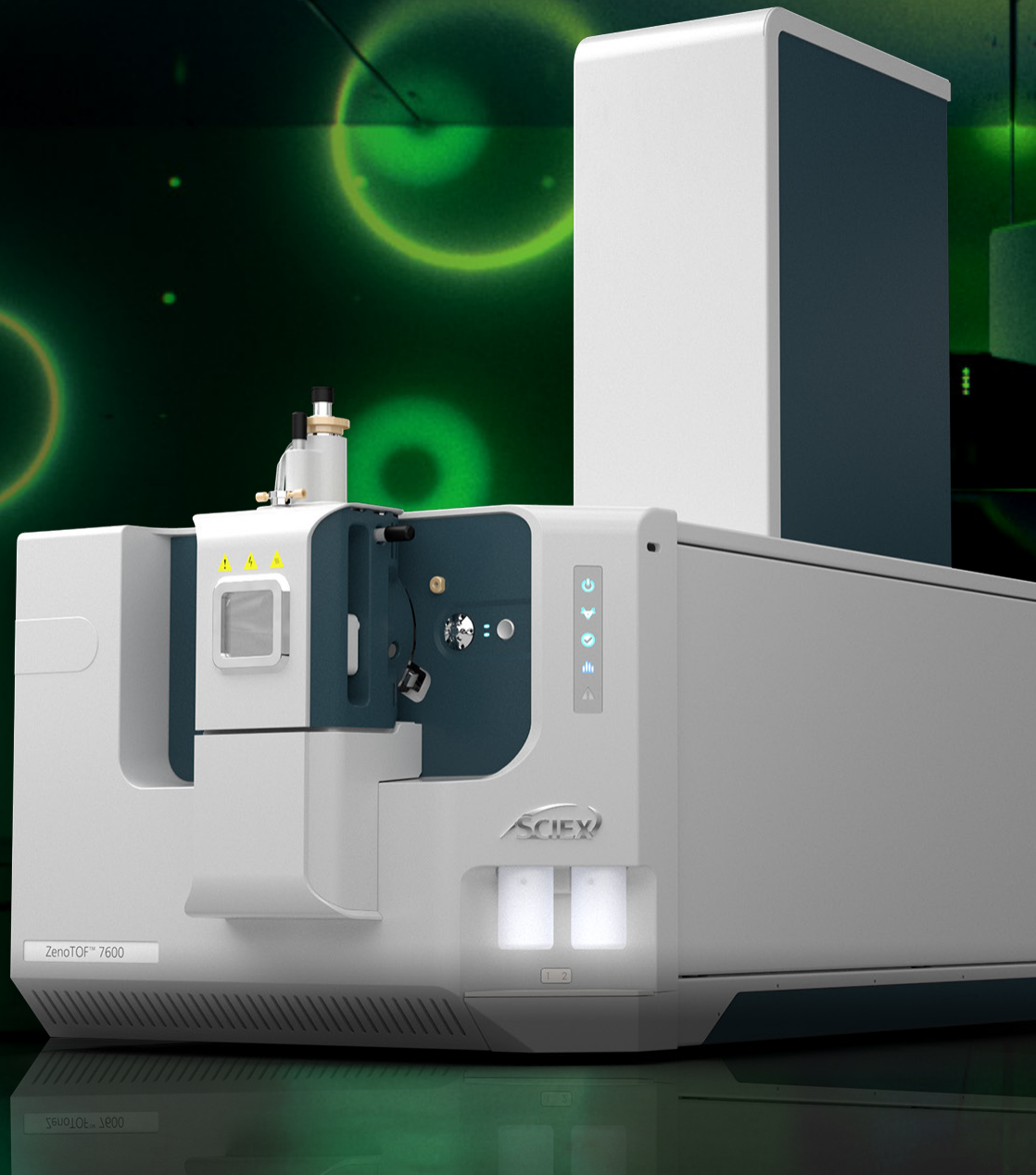
ZenoTOF 7600 system

The ZenoTOF 7600 system is an accurate mass spectrometry solution that combines powerful MS/MS sensitivity, innovative fragmentation technology and a step-change in data-independent acquisition (DIA).



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ZenoTOF 7600 system

Unlock sensitivity gains that reveal new, rare or even previously undetected information every day. A powerful leap in proprietary innovation, this accurate mass system combines the power of the Zeno trap with electron activated dissociation (EAD) fragmentation. Detect up to 20x more ions in every experiment and access a spectrum of tunable fragmentation techniques to uncover new perspectives for every molecule, in every experiment. And now, Zeno SWATH DIA capitalizes on these gains, revealing tens, hundreds and even thousands more identified and quantified analytes in a shorter time, and with higher precision than ever before. Reaching new depths of coverage, Zeno SWATH DIA delivers maximal information in minimal time.

Zeno SWATH DIA

Get high-quality, high-resolution MS/MS data for large-scale quantitation and identification, with high sensitivity and fast acquisition speed.

Ion sources

Compatibility with advanced source designs that minimizes contamination and allows you to obtain fast, automated calibrations across flow rate ranges.

Sources and flow rates supported include:

- Turbo V ion source
  - ESI: 5µL/min to 3mL/min
  - APCI: 200µL/min to 3mL/min
- OptiFlow Turbo V ion source
  - Microflow: 1µL/min to 200µL/min
  - Nanoflow 100nL/min to 1,000nL/min

Software

Powered by SCIEX OS software, intuitive algorithms and automation enable you to make informed decisions quickly. Transform your LC-MS/MS workflows with remarkable quantitative usability, efficiency and integrity that streamline your entire lab.

Zeno trap

Gain more useful MS/MS information in every experiment, particularly on lower abundance species, with a 5-20x gain in MS^2 sensitivity coupled with either EAD or collision-induced dissociation (CID) fragmentation.

Electron activated dissociation (EAD)

Fine-tune the fragmentation energies specific to your molecules of interest, and acquire key MS/MS features for large molecules, peptides, lipids and small molecules.

Calibration delivery system

A new calibration solution automates mass calibration and helps ensure that the accuracy of the system is maintained throughout acquisition.

A new mindset in accurate mass LC-MS/MS technology

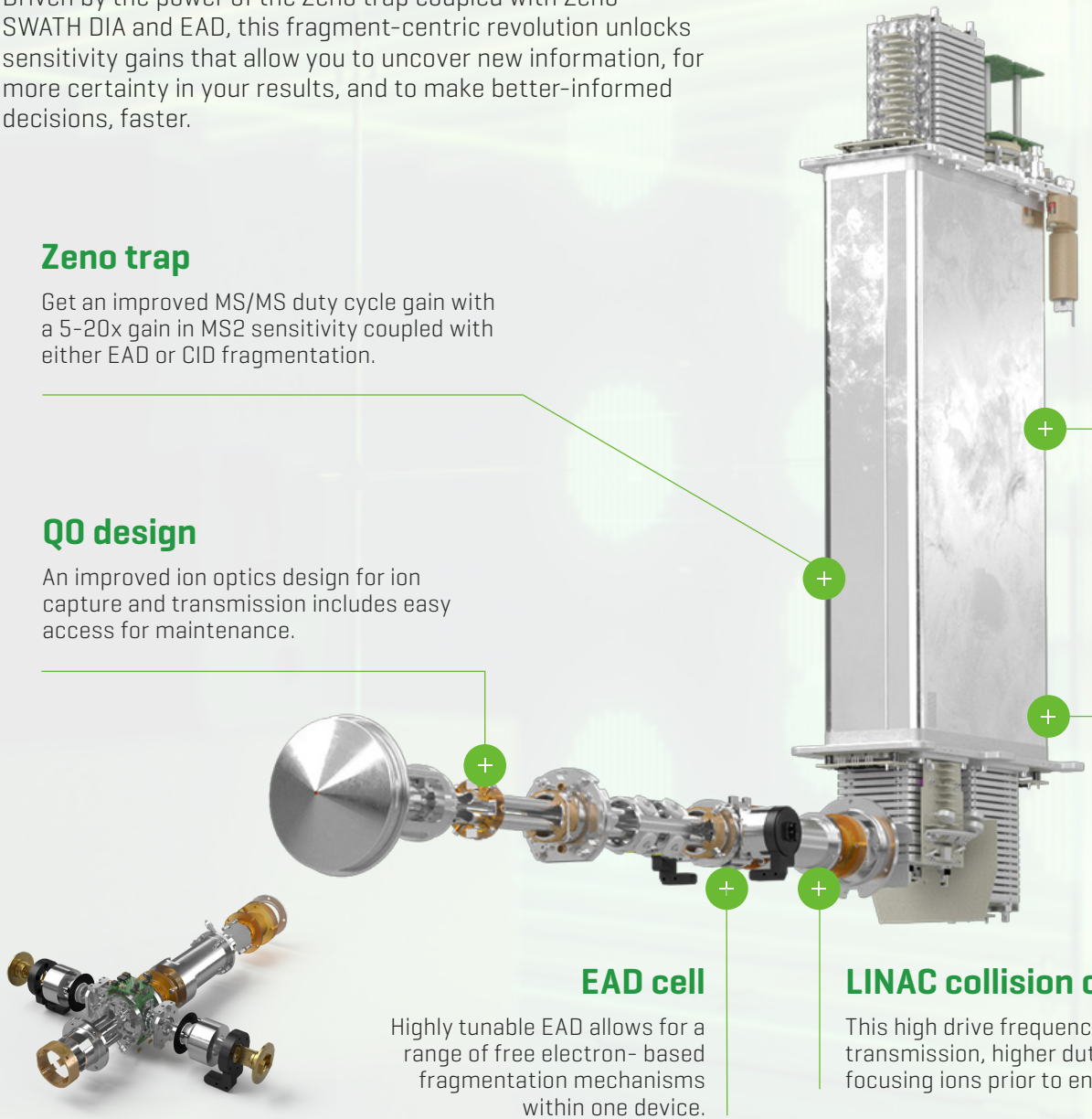
Driven by the power of the Zeno trap coupled with Zeno SWATH DIA and EAD, this fragment-centric revolution unlocks sensitivity gains that allow you to uncover new information, for more certainty in your results, and to make better-informed decisions, faster.

Zeno trap

Get an improved MS/MS duty cycle gain with a 5-20x gain in MS2 sensitivity coupled with either EAD or CID fragmentation.

QO design

An improved ion optics design for ion capture and transmission includes easy access for maintenance.



TOF

An N-optic TOF design provides optimal mass accuracy and resolution without compromising sensitivity.
Features include:

- Heated TOF path and drone heaters
- Mass range: 40 to 40 kDa in TOF
- Resolution: ≥42,000 at m/z 956
- MS/MS speed: 133 Hz
- Mass accuracy: <2 ppm RMS (external), <1 ppm RMS (Internal)
- Positive and negative linear dynamic range (LDR): interscan LDR of 5 orders of magnitude

Zeno SWATH DIA

Gain 6-10x more MS/MS sensitivity, which amounts to a ~1.7–3x increase in proteins identified and a 3–6x increase in proteins quantified at loads <20 ng.

EAD cell

Highly tunable EAD allows for a range of free electron- based fragmentation mechanisms within one device.

LINAC collision cell

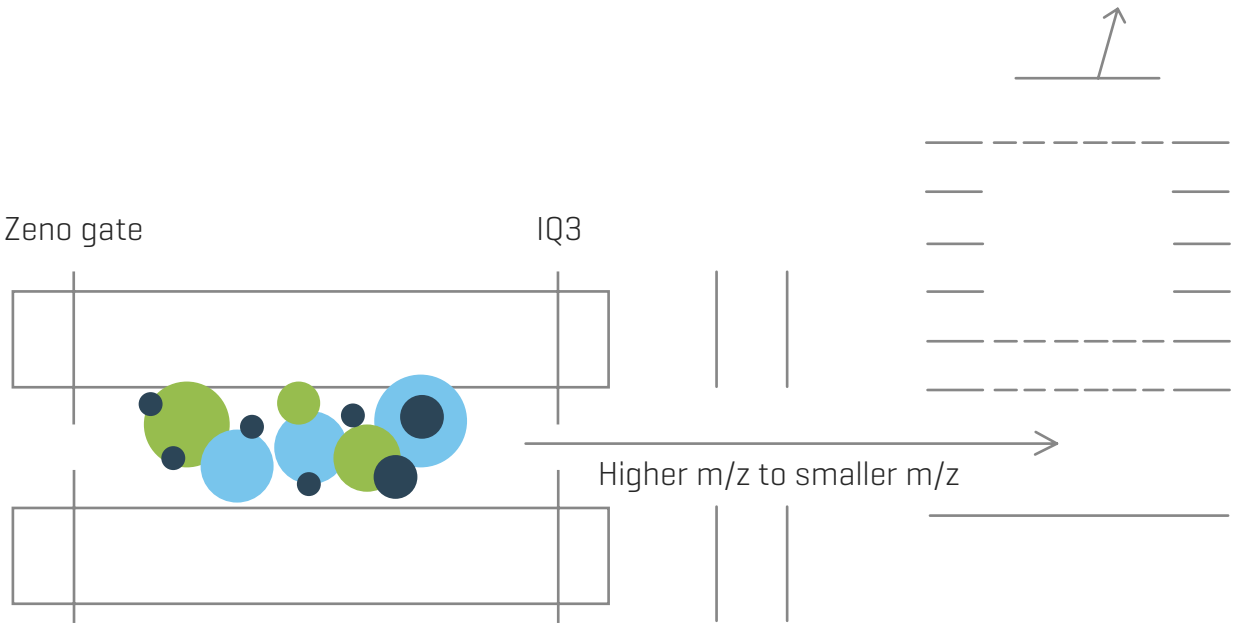
This high drive frequency collision cell provides a better ion transmission, higher duty cycle and improved resolution by focusing ions prior to entering the TOF accelerator.

The Zeno revolution is now

The ZenoTOF 7600 system is an accurate mass spectrometry solution that combines **powerful MS/MS sensitivity**, innovative **fragmentation technology** and a step-change in **DIA** enabling you to:

- Characterize large molecules, including post-translational modifications (PTMs)
- Elucidate positional isomers on small molecules and lipids
- Identify and quantify proteins and peptides at unparalleled speed
- Deliver a high depth of coverage, particularly on low abundance species, quickly and robustly

- **Overcome QTOF MS/MS duty cycle deficiencies** with >90% ions injected into the TOF
- **Achieve sensitivity gains of 50–20x with Zeno trap**
- **Identify and quantify low abundance species**
- **Enable tunable fragmentation of all molecule types**
- **Utilize controlled EAD**
- **Reach MS/MS scan rates of up to 133 Hz**
- **Improved DDA, DIA and MRM^{HR}**



All ions enter the TOF at the same time, achieving >90% duty cycle

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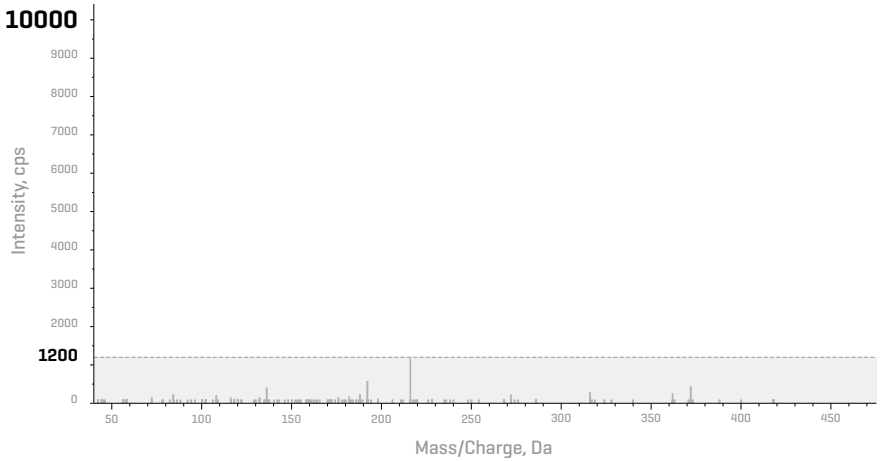
Zeno trap

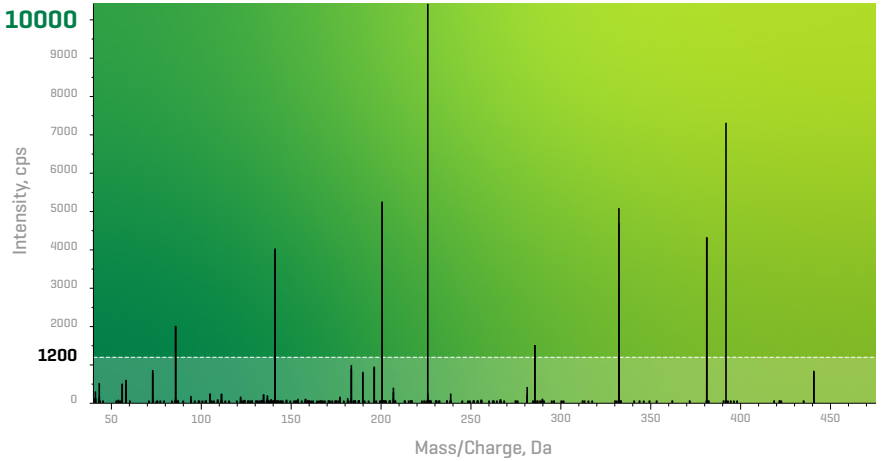
The next era of sensitivity for accurate mass

Ions are accumulated in the Zeno trap before being pulsed rapidly into the TOF, meaning up to 20x more fragment ions can be detected. Enabled by a new level of sensitivity, each MS/MS experiment contains more useful information-particularly on lower abundance species that were previously undetectable-than ever before.

Without the Zeno trap pulsing



With the Zeno trap



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Zeno SWATH DIA enabled by the Zeno trap

Learn more →

Zeno SWATH DIA combines the power of the Zeno trap with SWATH DIA. Similar to SWATH DIA, Zeno SWATH DIA identifies and quantifies analytes using MS/MS data. Thus, the rapid acquisition of high-quality MS/MS data across the entire precursor ion space is fundamental to operation.

In Zeno SWATH DIA, the Zeno trap, when activated, is used to increase the MS/MS sensitivity for each variable window acquired. The Zeno trap provides a 4-20x gain in sensitivity for Zeno SWATH DIA, while also maintaining other key performance attributes.

Fast scan rate

Zeno SWATH DIA uses the combination of fast scanning and detection to maximize the total number of high-quality MS/MS spectra generated per cycle. This enables a higher number of variable windows, which increases specificity and, therefore, confidence in the total number of identified and quantified analytes. Faster scanning also enables the use of shorter LC run times, greatly improving throughput and laboratory productivity.

Resolution and mass accuracy

Co-eluting isobaric analytes, contaminants and high background noise can interfere with the quantitation of analytes, especially at the MS level, even when using very high-resolution instruments. Zeno SWATH DIA maximizes the accuracy and precision of quantitation by utilizing the selectivity of MS/MS. When combined with the highest scan rates, these attributes (mass resolution and accuracy) are preserved to maintain the maximum number of identified and quantified analytes.

Dynamic range

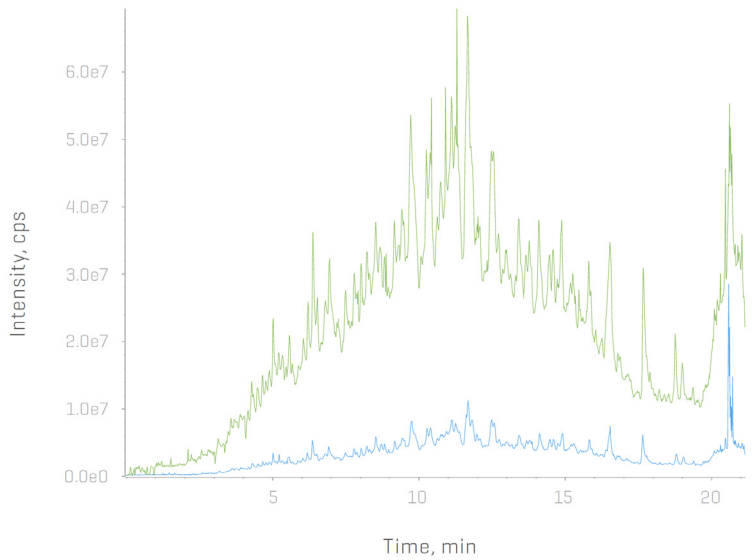
Both intrascan and interscan dynamic ranges are important for identification and quantitation. Zeno SWATH DIA features a wide intrascan LDR that allows low-level analytes to be detected in the presence of high-abundance analytes within the same scan, without peak distortion or saturation. Additionally, Zeno SWATH DIA possesses a wide interscan LDR, allowing analytes that span a range of abundances to be detected and quantified within a single run.

Zeno SWATH DIA

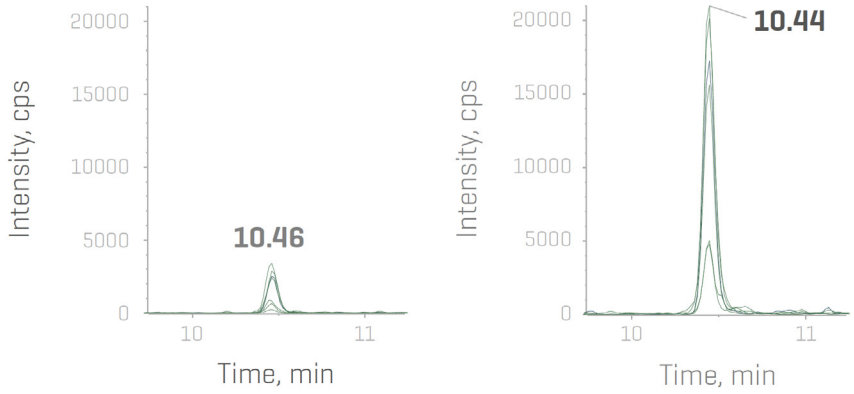
Learn more →

The 4—20x increase in MS/MS sensitivity that the Zeno trap provides while maintaining all other critical performance specifications, translates into more high-quality MS/MS spectra.

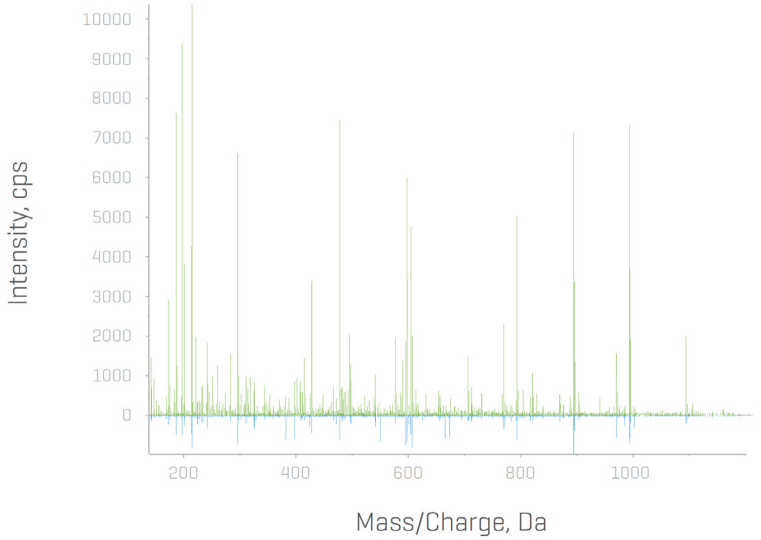
With Zeno SWATH DIA, this translates the raw MS/MS spectra into the MS/MS extracted ion chromatograms (XICs) and to the total peptide ion current.



Total ion chromatograms (TICs) with and without the Zeno trap activated: SWATH DIA (bottom, blue) and Zeno SWATH DIA (top, green).



MS/MS XICs with and without the Zeno trap activated for peptide ITVTSEVPFSK (P35268): SWATH DIA (left) and Zeno SWATH DIA (right).



MS/MS spectra with and without the Zeno trap activated for peptide ITVTSEVPFSK (P35268): SWATH DIA mirror (bottom) and Zeno SWATH DIA (top).

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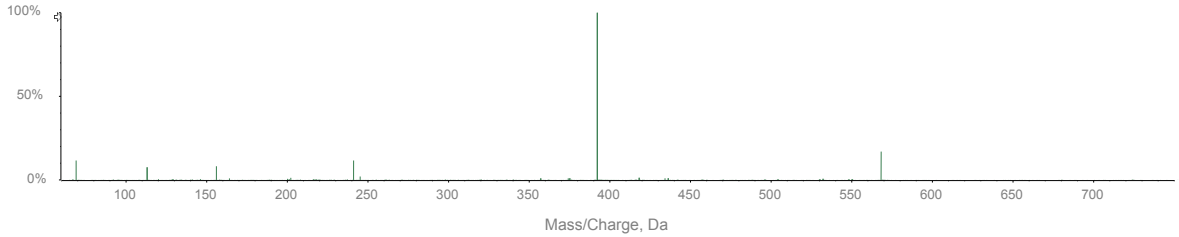
The Zeno revolution is now

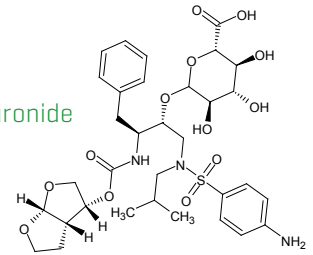
A step change in fragmentation technology: using EAD when CID is not enough

The ability to tune electron kinetic energy extends the utility of the approach to all molecule types, from singly charged small molecules to large multiply charged proteins. EAD allows for a range of reagent-free electron-based fragmentation mechanisms with a single device, and it has the capability to fragment peptides while retaining critical MS/MS information for both identification and localization of PTMs. Unlike other electron-based fragmentation techniques, EAD delivers reproducible, consistent data, even at fast scan speeds, and it is compatible with UHPLC time frames, delivering higher efficiency than electron-transfer dissociation (ETD). In this instrument, geometry coupling EAD with the Zeno trap allows for detection of very low abundant diagnostic fragment ion species, leading to greater sequence coverage.

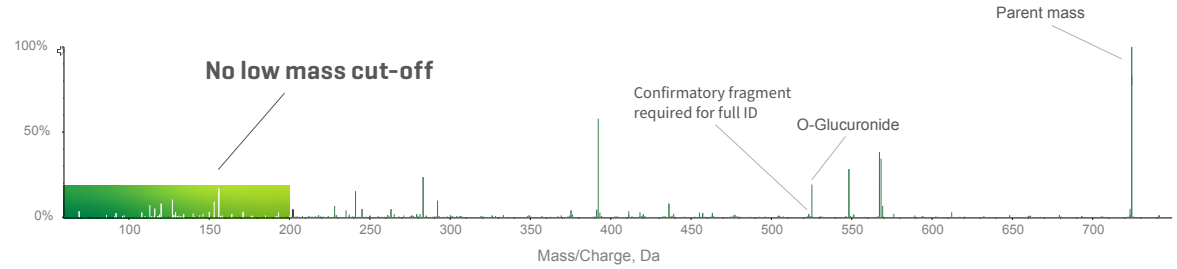
Zeno CID



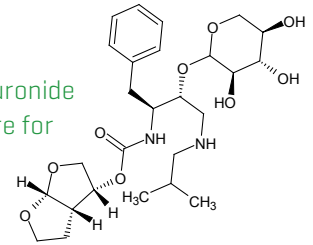
Darunavir-o-glucuronide



Zeno EAD



Darunavir-o-glucuronide fragment structure for confirmation



The EAD spectrum produces an important fragment ion with the glucuronide preserved, which allows localization of the glucuronide modification. Also, low mass fragment ions are preserved by using a QTOF-based platform.

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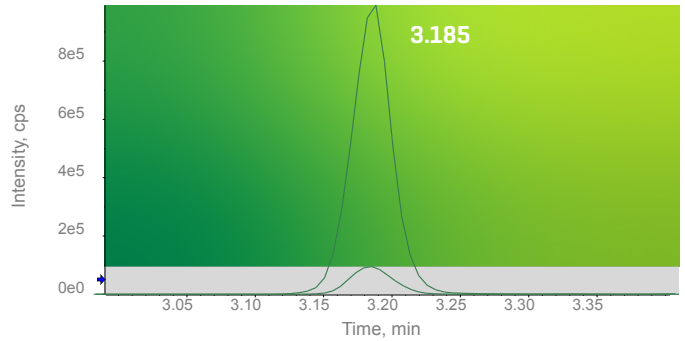
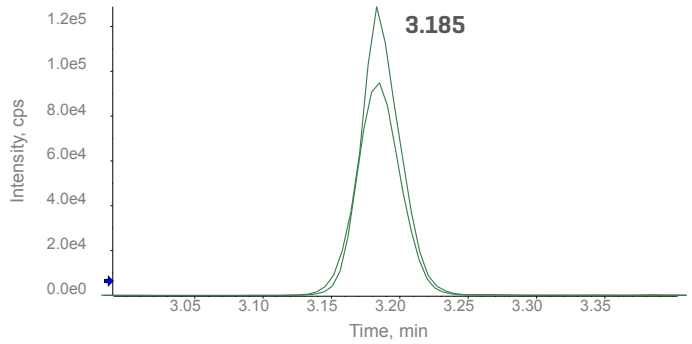
Zeno MRM^{HR} unlocks new levels of sensitivity

Zeno trap activation on demand gives the ability to detect lower abundance ions at the same times as those in abundance, redefining the limits of quantitation achievable with accurate mass. MRM^{HR} is a targeted approach that delivers high sensitivity and selectivity for screening and targeted quantitation

Small molecule

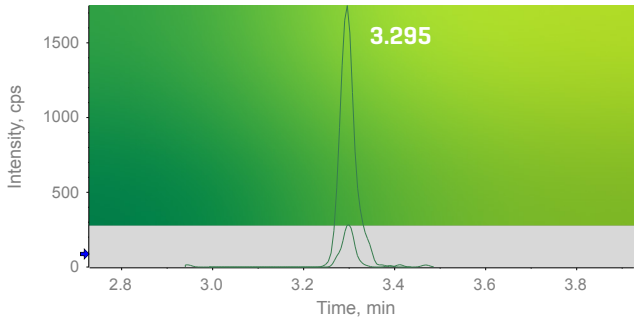


Targeted metabolite quantitation - Significant sensitivity gains in MS/MS. Comparison of extracted ion chromatograms (XICs) for cAMP fragments obtained from MS/MS collect with Zeno trap on vs. Zeno trap off. Signal/noise ratio improved ~12.5 fold when using the Zeno trap.

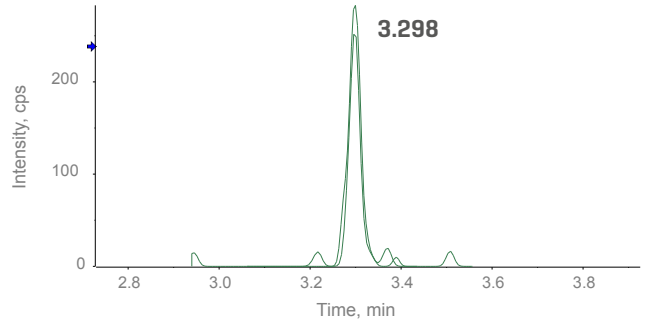


Better sensitivity in MS/MS with 10x less sample. Comparison of XICs for cAMP fragments obtained from MS/MS collect with Zeno trap on (0.2 µL injection) vs. Zeno trap off (2 µL injection).

Peptide quantitation



Targeted peptide quantitation - Significant sensitivity gains in MS/MS. Comparison of XICs for LILTLTHGTAVC[CAM]TR fragments obtained from MS/MS collected with Zeno trap on vs. Zeno trap off. Signal/noise ratio improved ~8 fold when using the Zeno trap.



Better sensitivity in MS/MS with 8x lower concentration. Comparison of XICs for LILTLTHGTAVC[CAM]TR fragments obtained from MS/MS collect with Zeno trap on vs. Zeno trap off. Zeno trap off at 6.18ng/mL and Zeno trap on at 0.757 ng/mL.

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Software that powers the modern laboratory

The ZenoTOF 7600 system is powered by the fully integrated SCIEX OS software, which acquires, processes and reports your accurate mass data. Since its launch, SCIEX OS software continues to evolve its functionality to meet the ever-expanding challenges and opportunities of analytical science.

Consistency, accuracy and connectivity are present throughout all the workspaces in SCIEX OS software, along with powerful algorithms and automation that will enable you to cut through complexity, straight to insight. SCIEX OS software streamlines your lab, delivering high-quality, actionable data for a wide range of applications. With SCIEX OS software, you can:

- Use a single platform for acquisition, processing and data management
- Customize the software for specific workflow requirements
- Enable routine and easily transferable method development transferable
- Increase efficiency and reduce method maintenance with scout triggered (stMRM)
- Configure workstations, user roles, permissions, projects and workgroups from a single workstation with the Central Administrator Console

"In new innovations, the software is key, as the software enables the creation of results. Software that integrates data acquisition, processing, interrogation and reporting gives added value in terms of the efficiency with which these results can be generated."

LIEVE DILLEN
Senior Principal Scientist for Assay Development and Analytical Support, Development Bioanalysis group, Janssen R&D, Belgium

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Delivering insight

Software is the vital connector between technology and insights that will drive discovery. Whether you are characterizing potentially complex proteins, routinely screening or quantifying modalities in complex matrices, they each require advanced data processing technologies to interrogate data and deliver actionable insight. The ZenoTOF 7600 system is powered by a suite of software tools that will help you make these discoveries within your existing data pipeline.

SCIEX OS software empowers you with more than just processing. Take advantage of automated functionality, library management and audit trails for compliance. Get all the tools you need for any LC-MS/MS workflow, from routine to the most complex, in a single location

Learn more>.

Big data needs the power of the cloud to process it. Whether you are conducting proteomics, metabolomics or genomics research the **OneOmics suite** has the power, precision and capacity to derive insight from large multi-omics cohorts. One cloud. Countless opportunities.

Learn more>

Achieve clarity with your biotherapeutic by Leveraging the latest acquisition techniques. Built on a heritage of proven performance, **Biologics Explorer software** delivers highly accurate and informative workflows for fully characterizing protein biotherapeutics. Reach decisions on the most important critical quality attributes for biopharmaceuticals faster and with more confidence

Learn more>

Molecule Profiler software delivers a highly accurate and flexible workflow for impurities and biotransformations for a wide variety of therapeutic molecules,. Built into the architecture of SCIEX OS software, Molecule Profiler software ensures a seamless acquisition and data analysis experience.

Learn more>

To gain valuable insight into any trends within their mass spectral data, many scientists will visualize their data by performing PCA and statistical analysis on large data sets, MarkerView software enables SCIEX users to quickly and efficiently explore statistical correlations with direct connections back to the raw data. **MarkerView software** is now incorporated into the evolving SCIEX OS software ecosystem and provides a single software solution for find meaningful relationships more rapidly, reducing cross-platform navigation.

Learn more>

Third Party software compatibility:

PROTEIN METRICS Clearing the Path for Analytical Scientists

Mass-MetaSite HIGH-THROUGHPUT METID

Genedata solutions in silico

Spectronaut™ Pulsar

Skyline

PEAKS

The ZenoTOF 7600 system in action
application examples

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Zeno SWATH DIA for higher-throughput proteomics

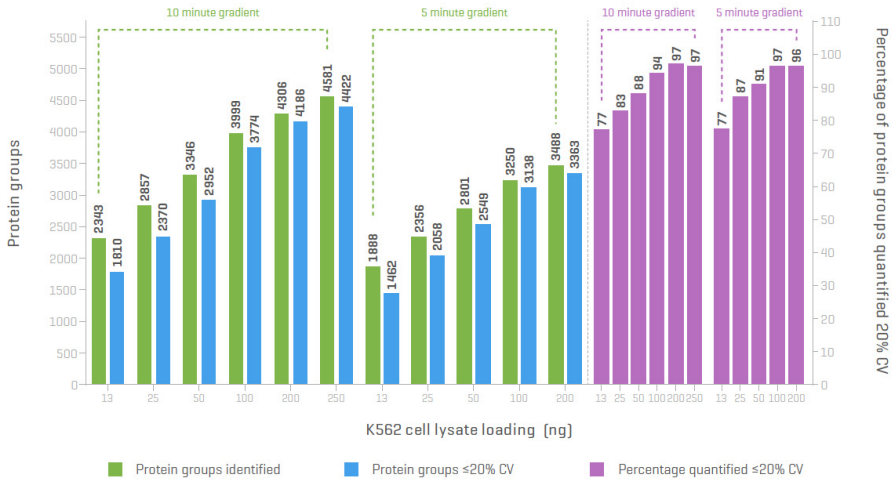
Because of its depth of proteome coverage and quantitative reproducibility, SWATH DIA has quickly become the method of choicefor large-scale proteomics studies. Zeno SWATH DIA takes this a step further with the added sensitivity gains that the Zeno trap provides. With its increased sensitivity, Zeno SWATH DIA now opens the door for fast and precise large-scale proteomics studies using higher flow rates and lower sample loadings.

With Zeno SWATH DIA, you can:

- Identify and quantify up to 2x as many proteins compared to traditional SWATH DIA approaches
- Shorten ru ntimes to as little as 5 minutes with minimal compromise in proteome coverage
- Reduce sample size to a tenth or twentieth with low loads of 10 ng

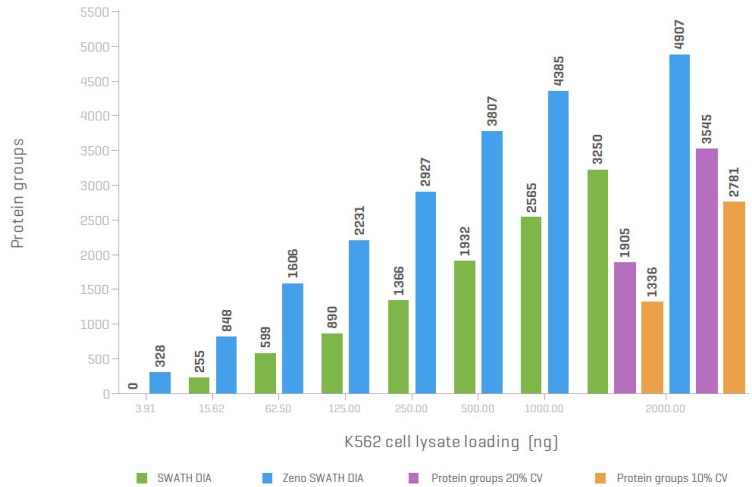
Learn more →

K562 cell lysate protein groups identified and quantified using fast gradients



Comparing 10 min and 5 min gradients. The number of proteins identified at <1% FDR and quantified at <20% CV across a range of loadings was studied. 80-90% of proteins identified are also quantified with these fast gradients.

Comparison of SWATH DIA and Zeno SWATH DIA at analytical flow rates



Comparison of SWATH DIA with Zeno SWATH DIA for high flow rate proteomics experiments (K562 using 800 µL/min, 5 min gradient). Left: Zeno SWATH DIA identifies and quantifies significantly more proteins and peptides than SWATH DIA across many different sample loading amounts. Right: Comparison of average number of IDs across 3 replicates (faint gray), number of consistent IDs (dark gray), quant < 20% CV (medium gray), quant < 10% CV (light gray).

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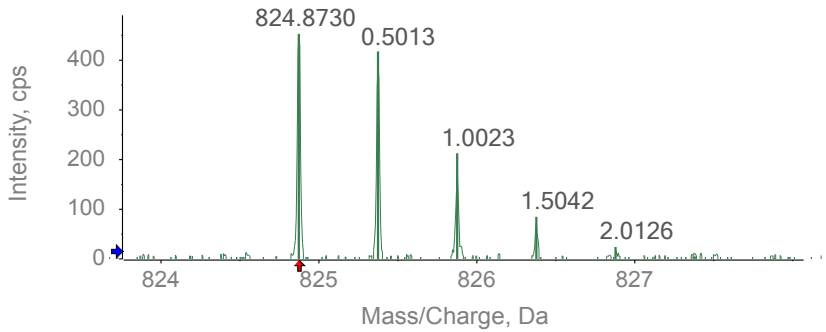
Over 40% more proteins identified using Zeno MS/MS

Utilizing high-throughput microflow methodologies, the ZenoTOF 7600 system breaks through the 3,000 protein groups in 21 minutes for the first time. Unique Zeno trap activation provides significant gains in peptide and protein identifications for proteomics experiments. Protein identifications improved by up to ~45% and peptide identifications improved by up to 145% comparedto previous TripleTOF systems.

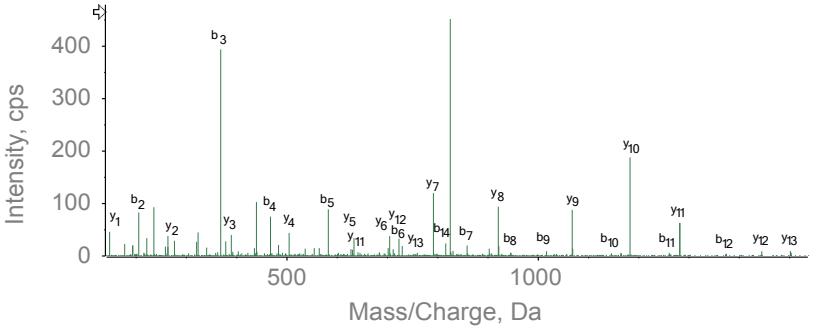
Read technical note →

Zeno DDA



Impact of using the Zeno trap for DDA. The TOF MS is shown for a peptide at 25 ng sample load, which was triggered for the Zeno MS/MS. The isotopic fidelity is shown up to the M+4 isotope.

Zeno MS/MS



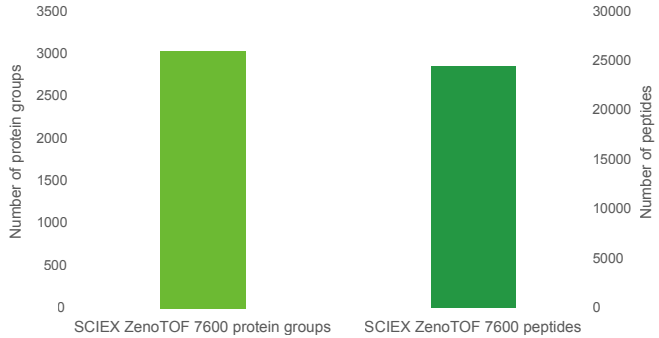
Impact of using Zeno trap for IDA. The Zeno CID MS/MS is shown for the precursor in figure 15. For a low abundant precursor a high quality MS/MS for identification is acquired with near complete sequence coverage and excellent signal to noise.

Peptide and protein gains

	Gradient duration (min)	1000 ng
Peptide Gains	10	72%
	45	145%
Protein Gains	10	41%
	45	46%

The impact of the Zeno trap on CID DDA over previous platforms is shown. Significant improvements in both peptide and protein numbers are observed at short and medium gradient lengths.

Peptide and protein IDs for HeLa at 500 ng on 60 SPD method*



Routinely achieving high protein and peptide identifications at high throughput is difficult. When coupled with a highly reproducible microflow solution, the ZenoTOF 7600 system drives significant protein and peptide identifications, breaking through >3,000 protein groups and >20,000 peptides using technical quadruplicates. [*Evosep: Towards a Standardized Omics Platform with the 60 SPD.]

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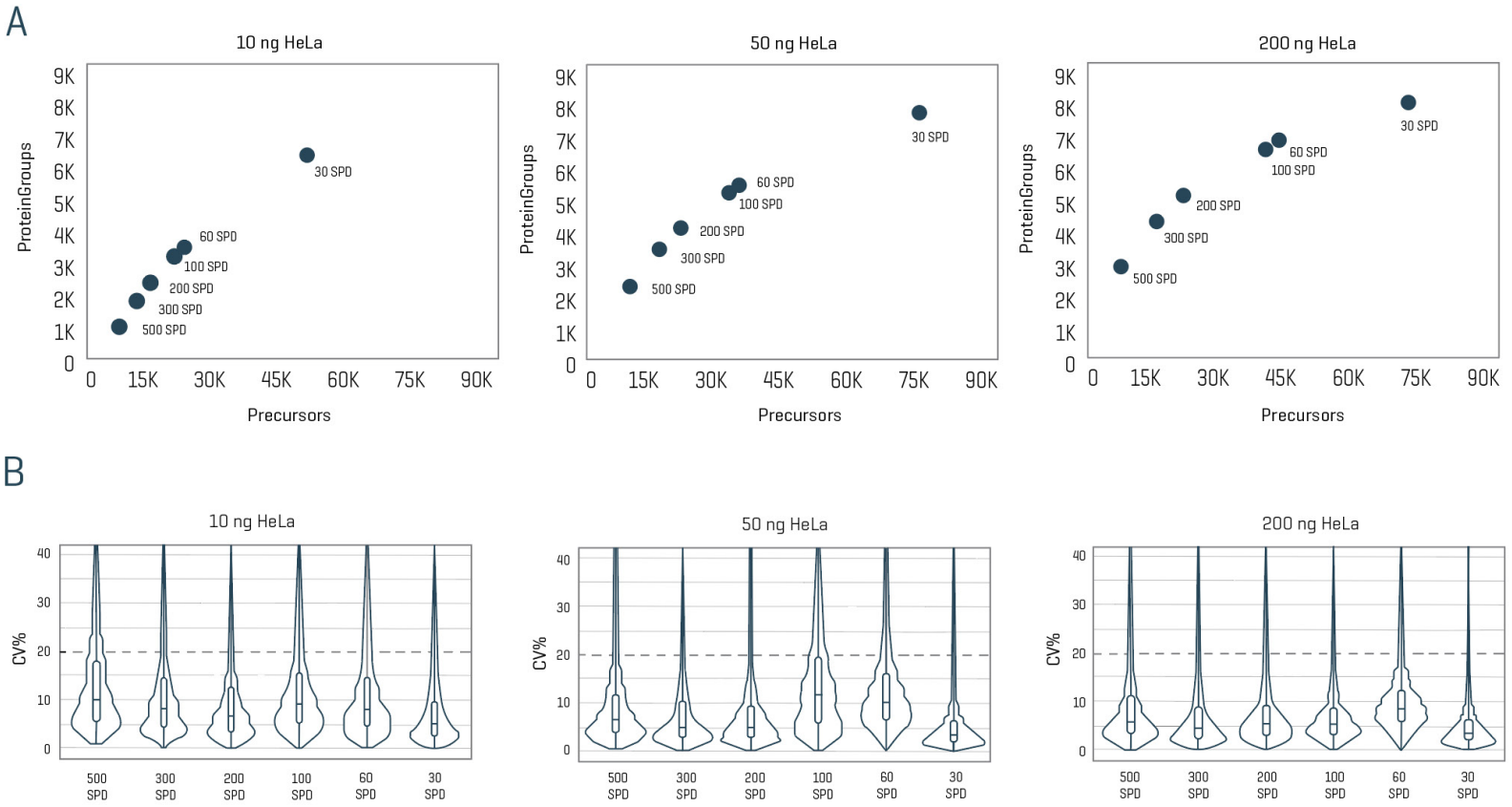
Proteomics example: moving towards industrialized nanoflow proteomics using Evosep One with Zeno SWATH DIA



Quantitative proteomics results with HeLa cell digest at various samples-per-day (SPD) throughput methods using Zeno SWATH DIA. (A) Numbers of protein groups and precursors quantified from different on-column loadings of HeLa cell digest using different SPD methods. Data were obtained from library-free searches of Zeno SWATH DIA triplicate injections for each experiment using DIA-NN software. The resulting "pg.matrix.tsv" and "pr.matrix.tsv" files were used to report the numbers of protein groups and precursors, respectively. (B) Violin plots showing %CV distributions for precursors from the different on-column HeLa cell loadings using the different SPD methods.

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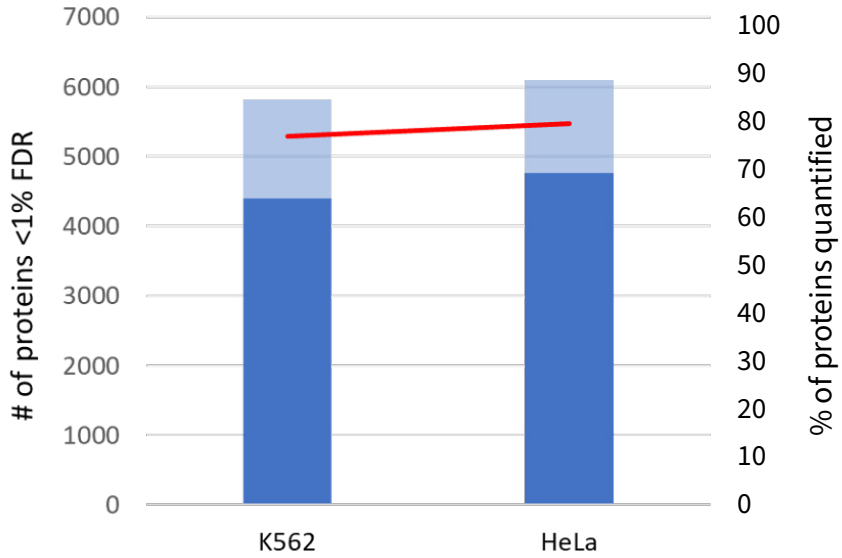
Proteomics example:
leveraging the speed of Zeno SWATH DIA for quantifying proteins/peptides using fast (5-minute) gradients



Numbers of protein groups identified with <1% FDR and quantified with <20% CV. These analyses were performed for 200 ng injections of K562 and HeLa human cell lysate tryptic digests using Zeno SWATH DIA on the ZenoTOF 7600 system with a 5-minute microflow gradient.

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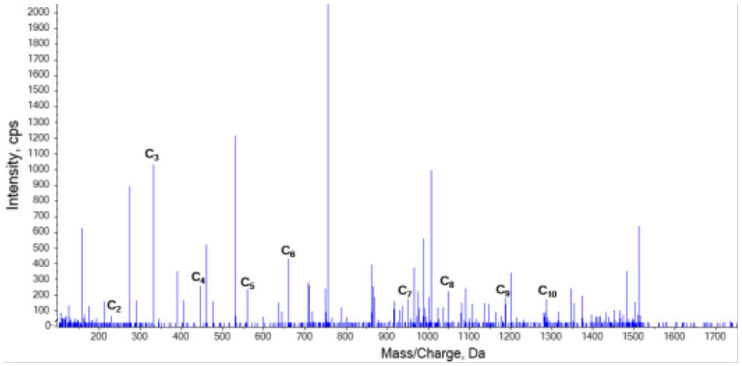
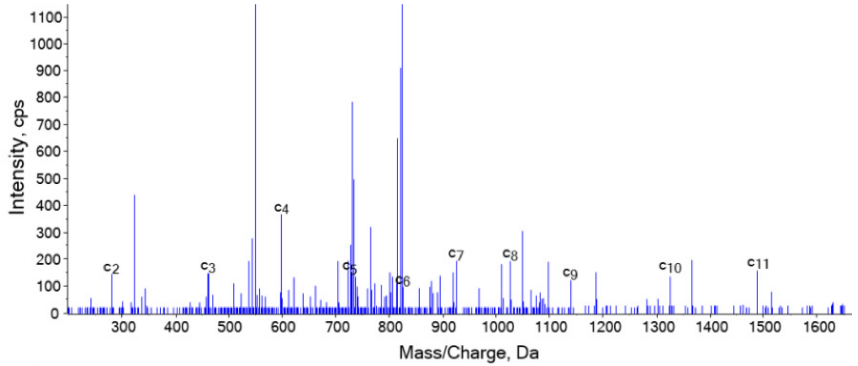
Proteomics example: using EAD at LC timescale for characterization of PTMs on peptides

EAD fragmentation of a glycated peptide from human serum albumin protein. A hexose modification was localized on a lysine using a near complete c' ion series. Detected fragment ion masses are shown in red in the table below the EAD spectrum. The hexose modification was located with 100% probability in Mascot software. Bold red indicates the fragments found with +1 charge state, while the red italics indicate fragments found with a different charge state.



Symbol	Res. Mass	# (N)	b	c	y	z	z + 1	z + 2	# (C)
L	113.08406	1	114.09134	131.11789	*3019.34417*	*3002.31762*	*3003.32544*	*3004.33327*	24
V	99.06841	2	***213.15975***	**230.18630**	2906.26010	2889.23355	2890.24138	2891.24920	23
T	101.04768	3	314.20743	***331.23398***	2807.19169	2790.16514	2791.17297	*2792.18079*	22
D	115.02694	4	429.23438	**446.26093**	2706.14401	2689.11746	*2690.12529*	*2691.13311*	21
L	113.08406	5	542.31844	**559.34499**	2591.11707	*2574.09052*	*2575.09834*	*2576.10617*	20
T	101.04768	6	643.36612	**660.39267**	2478.03300	2461.00645	2462.01428	2463.02210	19
K[Hex]	290.14779	7	933.51391	**950.54045**	*2376.98533*	2359.95878	2360.96660	2361.97443	18
V	99.06841	8	1032.58232	**1049.60887**	2086.83754	2069.81099	*2070.81881*	*2071.82664*	17
H	137.05891	9	1169.64123	**1186.66778**	1987.76912	1970.74258	*1971.75040*	1972.75823	16
T	101.04768	10	1270.68891	***1287.71546***	1850.71021	1833.68366	*1834.69149*	***1835.69931***	15
E	129.04259	11	1399.73150	***1416.75805***	1749.66253	1732.63598	*1733.64381*	*1734.65164*	14
C[CAM]	160.03065	12	1559.76215	*1576.78870*	1620.61994	*1603.59339*	1604.60122	1605.60904	13
C[CAM]	160.03065	13	1719.79280	*1736.81935*	1460.58929	1443.56274	1444.57057	1445.57839	12
H	137.05891	14	1856.85171	*1873.87826*	1300.55864	1283.53209	**1284.53992**	1285.54774	11
G	57.02146	15	1913.87318	*1930.89973*	**1163.49973**	1146.47318	**1147.48101**	1148.48883	10
D	115.02694	16	2028.90012	*2045.92667*	1106.47827	1089.45172	**1090.45954**	**1091.46737**	9
L	113.08406	17	2141.98419	*2159.01073*	*991.45132*	974.42477	**975.43260**	**976.44042**	8
L	113.08406	18	2255.06825	*2272.09480*	**878.36726**	861.34071	**862.34854**	**863.35636**	7
E	129.04259	19	2384.11084	*2401.13739*	**765.28320**	748.25665	**749.26447**	**750.27230**	6
C[CAM]	160.03065	20	2544.14149	*2561.16804*	**636.24060**	619.21405	620.22188	621.22970	5
A	71.03711	21	2615.17861	*2632.20515*	**476.20995**	*459.18340*	**460.19123**	**461.19905**	4
D	115.02694	22	2730.20555	*2747.23210*	**405.17284**	388.14629	**389.15411**	**390.16194**	3
D	115.02694	23	2845.23249	*2862.25904*	**290.14590**	273.11935	**274.12717**	**275.13500**	2
R	156.10111	24	3001.33360		**175.11895**	158.09240	**159.10023**	**160.10805**	1

Localization of a phosphorylation site near the N-terminus of a peptide with tyrosine and threonine. The c' fragment ion series enables localization of a phosphorylated threonine adjacent to a tyrosine. The c' ion series is shown in the spectrum and the modification site was located with 99.98% probability in Mascot software. Both the c' and z· (z+1) ion series are highlighted in the table below the EAD spectrum and the detected fragments (+1 charge state) are highlighted in bold red.



Symbol	Res. Mass	# (N)	b	c	y	z	z + 1	z + 2	# (C)
V	99.06841	1	100.07569	117.10224	*1645.77742*	*1628.75087*	***1629.75870***	***1630.76652***	12
Y	163.06333	2	263.13902	**280.16557**	*1546.70901*	*1529.68246*	*1530.69029*	*1531.69811*	11
T[Pho]	181.01401	3	444.15303	**461.17958**	1383.64568	1366.61913	**1367.62696**	1368.63478	10
H	137.05891	4	581.21194	**598.23849**	1202.63167	1185.60512	**1186.61295**	**1187.62077**	9
E	129.04259	5	710.25454	**727.28108**	**1065.57276**	1048.54621	**1049.55403**	**1050.56186**	8
V	99.06841	6	809.32295	**826.34950**	936.53016	919.50362	**920.51144**	***921.51927***	7
V	99.06841	7	908.39136	**925.41791**	837.46175	820.43520	**821.44303**	**822.45085**	6
T	101.04768	8	1009.43904	**1026.46559**	**738.39334**	721.36679	**722.37461**	**723.38244**	5
L	113.08406	9	1122.52311	**1139.54965**	**637.34566**	620.31911	**621.32693**	**622.33476**	4
W	186.07931	10	1308.60242	**1325.62897**	**524.26159**	507.23504	**508.24287**	**509.25069**	3
Y	163.06333	11	1471.66575	**1488.69230**	**338.18228**	321.15573	**322.16356**	323.17138	2
R	156.10111	12	*1627.76686*		175.11895	158.09240	159.10023	160.10805	1

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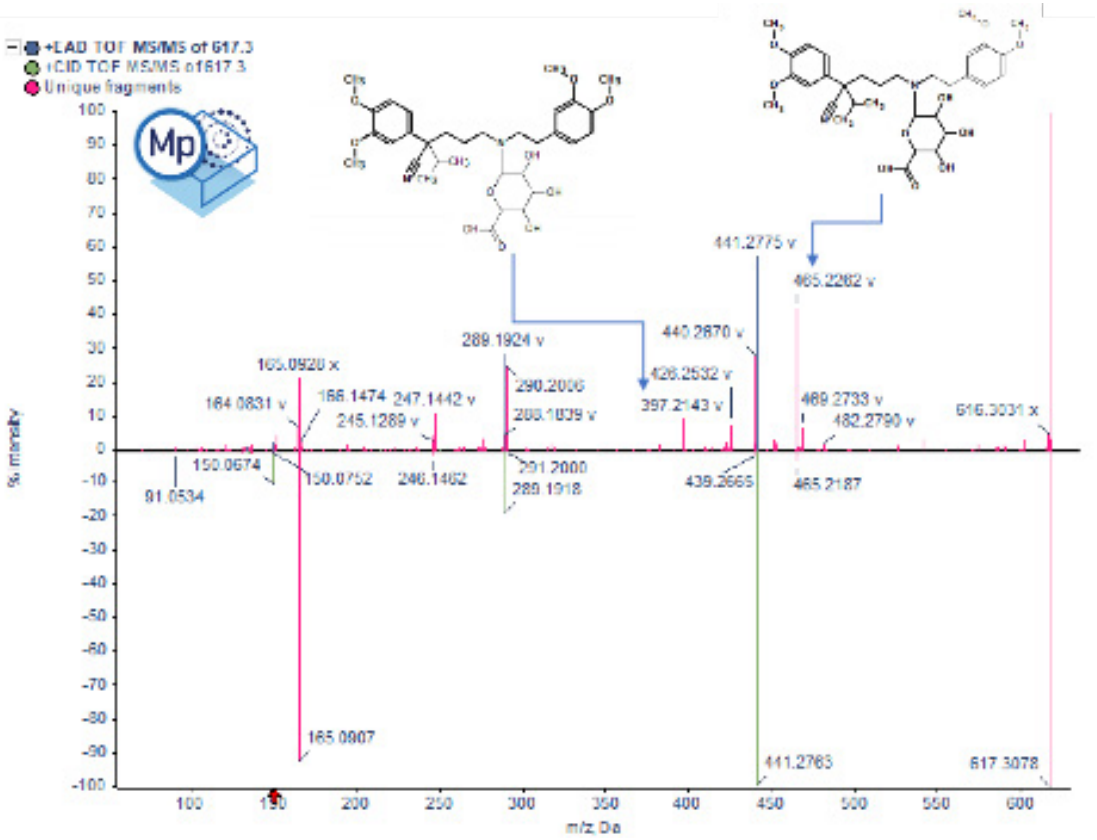
Comprehensive metabolite identification with electron-activated dissociation EAD and CID

Read technical note →



Through the enhanced sensitivity provided by the Zeno trap, the ZenoTOF 7600 system enables comprehensive and confident characterization and identification of metabolites, along with the ability to detect low-level metabolites. These capabilities are essential to critical processes such as drug discovery, where the ability to produce data promptly must be in alignment with the pace of the process. To demonstrate these capabilities, the figure to the left compares the fragments indicated by comparing results from EAD MS/MS spectra (top) with CID MS/MS spectra (bottom) for precursor ion m/z 617.3. Fragment ions in pink highlight the unique fragments comparing the CID MS/MS and EAD MS/MS spectra. A greater percentage of unique fragments were identified using EAD. Diagnostic fragments such as m/z 397.2143 and m/z 465.2262 support the N-glucuronide conjugation of verapamil. EAD TOF MS/MS fragment mass accuracy was within 5 ppm, enabling confident metabolite confirmation and identification.

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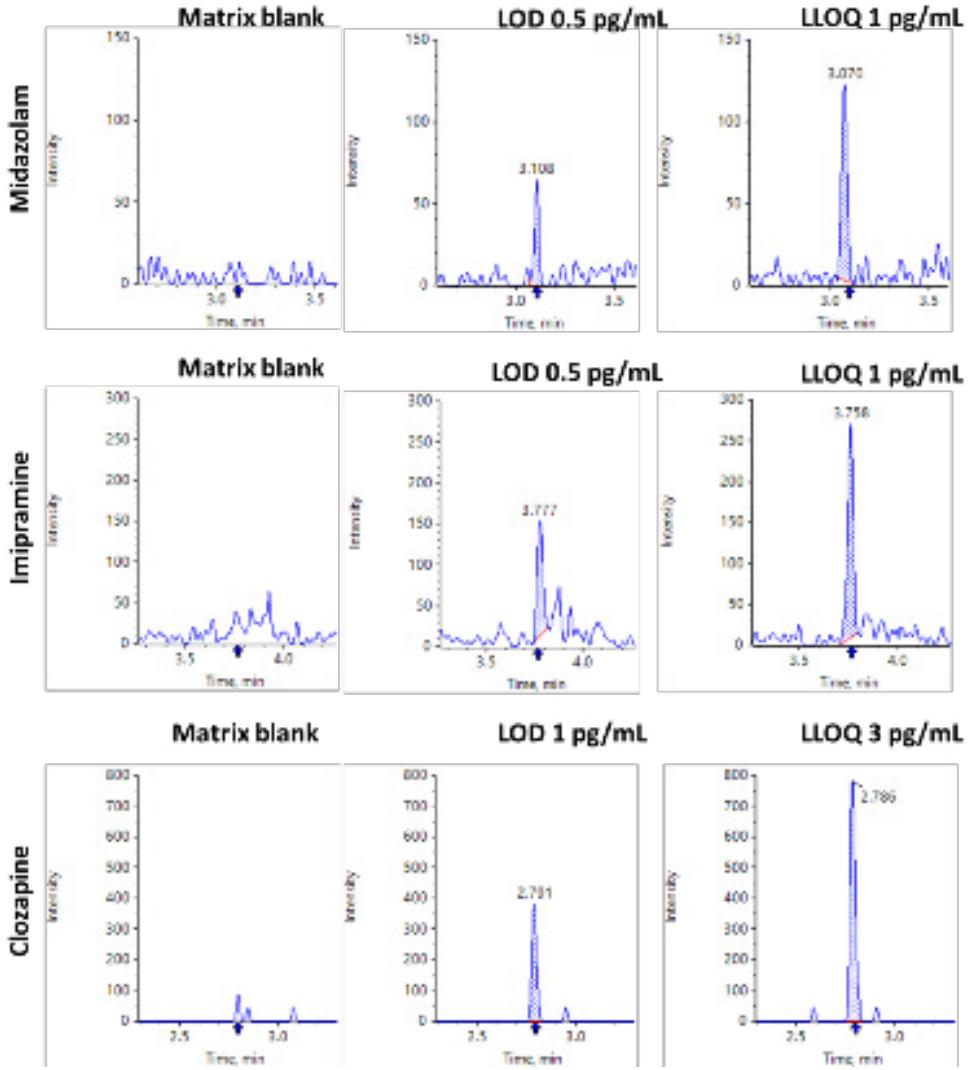
Accomplish outstanding quantitative performance for bioanalysis of small molecule pharmaceuticals using accurate mass spectrometry

Read technical note →



Demands for improved sensitivity in routine bioanalytical assays continue to increase as drug discovery and development programs focus on more effective, lower dosage compounds. Pharma development scientists supporting this work therefore require highly sensitive and selective bioanalytical methods for quantitation. More recently, accurate mass spectrometers, such as time-of-flight (TOF) instruments, have been increasingly adopted for quantitative bioanalysis because they demonstrate high selectivity. However, current TOF platforms still encounter challenges with sensitivity when used for quantitation because of the loss of ion transmission between TOF pulses. An accurate mass spectrometer with improved MS/MS sampling efficiency offers a robust and sensitive platform to support routine bioanalysi. The ZenoTOF 7600 system features a Zeno trap that controls the ion beam from the collision cell, facilitates greater ion transmission to the TOF accelerator and improves the duty cycle to ≥90% (traditional TOF is <30%). With the enhancement in the overall MS/MS sampling efficiency, the ZenoTOF 7600 system is highly advantageous for quantitative workflows that require high sensitivity.

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Confident structural elucidation of xenobiotics

The ZenoTOF 7600 system brings a new level and depth of information to qualitative and quantitative workflows with EAD. When combined with the Zeno trap, comprehensive fragment coverage can be obtained to enable more confident structural elucidation.

The hardest challenge for CID is the fragmentation of conjugated metabolites, such as glucuronidation. EAD generates unique fragments, pathways which enables the differentiation of isomers including, N- and O-glucuronides. These are otherwise lost during the CID fragmentation step, and without the use of chemically synthesized standards, elucidation is rather challenging . With the EAD approach, 32 diagnostic fragments were detected. This was possible because with the Zeno trap, the signal is considerably enhanced. Therefore, the use of EAD is a step forward towards improved productivity with fewer experiments needed.

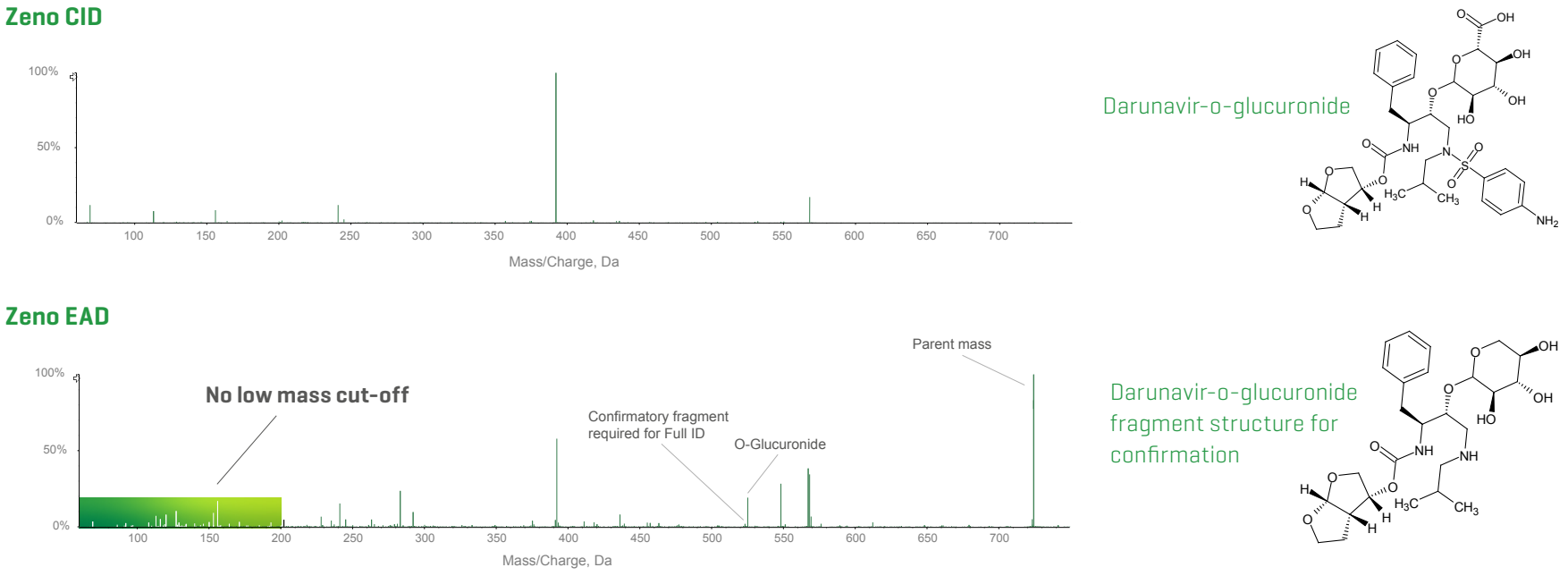
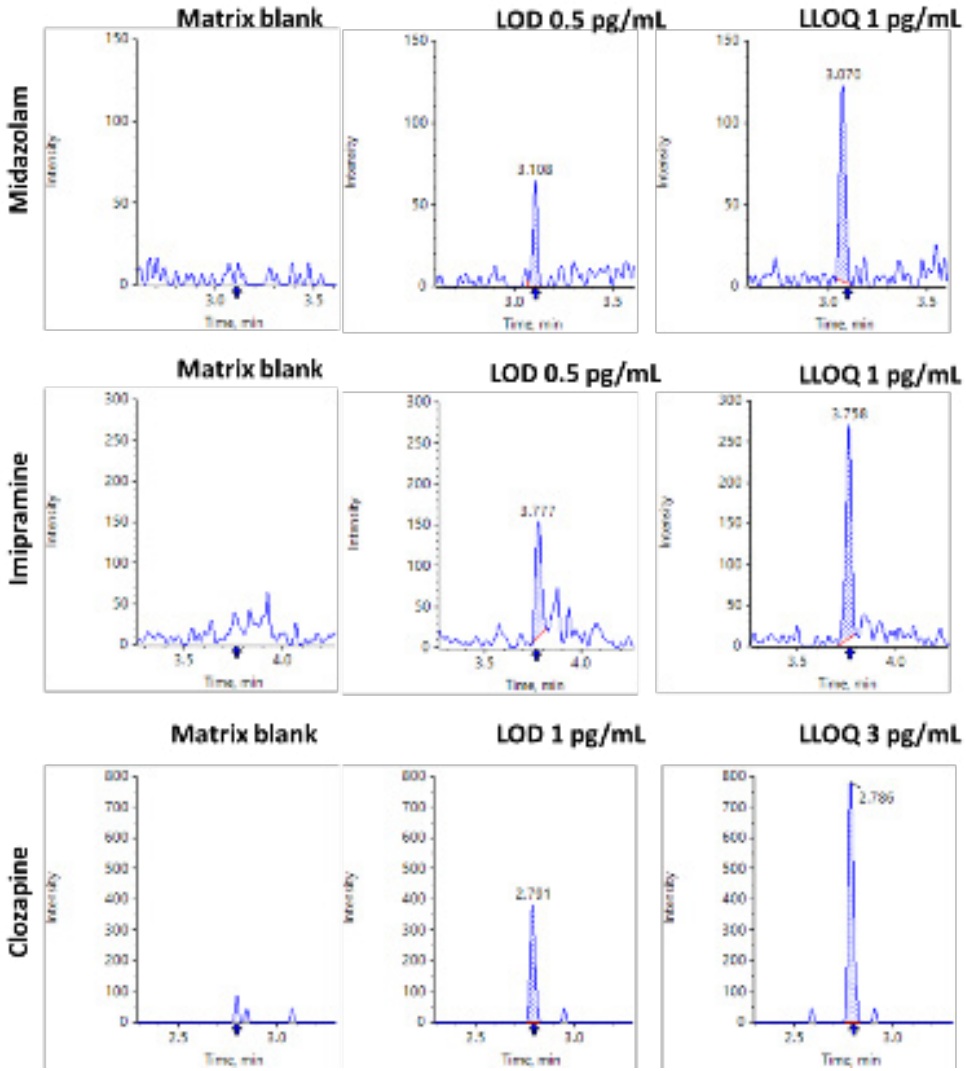


Figure 5. The EAD Spectrum. EAD spectrum which produces an important fragment ion with the glucuronide preserved which allows localization of the glucuronide modification. Also, low mass fragment ions are preserved by using a QTOF-based platform.

Multiple approaches for routine early-stage bioanalytical quantitation

Read technical note →



The ZenoTOF 7600 system is a highly sensitive accurate mass platform that is well suited for use in a routine, early-stage bioanalytical laboratory setting. While Zeno MRM^{HR} will be the approach of choice for most small molecule applications with higher sensitivity requirements, in situations where compound throughput limits method optimization time, a Zeno SIM approach can produce higher quality quantitative data than a typical accurate mass approach, with reduced MS development time. For compounds that do not produce good quantitative fragments under CID, and where Zeno SIM is not selective enough, Zeno EAD MRM^{HR} is a viable, quantitative option that was not previously available to bioanalytical scientists.

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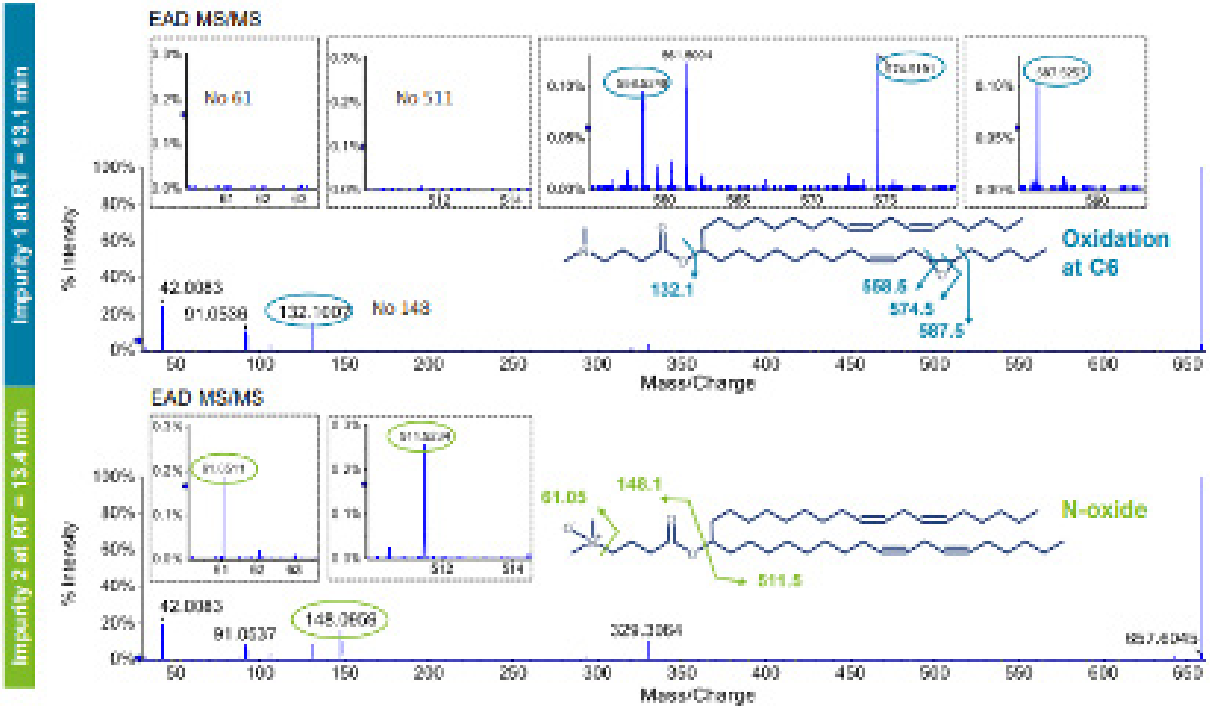
Lipid characterization in lipid nanoparticles (LNPs)

Read technical note →

Lipid nanoparticles (LNPs) are effective non-viral vectors, which are widely used delivery vehicles for genetic medicines such as messenger RNA (mRNA). As a result, it is important to understand and limit LNP-related impurities to help ensure genetic product integrity and mitigate risks to patient safety and product efficacy.

Zeno EAD can help you fully understand the structure of your ionizable lipid and related impurities by differentiating between oxidated species and accurately localizing double bonds or saturations. Avoid missing relevant product excipients by leveraging a linear dynamic range >5 orders of magnitude and signal-to-noise enhancement with the Zeno trap.



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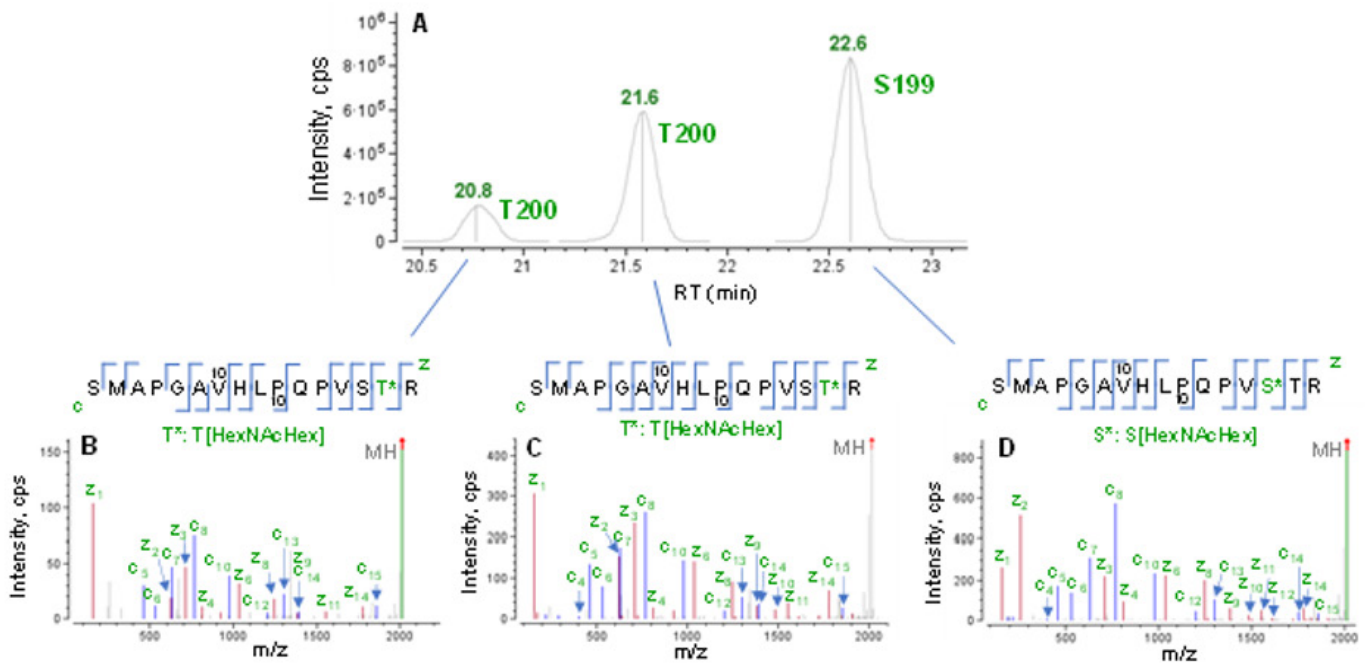
Characterization of O-linked glycosylation inetanercept by EAD

Read technical note →

Peptide mapping analysis is widely used for glycopeptide characterization, providing protein sequence information and glycan profiling simultaneously. However, traditional CID often fragments the glycan structures and fails to provide an accurate confirmation of the peptide backbone and glycan localization information, especially with complex O-glycoproteins, which contains multiple partially occupied glycosylation sites. Achieving accurate and comprehensive information is becoming increasingly challenging.

EAD allows for optimized peptide fragmentation on glycopeptides. Through high-sequence coverage, it enables accurate localization of glycans and confident identification of peptides. The figure below highlights the power of EAD for identification and localization of O-linked glycosylation in etanercept. The unique ability of EAD to pinpoint the positions of glycosylation further enables the differentiation of positional isomers of O-glycopeptides.



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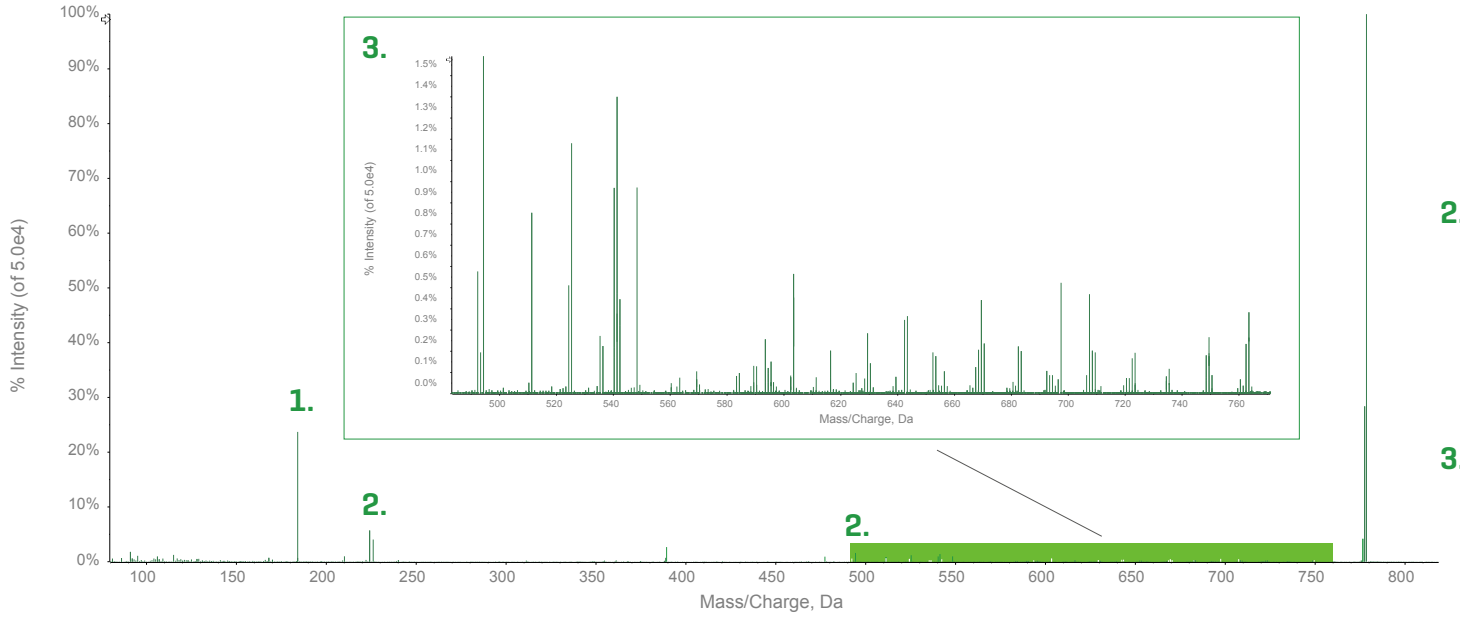
Complete characterization of lipids in a single experiment

Lipids are a complex group of compounds with subtypes that share a similar high-level structure. For example, triglycerides consist of a glycerol group bonded to 3 long hydrocarbon chains with additional functional head groups attached in some cases. Small but meaningful differences between lipid species such as the location of a single double bond along the hydrocarbon chain, can have important implications for health and disease. In a single experiment, EAD provides all of the information for complete lipid characterization that normally requires multiple technologies and experiments.

Complete characterization of lipids involves the identification of:

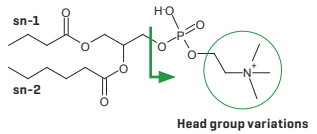
- Head group
- Backbone
- Regio-isomerism
- Double bonds
- Cis/trans isomerism

Single experiment lipid characterization

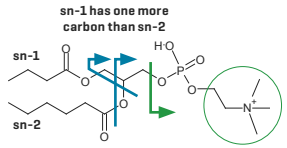


Fragmentation patterns

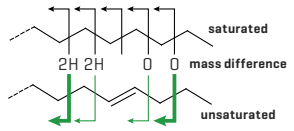
1. EAD produces diagnostic fragments of:
- Head group
  - PC (SM), PE, PS, PI, PA, PG



2. Backbone (glycerol/sphingoid)
- Regioisomerism (sn-1, sn-2, etc.)



3. Chain structure
- Length and double bonded positions
- Double bond stereochemistry



Single experiment lipid characterization. The complete de novo identification and characterization of the lipid PC 16:0 / 18:1(n-9:cis) in a single experiment.

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