



A comprehensive CE/ESI-MS solution for BioPharma applications

Thermo Scientific Q Exactive hybrid quadrupole-Orbitrap
mass spectrometers with ZipChip system

*Fast CE Separation
Nanospray Sensitivity
HRAM Spectrometry*

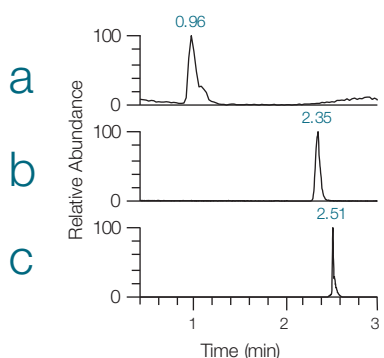


A unique and powerful combination of CE/ESI and MS technology designed for BioPharmaceutical applications

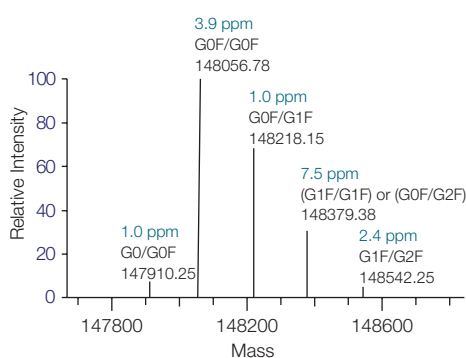
Thermo Scientific™ Q Exactive™ hybrid quadrupole-Orbitrap™ mass spectrometer platforms coupled with the 908 Devices™ ZipChip™ system can characterize a wide range of bio-analytes via unique microfluidic capillary electrophoresis (CE) separation and high resolution accurate mass (HRAM) spectrometry identification. This exceptionally fast, sensitive, and accurate CE/ESI-MS workflow complements LC-MS technology to address analytical challenges in BioPharma.

The unique ZipChip system and powerful Q Exactive MS combine with Thermo Scientific™ BioPharma Finder™ software and ZipChip consumables to offer **a comprehensive CE/ESI-MS solution for intact antibodies and antibody drug conjugates (ADC), antibody subunits, and peptide analyses.**

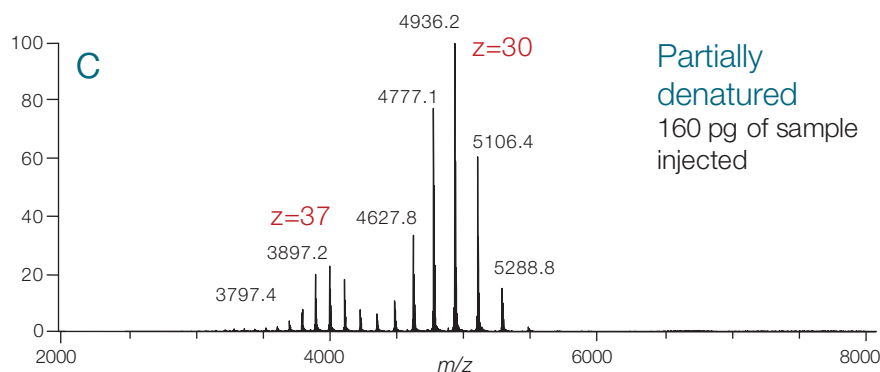
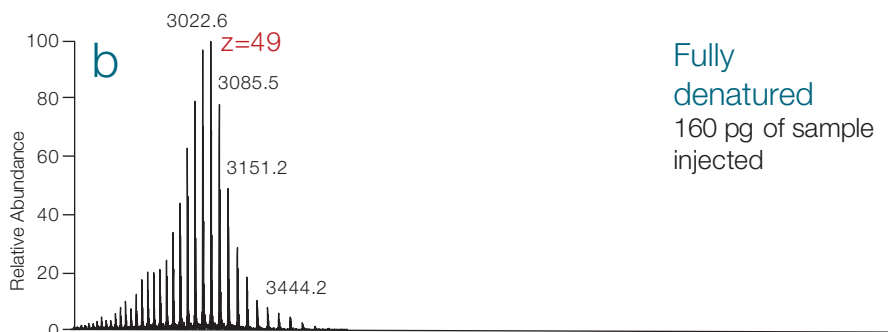
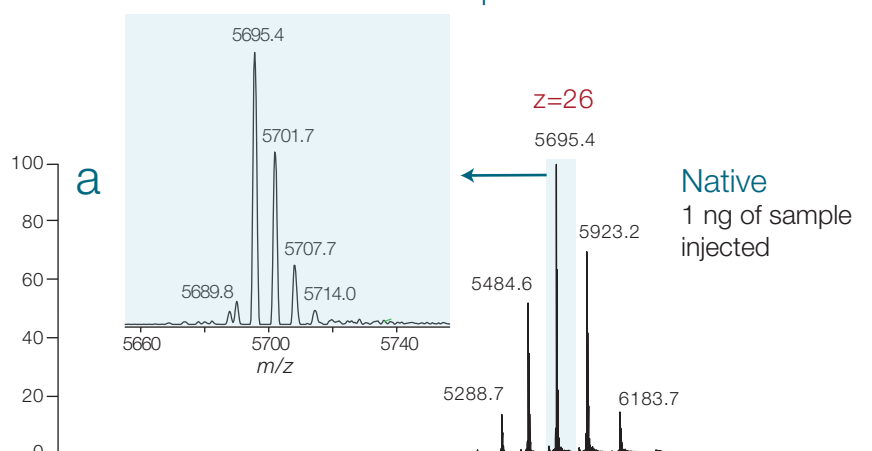
Electropherograms of intact trastuzumab corresponding to spectra a,b,c shown below



Deconvoluted spectrum



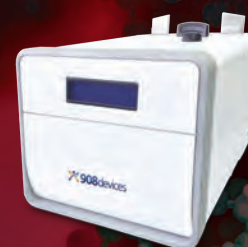
Full MS spectra



Intact mAb Analysis in HMR mode

The ZipChip system and Q Exactive MS platforms can quickly analyze intact mAbs in native, partially denatured, and fully denatured conditions to support characterization of biotherapeutics under a diverse range of conditions.

- The CE/ESI-MS analysis can be completed within 3 minutes
- Confidently achieve high resolution accurate mass spectra in intact native, partially denatured, and fully denatured states on the Thermo Scientific™ Q Exactive Plus, HF, HF-X hybrid quadrupole-Orbitrap™ MS with the BioPharma option
- Sample consumption can be as low as picograms to nanograms
- Major glycoforms are identified by BioPharma Finder software



ZipChip interface



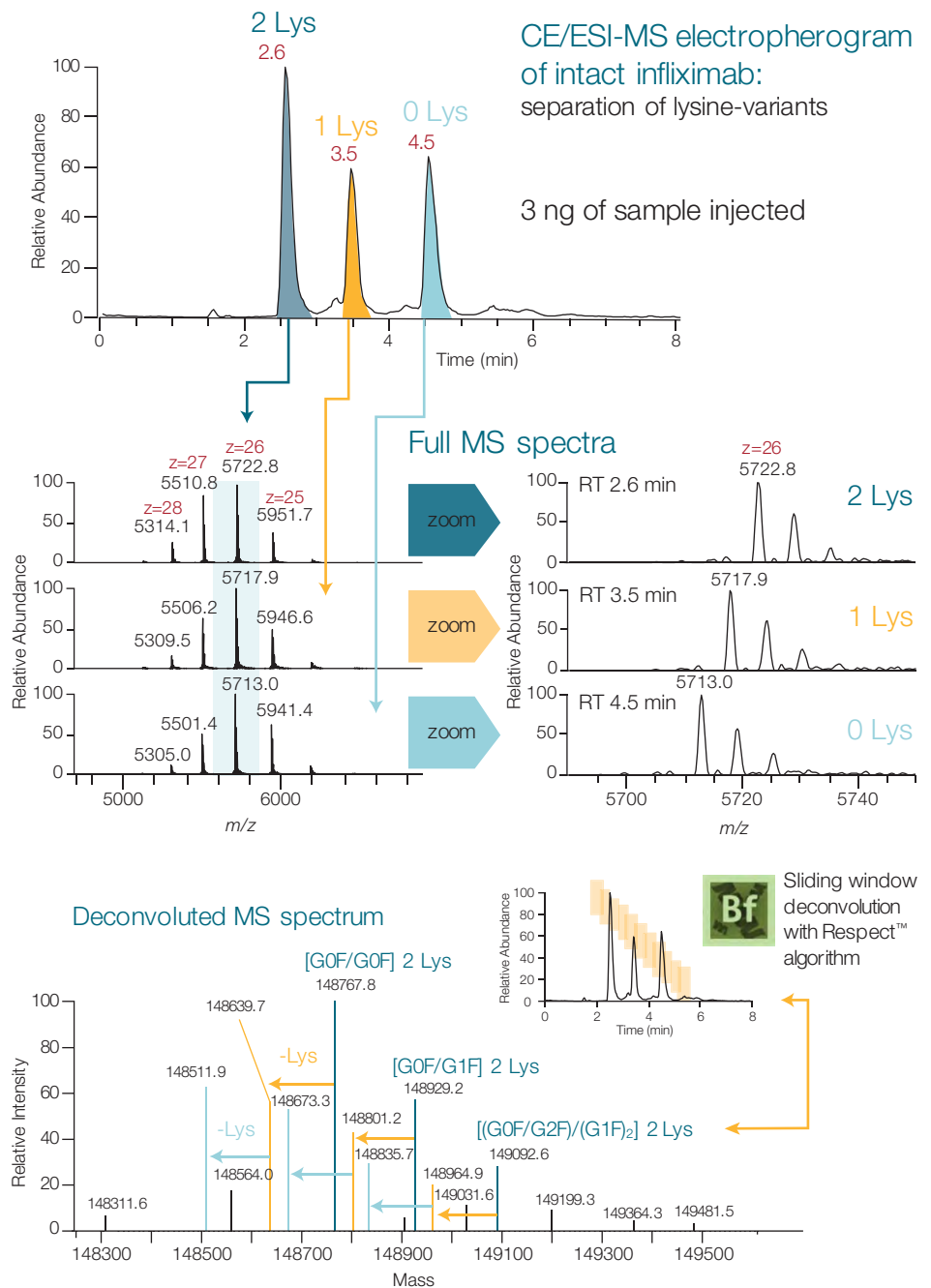
BioPharma Finder software

MS data were acquired on the Q Exactive HF-X mass spectrometer equipped with the BioPharma option

Intact mAb Analysis in HMR mode

The ZipChip system and Q Exactive MS platforms are unique and powerful in their ability to separate and identify different intact antibody charge variants in native and denaturing conditions.

- Baseline separation of intact mAb charge variants resulting from different levels of Lys-clipping can be achieved within three minutes by the ZipChip system
- High resolution accurate mass spectra of all lysine variants are confidently detected on Q Exactive Plus/HF/HF-X MS with the BioPharma option*
- Three major glycoforms from each of the three lysine variants are identified by BioPharma Finder software with mass accuracies better than 10 ppm



Theoretical and experimental masses of infliximab glycoforms of lysine variants

Lys-Variant	Glycoform	Theor. Average Mass	Exp. Average Mass	Δ Mass (ppm)
2 Lys	G0F/G0F	148768.5	148767.8	4.8
2 Lys	G0F/G1F	148930.7	148929.2	9.8
2 Lys	(G1F)2 or (G0F/G2F)	149092.8	49092.6	1.3
1 Lys	G0F/G0F	148640.3	148639.7	4.3
1 Lys	G0F/G1F	148802.5	148801.2	8.6
1 Lys	(G1F)2 or (G0F/G2F)	148964.6	148964.9	-1.8
0 Lys	G0F/G0F	148512.2	148511.9	1.6
0 Lys	G0F/G1F	148674.3	148673.3	6.8
0 Lys	G1F)2 or (G0F/G2F)	148836.5	148835.7	5.1

*MS data were acquired on the Q Exactive HF-X mass spectrometer equipped with the BioPharma option

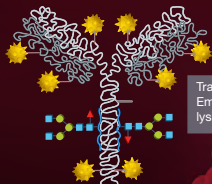
Antibody-Drug Conjugate Analysis in HMR mode

Heterogeneous ADCs can be successfully characterized within 1 minute by utilizing a ZipChip system and Q Exactive Orbitrap MS workflow with BioPharma Finder software.

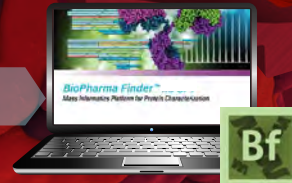
- Powerful sliding window capability enabled by BioPharma Finder software allows for highly accurate average masses

- All the different forms of Trastuzumab Emtansine can be analyzed extremely fast with extremely low sample consumption
- No sample pre-treatment is needed
- The calculated average DAR values are consistent with previous published data

Trastuzumab Emtansine



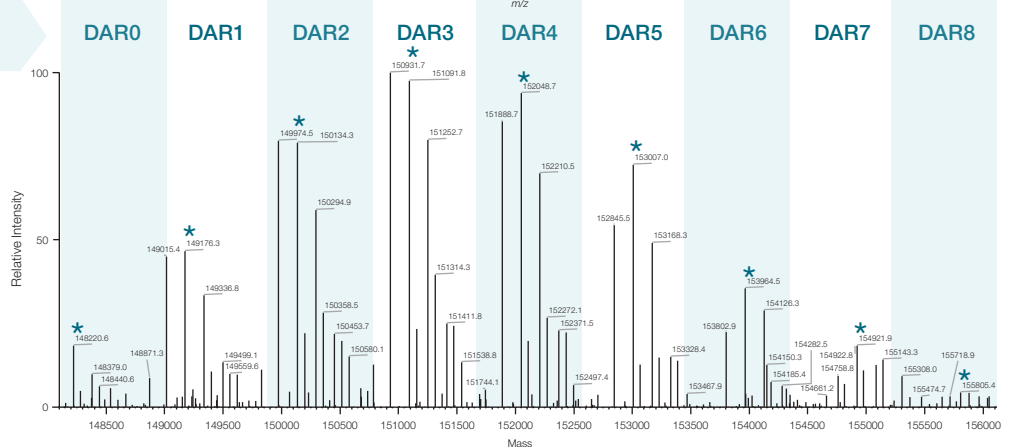
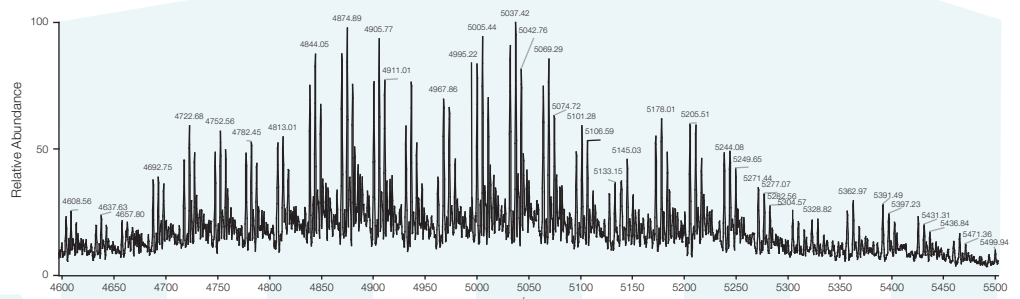
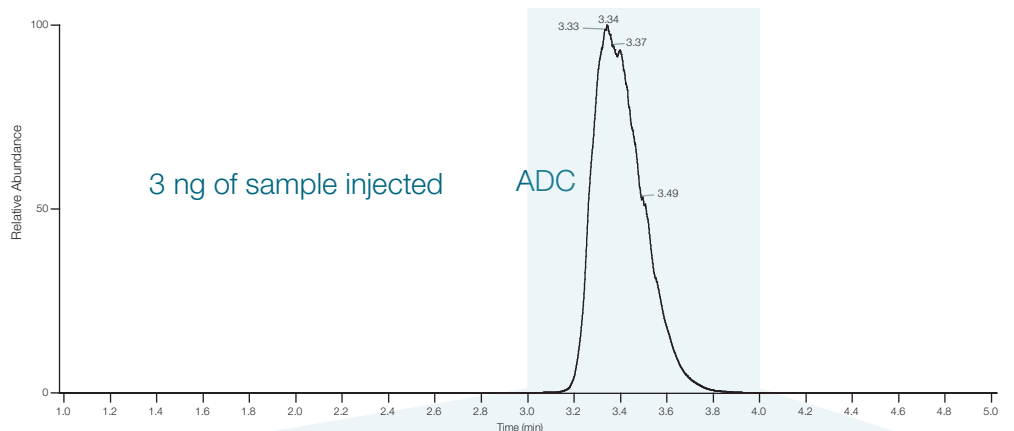
Trastuzumab Emtansine lysine-linked ADC



Average Drug-to-Antibody (DAR) Ratio

3.47

* G0F/G1F DAR Form	Mass Accuracy (ppm)	Relative Abundance
DAR0	10.72	9.95
DAR1	7.45	33.47
DAR2	1.23	58.97
DAR3	2.37	79.90
DAR4	5.63	69.92
DAR5	9.08	49.14
DAR6	13.89	28.97
DAR7	9.93	12.64
DAR8	8.41	2.83

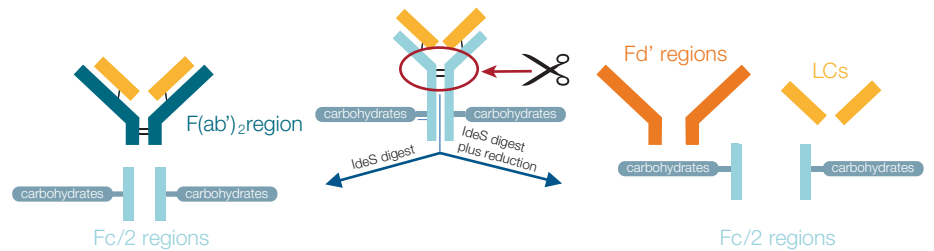


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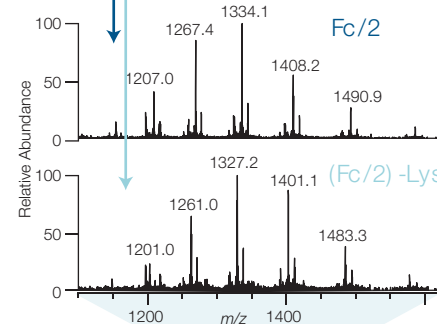
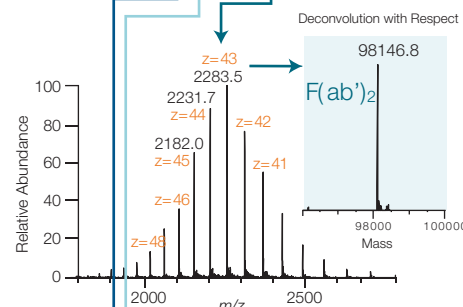
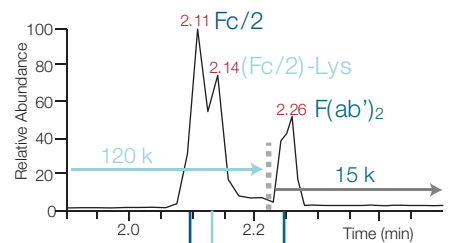
mAb Sub-unit Analysis in Protein Mode

Fast, sensitive, and accurate antibody subunit analysis can be accomplished by the ZipChip system and Q Exactive Plus or HF/HF-X MS platforms.*

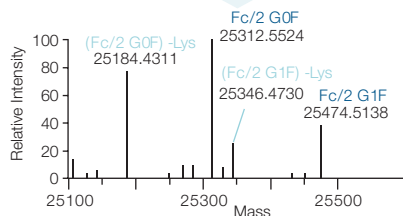
- Separation of infliximab mAb subunits can be achieved in 3 minutes by the ZipChip system
- The sliding window method combined with Thermo Scientific™ Xtract™ deconvolution algorithm in BioPharma Finder software enables monoisotopic mass determination of each subunit
- The subunits of the infliximab antibody mAb and the lysine variant have different migration times and were identified at less than with Δ 5 ppm after processing with BioPharma Finder software



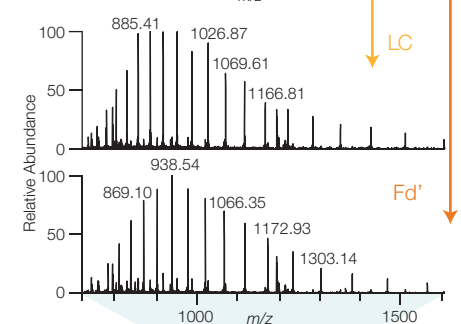
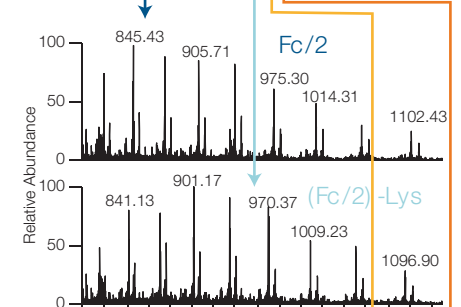
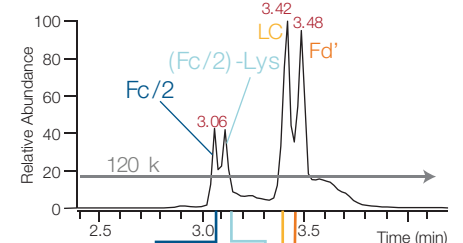
IdeS digested infliximab



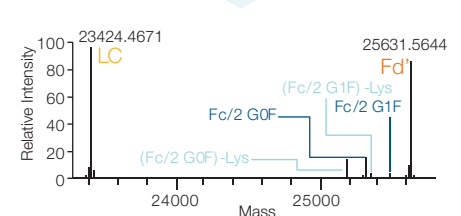
Deconvolution with Xtract



IdeS digested + reduced infliximab



Deconvolution with Xtract



	Subunit	Monoisotopic Theo. Mass	Experimental Mass	Δ Mass (ppm)
IdeS digest plus reduction	Light chain	23424.3946	23424.4671	3.1
	Fd'	25631.5325	25631.5644	1.2
	Fc/2 G0F	25316.5863	25316.6345	1.9
	Fc/2 G1F	25478.6391	25478.5753	2.5
	(Fc/2 G0F)-Lys	25188.49131	25188.5763	3.3
	(Fc/2 G1F)-Lys	25350.54413	25350.5246	0.8
IdeS digest	F(ab)2	98146.3 (av.)	98146.8	-4.8
	Fc/2 G0F (2 SS bonds)	25312.5550	25312.5524	0.1
	Fc/2 G1F (2 SS bonds)	25474.6078	25474.5138	3.7
	(Fc/2 G0F)-Lys (2 SS bonds)	25184.4600	25184.4311	1.1
	(Fc/2 G1F)-Lys (2 SS bonds)	25346.5128	25346.4730	1.6

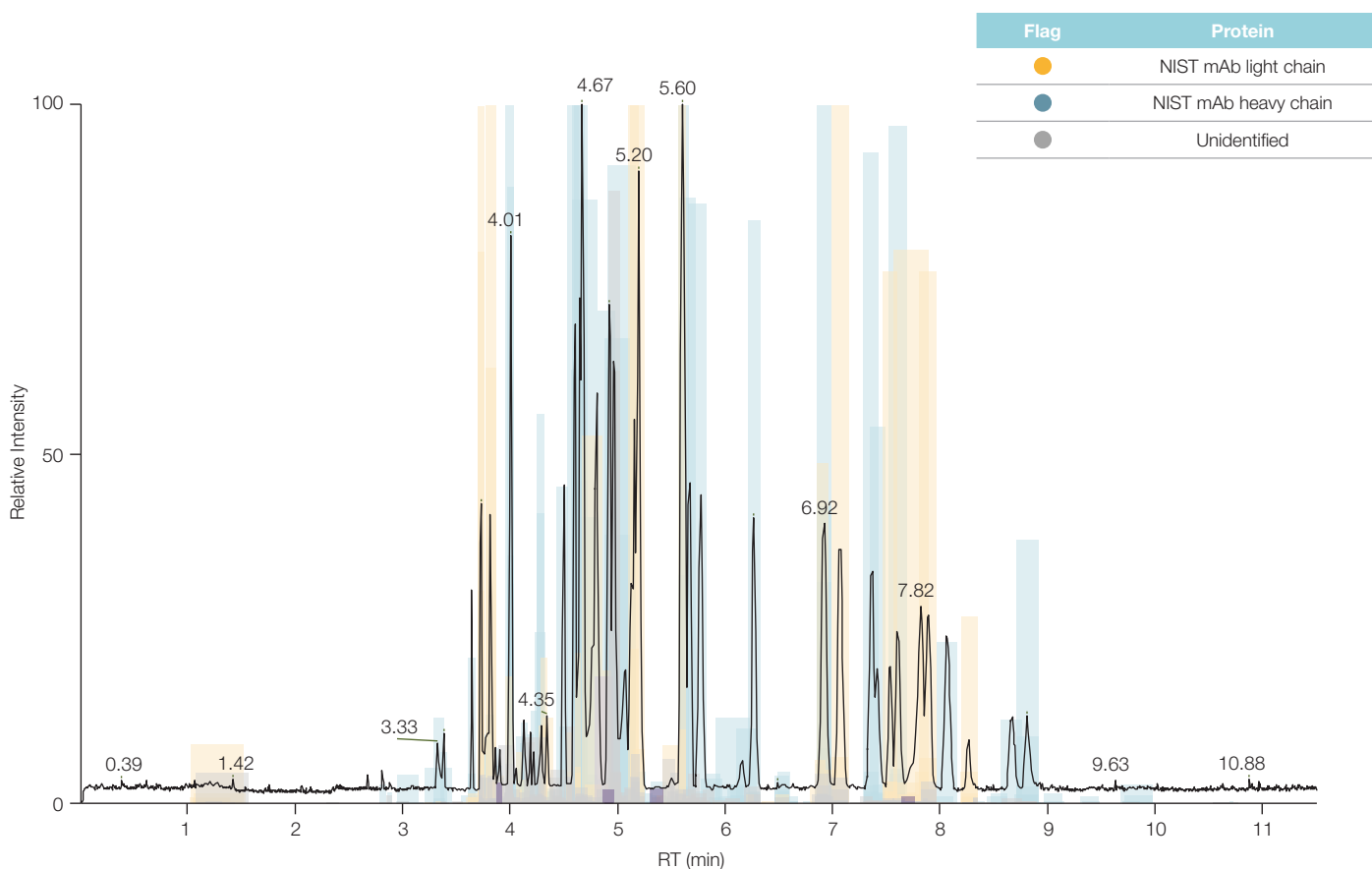
*MS data was acquired on the Q Exactive HF-X mass spectrometer equipped with BioPharma option

Peptide Mapping Analysis in standard mode

The combination of ZipChip sample separation, Q Exactive produced HRAM MS and MS/MS spectra, and BioPharma Finder software enables fast and accurate peptide identification.

- The plug-and-play ZipChip system delivers stable nanospray and nanospray level sensitivity with only 1 nanogram of sample injected for analysis

- Peptides can be separated and analyzed in a 10-minute CE-MS/MS experiment
- 98% sequence coverage based on MS/MS data for the light chain and heavy chain can be confidently achieved



Proteins	Number of MS Peaks	MS Peak Area	Sequence Coverage	Abundance (mol)
NSIT mAb light chain	141	26.4%	100.0%	41.67%
NSIT mAb heavy chain	339	60.5%	97.6%	56.35%
Unidentified	1441	12.6%		

MS data was acquired on the Q Exactive HF mass spectrometer equipped with BioPharma option

Ordering information

Product	Cat. No.
Mass Spectrometer	
Q Exactive Plus MS	0726030
BioPharma Option for Q Exactive Plus	0726055
Q Exactive HF MS	0726041
BioPharma Option for Q Exactive HF	0726060
Q Exactive HF-X MS	0726042
BioPharma Option for Q Exactive HF-X	0726060
BioPharma Finder software	OPTON-30592
CE/ESI	
ZipChip Interface (Autosampler version)	00950-01-00492
ZipChip Interface (Manual version)	00950-01-00493
ZipChip Autosampler	00950-01-00494
Consumables	
ZipChip HS	00950-01-00498
ZipChip HR	00950-01-00499
ZipChip Metabolites Assay Kit	00950-01-00500
ZipChip Peptides Assay Kit	00950-01-00501
ZipChip Intact Protein Assay Kit	00950-01-00502

Find out more at thermofisher.com/zipchip

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