

**Thermo Scientific Orbitrap Fusion  
Tribid Mass Spectrometer**



**Unmatched analytical performance**  
Revolutionary MS architecture

**Thermo**  
SCIENTIFIC



## Transforming biological research

In the world of systems and structural biology, research objectives continue to become more challenging: digging deeper into the proteome, identifying lower-abundance analytes in more-complex samples, making quantitative comparisons over more experimental conditions, elucidating structures faster. Meeting such challenges is the Thermo Scientific™ Orbitrap Fusion™ mass spectrometer. Its revolutionary Thermo Scientific™ Tribrid™ architecture combines the best of quadrupole, Orbitrap, and linear ion trap mass analyzers in a new class of instrument. Tribrid architecture provides unprecedented depth of analysis, enabling scientists analyzing even the most challenging low-abundance, high-complexity, or difficult samples to identify more compounds faster, quantify more accurately, and elucidate structures more thoroughly. With a simplicity of operation that belies its sophistication, the Orbitrap Fusion MS lets researchers concentrate on their science rather than method development and instrument operation.





### Identify more analytes more quickly

Increased sensitivity, scan rate, and mass resolution enhance the ability to positively identify more low-abundance proteins, such as transcription factors, in less time. Productivity is enhanced through the massive parallelization enabled by Tribrid architecture and Dynamic Scan Management.

### Quantify more accurately

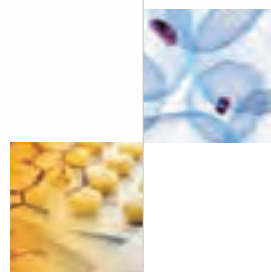
Synchronous Precursor Selection combined with MS<sup>3</sup> significantly improves quantitative accuracy when using isobaric mass tags for relative quantitation of proteins.

### Elucidate structures more thoroughly

The ability to use any fragmentation mode, at any stage of MS<sup>n</sup> analysis, with detection by ion trap or Orbitrap mass analyzer, maximizes structural information from metabolites, glycans, PTMs, and sequence polymorphisms.

### Work more efficiently

Next-generation hardware and software make methods more universal and setup easier. Users can spend more time thinking about their research and less time optimizing their methods.





# Revolutionary Tribrid architecture

Tribrid architecture, with an independent ion-routing multipole controlled by Dynamic Scan Management, enables massive parallelization, significantly increases scan rates, and maximizes versatility. Any of three dissociation techniques—CID, HCD, and ETD—can be performed at any fragmentation stage, followed by analysis in either the linear ion trap or Orbitrap mass analyzer.

## REDUCED NOISE AND INCREASED ROBUSTNESS

Active beam guide with an axial field reduces noise by preventing neutrals and high-velocity clusters from entering the quadrupole.

## EXCELLENT SENSITIVITY AND SELECTIVITY

Precursor selection using a quadrupole mass filter allows the ion trap and Orbitrap mass analyzers to operate in parallel. High ion transmission at isolation widths down to 0.4 amu improves both sensitivity and selectivity.

## EASY, RELIABLE ETD

Optional EASY-ETD electron-transfer dissociation ion source is extremely compact and uses Townsend discharge for ionization rather than a filament, making it reliable and easy to use.

## SUPERB MASS ACCURACY

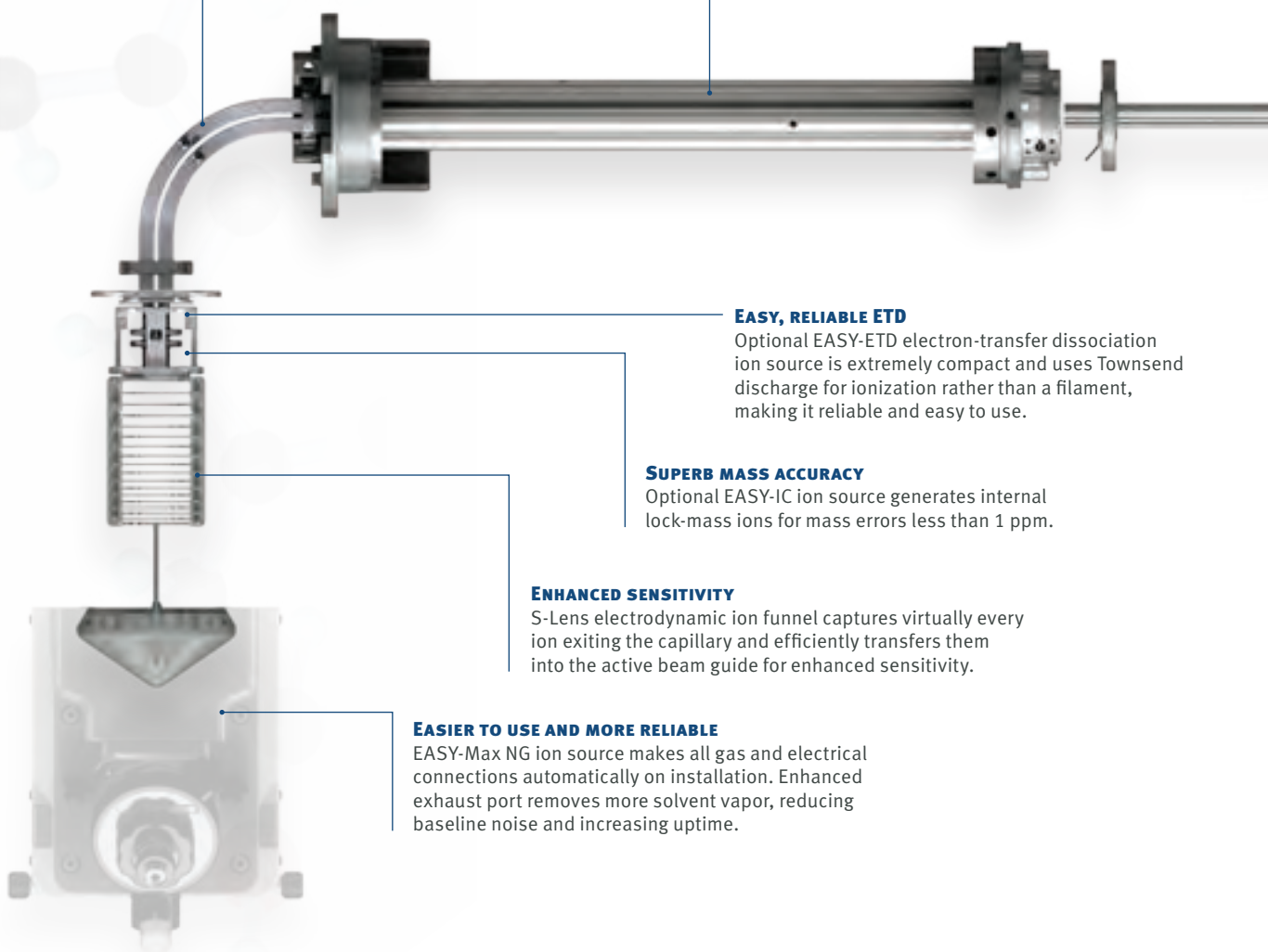
Optional EASY-IC ion source generates internal lock-mass ions for mass errors less than 1 ppm.

## ENHANCED SENSITIVITY

S-Lens electrodynamic ion funnel captures virtually every ion exiting the capillary and efficiently transfers them into the active beam guide for enhanced sensitivity.

## EASIER TO USE AND MORE RELIABLE

EASY-Max NG ion source makes all gas and electrical connections automatically on installation. Enhanced exhaust port removes more solvent vapor, reducing baseline noise and increasing uptime.



#### UNSURPASSED RESOLUTION AND INCREASED SCAN RATE

Ultra-high-field Orbitrap mass analyzer offers resolution in excess of 450,000 for unsurpassed separation of isobaric interferences. This novel Orbitrap design also allows for MS/MS scan rates up to 15 Hz, with unmatched spectral quality.

#### MAXIMUM THROUGHPUT BY MASSIVE PARALLELIZATION

Ion-routing multipole, controlled by Dynamic Scan Management, increases effective scan rates and facilitates parallel detection in the ion trap and Orbitrap mass analyzers. It also performs higher-energy collisional dissociation (HCD) at any fragmentation stage.

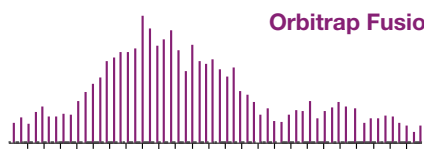
#### MULTISTAGE PRECURSOR ION ACTIVATION (MS<sup>n</sup>) AND SENSITIVE MASS ANALYSIS

Dual-pressure configuration of the linear ion trap enables scan rates up to 20 Hz. Synchronous Precursor Selection (SPS) increases S/N in experiments such as MS<sup>3</sup>-based multiplexed peptide quantification.

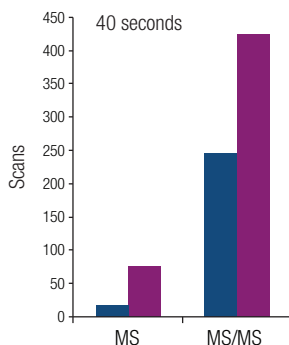
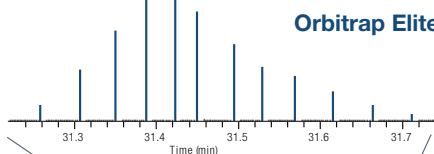
#### LONGER DETECTOR LIFE

Large-surface-area detector has two dynodes to capture the complete ion flux from the ion trap. The single multiplier features a very large surface area for extended lifetime.

#### Orbitrap Fusion MS



#### Orbitrap Elite MS

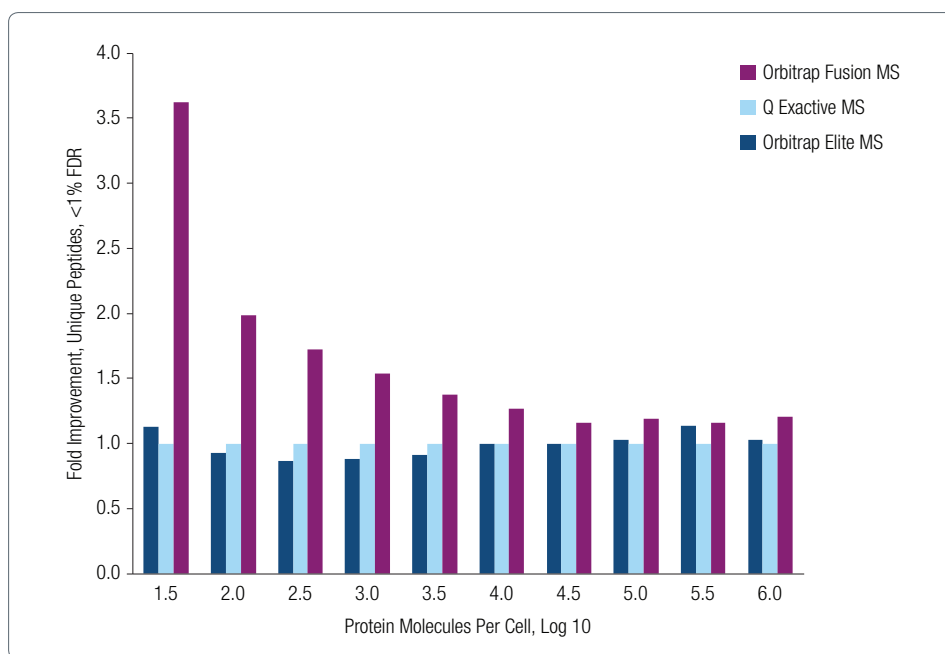


#### MASSIVE PARALLELIZATION

The unique Tribrid architecture and Dynamic Scan Management enable simultaneous precursor isolation, fragmentation, and data acquisition in both the Orbitrap and ion trap mass analyzers, maximizing the amount of high-quality data acquired and expanding the range of possible experiments.

## Discover more low-abundance proteins

Small changes in the proteome—phosphorylation of a protein kinase, induction of a rare transcription factor—can have dramatic biological effects. Detecting these changes amid a background of abundant housekeeping and structural proteins can be challenging. Proving statistical significance can be even more difficult. The wide dynamic range and ultrahigh mass resolution of the Orbitrap Fusion mass spectrometer make it the unrivaled choice for looking deeper into the proteome and confidently identifying more low-abundance proteins.

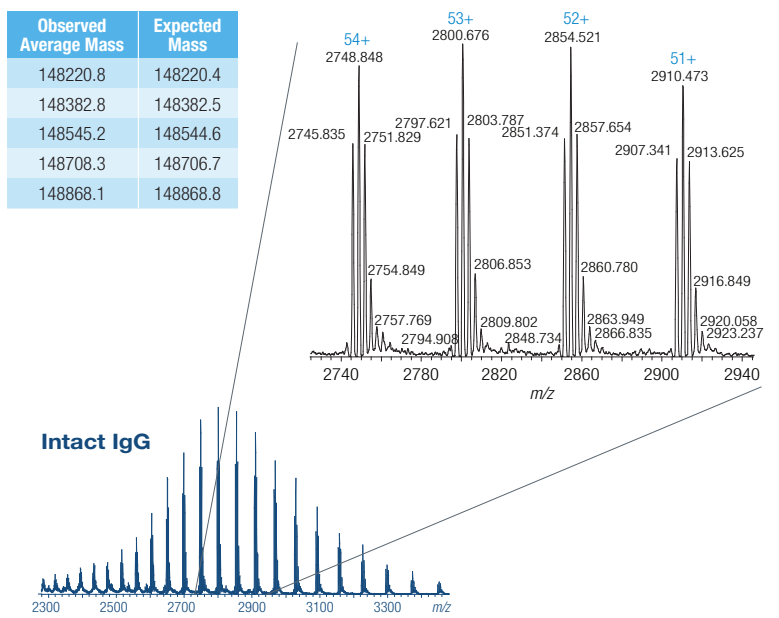


Orbitrap Fusion MS identifies more proteins with greater sequence coverage, particularly the low-copy-number proteins that are frequently of great biological interest

## Clearly assess intact proteins

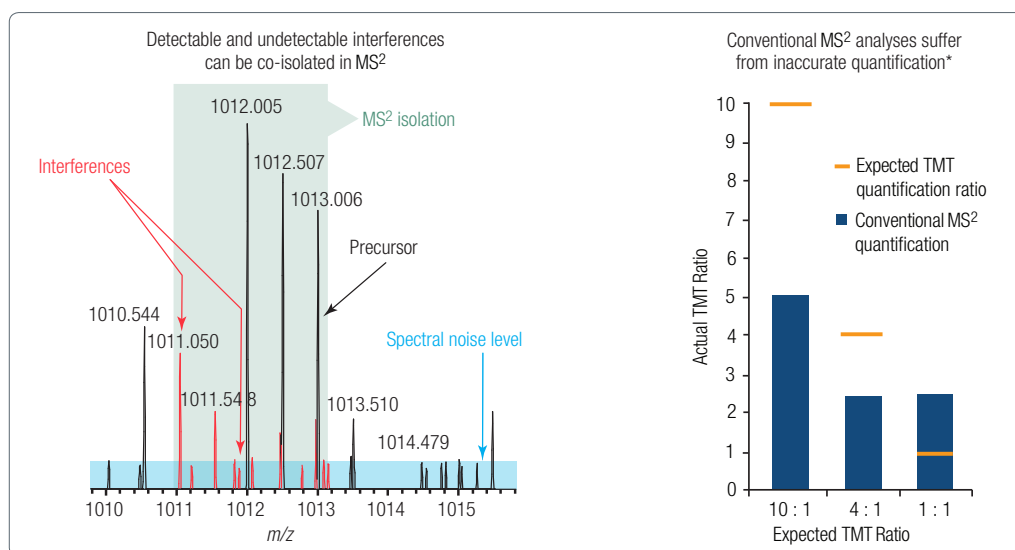
Therapeutic proteins and monoclonal antibodies have transformed biotechnology and the pharmaceutical industry. Essential to the development of new biotherapeutics is ability to quickly and accurately assess product quality and safety—including sequence integrity, glycan heterogeneity, and purity—at each step. The superior resolution and unprecedented versatility of the Orbitrap Fusion mass spectrometer make it ideal for analysis of monoclonal antibodies and other intact proteins.

Orbitrap Fusion MS provides outstanding analysis of intact IgG



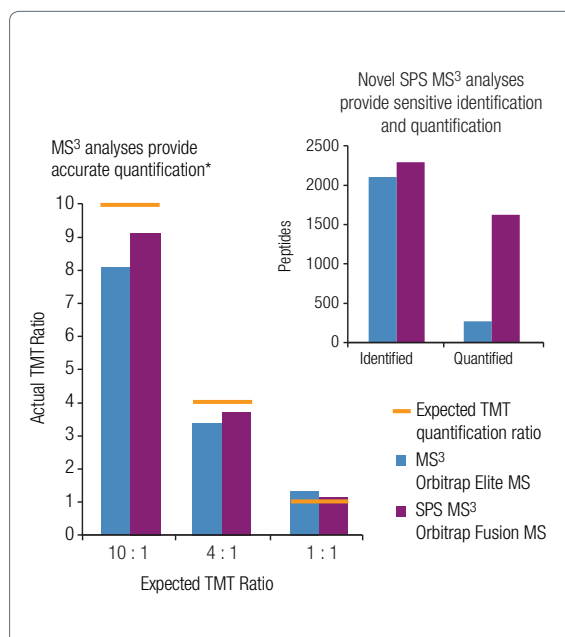
## More accurate protein quantification

Multiplexed analysis using isobaric mass tags such as TMT™ or iTRAQ® is a powerful tool, enabling quantitative comparison of protein abundances across time, conditions, tissues, subcellular locations, or other experimental variables. In conventional mass tagging experiments, reporter ions are generated at the MS<sup>2</sup> stage. However, in complex samples, co-isolation of isobaric background peptides distorts reporter ion ratios, yielding inaccurate quantitation and masking subtle but biologically significant changes in abundance.



▲ In isobaric mass tagging experiments with conventional MS<sup>2</sup> analysis, both detectable and undetectable interferences can compress the measured reporter ion ratios, yielding inaccurate quantification results

► MS<sup>3</sup> provides expected TMT ion ratios and good ID, but the number of quantified peptides is significantly reduced. Only SPS MS<sup>3</sup> on the Orbitrap Fusion MS provides accurate quantification of most identified peptides.



Conventional MS<sup>3</sup> significantly increases the precision and accuracy of TMT-based quantitation, but at the cost of a dramatically reduced number of peptides quantified. The Orbitrap Fusion MS can attain the same increased precision and accuracy of TMT-based quantitation while vastly increasing the number of peptides accurately quantified. It uses Synchronous Precursor Selection (SPS) in the ion trap to isolate multiple MS<sup>2</sup> product ions simultaneously. These product ions are fragmented to yield clean reporter ion signals and analyzed with high resolution at the MS<sup>3</sup> stage. Efficient scheduling of scan events via Dynamic Scan Management ensures quantitative accuracy, sensitivity, and excellent protein identification.

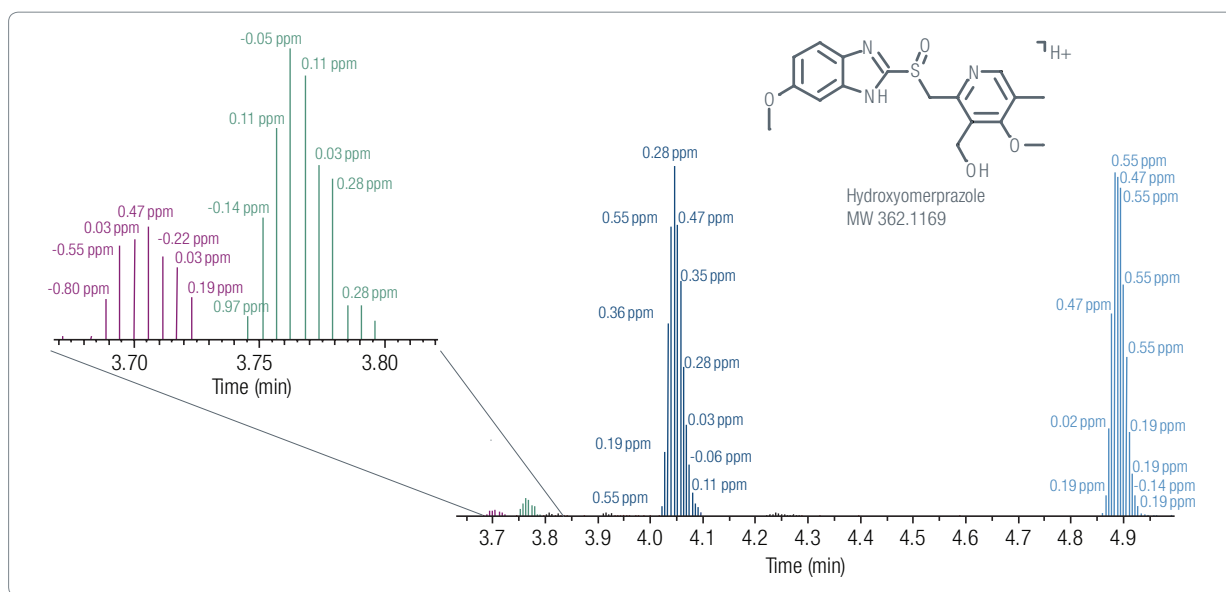
\* Using the model system developed by Ting et al., *Nature Methods*, Vol 8, No 11, 2011. Data Courtesy: Graeme McAllister, Steven Gygi Lab, Harvard University



## Internal calibration for added confidence

Mass accuracy improves analytical confidence. With the optional Thermo Scientific™ EASY-IC™ source providing internal calibration (IC), the Orbitrap Fusion MS can achieve a confidence-building sub-1-ppm mass accuracy in every scan.

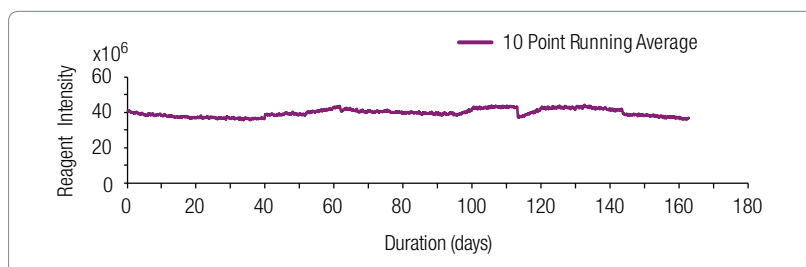
Four structural isomers of hydroxymerprazole varying in concentration are measured with ppb mass accuracy



## Simple, reliable ETD enhances characterization of complex PTMs

Electron-transfer dissociation (ETD) is a powerful complement to CID and HCD for the analysis of proteins. It cleaves primarily along the peptide backbone, generating c and z ions, often with increased fragment coverage compared to b and y ions that dominate CID spectra. ETD leaves side chains and modifications largely intact, making it particularly useful when analyzing post-translationally modified proteins. The optional Thermo Scientific™ EASY-ETD™ ion source, designed specifically for the Orbitrap Fusion MS, is robust, easy to maintain, and easy to use.

- Compact design fits entirely within the mass spectrometer, with front access to the reagent reservoir
- Single-step reaction calibration allows for easy ETD optimization
- Dynamic Scan Management, based on precursor charge and  $m/z$ , ensures ETD is applied when it will be most useful
- Fully parallel isolation, accumulation, fragmentation, and detection increases speed and sensitivity of ETD analyses



Townsend-discharge-based EASY-ETD source produces a reagent-ion flux that is stable for months



An abstract graphic featuring several overlapping, translucent blue and purple organic shapes, possibly representing cells or molecules. A faint, light gray wireframe sphere is visible in the upper right corner. The background is white with a subtle pattern of thin, light gray lines forming a network or mesh.

Hemoporexin peptide

GHGHRNGTGHGNSLTHHGPEYMR

1214.989

972.192

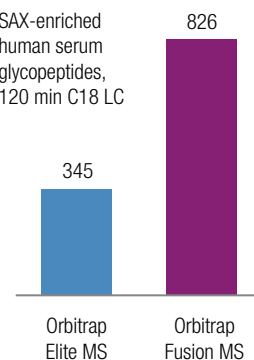
813.160

1619.984

1354.520

393.726

$m/z$



The Tribrid architecture and Dynamic Scan Management of the Orbitrap Fusion MS allow any dissociation technique to be performed at any fragmentation stage, followed by analysis in either mass analyzer. This can be of tremendous benefit in top-down analysis of intact proteins where multistage MS<sup>n</sup> analysis such as HCD followed by ETD can further increase the sequence coverage.



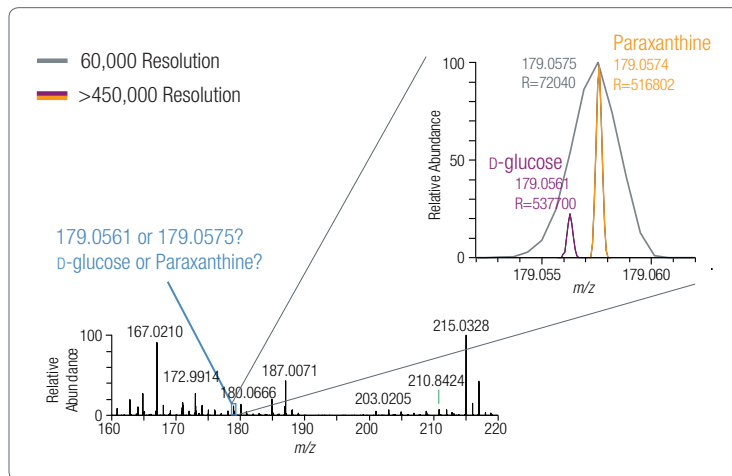
# Determine structures more quickly and accurately

## Resolution of isobaric interferences

With mass resolution in excess of 450,000, the Orbitrap Fusion mass spectrometer can easily separate and identify isobaric compounds indistinguishable by other MS technologies.

## Structural characterization on a UHPLC timescale

The Tribrid architecture and Dynamic Scan Management of the Orbitrap Fusion MS deliver exceptional scan rates for applications where high throughput and fast chromatography demand the most MS<sup>n</sup> data from a single run. The quadrupole mass filter, ion-routing multipole, ion trap, and Orbitrap analyzer work simultaneously to deliver high-quality data from the narrowest of LC peaks.



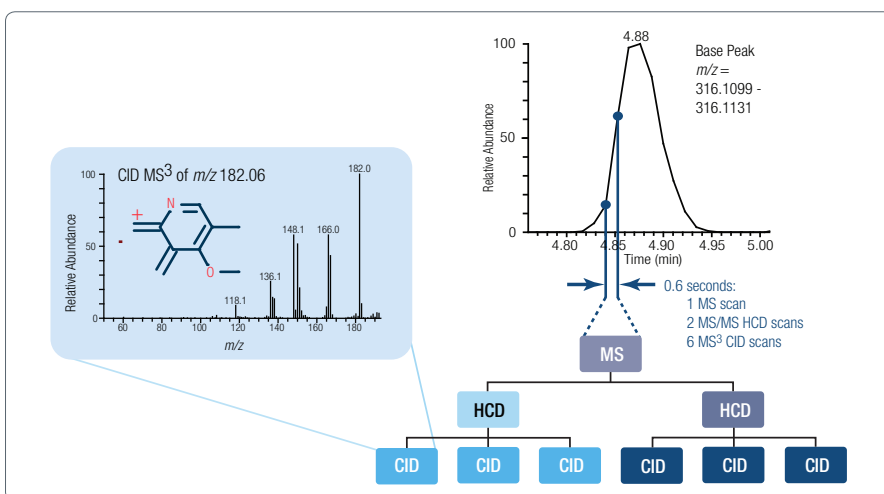
The Orbitrap Fusion MS easily separates D-glucose and paraxanthine, isobaric analytes commonly found at significantly different concentrations in blood. D-glucose is vastly more abundant, but difficult to detect due to its low ionization efficiency.

## More complete structural information in less time

For detailed structure determination of metabolites, glycans, and other small molecules, the Orbitrap Fusion MS uniquely offers ultimate flexibility—any fragmentation type, at any stage of MS<sup>n</sup> analysis, with fragment ions detected by either mass analyzer. CID-HCD, HCD-CID, and HCD-HCD experiments are all as simple as conventional CID. Combined with parallel data acquisition for greater speed and throughput, this flexibility facilitates the acquisition of more structural information in less time.

- Faster – MS<sup>n</sup> CID provides faster structural elucidation
- Richer – MS<sup>n</sup> HCD provides more structural information over a wider mass range with fewer stages of MS<sup>n</sup>
- More confident – high-resolution scans elucidate isobaric compounds and sub-ppm mass accuracy ensures accurate elemental assignment

The Orbitrap Fusion MS acquires more, richer data in less time for faster, more-complete structural elucidation



## Maximum performance with less effort

The Orbitrap Fusion Tribrid mass spectrometer delivers more, higher-quality information from more types of samples faster than any mass spectrometer available today. But *more* is only part of the story; the other part is *less*, less effort. The intelligence built into the Orbitrap Fusion instrument and software makes it possible to achieve exemplary results with far less effort than required by previous generations of mass spectrometers. This built-in intelligence helps researchers focus on their science instead of method development and instrument operation.

- Dynamic Scan Management not only schedules the scan events most efficiently, it also intelligently matches each precursor with the optimum fragmentation mode and mass analyzer, based on precursor  $m/z$ , intensity, and/or charge state
- A library of templates with application specific defaults is available for common experiments
- Automated Synchronous Precursor Selection for MS<sup>3</sup> significantly increases the number of peptides and proteins identified and quantified by isobaric mass tagging
- Top-speed mode efficiently schedules MS and data-dependant MS<sup>n</sup> scans based on user-definable parameters and maximizes the number of high-quality MS<sup>n</sup> spectra acquired
- Simultaneous identification, quantitation, and confirmation are achieved by high-resolution, accurate-mass, low-detection-limit SIM quantification with the Orbitrap mass analyzer and sensitive full-scan MS/MS confirmation with the ion trap



▲ Intuitive method editor with a drag-and-drop interface simplifies development of custom experiments without restricting access to important parameters. Tune parameters are incorporated into experimental methods, eliminating separate tune files.

# Transforming science with the next generation of mass spectrometers

The Orbitrap Fusion Tribrid mass spectrometer is one of a family of transformational, next-generation Thermo Scientific mass spectrometers that combine unprecedented performance and usability. Others include:

- Thermo Scientific™ TSQ Quantiva™ triple-stage quadrupole mass spectrometer
- Thermo Scientific™ TSQ Endura™ triple-stage quadrupole mass spectrometer

These next-generation instruments are built on a foundation of shared, state-of-the-art hardware and software components. This commonality makes it easier to transfer methods from one instrument to another when research progresses from single-sample-based experiments to validation and high-volume screening or routine quantification.



All of these Thermo Scientific mass spectrometers can be paired with a range of high-performance Thermo Scientific LC systems. Regardless of application, there is an LC that will ensure the highest possible performance.



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**Australia** +61 3 9757 4300  
**Austria** +43 1 333 50 34 0  
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**Canada** +1 800 530 8447  
**China** +86 10 8419 3588  
**Denmark** +45 70 23 62 60

**Europe-Other** +43 1 333 50 34 0  
**Finland/Norway/Sweden**  
+46 8 556 468 00  
**France** +33 1 60 92 48 00  
**Germany** +49 6103 408 1014  
**India** +91 22 6742 9434  
**Italy** +39 02 950 591

**Japan** +81 45 453 9100  
**Latin America** +1 561 688 8700  
**Middle East** +43 1 333 50 34 0  
**Netherlands** +31 76 579 55 55  
**New Zealand** +64 9 980 6700  
**Russia/CIS** +43 1 333 50 34 0  
**South Africa** +27 11 570 1840

**Spain** +34 914 845 965  
**Switzerland** +41 61 716 77 00  
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**USA** +1 800 532 4752

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