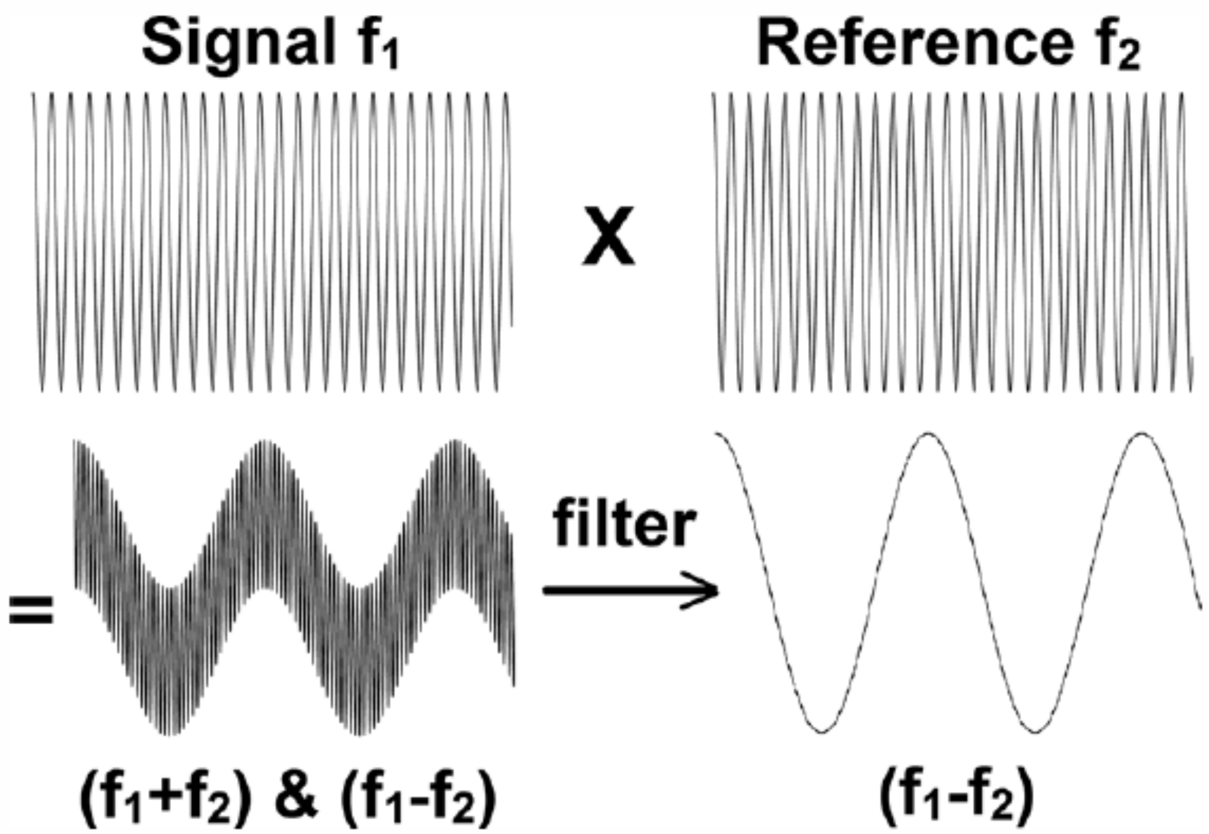
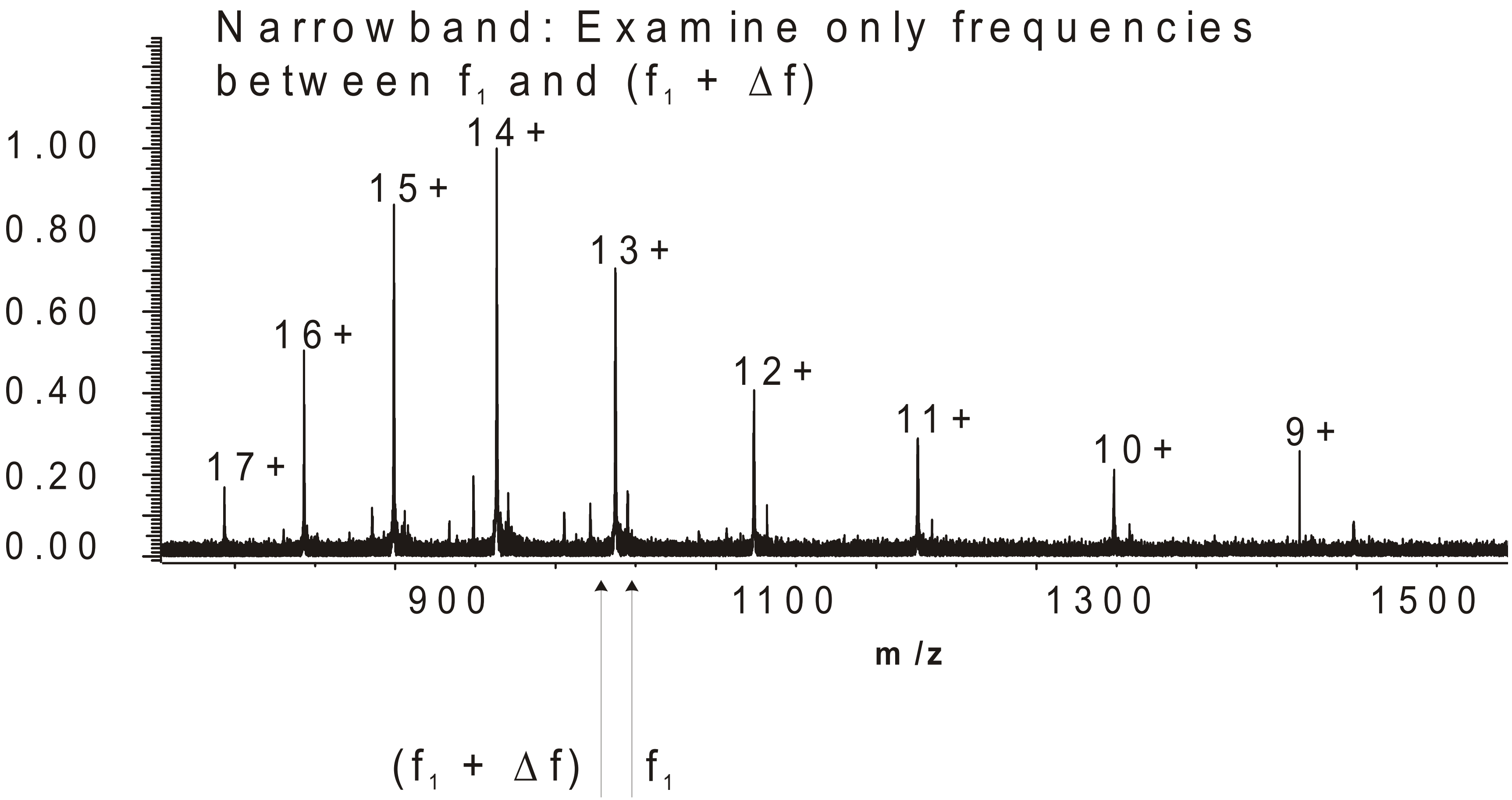


FIGURE 9. Principle of the heterodyne mode detection. Adapted from Amster (1996).

Heterodyne Detection

1. Focuses data collection on narrow region of mass spectrum
2. Must only excite ions in region of interest or will get aliasing



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Phasing

$$H(f) = \int_{-\infty}^{\infty} h(t) e^{-i\omega t + \phi} \, dt$$

$$H(f) = \int_{-\infty}^{\infty} h(t) e^{-j\omega t} e^{\phi} \, dt$$

$$H(f) = \int_{-\infty}^{\infty} h(t) e^{-j\omega t} e^{\phi(\omega)} \, dt$$

$$\Phi(\omega) = C_2 \omega^2 + C_1 \omega + C_0$$

Phasing

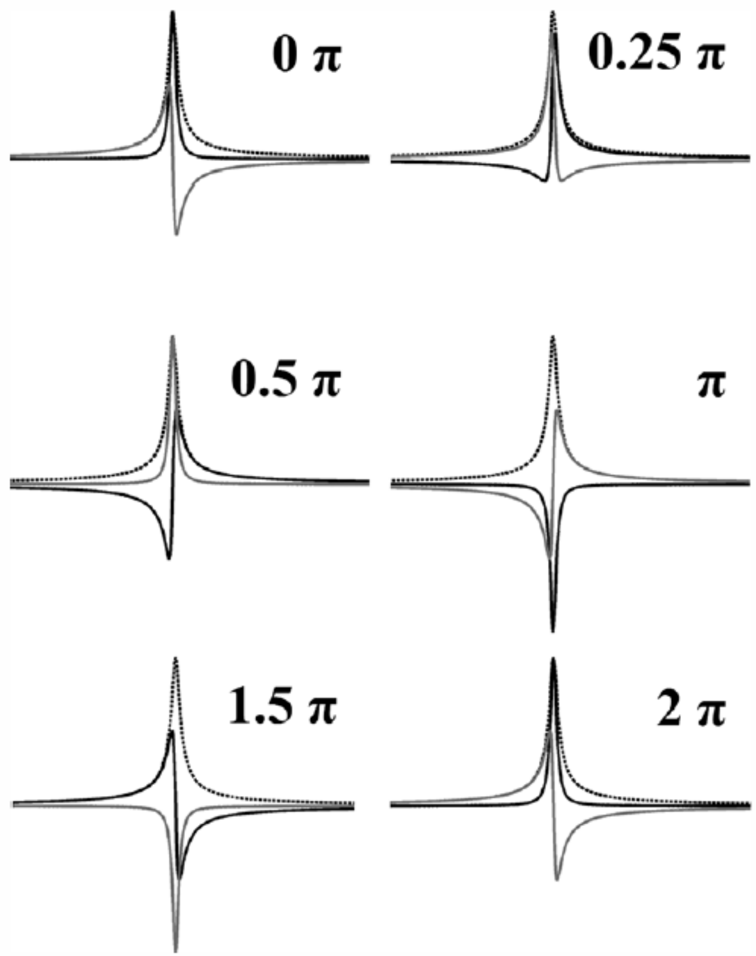
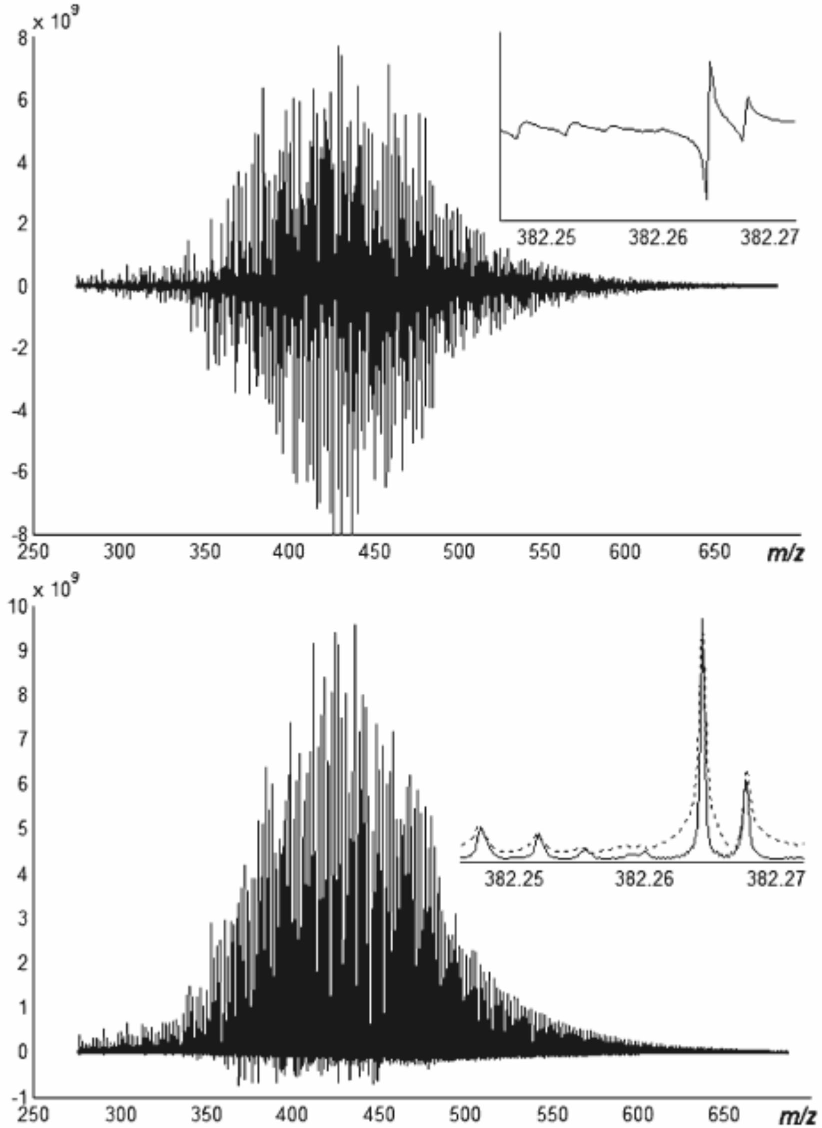


FIGURE 10. Peak shape of pure absorption- (black), dispersion- (gray), and magnitude-mode (dash line) spectra in Lorentzian function at different phase values.

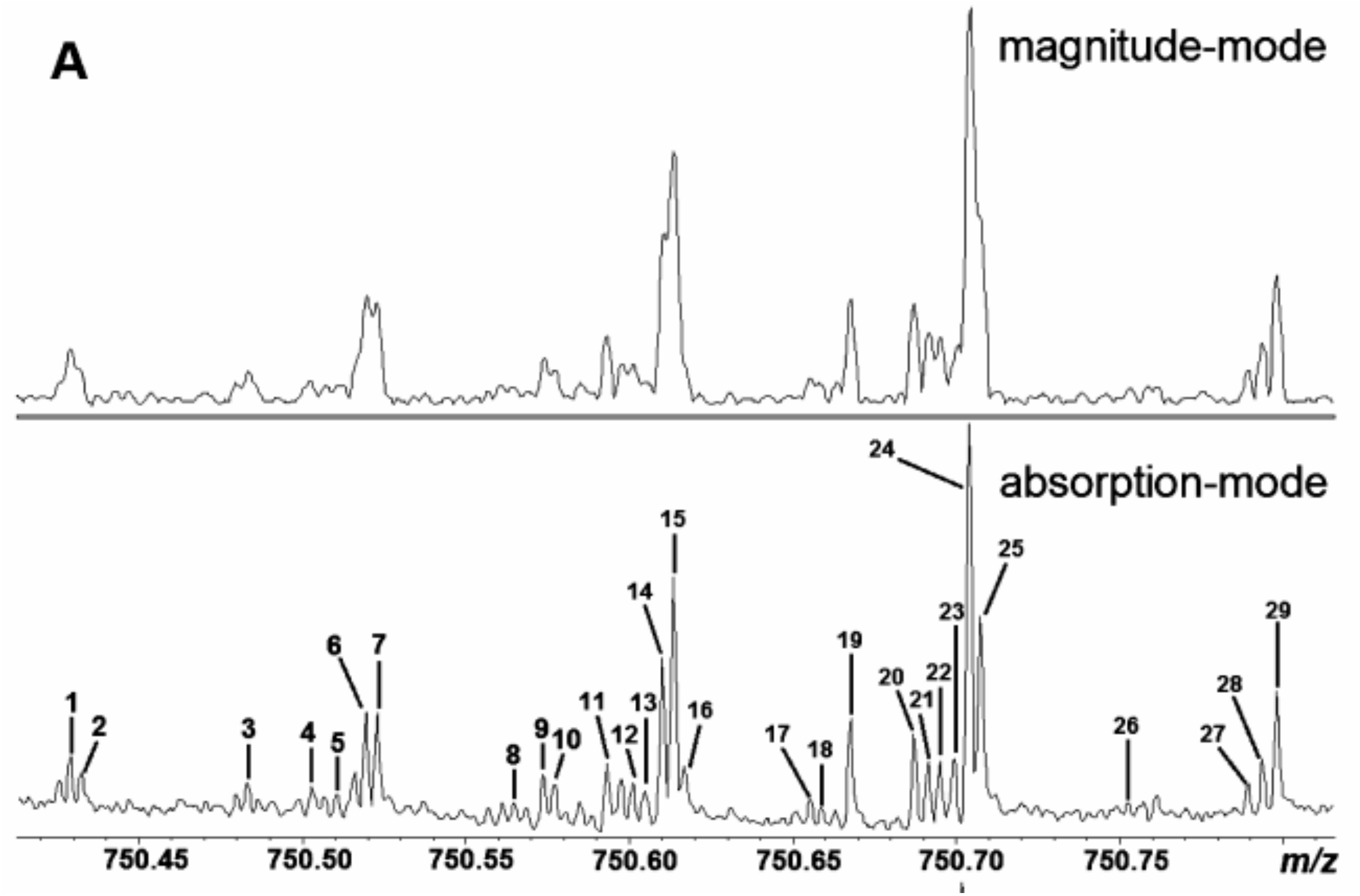
Qi, Y.; O'Connor, P. B., Data processing in Fourier transform ion cyclotron resonance mass spectrometry. *Mass Spectrometry Reviews* ***2014, 33 (5), 333-352.***

Phasing



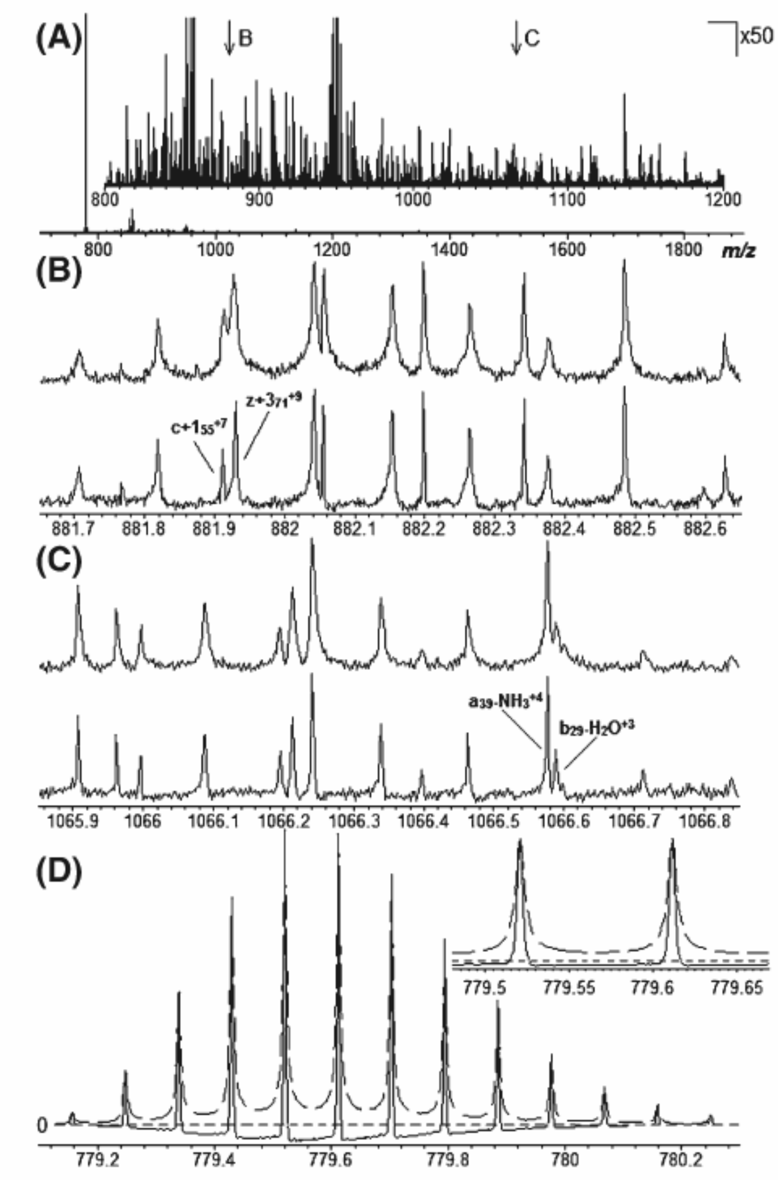
Qi, Y.; Thompson, C. J.; Van Orden, S. L.; O'Connor, P. B., Phase Correction of Fourier Transform Ion Cyclotron Resonance Mass Spectra Using MatLab. *J Am Soc Mass Spectrom* ***2011, 22 (1), 138-147.***

Phasing



Qi, Y.; Barrow, M. P.; Li, H.; Meier, J. E.; Van Orden, S. L.; Thompson, C. J.; O'Connor, P. B., Absorption-Mode: The Next Generation of Fourier Transform Mass Spectra. *Anal Chem* ***2012, 84 (6), 2923-2929.***

Phasing



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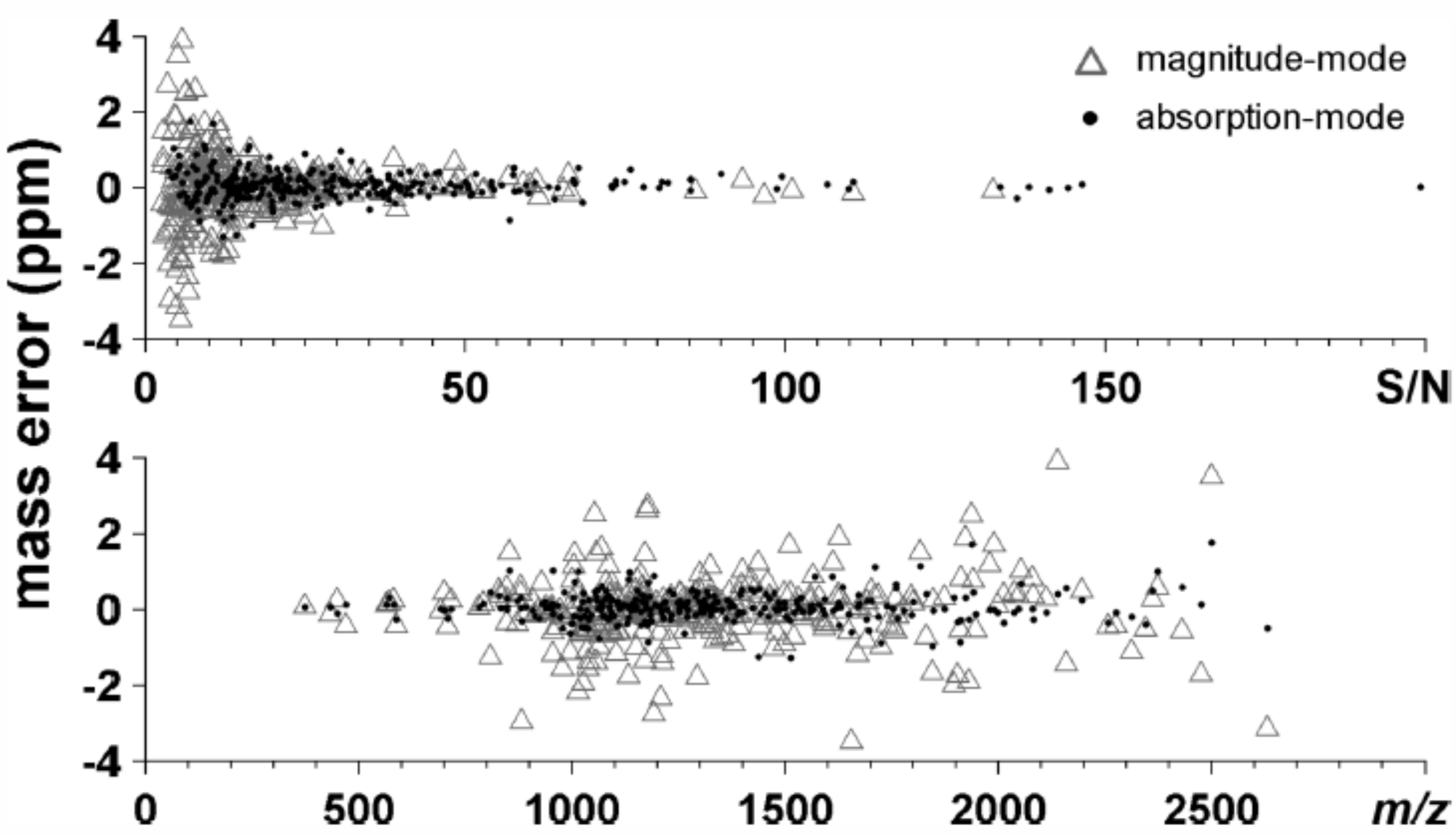

Figure 2. Mass error distribution (ppm) versus the S/N (top) and *m/z* (bottom) domains of the camodulin spectrum for both magnitude and absorption-mode.

Qi, Y.; Barrow, M. P.; Li, H.; Meier, J. E.; Van Orden, S. L.; Thompson, C. J.; O'Connor, P. B., Absorption-Mode: The Next Generation of Fourier Transform Mass Spectra. *Anal Chem* ***2012, 84 (6), 2923-2929.***

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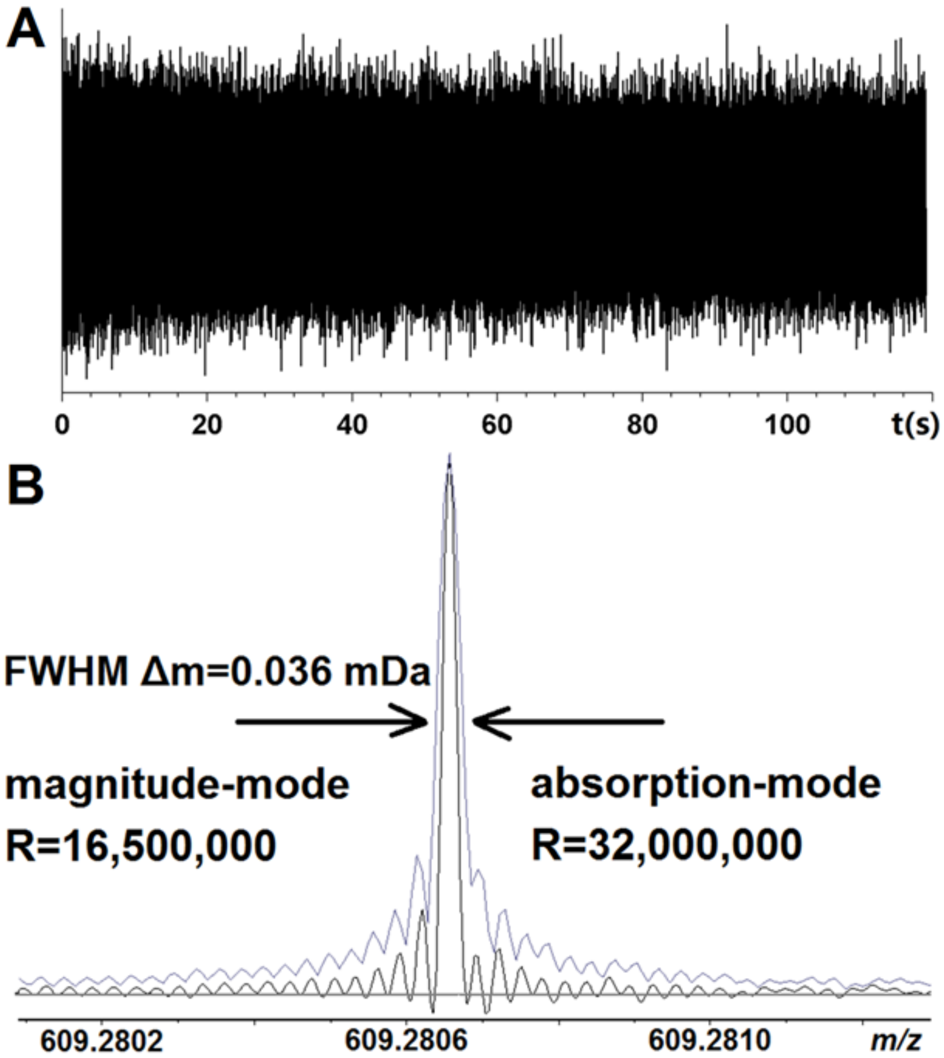

Figure 1. A: Time-domain transient of the $[Res+H]^+$ in heterodyne mode, acquired for 2 min. B: spectrum in both magnitude (grey) and absorption-mode (black), the peak width of the magnitude-mode is labelled.

Qi, Y.; Witt, M.; Jertz, R.; Baykut, G.; Barrow, M. P.; Nikolaev, E. N.; O'Connor, P. B., Absorption-mode spectra on the dynamically harmonized Fourier transform ion cyclotron resonance cell. *Rapid Communications in Mass Spectrometry* ***2012, 26 (17), 2021-2026.***

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- EPSRC (J003022/1, N021630/1)

EPSRC
Engineering and Physical Sciences Research Council

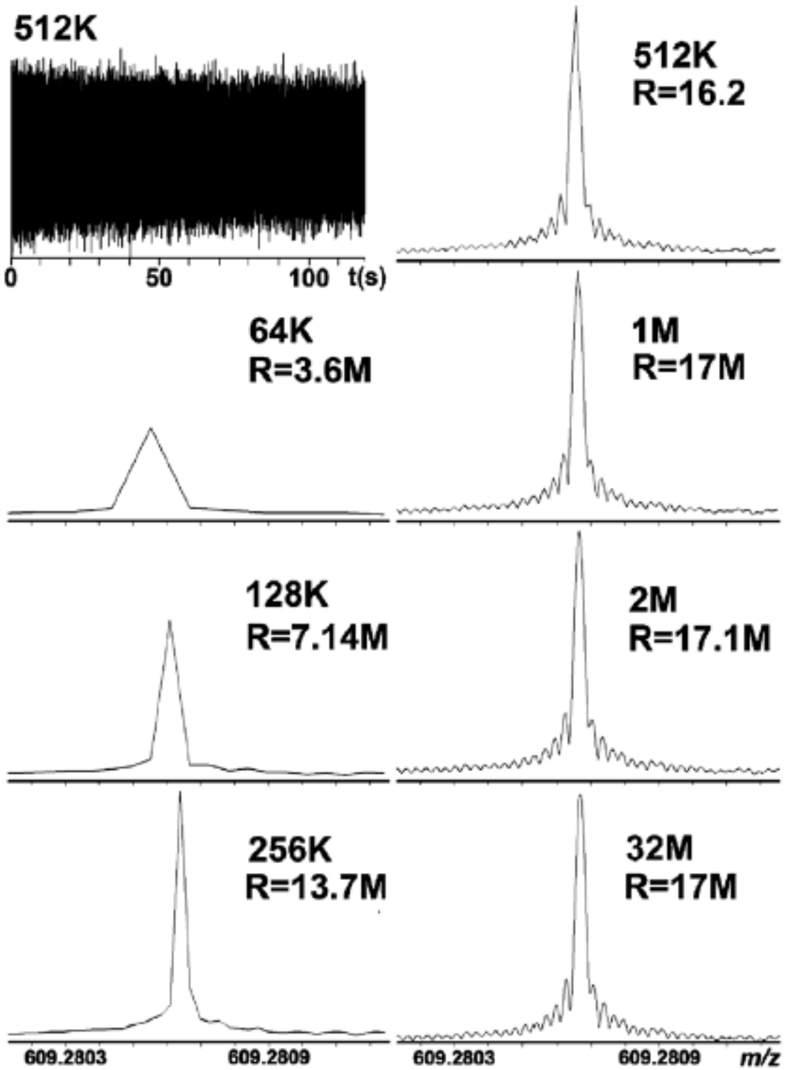

FIGURE 14. A 2-min transient (512 K data points) of the reserpine $[M+H]^+$ ion acquired in heterodyne mode, and the corresponding *m/z* spectra with different number of zero fills in magnitude-mode.

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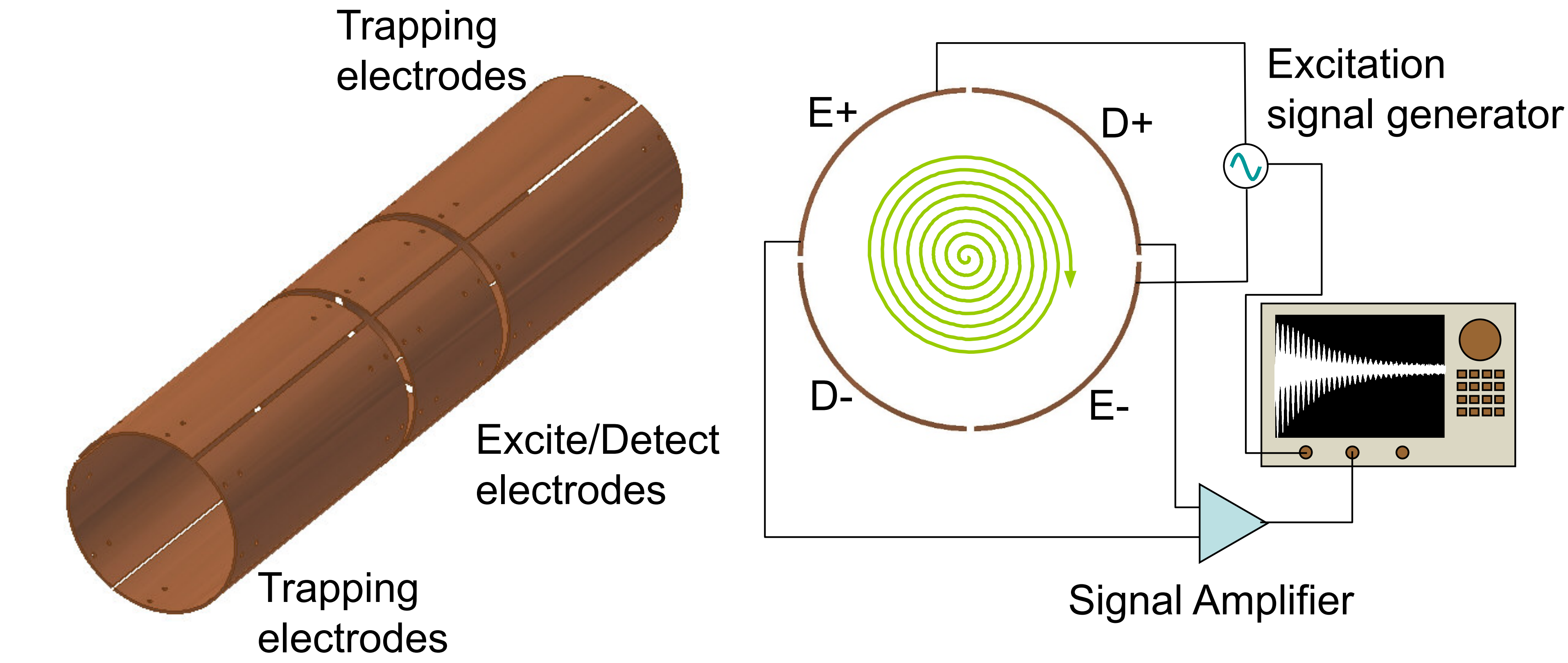
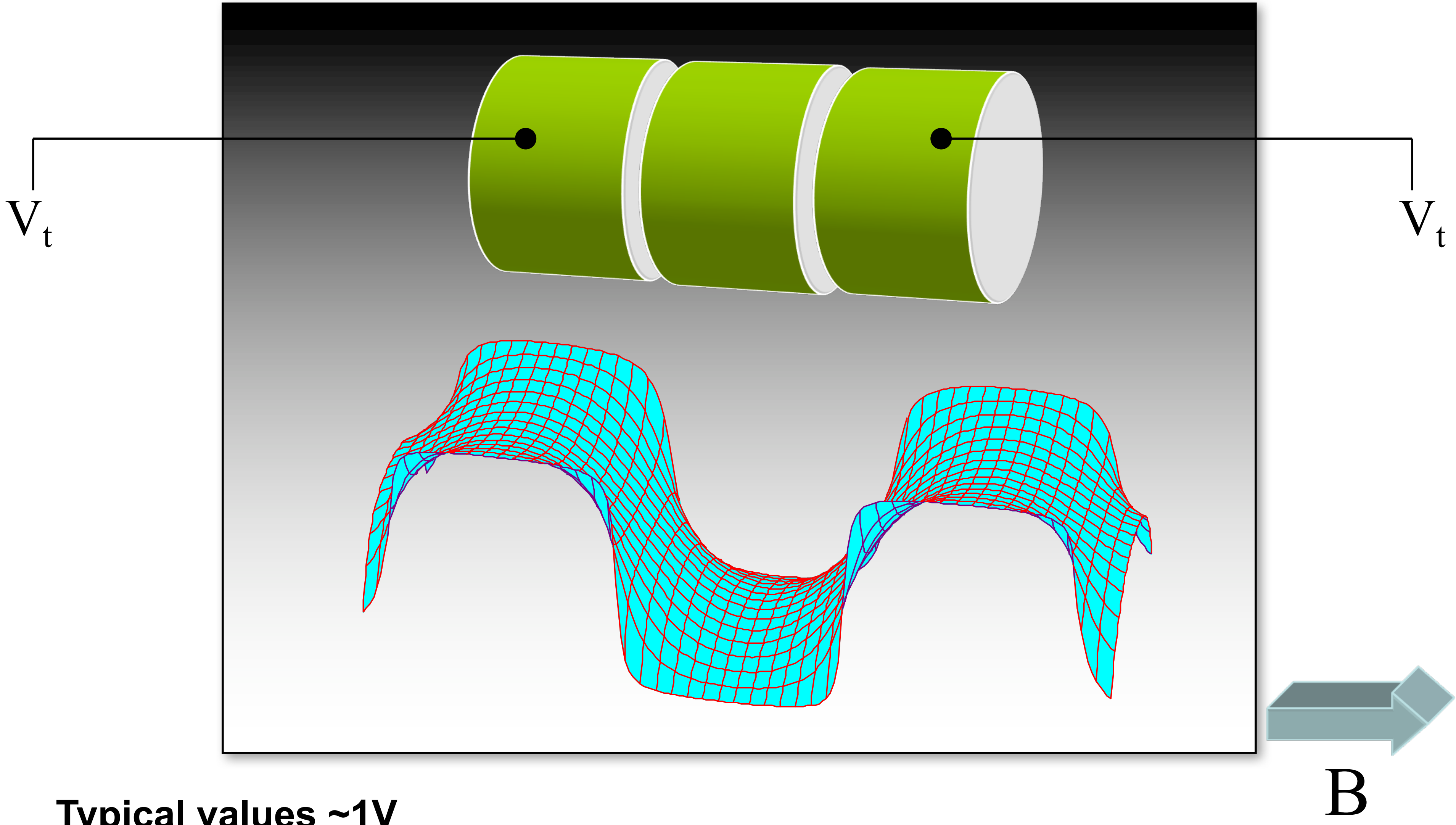


A. Typical open cylindrical cell

B. Typical Excite/Detect geometry

Figure 5. The principle of FT-ICR-MS.

Initialize Trap Voltages



Typical values ~1V

Cyclotron Motion

$$\frac{d^2x}{dt^2} + \xi\frac{dx}{dt} - \frac{q}{m}\frac{V_{eff}x}{a} - \omega_c\frac{dy}{dt} = 0$$

$$\frac{d^2y}{dt^2} + \xi\frac{dy}{dt} - \frac{q}{m}\frac{V_{eff}y}{a} - \omega_c\frac{dx}{dt} = 0$$

if ξ=0 (somewhat good assumption) this equation can be solved by the quadratic equation:

$$\omega_{obsd}^2 - \omega_c\omega_{obsd} + \frac{V_{eff}}{a}\frac{q}{m} = 0$$

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

$$\omega_{obsd} = \frac{\omega_c \pm \sqrt{\omega_c^2 - 4(\frac{V_{eff}q}{am})}}{2}$$

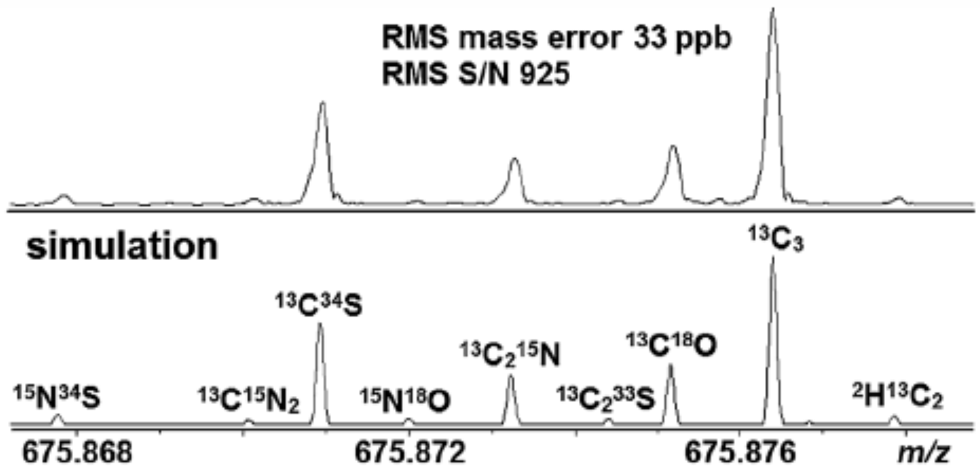
Calibration Equations

Zhang, L. K.; Rempel, D.; Pramanik, B. N.; Gross, M. L. Accurate mass measurements by Fourier transform mass spectrometry *Mass Spectrom. Rev.* **2005**, *24*, 286-309.

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)
$f_{estimated} = f_{measured} + c(I_{calibrant} - I_{analyte})$ $\frac{m}{z} = \frac{A}{f_{estimated}} + \frac{B}{f^2_{estimated}} + \frac{C}{f^3_{estimated}}$	(Easterling et al., 1999)
$M = (\frac{kB}{f_n + \Delta f})n - n(M_c)$	(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)
$\frac{m}{z} = \frac{A}{\nu} + \frac{B}{\nu^2} + \frac{C}{\nu^3} + \frac{BC}{A\nu^4}$	(Wang et al., 1988)

Francl, T. J.; *et al*, *Int. J. Mass Spec.* ***1983, 54, 189-199.***
Ledford, E. B., Jr.; Rempel, D. L.; Gross, M. L., *Anal. Chem.* ***1984, 56, 2744-2748.***



Formula	Measured m/z	Error (ppb)	Resolving power	S/N ratio	Calculated intensity	Measured intensity	Intensity difference
$^{15}N^{34}S$	675.867834	25	4.1M	118	5.9%	4.8%	-18.6%
$^{13}C^{15}N_2$	675.870143	58	4.1M	72	2.8%	3.0%	7.1%
$^{13}C^{34}S$	**675.870951**	**-19**	**4.0M**	**1363**	**60.7%**	**52.4%**	**-13.7%**
$^{13}C_2{}^{15}N$	**675.873268**	**25**	**4.0M**	**613**	**30.3%**	**23.7%**	**-21.8%**
$^{13}C^{18}O$	**675.875185**	**19**	**4.0M**	**781**	**36.2%**	**30.2%**	**-16.6%**
$^{13}C_3$	**675.876382**	**-25**	**4.1M**	**2607**	**100.0%**	**100.0%**	**0%**
$^{2}H^{13}C_2$	675.877895	61	4.7M	80	5.2%	3.4%	-34.6%
RMS		33		925			14%

FIGURE 6. Top: fine structure of $A + 3$ isotopic clusters for substance P $[M+2H]^{2+}$ ion, the recorded transient is 45-sec long. Middle: Simulation of the fine isotopic pattern. Bottom: Details of peak assignment (peaks used for mass calibration are in bold). Reprinted from Qi et al. (2012b), with permission from Wiley, copyright 2012.

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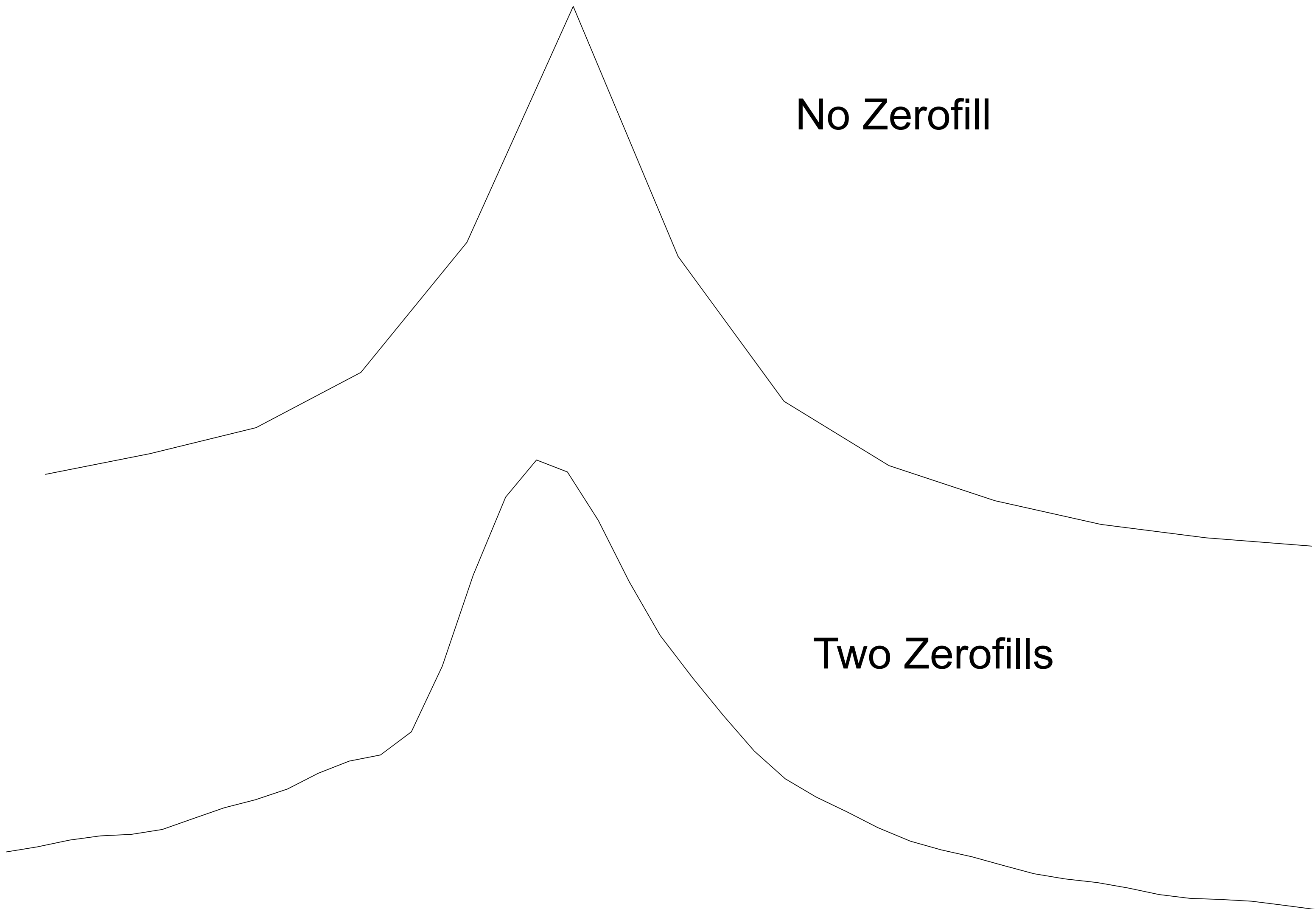
Ubiquitin 11$^+$: A+4 isotope



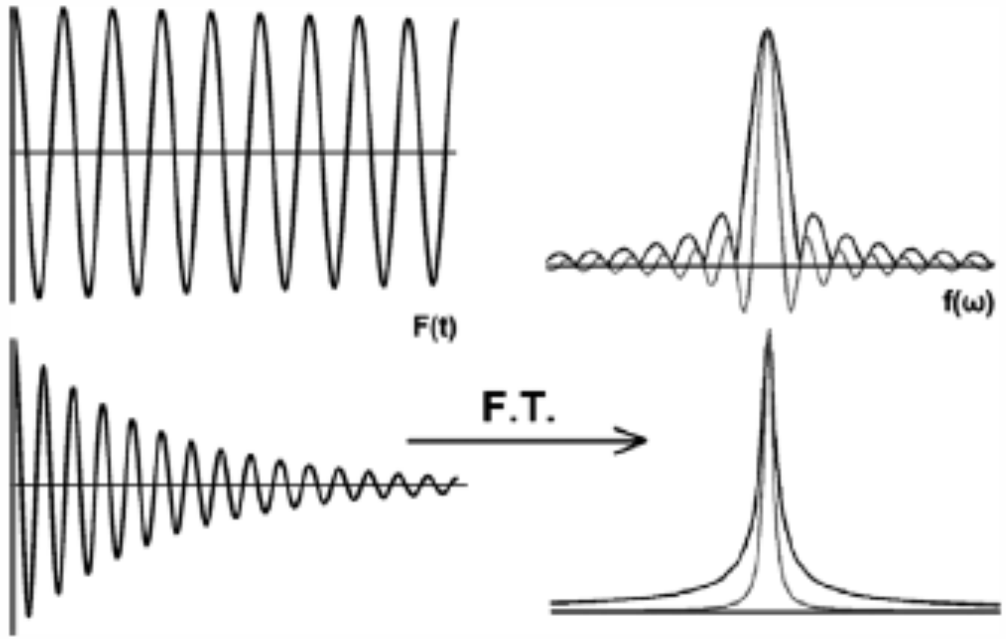


FIGURE 8. Simulated time-domain signals (left) and corresponding frequency-domain spectra after FT, with magnitude (black) and absorption-mode (defined below, gray) spectra (right). For $T \ll \tau$, peak shape is Sinc function (top), for $T \gg \tau$, peak shape is Lorentzian function (bottom). Adapted from Qi et al. (2011a).

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Zerofilling

•Every Zerofill roughly doubles the number of points/peak
•Zerofilling is effectively a smoothing operation that doesn’t change peak width
•Zerofilling is necessary for good peak fitting and centroiding