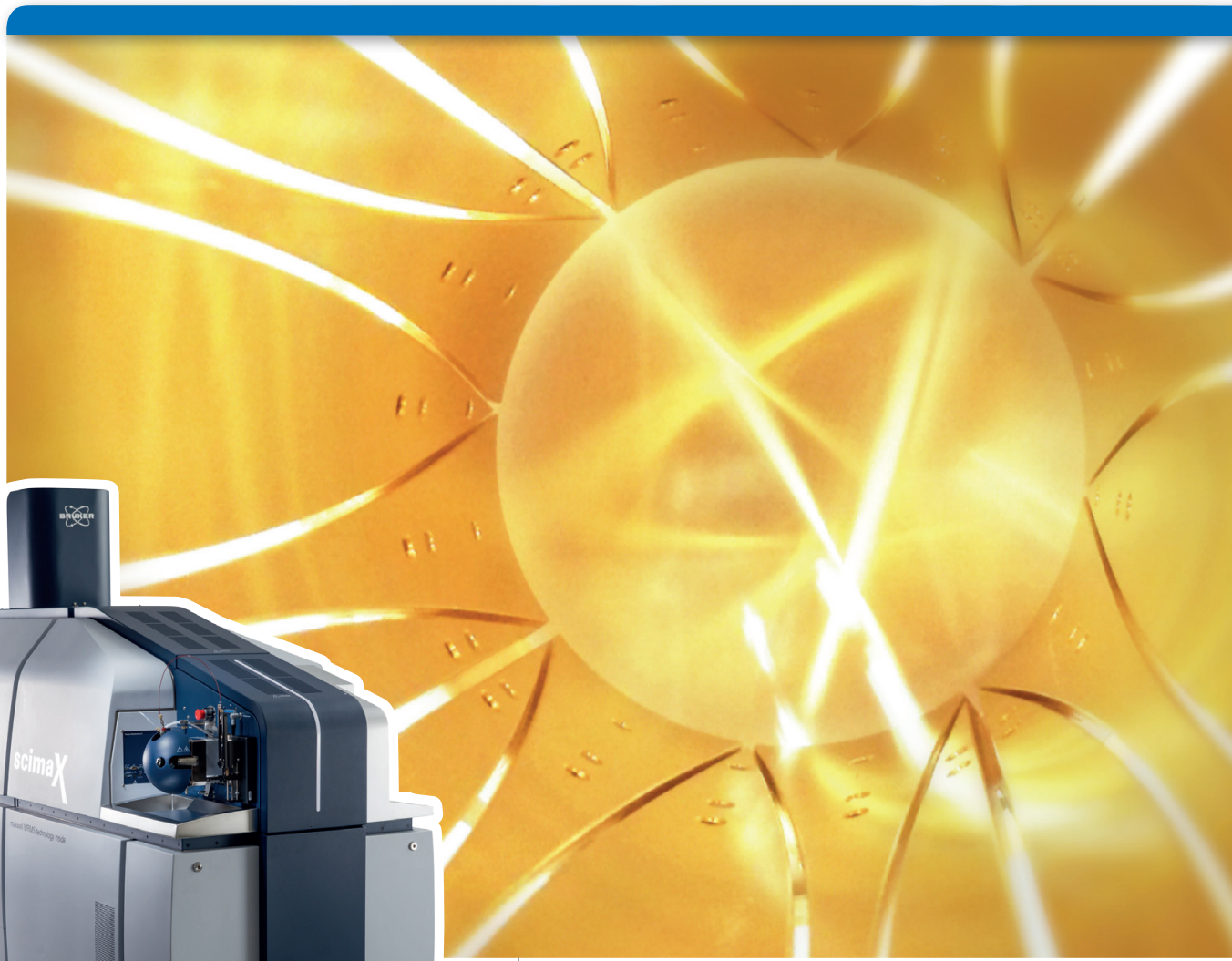
BRUKER



scimaX

The Applications Book

Innovation with Integrity

MRMS

scimaX MRMS

Enabling High Field Performance at 7T

Magnetic Resonance Mass Spectrometry (MRMS) is the panicle of mass spec in terms of mass accuracy, resolving power and flexibility.

scimaX MRMS opens new analytical doors, is reliable and easy to use, providing answers no other instrument can obtain.

Maxwell magnet technology does not require liquid cryogen fills, ever, enabling a smaller footprint that can fit in any standard laboratory.

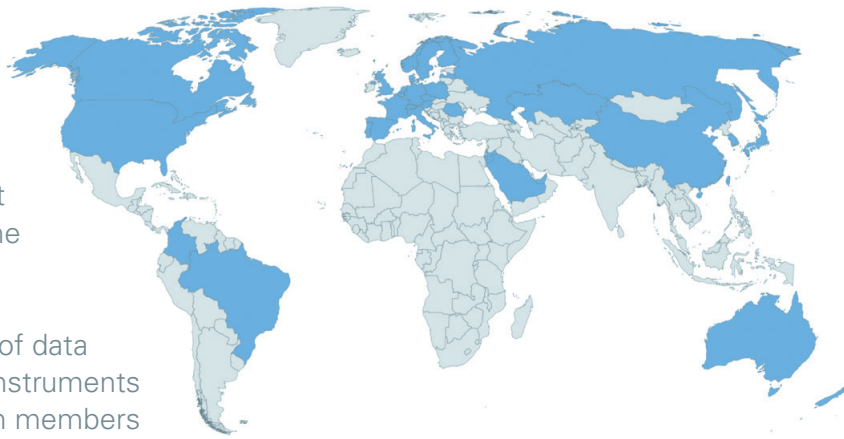
scimaX MRMS

Welcome Letter

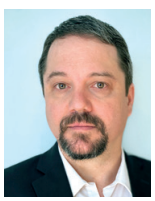
Dear Mass Spec Customer,

Thank you for your interest in Bruker's scimaX. Powered by MRMS (Magnetic Resonance Mass Spectrometry) and building on a tradition of record setting magnet designs (1.2 GHz NMR, 18T MRI and 21T ICR), Bruker's novel Maxwell magnet means no liquid cryogen fills – ever.

At the heart of scimaX is the ParaCell with 2xR detection, enabling high field performance at 7T. Having a maximum resolving power in excess of 20M, MRMS brings access to large scale research projects that can benefit population health, global energy, and the environment.



We are happy to provide this synopsis of data acquired on the scimaX MRMS. With instruments in 35 countries, our global MRMS team members are there for you. Please reach out to your local representative to lean how we can integrate this technology into your lab.



Christopher J. Thompson, Ph.D., Business Manager MRMS,
Bruker Scientific LLC, Billerica, MA, USA

Professor Joe Loo, University of California, Los Angeles, USA

"The development of the scimaX® will surely be a game-changer for ultra-high resolving power mass spectrometry."

Professor Eugene Nikolaev, ParaCell Inventor, Russian Academy of Sciences, Moscow

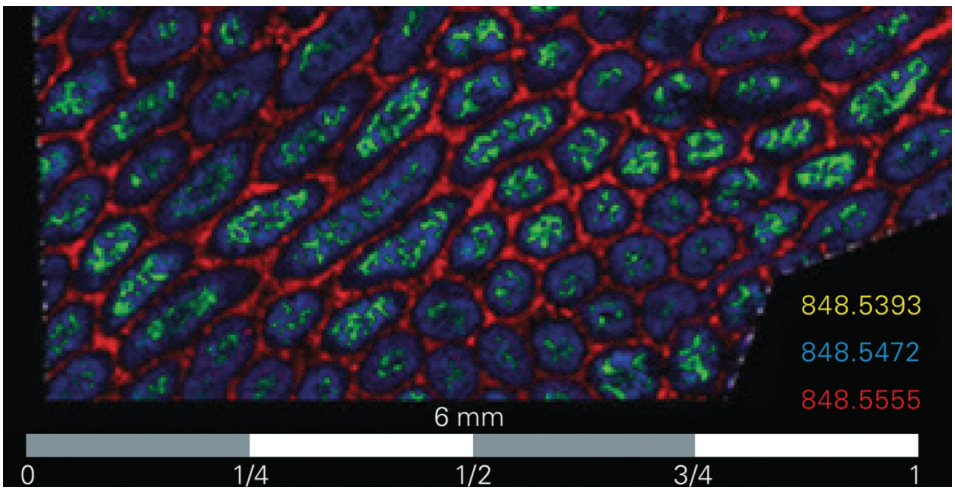
"Continuing the tradition of Bruker innovation, the ParaCell is a new enabling technology for solariX XR. This radical concept is a departure from traditional ICR cell strategies and provides uncommon broadband ion stability resulting in resolution orders of magnitude above other detection schemes. This power enables the user to effortlessly obtain the extreme resolving power needed to probe isotopic fine structure or highly complex mixtures."

Overview of Applications

MALDI Imaging

Requirements for MALDI Imaging

scimaX is the ultimate MALDI Imaging system for analyzing small to medium molecules, *m/z* 100-1500. Its unrivaled eXtreme Resolution capability and sub-ppm mass accuracy, over a wide mass range, can differentiate images that are only mDa apart and are prerequisite for Isotopic Fine Structure (IFS) analysis and molecular formula confirmation.



Realize the full benefit of eXtreme Resolution. Above, a 3-color image from rat testis showing distributions of three ions at nominal *m/z* 848 and differing only by less than 20 mDa.

MALDI Imaging

Customer Insights

Professor Jonathan Sweedler, Ph.D., University of Illinois at Urbana Champaign

"If I had to pick one instrument to save in a fire (and did not have to worry about its size or weight), it would be the solariX XR."

Professor Richard R. Drake, Ph.D., MUSC Proteomics Center, Medical University of South Carolina

"We have developed and continue to evolve new glycan and glycoprotein methods for MALDI imaging. Bruker has been a strong partner in facilitating and supporting these efforts with their innovative instrumentation and software solutions."

Professor Dr. Per Andrén, Mass Spectrometry Imaging, Department of Pharmaceutical Biosciences, University of Uppsala, Sweden and Director of the National Resource for Mass Spectrometry Imaging (NRMSI).

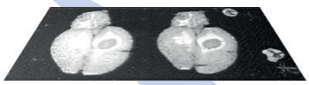
"The solariX is never resting. This is why I am so eager to buy a second one. If I had two, I could obtain my data a lot faster, and also complete more collaborations."

MALDI Imaging

The workflow

Sample cohort

Mount sections

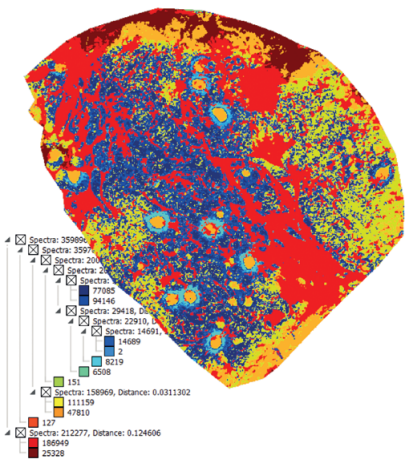


Apply matrix

Acquire data

View/analyze data

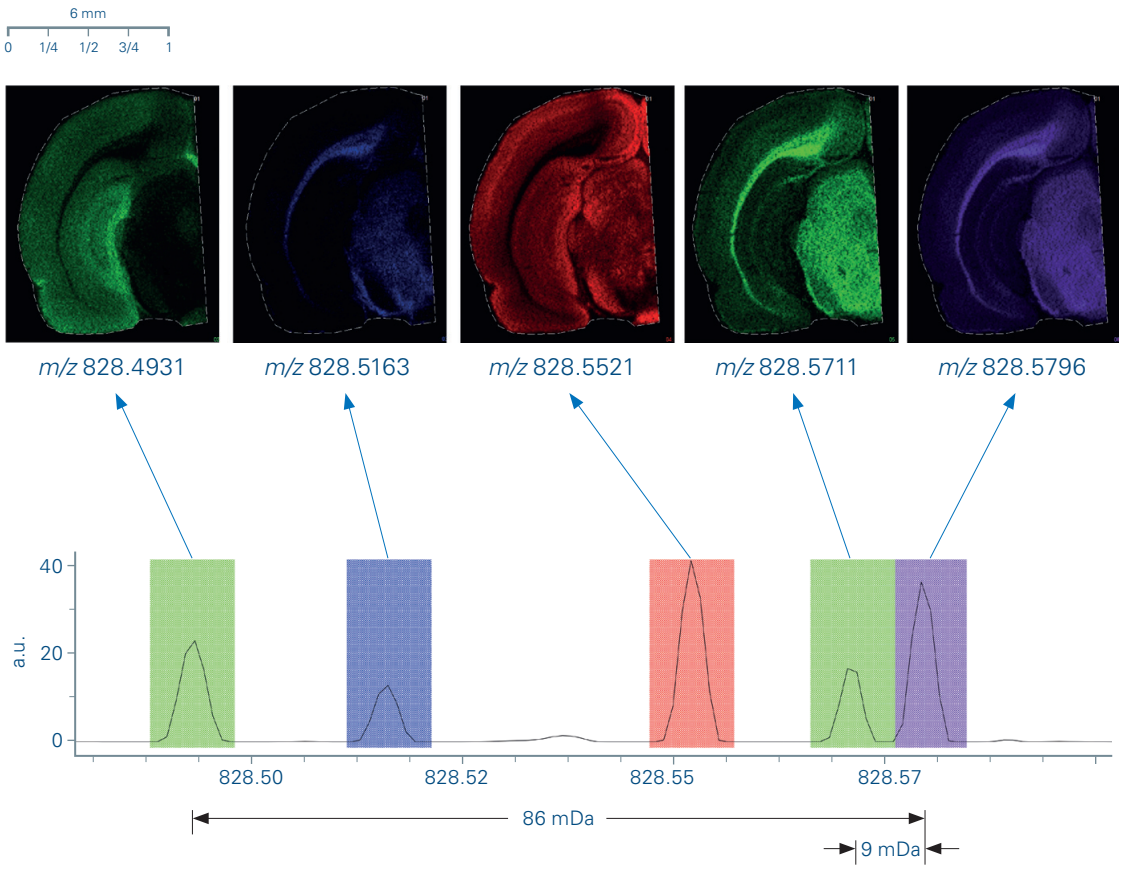
SCiLS



MALDI Imaging

Rat brain

2xR MALDI Imaging



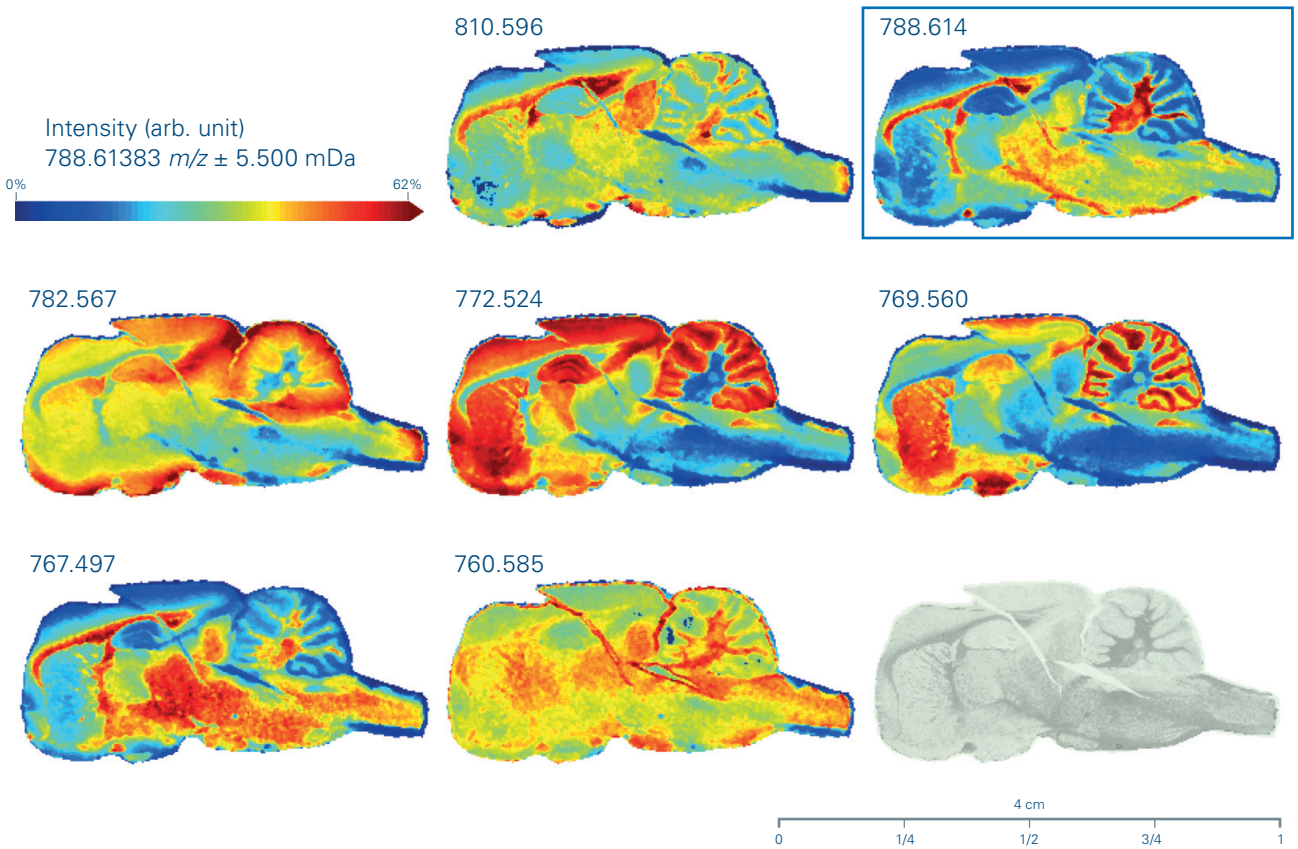
Compared to XR Imaging, 2xR offers the choice to acquire mass resolution in almost half the time without compromising or to acquire at double mass resolution without increasing acquisition time. Here, data is acquired in less than 7 hours at mass resolution of 800,000.

Imaging of rat brain
lateral resolution: 50 µm
R: 820,000 (2ω)
@ *m/z* 273

MALDI Imaging

Rat brain

2xR MALDI Imaging



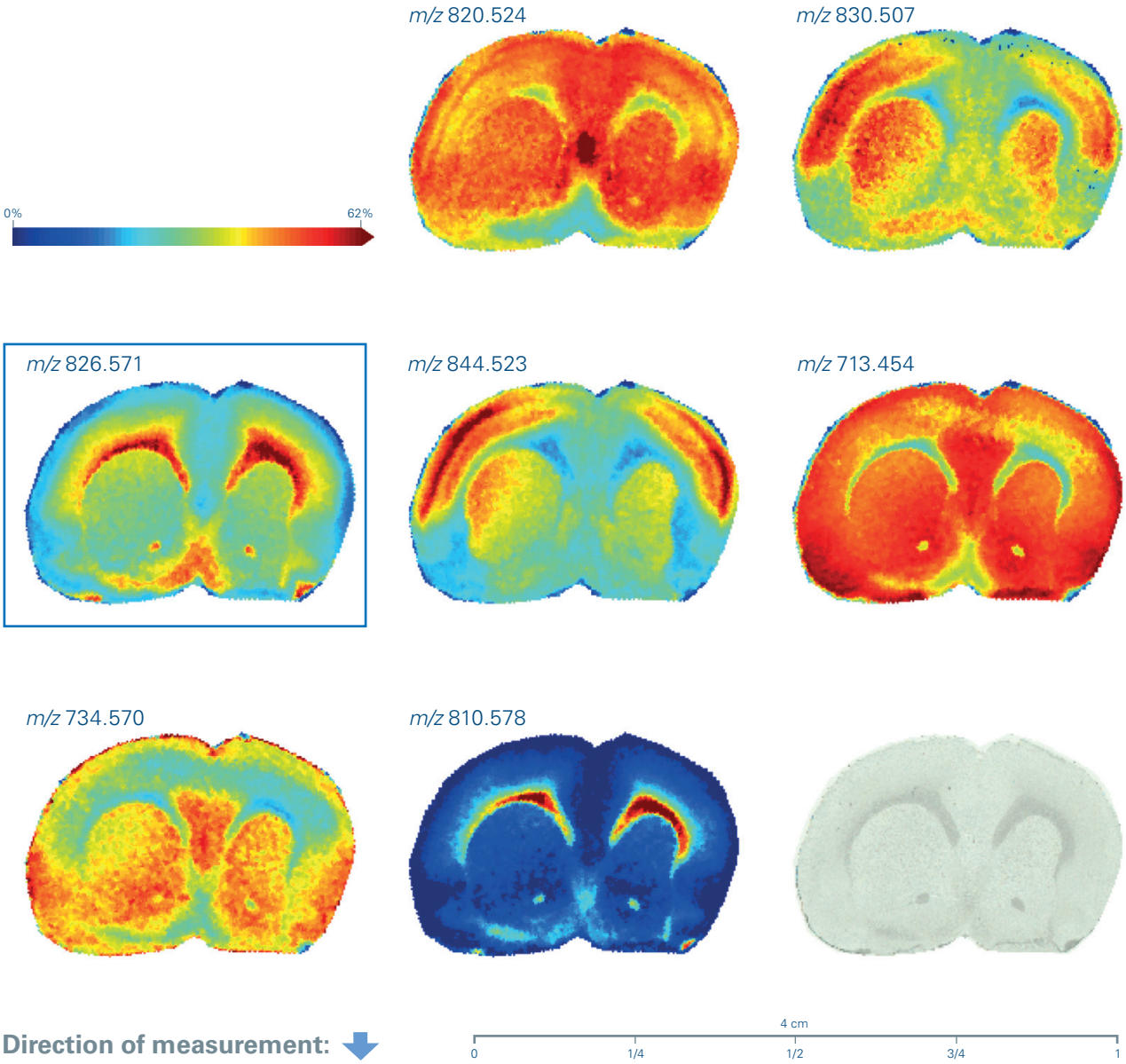
scimaX Imaging of a rat brain with standard 2xR detection provides fast imaging speed while retaining eXtreme mass resolution.

Imaging of rat brain (sagital cut)
Lateral resolution: 70 μm
R: 250,000
@ *m/z* 400

MALDI Imaging

Rat brain

2xR MALDI Imaging



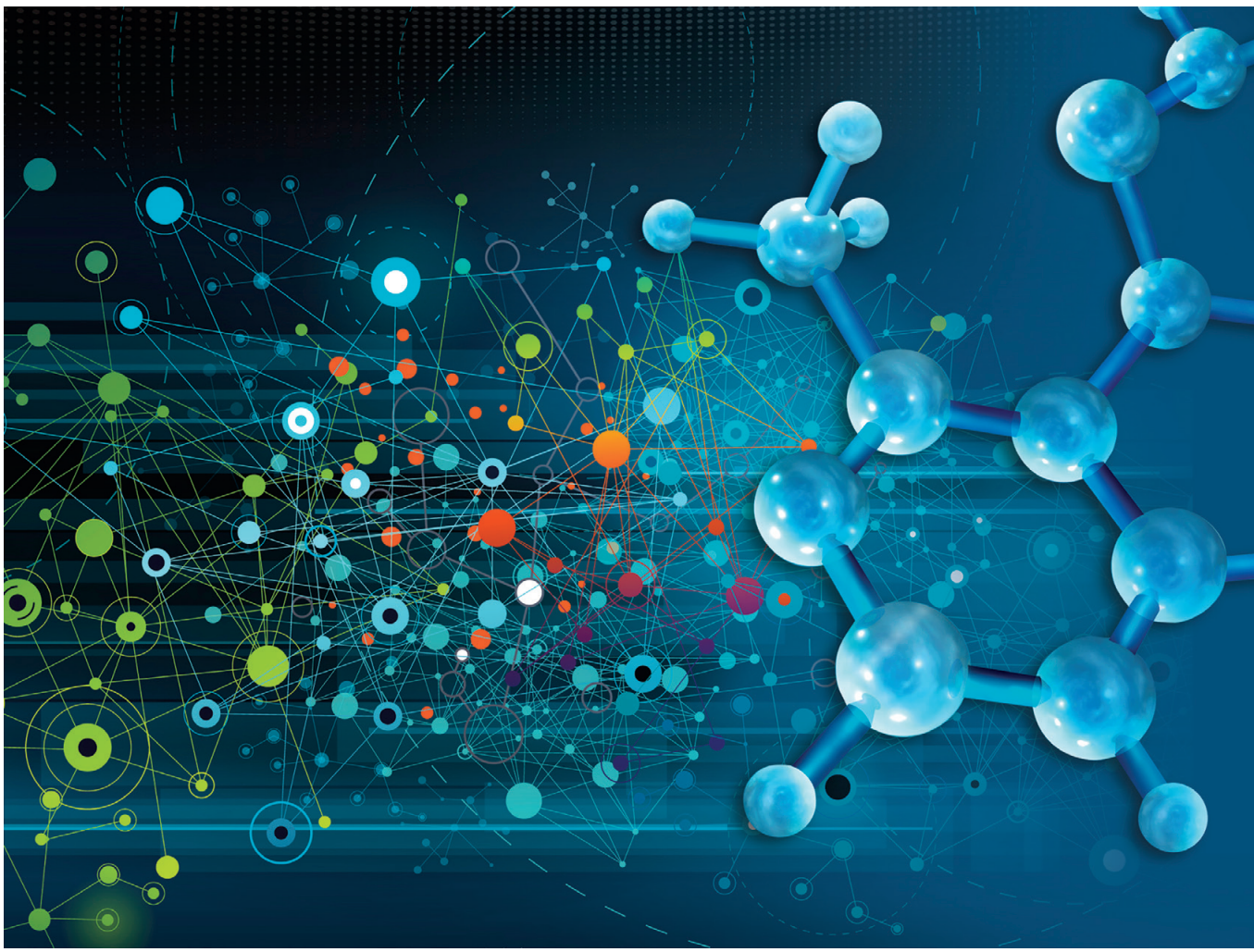
scimaX Imaging of a rat brain with standard 2xR detection provides fast imaging speed while retaining eXtreme mass resolution

Imaging of rat brain (coronal cut)
Lateral resolution: 70 µm
R: 250,000
@ *m/z* 400

Metabolomics

Requirements

Whether Metabolomics, Phenomics or any other complex sample analysis, large scale sample evaluation is now possible with scimaX and the MRMS aXelerate workflow. The eXtreme Resolution allows for direct sample analysis and enables true high sample throughput complementary to established NMR based solutions. From the largest unknown to the smallest, scimaX ensures confident molecular formula assignment at any level.



Metabolomics

Customer Insights

Professor Jeremy Nicholson, Ph.D., Director of the Australian National Phenome Center, ProVice Chancellor for Health, Murdoch University

"The performance of our new solariX 7 Tesla MRMS system has met and exceeded all our expectations across a variety of high end metabolic phenotyping challenges in molecular profiling, structure elucidation and imaging – and it is highly user friendly – every laboratory should have one!"

Professor Arthur S. Edison, Ph.D., and GRA Eminent Scholar, Departments of Biochemistry and Molecular Biology and Genetics Institute of Bioinformatics, Complex Carbohydrate Research Center, University of Georgia, Athens, GA

"Virtually every metabolomics project we have going right now will benefit from this new instrumentation ... "

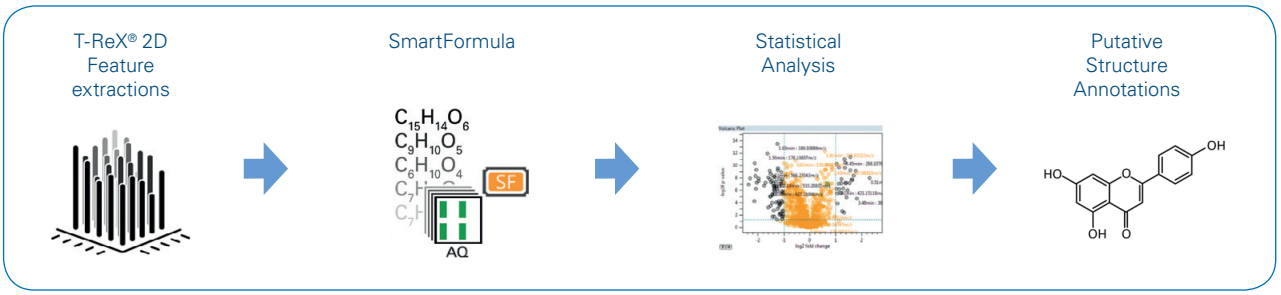
Professor Philippe Schmitt-Kopplin, Ph.D., Analytical BioGeoChemistry, Helmholtz Zentrum München, Germany

"We set up new discovery approaches to describe the compositional space of any complex system in biology and geochemistry. MRMS eXtreme Resolution enables us to address next generation metabotyping, i.e. simultaneous rapid description of hundreds of known and thousands of new metabolites relevant for dynamic biological/chemical processes. MRMS in combination with MetaboScape will also enable other researchers to shed light to this new exiting research field of this yet dark metabolome."

Metabolomics

MRMS aXelerate Workflow

Rapid, LC-free MS followed by statistical analysis provides a sensitive, high-throughput workflow for modern phenotyping and metabotyping.

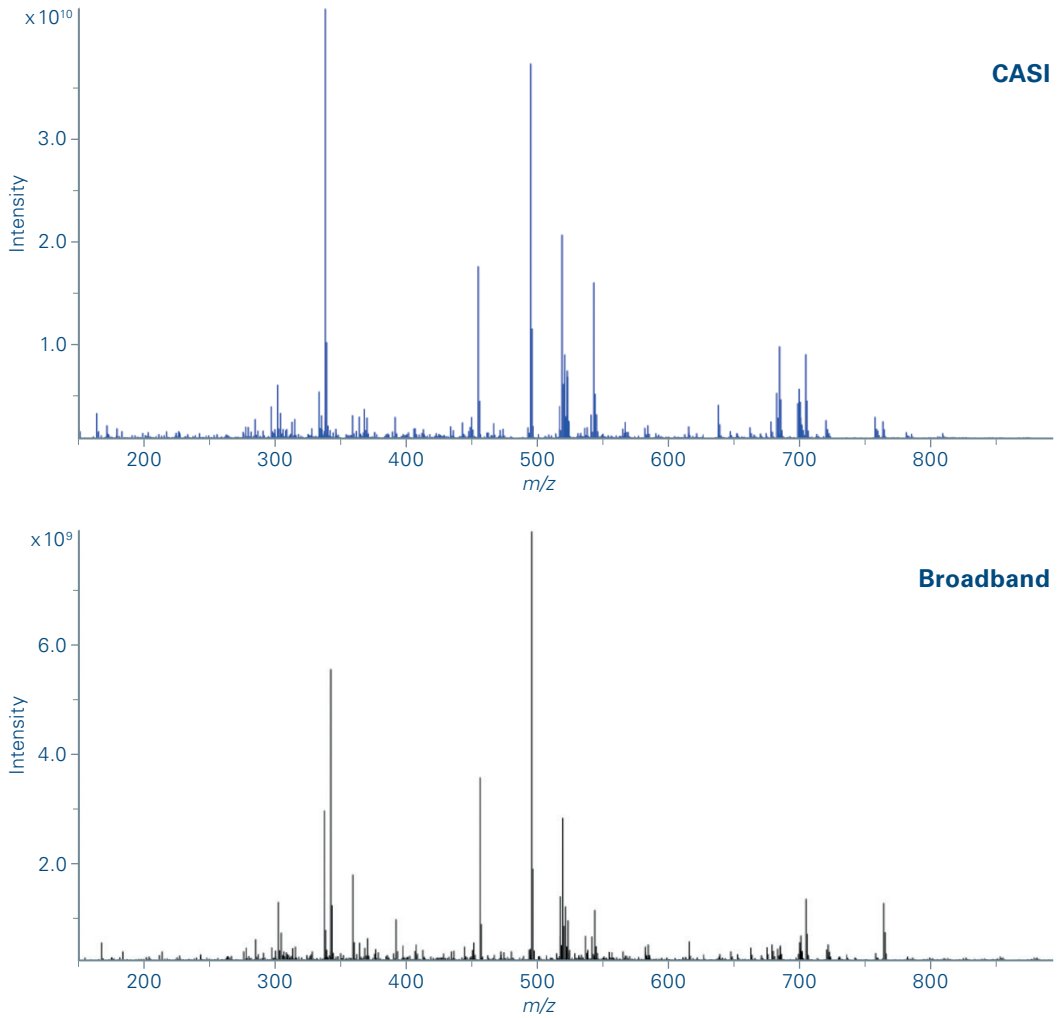


- Accelerate throughput (> 200 samples/day)
- Complementary to established NMR based solutions
- Simultaneous analysis of known and unknown metabolites
- Access compounds not readily detectable by LCMS analysis
- 3-tiered confidence in annotation

Metabolomics: FIA

FIA and CASI, plasma, ESI(+)

High-throughput clinical metabolomics

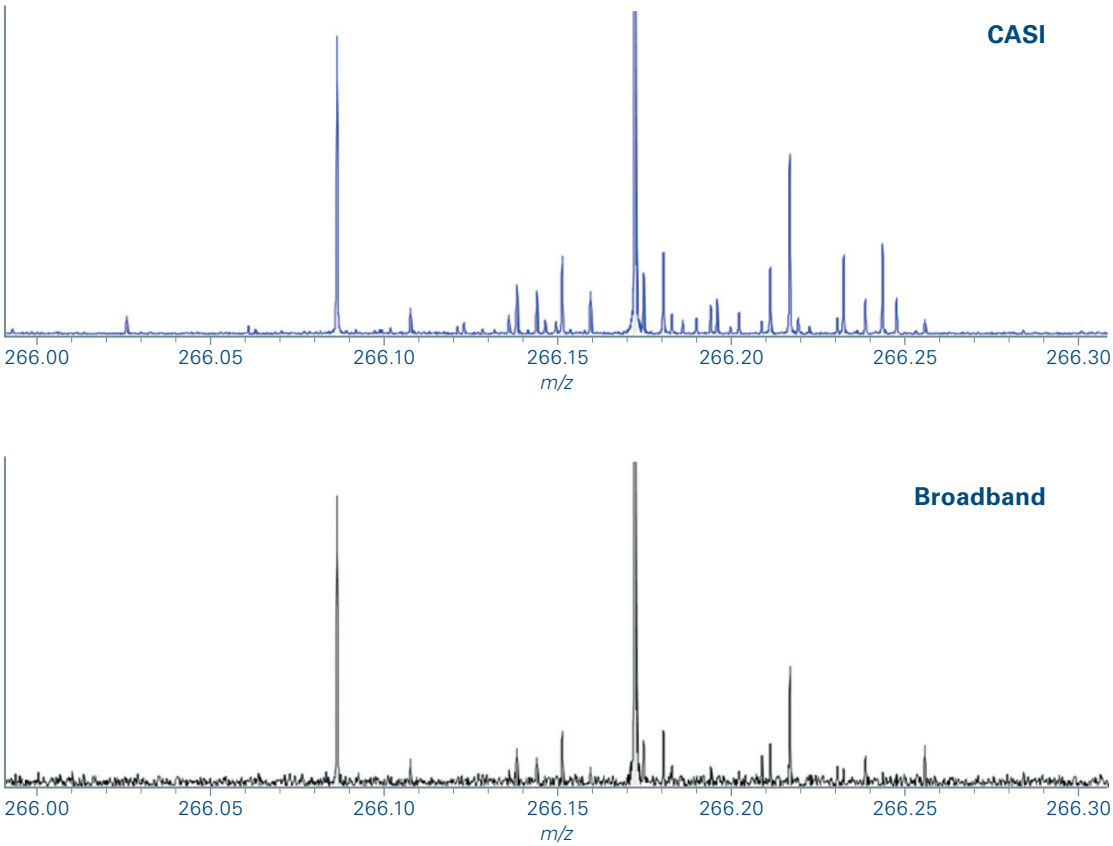


Flow injection analysis (FIA) enables high-throughput sample analysis by eliminating the time-consuming LC step. This also provides increased chemical coverage as the experiment is not bound to the chemistry of the LC column. The combination of these provides a great cost savings to any lab.

Metabolomics: FIA

FIA and CASI, plasma, ESI(+)

High-throughput clinical metabolomics

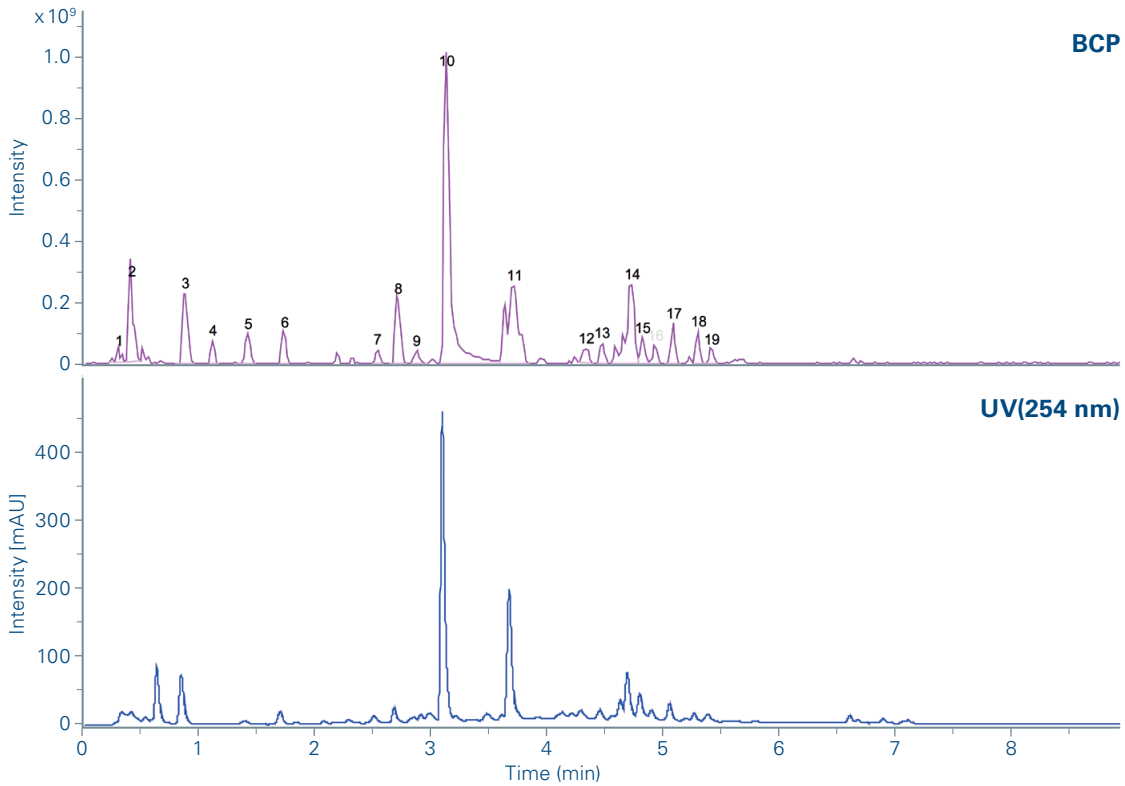


The continuous accumulation of selected ions (CASI) is an enhanced dynamic range experiment that provides increased sensitivity of low intensity species. This sensitivity also brings great utility through the ability to utilize isotopic fine structure for the unambiguous identification of unknown metabolites.

Metabolomics: LCMS

Darjeeling tea, ESI(+), @ 1 Hz

Isotopic fine structure on an LC timescale



scimaX's eXtreme Resolution is also compatible to LC analysis. An example is shown for the analysis of metabolites in Darjeeling tea. The following pages show the use of isotopic fine structure for the identification of compounds during a short gradient LC run.

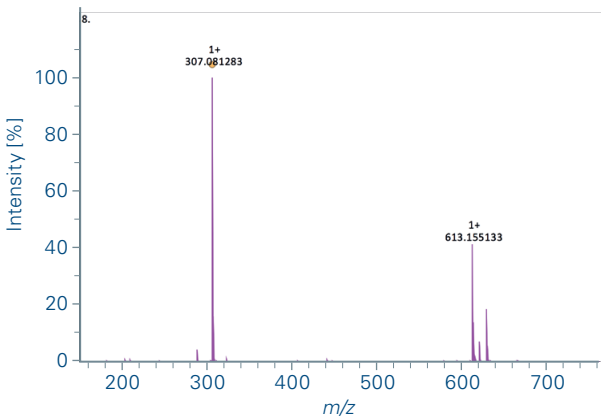
Metabolomics: LCMS

Darjeeling tea, ESI(+), @ 1 Hz

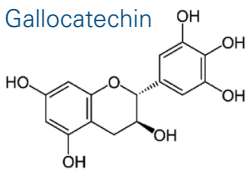
Isotopic fine structure on an LC timescale

Compound 8

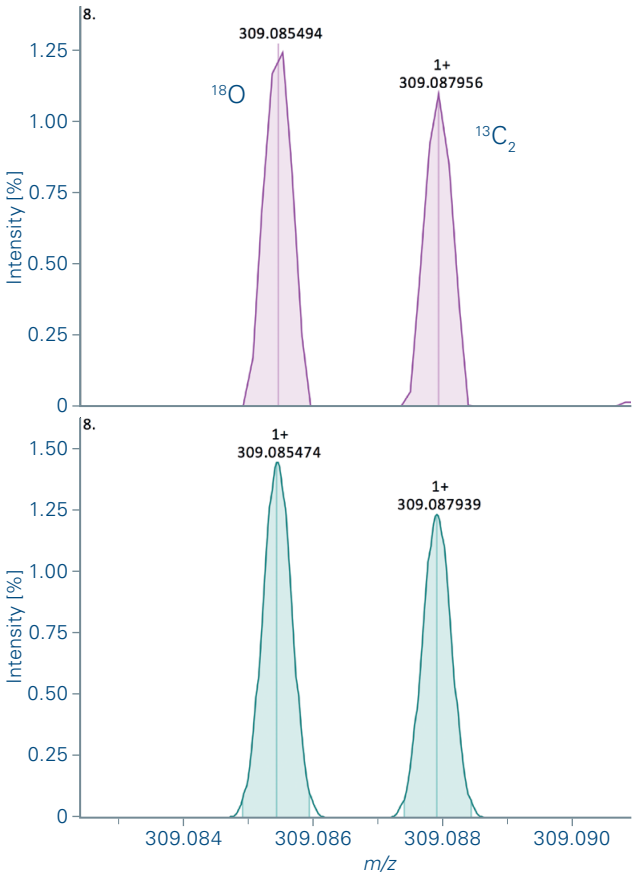
Detection of Gallocatechin



Gallocatechin



A+2 isotopic pattern



Compound 8 in the chromatogram is confidently assigned to Gallocatechin. The ^{18}O isotope is baseline resolved and the peak fidelity yield the correct number of Oxygen atoms in the molecule.

Mass error: 175 ppb

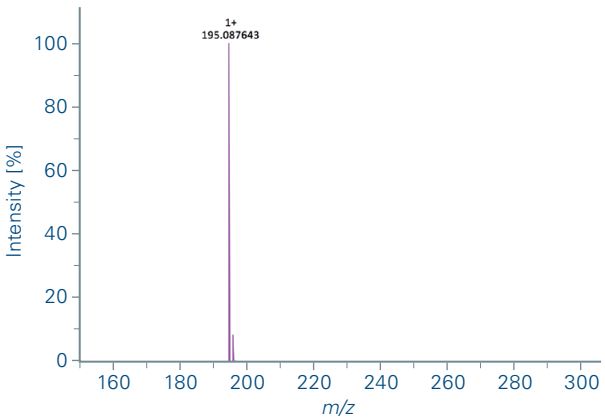
Metabolomics: LCMS

Darjeeling tea, ESI(+), @ 1 Hz

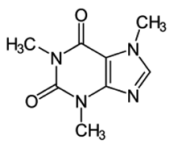
Isotopic fine structure on an LC timescale

Compound 10

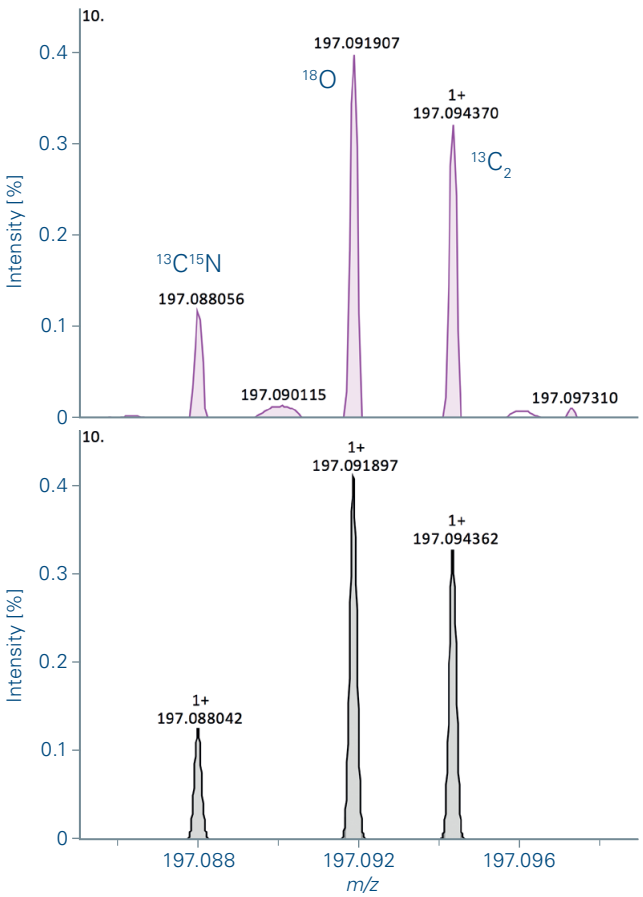
Detection of caffeine



Caffeine



A+2 isotopic pattern



Compound 10 in the chromatogram is confidently assigned to Caffeine. In this example, the A+2 isotope distribution clearly shows three distinct IFS species: $^{13}C_1{}^{15}N_1$, $^{18}O_1$ and $^{13}C_2$

Mass error: 47 ppb

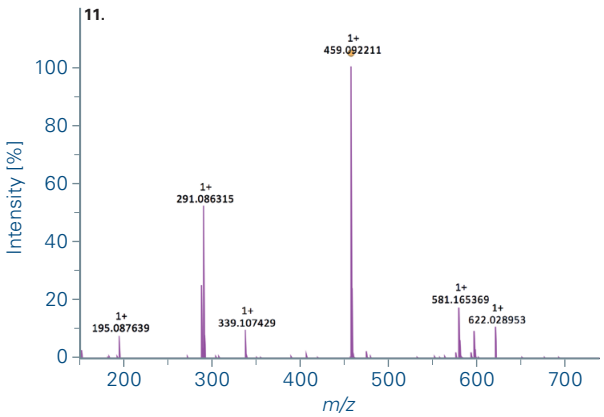
Metabolomics: LCMS

Darjeeling tea, ESI(+), @ 1 Hz

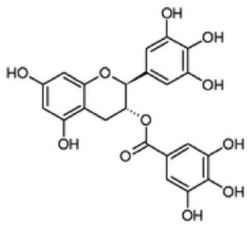
Isotopic fine structure on an LC timescale

Compound 11

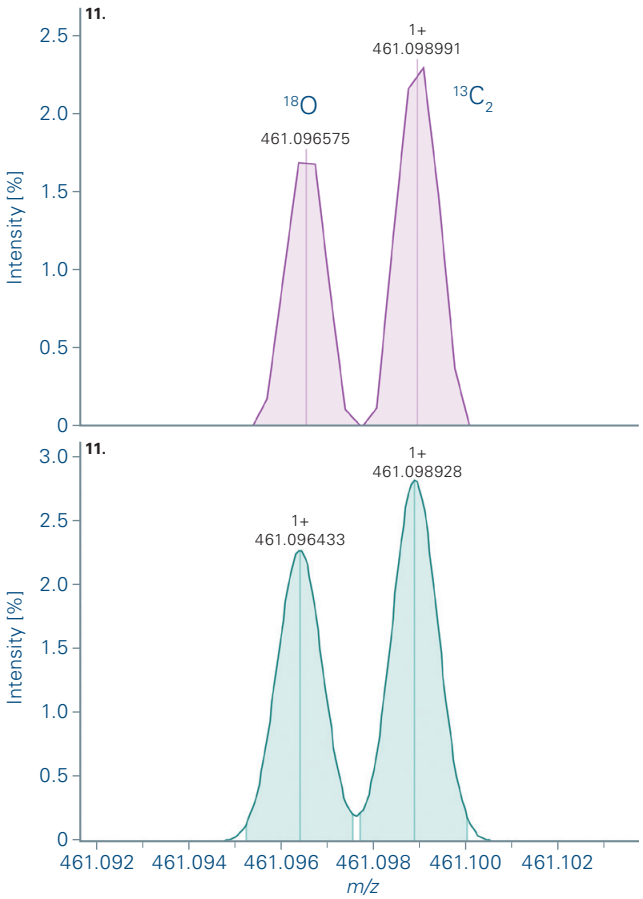
Detection of Epigallocatechin gallate



Epigallocatechin gallate



A+2 isotopic pattern

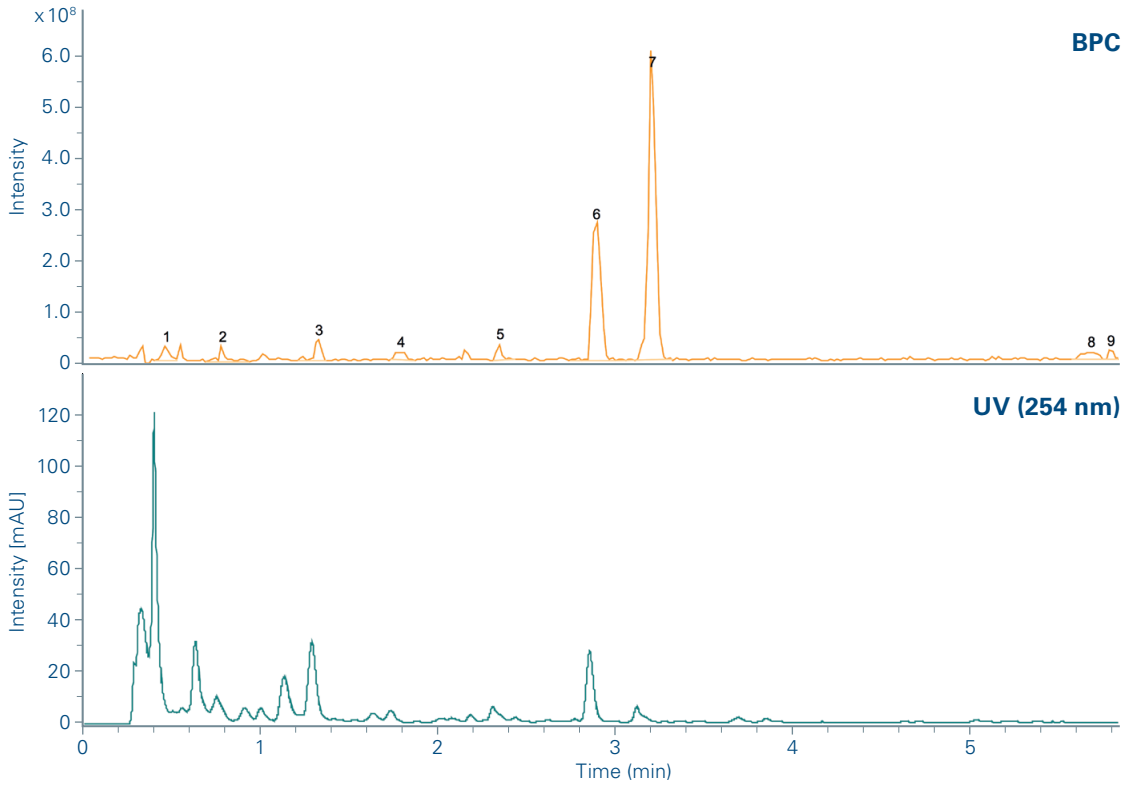


IFS is again present in Compound 11 assigned as epigallocatechin gallate.	Mass error: 51 ppb

Metabolomics: LCMS

Urine, ESI(+), @ 1 Hz

Isotopic fine structure on an LC timescale



Global health concerns are the focus of many groups across the globe. The analysis of complex samples such as blood and urine are routinely analyzed by LCMS. This example shows the LCMS separation of Urine at 1Hz acquisition rate.

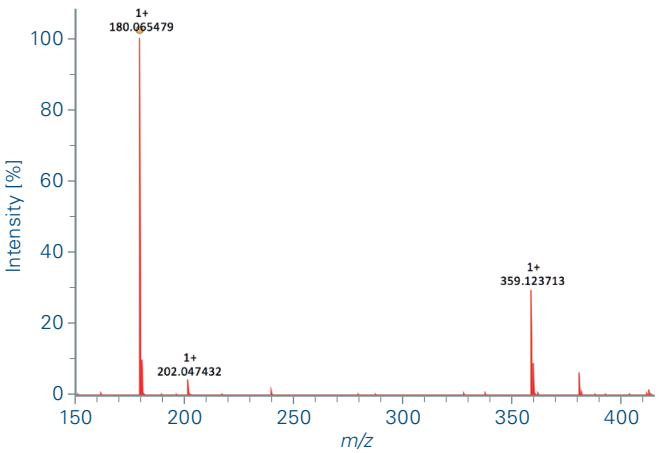
Metabolomics: LCMS

Urine, ESI(+), @ 1 Hz

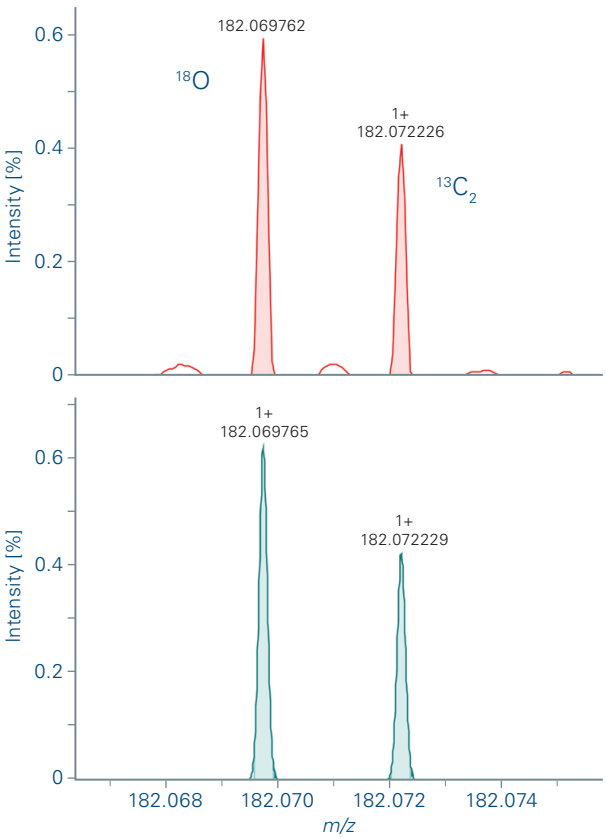
Isotopic fine structure on an LC timescale

Compound 6

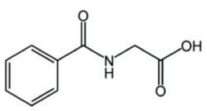
Detection of Hippuric acid



A+2 isotopic pattern



Hippuric acid



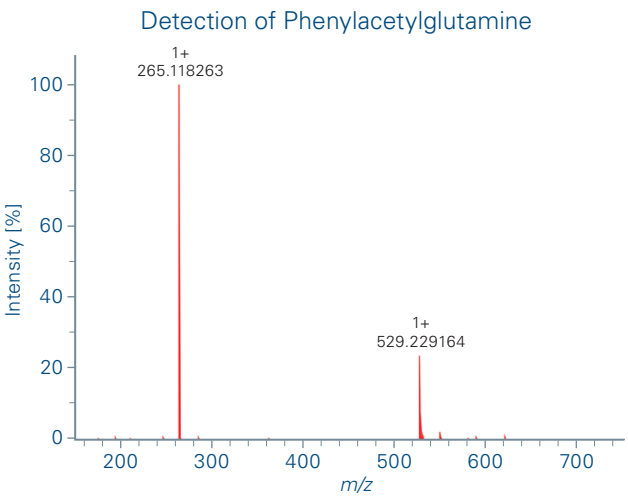
Hippuric acid is assigned as compound 6 through the detection of IFS. The combination of high mass accuracy and resolving power provides an unambiguous molecular formula assignment.	Mass error: 227 ppb

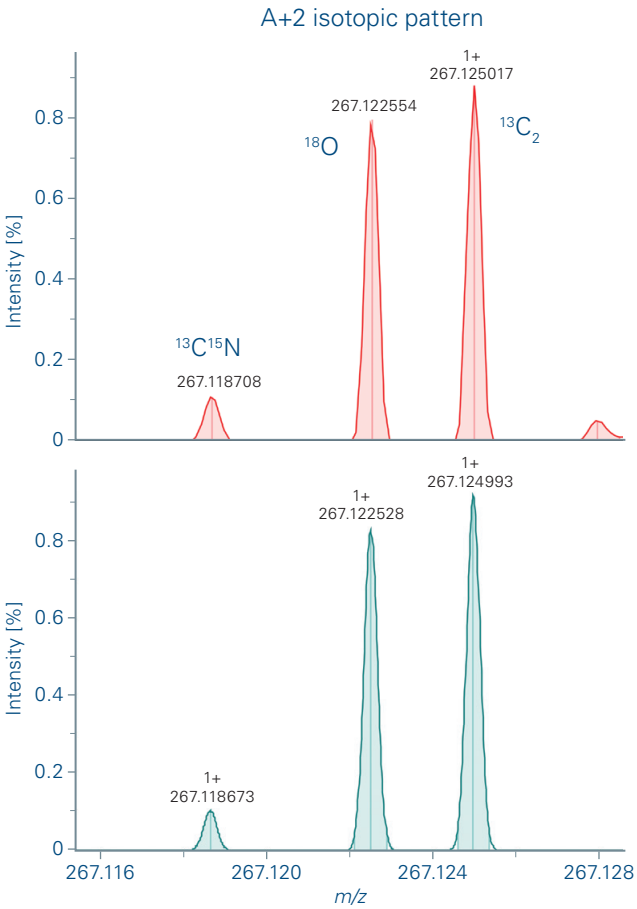
Metabolomics: LCMS

Urine, ESI(+), @ 1Hz

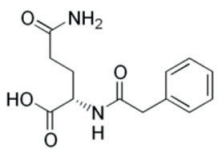
Isotopic fine structure on an LC timescale

Compound 7





Phenylacetylglutamine

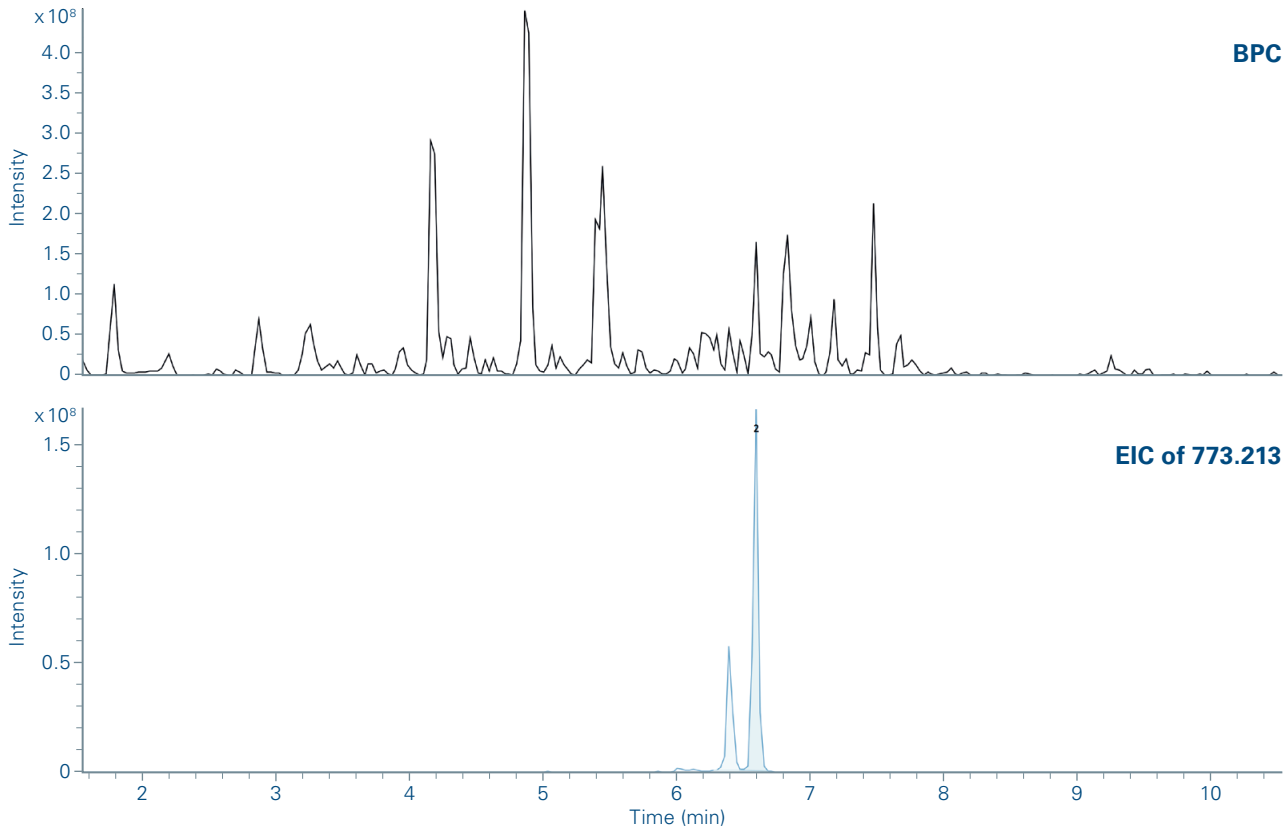


^{15}N and ^{18}O are used to assign the molecular formula of Phenylacetylglutamine to compound 7.	Mass error: 77 ppb

Metabolomics: LCMS

Green tea, ESI(+), @ 0.6 Hz

Isotopic fine structure on an LC timescale



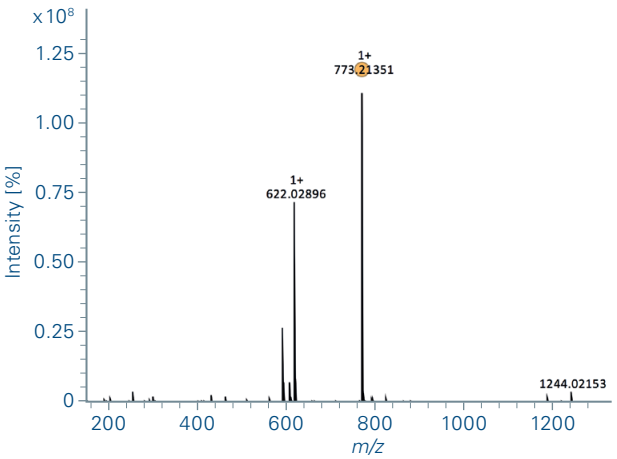
Green tea is analyzed with an acquisition rate of 0.6 Hz. The extracted ion chromatogram of *m/z* 773.214 is shown in the lower panel.

Metabolomics: LCMS

Green tea, ESI(+), @ 0.6 Hz

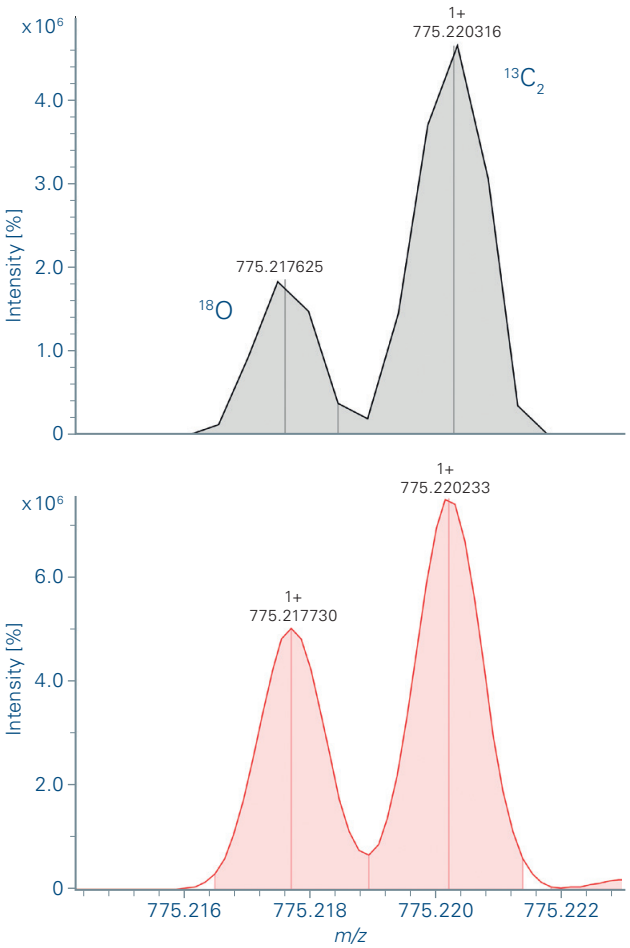
Isotopic fine structure on an LC timescale

Compound at RT 6.6 min



$C_{33}H_{41}O_{21}$

A+2 isotopic pattern



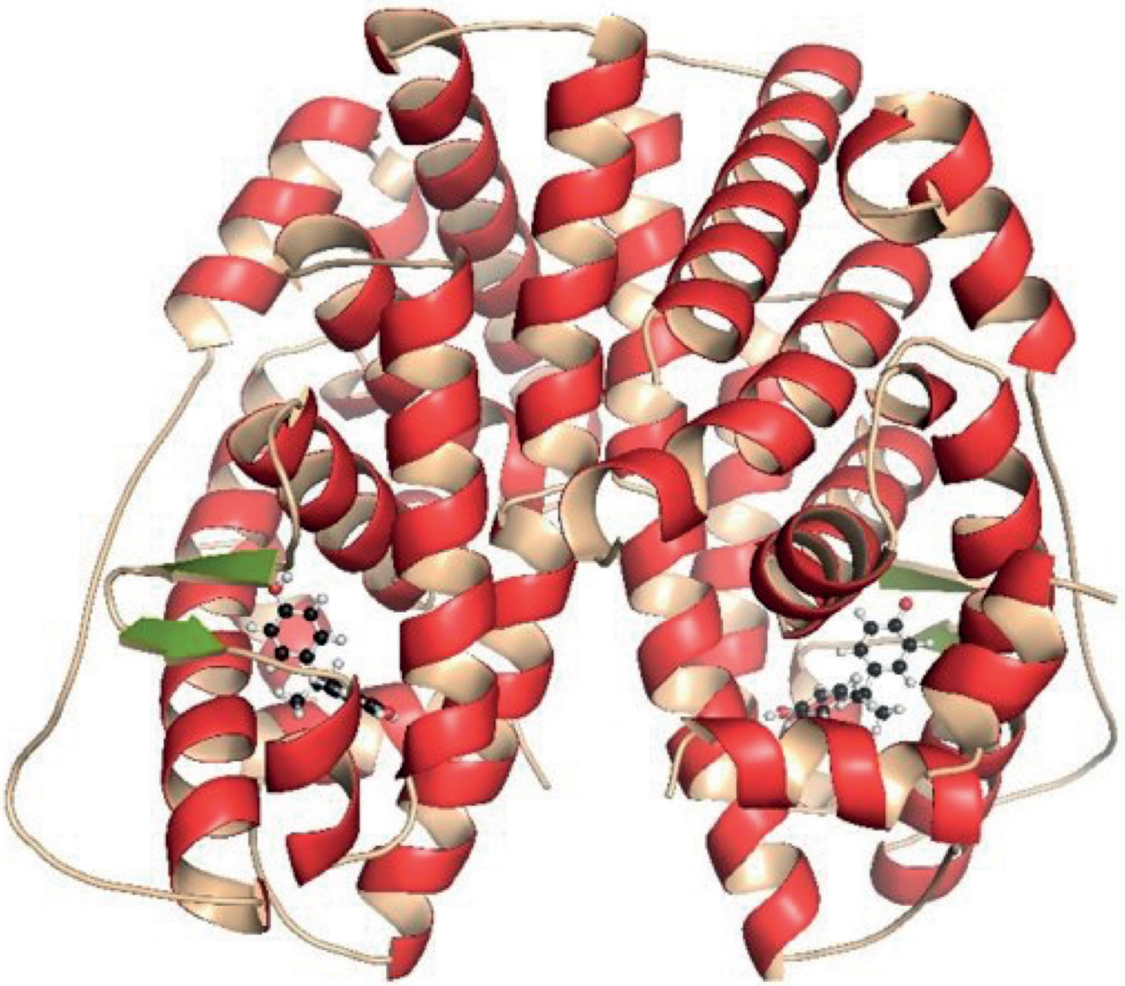
With an acquisition rate of 0.6 Hz, IFS is observed at *m/z* 775 for the chromatographic peak at 6.6 minutes. The molecular formula for Quercitin-3-O-glycosyl-rhamnosyl-galactosid is assigned easily with a mass resolving power of 550,000.

R: 550k @ *m/z* 773
mSigma: 37.3
Mass error: 27 ppb

Native and Intact Proteins

Requirements for Native MS

The critical requirement for native MS is an optimal pressure gradient between the electrospray source and the mass analyzer. The ion path on the scimaX MRMS enables the transmission of intact biomolecular complexes into the ParaCell, allowing for analysis of protein and protein complexes with isotopic resolution.



Now fragile fragment-protein, protein-substrate, multi-protein biomolecular complexes, membrane proteins with nanodiscs, mAbs, and native protein top-down analysis can all be analyzed on a standard (unmodified) scimaX.

Native and Intact Proteins

Customer Perspectives

Professor Joe Loo, University of California, Los Angeles, USA

"Native mass spectrometry and top-down proteomics are starting to impact studies in structural biology and medicine – and Bruker has all of the tools necessary for these growing technologies."

Dr. Sally Ann Poulsen, Professor of Chemical Biology at the Griffith Institute for Drug Discovery (GRIDD), Griffith University, Brisbane, Queensland, Australia

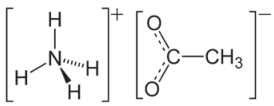
"The MRMS method means you avoid wasting valuable time on compounds that will not advance drug discovery"

Professor Ronald Quinn, Griffith Institute for Drug Discovery, Brisbane, Australia

"Our first experiments worked beautifully. Bruker MRMS retains weak non-covalent complexes and also easily handles screening of pools of compounds. The high resolution is perfect to resolve the complex mixtures."

Native and Intact Proteins

The workflow



Buffer exchange into ammonium acetate (50 mM)

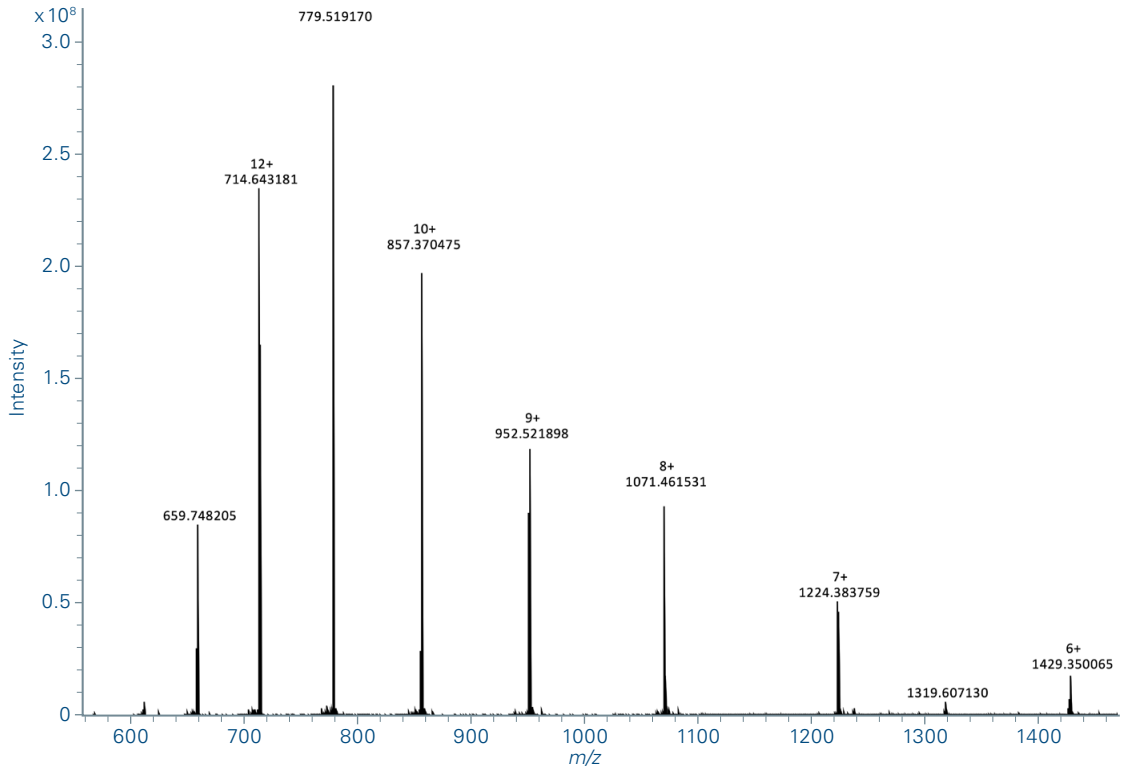
Infuse with syringe pump or automation (4 µl/min)

Acquire (7 sec/sample) with standard ESI source

Proteins

Ubiquitin, ESI(+)

High resolution protein analysis



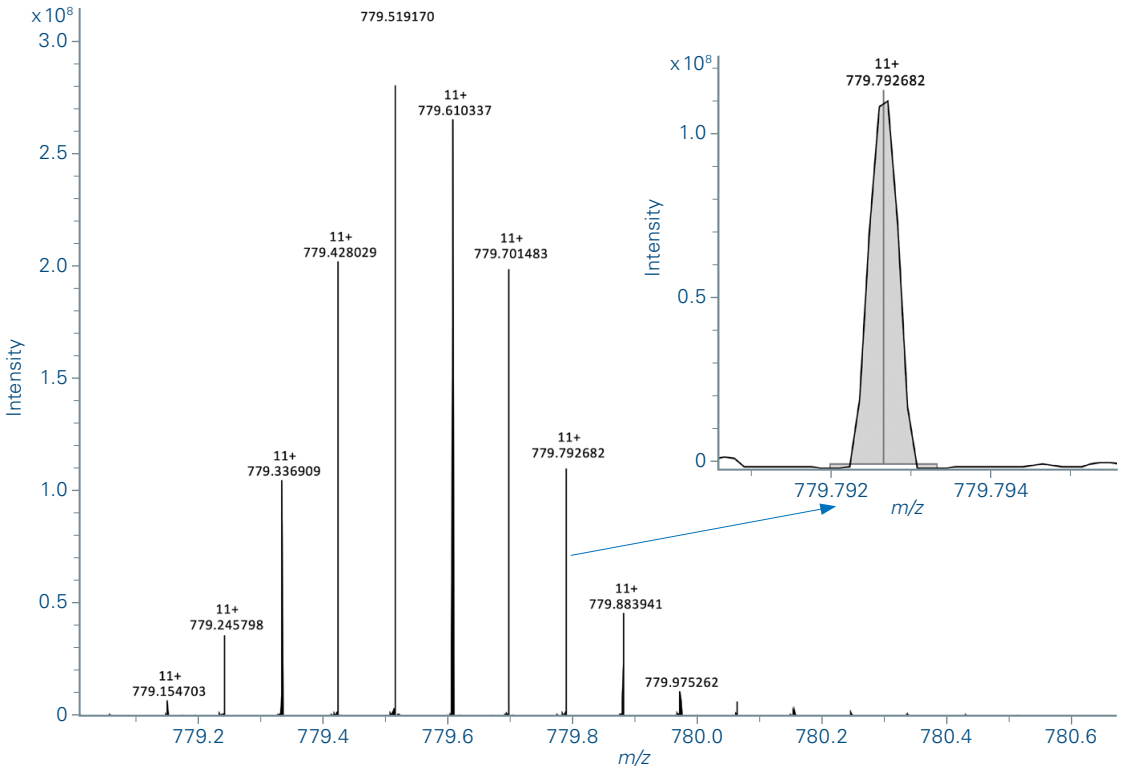
scimaX is not limited to the realm of small molecules. Its gentle source design is made to efficiently transfer intact proteins and other large molecular species, without any modifications to the instrument.

R: 2,000,000 @ *m/z* 779
transient: 5.86 s, 2ω, AMP (Kilgour)

Proteins

Ubiquitin 10+ Charge State, ESI(+)

Baseline resolved isotopic distribution



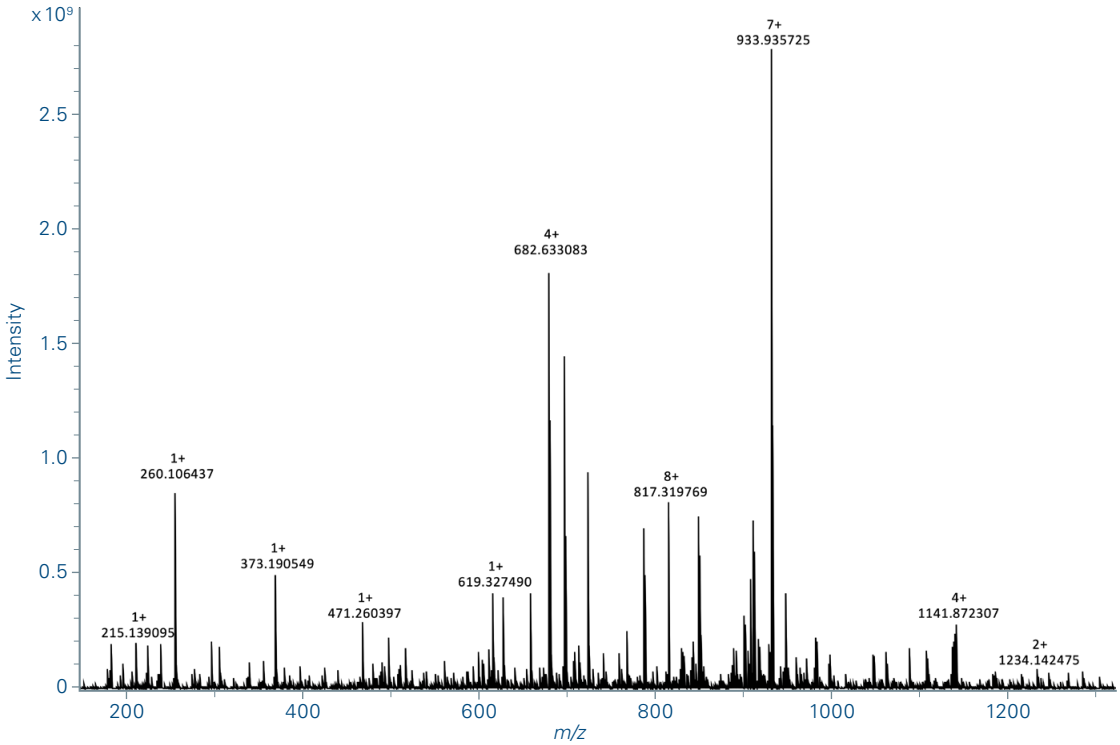
The eXtreme Resolution of scimaX produces baseline resolved isotopic peaks that provide confident molecular weight calculation via SNAP deconvolution.

R: 2,100,000

Protein Fragmentation

CID of Ubiquitin 10+ Charge State, ESI(+)

87% sequence coverage



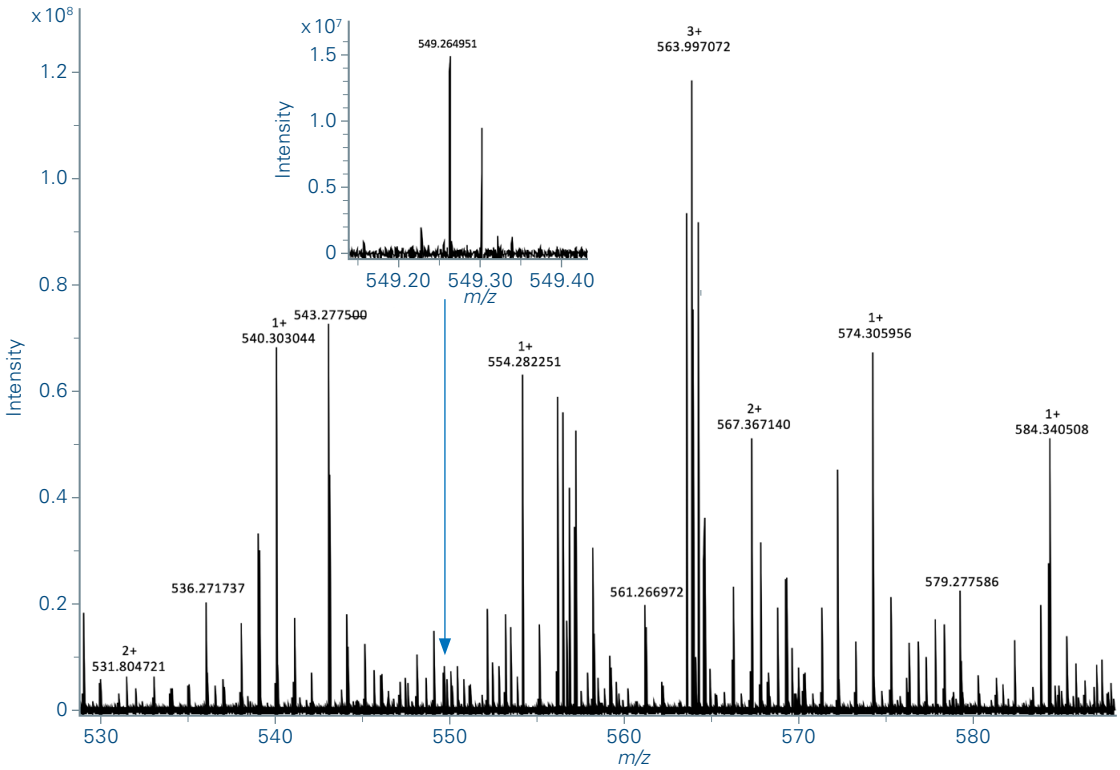
Rich MS/MS fragmentation provides sequence coverage that benefit from both the high mass accuracy and resolving power, to clearly separate the dense fragment ions.

R: 1,100,000 @ *m/z* 400
transient: 1.47 s, 2ω, AMP
(Kilgour)

Protein Fragmentation

CID of Ubiquitin 10+ Charge State, ESI(+)

87% sequence coverage

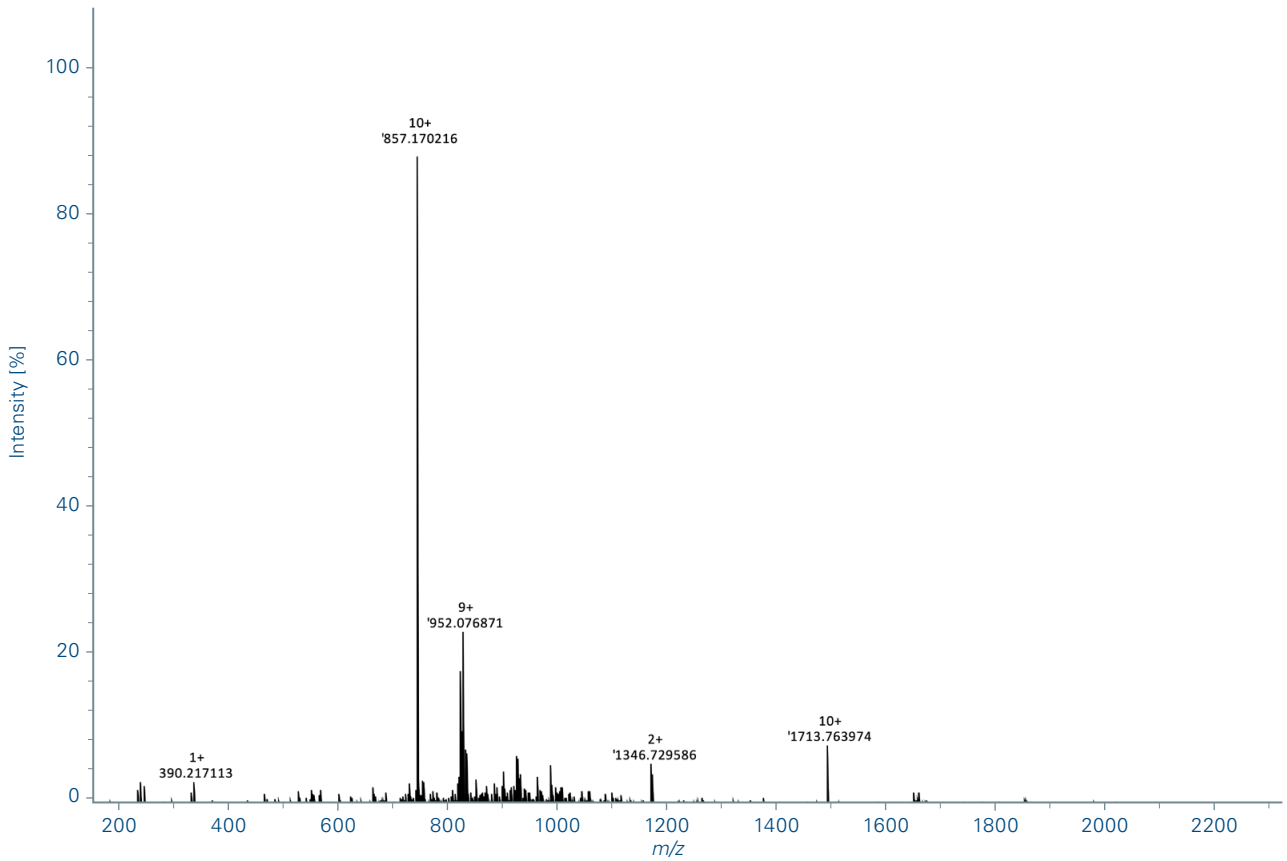


Looking closer reveals isotopically resolved fragment ions.	R: 1,100,000 @ *m/z* 400 transient: 1.47 s, 2ω, AMP (Kilgour)

Protein Fragmentation

ECD of Ubiquitin 10+ Charge State, ESI(+)

88% sequence coverage



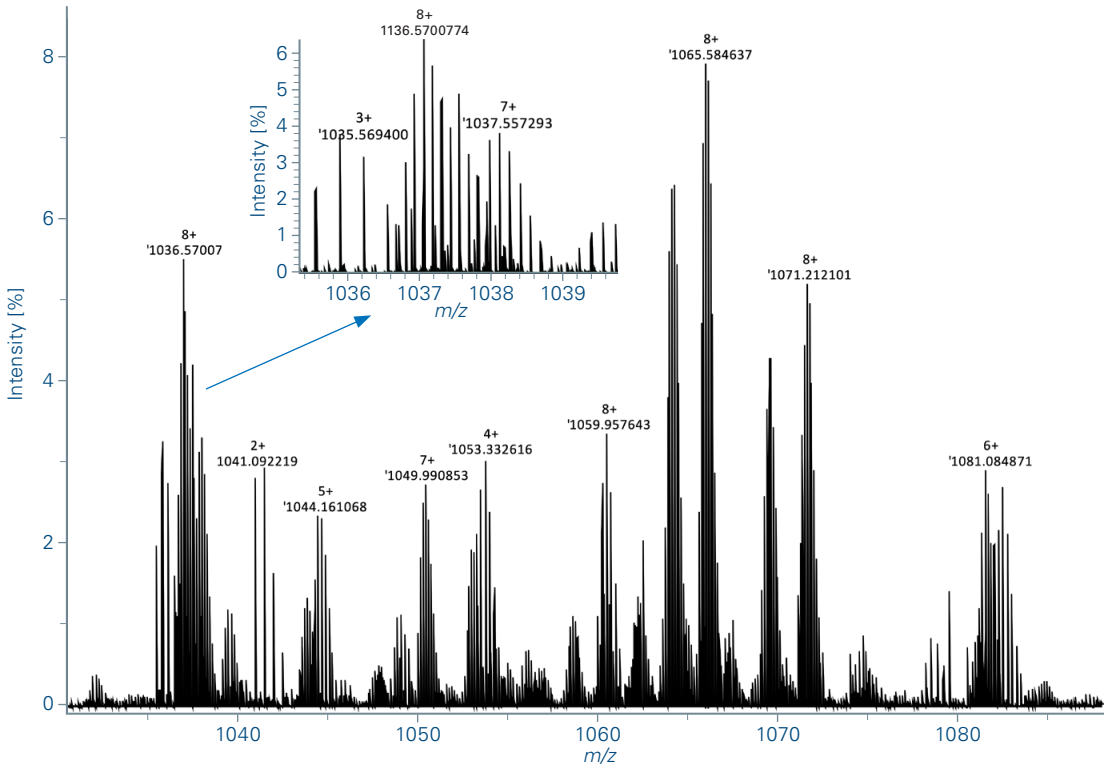
One of scimaX's many dissociation techniques, electron capture dissociation (ECD), provides complimentary fragmentation to traditional CID.

R: 1,100,000 @ *m/z* 400
transient: 1.47 s, 2ω, AMP
(Kilgour)

Protein Fragmentation

ECD of Ubiquitin 10+ Charge State, ESI(+)

88% sequence coverage



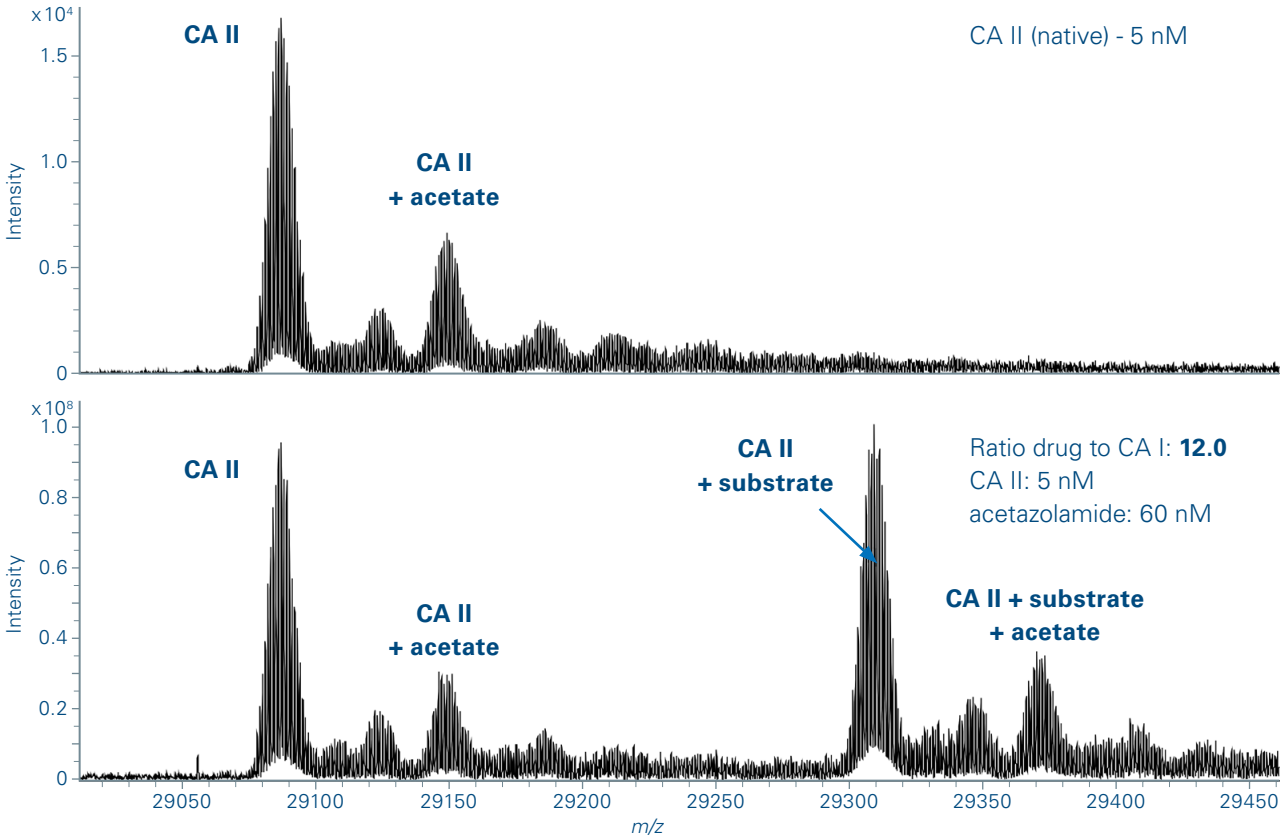
With SNAP, complex data is quickly and confidently deconvoluted to provide rich MS/MS information.

R: 1,100,000 @ *m/z* 400
transient: 1.47 s, 2ω, AMP
(Kilgour)

Fragment Based Drug Discovery

Native CA II and Acetazolamide, ESI(+)

5 nM sensitivity at normal ESI flow



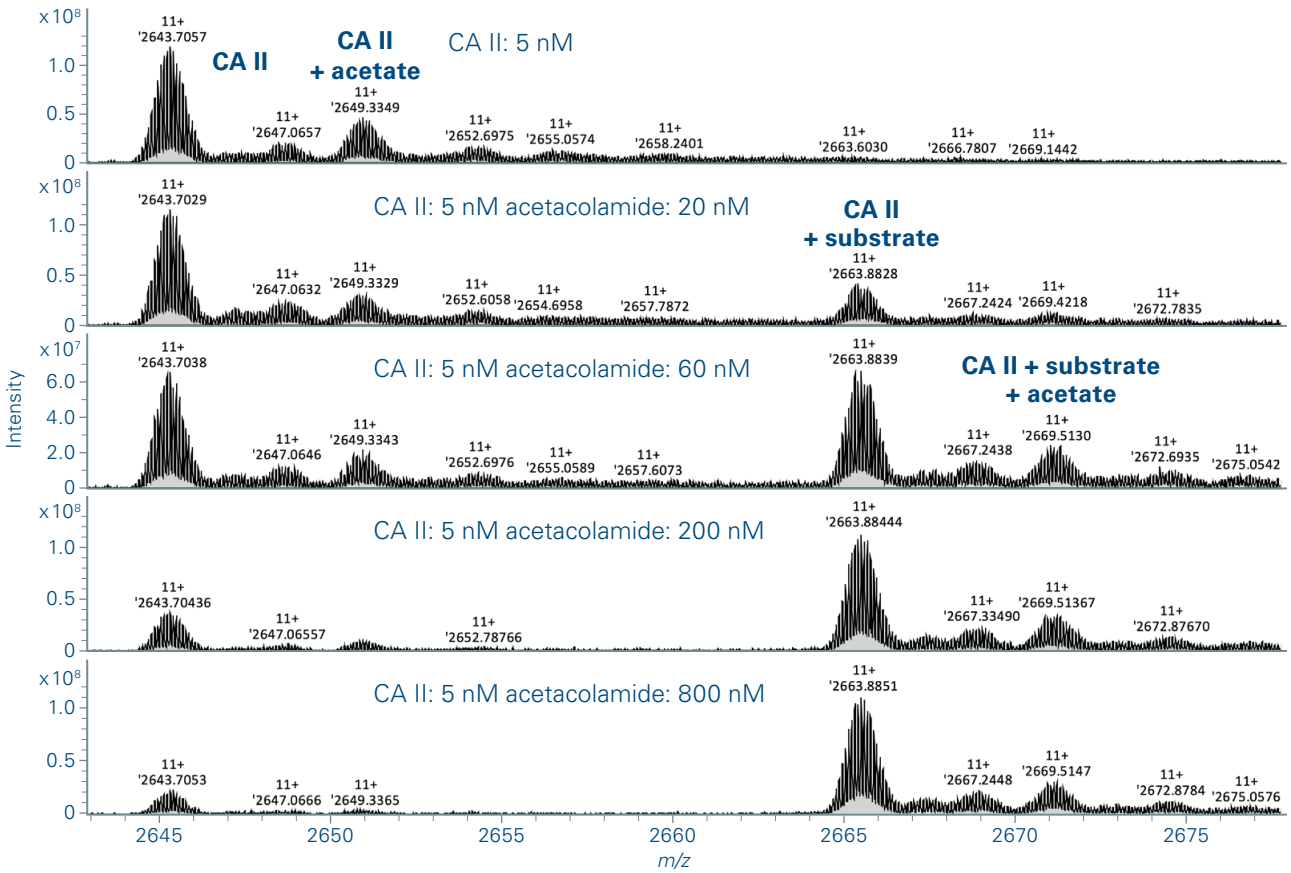
Using the standard scimaX ESI source for native MS, nanomolar levels of protein are detected with isotopic resolution, in a robust manner suitable for high throughput screening.

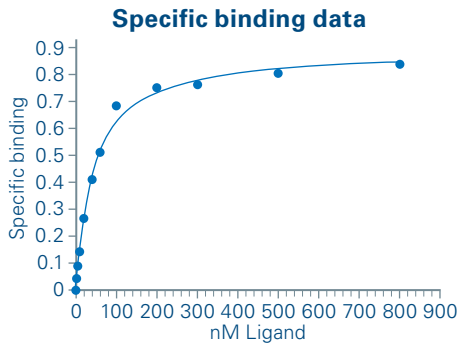
R: 70,000 @ *m/z* 2,620
Flow rate: 2 ul/min

Fragment Based Drug Discovery

Native CA II and Acetazolamide, ESI(+)

Rapidly determine binding constants





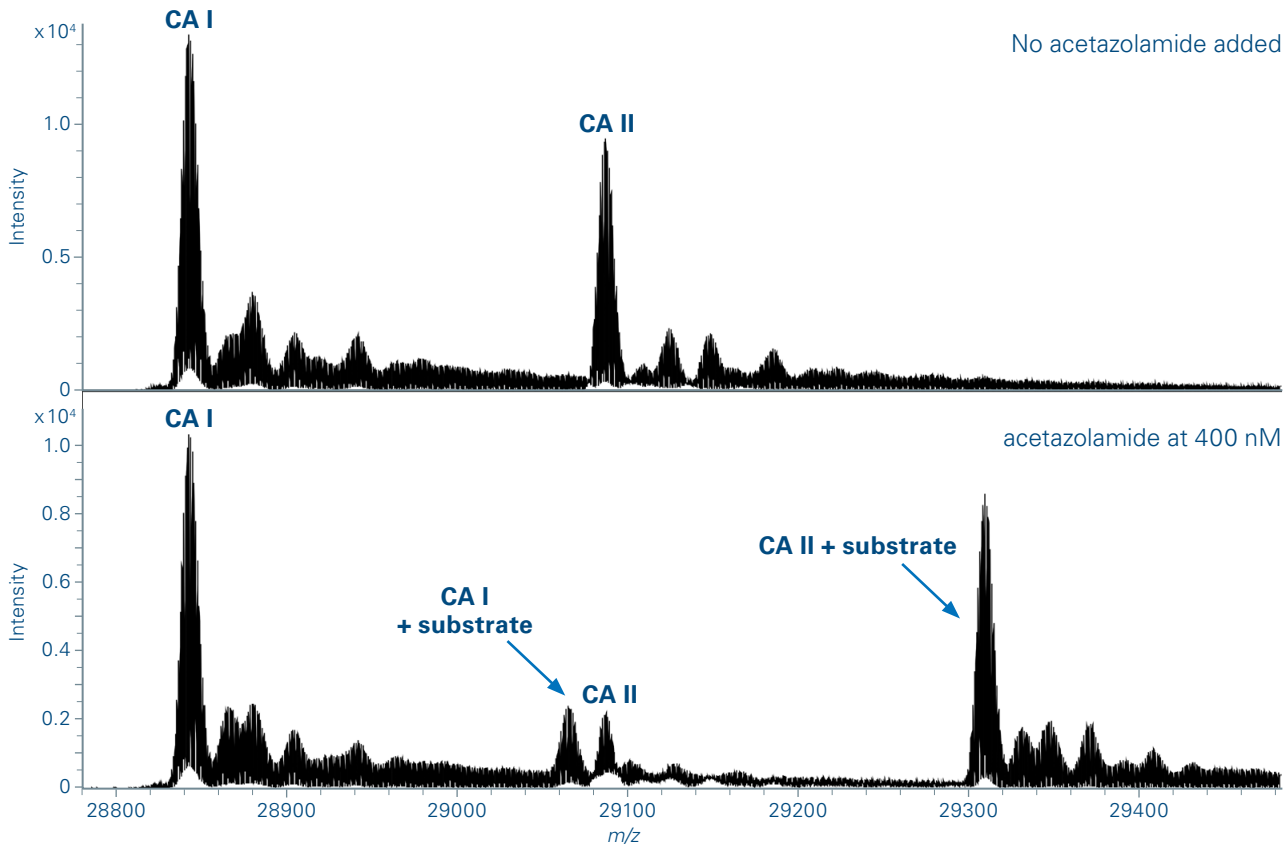
The robust source enables native protein-ligand screening of weak and strong complexes with the right balance of desolvation and high sensitivity.

R: 70,000 @ *m/z* 2,620
Flow rate: 2ul/min

Fragment Based Drug Discovery

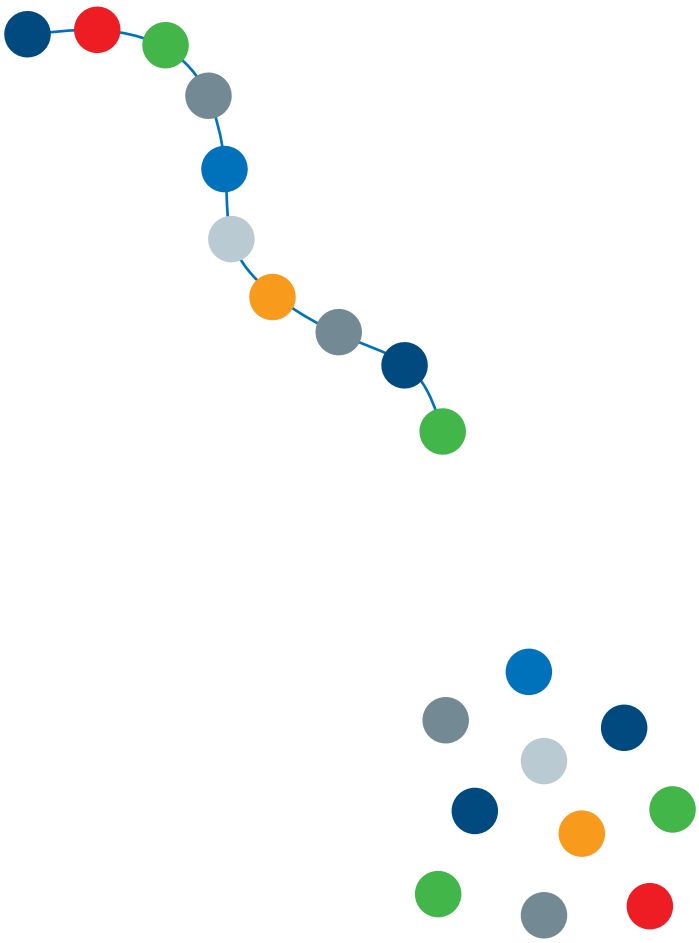
Native CAI and II with Acetazolamide, ESI(+)

Competitive binding of isoforms



Direct observation ligand specificity for protein isoforms is possible on scimaX, reducing need for multiple assays in your screening cascade.	R: 70,000 @ *m/z* 2,620 Flow rate: 2 ul/min

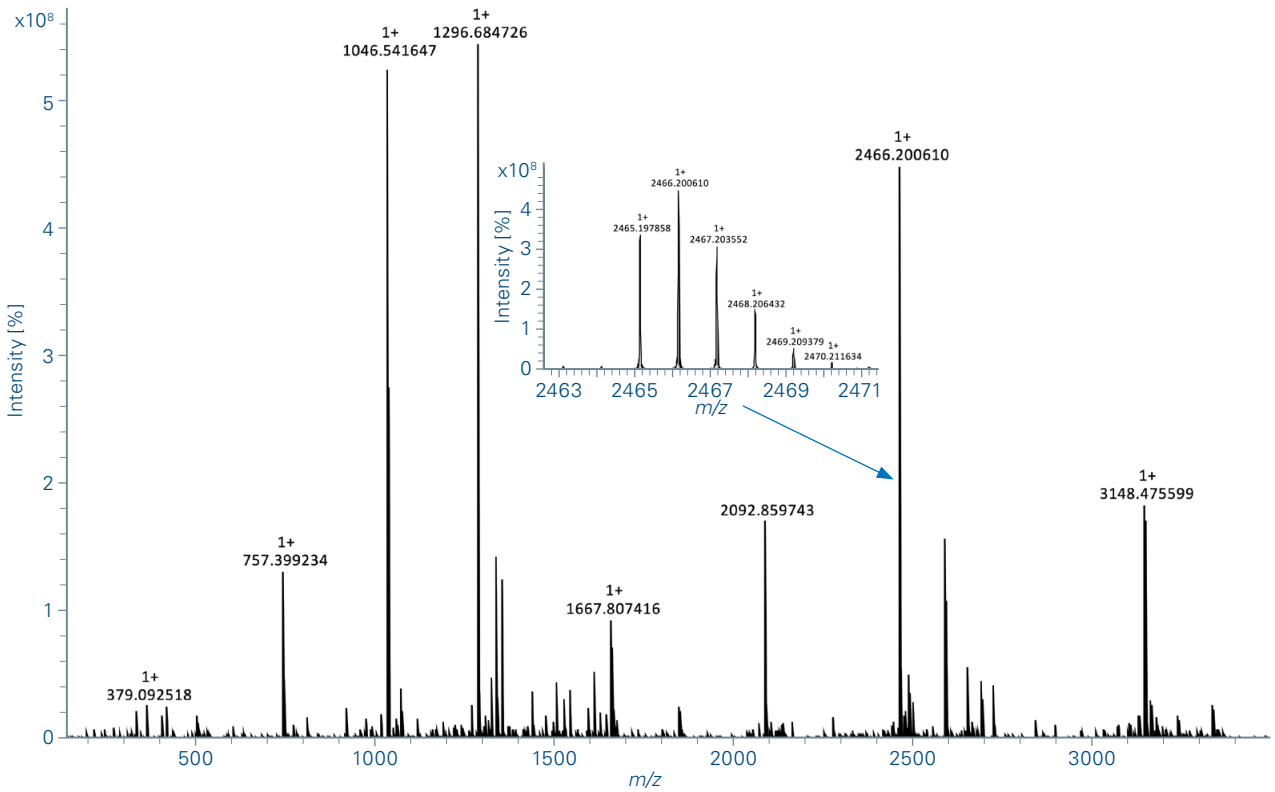
Peptide MS, MS/MS and MS^n



Peptides

PepMix, MALDI(+)

High accuracy and resolution

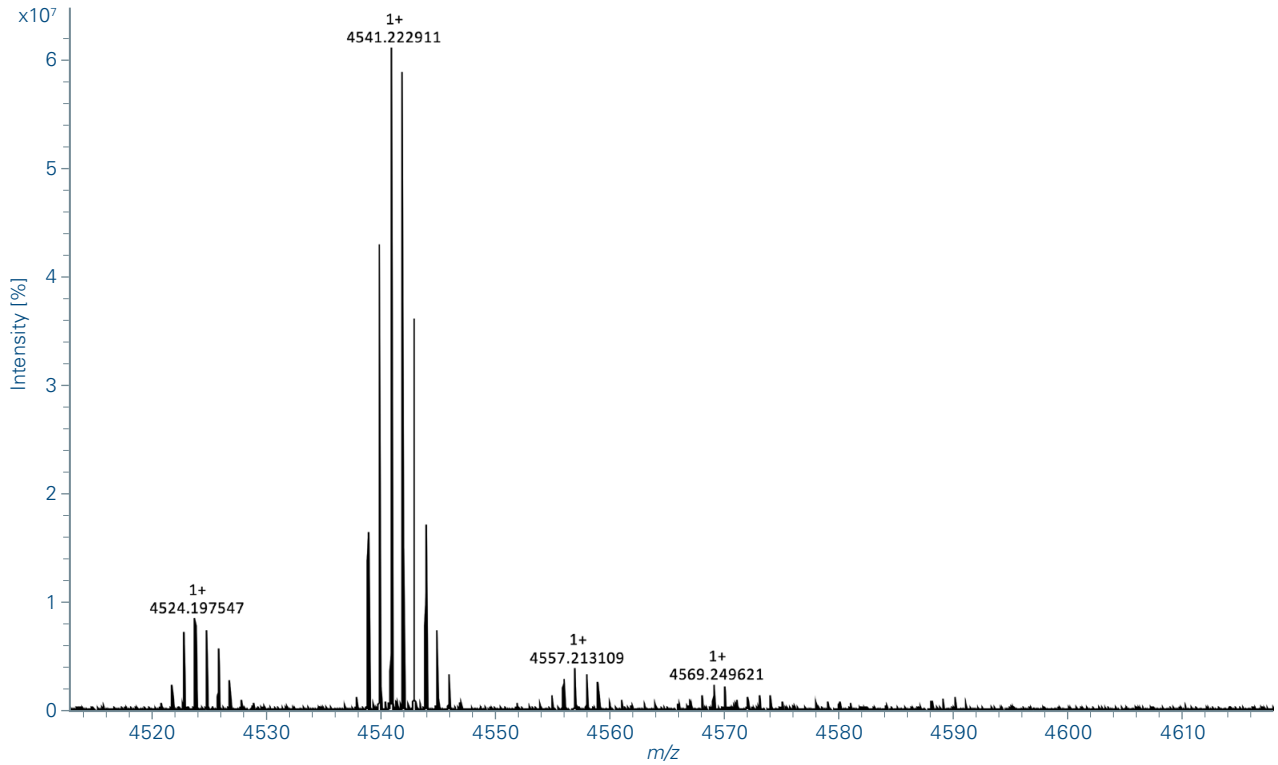


R: 500,000 @ *m/z* 400
transient: 1.47 s, 2ω
RMS mass error of calibration: 303 ppb

Peptides

ACTH (1-39), MALDI(+)

High accuracy and resolution

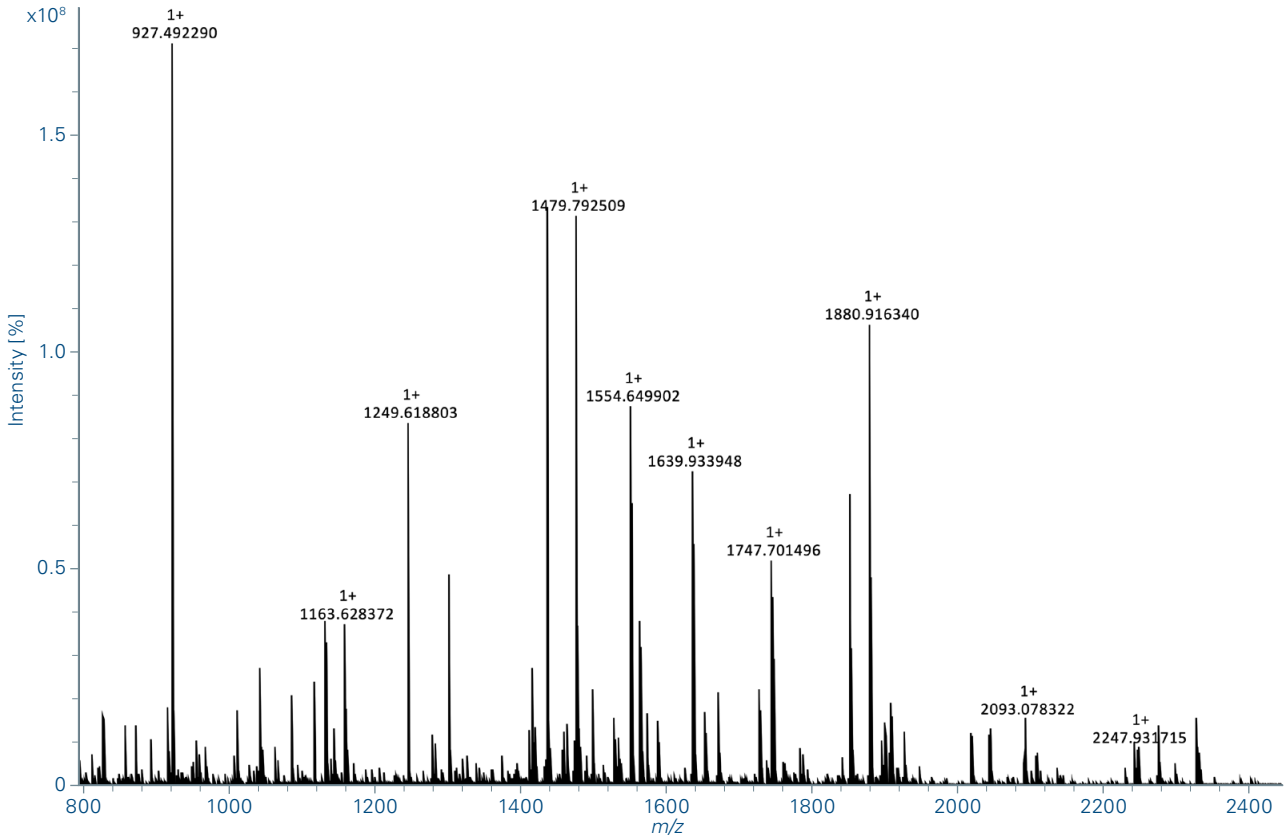


R: 165,000 @ *m/z* 4,541
transient: 5.94 s, 2ω

Peptides

BSA digest (10 fmol), MALDI(+)

High accuracy and resolution

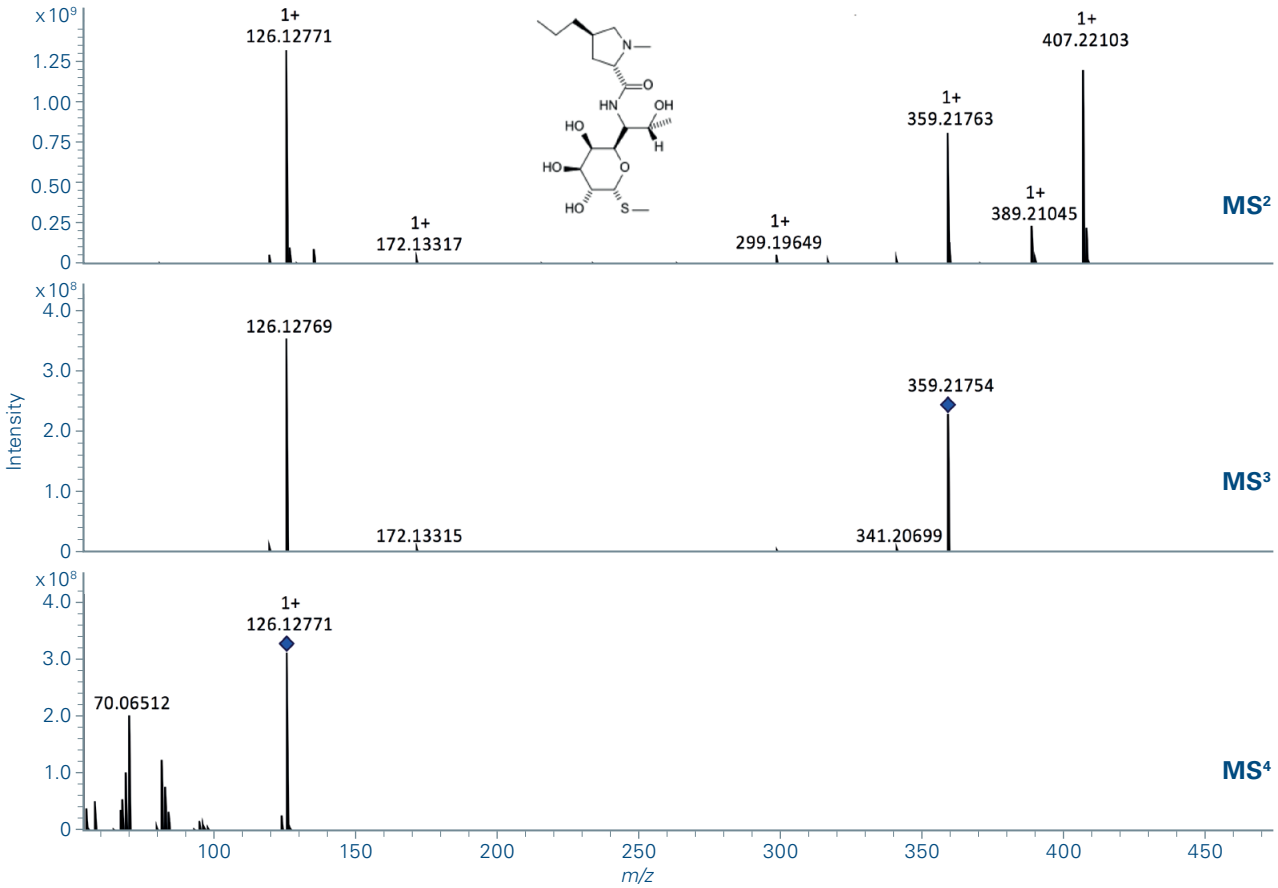


R: 500,000 @ *m/z* 400
transient: 1.47 s, 2ω

MS^n

Lincomycin

Full structural information: MS^n

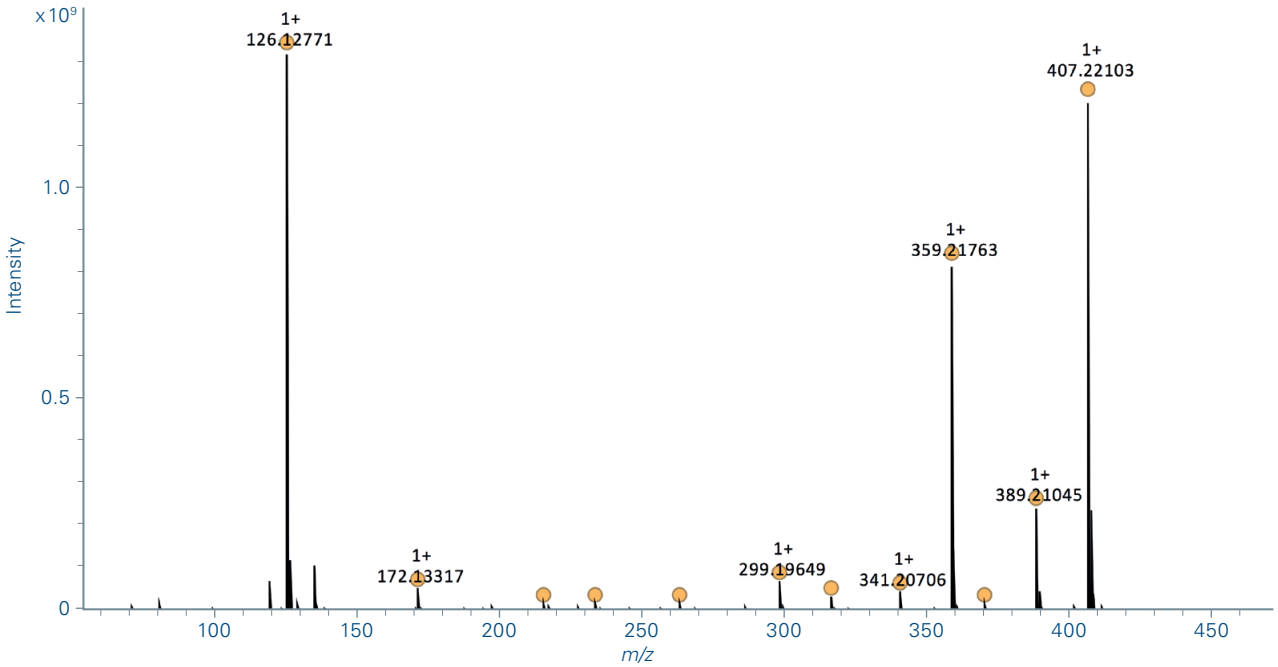


scimaX provides complex structural characterization via MS^n, using a combination of CID and SORI-CID. MS^2 is achieved in the front-end collision cell. The remaining stages of MSMS are done in the ParaCell with SORI-CID.

MS²

Lincomycin

Full structural information: MS²



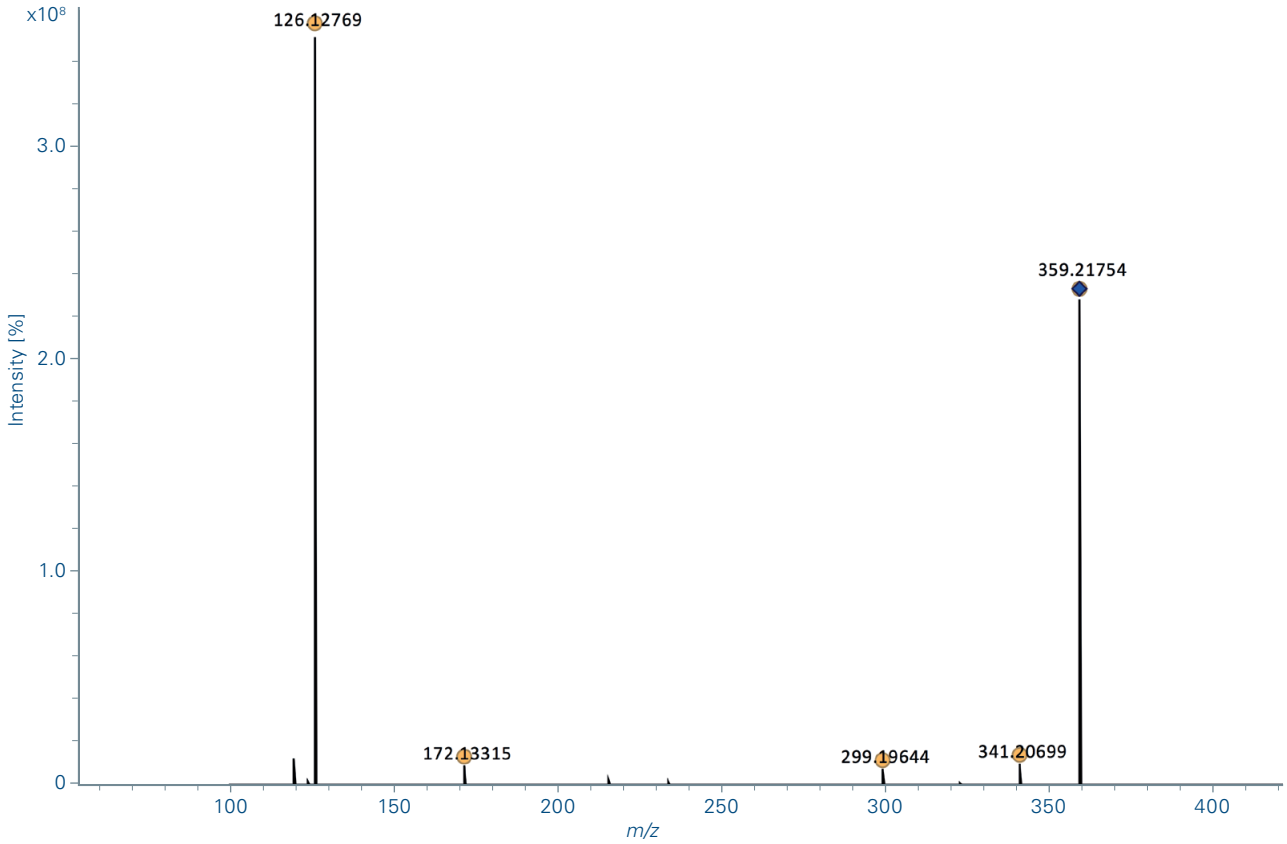
Meas. *m/z*	Ion Formula	err [ppm]	mSigma
126.12771	$C_8H_{16}N$	0.15	2.2
172.13317	$C_9H_{18}NO_2$	0.21	8.1
216.08661	$C_9H_{14}NO_5$	0.19	14.5
234.09717	$C_9H_{16}NO_6$	0.20	14.8
264.08996	$C_{10}H_{18}NO_5S$	0.22	12.2
299.19649	$C_{15}H_{27}N_2O_4$	0.15	9
317.20705	$C_{15}H_{29}N_2O_5$	0.14	13.1
341.20706	$C_{17}H_{29}N_2O_5$	0.11	16.8
359.21763	$C_{17}H_{31}N_2O_6$	0.08	5.8
371.19987	$C_{18}H_{31}N_2O_4S$	0.09	93.3
389.21045	$C_{18}H_{33}N_2O_5S$	0.05	8
407.22103	$C_{18}H_{35}N_2O_6S$	0	8.4

The first stage of MS/MS is done by isolation with the mass selective quadrupole, followed by CID fragmentation in the collision cell. For MS² only analysis, fragment ions are then sent to the ParaCell for detection.

MS³

Lincomycin

Full structural information: MS³



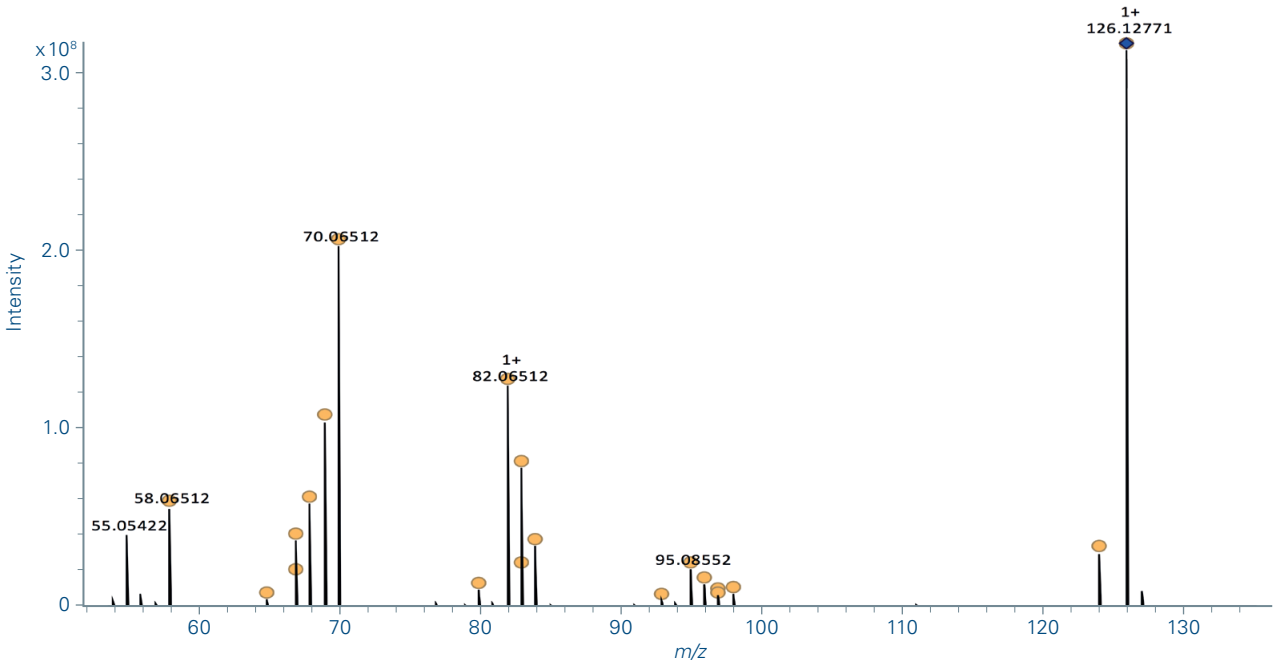
Meas. *m/z*	Ion Formula	err [ppm]	mSigma
126.12769	$C_8H_{16}N$	0.28	48.8
172.13315	$C_9H_{18}NO_2$	0.30	49.2
299.19644	$C_{15}H_{27}N_2O_4$	0.32	n.a.
341.20699	$C_{17}H_{29}N_2O_5$	0.33	n.a.
359.21754	$C_{17}H_{31}N_2O_6$	0.34	n.a.

Subsequent stages of MS/MS are performed by isolation and fragmentation in the ParaCell. Ions are fragmentated through the process of sustained off-resonance irradiation collision-induced dissociation, SORI-CID.

MS^4

Lincomycin

Full structural information: MS^4



Meas. *m/z*	Ion Formula	err [ppm]	mSigma
54.03382	C_3H_4N	0.03	n.a.
55.04165	C_3H_5N	0.06	n.a.
55.05422	C_4H_7	0.05	n.a.
56.04947	C_3H_6N	0.05	n.a.
58.06512	C_3H_8N	0.05	16.2
65.03857	C_5H_5	0.06	52.5
67.04164	C_4H_5N	0.09	n.a.
67.05422	C_5H_7	0.09	n.a.
68.04947	C_4H_6N	0.08	n.a.
69.06987	C_5H_9	0.09	29.3
70.06512	C_4H_8N	0.10	24.2
80.04947	C_5H_6N	0.11	n.a.
82.06512	C_5H_8N	0.11	29.8
83.07294	C_5H_9N	0.12	n.a.
83.08552	C_6H_{11}	0.12	30.3
84.08077	$C_5H_{10}N$	0.12	n.a.
93.06986	C_7H_9	0.14	59.2
95.08552	C_7H_{11}	0.12	n.a.
96.08076	$C_6H_{10}N$	0.13	27.5
97.08859	$C_6H_{11}N$	0.13	n.a.
97.10116	C_7H_{13}	0.12	n.a.
98.09641	$C_6H_{12}N$	0.14	n.a.
124.11206	$C_8H_{14}N$	0.13	41.3
126.12771	$C_8H_{16}N$	0.14	34.0

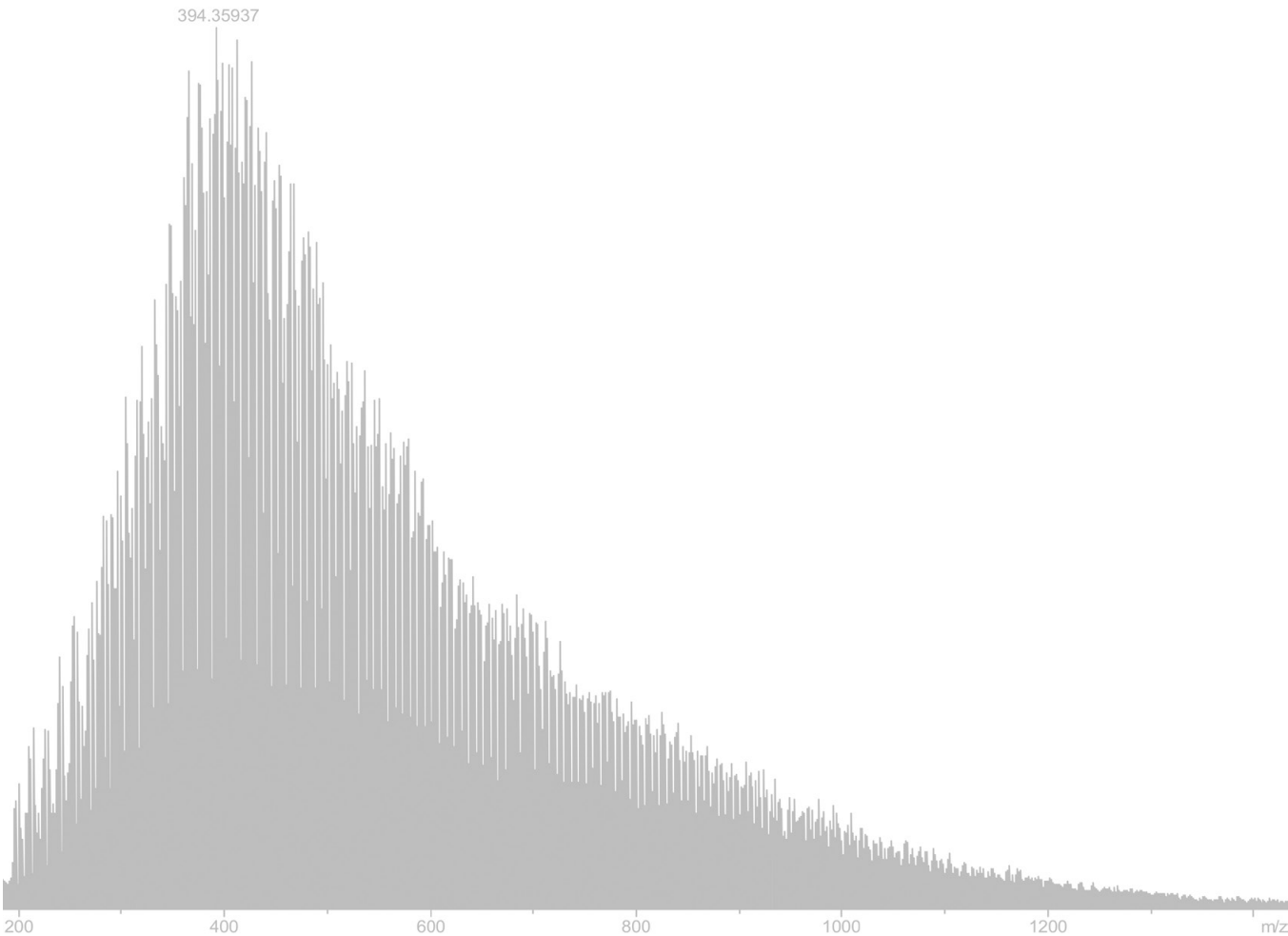
The remaining stages of MS^n are all achieved with SORI-CID. Even by the fourth stage, rich fragment ions produced with sub-ppm mass accuracy.

Petroleomics and Environmental

Requirements

When knowing every molecule matters, scimaX empowers 7T systems with high field performance for any complex mixture.

scimaX powered by 2xR technology is easily matching or surpassing the resolving power of many conventional high field MRMS systems. Now such high field systems are no longer mandatory for crude oils, bio-fuels, DOM/NOM or any complex mixture



Petroleomics and Environmental

Customer Insights

Carlos Afonso, University of Rouen
Pierre Giusti, TOTAL
C2MC – Complex Matrices Molecular Characterization, Joint Laboratory

"With our Bruker MRMS in Rouen the analysis of highly Complex Mixtures has been pushed further than ever and could also be made on a routine basis in the framework of the C2MC joint lab."

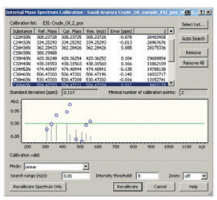
Janne Jänis, University of Eastern Finland – Joensuu
Laboratory of Bio-organic Chemistry

"Most of our research at UEF heavily relies on the use of Bruker MRMS technology to dig deep into chemistry of bio-oils, natural extracts and highly complex environmental samples"

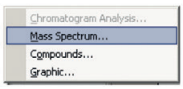
Petroleomics and Environmental

Processing workflow

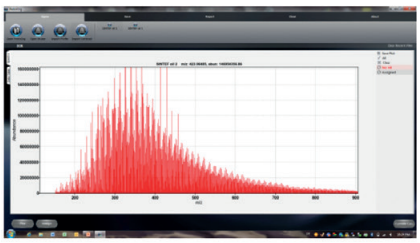
Internal recalibration



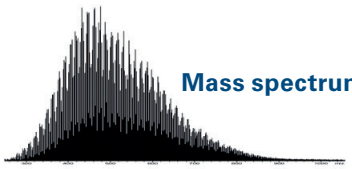
Export mass spectrum



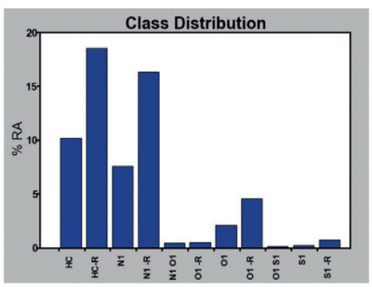
PetroOrg software
Molecular Formula calculation



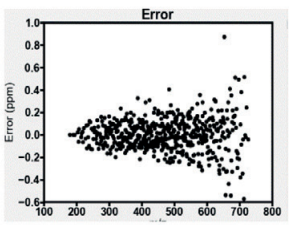
Mass spectrum



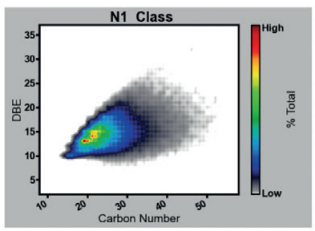
Class distribution plot



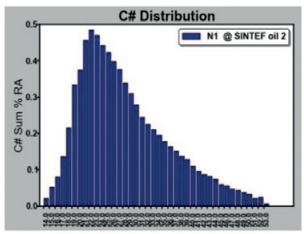
Mass error plot



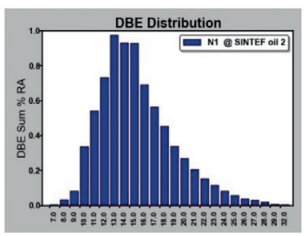
DBE vs. C plot



Carbon number distribution plot



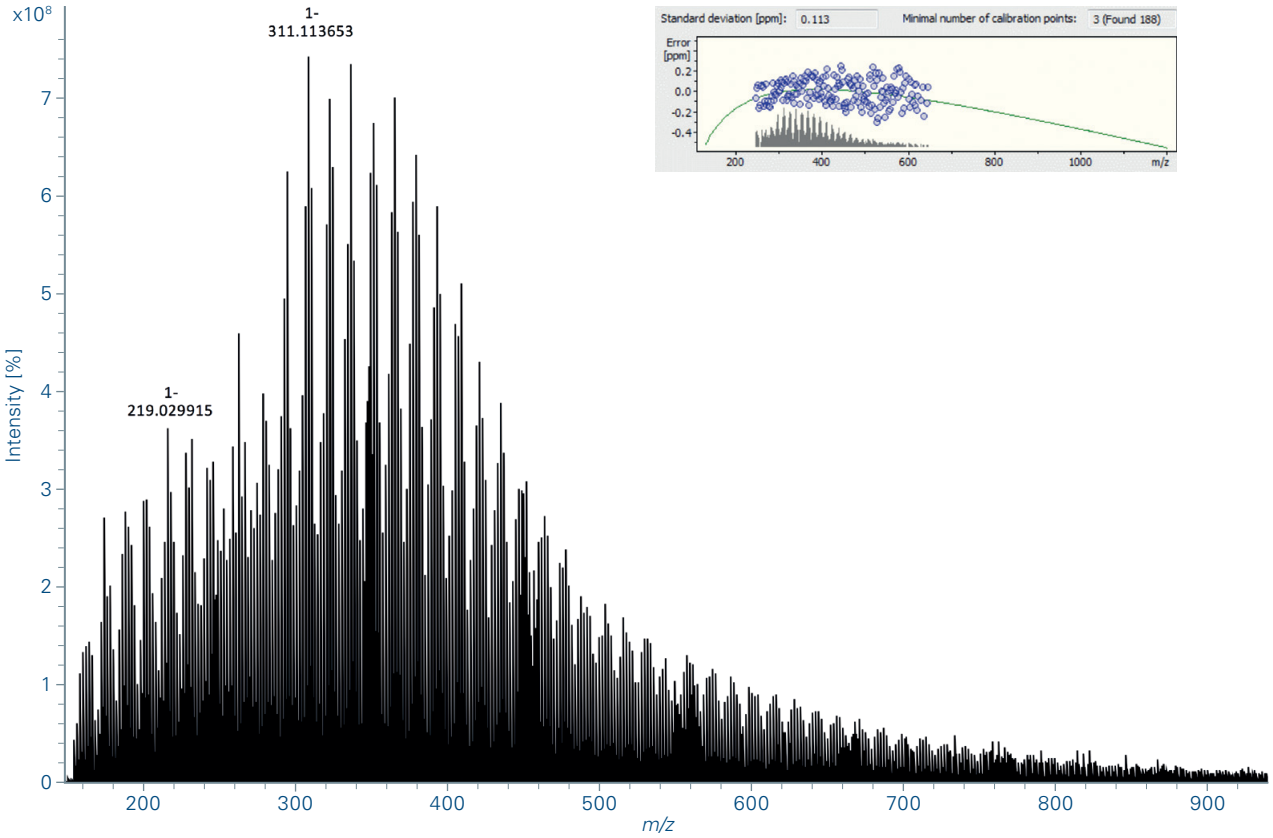
DBE distribution plot



Environmental

SRFA, ESI(-)

Environmental analysis

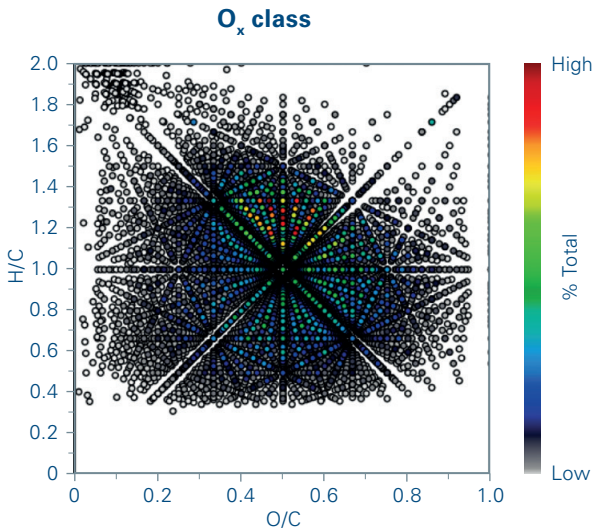


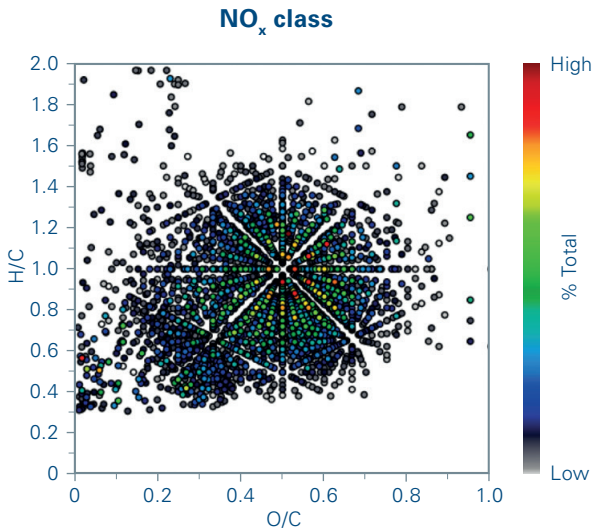
R: 1,400,000 @ *m/z* 400
Transient length: 2.96s
2ω detection, AMP
100 scans

Environmental

SRFA, ESI(-)

Van Krevelen plots



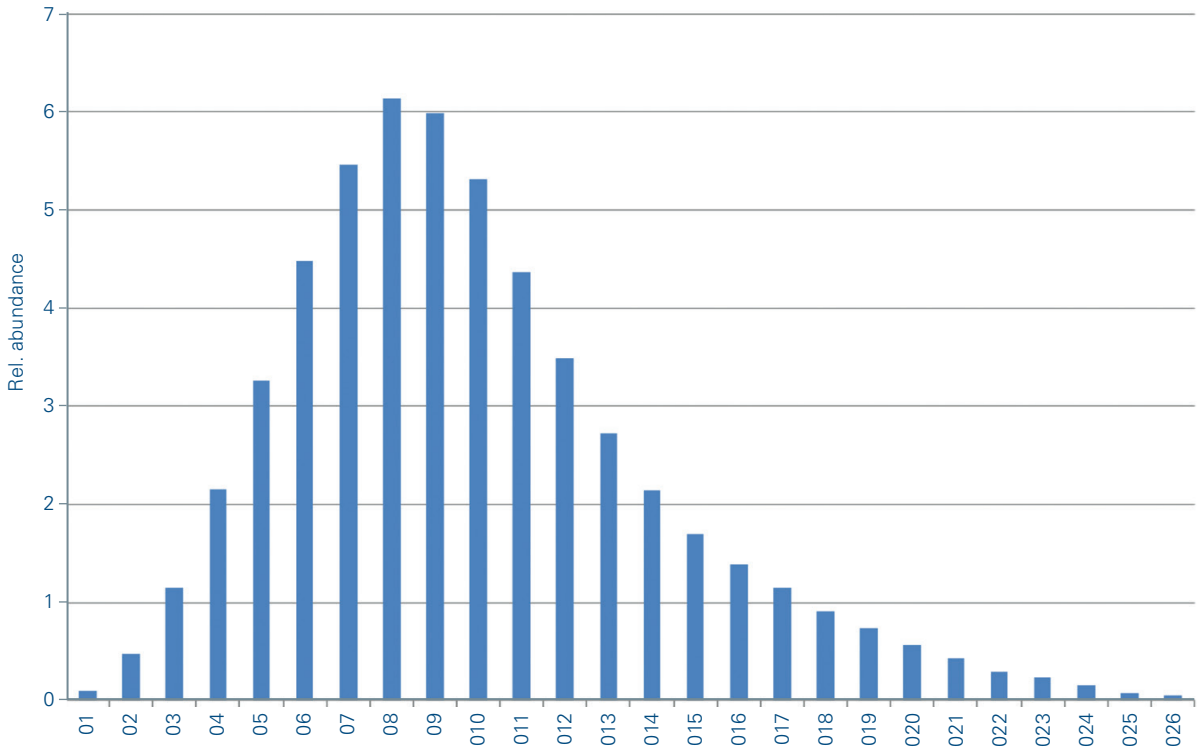


R: 1,400,000 @ *m/z* 400
Transient length: 2.96s
2ω detection, AMP
100 scans

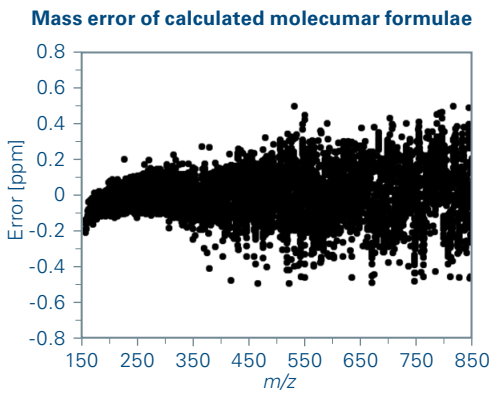
Environmental

SRFA, ESI(-)

Class plot of O_x Class



Mass error plot of O_x class

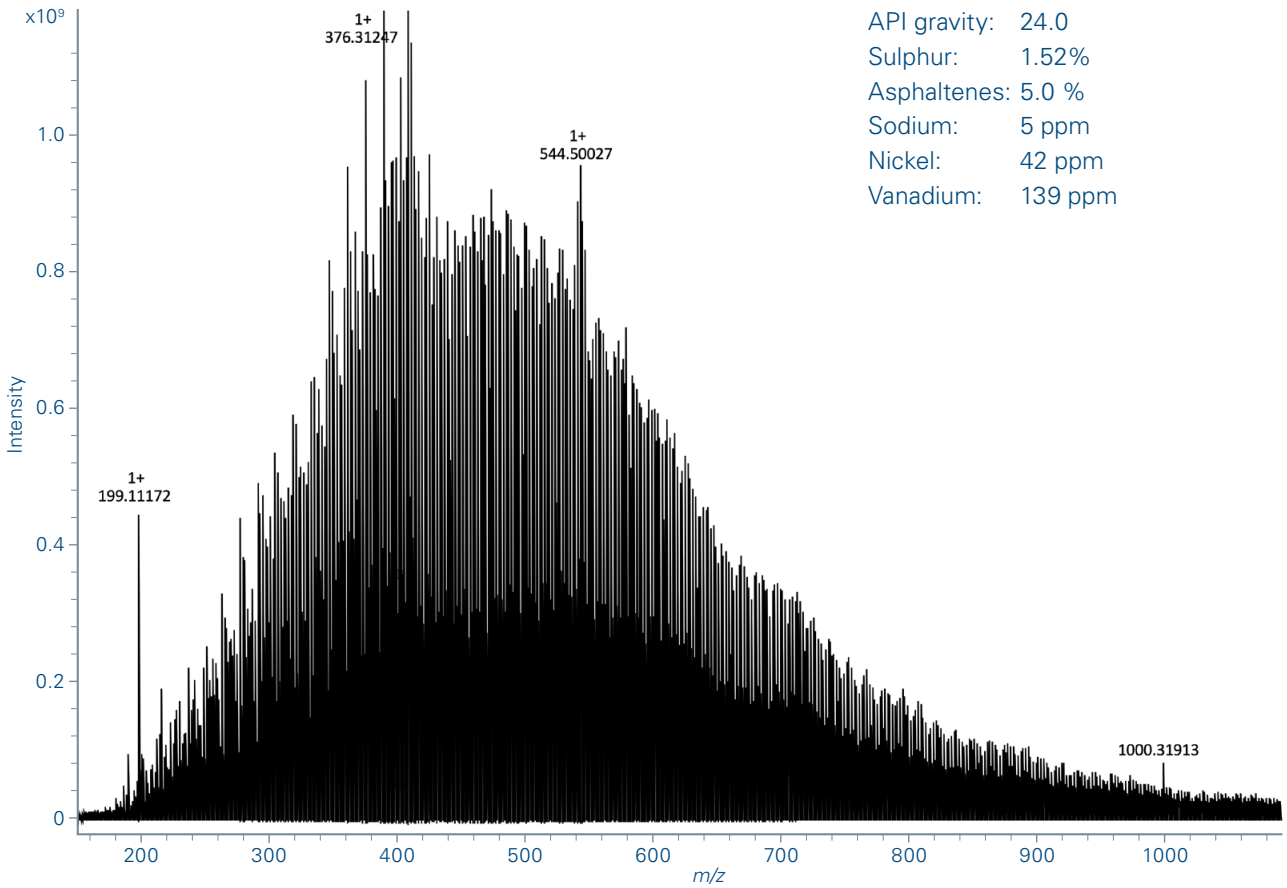


Molecular formulae: ca. 15960 (incl. ^{13}C peaks)	R: 1,400,000 @ *m/z* 400 Transient length: 2.96s 2ω detection, AMP 100 scans Average mass error: 124 ppb

Petroleomics

Crude oil, APPI(+)

Complex mixture analysis via APPI



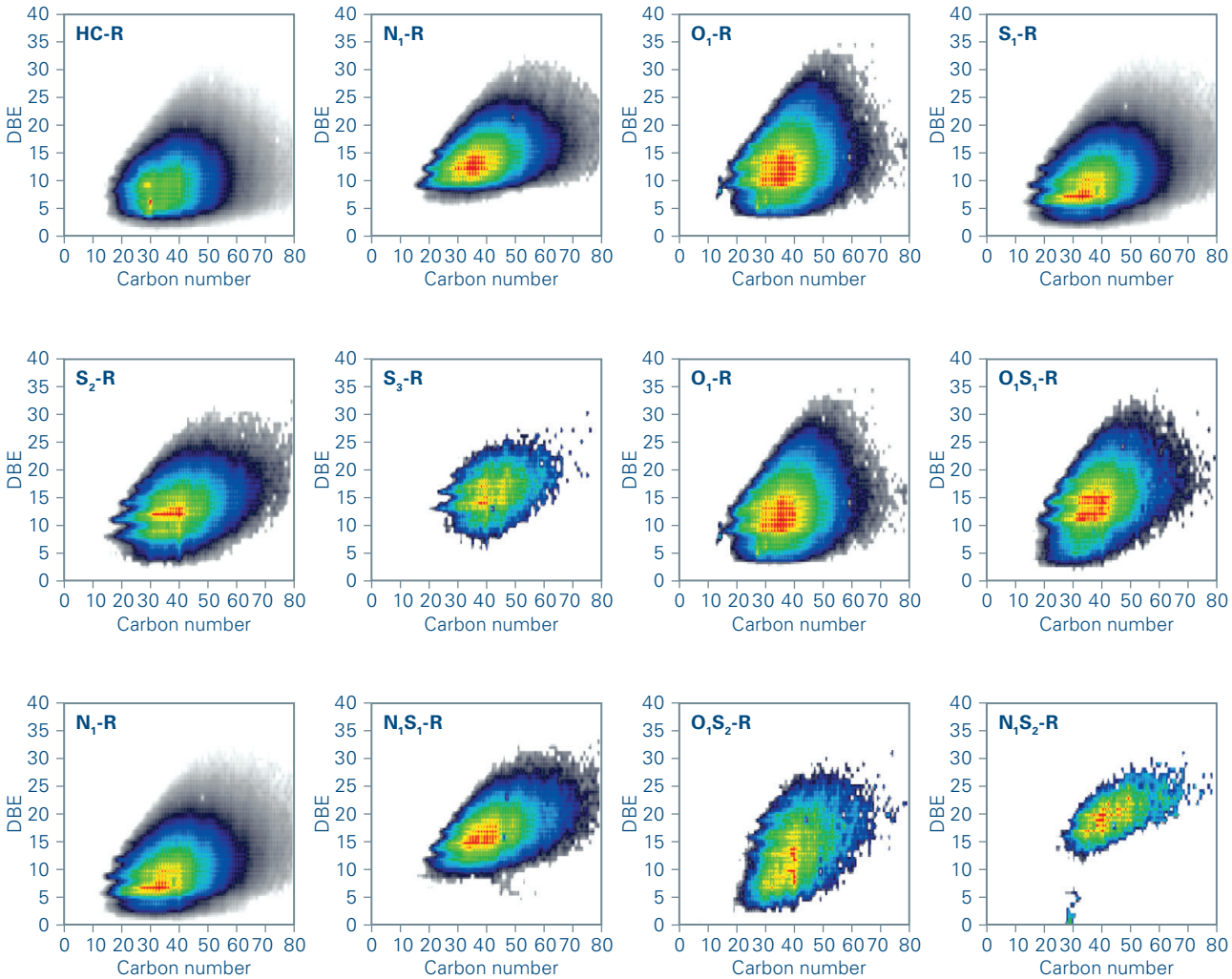
API gravity: 24.0
Sulphur: 1.52%
Asphaltenes: 5.0 %
Sodium: 5 ppm
Nickel: 42 ppm
Vanadium: 139 ppm

R: 1,750,000 @ *m/z* 400
transient: 2.93 s, 2ω,
AMP (Kilgour)
3,000 scans

Petroleomics

Crude oil, APPI(+)

DBE vs. carbon number



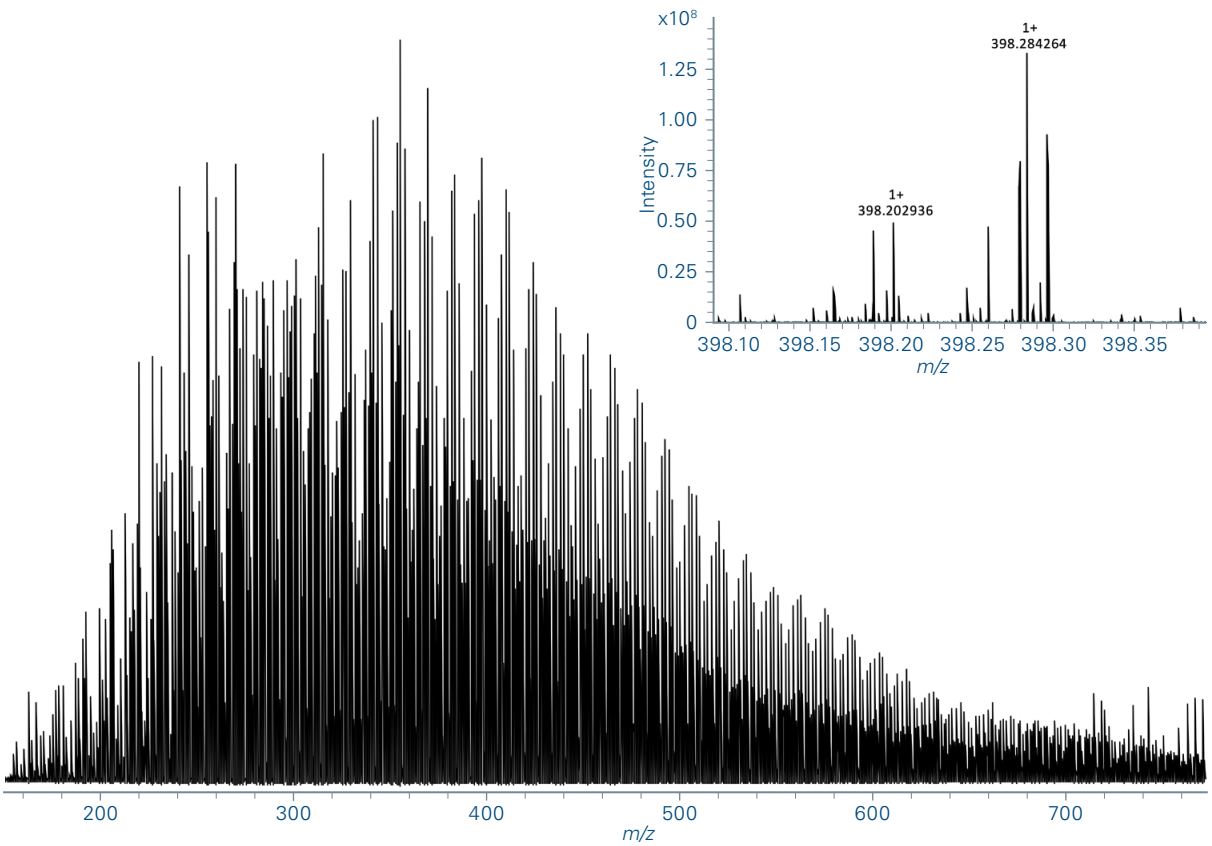
Crude oil sample and their compound classes can be analyzed in detail concerning carbon distribution and aromaticity.

R: 1,750,000 @ *m/z* 400
transient: 2.93 s, 2ω,
AMP (Kilgour)
3,000 scans

Petroleomics

Crude oil, LDI(+)

Complex mixture analysis via LDI



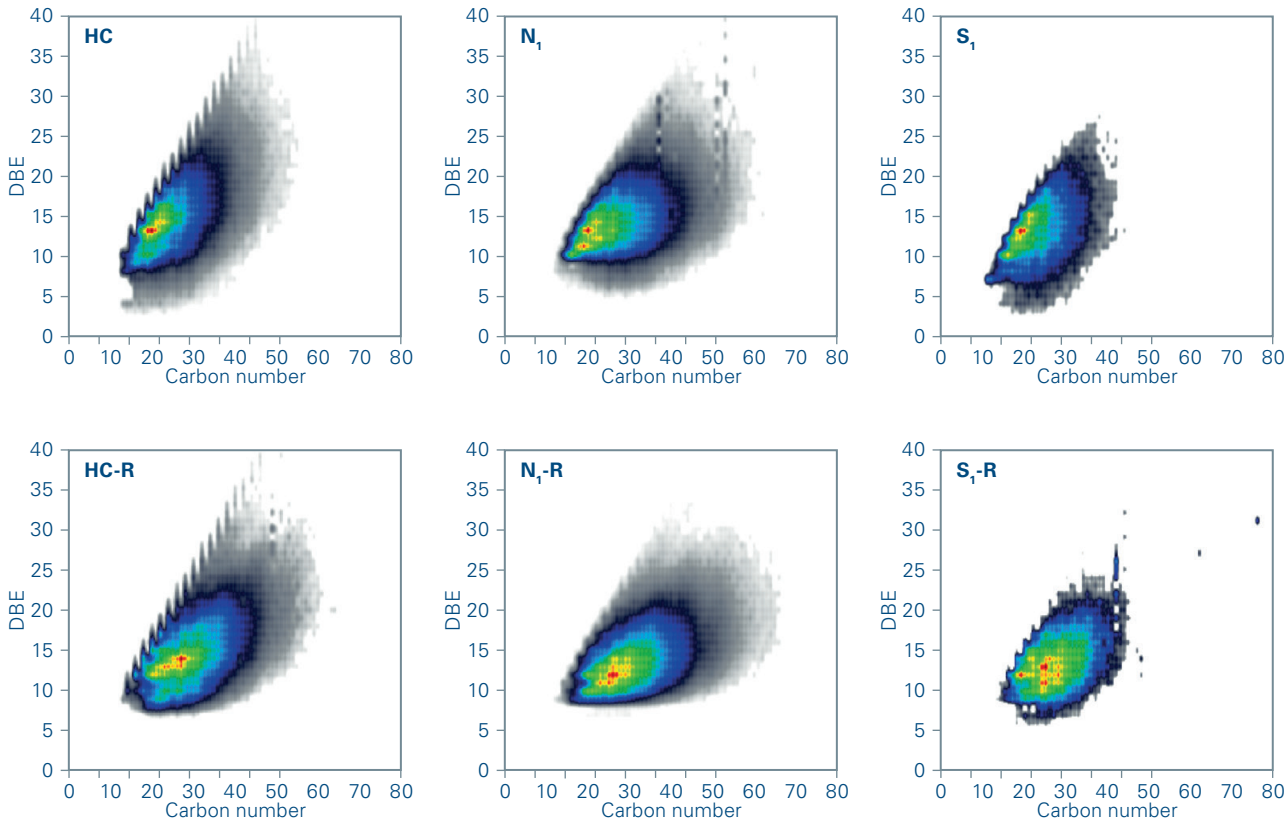
Many samples require solvents that are not amicable to ESI. The dual ESI/MALDI source of scimaX allows for easy laser desorption ionization for these types of samples.

R: 1,900,000
Transient length: 2.96s
2ω detection, AMP
300 scans

Petroleomics

Crude oil, CASI-LDI(+)

Enhanced dynamic range by CASI



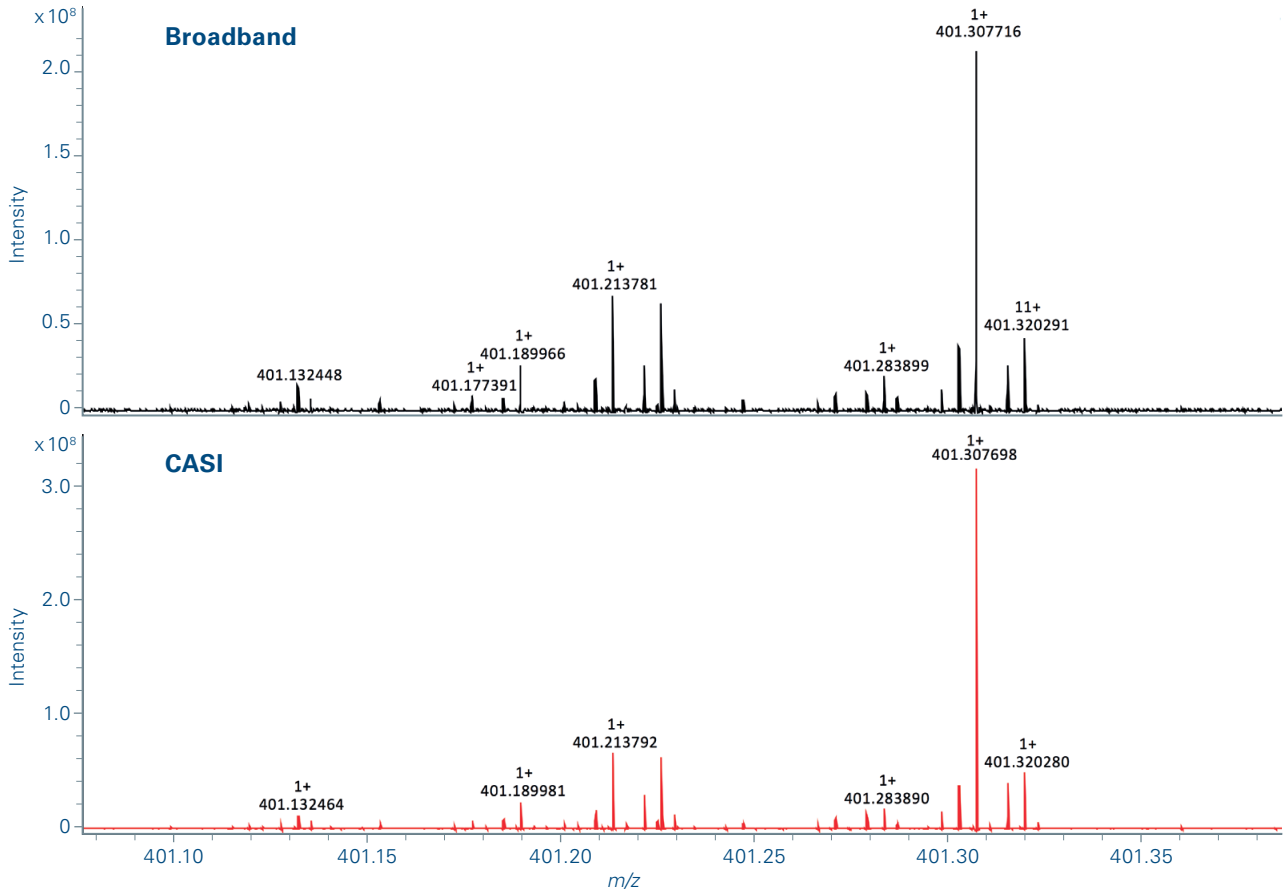
Broadband
R: 1,900,000 @ m/z 401

CASI
R: 3,200,000 @ m/z 401

Petroleomics

Crude oil, CASI-LDI(+)

Enhanced dynamic range by CASI



The CASI spectrum detected 54 peaks and assigned 50 molecular formula annotations with average error of 39 ppb in 1 Da window (*m/z* 401).

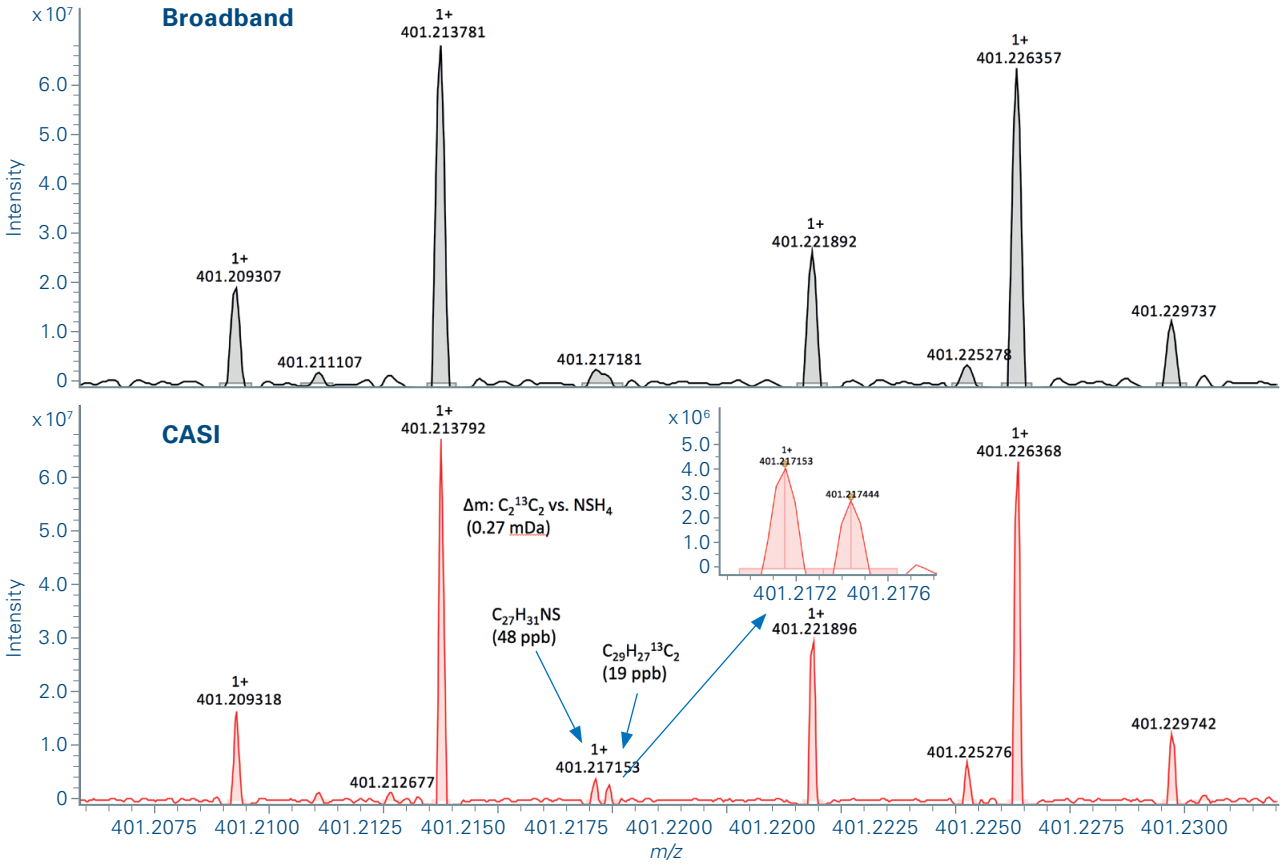
Broadband
R: 1,900,000 @ *m/z* 401

CASI
R: 3,200,000 @ *m/z* 401

Petroleomics

Crude oil, CASI-LDI(+)

Enhanced dynamic range by CASI

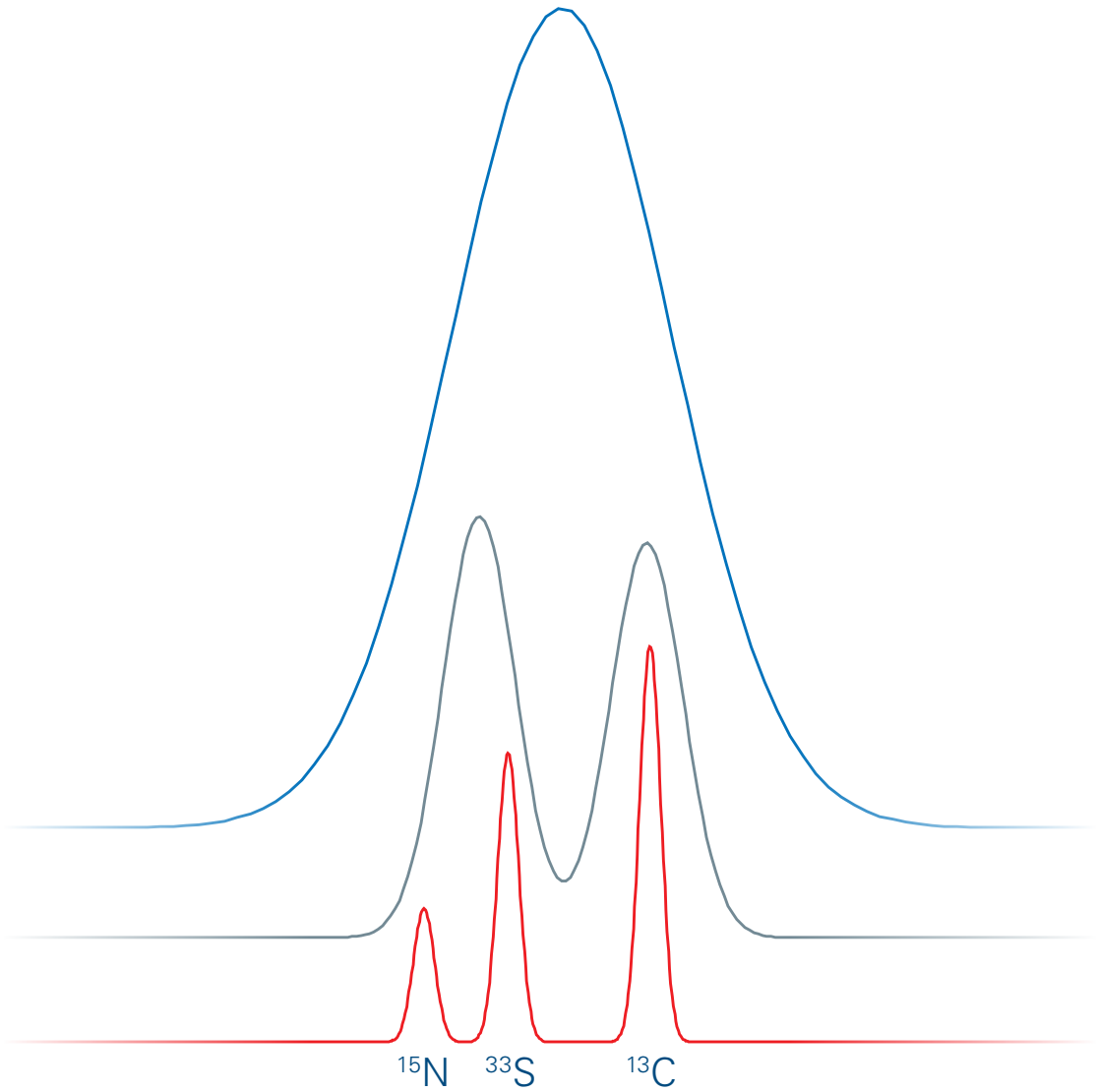


The insert shows two peaks baseline resolved that are only 0.27 mDa apart. This difference is less than the mass of an electron (0.59 mDa).

Broadband
R: 1,900,000 @ *m/z* 401

CASI
R: 3,200,000 @ *m/z* 401

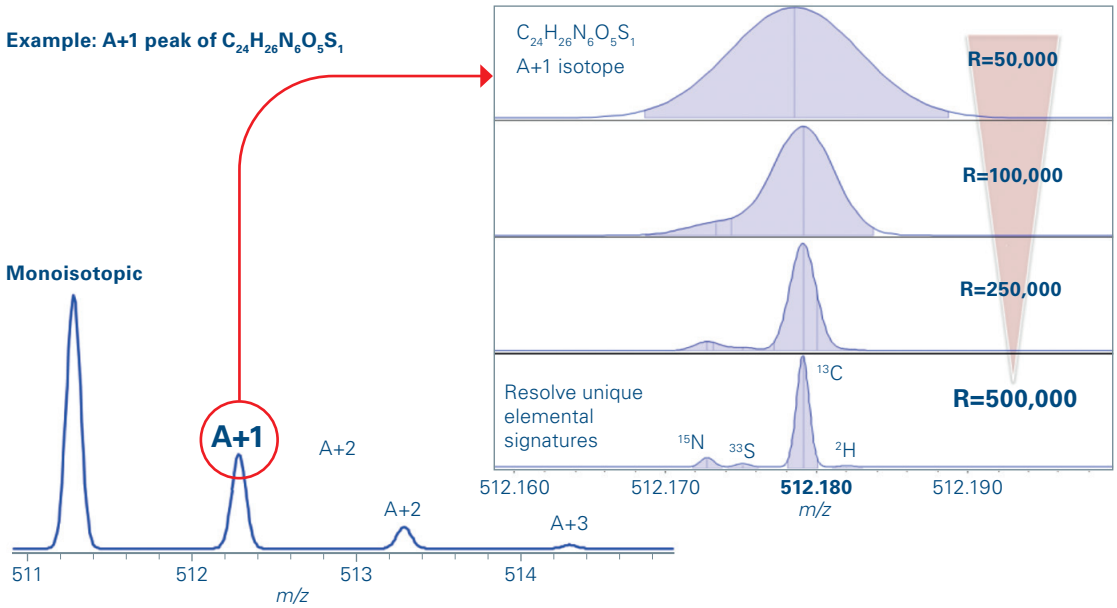
Isotopic Fine Structure



Isotopic Fine Structure

Requirements for IFS

Improvement in resolving power is more than simply a larger number. Rather improvements are gained only when new information is obtained. scimaX is the panicle of resolving power through routine isotopic fine structure analysis.



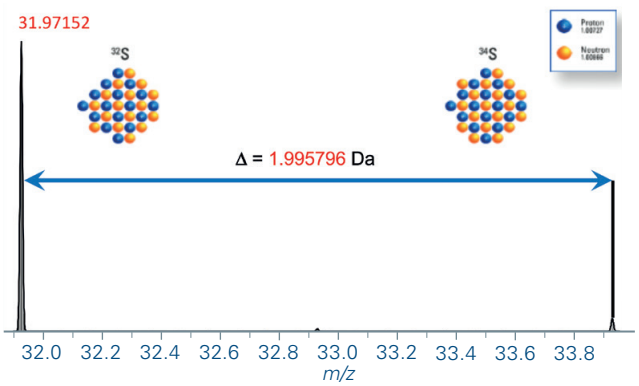
Isotopic Fine Structure

Customer Insights

The IFS approach enables the ability to rapidly identify sulfur containing metabolites and calculate single sum formulas for each, increasing both the speed and accuracy of the workflow. The incredible power of this workflow is that with extreme resolving power and sum formula determination, rapid screening for other heteroatom (N and O) containing metabolites is also possible.

"This S-atom-driven approach afforded an efficient chemical assignment of S-containing metabolites, suggesting its potential application for screening not only S but also other heteroatom-containing metabolites in MS-based metabolomics."

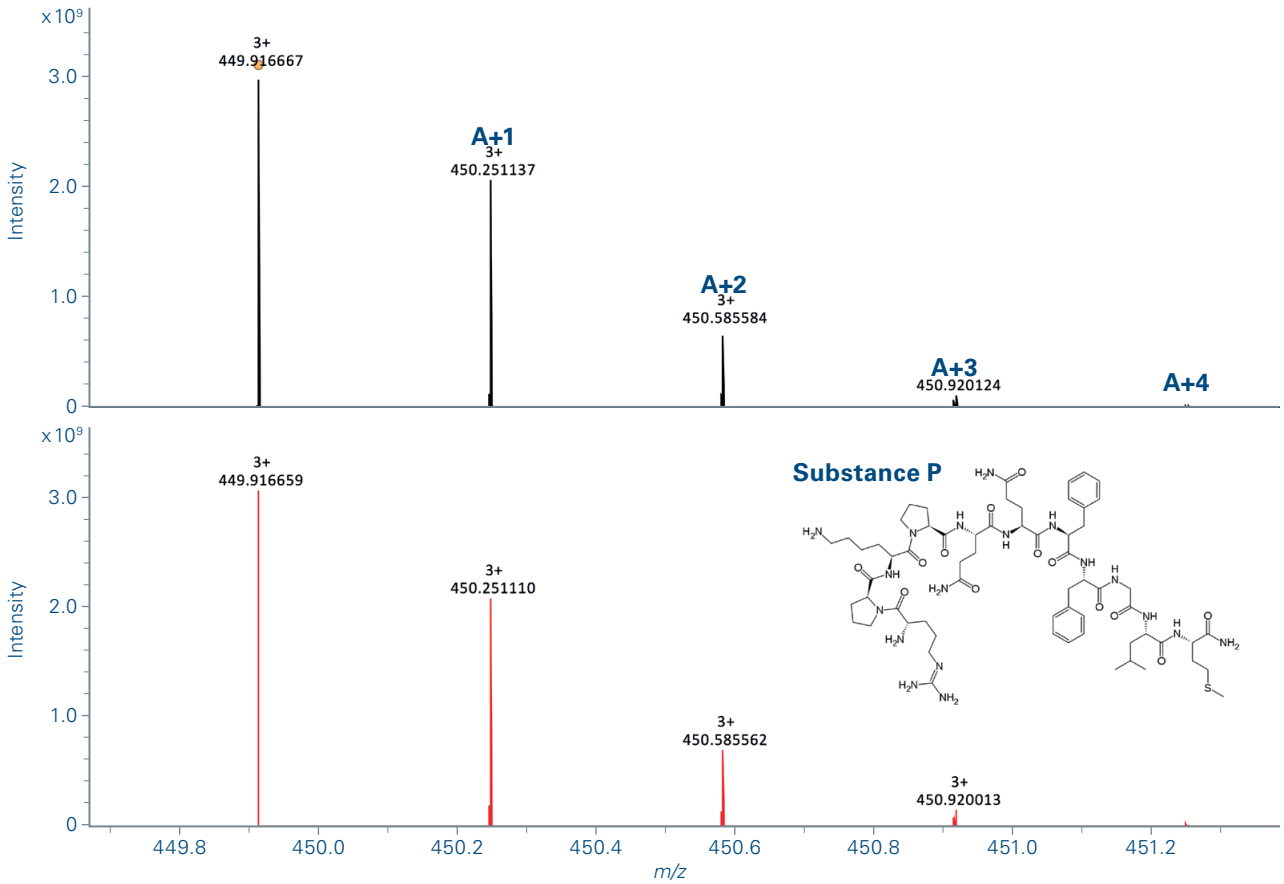
In 2013, Prof. Kazuki Saito, of the RIKEN Plant Science Center (group photo shown), was acknowledged with an award for one of the top downloaded papers. Prof. Kazuki Saito has been selected as a highly cited Researcher in 2014 and 2015 by Thomson Reuters in the Plant and Animal Science field and won the 2016 Japanese Society of Plant Physiologists award.



Isotopic Fine Structure

Substance P, ESI(+)

Unambiguous molecular formula determination



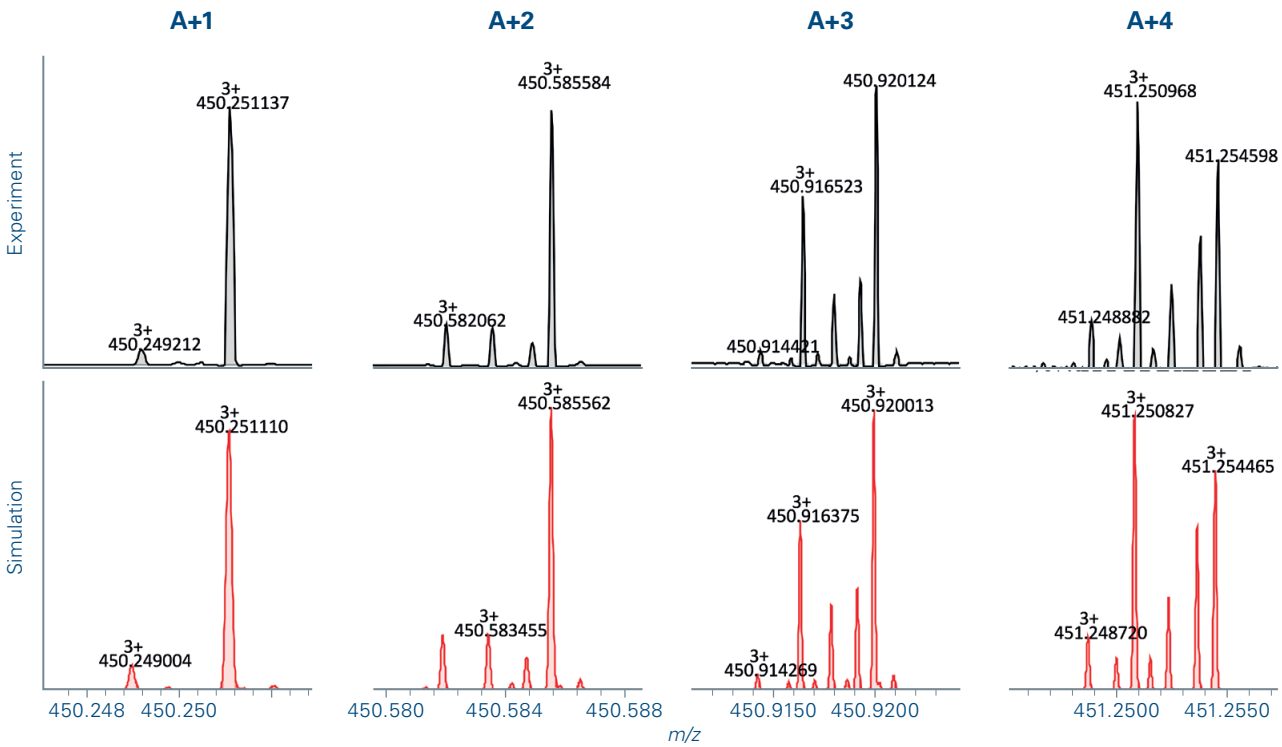
scimaX reveals nature's signature through the ability to see isotopic fine structure, providing unambiguous molecular formula determination. ParaCell technology allows you to work beyond the molecular realm.

R: 3,200,000 @ *m/z* 449
transient: 5.86 s, 2ω,
AMP (Kilgour)

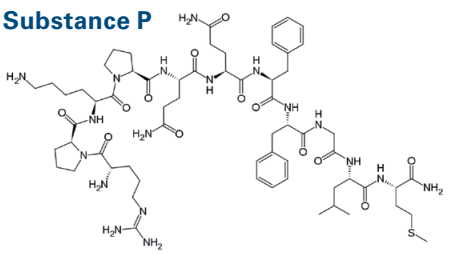
Isotopic Fine Structure

Substance P, ESI(+)

Unambiguous molecular formula determination



Substance P



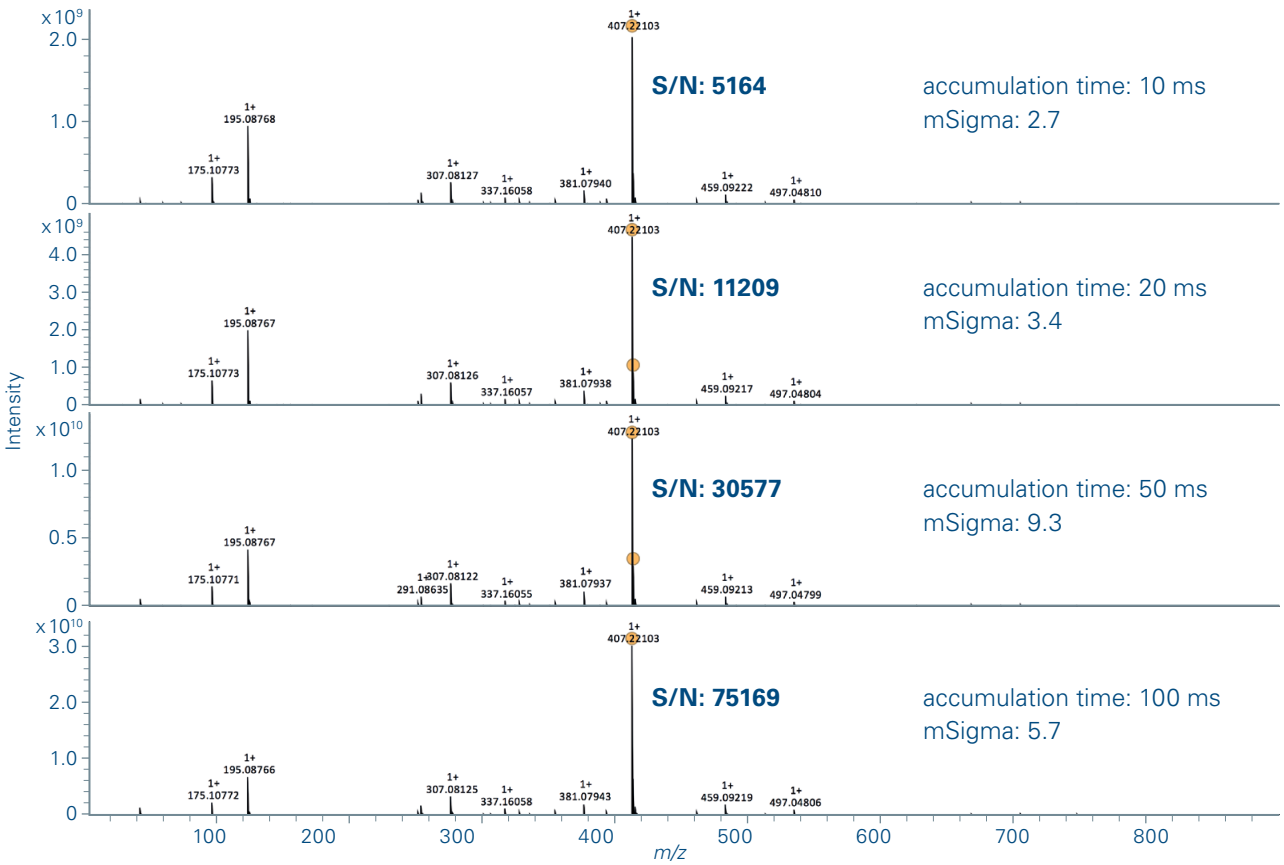
The molecular formula of Substance P is clearly shown by resolving the heavy isotopes for all the elements present in the molecule.

R: 3,200,000 @ m/z 449
transient: 5.86 s, 2ω,
AMP (Kilgour)

Isotopic Fidelity and Ion Population

Lincomycin, ESI(+)

Maintains isotopic fidelity at high ion population



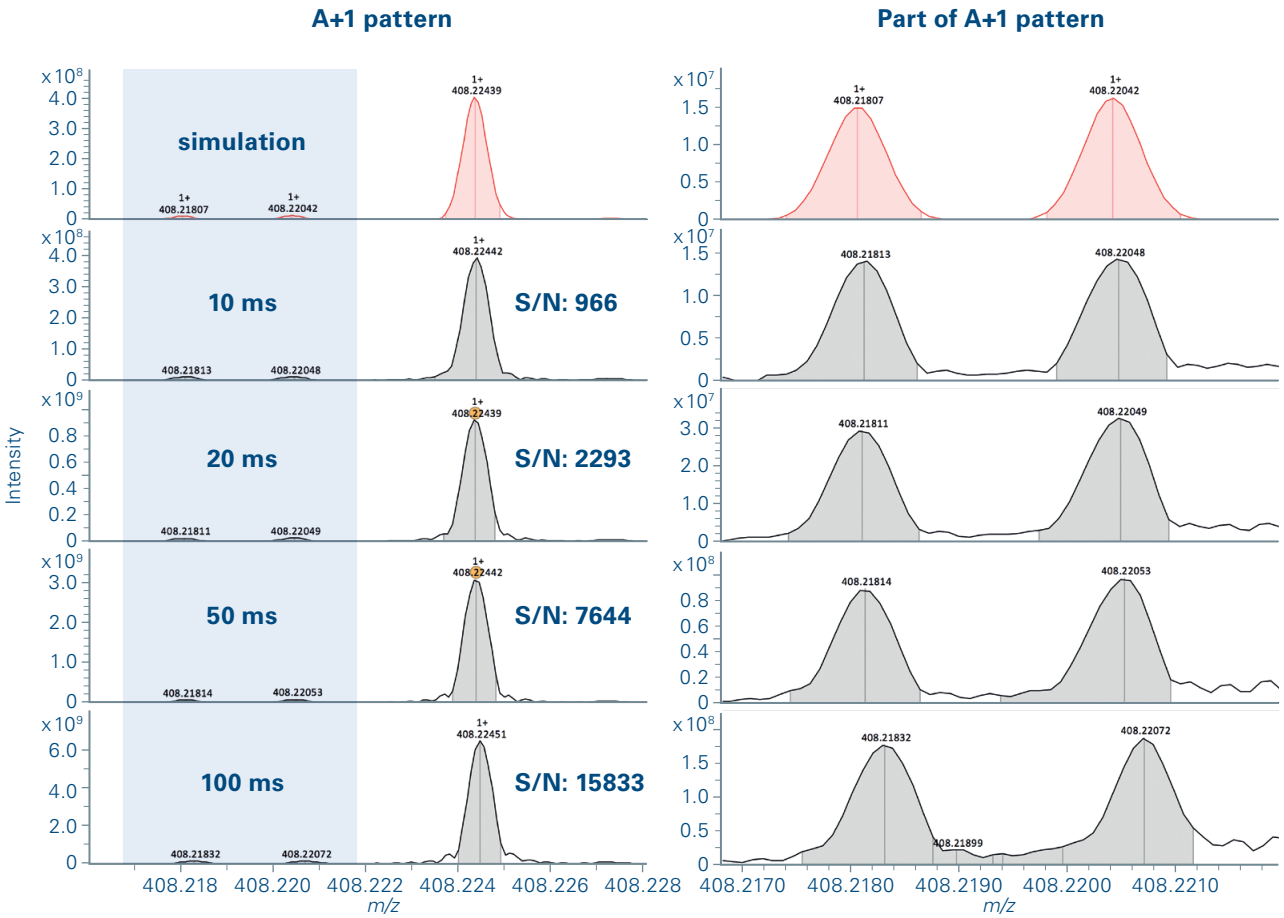
The high dynamic range of the ParaCell maintains peak fidelity even as the number of ions varies.

R: 650k @ *m/z* 407
Calibrated on Lincomycin ^{12}C peak

Isotopic Fidelity and Ion Population

Lincomycin, ESI(+)

Maintains isotopic fidelity at high ion population



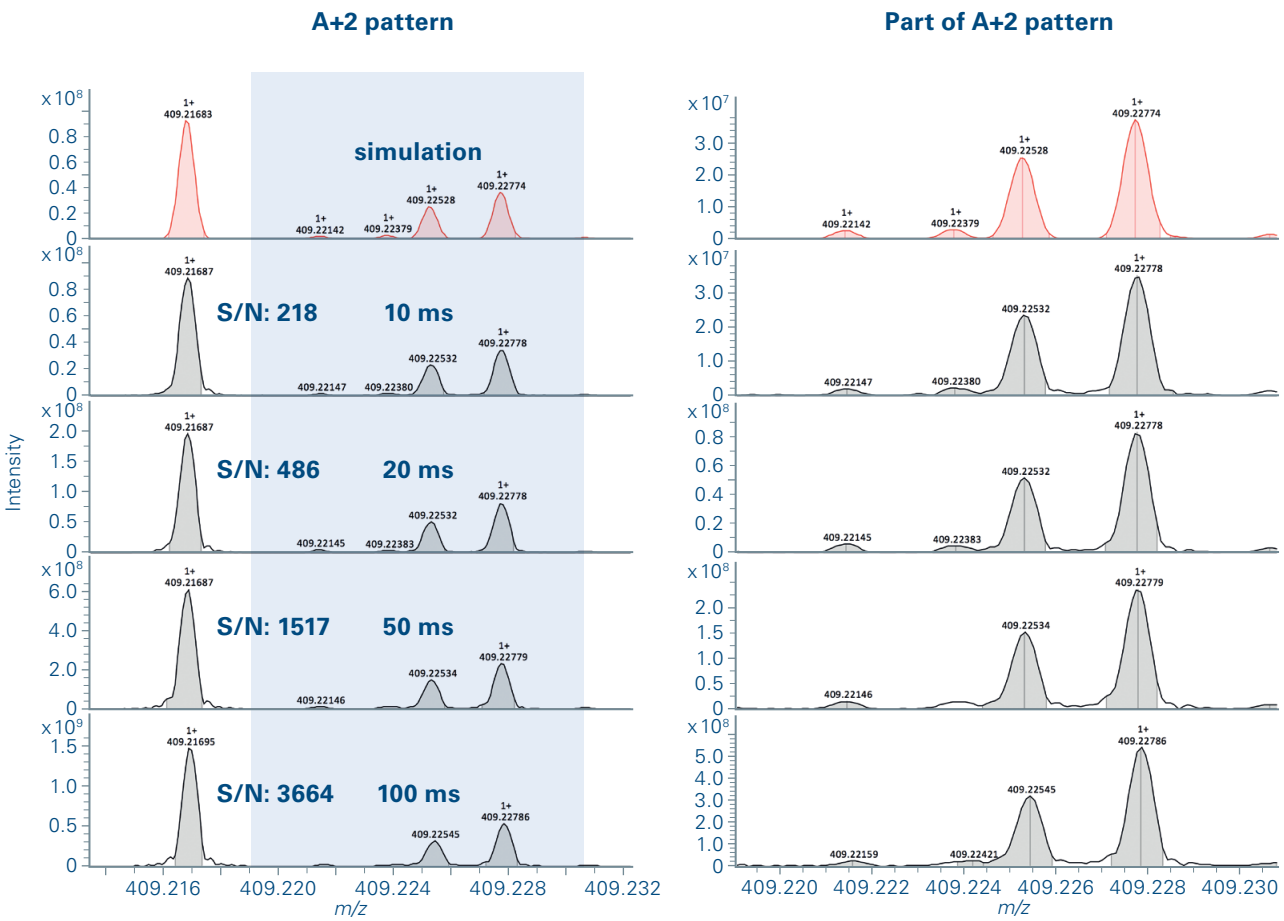
As the number of ions increases there is no change in the observed isotopic fine structure of Lincomycin.

R: 650k @ *m/z* 407
Calibrated on Lincomycin ^{12}C peak

Isotopic Fidelity and Ion Population

Lincomycin, ESI(+)

Maintains isotopic fidelity at high ion population



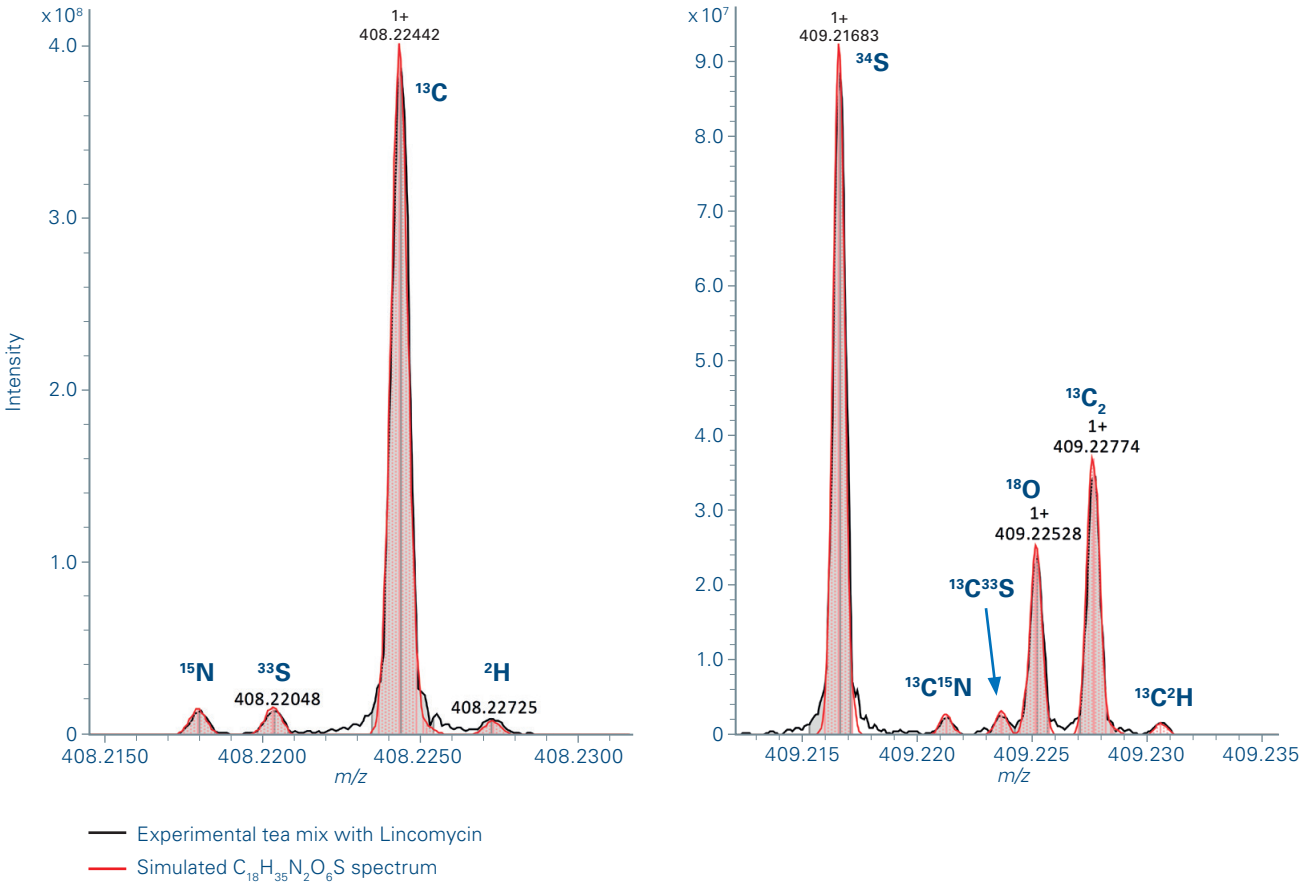
No change of IFS with high ion load in analyzer.

R: 650k @ *m/z* 407
Calibrated on Lincomycin ^{12}C peak

Isotopic Fidelity and Ion Population

Lincomycin, ESI(+), 10 ms

Maintains isotopic fidelity at high ion population

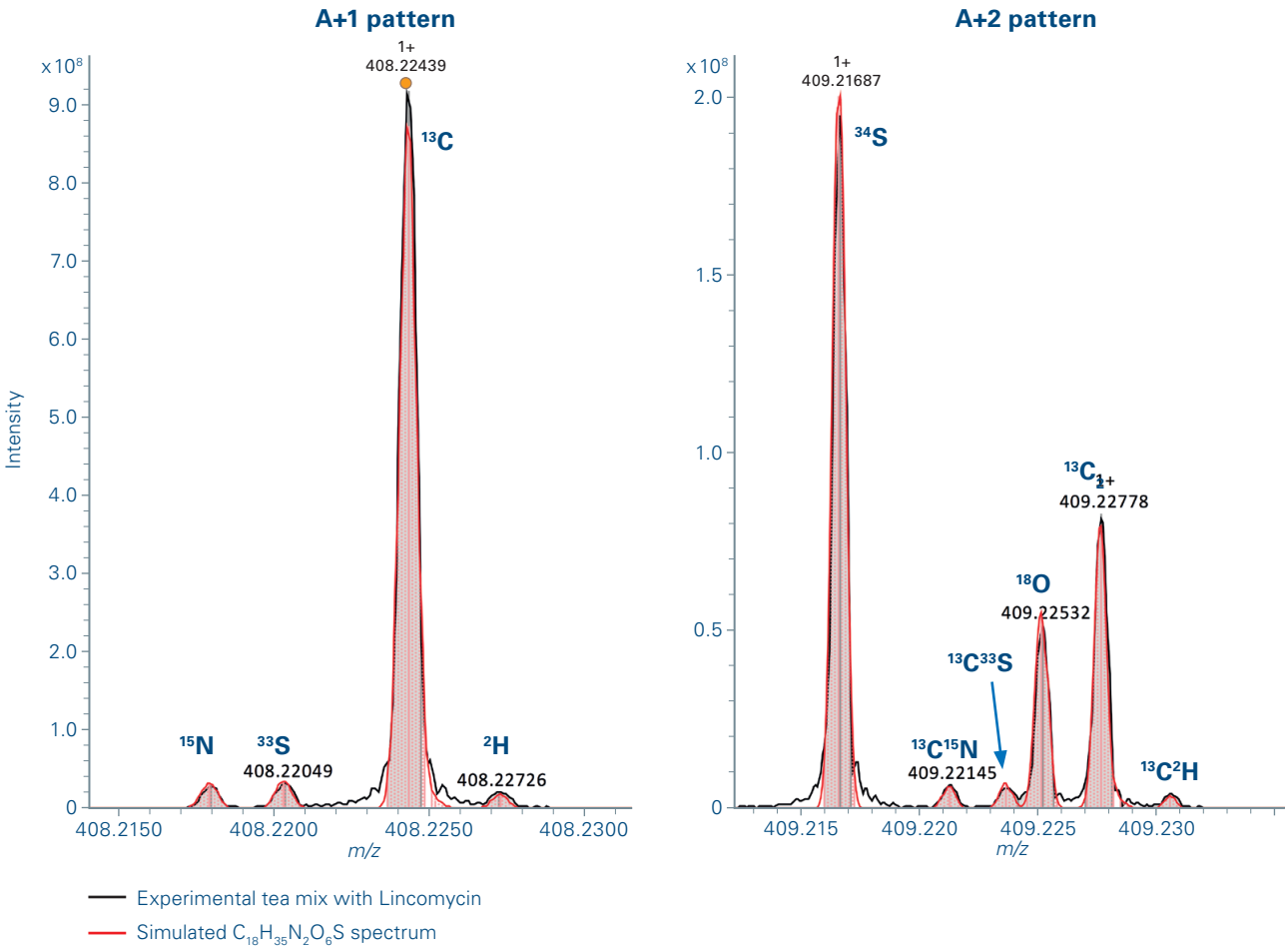


10 ms accumulation time
mSigma: 2.7
R: 650k @ *m/z* 407
Calibrated on Lincomycin ^{12}C peak

Isotopic Fidelity and Ion Population

Lincomycin, ESI(+), 20 ms

Maintains isotopic fidelity at high ion population

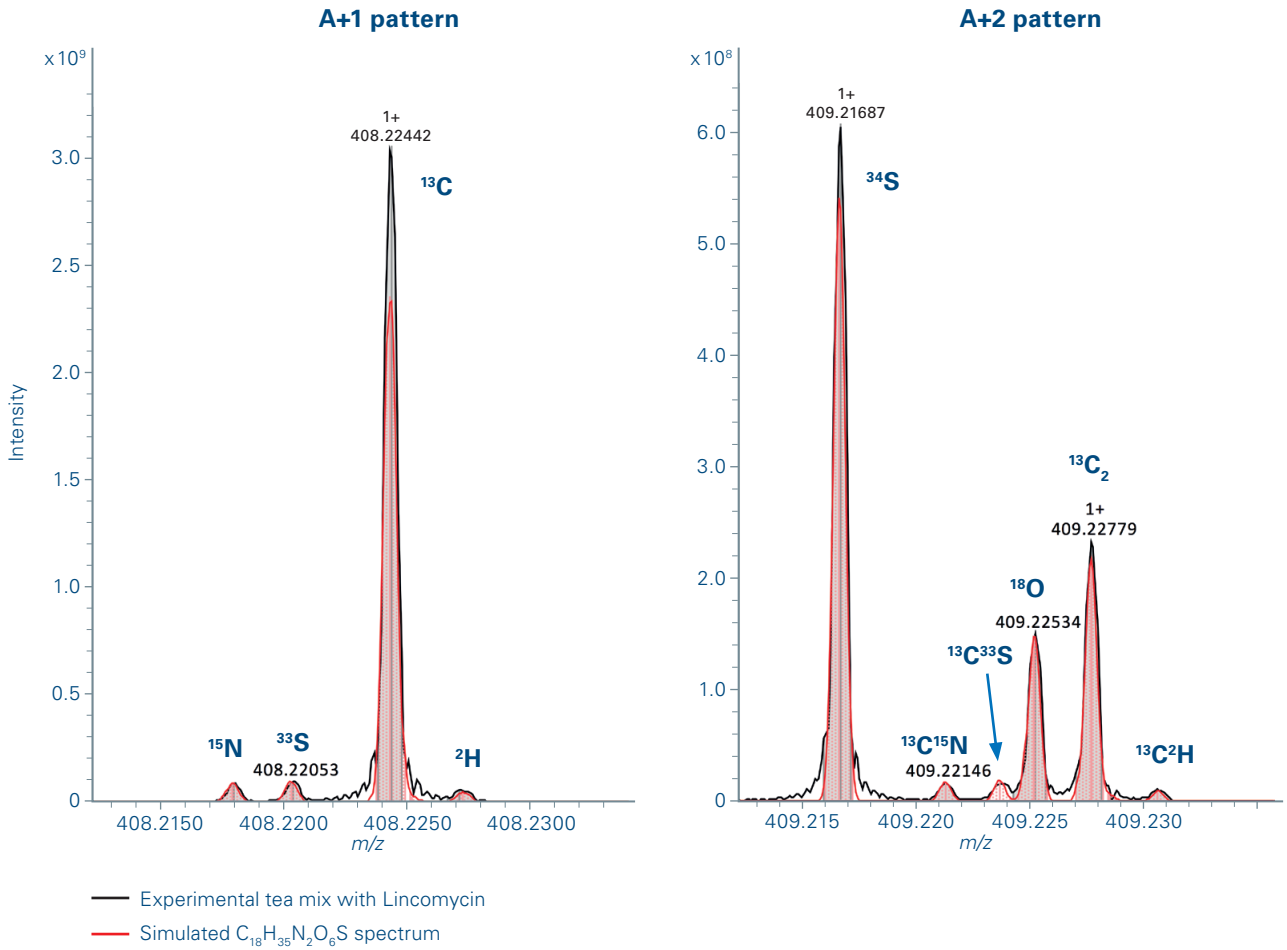


20 ms accumulation time
mSigma: 3.4
R: 650k @ *m/z* 407
Calibrated on Lincomycin ^{12}C peak

Isotopic Fidelity and Ion Population

Lincomycin, ESI(+), 50 ms

Maintains isotopic fidelity at high ion population

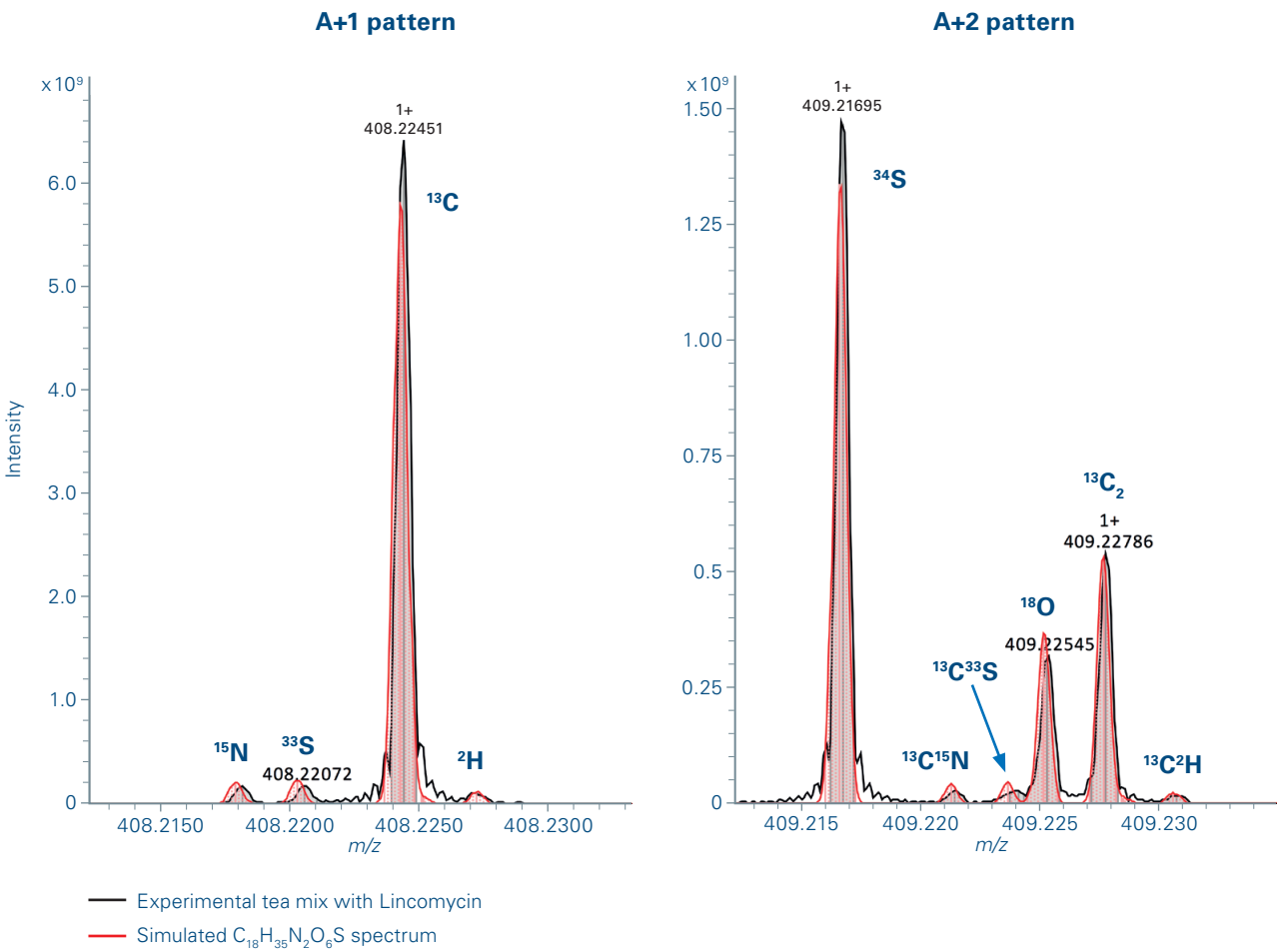


50 ms accumulation time
mSigma: 9.3
R: 650k @ *m/z* 407
Calibrated on Lincomycin ^{12}C peak

Isotopic Fidelity and Ion Population

Lincomycin, ESI(+), 100 ms

Maintains isotopic fidelity at high ion population

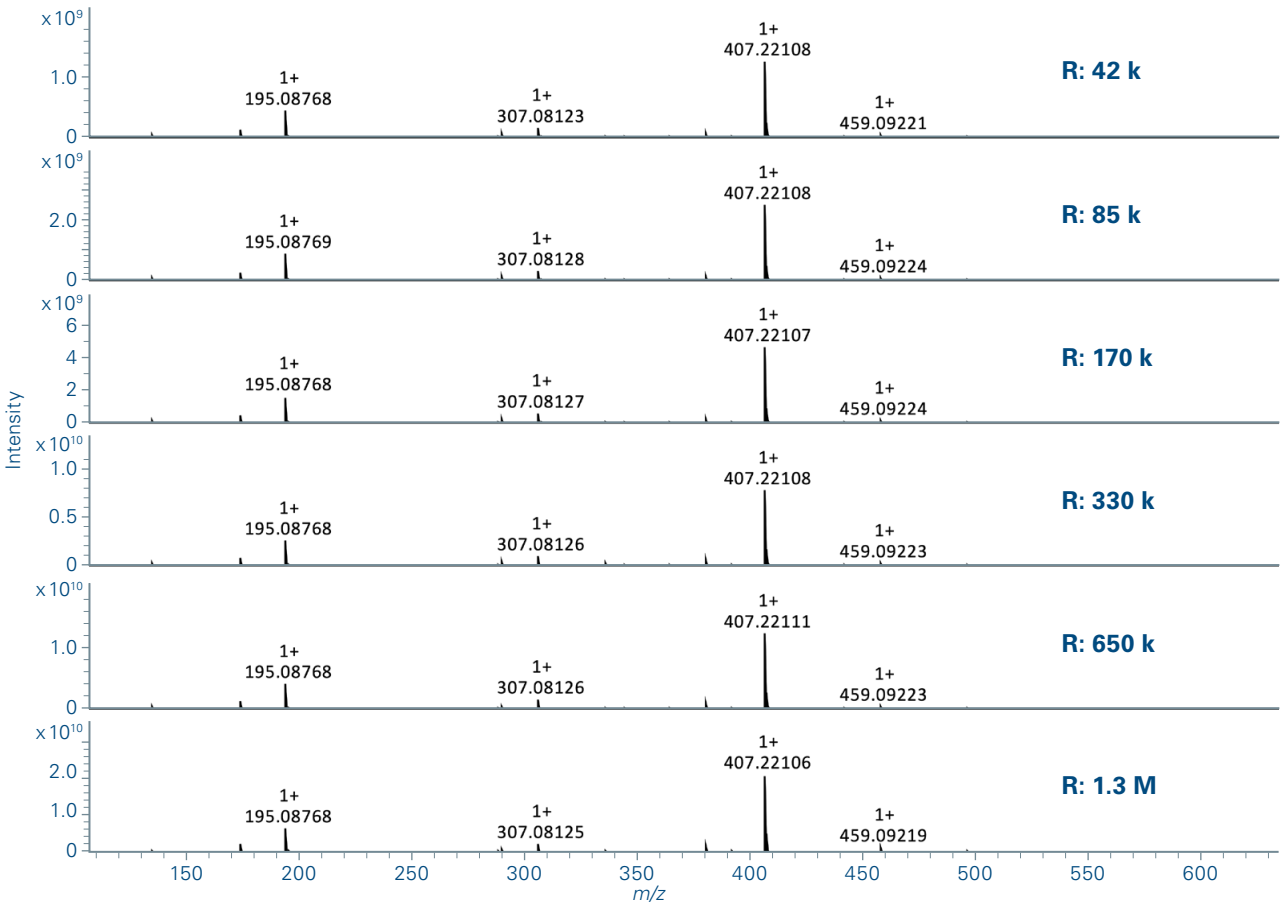


100 ms accumulation time
mSigma: 5.7
R: 650k @ *m/z* 407
Calibrated on Lincomycin ^{12}C peak

Isotopic Fidelity and Resolving Power

Lincomycin, ESI(+)

Maintains isotopic fidelity at high resolving power



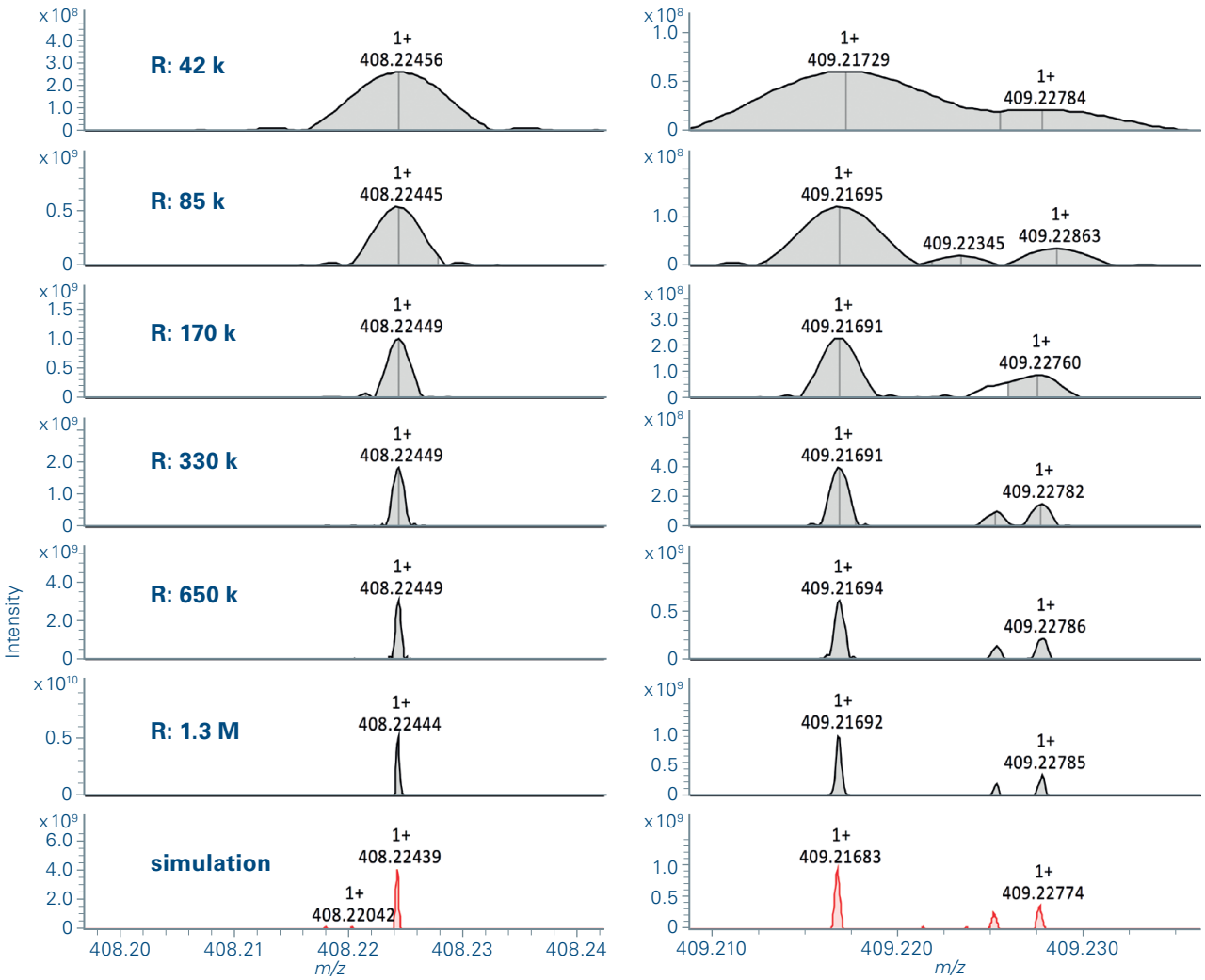
Unlike other MS instrumentation, scimaX has the ability to change resolving power from low resolution to eXtreme resolution. Isotopic peak fidelity is maintained across all settings.

R: 42k to 1300k @ *m/z* 407
Calibrated on $C_{12}H_{18}F_{12}N_3O_6P_3$

Isotopic Fidelity and Resolving Power

Lincomycin, ESI(+)

Maintains isotopic fidelity at high resolving power

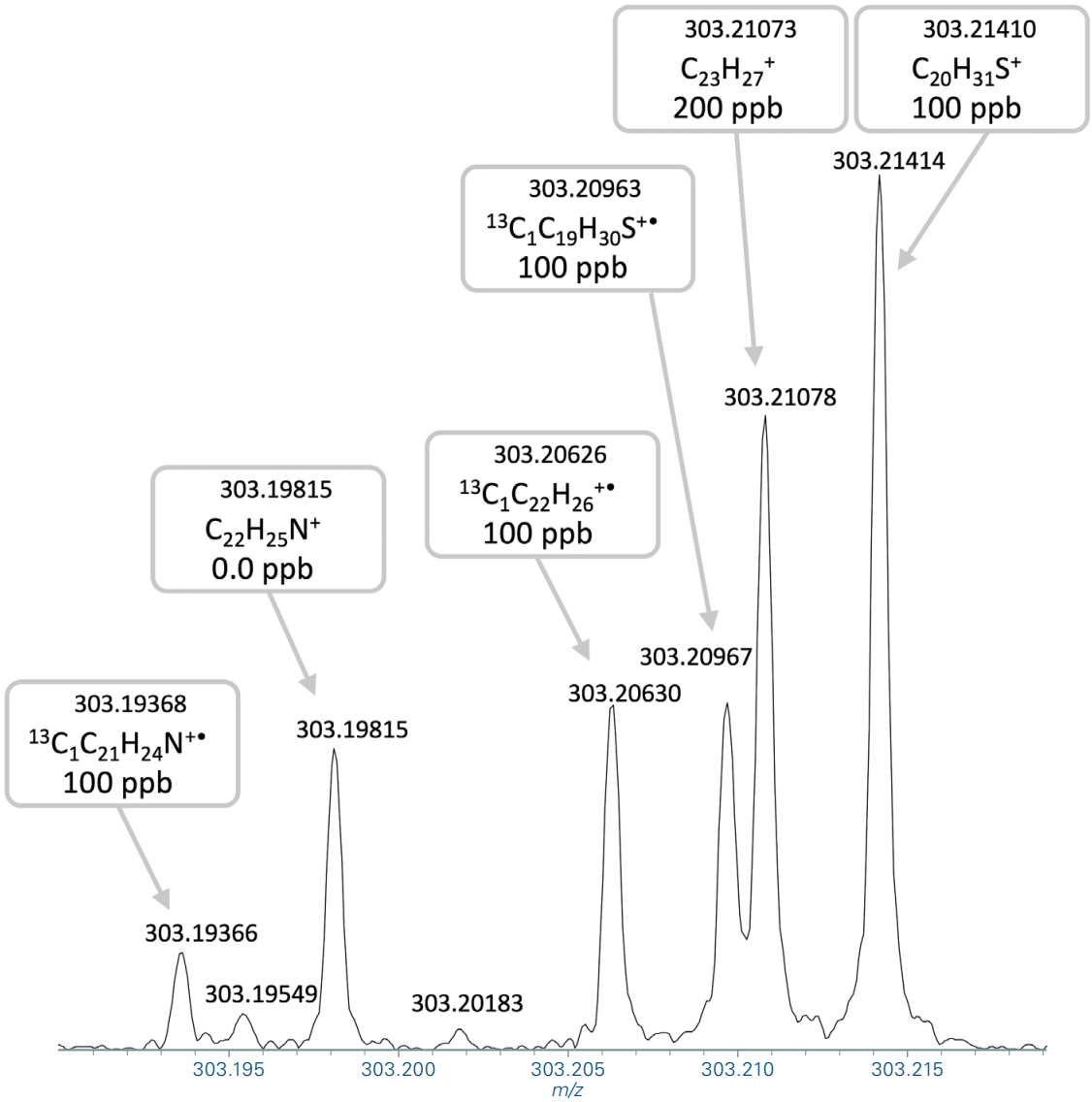


Isotopic peak fidelity is maintained even above 1M resolving power (RP), while high mass accuracy and peak fidelity is maintained at low RP.

R: 42k to 1300k @ *m/z* 407
Calibrated on $C_{12}H_{18}F_{12}N_3O_6P_3$

Mass Accuracy

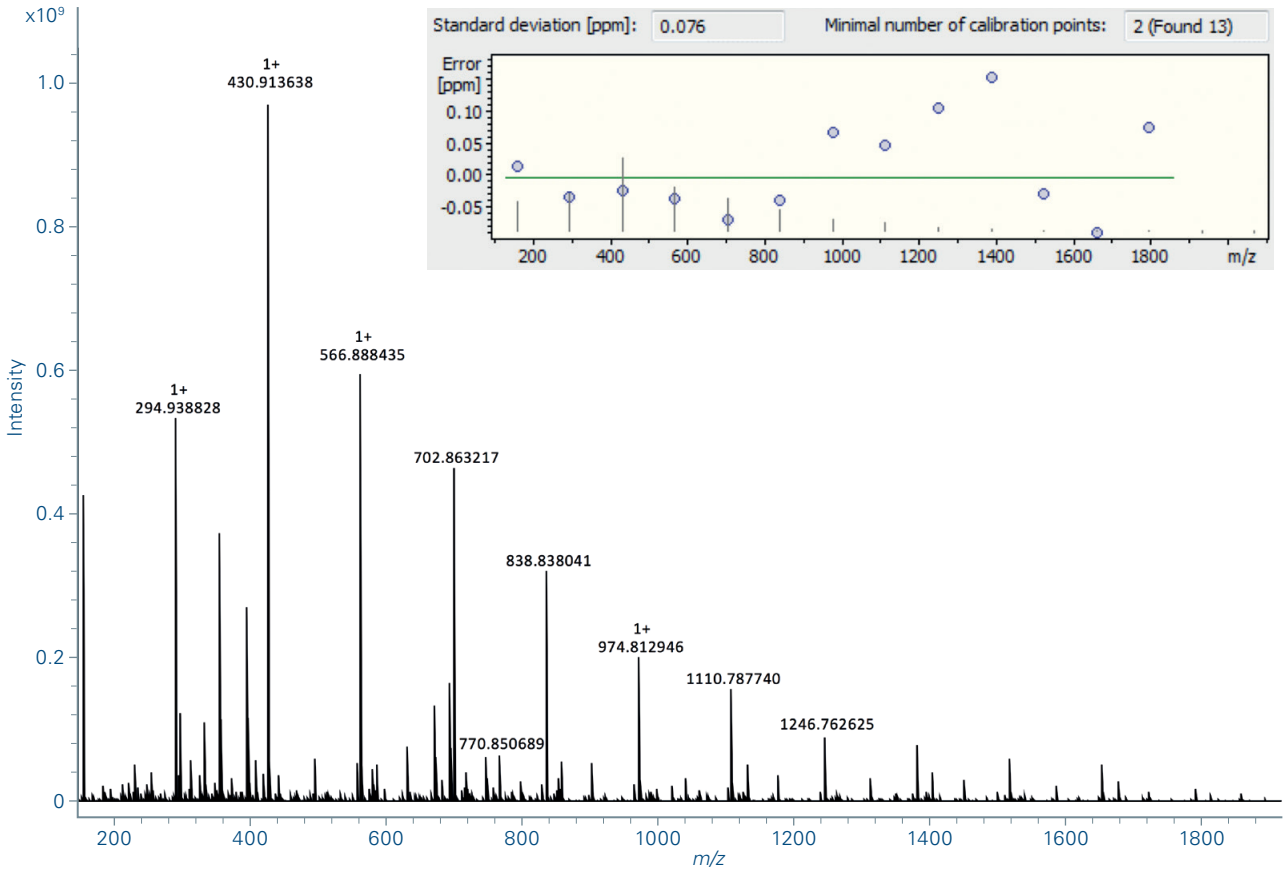
Routine Parts Per Billion



Calibration Mass Accuracy

ESI(+), NaTFA

ppb mass accuracy

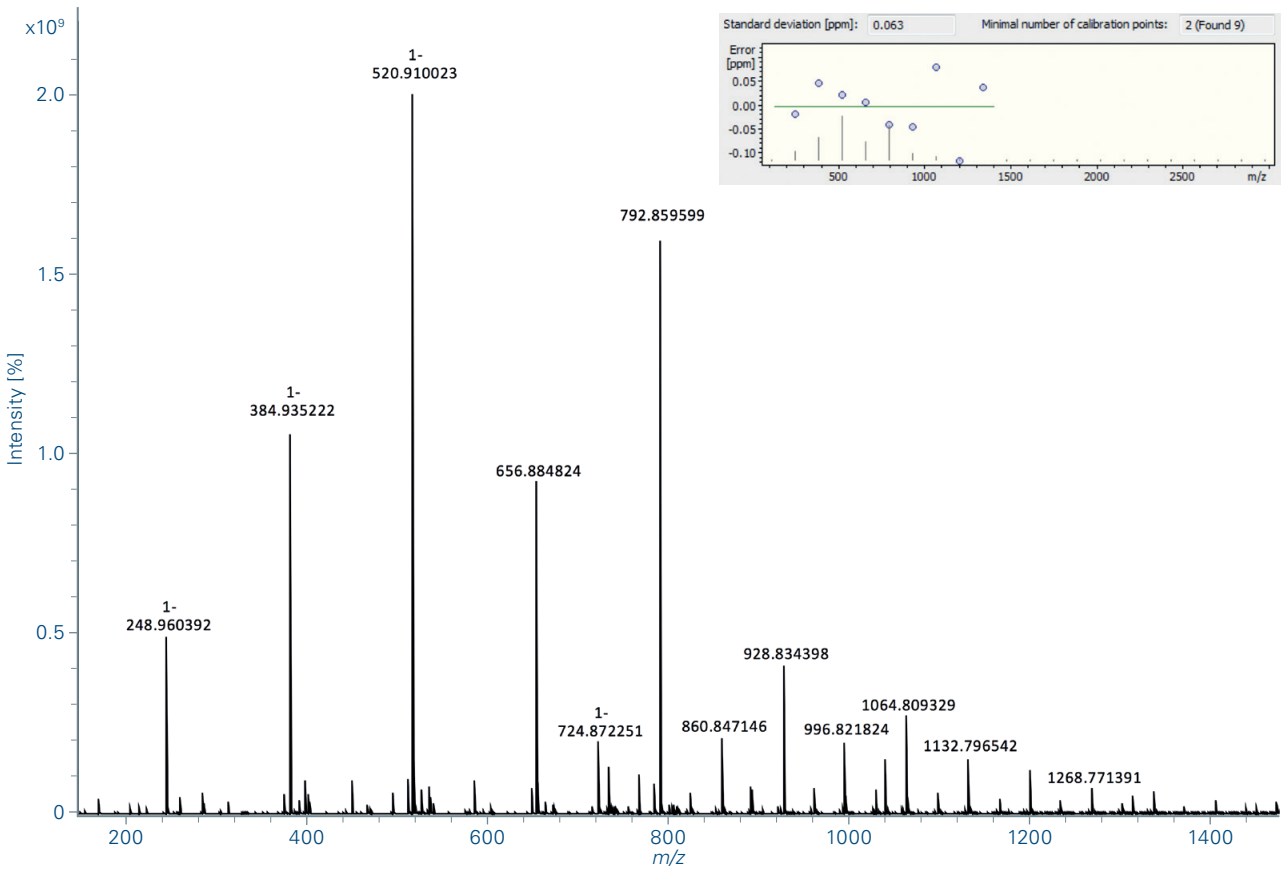


R: 1,550,000 @ *m/z* 430
RMS mass error: 76 ppb
Transient length: 2.96 s
2ω detection
absorption mode

Calibration Mass Accuracy

ESI(-), NaTFA

ppb mass accuracy

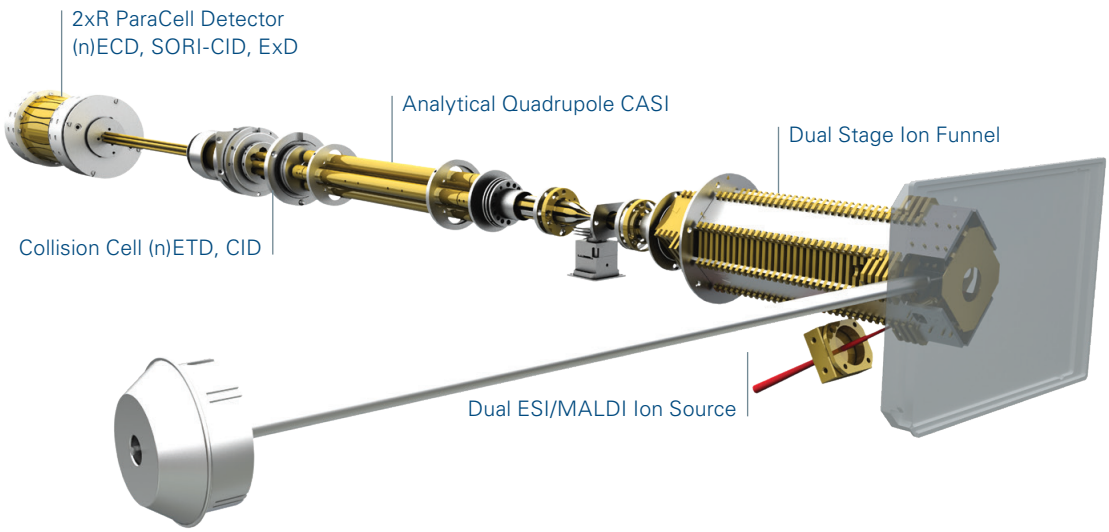


R: 1,760,000 @ *m/z* 384
RMS mass error: 63 ppb
Transient length: 2.96 s
2ω detection
absorption mode

Technology

scimaX MRMS

Technology



Maxwell Magnet Technology

No Liquid Cryogens – Ever

scimaX MRMS introduces Maxwell magnet technology to the field of mass spectrometry. This revolutionary design does not require liquid cryogens fills – ever.

This eliminates the need of monthly and yearly cryogen fills. It also eliminates the cost and hassle of obtaining cryogens.

Additionally, the reduced footprint allows for the placement of scimaX into any standard laboratory. Eliminating the need for quench ducts and simplifying the installation to that of any traditional mass spectrometry instrument.

All of the performance without the headaches of the past.

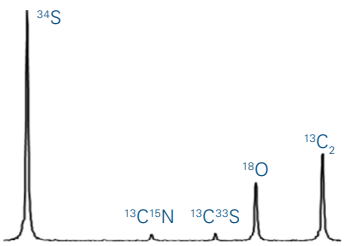
- 7T magnet
- Ultra-Stable Field
- Very compact design
- Small stray field
- **No** Liquid Nitrogen
- **No** Liquid Helium fill needed
- Biennial cold-head exchange
- **No** Quench duct required

scimaX MRMS

Unique Feature List

Appendix: Specifications for scimaX

scimaX is powered by Magnetic Resonance Mass Spectrometry (MRMS) technology which provides superior eXtreme Resolution and mass accuracy, enables routine Isotopic Fine Structure (IFS) analysis for a broad mass range and results in unmatched confidence for compound identification.

Analytic Performance	
Mass Range	100–10,000 *m/z*
Quadrupole Isolation Mass Range	100–6000 *m/z*
Quadrupole Isolation Efficiency	> 60%
Mass Accuracy (*m/z* 100–1500)	With internal calibrant: < 600 ppb average error With external calibrant: < 1500 ppb average error
Resolving Power @ *m/z* 400 (Lincomycin)	≥ 450,000 @ 1 Hz for LC experiments 20,000,000 maximum resolving power
Isotopic Fine Structure (IFS) @ *m/z* 400 (Lincomycin)	Separation of ^{13}C, ^{15}N, ^{18}O, ^{34}S isotopic peaks in M+1 or M+2 isotopic cluster, e.g.: 
Sensitivity	ESI (Ubiquitin): S/N > 20:1 for < 100 amol (consumed) MALDI (GluFib): S/N ≥ 20:1 @ *m/z* 1570.68 for 250 amol on target
MS/MS Efficiency (CID in collision cell, LHRH, $[M+2H]^{2+}$	> 50% conversion from isolated precursor
Multistage MS (MS^3 guaranteed) (LHRH)	LHRH MS/MS (collision cell) -> MS/MS/MS (ParaCell)
Negative Ions	Functionality shown on Fibrinopeptide B
Fragmentation Techniques	• In Source CID • CID in collision cell • (n)ECD and EID in ParaCell; ECD sensitivity for c5 fragment of Substance P @ *m/z* 624 S/N > 10:1 for 5 fmol consumed • SORI • (n)ETD
MS/MS Capabilities	Automated selection, isolation and MS/MS utilizing CID, (n)ECD or (n)ETD

scimaX MRMS

Unique Feature List

System Properties	
Vacuum System	6 stage differentially pumped vacuum system • 2 rough pumps (28 m3/h and 5 m3/h) and 4 turbo pumps (each 260 l/s) • Continuous sample introduction at atmospheric pressure while maintaining ultra-high vacuum (UHV) analyzer conditions
Dual ESI/MALDI source	• Apollo II Electrospray Source, flow rate: 1 µL/min – 1 mL/min • Highly sensitive MALDI source in conjunction with microtiter plate formatted MALDI targets and 1 kHz SmartBeam-II laser • Fast software controlled switchover between MALDI and ESI operation or simultaneous ESI/MALDI operation • Dual ion funnel for high ion transmission efficiency over broad mass range • In Source Collision Induced Dissociation (IS-CID) control
ETD	Electron Transfer Dissociation (ETD) • Robust third generation design • Provides extensive fragmentation for top-down studies • Superb tool for studying labile PTMs
Analytic Quadrupole	• Facile Q-CID for top-down and LC-MS/MS • Supports CASI for enrichment of low abundant species
Ion Optics	Optimized ion optics to guide the ions, enabling • Sensitive transmission of broad mass range • Easy and quick workflow and sample changes
Magnet	7T conduction cooled magnet • Very stable and homogenous 7T magnetic field for ultimate MRMS performance • Very compact design with small stray field • No liquid nitrogen • No liquid helium fill needed • No quench duct required
Mass Analyzer	Proprietary ParaCell MRMS detector with patented **2XR** magnetron control technology • Dynamic Field shape and shimming enables e**X**treme **R**esolution applications with speed • Ultrahigh performance low noise **2XR** preamplifier for improved sensitivity • Allows for high resolution, in-cell isolation • Integrated computer controlled indirectly heated cathode for Electron Capture Dissociation (ECD) and Electron Induced Dissociation (EID) of trapped ions
Acquisition Electronics	Nanobay-E featuring • Fully computer controlled data acquisition • Data streaming, enabling e**X**treme broad-band **R**esolution • Flexible and fast data acquisition
Size	• Floor standing, L 2.30m x B 0.93m x H 2.04 m
Weight	• Mass spectrometer ~ 1450 kg, Accessories ~ 255 kg

scimaX MRMS

Unique Feature List

scimaX

Magnetic Resonance Mass Spectrometry (MRMS) system

Unique Feature List
applicable to
BDAL #188807050 (for regions with 50Hz power requirements) or
BDAL #188807060 (for regions with 60Hz power requirements)

A. Dual ESI/MALDI source

Mass spectrometer with an electrospray ionization (ESI) source allowing for positive and negative ion detection.

- The needle of the near-orthogonal ESI source must be on ground potential.
- Ions from the ESI source need to be deflected orthogonally into the mass spectrometer for minimum neutral gas background.
- Atmospheric Pressure Ionization (API) spray chamber shall be compatible with a wide range of ionization sources including ESI, APPI, APCI, CaptiveSpray, and GC-APCI.
- The source shall be compatible with a direct insertion probe (DIP) solution for facile introduction of volatile compounds.
- Fast polarity switching shall be possible in less than a second.

A mass spectrometric source setup including

- An ion source with dual ion funnel system enabling simultaneous transfer of a broad m/z-range by monolithic rf design eliminating compound specific tuning.
- A lens system enabling switching from soft ion transfer to in-source-CID experiments.

Mass spectrometer with a combined ESI/MALDI source allowing for positive and negative ion detection.

Switching between ESI and MALDI operation must be fully automatic and SW controlled, the switchover time shall be fast and not exceed 1 minute.

- Simultaneous acquisition of ions originating from ESI and MALDI shall be possible.
- Mixing of ions generated by ESI into the MALDI ions from the e.g. tissue sample shall allow for internal calibration leading to a further increase of mass stability and accuracy.

Solid-state laser capable of at least 1 kHz repetition rate with dynamical shaped beam profile for optimized MALDI performance.

Technology using n^{th} ($n \geq 2$) harmonics detection enabling fast MALDI imaging acquisitions while maintaining resolution required for Isotopic Fine Structure (IFS) investigations.

Co-registration for MALDI Imaging data within the suppliers MS software including visualization of mass spectrometry imaging data.

B. Mass Spectrometer

Support of a technique for the selective enrichment of low abundant species, including

- Quadrupole mass filter for Continuous Accumulation of Selected Ions (CASI) to increase the dynamic range and spectral quality over a selected mass range.
- Continuous Accumulation of Selected Ions (CASI) providing added sensitivity and mass resolution for target m/z ranges.

Transmission of a wide m/z range (~100 – 10,000 m/z)

Provision of various fragmentation techniques

- CID in source and collision cell
- (n)ECD in MRMS analyzer
- SORI-CID in MRMS analyzer
- (n)ETD
- EID

C. Mass Analyzer Technique

A mass spectrometric analyzer with the following properties:

- Differential pumping system with ≥ 6 differential pumping stages to achieve ultimate vacuum at the analyzer and best mass spectrometric performance characteristics.
- Fourier Transform Mass Spectrometer (FTMS) based on Magnetic Resonance Mass spectrometric (MRMS) detection system enabling routine Isotopic Fine Structure (IFS) analysis for a broad mass range.

An MRMS system featuring a conduction cooled 7T magnet:

- No filling of liquid cryogens needed
- No quench line needed

A mass spectrometric detection device as specified below:

- Cylindrical MRMS detection cell equipped with ECD capabilities
- Capability of mass isolation in the detector cell
- MRMS detector with magnetron control features
- Exploitation of n^{th} ($n \geq 2$) harmonics detection to enable routine Isotopic Fine Structure analysis (IFS) with speed
- Mass accuracy (internally calibrated) of 600 ppb or better
- Ultimate resolving power in excess of 20 Million at *m/z* 400
- Allowing for LC experiments with an acquisition speed of 1 Hz while maintaining mass resolution of ≥ 400,000 at *m/z* 400 or ≥ 800,000 at *m/z* 200.
- Allowing for MALDI experiments with an acquisition speed of 1 Hz while maintaining mass resolution of ≥ 400,000 at *m/z* 400.

D. Software

Flexibility to control HPLC systems of various vendors (Agilent, Bruker, Thermo, Waters) within the original MS vendor software offered (START/STOP signal is insufficient)

Absorption Mode Processing (AMP) enabling

- Faster acquisitions for LC and MALDI based applications
- Enhanced mass resolution for Isotopic Fine Structure (IFS) interrogation

SW for elemental formula determination from isotopic profile evaluation

E. Further requirements

Possibility of remote service diagnostics via secured Internet connection

scimaX MRMS

Unique Feature List

Appendix: Patents

Electro-Spray Ion Source: Apollo II Ion Source with Ion Funnel

- Title: "Ionization chamber for atmospheric pressure ionization mass spectrometry"
  Patent granted: US731502082
- Title: "Ion guide for mass spectrometers"
  Patents granted: CA2463433C; CA2747956C; EP1465234B; US7495212B2; US7459693 B2; US785l752B2; US8222597B2
- Title: "Ion funnel with improved ion screening"
  Patents granted: GB2402261B; US7064321B2

High Precision Multipole Rod Ion Guides

- Title: "Multiple rod systems produced by wire erosion"
  Patents granted: DE102004037B4; GB2416915B; US7351963B2

Electron Capture Dissociation in an ICR cell

- Title: "Method and device for irradiating ions in an ion cyclotron resonance trap with photons and electrons"
  Patents granted: DE10213652B4; GB2390937B; US6803S69B2

ParaCell XR and 2xR Detector

- Title: "Ion cyclotron resonance measuring cells with harmonic trapping potential"
  Patents granted: DE102009050039B4; US8704173B2
- Title: "Correction of asymmetric electric fields in ion cyclotron resonance cells"
  Patents granted: US8859953B2; US8766174BI
- Title: "ICR cell operating with a duplexer"
  Patents granted: DE102014226498B4; US9620349B2
- Title: "Introduction of ions into ion cyclotron resonance cells"
  Patents granted: EP 285809061; US935583082

Isotopic Fine Structure MRMS

- Title: "Determination of elemental composition of substances from ultrahigh-resolved isotopic fine structure mass spectra
  Patent granted: US9111735BI

Smart Beam MALDI source

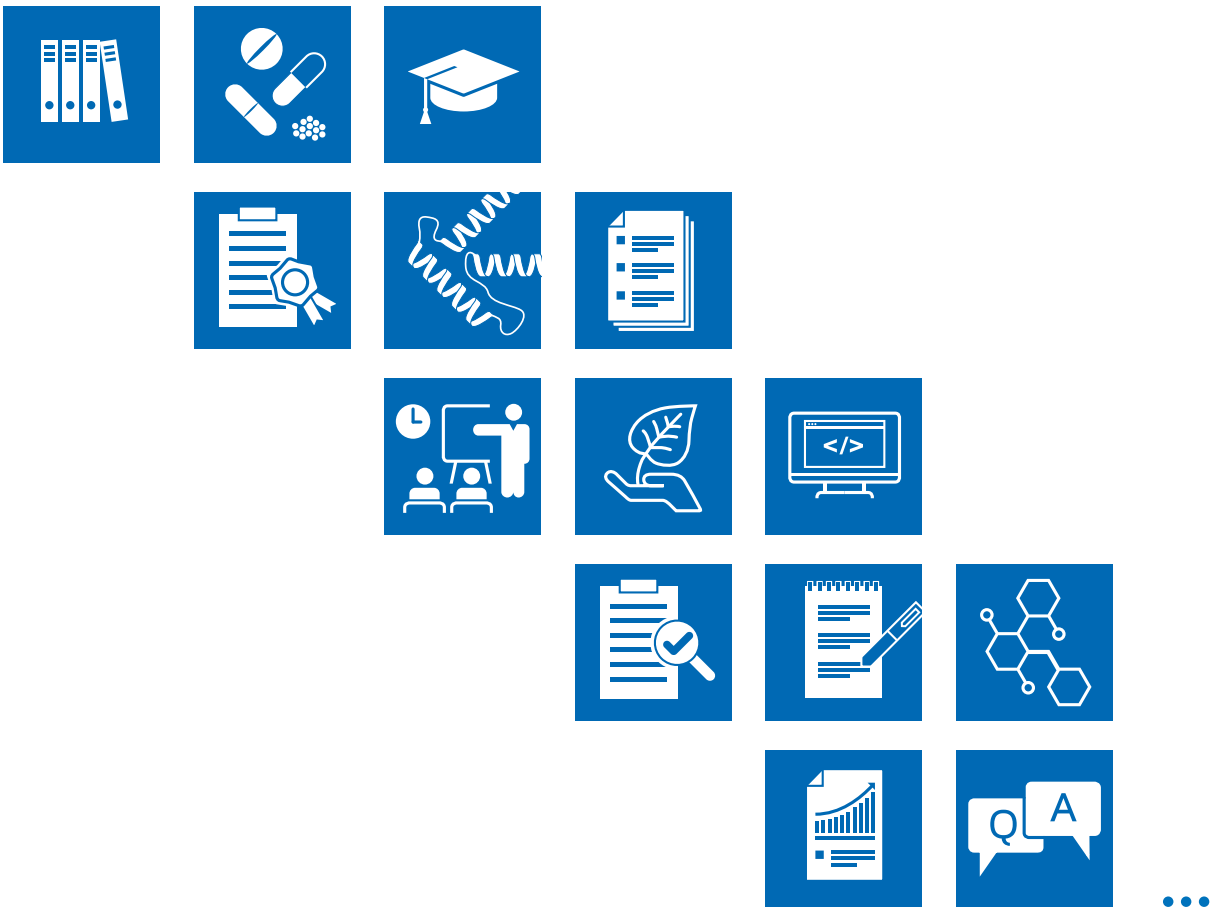
- Title: "Laser system for the ionization of a sample by matrix-assisted laser desorption in mass spectrometric analysis"
  Patents granted: GB2421352B; US7235781B2
- Title: "A method and system for providing a choice of spatial intensity distributions of laser radiation in MALDI mass spectroscopy"

Patents granted: GB2423187B; US7385192B2

Electron Transfer Dissociation

- Title: "Ion fragmentation by electron transfer in ion traps"
  Patents granted: GB2423865 B; US7456397B2

Additional Resources



MRMS Literature

Resources for researchers

MALDI Imaging

High-resolution climate reconstruction using MRMS MALDI Imaging

Designer drug analysis by forensic MALDI techniques

Interrogation of the Spatial Metabolome of Ginkgo biloba with high-resolution MALDI and LDI Mass Spectrometry Imaging

Integrating Ultra-High Speed MALDI-TOF and MALDI MRMS Imaging For Spatial Proteomics

Single Cell Lipid Analysis using Mass Spectrometry

MALDI FTMS Imaging Mass Spectrometry of N-glycans as Tissue Biomarkers of Cancer

MALDI Imaging Success Stories

Microbial Imaging Mass Spectrometry With Fourier Transform Mass Spectrometry

Metabolomics

Fast profiling of sphingolipids alteration in hypertension by MRMS

MRMS aXelerate for targeted metabolomics profiling of myxobacterial extracts

Rapid elucidation of carotenoids in microalgae formulations by MRMS aXelerate

A strategy using isotopic fine structure to reveal potential biomarkers showing the effects of traditional Chinese medicines on Alzheimer disease in rats

Analysis of metabolic changes in murine hair follicles treated with Procyanidin-B2 rich nutraceuticals by DI-MRMS

MRMS aXelerate – rapidly detected micropollutants and plant response metabolites in poplar leaves

Automated MALDI Magnetic Resonance Mass Spectrometry (MRMS) for biomarker identification in large clinical sample sets

Unambiguous Natural Product ID

Electron Induced Dissociation for the Differentiation of Isomeric Metabolites of Diclofenac

Ultrafast Statistical Profiling of Bacterial Metabolite Extracts

Definitive Elemental Formula Determination Debuts with SmartFormula-XR

Native and Glycans

Glycan Sequencing by Electronic Excitation Dissociation Tandem Mass Spectrometry

Comparison of CID and EID Mass Spectrum of Glycosides from solarix XR

Top Down Analysis of Histone H4

Expanded Collisional Energy Files for Automated Top Down and Bottom up Analysis on solariX

MALDI In-Source Decay for Top-Down Analysis of Proteins using Fourier Transform Mass Spectrometry

Petroleomics

Characterization of Petroleum Samples via Thermal Analysis Coupled to APCI FTMS

Reproducibility of Crude Oil Characterization by Flow Injection APPI-FT-ICR Mass Spectrometry

LDI FT-ICR MS as a Tool for Statistical Analysis of Crude Oils

solarix XR: Analysis of Complex Mixtures

Analysis of peat bog after solid phase extraction by FTMS

Analysis of sulfur-rich crude oil and bitumen by FTMS

Analysis of Gas Oil by GC/APCI FTMS

MRMS Literature

Resources for researchers

Customer Insights

Prof. Richard Drake, MUSC, Translating Cancer Biomarkers into the Clinic with MALDI Mass Spectrometry Imaging

Prof. Ying Ge, University of Wisconsin, Top-Down Proteomics: An Emerging Technique Driven By Cutting-Edge Mass Spectrometer

Prof. Jonathan Sweedler, University of Illinois at Urbana Champaign, How Mass Spectrometry Techniques are Propelling the Advancements of Single Cell Biology

Prof. Sally-Ann Poulsen, Griffith University, Innovating in medicinal chemistry using Fragment Based Drug Discovery combined with Native Mass Spectrometry

Prof. Per Andren, Uppsala University, MALDI Imaging in Neuroscience, Revealing the Biomolecular Map of the Brain

Solutions

Isotopic Fine Structure, Beyond the Molecular Realm: Unambiguous Elemental Formula Determination

Label-Free Molecular Imaging, Discover, localize and quantify biochemical changes and molecular markers

MRMS aXelerate: Phenomics, Metabolomics and beyond

Metabolomics, Novel solutions for Metabolomics, Lipidomics and high-throughput Phenomics

Native MS Solutions, scimaX MRMS: Perfectly designed for Native MS

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18T MRMS

Pushing the boundaries of science

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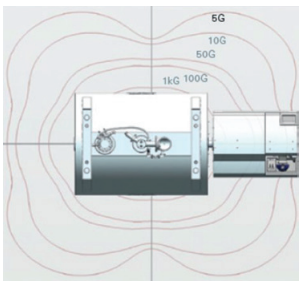
Magnetic Resonance
Mass Spectrometer

scimaX represents a revolutionary step in extreme resolution mass spec, bringing high field performance to 7T. However, there remain heroic global problems that require a solution that can address these issues that go beyond the current standard. The net effect of increasing magnetic field is not incremental, it is transformative. The cumulative effect of increased field strength takes the performance of scimaX to a level beyond currently available production systems. For these applications, Bruker offers an 18T magnet that will define a new class of experimentation. Please contact your local Bruker representative to learn more.



18T MRMS design study: In normal operation the 5G line extends from the magnetic center less than 2.5 m in z (magnetic axis) direction and less than 2.5 m radial.

Technical Specifications (preliminary)	
Magnet Type	B-C 180/11 USR-TT
Magnetic Field	18T
Cold Head	Dual stage
Magnet Dewar	Asymmetric, ca. 85cm to magnetic center
Stray Field (5G, axial/radial)	<3.6m/ <3.6m; in normal operation <2.5m/ <2.5m
Ion Source	ESI/MALDI dual source
Ion Optics	rf and dc ion guides, quadrupole, collision cell, ExD
Detector	ParaCell MRMS
Foot print	ca. 3.4 m x 1.6 m
Height	ca. 2.6m; ceiling ≥2.9m
Total Weight	ca. 7.5 t
Certification	CE
Maintenance	magnet every 2nd year, no field ramping required; mass spectrometer cart yearly
Liquid Helium Volume	ca. 1000 Liter
Liquid Helium Refill Volume	None between biennial maintenance; ca. 10 Liter LHe at maintenance

Notes

scimaX

Pushing science to the max

For Research Use Only. Not for Use in Clinical Diagnostic Procedures.

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