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Introduction to novel Mass Spectrometer & Chromatography

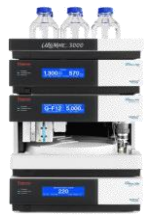
Sofia 2017, October

Gerhard Stadlmann

Portfolio Overview

Routine Analysis

UltiMate 3000 Basic
- Highly economic & reliable
- 620 bar UHPLC compatible



UltiMate 3000 Standard
- Highest flexibility with Dual solutions
- 620 bar UHPLC compatible

620 bar

Flexibility, More Performance and Method Development

UltiMate 3000 RS/BioRS
- Advanced workflows with Dual systems
- Flow rates up to 8 mL/min
- Binary and Quaternary UHPLC systems

Vanquish Flex

Quaternary System
- Quaternary solvent blending
- Pressures up to 1000 bar
- Flow rates of up to 8 mL/min
- Biocompatible

Binary System
- Binary high pressure solvent mixing
- Pressures up to 1000 bar
- Flow rates of up to 8 mL/min
- Biocompatible

Up to 1000 bar

Research & HT

Vanquish Horizon
- Highest pressure capability up to 1500 bar
- Flow rates up to 5 mL/min
- Lowest system dispersion and GDV
- Unmatched detection sensitivity and linearity
- Biocompatible

1500 bar

ISQ EC introduced at the HPLC 2017

Unique robustness and performance in a routine MS.

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Stacking up ISQ EC vs MSQ Plus: Instrument Specifications

Specification	ISQ EC	MSQ Plus
Mass Range (m/z)	**10**–1250	17–**2000**
Source Type	ESI	ESI / **APCI**
Supported Modes	Full scan / SIM	Full scan / SIM
ESI Max Flow Rate	2 mL/min	2 mL/min
Scan Rate, max (Da/s)	**20,000**	12,000
SIM Sensitivity (ESI+)	**10 pg Reserpine 400:1**	50 pg erythromycin 1,000:1
Polarity Switching	Yes, **25 ms**	Yes, 240 ms
Mass Resolution	Unit (≤ 1.0 Da)	Unit (≤ 1.0 Da)
Mass Accuracy / Stability	**≤ ± 0.1 Da** ≤ 0.1 Da over 24 h	≤ ± 0.3 Da ≤ 0.1 Da over 24 h
Digital Dynamic Range	**10^7**	10^4
Roughing Pump	External oil-based rotary	External oil-based rotary
Power	**100-240 VAC 50/60Hz**	240 VAC 50/60 Hz
Reserpine MDL* (pg)	0.3 ← 3x better →	1.0
Erythromycin MDL* (pg)	0.08 ← 3x better →	0.25

* SIM mode

Introduction to TSQ Altis and TSQ Quantis

Performance: Sensitivity, Selectivity (H-SRM)

TSQ Altis

TSQ Quantis

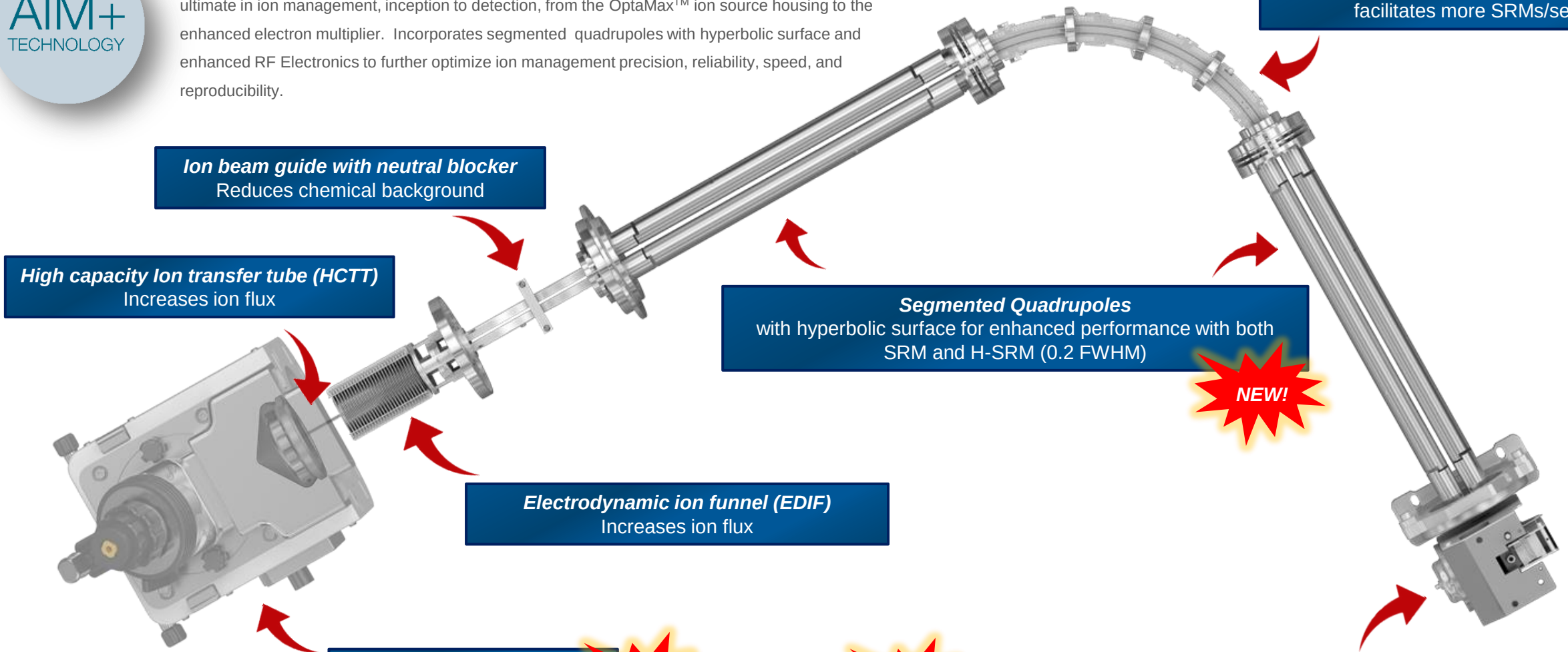
	TSQ Altis *High-end*	TSQ Quantis *Mid-tier*
Mass Range	5-2000	5-3000
SRM/sec	600	600
Selectivity (H-SRM)	0.2 Da FWHM	0.4 Da FWHM
Sensitivity (HESI Reserpine 1 pg)	500,000:1	150,000:1
Targeted Market	Omics, Research, Pharma/Biopharma, Clinical Research and Forensic Toxicology	Environmental and Food Safety, Clinical Research, and Forensic Toxicology

Robustness, Reproducibility, Speed, Ease-of-Use, Flexibility

TSQ Altis: Sensitivity with Robustness, No Compromises

AIM+ TECHNOLOGY

Active Ion Management Plus (*AIM+*) - The next step in precision design delivers the ultimate in ion management, inception to detection, from the OptaMax™ ion source housing to the enhanced electron multiplier. Incorporates segmented quadrupoles with hyperbolic surface and enhanced RF Electronics to further optimize ion management precision, reliability, speed, and reproducibility.



Active collision cell with axial DC field
facilitates more SRMs/sec

Ion beam guide with neutral blocker
Reduces chemical background

High capacity Ion transfer tube (HCTT)
Increases ion flux

Segmented Quadrupoles
with hyperbolic surface for enhanced performance with both SRM and H-SRM (0.2 FWHM)

NEW!

Electrodynamic ion funnel (EDIF)
Increases ion flux

OptaMax™ NG
APCI ready

NEW!

NEW!

Enhanced dual-mode electron multiplier detector
Ensures excellent linearity and dynamic range

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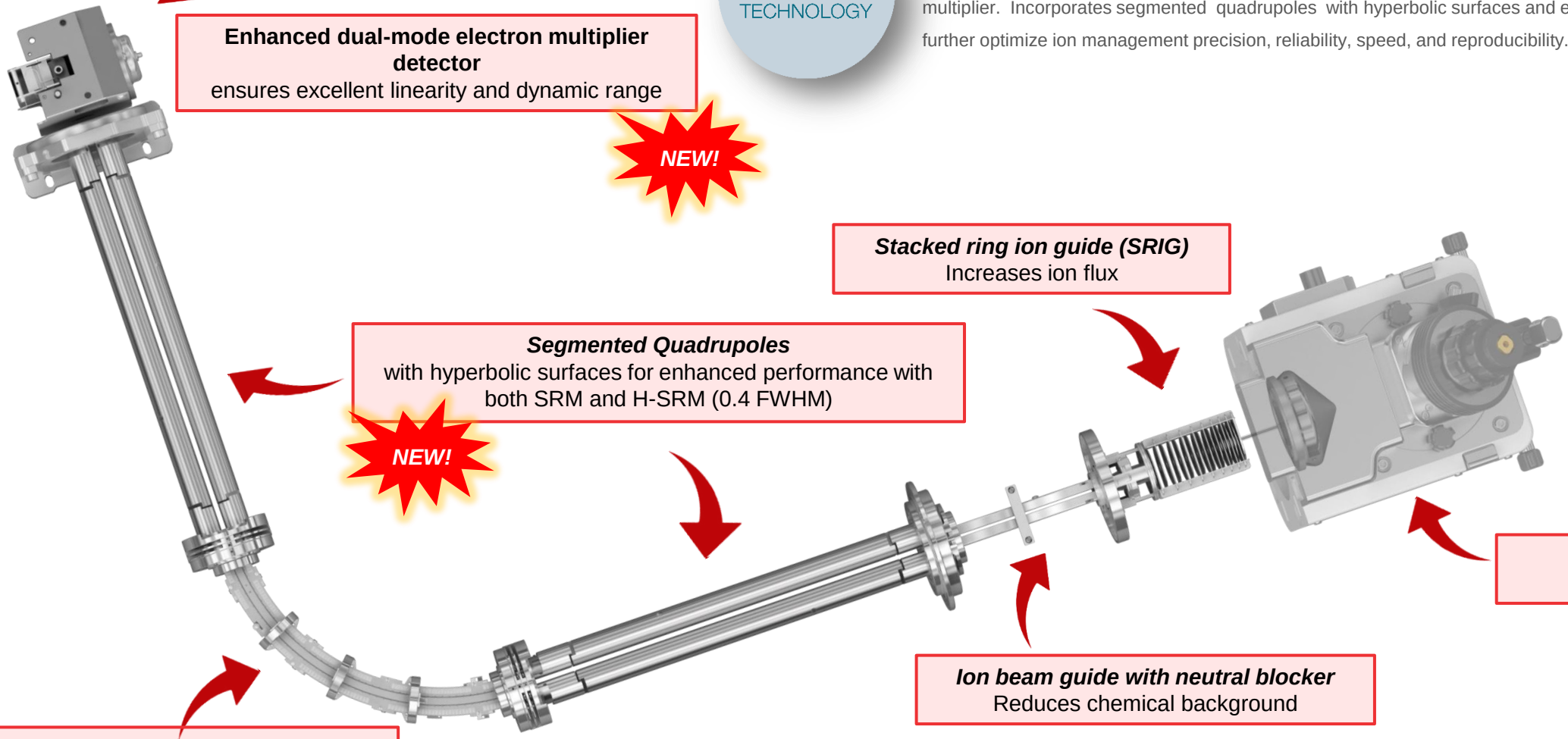
TSQ Quantis: Unprecedented Robustness, Day After Day

AIM+ TECHNOLOGY

Active Ion Management Plus (*AIM+*) - The next step in precision design delivers the ultimate in ion management, inception to detection, from the OptaMax™ ion source housing to the enhanced electron multiplier. Incorporates segmented quadrupoles with hyperbolic surfaces and enhanced RF Electronics to further optimize ion management precision, reliability, speed, and reproducibility.



Enhanced dual-mode electron multiplier detector
ensures excellent linearity and dynamic range

NEW!

Stacked ring ion guide (SRIG)
Increases ion flux

Segmented Quadrupoles
with hyperbolic surfaces for enhanced performance with both SRM and H-SRM (0.4 FWHM)

NEW!

OptaMax™ NG
APCI ready

NEW!

Ion beam guide with neutral blocker
Reduces chemical background

Active collision cell with axial DC field
facilitates more SRMs/sec

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Exactive Series 2.9 ICSW

This is a “one fits all” solution – suitable for all members of the Exactive Series family *

- Exactive Plus
- Exactive Plus EMR
- Q Exactive Focus
- Q Exactive
- Q Exactive Plus
- Q Exactive HF
- Q Exactive HF-X
- Q Exactive GC
- Exactive GC

Thermo Scientific Q Exactive HF-X representing the latest member of the Exactive Series instruments family

- **Exactive Series 2.9: P/Ns BRE0011868 and BRE0011869**

* (except Exactive MS)

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Thermo Scientific Q Exactive HF-X Hybrid Quadrupole-Orbitrap MS

Pushing the leading edge in protein analysis

- Revolutionizing insights, from discovery to verification
- Enhance your productivity
- Achieve faster than ever scan speed
- Confirm with greater confidence
- Superior consistency in quantitative accuracy, sensitivity and reproducibility
- Enhanced sensitivity of intact proteins with optional BioPharma option

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Q Exactive HF-X Specifications

Scan rate	Up to 40 Hz
Resolution	240,000 (FWHM) at m/z 200
Mass range	50 to 6,000 m/z Up to 8,000 m/z in BioPharma option
Mass Accuracy	3 ppm external, 1 ppm internal
Dissociation	Source CID, HCD
Multiplexing	Up to 10 precursor ions
Detectors	Orbitrap device
Polarity Switching	one full cycle in <1 sec (one full positive mode scan and one full negative mode scan at a resolution setting of 60,000)
Scan Functions	FS: Full Scan AIF: All Ion Fragmentation, SIM: Selected Ion Monitoring, PRM: Parallel Reaction Monitoring, DIA: Data Independent Acquisition, ddHCD: data dependent HCD
Options	BioPharma option

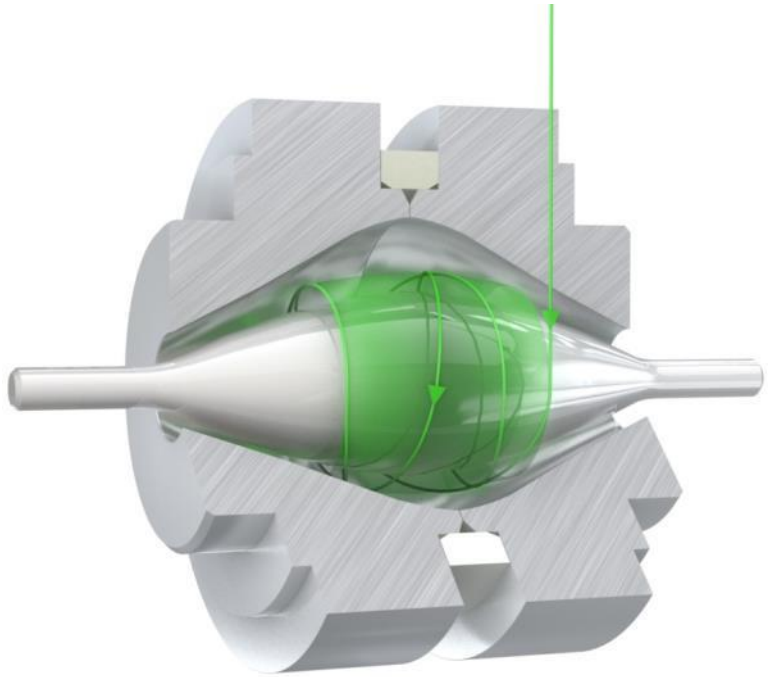
Thermo Scientific Q Exactive HF-X Hybrid Quadrupole-Orbitrap MS

Ultra-high field Orbitrap analyzer

- 40 Hz data acquisition speed
- 240,000 resolution at *m/z* 200

Novel architecture with a high capacity transfer tube and electrodynamic ion funnel

BioPharma Option for intact protein



Q Exactive HF-X – new architecture

Optimized Scan Matrix with accelerated HCD 40 Hz MS/MS

Advanced DDA for bottom-up and top-down

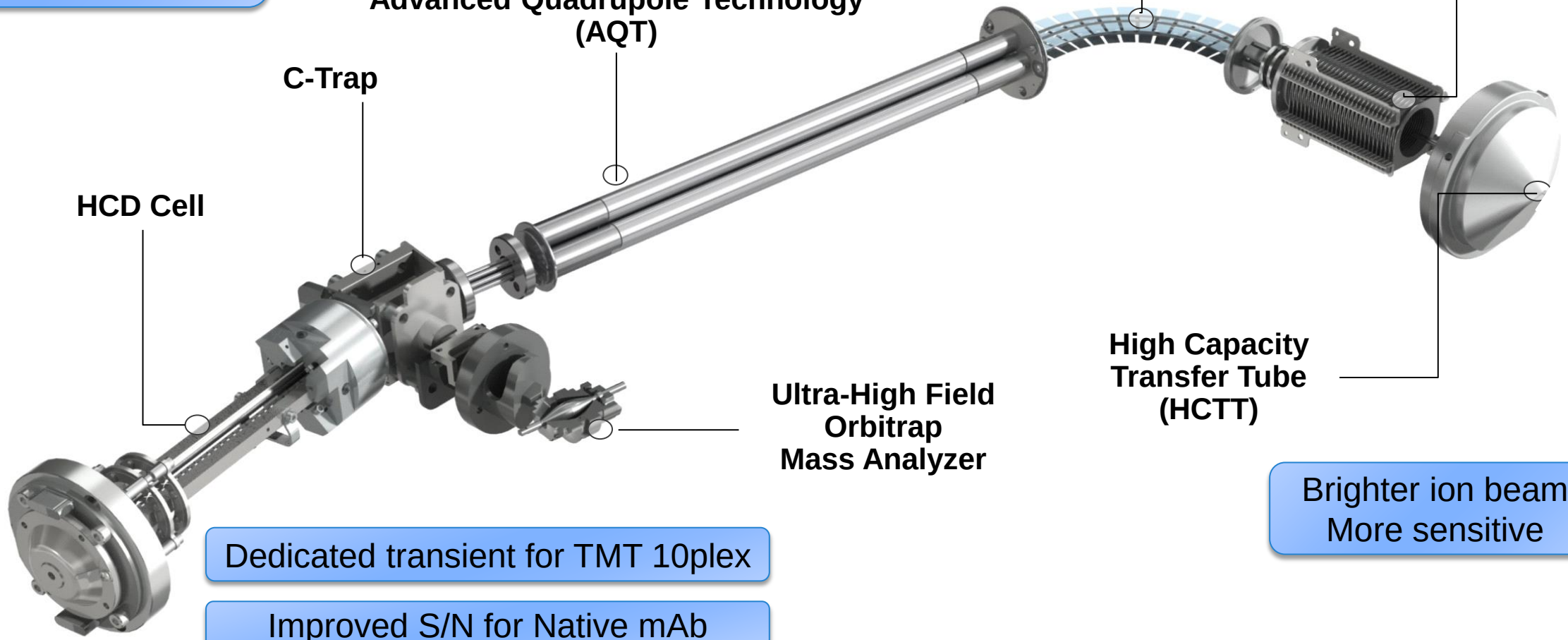
HyperQuad Mass Filter with Advanced Quadrupole Technology (AQT)

Advanced Active Beam Guide (AABG)

Electrodynamic Ion Funnel

C-Trap

HCD Cell



Ultra-High Field Orbitrap Mass Analyzer

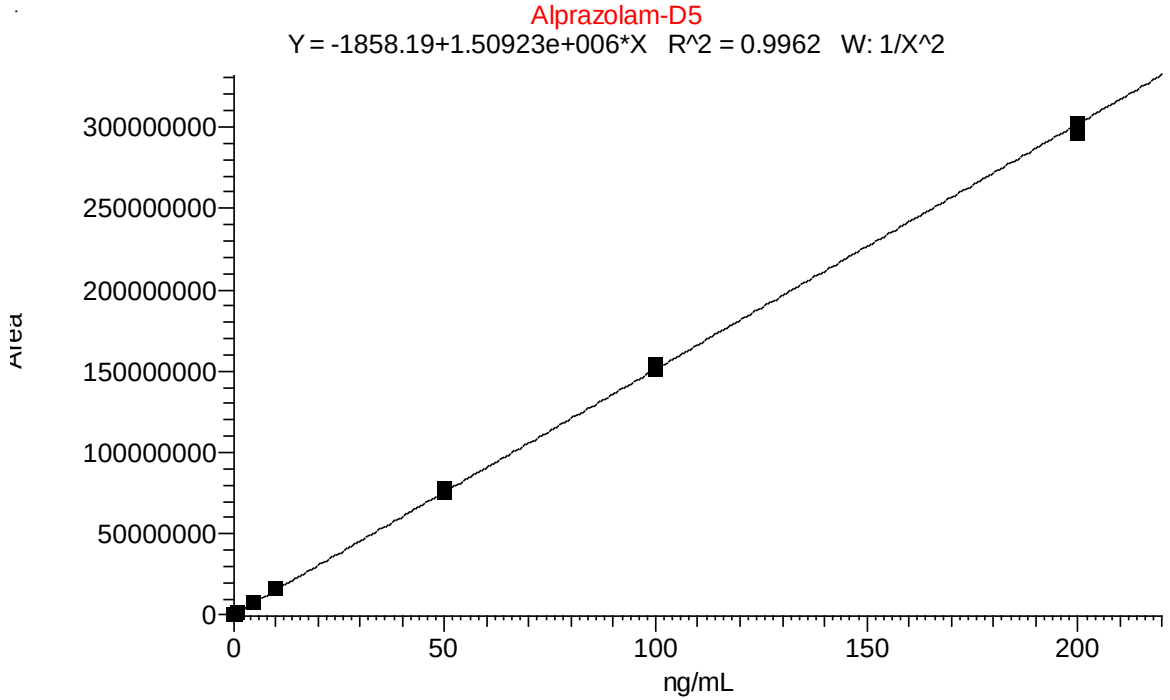
High Capacity Transfer Tube (HCTT)

Brighter ion beam
More sensitive

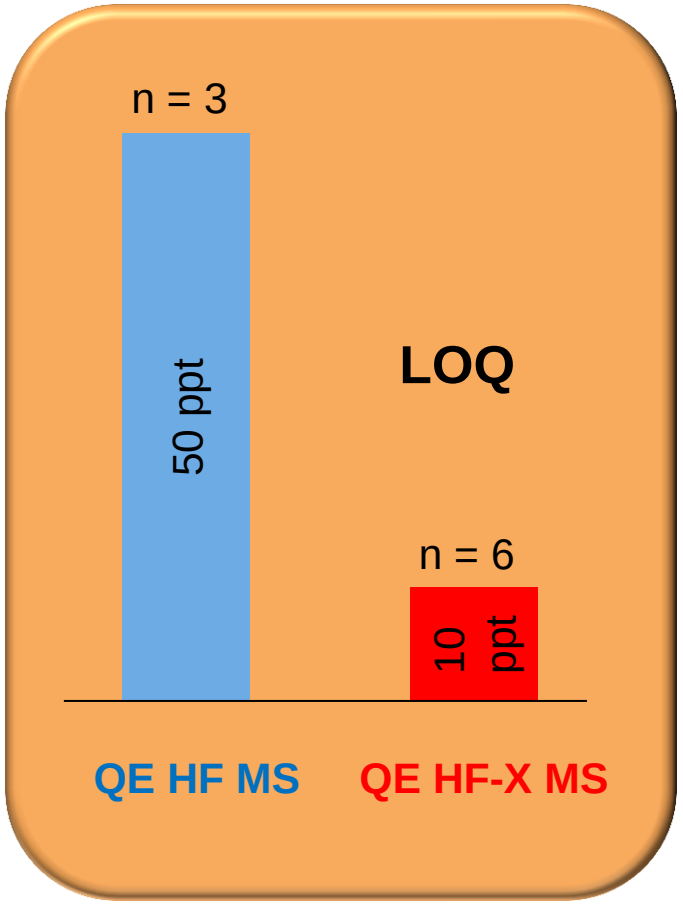
Dedicated transient for TMT 10plex

Improved S/N for Native mAb

Sensitivity and Linear Dynamic Range in Quantitation



- tSIM, Resolution 60K, maxIT 119ms, Iso 8 amu
- 3 replicates
- Sample: **Alprazolam** spiked into crashed plasma
- LOQ = 10 fg/µL = 10 ppt
- Range = 10 - 200,000 pg/mL



>10^4 linear dynamic range - LOQ at low ppt level

ASMS'17: TP 389, T.N. Arrey et al. New innovations implemented on the Q Exactive HF mass spectrometer.

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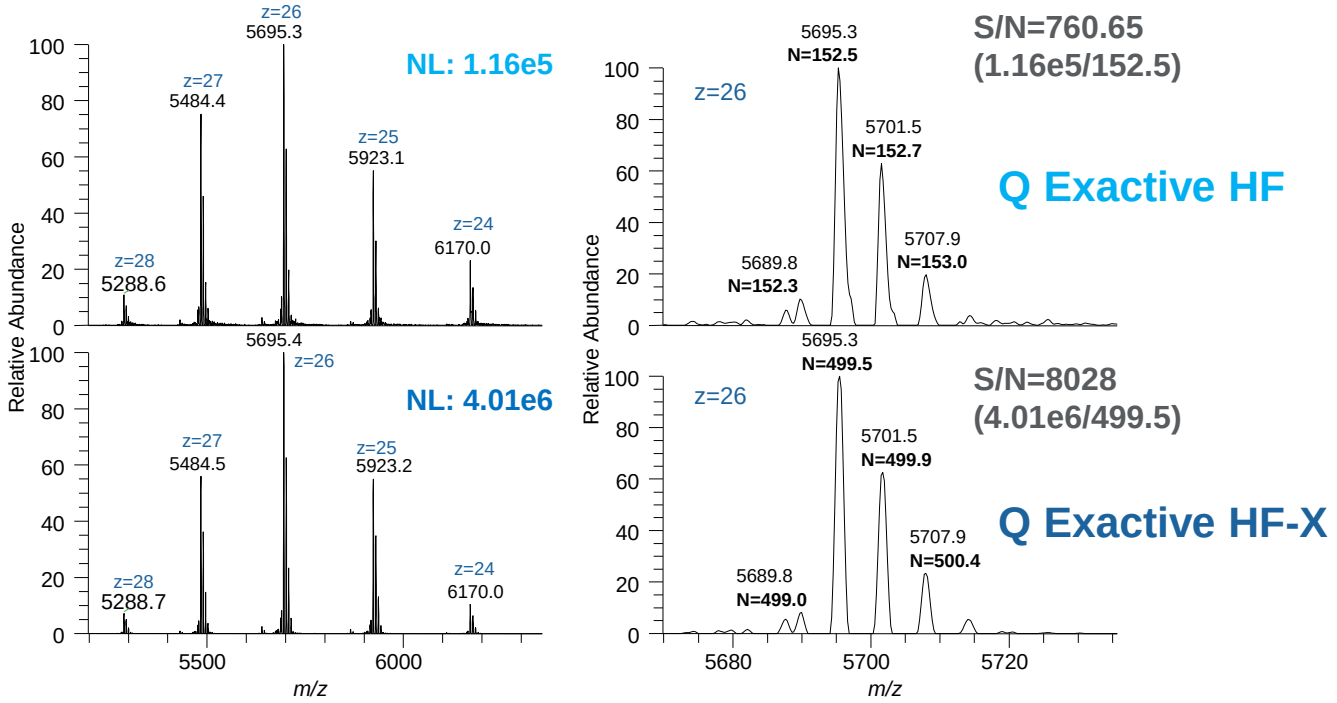
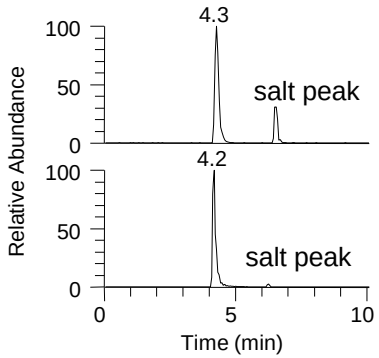
Analysis of Intact Trastuzumab under Native Conditions in HMR Mode

Improved S/N ratio on the Q Exactive HF-X by a factor of ~5-10.



TIC, size exclusion chromatography using Acclaim SEC column



SEC-LC/MS analysis of intact Trastuzumab monoclonal antibody using Acclaim SEC column, 4.6 x 300 mm, 300 µl/min flow rate, 50 mM ammonium acetate. Full MS, HMR mode, m/z 2500–8000, resolution setting 30k, 10 µscans. Spectra show an average of 3 scans (10 µscans each).

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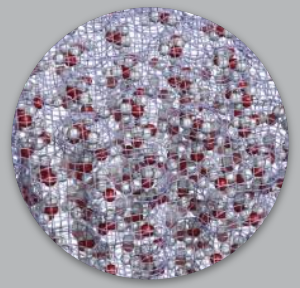
NEW on Orbitrap Fusion Lumos Tribrid Mass Spectrometer

06/05/2017

Challenges In Life Science Mass Spectrometry



Complex samples, insufficient depth of analysis

$C_{28}H_{35}NO_7S$
vs.
$C_{30}H_{32}N_3O_4P$

Isobaric analytes, confirmation of elemental composition

Comprehensive sequence characterization of protein drugs

Structural elucidation of lipids, metabolites, xenobiotics and others

Thermo Scientific™ Orbitrap Fusion™ Lumos™ Tribrid™ Mass Spectrometer is the most sensitive and versatile MS system

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ASMS 2017: NEW On Orbitrap Fusion Lumos MS

ADVANCED PEAK DETERMINATION ALGORITHM RESULTS IN SIGNIFICANT IMPROVEMENT IN PROTEOMICS EXPERIMENTS

APD

STANDARD ON NEW SYSTEMS
OPTIONAL ON EXISTING SYSTEMS

NEW
30 Hz
OT MS^2

UNIQUE FRAGMENTATION FOR TOP-DOWN AND SMALL MOLECULES CHARACTERIZATION

UVPD

OPTIONAL ON NEW AND EXISTING SYSTEMS

ULTRA-HIGH RESOLUTION FOR FINE ISOTOPE STRUCTURE

1M

OPTIONAL ON NEW AND EXISTING SYSTEMS

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Orbitrap Fusion Lumos MS with UV Photodissociation (UVPD)

Product Manager: Romain Huguet

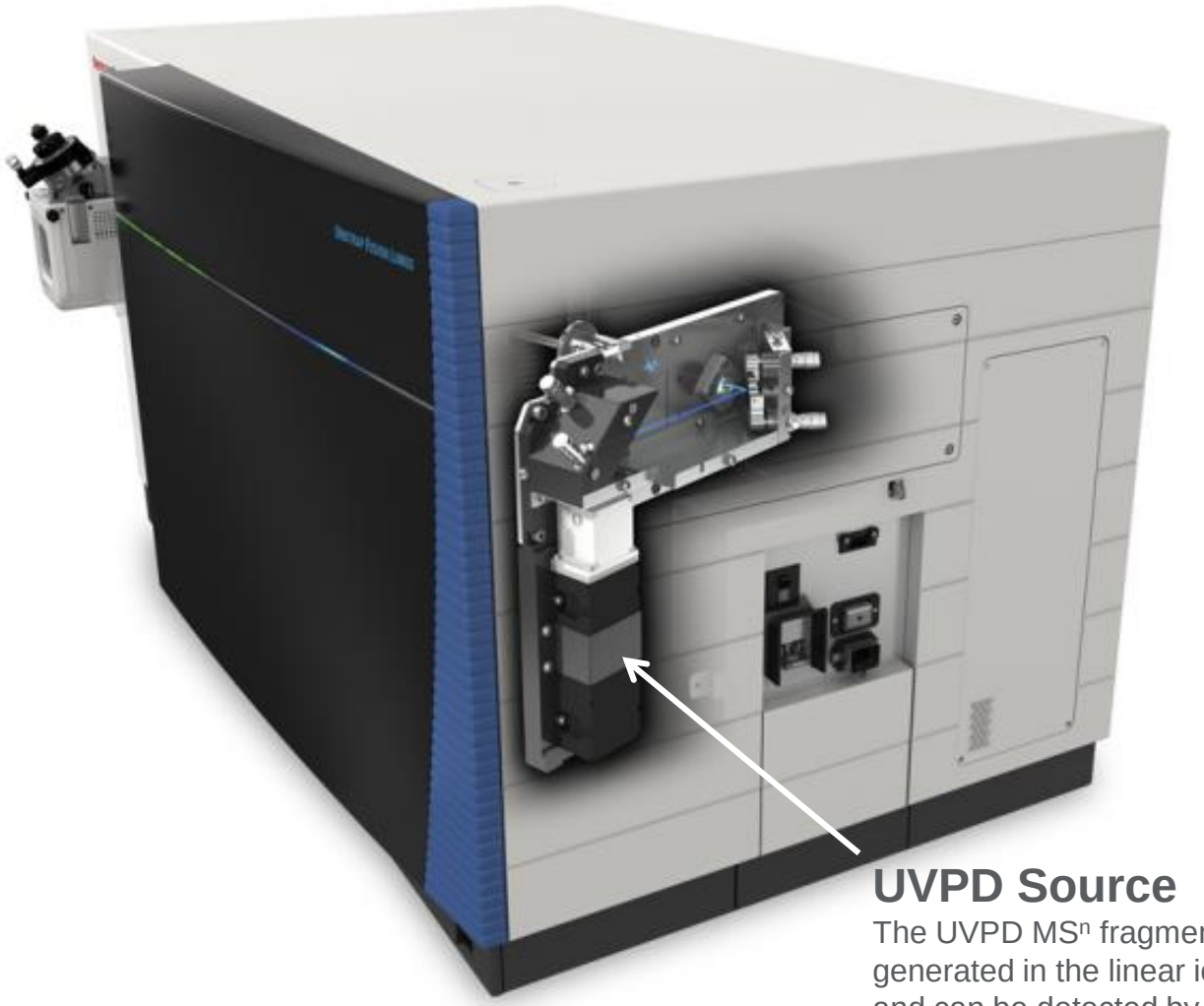
Challenge

Dissociation techniques currently available (CID, HCD and ETD) can be insufficient for comprehensive characterization of analytes of interest

UV Photodissociation (UVPD) option

- Provides unique fragments vs. other dissociations increasing sequence coverage of proteins
- Provides unique fragments when analyzing small molecules, including those around double bonds in lipids, allowing for complete characterization of molecular species vs. other methods
- Available only on Orbitrap Fusion Lumos MS

UVPD Implementation (Class 1 Laser System)



UVPD Source

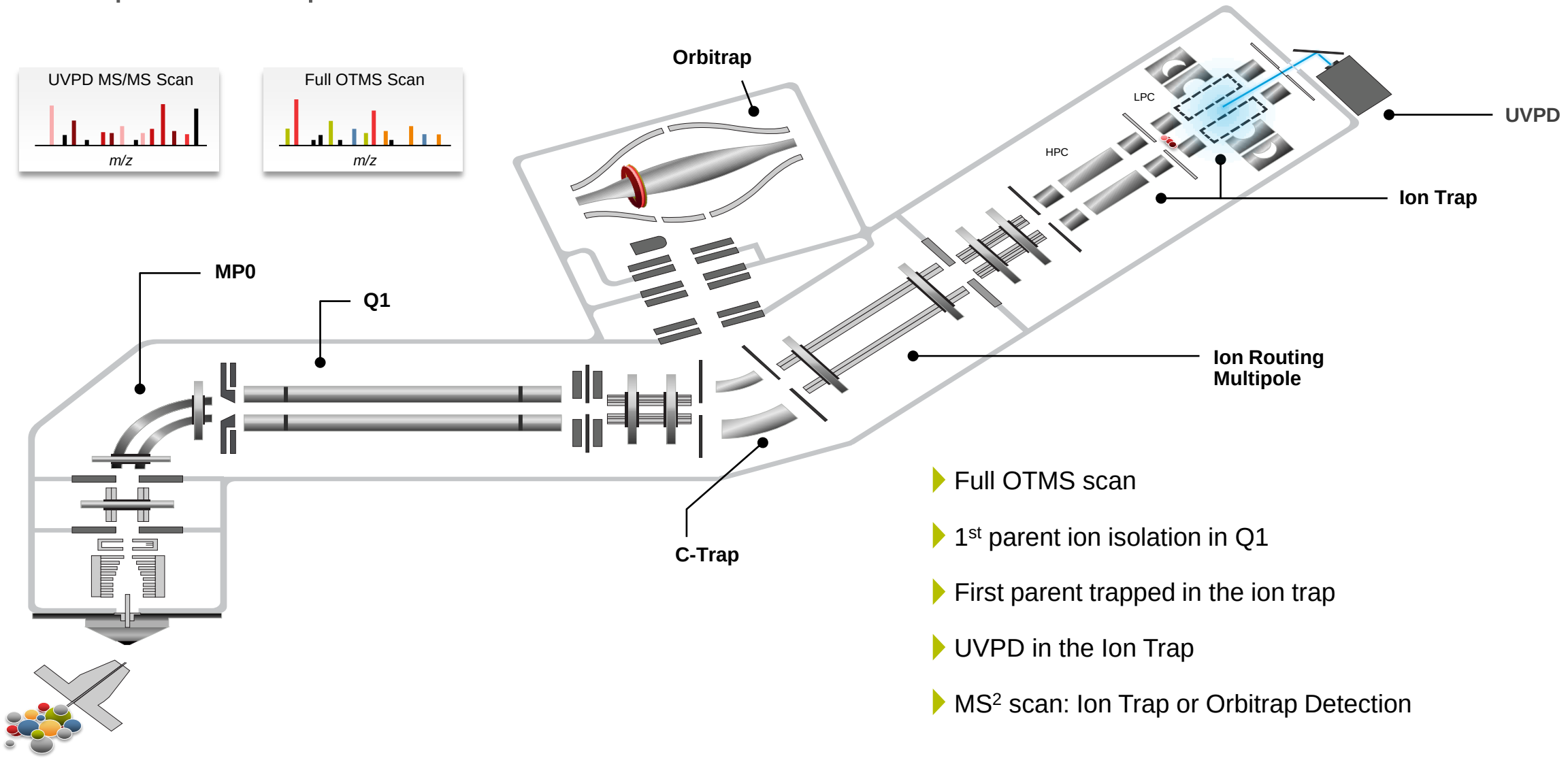
The UVPD MS^n fragments are generated in the linear ion trap and can be detected by either the ion trap or Orbitrap

Compact Footprint

- UVPD source is embedded inside the instrument, directly connected to the dual-pressure linear ion trap
- UVPD source employs a 213 nm laser with 2.5 kHz repetition rate delivering >1.2 µJ/pulse
- UVPD is a field upgradable option

UVPD Is Unique To The Orbitrap Fusion Lumos MS

Data Dependent Experiment: OTMS>UVPD OTMS^2



- Full OTMS scan
- 1st parent ion isolation in Q1
- First parent trapped in the ion trap
- UVPD in the Ion Trap
- MS^2 scan: Ion Trap or Orbitrap Detection

Example Applications Of UVPD

Comprehensive sequence characterization/confirmation of protein drugs

Identification and characterization of intact proteins by MS

Structural elucidation of lipids, metabolites, xenobiotics and others