

To identify components in your sample, do you need to:

- Determine elemental composition?
- Elucidate structural characteristics?
- *De novo* sequence peptides with the highest confidence?
- Eliminate false positive protein identifications?
- Identify components in complex matrices?
- Distinguish between nominally isobaric amino acids?

Combined accuracy and sensitivity

Whether you want to identify and characterize proteins or perform structural elucidation of small molecules, exact mass measurement is as important as having the sensitivity to detect them. The Waters® Micromass® Q-ToF micro™ Mass Spectrometer enables you to combine sensitive LC/MS/MS with simple, automated exact mass measurement, increasing confidence in your results. The high quality data delivered by the Q-ToF micro can provide information on elemental composition, structural characteristics and excellent specificity for identifying your compounds in complex matrices.



This benchtop, total solution integrates the Micromass® Q-ToF micro™ Mass Spectrometer with NanoLockSpray™ and the Waters CapLC® Pump and Autosampler using MassLynx™ 4.0 Software.

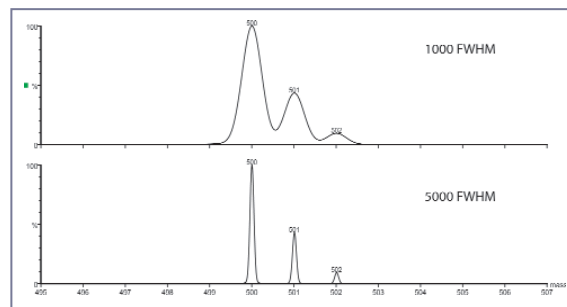
Why exact mass?

So, do you really know the mass of your compound? Are you confident that you've identified the correct component? As with every analytical tool, the more accurately you make your measurement the more confidence you'll have in your results. Exact mass measurement enables you to determine the elemental composition of compounds with greater confidence. When you detect a drug metabolite at 500.2 m/z in an *in vivo* sample, are you sure which bio-transformation has taken place? When you detect a peptide at 976.6 m/z, can you be sure which post-translational modification is present?

With exact mass measurement you can:

- Determine elemental composition
- Distinguish nominally isobaric components
- Improve specificity of detection for MS/MS analyses
- Improve data processing speed and specificity

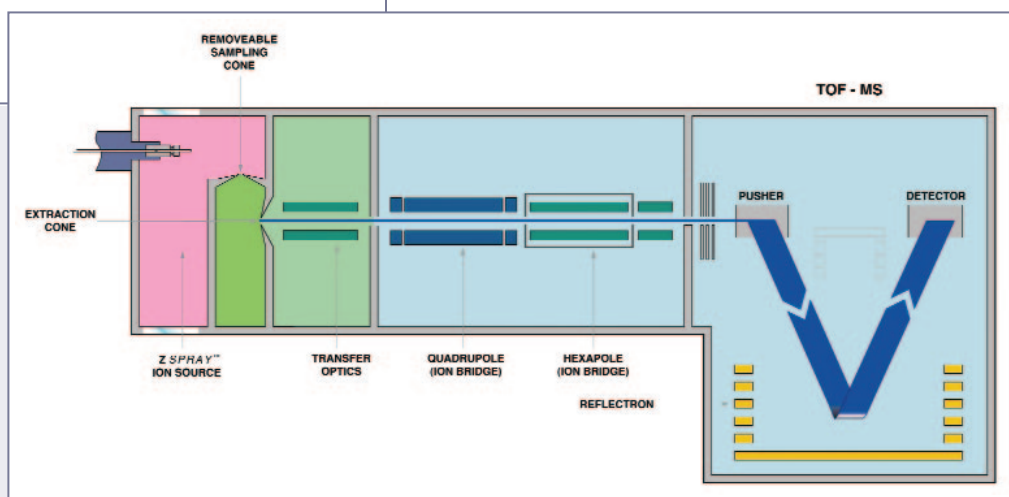
The inherent high resolution and mass accuracy of an orthogonal time-of-flight (oa-ToF) mass spectrometer minimizes co-eluting and matrix interferences, enabling components of interest to be resolved. Automated exact mass measurements can then be performed "on the fly".



The resolution of the Q-ToF micro is shown relative to the typical unit resolution used for full scan LC/MS analyses on a quadrupole or ion trap mass analyzer. The higher resolution of the ToF analyzer across the full m/z range, in conjunction with exact mass measurement, enables unknowns to be more easily identified without losing precious information due to scan speed restrictions.

The Waters Micromass Q-ToF micro Mass Spectrometer

The Micromass Q-ToF micro is a high resolution oa-ToF mass spectrometer that enables automated exact mass measurements in an easy-to-use benchtop instrument. The instrument also features a quadrupole mass filter and collision cell for MS/MS analyses. This powerful combination delivers simple exact mass measurement of fragment ions to yield increased confidence in structural elucidation and databank search results.



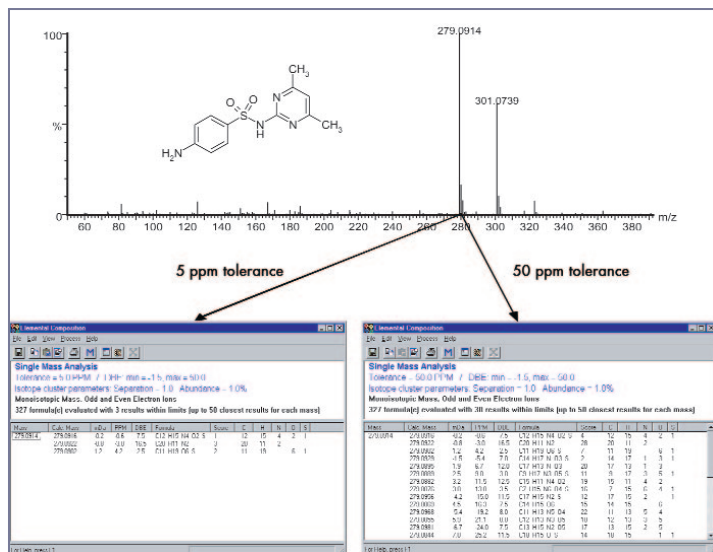
Waters Micromass Q-ToF micro technology

Why exact mass MS/MS?

Exact mass measurement becomes an increasingly powerful tool for determining elemental composition at lower m/z values, and is therefore particularly useful for identification of fragment ions in MS/MS. With the increased accuracy of exact mass measurement, peptide sequencing and the elucidation of small molecule structures is significantly enhanced. Data processing tools for automated interpretation rely heavily on the specificity of exact mass measurements.

With exact mass MS/MS you can:

- Eliminate false positive protein ID's apparent in nominal mass data
- *De novo* sequence peptides with the highest level of confidence
- Identify elemental composition of structural fragments
- Gain excellent specificity for quantitative analyses



Peptide sequence from BSA	LockSpray™ corrected data (MassSeq™ 10ppm tolerance)	Nominal mass data (MassSeq™ 100ppm)
FKDLGEEHFK	FKDLGEEHFK	FKDLGEE RK K
LCVLHEKTPVSEK	LCVLHEKTPVSEK	LCVL RLLLRID
CCTESLVNR	CCTESLVNR	CCTESL KKL
KVPGVSTPTLVEVSR	KVPGVSTPTLVEVSR	KVPGVSTPTLVEVSR
LVNELTEFAK	LVNELTEFAK	LVNEL HTPK
GFQNALLVR	GFQNALLVR	No result
YLYELAR	YLYELAR	YLYELAR

Green: Confident assignment
 Red: Incorrect assignment
 Yellow: Ambiguous assignment

De novo sequencing of peptides is significantly enhanced through the specificity of exact mass MS/MS. The table demonstrates how greater confidence in sequence assignment is achieved with improved mass accuracy. Results are shown for a digest of Bovine Serum Albumin using ProteinLynx™ Global SERVER 2.0 Software.

Exact mass MS measurement enables compounds to be more easily identified. Confirming a measured m/z to within 5 ppm significantly increases confidence in assigning elemental composition.

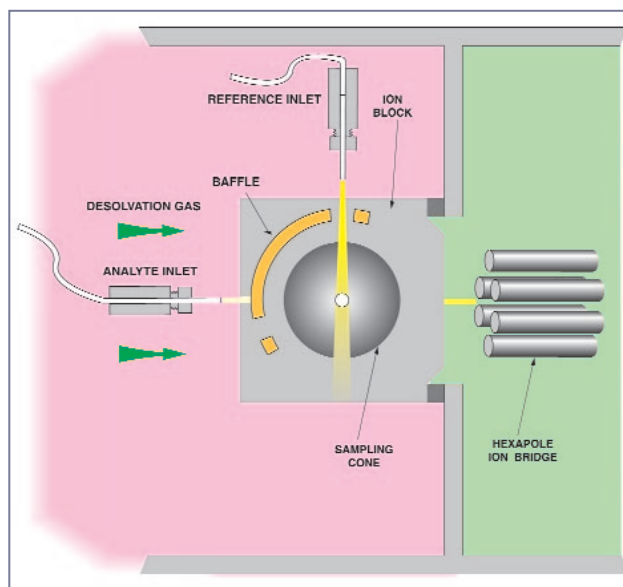
“...for materials with molecular weights below 1000, the measured mass should generally agree to 5ppm or better, with the calculated mass.” Notice to Authors of Papers: *J. Am. Chem. Soc.*, 1999 121(1), 7A 12A

A powerful technology platform

The Q-ToF micro provides a powerful platform for MS and MS/MS analyses, upon which total system solutions may be designed to maximize data quality for your application.

The Q-ToF micro Mass Spectrometer offers:

- A small footprint—powerful Q-ToF technology on your benchtop
- ZSpray™—dual orthogonal source technology for unsurpassed sensitivity and ruggedness
- High resolution—5000 FWHM for resolving nominally isobaric ions
- Exact mass measurement—sub 5 ppm RMS in both MS and MS/MS modes
- Extended linear dynamic range for quantitative analysis
- oa-ToF analyzer—wide acquisition range of up to 20,000 m/z
- Data Directed Analysis (DDA™)—intelligent detection of compounds of interest for automated switching from MS to MS/MS
- Precursor Ion Discovery—patented acquisition techniques for class-specific analyses (i.e. detection of specific structural motifs) using exact neutral loss or product ion detection
- Variable Flow Chromatography—with the Waters CapLC® System for enhanced MS/MS data quality
- Ease of use—wizard-driven system configuration and method editing for simplified operation



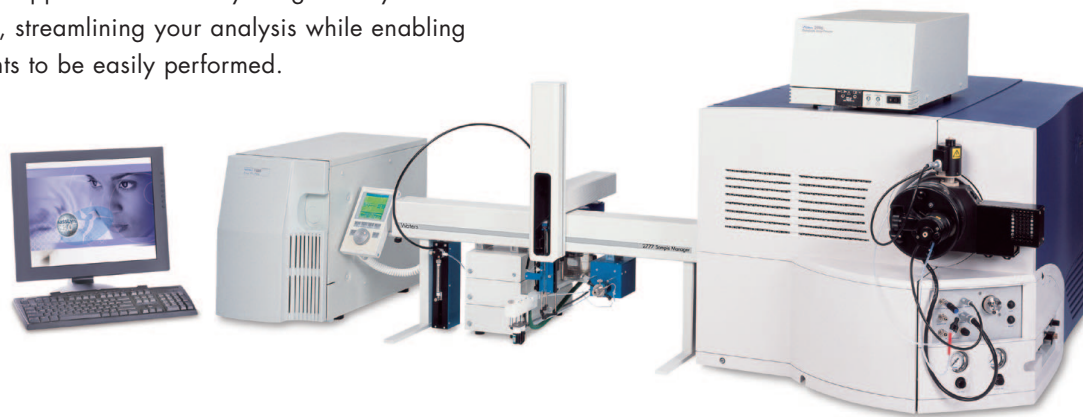
Exact mass MS/MS is achieved automatically using the Q-ToF's LockSpray™ dual electro spray source.

The LockSpray dual electro spray source enables automated exact mass measurement with an infused internal lockmass from a second sprayer, eliminating the need for T-plumbing and potential ionization interference between analytes and standard.

The NanoLockSpray dual electro spray source is optimized for exact mass data acquisition with nanoflow LC/MS/MS and is ideal for proteomics studies or low level metabolite identification.

Systematic productivity

Whether you are characterizing peptides and proteins, or identifying small molecules, such as metabolites or impurities, in complex matrices, Waters Mass Spectrometry Systems incorporating the Q-ToF micro maximize performance for your application. The fully integrated systems are controlled from a single data system, streamlining your analysis while enabling advanced experiments to be easily performed.



The Waters Mass Spectrometry System for Metabolite Identification integrates the Waters 1525 μ Binary HPLC Pump, 2777 Sample Manager, 2996 Photodiode Array Detector, Q-ToF micro with LockSpray, all controlled by MassLynx™ 4.0 Software with the Metabolynx™ Application Manager.

Protein Characterization

- Comprehensive chromatographic capabilities for complex mixture separation
- Exact mass MS and MS/MS for the highest confidence in databank searching and *de novo* sequencing
- Exact mass precursor ion discovery for confident detection and characterization of modified peptides
- Automated protein identification and characterization with MS-WorkFlow—ProteinLynx Global SERVER 2.0
- Determination of intact protein complexes with Maximum Entropy processing

Metabolite/Impurity Identification

- Sensitive full spectral acquisition for detection of predicted and unexpected components
- Exact mass MS and MS/MS for structural comparison with parent drug
- Metabolynx Application Manager for intelligent exclusion of endogenous components and automated processing of exact mass MS and MS/MS from a single analysis

Metabonomics

- Sensitive full scan MS for detection of low level endogenous metabolites
- Exact mass MS and MS/MS for accurate identification
- High quality liquid chromatography for efficient separation and high retention time reproducibility
- High quality LC/MS data for efficient statistical analysis of the samples

Natural Product Identification

- Sensitive full scan MS for detection of multiple components
- Exact mass MS and MS/MS for accurate identification
- Integrated high throughput LC with environmental control for samples
- Automated exact mass data processing

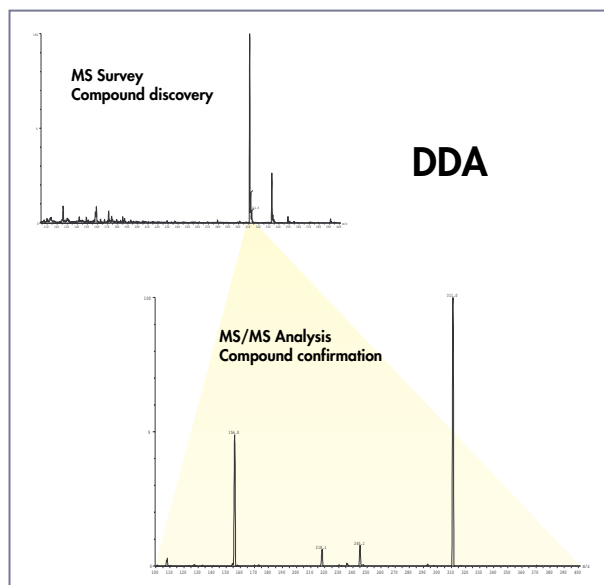
Intelligent LC/MS/MS

With both throughput and sample volume restrictions on many analyses, it is increasingly important to maximize the amount of real information that can be extracted from a single experiment. Integrating your Waters chromatography and MS instrumentation into an intelligent mass spectrometry system with MassLynx Software enables maximum sensitivity and selectivity for your components of interest.

Intelligent Data Directed Analysis (DDA)

DDA enables intelligent MS and MS/MS analyses to be performed automatically, maximizing the amount of real information acquired on components of interest. Using the easy-to-use DDA Wizard, your analysis can be targeted for detection of analytes based on charge state recognition, exact mass and peak intensity. Exclude lists can also be employed to avoid redundant analyses. Detection in the MS Survey mode triggers a switch to MS/MS where exact mass data are quickly acquired on structural fragments.

Advanced Application Managers such as ProteinLynx Global SERVER 2.0 and MetaboLynx have been designed for rapid processing of DDA data, increasing the efficiency of both your analysis and results reporting.

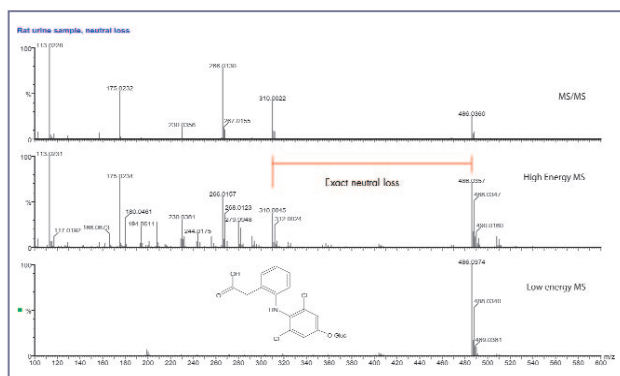


Intelligent MS and MS/MS data acquisition in a single run using Data Directed Analysis (DDA).

Precursor ion discovery (PID)

DDA can be used to automate precursor ion discovery. The Q-ToF micro employs a novel acquisition mode that enables highly selective detection of an exact neutral loss (e.g. from phosphopeptides) or product ion (e.g. glycans) to trigger MS/MS on components of the related precursor ion.

By cycling collision energy between high and low modes in MS survey, the software can very accurately detect targeted product ions or neutral losses. Identification of these triggers selection of the precursor for true MS/MS.



Exact neutral loss of the glucuronide conjugate (176.0321 Da) from a Phase II metabolite is detected in MS mode by cycling collision energy. The identified precursor is subsequently selected for MS/MS analysis.

Advanced chromatography integration

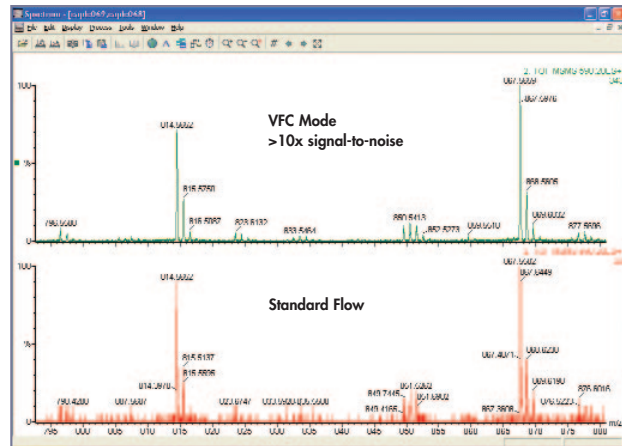
The integration of Waters LC and MS instruments through a single data system enables a simplification of operation, while also creating a platform for more advanced experiments. By using exact mass MS detection, analyses can be automatically directed in real time based on pre-defined criteria.

Maximizing efficiency and sensitivity

Capillary LC, utilizing the Waters CapLC System, benefits from very efficient chromatographic peaks, enabling complex mixtures to be resolved and more specific MS and MS/MS data to be obtained. An additional benefit is the inherent increase in sensitivity provided by the CapLC due to concentration effects, yielding much more sensitive MS detection.

Variable flow chromatography (VFC)

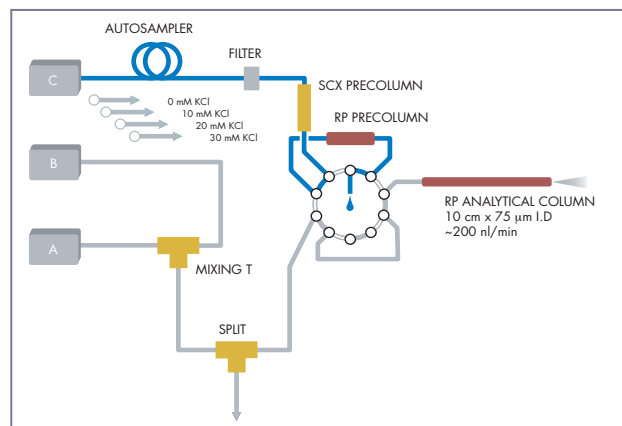
Variable flow chromatography can automatically reduce the flow rate of the CapLC upon detection of a specified ion by the Q-ToF micro Mass Spectrometer. This can be of particular use in a precursor ion discovery experiment, increasing the length of MS/MS acquisition time available for the analysis of targeted precursor ions.



Phosphopeptide analysis by PID on the Q-ToF micro. VFC allows MS/MS data to be acquired from the targeted ion for 3 minutes (compared to only 30 seconds at standard flow rate), resulting in increased structural information and a >10x improvement in signal-to-noise.

2D LC

Multi-dimensional chromatography can also be driven through the Waters Mass Spectrometry System that features the CapLC and Q-ToF micro. The ability to resolve components across different column chemistries is particularly useful for complex mixture analysis. The Stream Select Module can be easily configured to include an additional ion exchange column, enabling complex peptide mixtures to be resolved based on charge prior to their separation on a reversed phase analytical column.



2D LC configured for the CapLC and Q-ToF micro using the Stream Select Module.

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