LRQ 4005852/B

Founded in 1875, Shimadzu Corporation, a leader in the development of advanced technologies, has a distinguished history of innovation built on the foundation of contributing to society through science and technology. We maintain a global network of sales, service, technical support and applications centers on six continents, and have established long-term relationships with a host of highly trained distributors located in over 100 countries. For information about Shimadzu, and to contact your local office, please visit our Web site at **www.shimadzu.com**

SHIMADZU

Kratos Analytical Ltd.
Wharfside, Trafford Wharf Road, Manchester M17 1GP, UK
Phone: +44 161 888 4400 Fax: +44 161 888 4402
URL http://www.shimadzu.com/an/

SHIMADZU
Excellence in Science

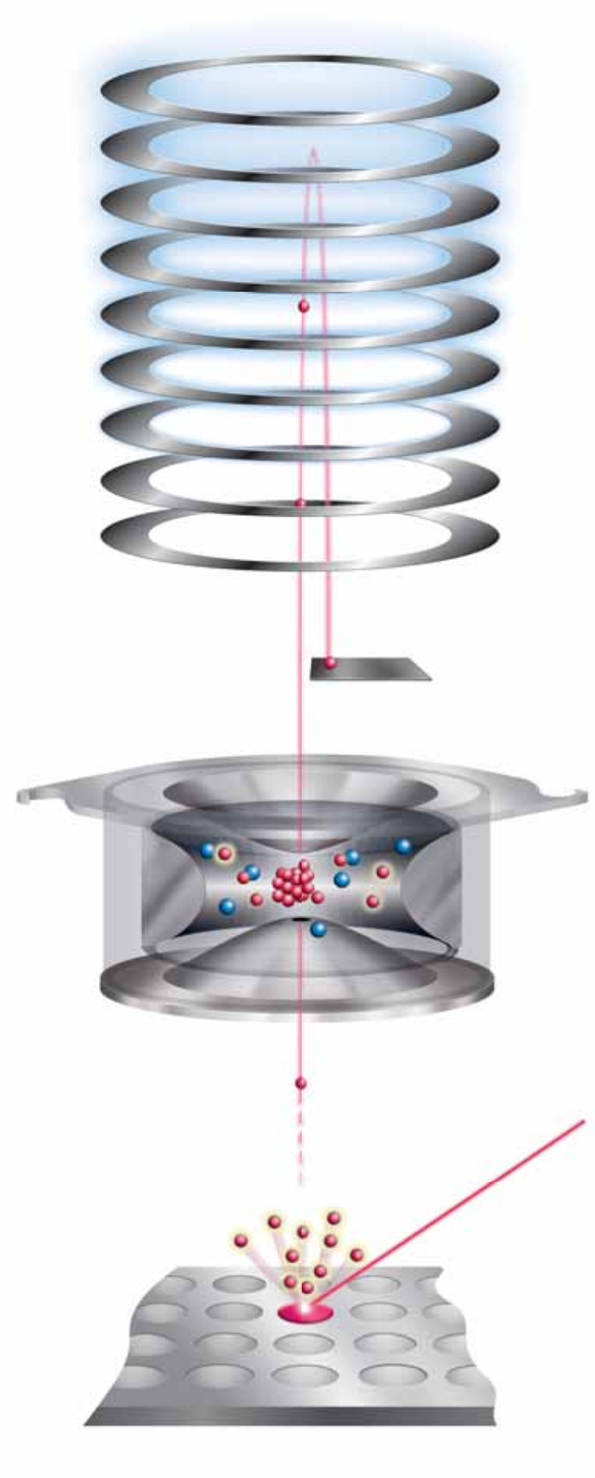
MO335

A Unique Mass Analyzer

AXIMA Resonance™

A unique MALDI QIT TOF MS designed for the structural characterization and sequencing of biomolecules - not just mass measurement.

- Quadrupole ion trap - True MS^n for structural studies
- Variable energy CID control on the fly
- High resolution precursor ion selection – up to 1000 FWHM
- High mass resolution and mass accuracy across MS and MS^n analyses
- Outstanding sensitivity - uncompromised design, to ensure highly efficient trapping functionality
- Low sample consumption- allowing many more MS^n experiments to be performed on the same sample spot
- Variable repetition rate N_2 laser
- Manual or fully automated operation allowing the seamless analysis of few or many samples as required



Essential features providing confident results

This next generation unique design MALDI system delivers all of the features expected of an AXIMA™ series mass spectrometer;

- High resolution MS data in for more accurate and confident peptide mass fingerprinting (PMF) and complex mixture analysis.
- Near-axis laser irradiation for enhanced ion transmission and sensitivity in all modes of operation.
- Advanced calibration algorithm with easy to use software providing more accurate data
- Stable simple calibration for accurate data and ease of use.
- Intuitive software incorporating data dependent workflows for achieving the maximum result with the minimum user input, making it ideal for novice and expert users alike.
- Suitable for use with most common MALDI matrices
- Flexibility – this is not just another proteomics workhorse. Polymers, oligonucleotides, SNPs, metabolites, carbohydrates and small molecules amongst others may all be analyzed and processed.

High performance with an innovative design

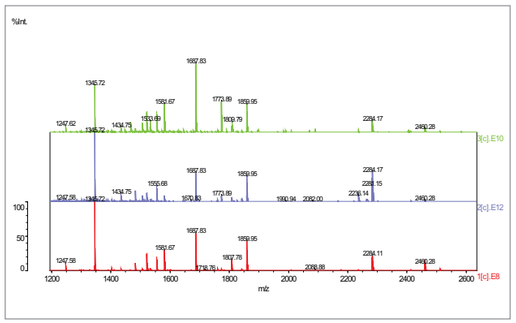
Advanced MS^n performance

The unique characteristics of the instrument allow controlled, flexible and complete searchable fragmentation for target identification and characterization.

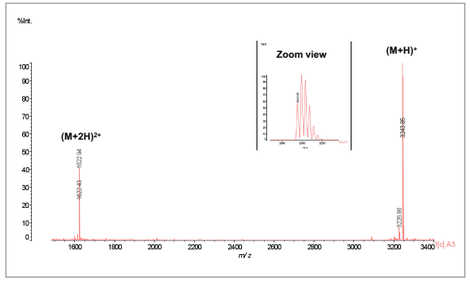
The unique combination of MALDI and quadrupole ion trap allows:

- generation of ions using a number of different matrices
- positive and negative ionization modes, switchable via software in seconds
- simple high resolution precursor ion selection for MS^n experiments
- controllable MSn fragmentation using argon as the collision gas
- high sensitivity allowing multiple MS^n acquisitions on the same sample spot through low sample consumption.

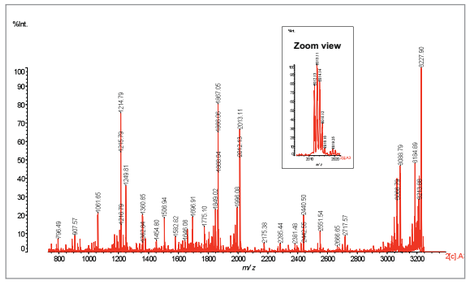
The incorporation of a TOF analyser promotes high resolution and high mass accuracy for all ions generated regardless of their origin – similar mass accuracy can be achieved for MS ions as that for MS^3 ions.



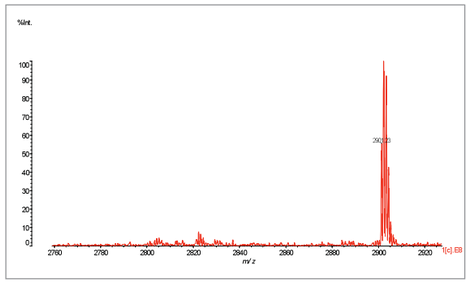
Chicken ovalbumin tryptic digest in a) DHB matrix, b) CI-CHCA matrix, c) CHCA matrix. Very similar peptide mass fingerprints are observed.



Des-Acyl Ghrelin (human), an extremely fragile molecule, in MS mode demonstrating excellent resolution and the presence of the doubly charged ion



MS/MS of Des-Acyl Ghrelin showing high resolution fragment ions (inset)



Phosphopeptide from an ovalbumin tryptic digest showing no metastable fragmentation or neutral loss of the phosphate moeity

Peptide mass fingerprinting Mascot search results for chicken ovalbumin tryptic digest. Excellent mass accuracy and extensive sequence coverage is routinely achieved.

Compatibility with other MALDI mass spectrometers

Samples may be screened in a high throughput manner using an Axima Confidence™ or Performance™ (or any other MALDI mass spectrometer using a microtitre plate target format or via an adaptor) and ions of particular interest, perhaps a post translationally modified peptide or glycan, may be interrogated further using the Axima Resonance™.

A practical and ergonomic package

The compact floor-standing geometry is designed to maximize laboratory space and allow easy installation and servicing. The system is delivered ready to install requiring no assembly on site.

As with all AXIMA™ series systems, a variety of industry standard microtitre plate format MALDI targets are used for convenience and simple experiment planning and tracking. This allows seamless integration with a variety of robotic sample handling systems including the CHIP™ and Accuspot™.

In addition, microscope slide design targets may also be used in conjunction with an adaptor, allowing lower throughput or multi user laboratories an economical alternative to the MTP format.

MS^n – using multiple fragmentation stages for structural elucidation

High performance MS/MS mode:

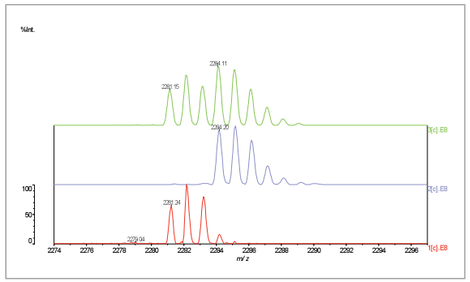
The combination of a QIT and high performance reflectron allows superior resolution and excellent sensitivity MS/MS spectra. The AXIMA Resonance™ permits MS/MS spectra of a wide range of analytes from pharmaceutical compounds, through peptides, glycans, lipids and polymers.

MS/MS can be performed on singly charged precursor ions as high as 6-7 kDa.

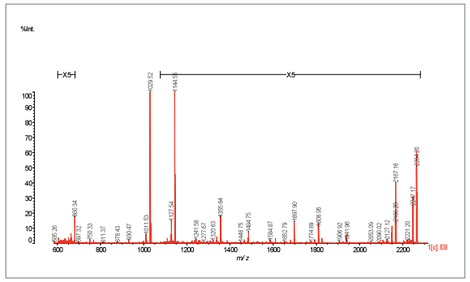
Excellent precursor ion selection:

The excellent precursor ion selection available on the Axima Resonance™ allows ions from complex mixtures or closely associated neighboring isotopic envelopes to be easily isolated and subsequently fragmented.

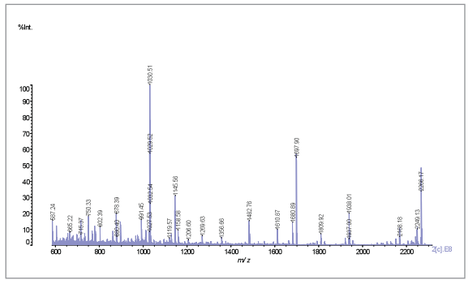
The trapping resolution of greater than 1,000 (FWHM) readily permits the analysis of samples with similar nominal mass, even with overlapping isotopic distributions.



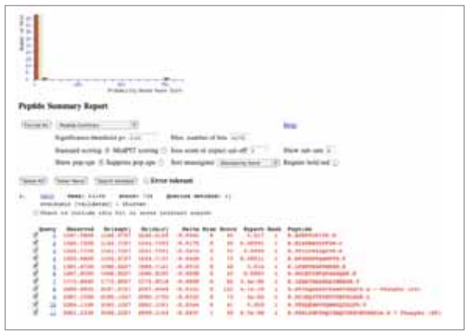
Isolation of two individual peptides from a chicken ovalbumin tryptic digest. The green trace shows the complex mixture with overlapping isotopic patterns and the red and blue traces demonstrate the high resolution precursor selection achieved using the ion trap to isolate both peptides.



MS/MS of m/z 2284 following isolation from the complex mixture of peptides



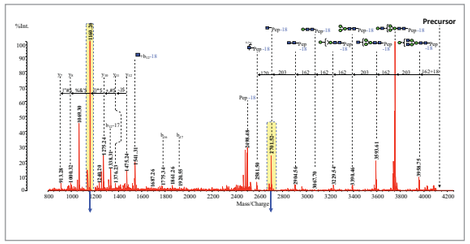
MS/MS of m/z 2281 following isolation from the complex mixture of peptides



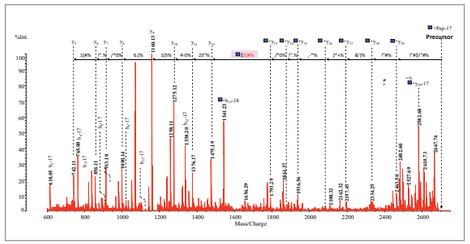
MS/MS search results for chicken ovalbumin tryptic digest

603-QQQHLFGSNVTDCSGNFCLFR-623 *m/z* 4136

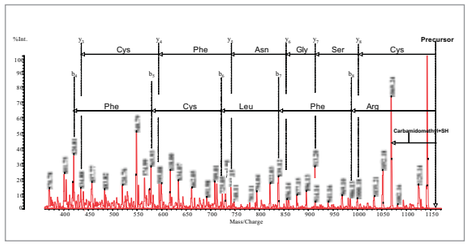
Structure of human transferrin glycopeptide (already having lost two sialic acid residues)



Positive ion mode MS/MS spectrum of human transferrin glycopeptide showing the sequential dissociation of the glycan structure following the loss of two sialic acid residues



Positive ion mode MS^3 spectrum of human transferrin glycopeptide (precursor mass m/z 2701) demonstrating the identification of the glycosylation site



Positive ion mode MS^3 spectrum of human transferrin glycopeptide (precursor mass m/z 1160) demonstrating the complete amino acid sequence of the peptide

Ultimate MS^n for flexible fragmentation:

Once selected for fragmentation, precursor ions are subjected to collision induced dissociation using argon as the collision gas, whilst user defined collision energies are allowed and may be varied on the fly.

Complete fragmentation is performed in the QIT. Ions are subsequently extracted to the flight tube incorporating a reflectron and detected by a high performance microchannel plate detector.

The QIT allows sequential dissociation of an ion via MS^n experiments. This is particularly useful when analysing post translational modifications where MS^2 is often not sufficient to determine both the nature and the location of the modification. Similarly, the composition of a glycan may be derived using MS^n, detailing branched structures and cross ring cleavages to allow full interpretation of the structure.

Software tools to empower researchers and aid investigation

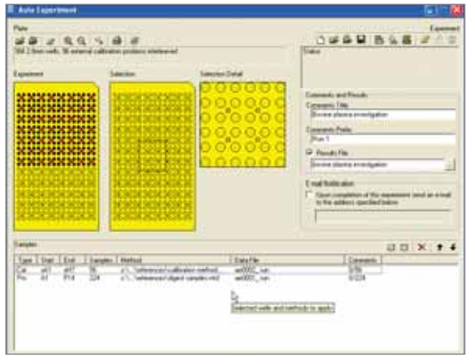
The Axima Resonance™ is complemented by a suite of software tools allowing many different types of analyses to be performed.

- Fully enabled for proteomics experiments – Intellimarque™ software suite for automated data dependent peptide mass fingerprinting and MS/MS of peptides with optional incorporated Mascot database searching
- LC-MALDI software allowing confident identification of off-line separated complex mixtures via automated MS^n
- Tissue imaging suite – allows full integration with the CHIP™ tissue sample preparation device, automated acquisition of data and interrogation using proprietary visualization software or automated export to BioMap
- Compatible with PEAKS de novo sequencing package
- Post translational modification investigation using the innovative PTM Finder™ software – empowers the researcher, allowing data mining to determine previously undetected peptide modifications

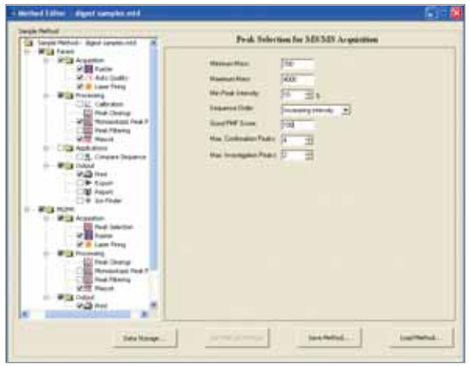
* Separate Mascot® server required

Intellimarque™ proteomics software suite

Fully automated protein identification experiments may be performed using Intellimarque software. Peptide mass fingerprinting with integrated Mascot searching can be followed by data dependent MS/MS acquisition and searching for confident protein assignment.*



Intellimarque™ Auto Experiment software – define the calibrants, samples, methods and results file



Intellimarque™ Method Editor software – define the method including acquisition and processing parameters, MS/MS peak selection criteria and Mascot search details

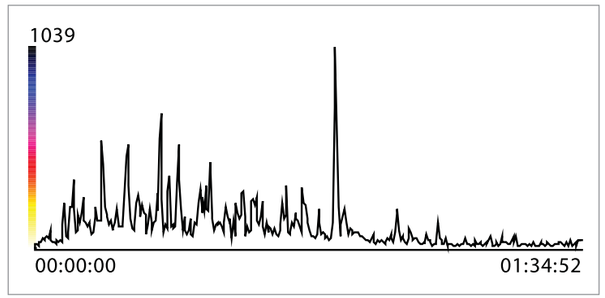
LC MALDI tools

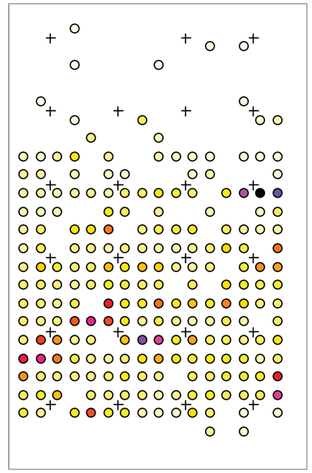
LC MALDI experiments may also be easily performed using our proprietary software and full integration with robotic sample deposition devices, for example, the Accuspot™

The software suite allows the fully automated acquisition of LC separated samples deposited onto MALDI targets ad the subsequent identification of proteins via MS/MS of the peptides detected.

The workflow automatically provides a provisional intensity map of all sample spots across the target to assess the distribution of peptides and identify the position of the apex of the chromatographic peaks. These are utilized to generate a candidate list and MS/MS data acquired for all discrete peptide ions. Exclusion lists are used to remove known contaminants or high abundance peptides.

MS/MS is automatically performed and the resultant peak lists are batch searched using the integrated Mascot database search engine*. Low sample consumption allows multiple spectra to be acquired from the same spot increasing the amount of MS/MS data obtained.





LC MALDI tools – a heat map is produced of peptide candidates for MS/MS distributed throughout the target along with a reconstructed ion chromatogram

Post translational modification analysis – PTM Finder™

AXIMA Resonance™ provides total support for many types of PTM analysis using the PTM Finder™ software suite of tools – software that facilitates the user's workflow when dealing with MS/MS data sets.

Phosphorylation, glycosylation, oxidation, methylation and acetylation amongst others can be characterized.

An MS/MS data set is interrogated for the presence of user defined post translational modifications following an initial Mascot search:-

- Peptides that are unmatched in this first pass are subjected to a second search using different search parameters.
- The remaining set of unidentified fragment ion spectra are subsequently interrogated for PTM's.
- Labile PTM's (for example, phosphorylated peptides) are detected via their characteristic neutral losses in MS and MS/MS spectra
- PTM's created by "shifts" (for example, acetylation adds +42 Da) are discovered by comparing 2 MS/MS Datasets and looking for similarities and/or differences

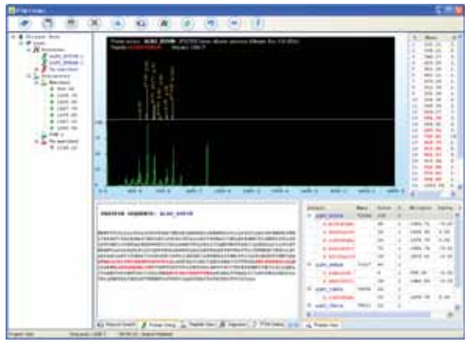
The user can also define specific modifications that can be used to search the acquired MS/MS spectra to unearth modified peptides not flagged in standard Mascot searches. Sequence coverage is improved and new modifications discovered.

System support

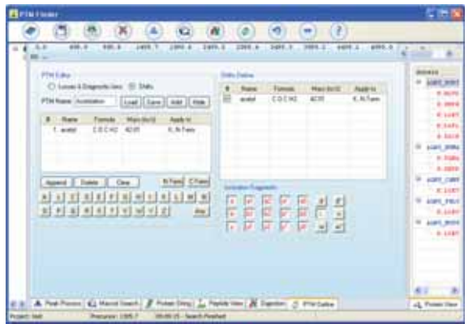
All Axima systems can be fully supported throughout their lifetime using sophisticated web based service diagnostics and real time remote monitoring.

Highly trained specialist local service support engineers are available to install and maintain Axima mass spectrometers. A wide range of service contracts are available, catering for all budgets and requirements, including IQ/OQ environments.

Full training courses are offered by MALDI experts at our regional corporate training centers or at the customer site and may be tailored for specific requirements and applications.



PTM Finder™ - discover post translational modifications within a set of MS/MS data



PTM Finder™ - define post translational modifications that may be used to interrogate the data set.

PTM Finder™ - create a list of modifications to search for

NB. PTM Finder™ software will be available May 2009

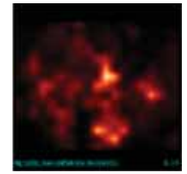
Integrated MALDI imaging made simple

Discover a completely integrated workflow designed to take the guess work out of tissue imaging. Reproducible automated matrix delivery directly to the sample surface is achieved using the CHIP™.

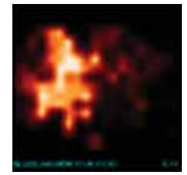
The CHIP allows deposition of discrete droplets minimizing diffusion and maintaining localization of components within the tissue. Seamless export of sample location to the Axima Resonance™ MALDI mass spectrometer and automated data acquisition routines are easily performed using the CHIP Imaging Experiment wizard driven software module. Profiling or imaging experiments are routinely executed.

Visualization of the spatial distribution of components of interest is demonstrated via proprietary intensity mapping software allowing the user to interrogate the data for compounds of interest. Easy automated export of data to alternative processing packages, including BioMAP, is also included.

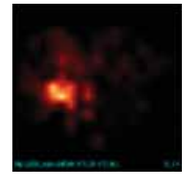
824.60 Da



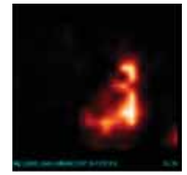
1112.44 Da



1172.50 Da



1237.50 Da



Typical heat maps generated following a tissue imaging experiment on the Axima Resonance