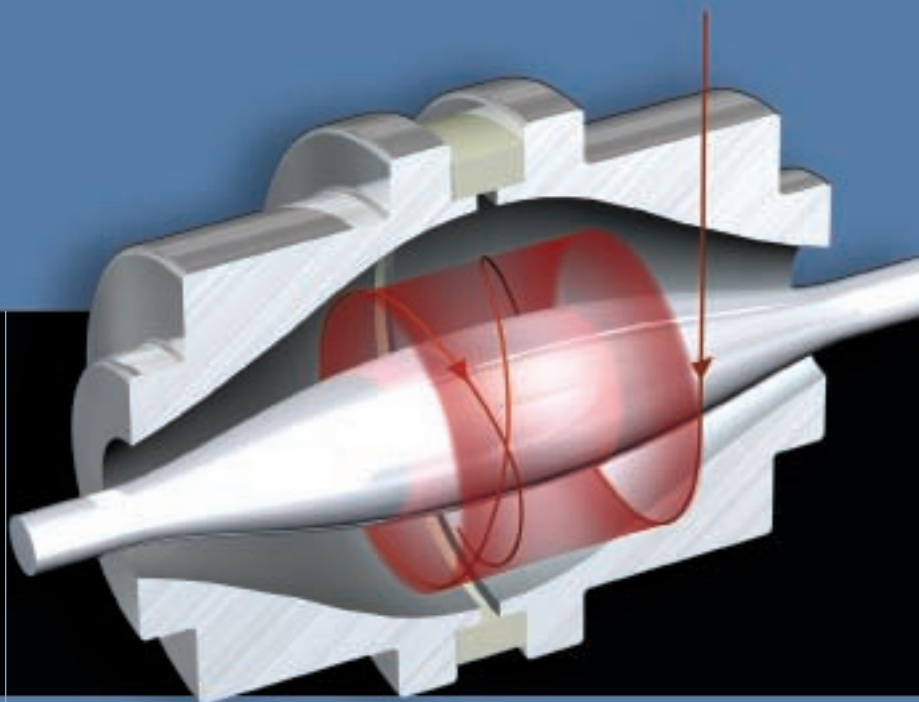


LTQ Orbitrap™
Hybrid FT Mass Spectrometer



**Breakthrough technology for proteomics
and small molecule research**

LTQ ORBITRAP: A NOVEL HYBRID MASS SPECTROMETER WITH SUPERIOR MASS ACCURACY, MASS RESOLUTION, DYNAMIC RANGE AND DETECTION POWER

Combining patented Orbitrap technology with the industry benchmark Finnigan™ LTQ™ linear ion trap, the LTQ Orbitrap provides faster, more sensitive and more reliable detection and identification of compounds in complex mixtures.

Outstanding mass accuracy, mass resolution and reliable high sensitivity MSⁿ performance make the LTQ Orbitrap a clear alternative to hybrid Time-of-Flight systems.

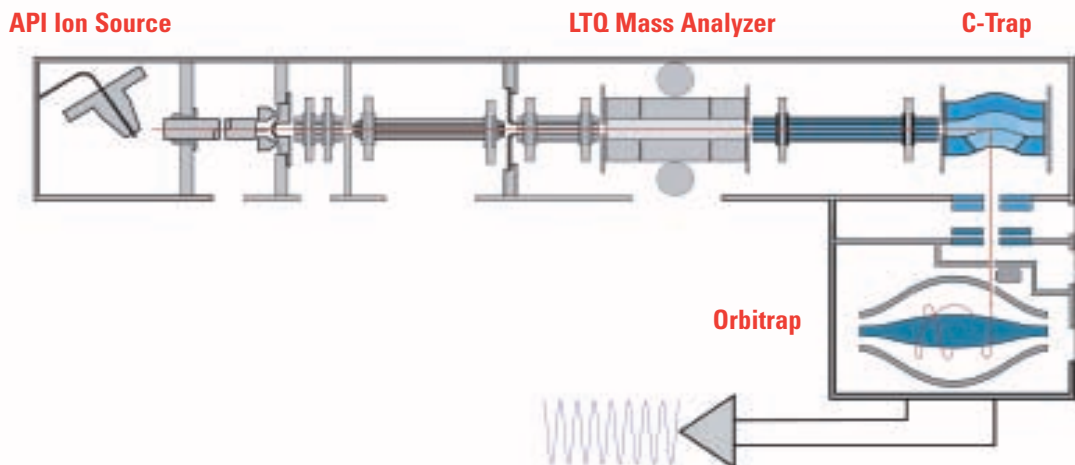
The LTQ Orbitrap supports a wide range of applications, from routine compound identification to the most demanding analysis of trace level components in complex mixtures.

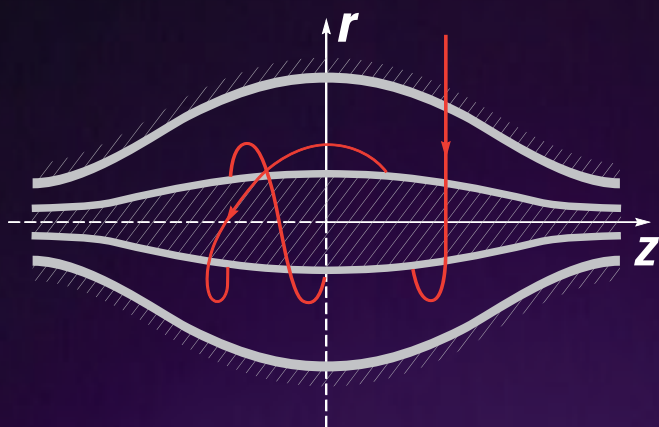
PRINCIPLE OF OPERATION

The LTQ Orbitrap mass spectrometer is a hybrid system combining the Finnigan LTQ linear ion trap mass spectrometer and the Orbitrap mass analyzer. Ions generated in the API ion source are trapped in the LTQ mass analyzer.

Once in the mass analyzer, the ions are analyzed using the MS and MSⁿ scan modes of the LTQ. Then, the ions are axially ejected from the LTQ and collected in a C-shaped ion trap (C-Trap) from which they are passed into the Orbitrap.

The ions transferred from the C-Trap are captured by rapidly increasing the voltage on the center electrode of the Orbitrap. The trapped ions assume circular trajectories around the center electrode and their axial oscillations, along the center electrode, are detected.





The axially oscillating ions produce a periodic signal on the outer electrodes, which is detected as an image current. After amplification, the image current signals are converted into a frequency spectrum using a Fourier transform algorithm. Because the frequency of oscillation is directly related to the mass-to-charge ratio, the frequency spectrum is readily converted into a mass spectrum.

ACCURATE MASS CAPABILITIES

- Parallel data acquisition using both the Finnigan LTQ and the Orbitrap
- Independent of signal intensity
- External mass calibration
- Optional internal calibration without sample introduction

UNSURPASSED LC/MS AND LC/MSⁿ PERFORMANCE

- Low detection limits
- Data acquisition rates suitable for HPLC separations
- Wide linear dynamic range
- Data Dependent™ acquisition with Dynamic Exclusion™

HIGH PRODUCTIVITY WITH LOW MAINTENANCE

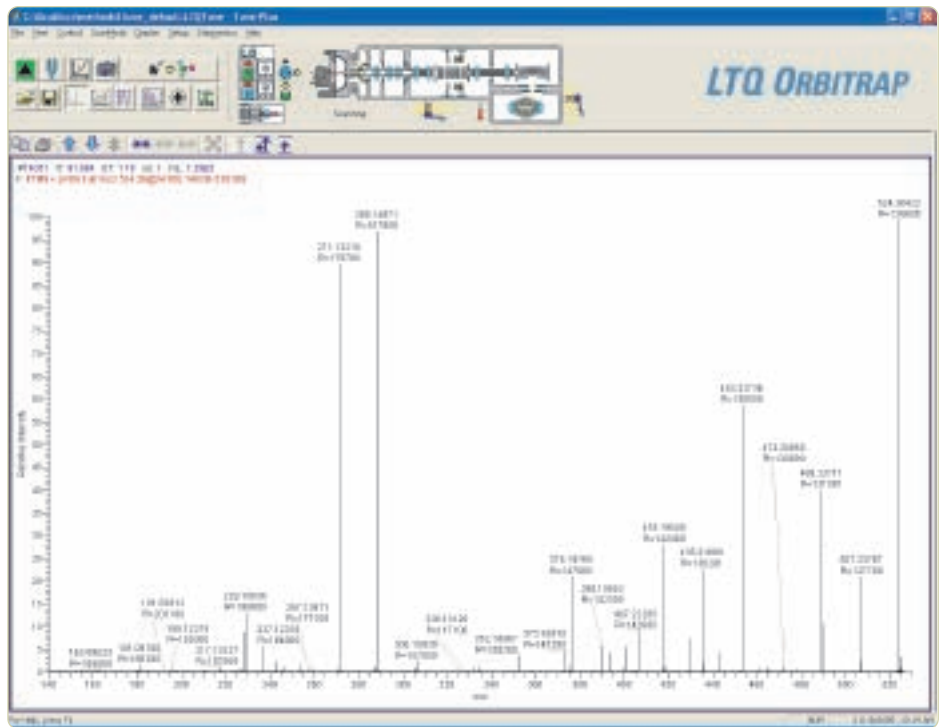
The LTO Orbitrap exemplifies Thermo's tradition of providing ultimate analytical performance in a reliable, easy-to-use, robust instrument platform.

All the performance and sample inlet features of the Finnigan LTO complement the wide dynamic range, outstanding sensitivity, high mass accuracy and high mass resolution of the Orbitrap.

Intelligent, Data Dependent instrument control provides unmatched flexibility, which is easily tailored to help solve the toughest analytical challenges.

Software for both data acquisition and data evaluation in metabolite identification and bottom-up proteomics research converts the analytical power of the LTO Orbitrap into ready-to-use analytical information. This includes intelligent use of accurate mass information in Mass Defect Filters as well as in structure elucidation and protein identification.

The LTO Orbitrap's small footprint accommodates any size laboratory and requires minimal laboratory infrastructure. This hybrid system installs rapidly to provide immediate productivity for high-throughput environments. Especially noteworthy; the Orbitrap analyzer cell requires no maintenance.



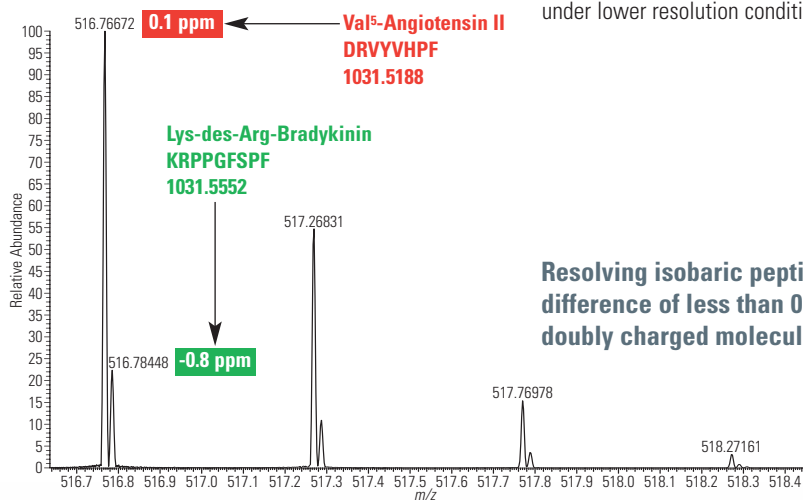
TUNE Plus window simplifies user interface

HIGH MASS RESOLUTION

Analysis of unknown samples requires both high resolution and high mass accuracy.

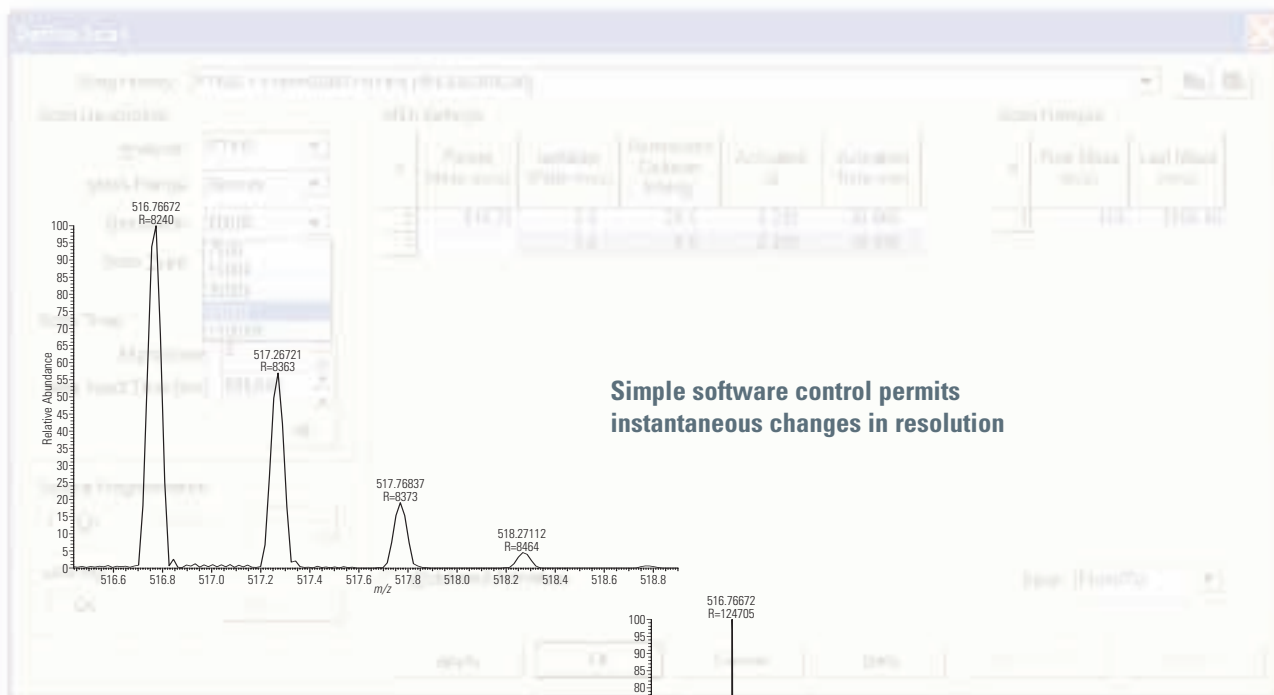
High resolution enables the detection and differentiation of isobaric signals, not discernable under lower resolution conditions.

Not only can these ions be detected, but their exact mass can be determined for unequivocal compositional and structural elucidation. Resolutions of 7,500, 15,000, 30,000, 60,000 and 100,000 (at m/z 400) are available on the LTQ Orbitrap.



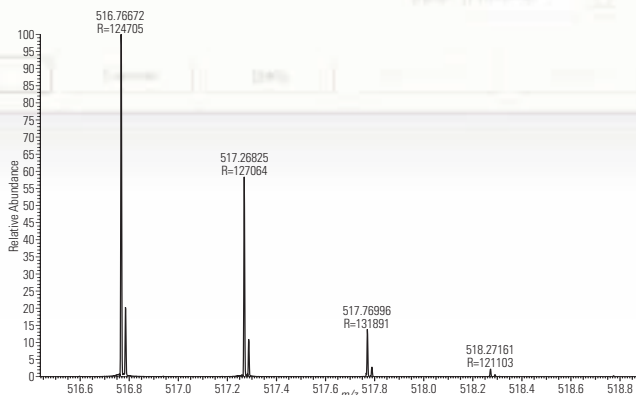
Resolving isobaric peptides with m/z difference of less than 0.02 Da on the doubly charged molecular ion

LTQ Orbitrap Full Scan (R = 60,000 at m/z 400)



Simple software control permits instantaneous changes in resolution

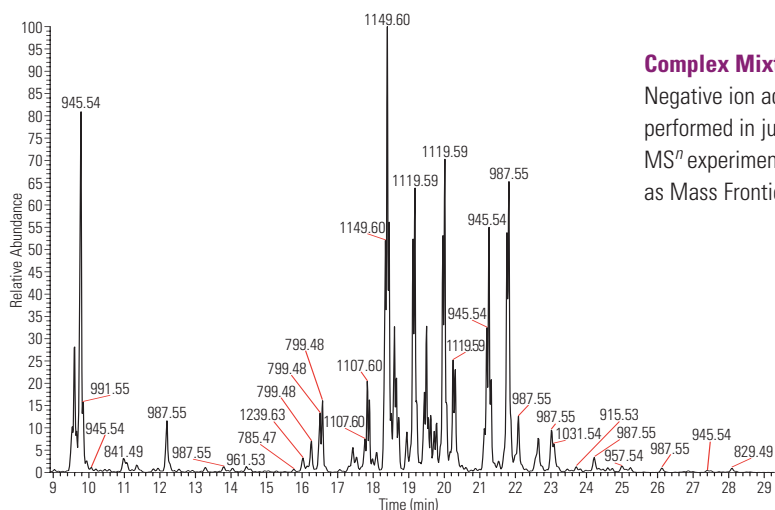
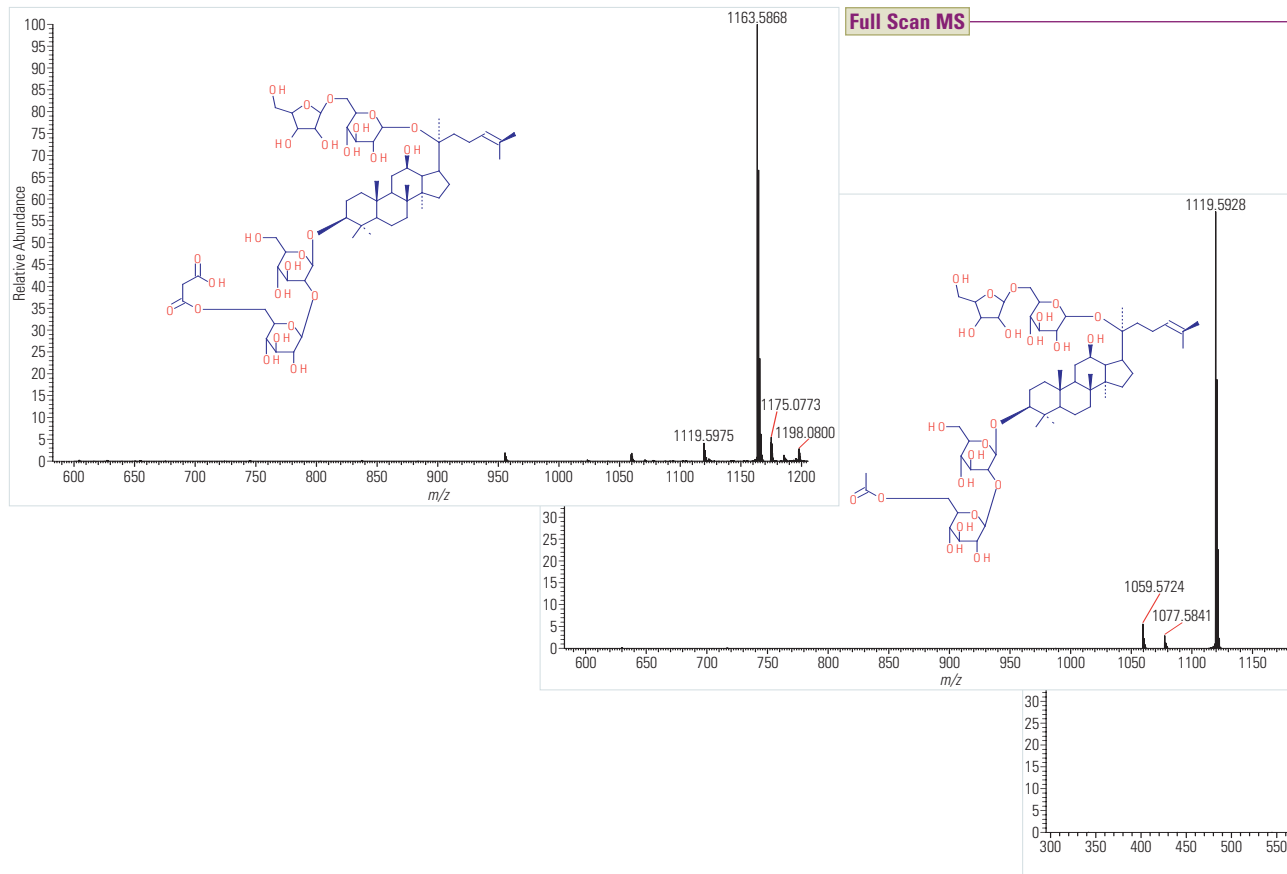
Real time change in resolution from 7,500 to 100,000



COMPOUND IDENTIFICATION OF COMPLEX MIXTURES

The LTO Orbitrap provides accurate mass MS and MSⁿ spectral data on a chromatographic time scale with scan cycles of one second (at R = 60,000) or less.

Accurate mass experiments yield the elemental composition of intact molecules, and MSⁿ fragment ions provide additional structural confirmation.



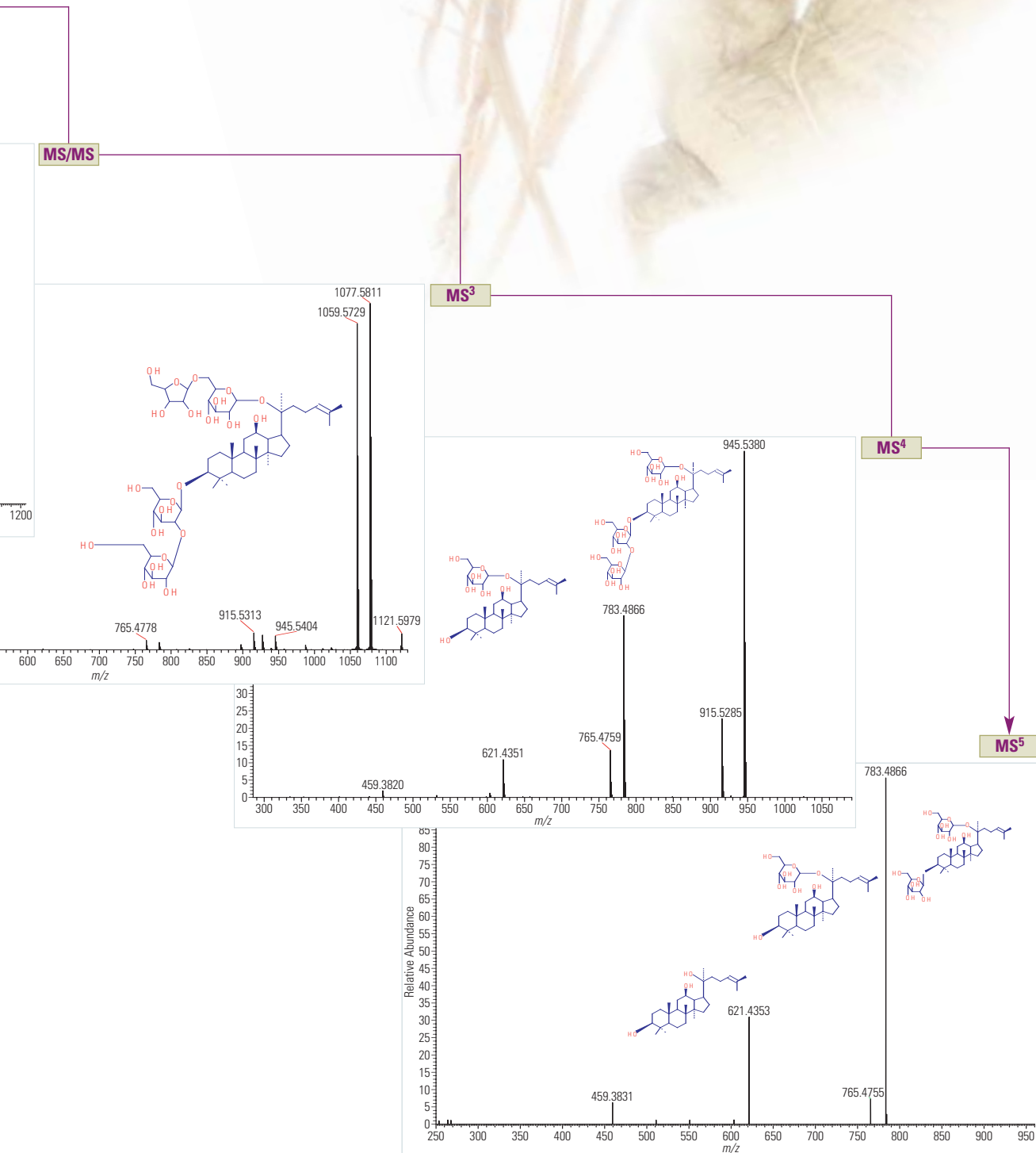
Complex Mixture Identification Strategy

Negative ion acquisition of one MS and four MSⁿ spectra are performed in just over one second. Using accurate mass MS and MSⁿ experiments combined with sophisticated software, such as Mass Frontier™, provides unambiguous structural elucidation.

Negative ion, base peak chromatogram of a Korean ginseng (*Panax ginseng*) root extract

Example: Ginsenosides from Korean Ginseng

- Analysis of ginsenosides and their malonyl esters
- On-line LC/MS measurement
- Negative electrospray ionization
- MS/MS to MS⁵ for structural elucidation
- Accurate masses with external calibration



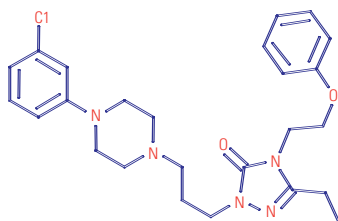
UNAMBIGUOUS IDENTIFICATION OF METABOLITES

Extensive preclinical studies require detailed analysis of metabolic profiles for regulatory approval of new drugs.

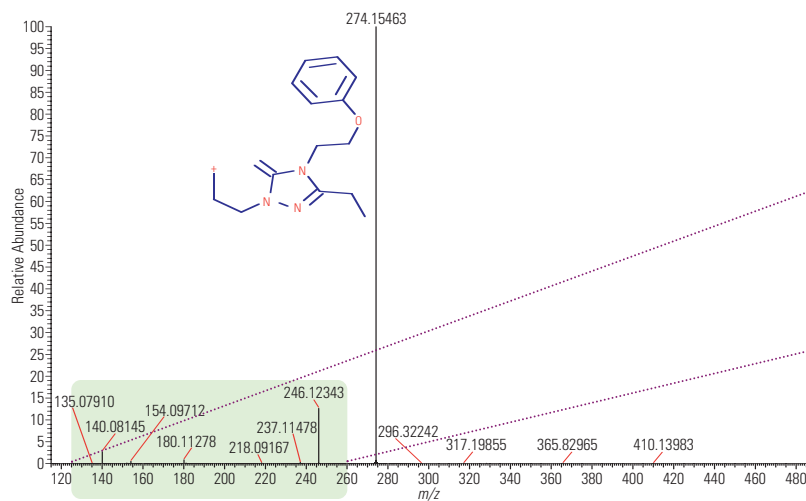
On-line accurate mass LC/MS and MSⁿ measurements provide key results for the unambiguous identification of metabolites. Selectivity and specificity in the search of metabolites are supported by software filters utilizing accurate mass defects and isotope ratios.

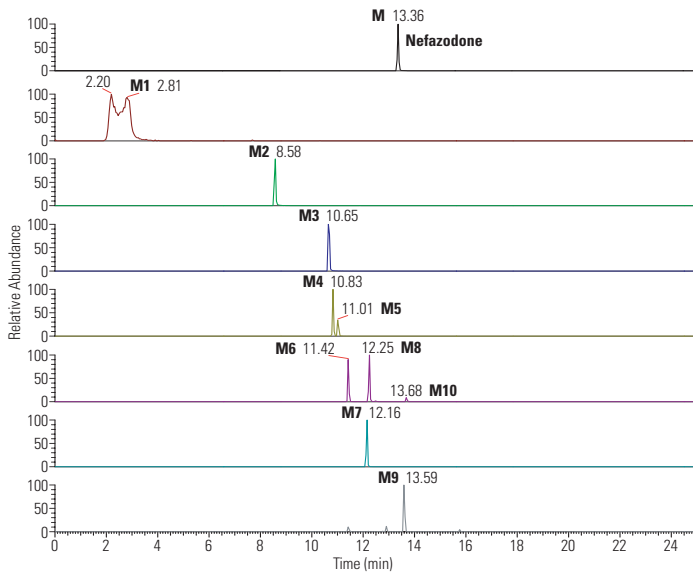
EXAMPLE: NEFAZODONE METABOLISM

- On-line LC/MS and MSⁿ
- High resolution and accurate mass for precursor and product ions
- Data Dependent acquisition mode
- Mass Frontier software for structural identification
- Accurate mass for structural confirmation



$C_{25}H_{32}N_5O_2$ $[M+H]^+ = 470.23173$

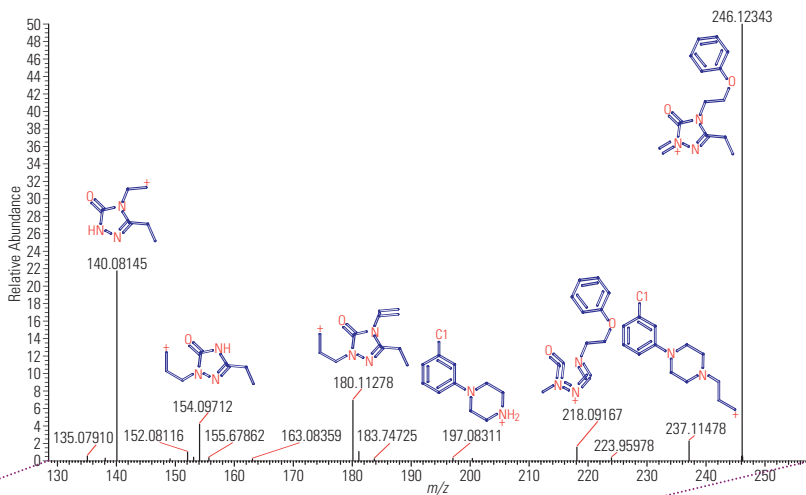




Mass chromatogram of Nefazodone and 10 metabolites measured from a 10 μ mol incubation experiment

Metabolite	Retention Time [min]	Theoretical Mass	Experimental Mass	Mass Error [ppm]
M	13.36	470.23173	470.23169	-0.08
M1	2.81	213.07892	213.07878	-0.65
M2	8.58	197.08400	197.08405	0.25
M3	10.65	292.16557	292.16580	0.78
M4	10.83	306.14483	306.14502	0.62
M5	11.01	306.14483	306.14526	1.40
M6	11.42	486.22664	486.22635	-0.59
M7	12.16	458.19534	458.19479	-1.20
M8	12.25	486.22664	486.22632	-0.65
M9	13.59	484.21099	484.21054	-0.92
M10	13.68	486.22664	486.22659	-0.10

Identified metabolites with their theoretical masses, experimental masses, and the observed mass error



Full scan and expanded mass range for the Nefazodone product ion spectrum

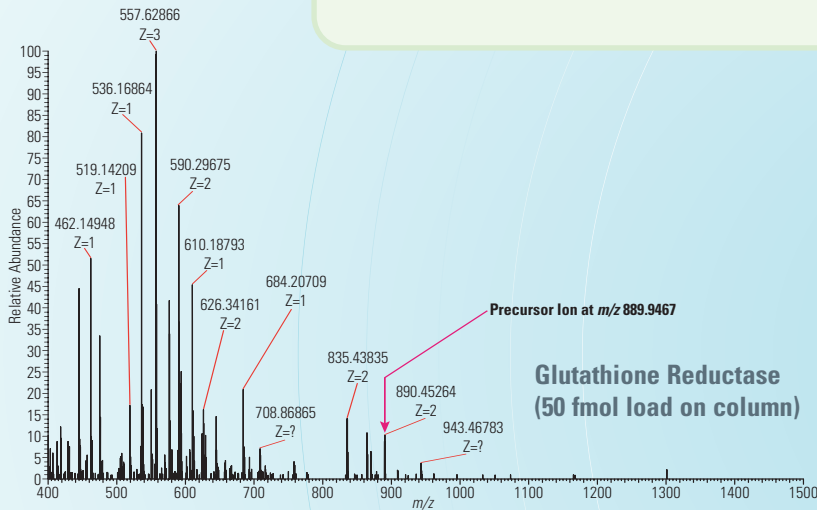
NOTE:
ALL MEASUREMENTS
WERE PERFORMED
USING EXTERNAL
CALIBRATION

EXCELLENT COVERAGE FOR CONFIDENT PROTEIN IDENTIFICATION

FIVE PROTEIN MIXTURE (DYNAMIC RANGE OF 10,000):

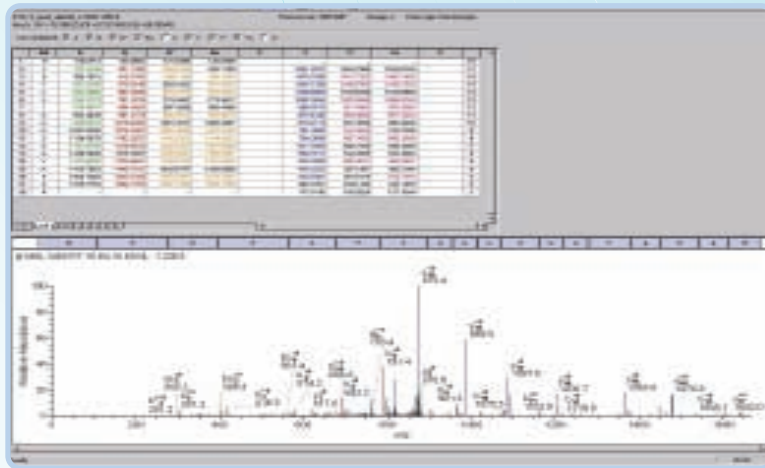
Alcohol Dehydrogenase	5 pmol
Enolase	500 fmol
Glutathione Reductase	50 fmol
Hexokinase	5 fmol
Phosphoglucose Isomerase	500 amol

- On-line nano-LC/MS and MS/MS
- Rapid duty cycle with parallel detection
- Improved probability scoring using BioWorks™



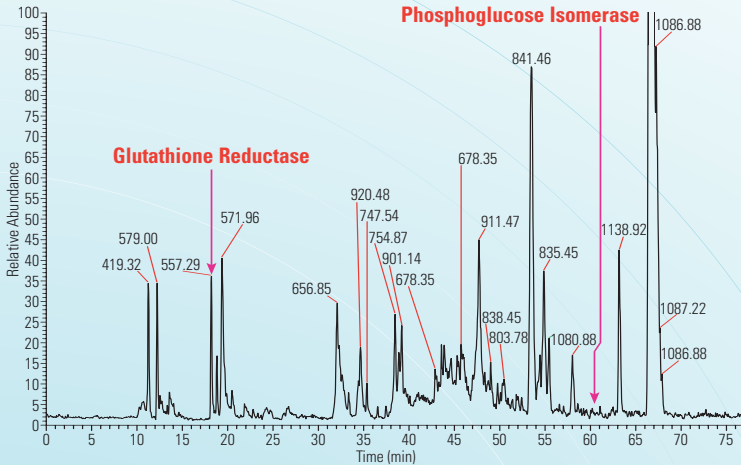
LTQ Orbitrap high resolution ($R = 60,000$ at m/z 400) full scan at RT 18 min

LTQ Or
+
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PK#	MS/MS	Sequence	IC	MCn	Sp	Wto	Items	Count	qf	Database
1	1.718.0242	...RHFDVLPDGGDQVWVWAL	6.508	8.008	2008.3	1	30.93	1	1.00	glutathione reductase
2	1.718.0242	...KIDPCPTIHWKGLFFK	2.008	8.008	468.4	3	17.08	3	0.72	glutathione reductase
3	1.718.0242	...DEKPTLGGKLLK	1.197	8.189	607.1	3	26.83	11.26	0.12	glutathione reductase
4	1.718.0242	...KSDHPVLSVDSVANK	1.111	8.114	328.8	8	18.83	3.40	0.13	glutathione reductase

BioWorks results of the database search showing Glutathione Reductase as first hit



Base peak chromatogram of the enzymatically digested protein mixture

EXPERIMENTAL METHOD:

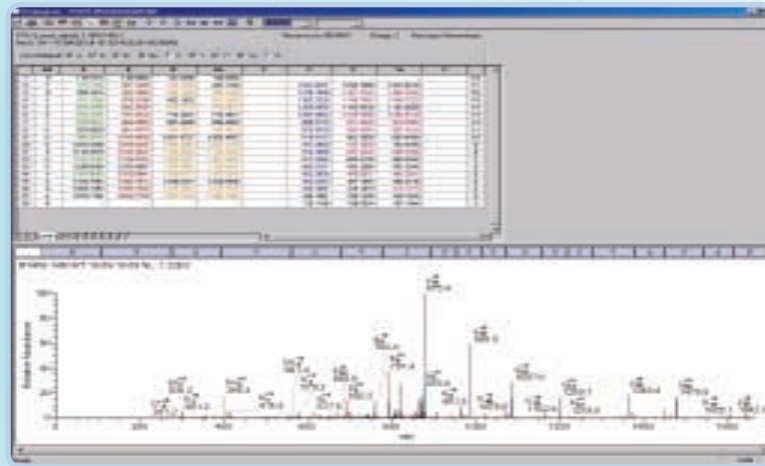
- LTQ Orbitrap full scan at 60,000 resolution
- Six Data Dependent ion trap MS/MS scans
- Dynamic Exclusion
- 60 minute gradient
- BioWorks database search against Yeast

The analyses of complex protein digests is one of the most challenging applications in mass spectrometry.

Important capabilities for successful protein identification:

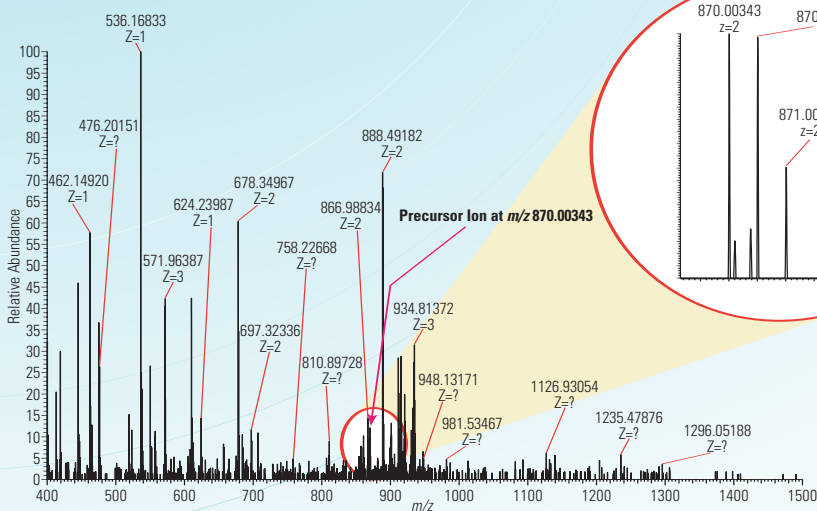
- High resolution accurate mass measurement
- Wide dynamic range
- External mass calibration

Orbitrap
+
BioWorks
=
Fast Protein
Identification



File	MS/MS	Scan	IC	MS	Sp	File	Scan	IC	MS	Sp	Reference
1	17280040	37	R	PHOSPHOGLUCOSE ISOMERASE	841.46	0.000	2421	1	2746	1.00	[P]PHOSPHOGLUCOSE ISOMERASE
2	17280037	33	R	GLUTATHIONE REDUCTASE	571.96	0.000	2421	1	2746	1.00	[P]GLUTATHIONE REDUCTASE
3	17280036	33	R	GLUTATHIONE REDUCTASE	571.96	0.000	2421	1	2746	1.00	[P]GLUTATHIONE REDUCTASE
4	17280035	33	R	GLUTATHIONE REDUCTASE	571.96	0.000	2421	1	2746	1.00	[P]GLUTATHIONE REDUCTASE

BioWorks results of the database search showing Phosphoglucose Isomerase as first hit



Phosphoglucose Isomerase
(500 attomol load on-column)

LTQ Orbitrap high resolution (R = 60,000 at m/z 400) full scan at RT 61 min

TURNING DATA INTO INFORMATION

Xcalibur™ data system

Stable operating platform

Xcalibur is the versatile, easy-to-use data system that controls all Thermo MS systems. Xcalibur's Home Page offers easy navigation through the process of instrument setup, sequence setup, and data acquisition. The new XReport reporting package simplifies custom reporting with drag-and-drop functionality.

ProteinCalculator

ProteinCalculator performs *in silico* digestion of proteins to produce CID or ECD fragments. Specify peptide sequences or import them from a fasta database, select post-translational modifications from a list or edit novel PTMs, then digest them with an enzyme of your choosing. The proteolytic fragment spectra can be saved as RAW data files for comparison with acquired spectra.

Xtract

Xtract deconvolutes isotopically resolved data, simplifying complex MS/MS spectra acquired in top-down, intact protein analysis. Specify the mass range, mass resolution, and S/N criteria for deconvolution and display in one of four modes: monoisotopic masses, isotopic pattern, or approved or disapproved signals. The results can be exported as RAW or ASCII file formats.

BioWorks protein identification software

Confident protein ID featuring the SEQUEST® algorithm

BioWorks utilizes the SEQUEST search algorithm to automatically identify proteins by comparing experimental tandem mass spectrometry (MS/MS) data with spectra created from standard protein and DNA databases.

Mass Frontier spectral elucidation software

Turning mass spectral data into results

Mass Frontier contains a state-of-the-art database and predictive fragmentation module which allows you to easily interrogate and assign the structure of your compounds.

Metabolite ID™ drug metabolism software

Simplify the interpretation of complex metabolism data

Metabolite ID simultaneously searches multiple modifications of one or more parent drugs and interprets simple to complex isotope patterns, or unexpected or low abundance metabolites.

Installation Requirements

Power

230 Vac ±10% 3 phase, 16 Amps, 50/60 Hz, with earth ground for the instrument

120 or 230 Vac single phase with earth ground for the data system

Gas

One high purity (99.5% pure, flow rate 15 L/min) nitrogen gas supply for the API source

One ultra high-purity helium gas supply (99.998%) with less than 1 ppm each of water, oxygen, and total hydrocarbons for the linear ion trap

Environment

System averages 2800 W (10,000 Btu/hr) output when considering air conditioning needs

Operating environment must be 15-27°C (59-80°F) and relative humidity must be 40-80% with no condensation

Optimum operating temperature is 18-21°C (65-70°F)

Weight

~590 kg

Dimensions

141.4 × 87 × 146.3 cm
(H × W × D)

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