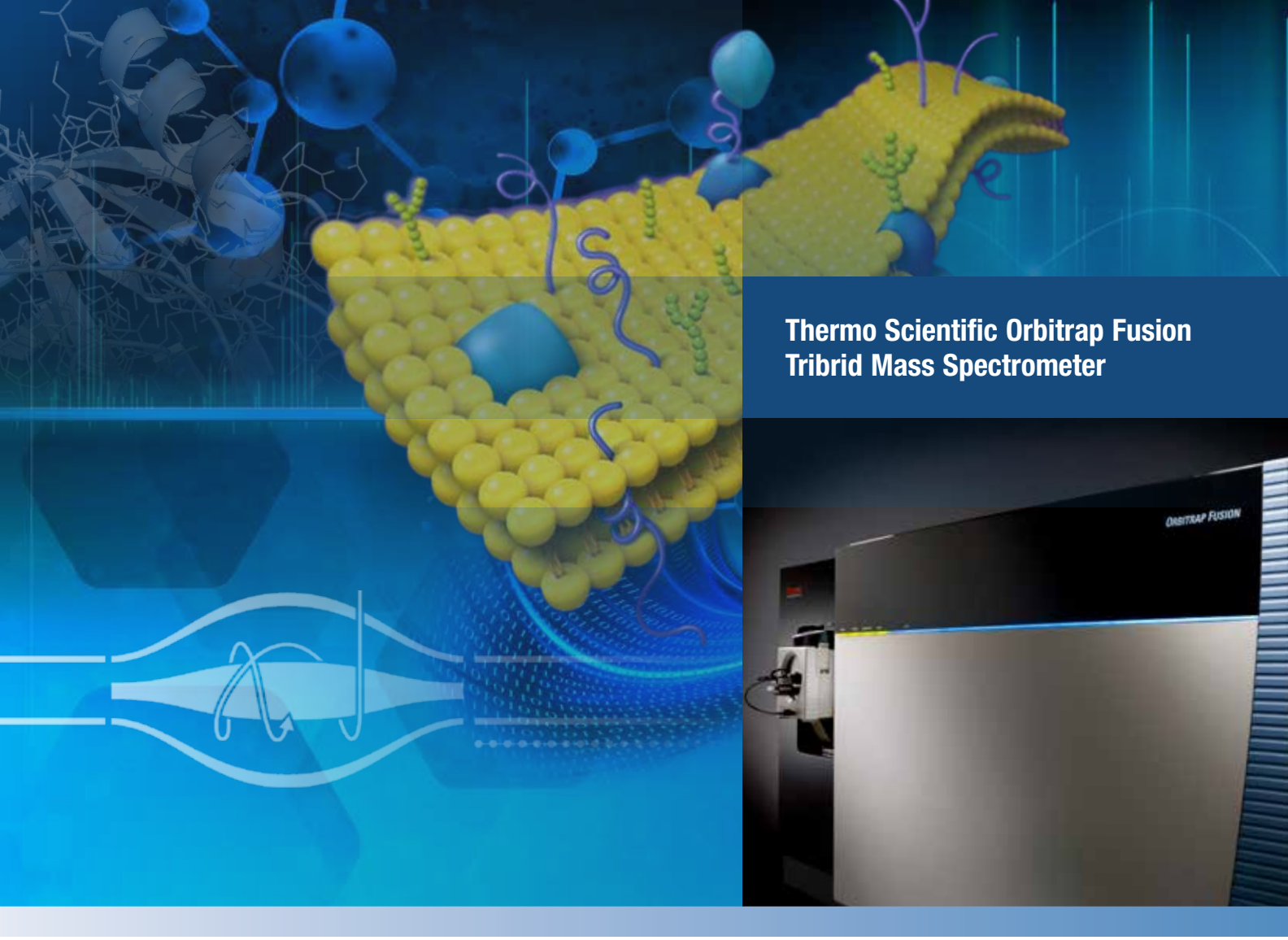


Thermo Scientific Orbitrap Fusion
Tribrid Mass Spectrometer

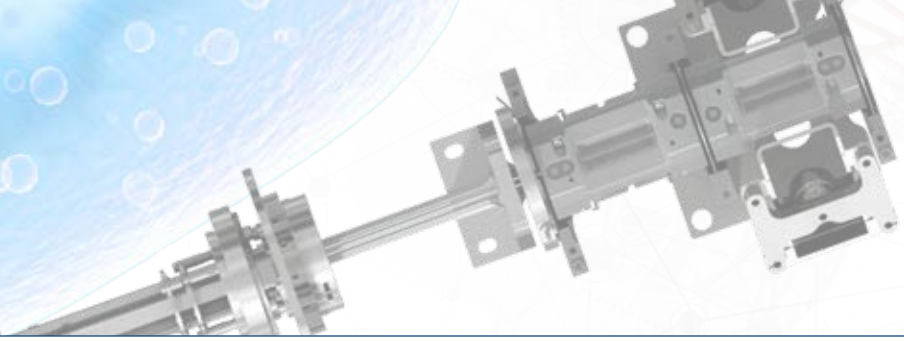
Unmatched analytical performance

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 goal of 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. The Tribrid architecture provides unprecedented depth of analysis, enabling scientists with the most challenging low-abundance, high-complexity, or difficult-to-analyze samples to identify more compounds faster, quantify more accurately, and elucidate structures more thoroughly. Easy to use, yet sophisticated, 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

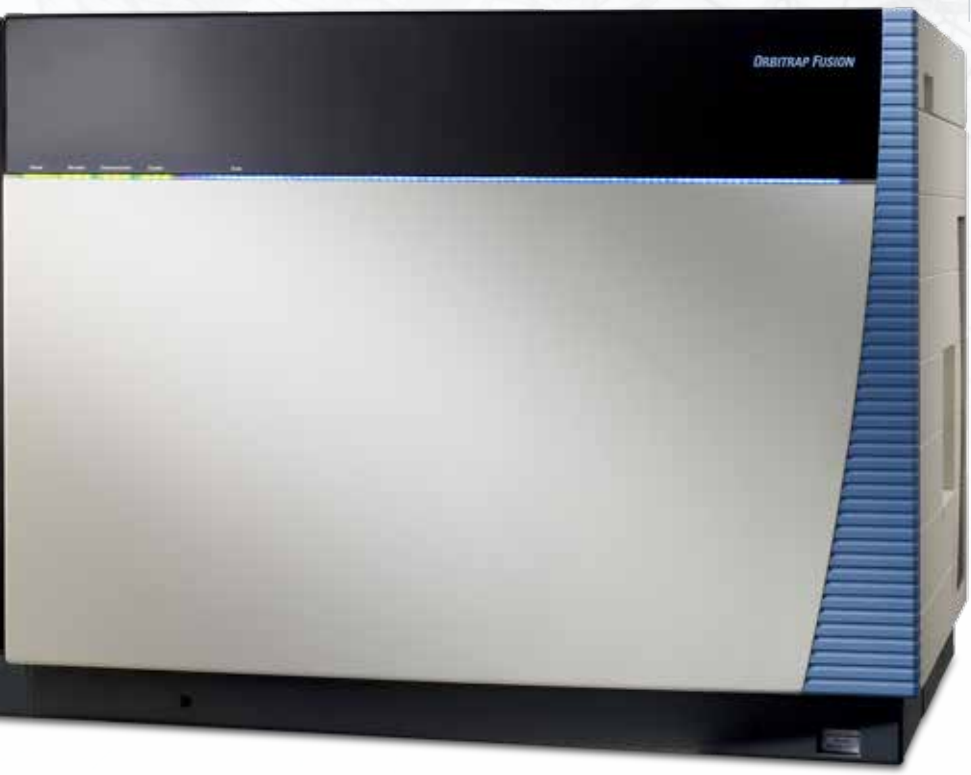
Synchronous Precursor Selection combined with MS^3 significantly improves quantitative accuracy when using isobaric mass tags for relative quantitation of proteins.

Elucidate structures more thoroughly

The ability to use any fragmentation mode, at any stage of MS^n analysis, with detection by ion trap or Thermo Scientific™ 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.

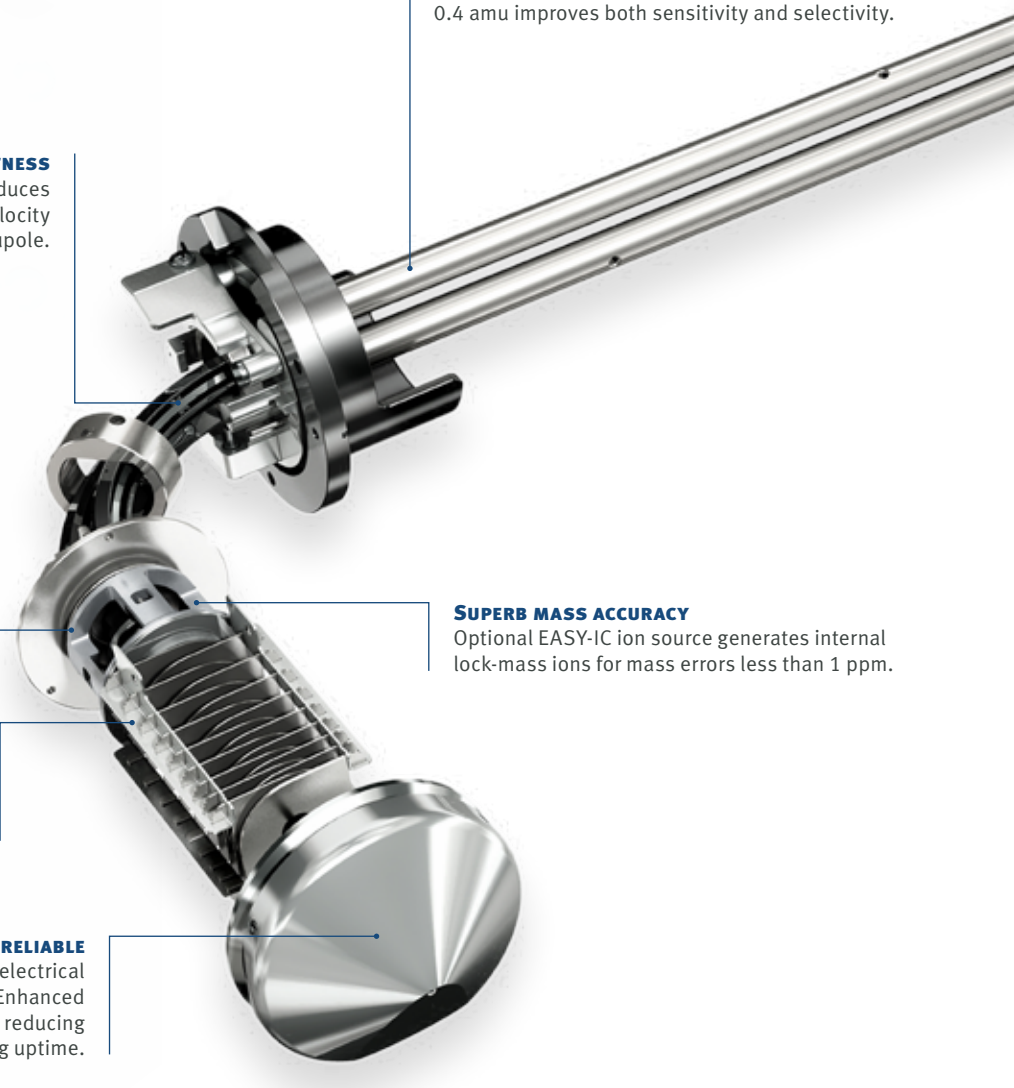


Revolutionary Tribrid architecture

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.

Excellent sensitivity and selectivity
Precursor selection using a quadrupole mass filter allows the ion trap and Orbitrap mass analyzers to operate in parallel. Wide mass range isolation improves signal to noise ratio in full scan detection. High ion transmission at isolation widths down to 0.4 amu improves both sensitivity and selectivity.

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.

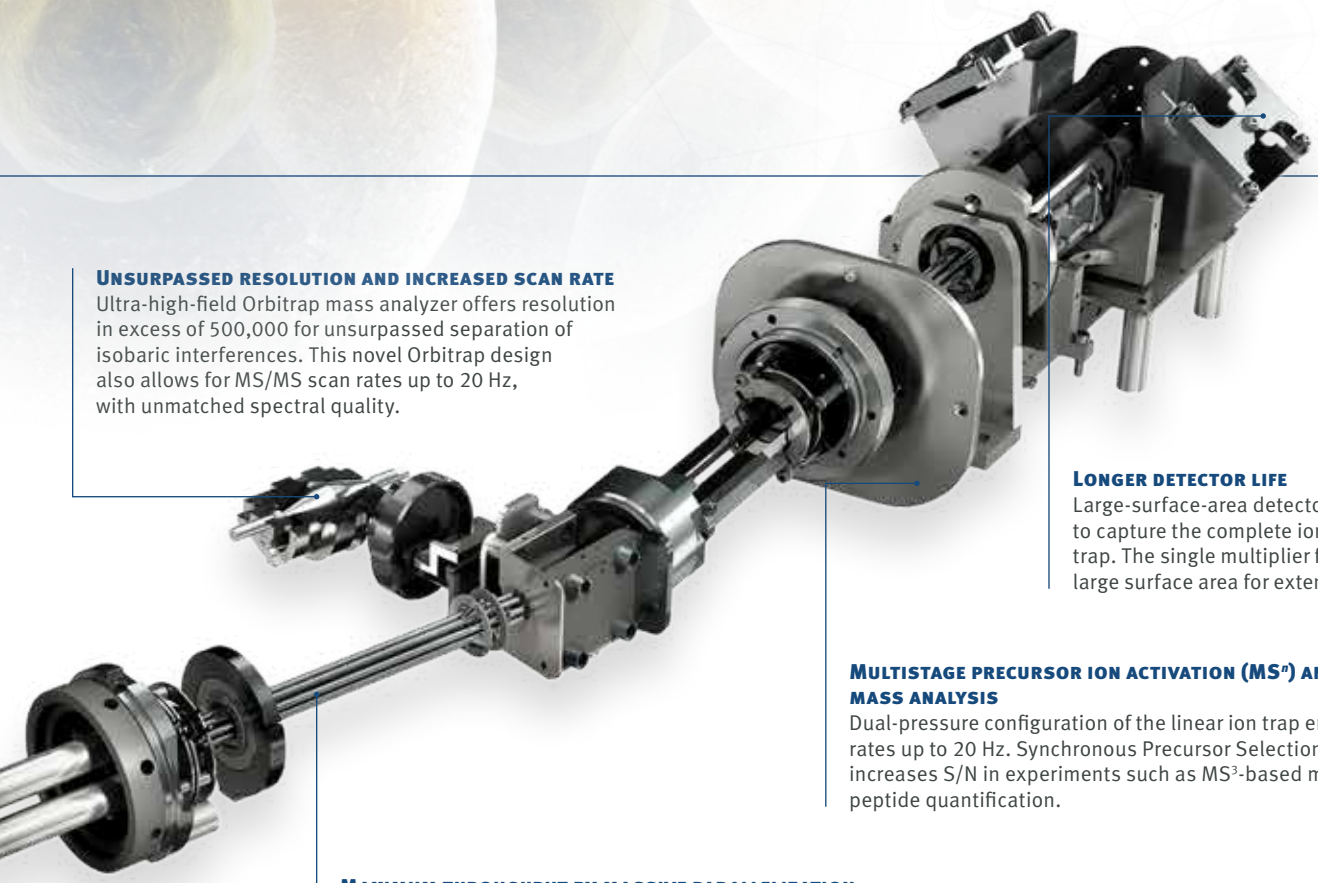


Easy, reliable ETD
Optional EASY-ETD electron-transfer dissociation ion source is extremely compact and uses Townsend discharge for ionization rather than a filament, making it reliable and easy to use.

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 500,000 for unsurpassed separation of isobaric interferences. This novel Orbitrap design also allows for MS/MS scan rates up to 20 Hz, with unmatched spectral quality.

Longer detector life

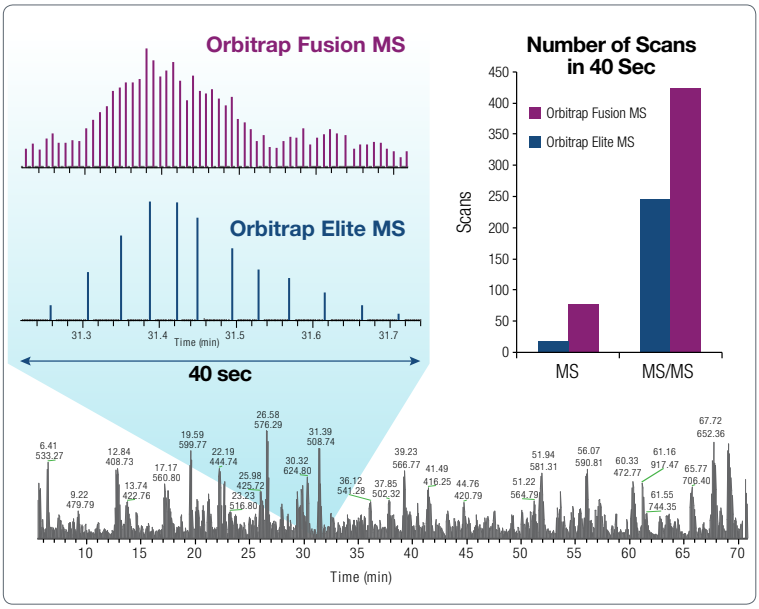
Large-surface-area detector has two dynodes to capture the complete ion flux from the ion trap. The single multiplier features a very large surface area for extended lifetime.

Multistage precursor ion activation (MS^n) 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^3-based multiplexed peptide quantification.

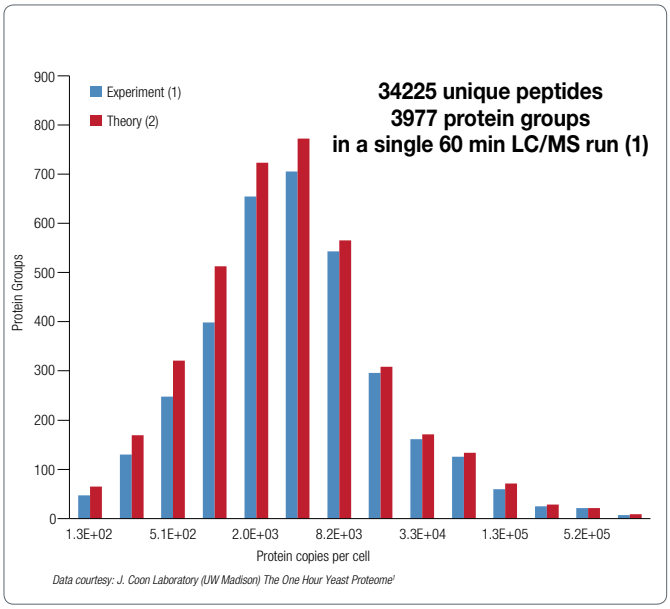
Maximum throughput by massive parallelization

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.



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 (as shown in the 40 sec window) and expanding the range of possible experiments.



Wide dynamic range for deep sequencing

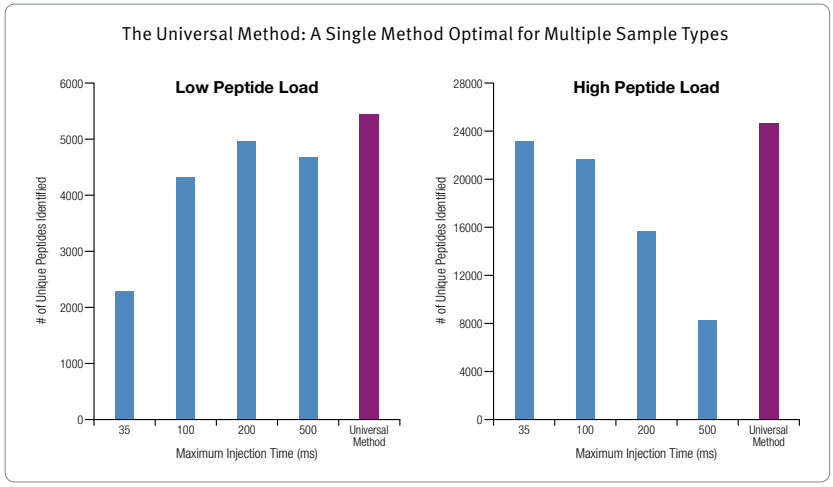
Orbitrap Fusion is capable of near complete sequencing of the yeast proteome in a single 60 minute analysis including those proteins present at greater that 5.2E+05 and less than 130 copies per cell.

(1) Mol Cell Proteomics. Jan 2014; 13(1): 339–347
(2) Nature. 2003; 16: 737–7341

The Universal Method eliminates method optimization for data-dependent analysis

Achieving the maximal number of peptide identifications from a given sample in a single run usually requires multiple LC/MS analyses for optimization of the method parameters to determine the best balance of scan rate and number of ions per spectrum. However, this is time consuming and sample intensive, particularly when sample concentration, complexity, and dynamic range are unknown. As a result, the same acquisition parameters are often applied to all samples, resulting in suboptimal spectral quality that compromises maximal identifications.

The Universal Method adjusts key acquisition parameters "on-the-fly" according to full scan spectral complexity and ion intensity without any prior knowledge of the sample amount. This approach allows for maximal identifications from an unknown sample in a single run, eliminating the need for lengthy parameter optimization and excessive sample usage.

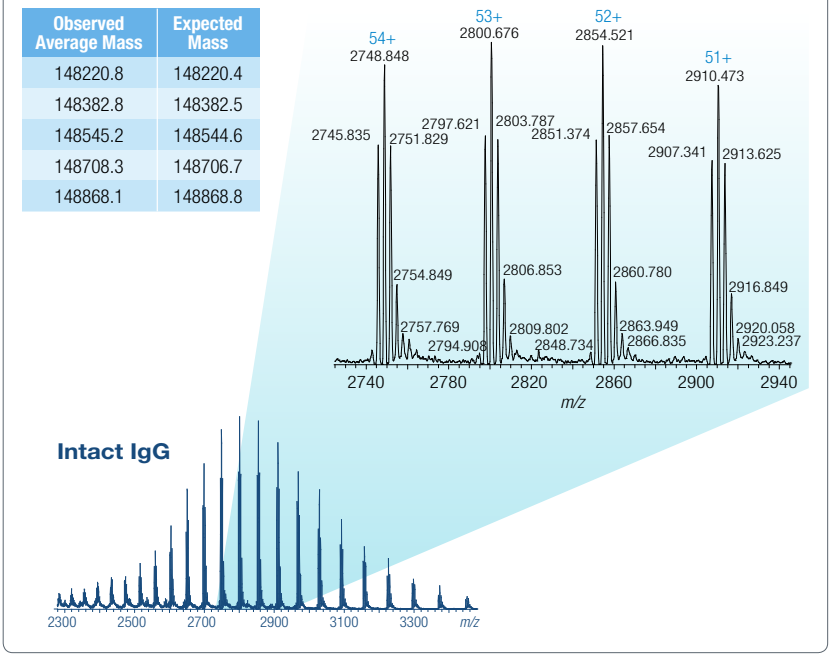


In order to maximize the number of unique peptides identified, injection times is one parameter to optimize with low and high peptide loads. The Universal Method, with no optimization, is shown here to perform equally as well as manual optimization without the added time and sample.

Analyze intact proteins

Therapeutic proteins and monoclonal antibodies have transformed biotechnology and the pharmaceutical industry. Essential to the development of new biotherapeutics is the 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 the analysis of monoclonal antibodies and other intact proteins.

Observed Average Mass	Expected Mass
148220.8	148220.4
148382.8	148382.5
148545.2	148544.6
148708.3	148706.7
148868.1	148868.8



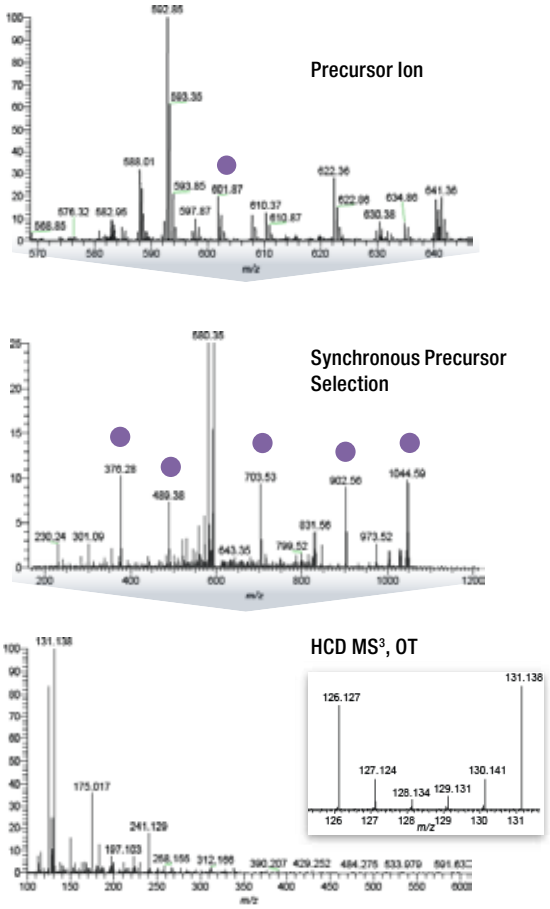
Orbitrap Fusion MS provides outstanding analysis of intact IgG

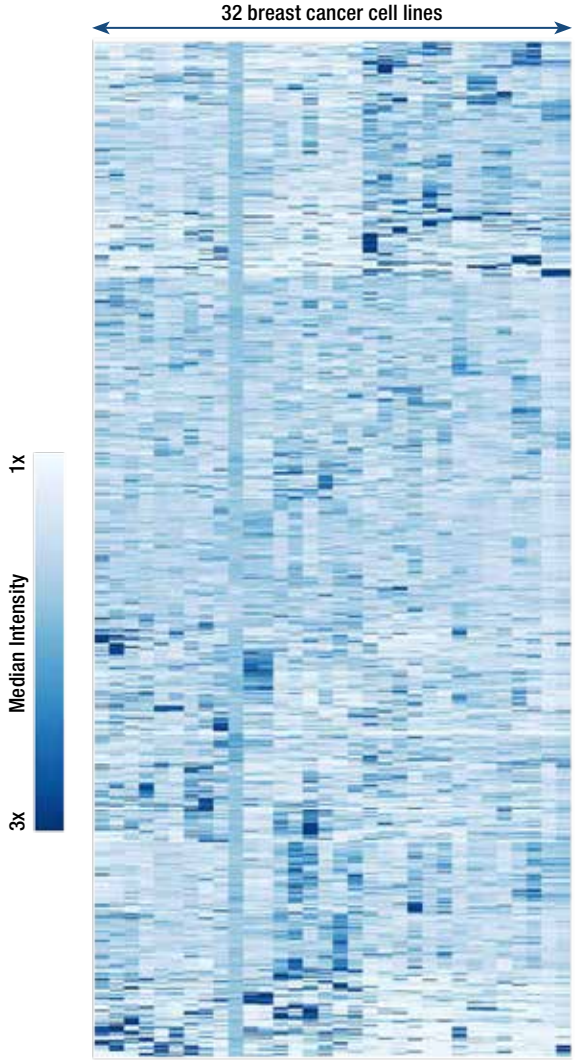
More accurate protein quantification

Multiplexed analysis using isobaric mass tags such as TMT™ reagents or iTRAQ® reagents 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^2 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.

- **Goal:** Comprehensive quantitative proteome maps of 32 breast cancer cell lines
- **Approach:** 4 TMT-10plex experiments using SPS TMT3 workflow
- **Duration:** 6 days
- **Results:** 9,196 quantified proteins across the experiments, more than 7,600 proteins in each experiment
- **Throughput:** 4.5 hours for a comprehensive proteome map per cell line

SPS TMT3 Workflow





"I think that the Orbitrap Fusion, in combination with TMT, is the first instrument that enables mass spectrometry to play a serious role in "genomics-like" studies. In a very short period of time, I already have full proteome data sets (~8,000 quantified proteins per sample) on more than 30 breast cancer cell lines."

Professor W. Haas, Harvard Medical School

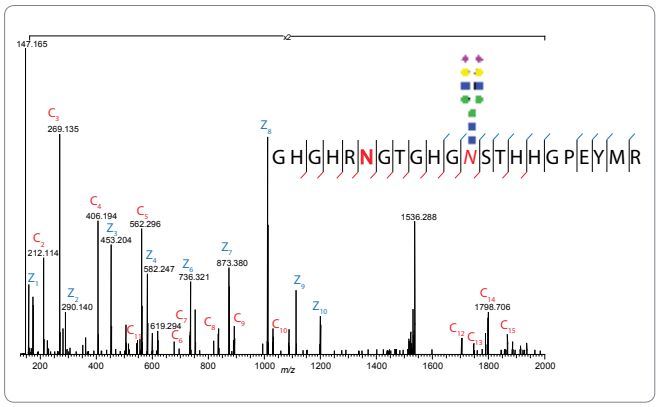
Data courtesy: W. Haas and C. Benes (HMS).

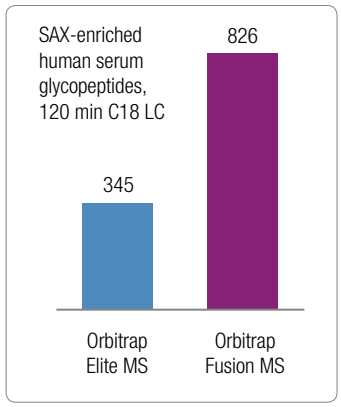
Simple, reliable ETD enhances characterization of complex PTMs

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

Comprehensive fragment ion coverage identifies the exact sites of modifications, in this case deamidation of Asn6 and GlycNAc on Asn12





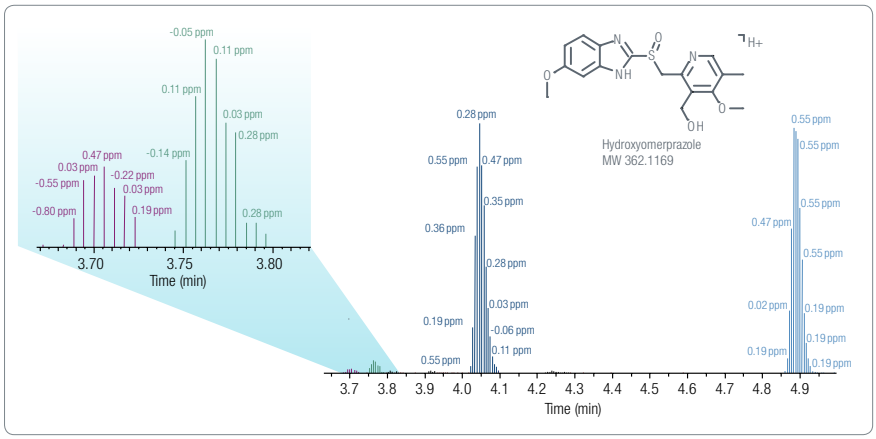
Easy-to-use ETD combined with Dynamic Scan Management, charge-state-dependent reaction time, and intelligent precursor prioritization on the Orbitrap Fusion MS results in significantly more identified glycopeptides

One example of the benefits of using ETD is the profiling of glycosylation sites on glycopeptides and glycoproteins. ETD provides extensive fragmentation along the peptide backbone, enabling sequencing of the peptide while preserving attachment of the glycans for localization of the glycosylation sites. CID or HCD provides complementary information about the glycan composition.

Internal calibration for added confidence

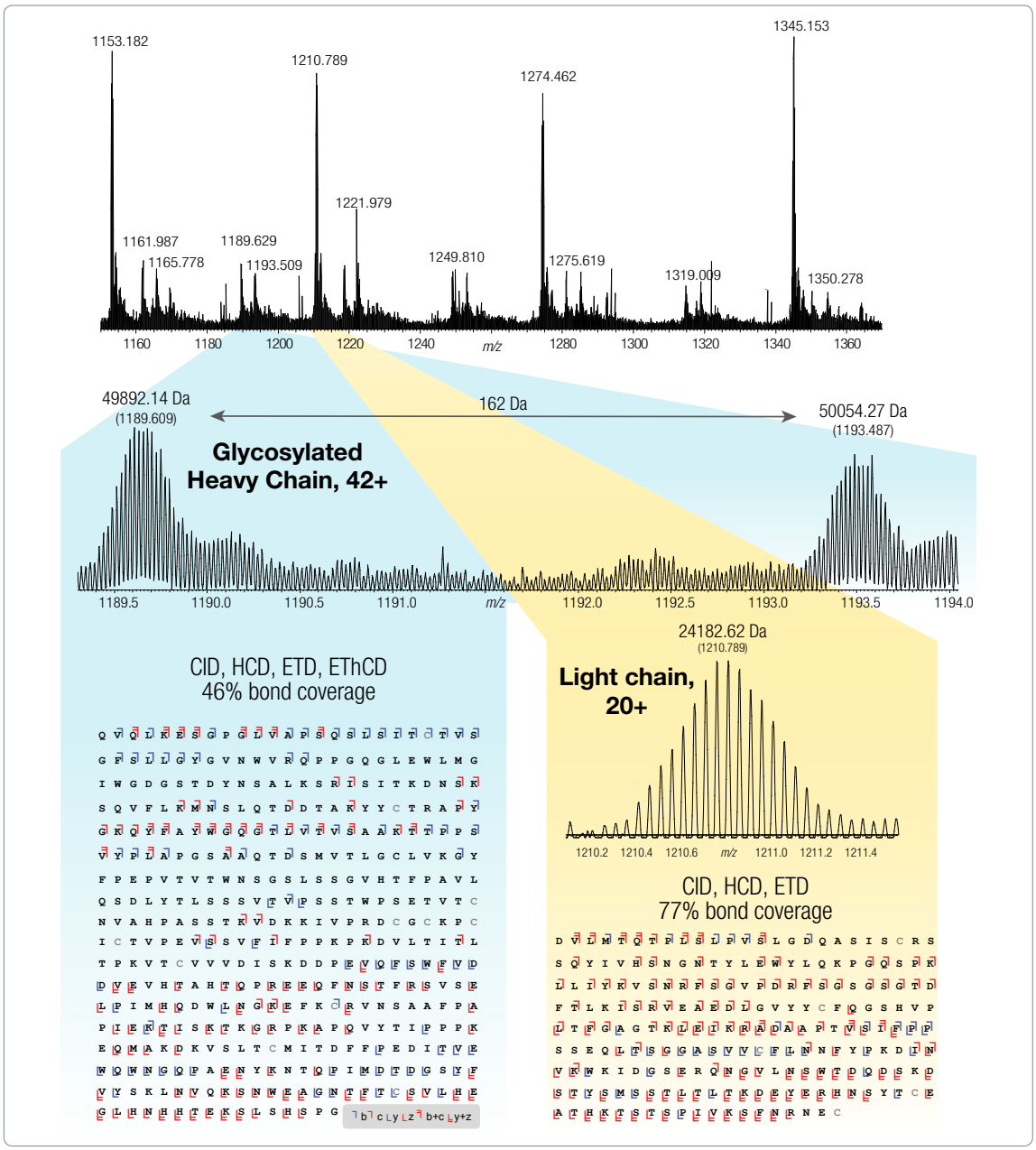
Mass accuracy improves analytical confidence. With the optional Thermo Scientific™ EASY-IC™ source providing internal calibration (IC), the Orbitrap Fusion MS can achieve a confidence-building sub-1-ppm mass accuracy in every scan.

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

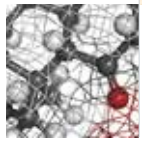


Multiple fragmentation types provide exceptional sequence coverage for top-down analyses

The Orbitrap Fusion MS has the high resolution and accurate mass necessary to fully resolve monoclonal antibody heavy and light chains, as well as to accurately assign the complex fragmentation spectra generated from top-down experiments on large species. To maximize fragmentation for sequence characterization, proteins can be analyzed using a combination of fragmentation types including CID, HCD, ETD, and EThcD which provide complementary information. More complex experiments such as MS^n analyses using any combination of fragmentations, including HCD- MS^2, ETD-MS^3, can easily be used to further characterize intact proteins in a unique fashion.



The unique combination of high resolution and versatile fragmentation modes combine to enhance top-down characterization of monoclonal antibodies



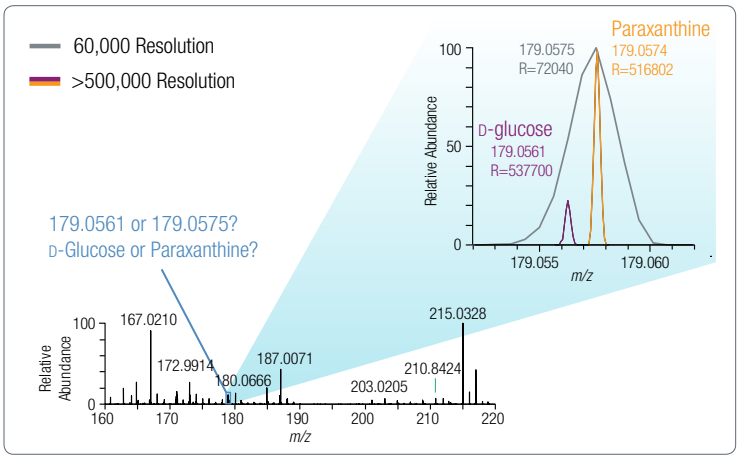
Determine structures more quickly and accurately

Resolution of isobaric interferences

With mass resolution in excess of 500,000, 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^n 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.



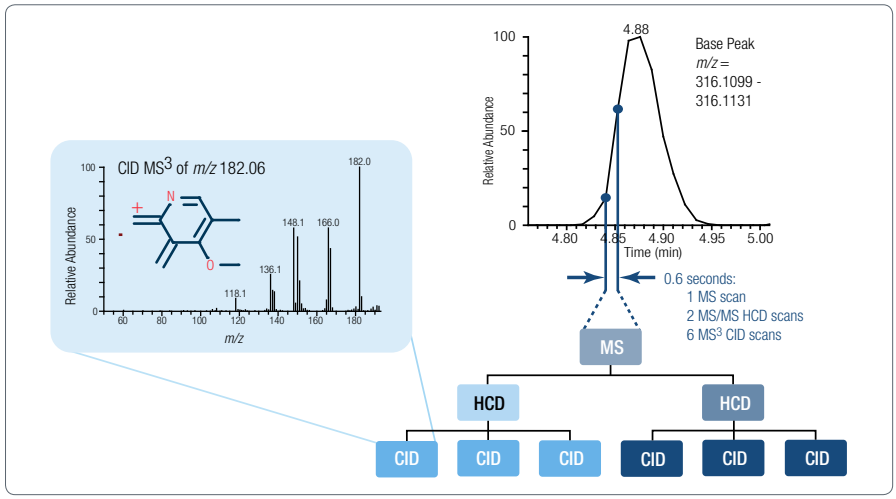
The Orbitrap Fusion MS with its unique high resolution easily separates D-glucose and paraxanthine, isobaric analytes commonly found at significantly different concentrations in blood. While impossible to resolve at 60000 resolution settings, the high res >500,000 enables the separation of these isobaric species. 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^n analysis, with fragment ions detected by either mass analyzer. Combined with parallel data acquisition for greater speed and throughput, this flexibility facilitates the acquisition of more structural information in less time.

- Faster – MS^n CID provides faster structural elucidation
- Richer – MS^n HCD provides more structural information over a wider mass range with fewer stages of MS^n
- 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



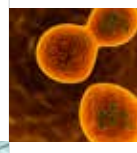
Maximum performance with less effort

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 schedules scan events to maximize MS efficiency, as well as intelligently prioritizing precursors for data dependent analysis with their optimum fragmentation mode and mass analyzer
- A library of templates with application specific defaults is available for common experiments allowing you to run guided methods with less effort. For unique experiments, customized method development is available for maximum flexibility.
- Automated Synchronous Precursor Selection (SPS) for MS^3 significantly increases the number of peptides and proteins identified and quantified by isobaric mass tagging
- Top-speed (Top S) mode efficiently schedules MS and data-dependent MS^n scans based on user-definable parameters and maximizes the number of high-quality MS^n spectra acquired
- Simultaneous identification, quantitation, and confirmation are achieved by a combination of 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. The Orbitrap Fusion MS enables the analysis of most challenging samples to identify more compounds faster, quantify more accurately, and elucidate structures more thoroughly. The next-generation SRM triple quadrupole MS systems for targeted quantitation include the Thermo Scientific™ TSQ Quantiva™ MS and TSQ Endura™ MS systems. These 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.

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