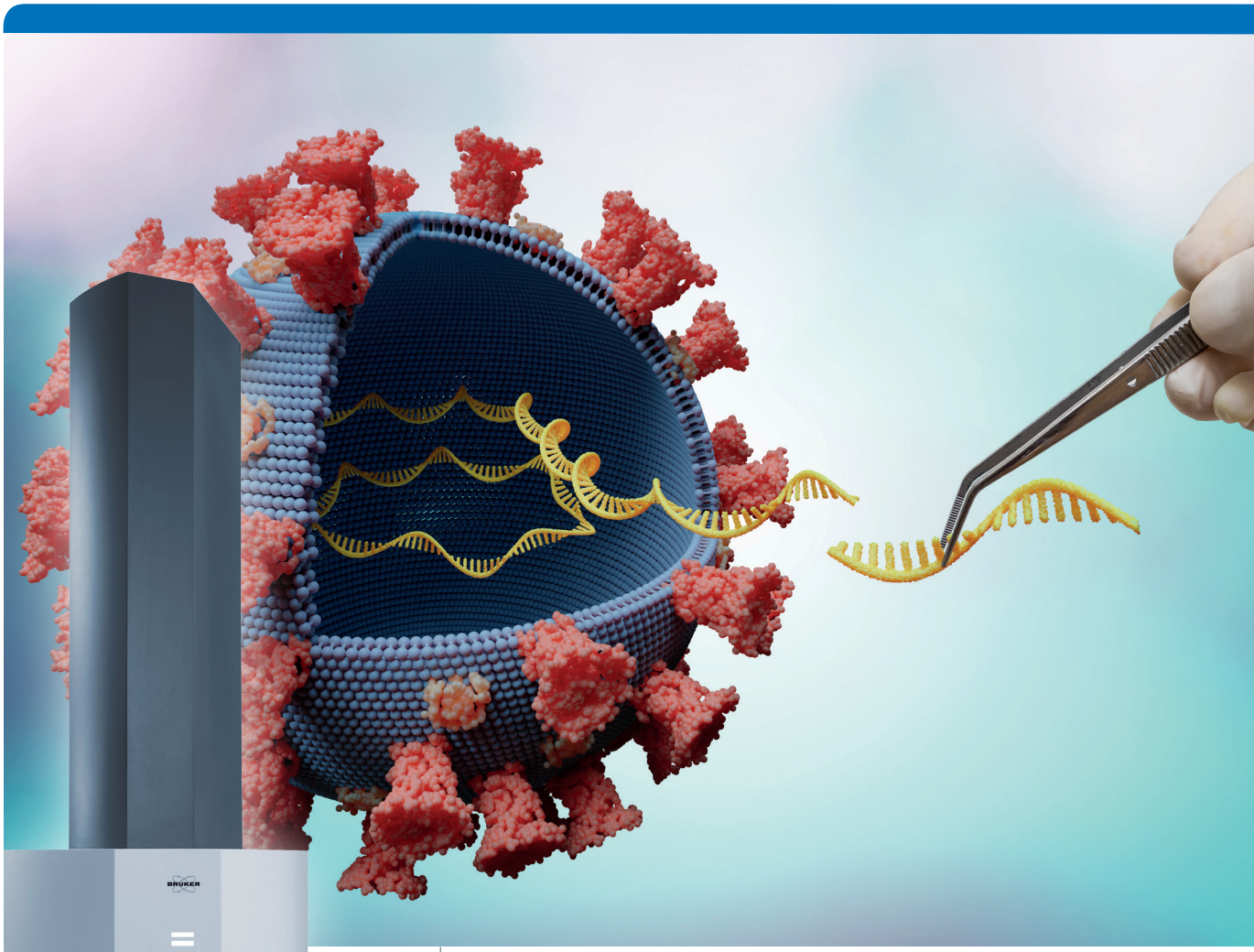


maXis II for BioPharma Analysis

- Biologics development made easy

Innovation with Integrity

BioPharma

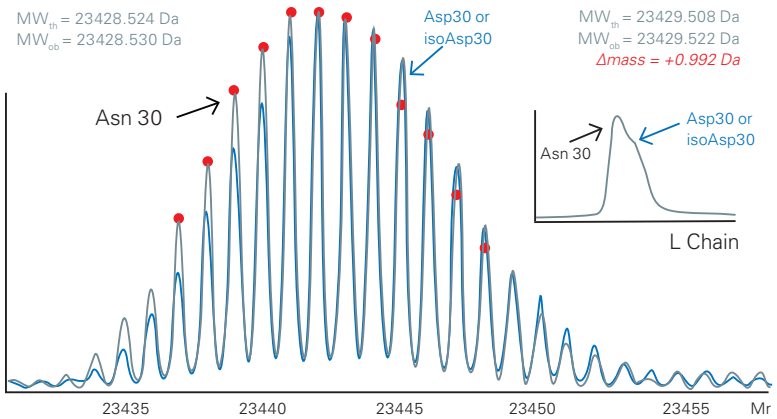
maXis II: Unmatched Performance

The maXis II UHR QTOF delivers a proven combination* of high isotopic fidelity (True Isotopic Pattern), algorithms to analyze large molecules with isotopic resolution (SNAP) and high sensitivity to analyze in positive and negative mode (VIP-HESI). This enables the characterization of mAb subunits, reduced mAbs, oligonucleotides and RNA with sub-ppm mass accuracy.

Confident mass assignments of proteins and RNA enables simpler assays for BioPharma scientists to accelerate their clone screening, glycan profiling and stress studies without compromising the ability to detect deamidated forms or complex glycan profiles.

Deamidation analysis on a mAb subunit

TRUE ISOTOPIC PATTERN (TIP)

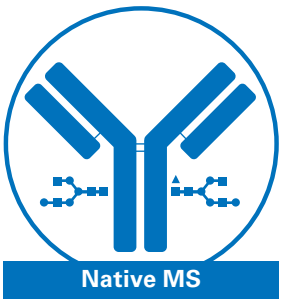


The maXis II acquires True Isotopic Pattern (TIP) raw data that allows for rapid determination of modifications such as deamidation of the light chain (LC). Coupled to the SNAP-II algorithm, these subtle modifications can be routinely characterized at the sub-unit level.

*Resemann et al (2016): Full validation of therapeutic antibody sequences by middle-up mass measurements and middle-down protein sequencing, mAbs, DOI: 10.1080/19420862.2015.1128607

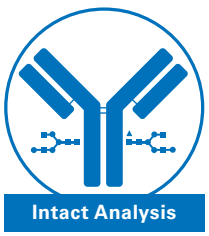
Simplified analysis of complex biologics

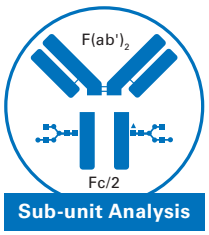
Support biotherapeutic development with clone screening, degradation and biotrans-formation studies with high quality data and seamless integration with BioPharma Compass®

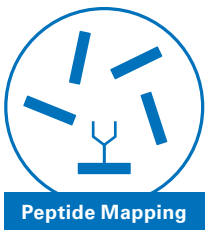


- Stable performance under high salt non-denaturing conditions give users access to wide range of eluents to analyze non-covalent mole-cules such as ADCs and multispecifics.

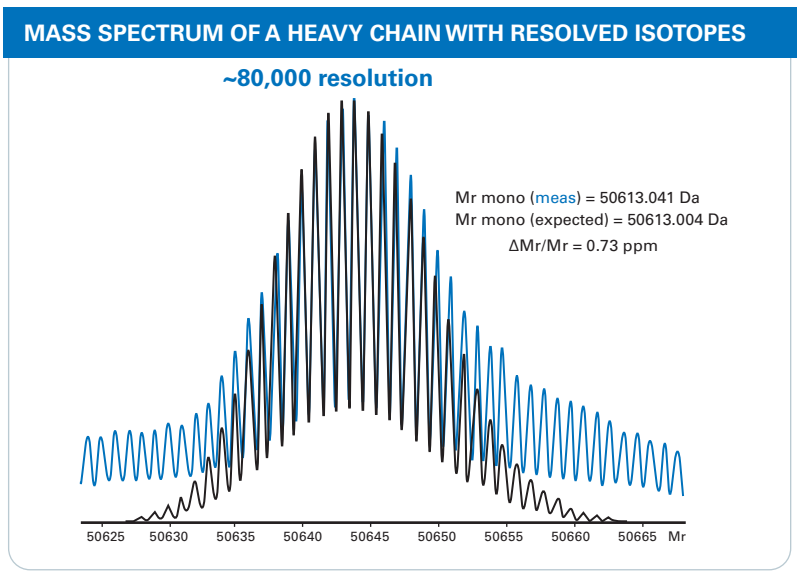
- High dynamic range and absence of space charging limitations allow full scan analysis of complex spectra to comprehensively characterize heterogeneities. High data quality, isotopic fidelity and mass accuracy equips project teams with actionable data.







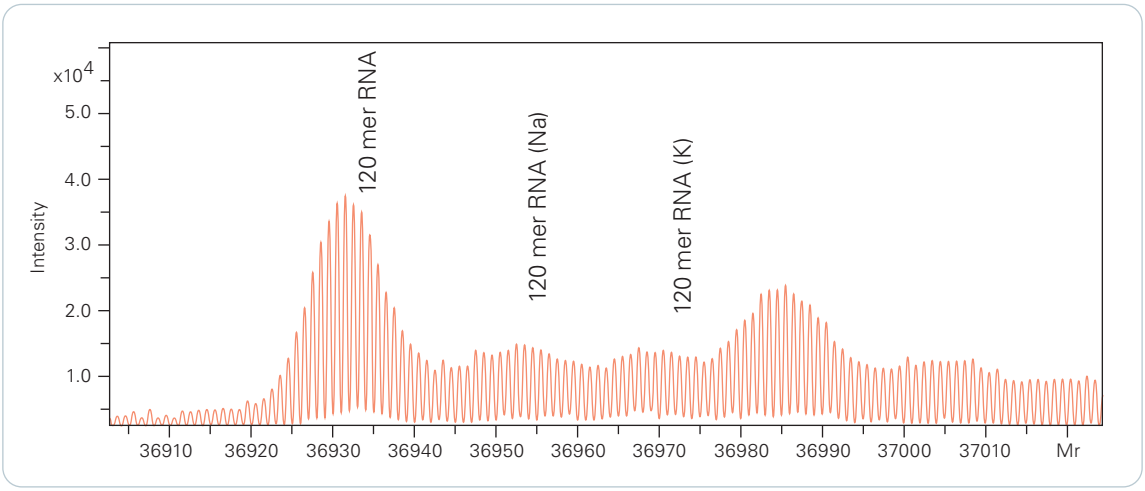
MASS SPECTRUM OF A HEAVY CHAIN WITH RESOLVED ISOTOPES



MaxEnt deconvolution spectrum measured in blue. Simulated mass spectrum in black.

Oligonucleotide sequence verification

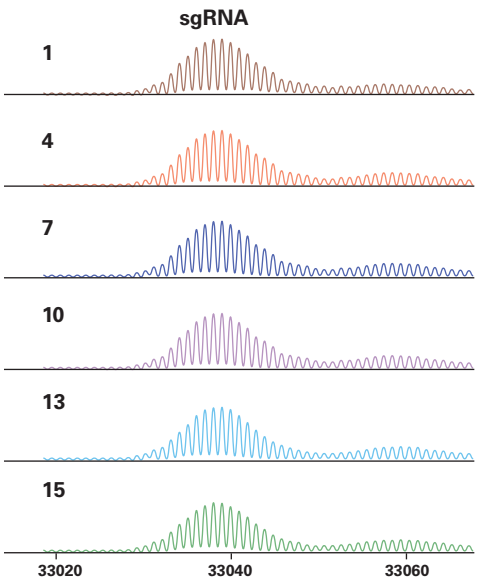
Superior negative mode analysis



Intact mass verification of a sgRNA with maximum entropy deconvolution and SNAP annotation

The maXis II with VIP-HESI high sensitivity in negative mode is ideal to analyze heterogeneities in oligonucleotides such as siRNA but also in larger molecules such as single guide RNA (sgRNA) used in CRISPR based gene editing.

Confident mass assignments in complex spectra with True Isotopic Pattern and SNAP enable confident sequence verification even for base substitution resulting in only 1 Da mass differences.



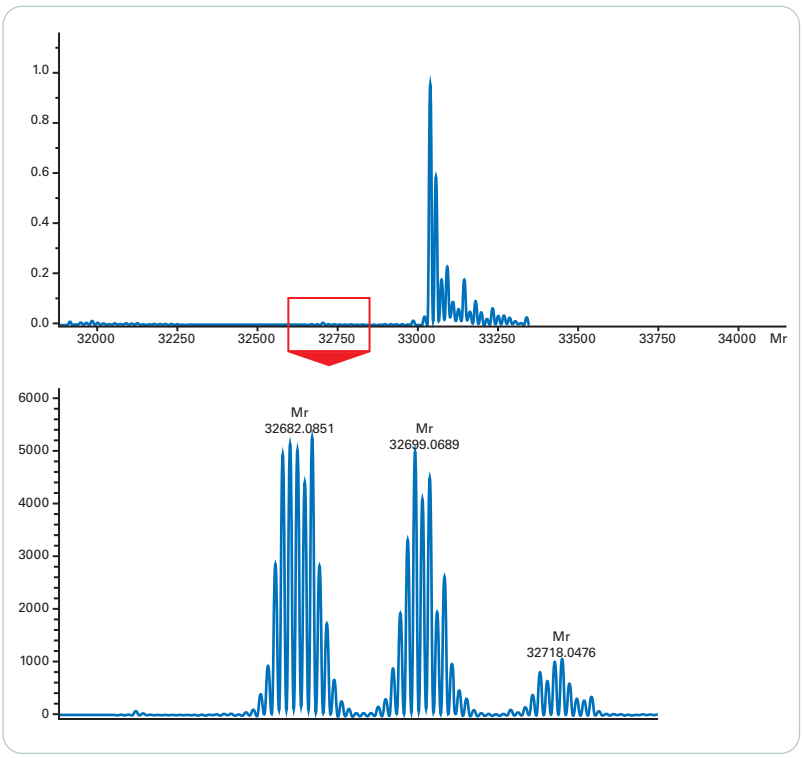
Intraday reproducibility (8h) for the analysis of a 100nt single guide RNA shows highly consistent isotopic pattern with no loss of performance during the batch.

"The introduction of this new suite of software, which will enable the routine analysis of larger and modified nucleic acids, will put us a step closer to realizing the broad range of analytical capabilities available now for protein analysis"

Dr. Dan Fabris, CEO of Ribodynamics and Harold S. Schwenk, Sr. Professor at University of Connecticut, MA, USA

Sequence verification of a 75-mer oligonucleotide by LC-MS/MS with OligoQuest™

The confident annotation of complex overlapping spectra is also essential for MS/MS based sequence confirmation. OligoQuest™ combines the SNAP deconvolution and advanced sequencing algorithms from RiboDynamics (embedded in BioPharma Compass®) and takes full advantage of the maXis II data quality to annotate terminal and internal fragments.



High intrascan dynamic range enables monoisotopic detection of impurities < 0.4% coeluting with a 100 nucleotides RNA

High dynamic range glycan profiling

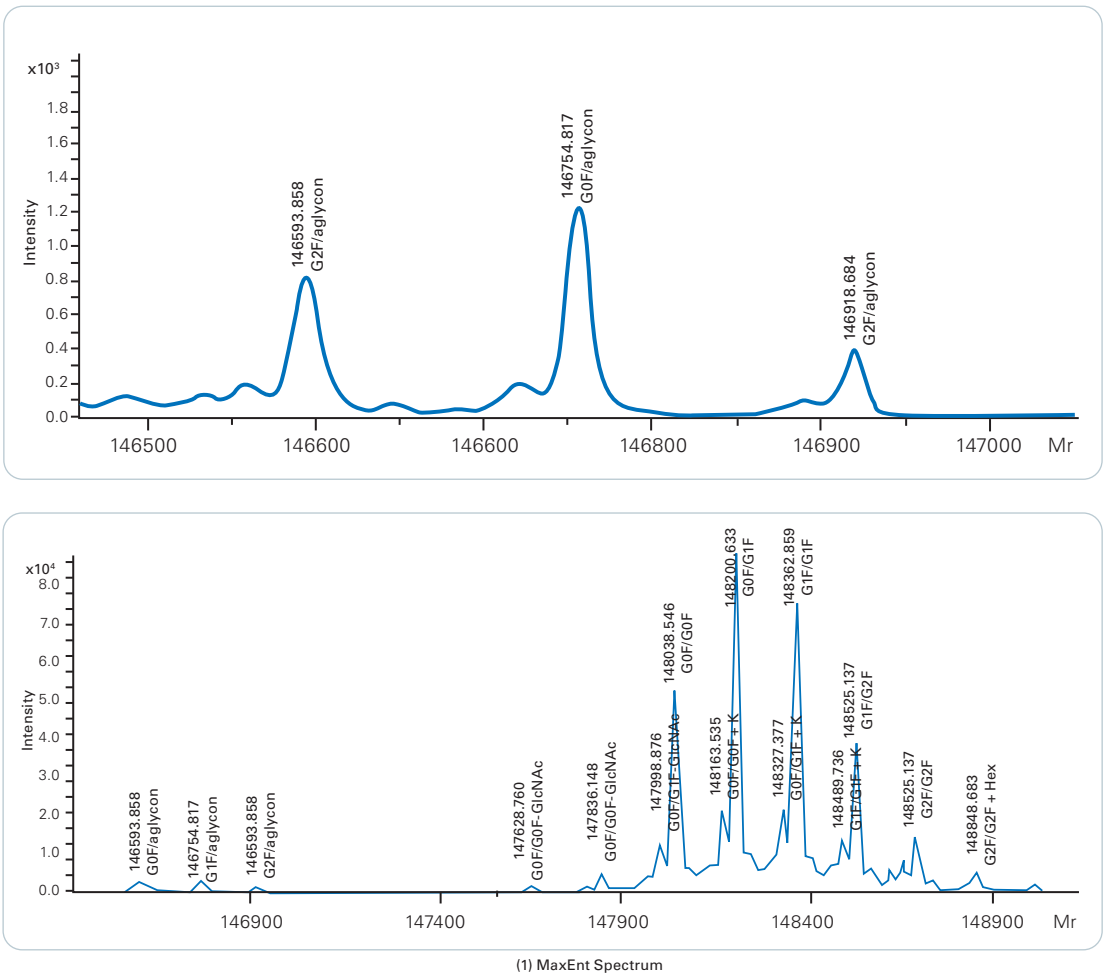
Identifying, monitoring and controlling the glycosylation levels is key for successful biopharmaceutical development.

High intrascan dynamic range is required for the confident assignments of coeluting glycoforms on subunits or intact mAbs.

The maXis II confidently addresses these key challenges in many pharmaceutical labs today at the intact, subunit, glycopeptide and released glycans level.

Confidently determine:

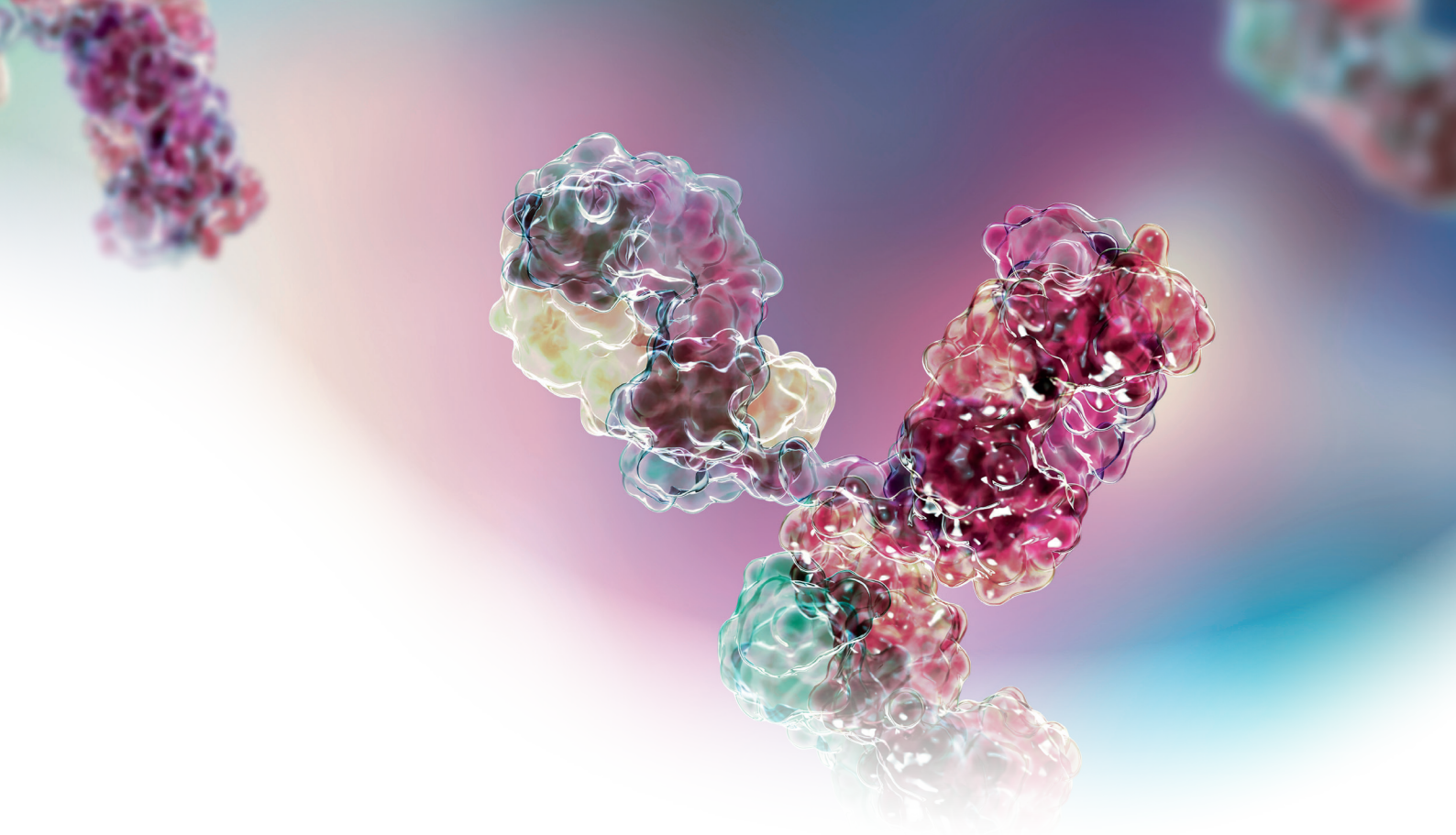
- **Relative abundances**
  (The most glycan IDs and 1-sigma groups in NISTmAb round robin study)*
- **Composition**
  (glycopeptide or released)**
- **Localization**
  within protein sequence (glycopeptide)



High dynamic range analysis of the intact NISTmAb glycoforms, including low intensities aglycon heterogeneities (<1%)

*Maria Lorna A. De Leoz et al: NIST Interlaboratory Study on the Glycosylation of NISTmAb, NIST Pubs (2017), DOI: 10.6028/NIST.IR.8186

**H. Hinneburg et al.: The Art of Glycopeptide Destruction, J. Am. Soc. Mass Spectrom. (2015), DOI: 10.1007/s13361-015-1308-6



Protein	Form	Annotation	Mr Ref	Mr Sample	Δ Mr [ppm]	Int. [a.u.]	Rel. Int. Ref [%]	Rel. Int. Sample [%]	Rt Ref [min]	Rt Sample [min]	Δ Rt [min]	Confirmed
NISTmab Fc/2	G0F	Fc/2 G0F	25220,4634	25220,4626	-0,03	6,964E+05	42,8	43,7	21,50	21,17	-0,33	Yes
NISTmab Fc/2	G1F	Fc/2 G1F	25382,5132	25382,5101	-0,12	6,798E+05	43,3	42,6	21,50	21,17	-0,33	Yes
NISTmab Fc/2	G2F	Fc/2 G2F	25544,5690	25544,5528	-0,64	1,797E+05	11,5	11,3	21,50	21,17	-0,33	Yes
NISTmab Fc/2	G2F Hex	Fc/2G2F H	25706,6219	25706,5934	-1,11	3,861E+04	2,4	2,4	21,50	21,17	-0,33	Yes
NISTmab Fd	pyro-Glu	Fd pyro-Glu	25672,8066	25672,7850	-0,84	5,303E+05	95,9	94,7	26,00	26,05	0,05	Yes
NISTmab Fd	pyro-Glu Hex	Fd pyro-Glu H	25834,8564	25834,8130	-1,68	2,941E+04	4,1	5,3	26,00	26,05	0,05	Yes
NISTmab LC	Hex	LC H	23275,3570	23275,2695	-3,76	4,991E+03	4,6	4,2	23,00	22,14	-0,86	Yes
NISTmab LC	native	LC	23113,3042	23113,3021	-0,09	1,128E+05	95,4	95,8	23,00	23,60	0,60	Yes

Average mass based profiling at the intact level usually has a mass accuracy of around 10 ppm. With resolved isotopes (< 50 kDa) it drops under 1 ppm (as illustrated above). The maXis II UHR QTOF sets the performance standard, with an unrivaled dynamic range for large proteins and glycoforms

"The Bruker maXis II ETD is LiVeritas Biosciences's instrument of choice to build MSaaS, an Automated Workflow System for Mass Spec R&D. We based the decision on prior experience with intact mass analysis of ADCs, including Native LC-MS. Data generated from the maXis II were critical for phase appropriate Mass Spec characterization of hundreds of candidates supporting the pioneers of accelerated drug development.

Our BioPharma clients are consistently impressed with the maXis's high performance and the generated actionable insights from the quality data for rapid analysis of ADCs, BsAbs, and oligonucleotides.

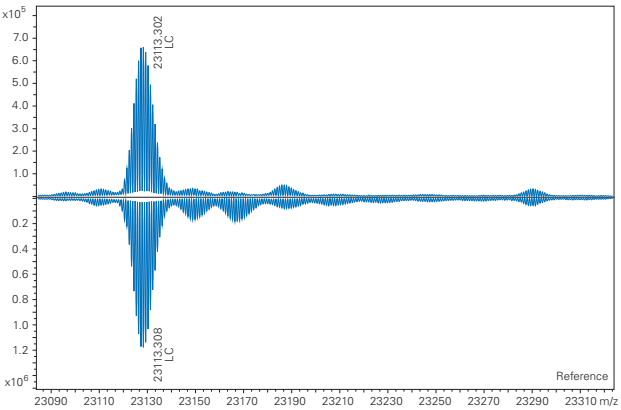
We will continue pushing boundaries of Mass Spec hardware and software solutions to meet the urgent and unmet needs of our clients for unambiguous data and actionable insight generation.
All empowers timely decision-making in all stages of drug development."

Dr Lieza Danan, CEO and Founder, LiVeritas Biosciences, Inc.

Powered by BioPharma Compass

- Single interface optimized for high fidelity data supports:
  - Intact protein and subunit characterization
  - Multi-Attribute Monitoring (MAM) at the protein and peptide level
  - Multi compound screening for QC of raw materials, synthetic or recombinant products
  - Analysis of RNA and oligonucleotide with ***OligoQuest***
- Analysis of LC-UV, MS and MS/MS data and MALDI compatible
- Integrated data acquisition. Simple GUI for starting and monitoring acquisition runs.
- Tools for 21 CFR Part 11 requirements implementation
- Data fully supported in vendor neutral packages (Protein Metrics, Genedata)

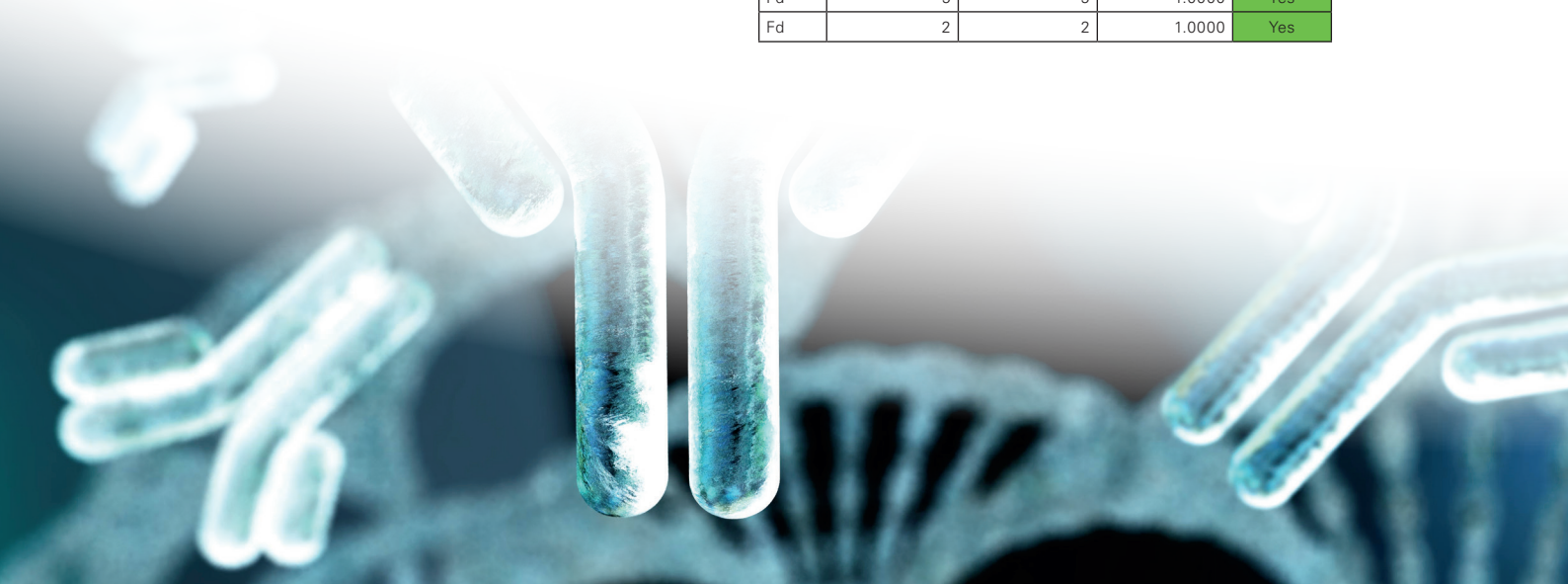
Butterfly plots for easy comparison of chromatograms and specta

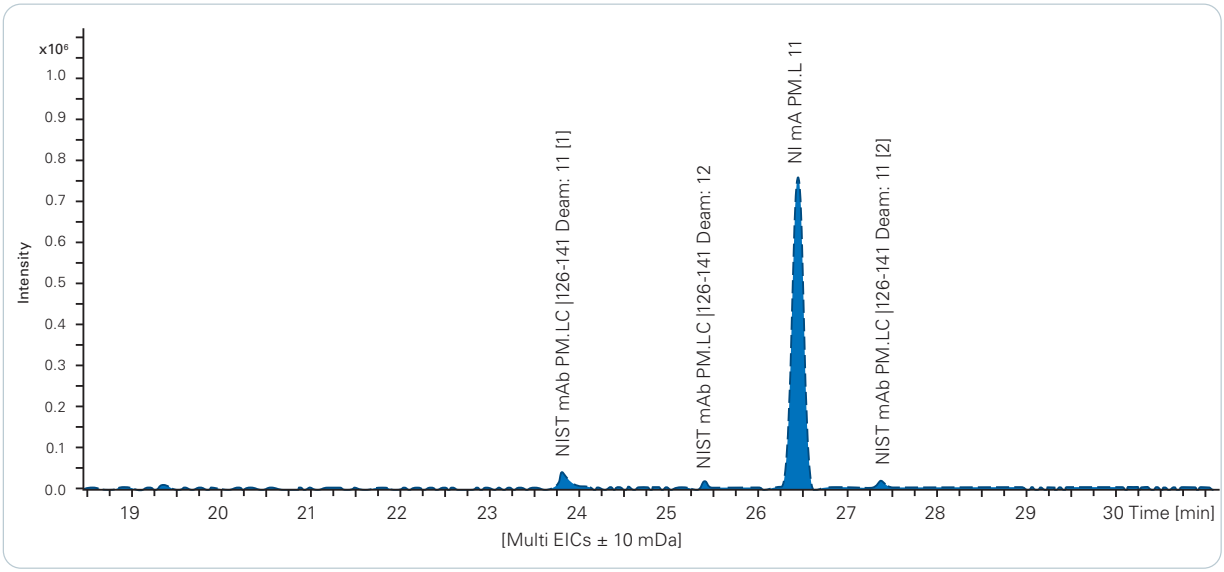


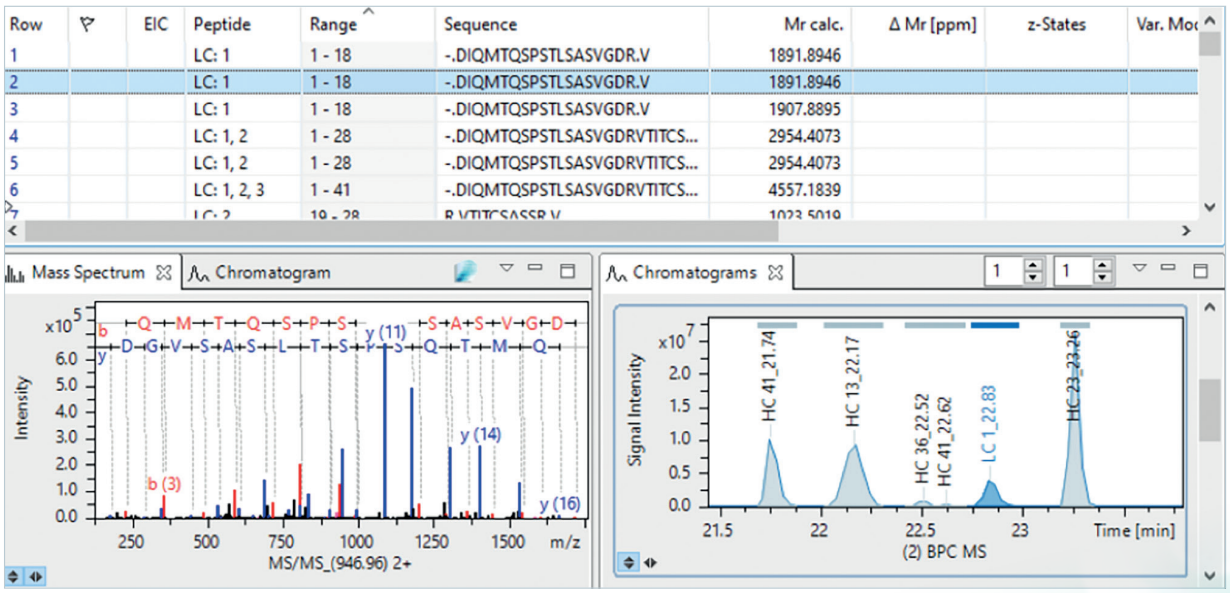
Automatic result assessment,

- Algorithm based similarity scoring

Protein	Peaks Expected	Peaks Confirmed	Cosine Similarity	Accepted
LC	2	2	1.0000	Yes
Fd²	9	9	1.0000	Yes
Fd	2	2	1.0000	Yes







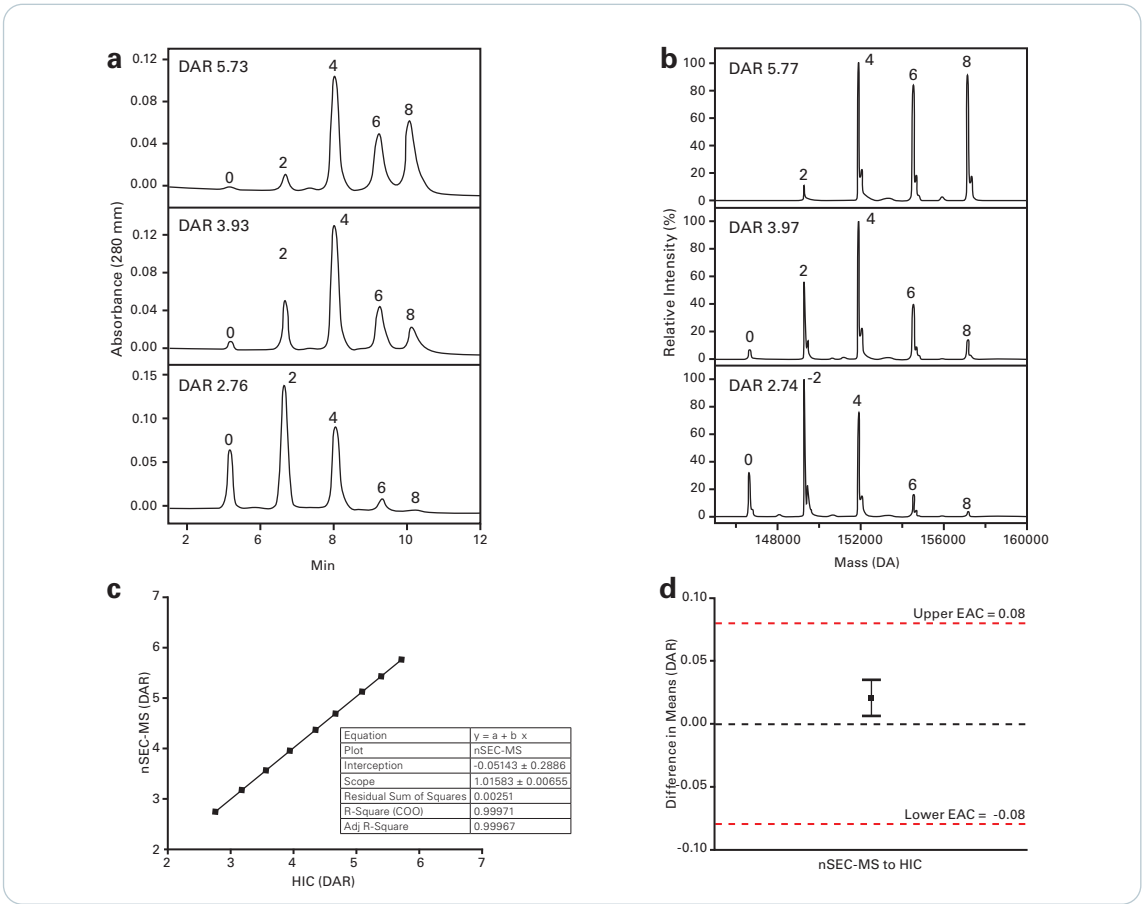
Interactive review of peptide mapping data

Antibody drug conjugates and multispecifics at the native MS level

Sustained performance even under high salt non-denaturing conditions makes the maXis II the perfect instrument to develop platform SEC-MS assays and measure ADC drug distribution or multispecifics assemblies

Article from Seagen in mAbs journal:

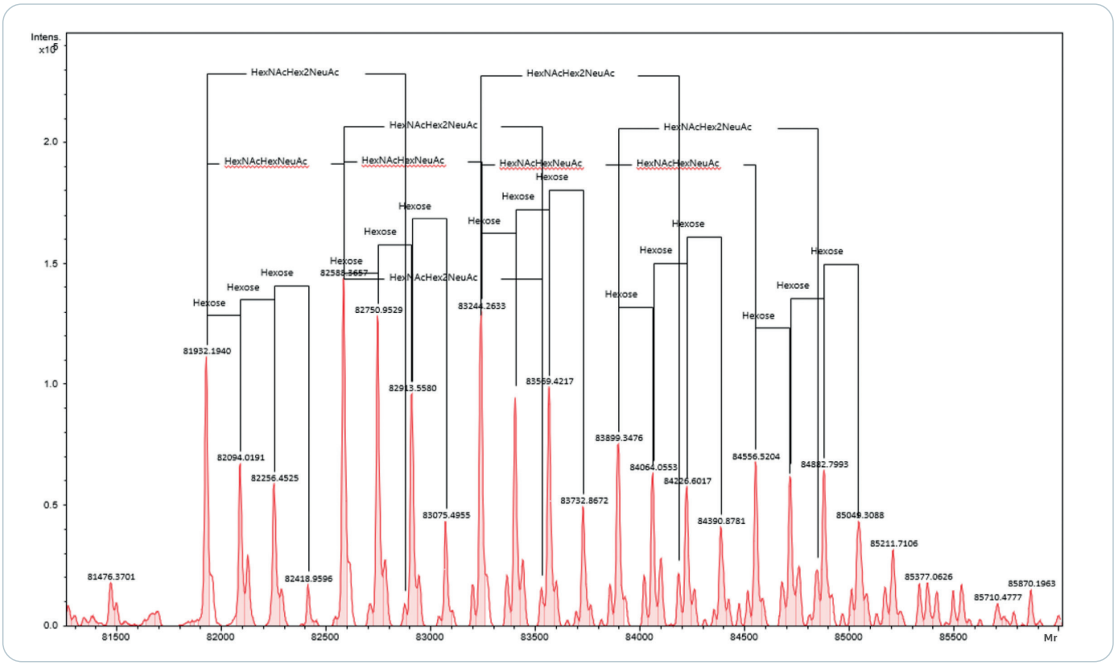
Jay Jones et al. - (2020) Native size-exclusion chromatography-mass spectrometry: suitability for antibody–drug conjugate drug-to-antibody ratio quantitation across a range of chemotypes and drug-loading levels, mAbs, 12:1, 1682895, DOI: 10.1080/19420862.2019.1682895



Comparison of HIC (Panel a) and nSEC-MS (panel b) profiles of ADC-A samples at three different DAR levels. Linear correlation of ADC-A DAR detemination by both methods is shown in panel c and a graphical representation of nSEC-MS equivalence to HIC for ADC-A DAR given previously established EAC is shown in panel d.

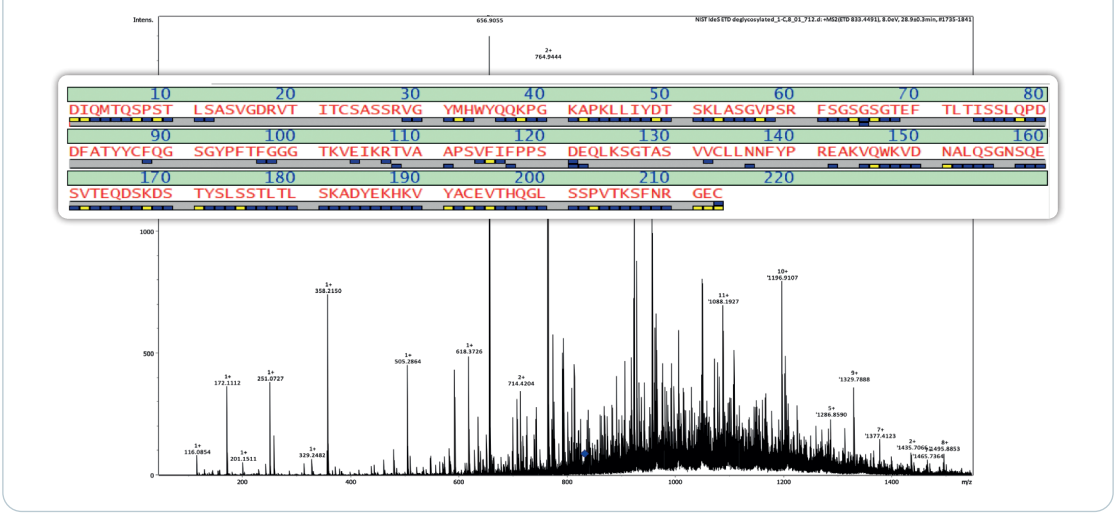
Tools for complex biologics characterization

Analysis of non-covalent interactions with native MS

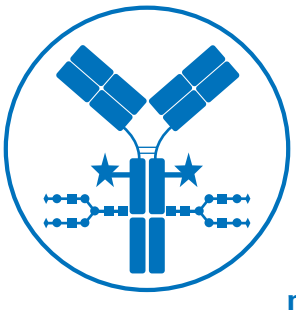


Elucidation of a glycosylated protein dimer (App note LCMS-142 with BMS)

Comprehensive middle-down sequence coverage with ETD at HPLC speed



65% sequence coverage of the Fc/2 NISTmAb subunit in a single LCMS run



maXis II delivers proven performance to accelerate your Biologics development

- Leading isotopic fidelity for the full scan analysis of large molecules
- Unmatched mass accuracy for biomolecules under 55 kDa, including subunits, reduced mAbs, siRNA, tRNA and single guide RNA (CRISPR)
- High dynamic range analysis from small molecules to complex biologics
- Facilitating the native analysis of non-covalent molecules such as ADCs and multispecifics
- MS2 sequencing for primary sequence verification and analysis of PTMs or heterogeneities
- Optional ETD capabilities to directly analyze protein impurities

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