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Review Article

FOURIER TRANSFORM ION CYCLOTRON MASS RESONANCE SPECTROSCOPY

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ABSTRACT
Mass spectrometry is essentially a technique for determining the molecular weight. Mass spectrometry is based upon the motion of a charged particle, called an ion, in an electric or magnetic field. Mass spectrometry relies on the formation of gas-phase ions (positively or negatively charged) that can be isolated electrically (or magnetically) based on their mass-to-charge ratio (*m/z*), where as in Fourier transform ion cyclotron mass resonance spectroscopy (FTICR-MS) the m/z ratio measurement of an ion is based upon the ion's motion or cyclotron frequency in a magnetic field. Ions are detected by passing near detection plates and thus differently from other mass detectors/analysers in which ions are hitting a detector (at different times or places), the ions are trapped in a magnetic field combined with electric field perpendicular to each other (Penning trap). They are excited to perform a cyclotron motion. The cyclotron frequency depends on the ratio of electric charge to mass (m/z) and strength of the magnetic field. This spectrometric analysis can provide important information about the analytes, including their structure, purity, and composition.
Key words: Cyclotron frequency, Fourier transform, mass-to-charge ratio, Weighing molecules.

INTRODUCTION

Mass spectrometry relies on the formation of gas-phase ions (positively or negatively charged) that can be isolated electrically (or magnetically) based on their mass-to-charge ratio (*m/z*). For FTICR-MS the m/z ratio measurement of an ion is based upon the ion's motion or cyclotron frequency in a magnetic field. Ions are detected by passing near detection plates and thus differently from other mass detectors/analysers in which ions are hitting a detector (at different times or places). The ions are trapped in a magnetic field combined with electric field perpendicular to each other (Penning trap). They are excited to perform a cyclotron motion. The cyclotron frequency depends on the ratio of electric charge to mass (m/z) and strength of the magnetic field. Applications of FTICR-MS include identifying and quantitating pesticides in water samples, also identifying steroids in athletes, determining metals at ppq (Parts Per Quadrillion) levels in water samples, looking for life on Mars, determining the mass of an 28Si atom with an accuracy of 70 ppt, and studying the effect of molecular collision angle on reaction mechanisms. This is an essential technique for "weighing" molecules. FTICR-MS differs significantly from other mass spectrometry techniques in that the ions are not detected by hitting a detector such as an electron multiplier but only by passing near detection plates. Additionally the masses are not resolved in space or time as with other techniques but only by the cyclotron (rotational) frequency that each ion produces as it rotates in a magnetic field. Thus, the different ions are not detected in different places as with sector instruments or at different times as with time-of-flight instruments but all ions are detected simultaneously over some given period of time. In FT-ICR MS, resolution can be improved by increasing the strength of the magnet (in teslas) or by increasing the detection duration[1-4]

Principle

In the simplest mass spectrometer, organic molecules(gas) are bombarded with electrons (high energy electron beam 70ev) by using tungsten or rhenium filament and converted to high energy positive charged ions (molecular ions), which can break up into smaller ions (fragment ions) the loss of an electron from a molecule leads to radical cation. This process can be represented as $M - M^+$ (molecular ion) (loss of electron) the molecular ion M^+ decomposes to pair of fragments, which may be either a radical cation. Where as in FTICR-MS, Ions can be generated in an external ion source outside of the magnet and transferred into the cell, or volatile substances can be ionized within the cell. The ions are confined in the cell by the strong magnetic field and by an electricfield created by the cell's two end-cap electrodes. The trapped ions describe a circular orbit with a characteristic orbital frequency, also known as the ion cyclotron frequency ω_c where[4-7],

$$\omega_c = qB_0/m$$

B_0 is the magnetic flux density; m/q is the mass-to-charge ratio of the ion. On applying an excitation signal with a frequency ω_c, the ions will absorb energy and the ion ensemble will describe a coherent cyclotron motion with a larger orbital radius. The ion packet induces an image current in a pair of detector electrodes. The Fourier transform is a mathematical tool to convert the induced transient signal from the time domain to the frequency domain, which directly gives the mass-to-charge ratio of the ion

When a positive potential is applied, as the molecule are positively charged, they get repelled and travel with a great speed in straight path.

i.e potential energy = kinetic energy of molecule

$$eV = \tfrac{1}{2} mv^2$$

e - Charged ion, V- Accelerating velocity, M- Mass, v - Velocity after acceleration

When a magnet or electric field is applied, the positive charged fragments travelling in a straight path, now travels in a carved path, when they travel in carved path under the influence of magnetic field, the fragments are separated into different masses because radius:

$$m/e \alpha r^2$$

r – radius of path, Therefore mass α radius of path ion, Since e = 1 (unit of positive charge)

In recent years, FT-ICR has proven itself to be an excellent mass analyzing technique, providing ultra-high resolving power, high mass accuracy and tandem and higher- order tandem mass spectrometry [$(MS/MS)^n$] capability through non-destructive detection. Advances in electronics and computers together with the development of electro spray ionization (ESI) have further improved the performance of FTICR mass spectrometry systems and have made it possible to analyze biological macromolecules.

Instrumentation

A basic mass spectrometer contains following parts

- Vacuum pump
- Sample introduction device
- Ionization source
- Mass analyzer or ion separatorIon
- Detector[8-11]

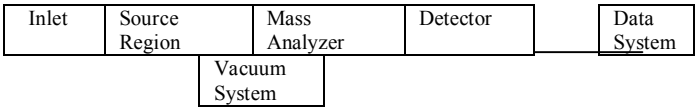

Figure 1: Block diagram of a mass spectrometer

Vacuum pump

To ensure the filament does not burn out in source. Helps to vaporize the sample to be vaporized and prevents ions, once formed being lost by collision with atmospheric gas also removes the sample from the instrument after analysis

Sample introduction: (inlet system)

The inlet system is used to introduce sample (milligram or nanogram) into the spectrometer. With the help of inlet system sample is converted to gaseous ions (system contains means for volatilizing solid or liquid samples). A sample studied by mass spectroscopy may be gas, liquid or solid. The sample should be finally converted to vapour state to obtain stream of molecules that must flow into the ionization chamber.

Ionization source

From the inlet system sample is introduced into ionization chamber, where a beam of electrons is bombarded with the molecules of sample, to convert the molecules into the ionized form. The ion sources used in mass spectroscopy is classified into two methods: 1.Gas phase source 2.Desorption source

These sources impart high or sufficient energy to analyte molecules, so that they are left in a highly excited energy state. Relaxation then involves rupture of bonds, producing fragment ions that have M/e ratio less than molecular ion.

Mass analyzers:

This is the part where separation of ions according to their masses is observed. An ideal mass analyzer should be capable of distinguishing between minute mass differences and should allow passage of sufficient number of ions to yield readily measurable ion currents. Also should have high resolution (R) and high transmission of ions (I), in order to undergo FT-ICR, a powerful mass analyzer where a sample must first be ionized. That means turning the liquid sample into a gas while applying a charge to it, making each of the atoms or molecules under study a positively or negatively charged particle (ion). The charge is critical to allowing the cyclotron's magnet to determine its mass.

Detectors:

Detection of ions is based upon their charge or momentum. For large signals a faraday cup is used to collect ions and measure the current. Older instruments used photographic plates to measure the ion abundance at each mass to charge ratio. Most detectors currently used to amplify the ion signal using a collector similar to a photomultiplier tube. These amplifying detectors include: electron multipliers, channeltrons and multichannel plates. The gain is controlled by changing the high voltage applied to the detector. A detector is selected for its speed, dynamic range, gain, and geometry. Some detectors are sensitive enough to detect single ions.

Along with these above mentioned there are also a horizontal bore magnet is aligned with a metal frame which supports vacuum system, ion sources and an inlet system for the introduction of volatile samples. From the main vacuum chamber a titanium tube leads into the centre of the magnet and ends with a cell where the ions are stored. The metal frame runs on tracks and can easily be moved away from the magnet to provide access to the cell. The instrument is controlled and data is retrieved and analyzed on a single Silicon Graphics O2 or Indy workstation. A number of remote workstations are used for subsequent data analysis.

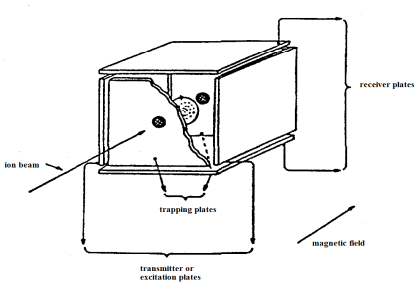

Figure 2: FTICR- Mass Spectrometer

WORKING

Pumps and vacuum:

The vacuum system is a differentially pumped, oil-free, ultra-high vacuum system capable of sustaining a base pressure of below 5×10^{-9} mbar using either turbomolecular pumps backed by mechanical rough pumps or cryogenic pumps (Warwick). The ESI source is equipped with a fore pumping system which includes one mechanical pump and a 250 Ls turbo molecular pump. The system is compatible with a wide range of reagent and buffer gases. The part of the system within the magnet bore can be cooled and heated from ambient temperature up to 150°C for baking or for blackbody infrared radiative dissociation (BIRD) experiments. A gate valve separates the cell side of the vacuum system from the source side allowing ion source changes or maintenance without disturbing the ultra-high vacuum.[12-15]

Magnet:

The magnet is a 9.4T central-field, superconducting (Nb_3Sn) magnet with passive shielding. The magnet system includes a He and N_2 monitor, an emergency quench unit, transfer lines for liquid He and liquid N_2 and a line for recycling He. The cryogen consumption is <15 L N_2 (liquid) / 24 h and <1.5 L He (liquid) / 24 h. About 90% of the He is

recycled in-house for the magnet. The room temperature bore is 160 mm length. The field homogeneity at the centre of the magnet within a cylindrical volume of 30 mm diameter and 60 mm length has been measured to be <8.2 ppm peak to-peak and <3.4 ppm within a 15 mm diameter cylindrical volume of the same length. The passive shielding surrounding the magnet consists of an iron cage with a weight of 11 metric tonnes. The shield reduces the outside fringing fields to <5 gauss radially at the outer surface of the magnet shield and <10 gauss axially at 2 m from the centre of the magnet.

The cell:

The INFINITY cell is of cylindrical geometry and consists of one pair of plates used for detection, offset by 90°, a second pair of plates that is used to introduce radio frequency excitation pulses. Two plates with annular entrance holes, cap the cell. The cell is equipped with an ion accumulation system and a quadrupolar excitation axialisation (QEA) system. The cell electronics include a pulse shaping system for generation of frequency shots, correlated frequency sweeps, on-resonance and sustained off-resonance irradiation (SORI) for collision induced dissociation (CID) experiments, electronics for dynamical trapping of ions, a preamplifier and detection electronics for direct and heterodyne-mode detection. Outside the cell is an electron gun for internal electron impact (EI) ionization and chemical ionization (CI) of volatile substances. This electron gun can also be used for electron capture dissociation (ECD). The electron gun can be removed and replaced with a laser for infrared multiphoton dissociation (IRMPD) experiments.

Data acquisition and control:

Data are acquired through a 12-bit fast (10 MHz, broad-band mode) and a 14/16-bit slow (400 kHz, heterodyne mode) digitizer, with an acquisition memory of 1 Mbytes. Data is subsequently transferred to either a Silicon Graphics workstation or an Indy workstation via a dedicated Ethernet connection between the acquisition computer and the workstation. The workstation is equipped with a second Ethernet card for external communication. The system is controlled by and data is retrieved and analyzed with the software package, presently at version 5.0.6.

Ion sources and sample introduction:

The mass spectrometer is equipped with four external ion sources and an electron gun for internal (in cell) electron impact (EI) ionization and low-pressure chemical ionization (CI). The four external sources are an electrospray ionization (ESI) source, matrix-assisted lasers desorption/ionization (MALDI) source, a secondary ion mass spectrometry (SIMS) ion source and a switchable EI/CI source. [16-18]

The ESI source is equipped with an inlet glass capillary (15 cm length and 0.5 mm i.d. with platinum capping at both ends). The spraying needle is a stainless steel capillary with 0.1 mm i.d. N_2 nebulising gas is used to assist the spray, and a counter-flow of heated drying gas is used to promote solvent evaporation from the electrosprayed droplets. The electrospray source is fitted with a holder for nanospray needles and a small aperture stainless steel cap for the glass capillary. Ions are accumulated in a computer-controlled hexapole ion trap behind a skimmer, and are pulsed into the spectrometer. The sample is infused using a syringe pump.

The MALDI source consists of an UV (337 nm) N_2 laser with optics, filters, attenuators, a manually-controlled sample probe and a CCD camera with a monitor for visual monitoring of the sample. The SIMS ion source has a pulsed 25 keV Cs^+ ion gun and uses a similar sample probe to the MALDI source.

The external EI/CI source uses a direct inlet probe (DIP) that can be heated up to 400°C. Alternatively, a dedicated port for introduction of volatile liquids and gases can be used for EI/CI. On the instrument, the SIMS source is always mounted. Switching between the external ion sources (MALDI, EI/CI or ESI) is relatively easy, as only the front flange of the source chamber has to be changed.

Computer-controlled fast valves for gas introduction:

Experiments that require introduction of gas, two computer-controlled fast gas-inlet valves are provided. By opening an inlet valve connecting the cell and a volume of collision gas (e.g. Ar or CO_2 at a pressure of 5 mbar) for ~10 ms, the pressure in the cell is raised to a level (~10^{-7} mbar) suitable for those experiments. [19-21]

MODIFICATIONS

A new electrospray has been assembled to allow lower flow rates to be used. This source has a stainless steel needle (0.1 mm i.d.) with a conical shape. This needle is connected to a syringe through a short piece of Teflon tubing. The sample is loaded to the spraying end of the needle. No nebulising or drying gas is used. Flow rates are between 0.2 and 0.4 μL min^{-1}. A further improvement to the electrospray source is the fitting of a computer controlled shutter. Thus a new electrospray source has been assembled in shutter, essentially closes the spectrometer so that no more ions are accumulated in the hexapole ion trap, allowing investigation of multipole storage-assisted dissociation (MSAD). A further advantage is that contamination of the source is reduced. The flexibility of the program has permitted the compilation of experimental pulse programs controlling not only this shutter, but also the internal EI gun used to perform ECD experiments. [22-26]

Negative-ion detection mode:

Switching from positive-ion detection to negative-ion detection mode can be easily achieved by changing the polarity of the ion source and transfer optics. Routine or advanced experiments can be performed either in the positive or in the negative mode, e.g. broadband and heterodyne detection, resonant and sustained off resonance irradiation CID.

Performance characteristics[27-30]

Mass-to-charge range:

Since the cyclotron frequency is inversely proportional to mass, the sampling rate and the bandwidth of the electronics set a lower mass limit. With a 9.4 T magnetic field and a sampling frequency of 10 MHz, the lower mass limit is m/z ~ 29 according to the Nyquist criterion. $C2H5^+$ ions (m/z = 29) formed using methane regent gas in the external chemical ionization source have been detected. The highest detected m/z value is singly-charged ubiquitin (m/z = 8565) formed by MALDI.

Resolving power:

Resolving power, here defined as $m/\Delta m_{FWHM}$, in excess of 4,000,000 (magnitude mode) has been achieved on a fragment ion at m/z=130.9916 (C_3F_{5+}) from perfluorotributyl-amine (PFTBA) using external EI ionisation and heterodyne detection. It must be born in mind that, in this context, measurement of a single peak does not provide a very useful figure of merit because of peak coalescence.

High mass performance:

Electrosprayed protein (45 kDa) and bovine serum albumin (BSA, 66 kDa) with charge states ranging from 30+ to 55+, have been fully isotopically resolved with a resolving power of over 150,000 for the 50+ charge state in broad-band mode (600 summed spectra). No ions were ejected prior to detection. Apotransferrin (77 kDa) has been successfully detected in broadband mode using ESI Electrosprayed streptokinase. A 47.3 kDa protein has been completely isotopically resolved with a resolving power over 150,000 in broadband mode for the 36+ charge state.

Mass accuracy:

Mass accuracy in the ESI mode has been shown to be of the order of a few ppm over the m/z range 200-2000. The m/z scale is externally calibrated using a pre made calibrant for ESI which generates seven peaks, viz. m/z = 118.0868, 322.0487, 622.0295, 922.0103, 1521.9719, 2121.9335 and 2721.8951. The software allows two- or three-point calibration formulae with linear or quadratic fitting to the calibration peaks. Typically, a calibration formula $m/z = a / f + b / f^2 + c$ is used, where f is the cyclotron frequency and a, b and c are calibration constants. In the analysis of tryptic digests, more than 100peptides have been identified in one spectrum where the distribution of mass measurement error was approximately normal with a standard deviation of 1.7 ppm (external calibration).

Sensitivity:

Angiotensin concentrations down to 1 nM (200 attomole consumed during the data acquisition period of 4 s) have been detected using the home-built ESI source and a spraying solvent comprising $CH_3OH + H_2O + HOAc$ (199 : 99 : 2 v/v). Low (20-40 attomole) amounts consumed during data acquisition of bradykinin, bradykinin fragment 1-5, leucine enkephalin and [Arg^8]-vasopressin have been detected simultaneously using nanospray and a spraying solvent comprising $CH_3CN + H_2O + HOAc$ (99:99:2v/v).

APPLICATIONS

The work and research conducted on the FT-ICR mass spectrometer is described and its applications were listed below. [31-34]

Peptides and proteins

ESI FT-ICR tandem mass spectrometry (MS/MS) provides both a sensitive and selective method for detection of peptides. In co-operation with other groups, neuropeptides present in small amounts are analysed. Biological samples have been analysed using liquid separation methods (capillary electrophoresis and micro-scale high performance liquid chromatography) coupled with FT-ICR mass spectrometry. Biological applications, particularly the study of non-covalent interactions of biological molecules and protein conformation, are priority for the FT-ICR. Evidence of non-covalent dimerisation of calmodulin has been reported.

Peptide fragmentation

In order to investigate novel approaches to peptide fragmentation, the internal electron gun was reprogrammed and used for electron capture dissociation. Another more recent approach to peptide dissociation is multipole-storage assisted dissociation (MSAD), where ions are accumulated and fragmented in the hexapole ion trap in the ESI source.

Oligonucleotides

Negative-ion detection has been applied for the study and characterization of oligonucleotide complexes on the instrument. It has been found that the nanospray ion source can be effective for negative-ion detection. This is partially due to the smaller number of vari-

ables associated with nanospray compared with the number associated with standard ESI. Extra parameters to be adjusted in standard ESI, compared with nanospray, are the drying and needle gases, the flow rate and the extra voltages associated with the spraying process.

Synthetic polymers

A wide range of polymers has been studied using ESI FT-ICR

Eg: PEG

Poly-ethylene glycol 3500 mass spectrum obtained with nano-electrospray ionisation using a 20 µM solution prepared using 50 : 50 water + methanol with the addition of 1% 1 mM NaOH**.**

Fullernes:

ESI FT-ICR has been successfully used for the first time to characterise fullerenes and fullerene derivatives with the combined benefits of the gentle ionisation process, high resolution and high mass-accuracy. Using the tandem capability of laser desorption/ionisation with FT-ICR, complexes of fullerenes with helium have been produced by resonant excitation of the fullerene ions in helium gas. The laboratory-frame collision energy was not determined accurately, but would have been approximately 3 keV.

Recent advanced applications:

- For complex mixtures or unknown analytes, ultra high mass resolution is a necessary prerequisite for ultra high mass accuracy (sub ppm) because each peak must be fully resolved before mass can be assigned uniquely.
- Assignment of element composition (metabolomics, fossil fuels, environmental mixtures) and amino acid composition are determined.
- Post translational modification of peptides and proteins and mapping of protein binding sites by Helium/Deuterium exchange followed by enzyme cleavage.
- Another place that FTICR-MS is useful is in dealing with complex mixtures since the resolution (narrow peak width) allows the signals of two ions of similar mass to charge (*m/z*) to be detected as distinct ions. [35-37]

CONCLUSION:

Finally we conclude that introduction of FT-ICR as mass analyzer is that ion mass-to-charge ratio is manifested as frequency, because frequency can be measured accurately than any other parameter, ICR MS, therefore, offers greater resolution than any other type of mass measurement. Introduction of FT techniques to ICR MS brought advantage of increased speed and sensitivity. The use fixed magnetic field rather than swept field increases resolution and mass range. Applications from these advantages include determinations of chemical formulas from the complex mixtures, detection limit in attomole range etc.

REFERENCES

1. Howe. I, D.H. Williams, Bowen R.D. Mass Spectrometry Principles and Applications. 2nd ed., New York: Mcgraw-Hill Inc; 1981: 25-83.
2. Comisarow MB, Marshall AG. Theory of Fourier transforms ion cyclotron resonance mass spectroscopy: Response to frequency-sweep excitation. J Chem Phys Lett 1974; 25: 282-289.
3. Comisarow MB, Marshall AG. Theory of Fourier transforms ion cyclotron resonance mass spectroscopy: Fundamental equations and low-pressure line shape. J Chem Phys Lett 1974; 26: 489-502.
4. Marshall AG, Schweikhard L. Quadrupolar excitation and collisional cooling for axialization and high pressure trapping of ions in Fourier transform ion cyclotron resonance mass spectrometry. Int J Mass Spectrom Ion Processes 1992; 37: 118-119.
5. Kanawati B, Wanczek K P. Characterization of a new open cylindrical ion cyclotron resonance cell with unusual geometry. Rev sci instrum 2007; 78: 7-23.
6. Holliman CL, Rempel DL, Gross ML. Fundamentals of Contemporary Mass Spectrometry. Mass Spectrom Rev 1994; 13: 105-111.
7. Marshall AG, Hendrickson CL, Jackson GS. Fourier transform ion cyclotron resonance mass spectrometry: a primer. Mass Spectrom Rev 1998; 17: 1-40.
8. Cody RB, Burnier RC, Freiser RS. Multiple-collision induced dissociation of trapped silver clusters. Anal Chem 1982; 54: 96-202.
9. Gauthier JW, Trautman TR, Jacobson DB. Filar ion cyclotron resonance ion trap: Spatially multiplexed dipolar and quadrupolar excitation for simultaneous ion axialization and detection. Anal Chem Acta 1991; 246: 21-46.
10. Fenn JB, Mann M, Meng CK, Wong SF, Whitehouse CM. Electron transfer collisions between isolated fullerene dianions and SF6. Mass Spectrom Rev 1990; 9: 37-48.
11. Henry KD, Williams ER, Wang BH, McLafferty FW, Shabanowitz J, Hunt DF. Fourier-transform mass spectrometry of large molecules by electrospray ionization. Proc Natl Acad Sci 1989; 86: 90-75.
12. Henry KD, McLafferty FW. High performance detection of biomolecules using a high magnetic field electrospray ionization source/Fourier transform ion cyclotron resonance mass spectrometer. Org Mass Spectrom 1990; 25: 490-553.
13. Caravati P, Allemann M. A new electrostatic transfer line for improved transmission in fourier transform laser microprobe mass spectrometry with external ion source. Org Mass Spectrom 1991; 26: 514-564.
14. Dale VC, Speir JP, Kruppa GH, Stacey CC, Mann M, Wilm M. Applications of sustained off-resonance irradiation (SORI) and quadrupolar excitation axialization (QEA) for the characterization of biomolecules by Fourier-transform mass spectrometry (FTMS). Biochem Soc Trans 1996; 24: 943-1008.
15. Savard G, Becker S, Bollen G, Kluge HJ, Moore RB, Otto T, *et al*. Trap-based Cluster Research and Cluster-based Investigations of Ion Storage at ClusterTrap. J Phys Lett 1991; 158: 247-252.
16. Guan S, Kim HS, Marshall AG, Wahl MG, Wood TD, Xiang X. Fourier transform Ion Cyclotron resonance Mass spectrometry in study of ion-molecule reaction. J Chem Rev 1994; 94: 21-61.
17. Kanawati B, Wanczek K. Characterization of a new open cylindrical ICR cell for ion–ion collision studies. Int J Mass Spectrometry 2008; 269: 12-57.
18. Axelsson J, Palmblad M, Hakansson K, Hakansson P. Identification and characterization of proteins and peptides by FTCR.MS. Rapid Commun Mass Spectrom 1999; 13: 4-74.
19. Woodlin RL, Bomse DS, Beauchamp JP. Probing the mechanisms of electron capture dissociation mass spectrometry with nitrated peptides. J Am Chem Soc 1978; 100: 32-48.
20. Price WD, Schnier PD, Willliams ER. A 9.4 T Fourier transform ion cyclotron resonance Mass spectrometry. Anal Chem 1996; 68: 859-950.
21. Axelsson J, Hakansson K, Palmblad M, Hakansson P. Electron capture dissociation of substance P using a commercially available Fourier transform ion cyclotron resonance mass spectrometer. Rapid Commun Mass Spectrom 1999; 13: 15-50.
22. Sannes-Lowery K, Griffey RH, Kruppa GH, Speir JP, Hofstadler S. The Use of a Hybrid Linear Trap/FT-ICR Mass Spectrometer for On-Line High Resolution/High Mass Accuracy Bottom-Up Sequencing. Rapid Commun Mass Spectrom 1998; 12: 19-57.
23. Hakansson K, Axelsson J, Palmblad M, Hakanssonn P. Instrumentation and woking of Ion cyclotron mass resonance spectroscopy. J Am Soc Mass Spectrom 2000; 11: 210-268.
24. Marshall AG, Guan S. Advantages of High Magnetic Field for Fourier Transform Ion Cyclotron Resonance Mass Spectrometry. Rapid Commun Mass Spectrom 1996; 10: 18-19.
25. Cody RB, Hein RE, Goodman S D, Marshall AG. Stored waveform inverse fourier transform excitation for obtaining increased parent ion selectivity in collisionally activated dissociation: Preliminary results. Rapid Commun Mass Spectrom 1987; 1 (6): 99-109.
26. He F, Hendrickson CL, Marshall AG. Baseline mass resolution of peptide isobars: a record for molecular mass resolution. Anal. Chem 2001; 73 (3): 647–750.
27. Feng X, Giannakopulos AE, Wallace J, Der- rick PJ. A comment on: New Mass spectrometric approaches to structural analysis in mixtures. Rapid Commun Mass Spectrom 2000; 14: 719-876.
28. Shi S, Drader Jared J, Freitas Michael A, Hendrickson, Christopher L, Marshall Alan G. Comparison and interconversion of the two most common frequency-to-mass calibration functions for Fourier transform ion cyclotron resonance mass spectrometry. Int J Mass Spectrometry 2000; 591: 195-196.
29. Smith DL, Zhang ZQ. Instrumental techniques, methods and awareness in biological Mass spectrometry. Mass Spectrom Rev 1994; 13:411-436.
30. Loo JA. Protein Mass spectrometry. Mass Spectrom Rev 1997; 16: 12-54.
31. Veenstra TD. Mass spectrometry. J Bio Phys Chem 1999; 79: 63-69.
32. Pramanik BN, Bartner PL, Mirza UA, Liu YH, Ganguly AK. Electrospray ionization mass spectrometry for the study of non-covalent complexes. J Mass Spectrom 1998; 33: 911-88.
33. Heck AJR, Derrick PJ. Selective fragmentation of single isotopic ions of proteins upto 17kDa using 9.4 Tesla Fourier transform ion cyclotron resonance. Anal Chem 1997; 69:36-73.
34. Blomqvist M, Bergquist J, Westman A, Hakansson K, Hakansson P, Fredman P. Combined infrared multphoton dissociation and electron capture in FT-ICR mass spectrometry. Eur J Biochem 1999; 263: 312-330.
35. Lafitte D, Heck AJ, Hill TJ, Jumel K, Harding SE, Derrick PJ. Ca4 complex in gas phase: electrospray ionsation and ion cyclotron resonance. Eur J Biochem 1999; 261: 3-37.
36. Marshall A. Fourier transform ion cyclotron resonance detection: principles and experimental configurations. Int J Mass Spectrom 2002; 215: 40-59.

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